

One Health Approach on AMR surveillance in Korea

Food Microbiology division, NIFDS, MFDS



Threats of AMR

- Antimicrobial resistance is a global public health concern and food safety issue

취재 현장
美 '치명적'...우리는 '남용'

KBS1

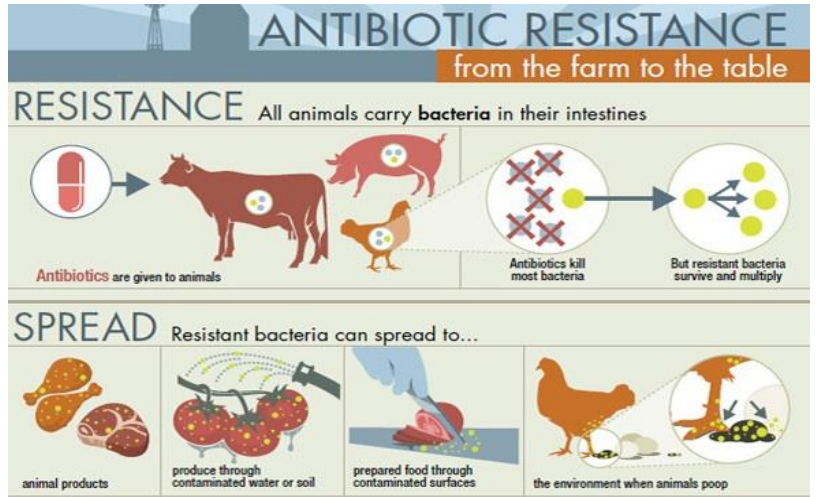
Livestock animals

Human

Antibiotic drugs

Infection of AMR

LIVE



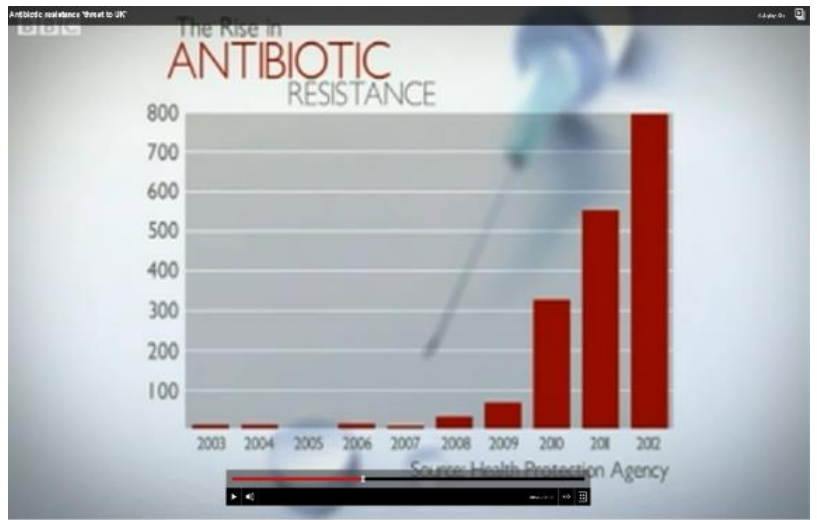
KBS1

COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

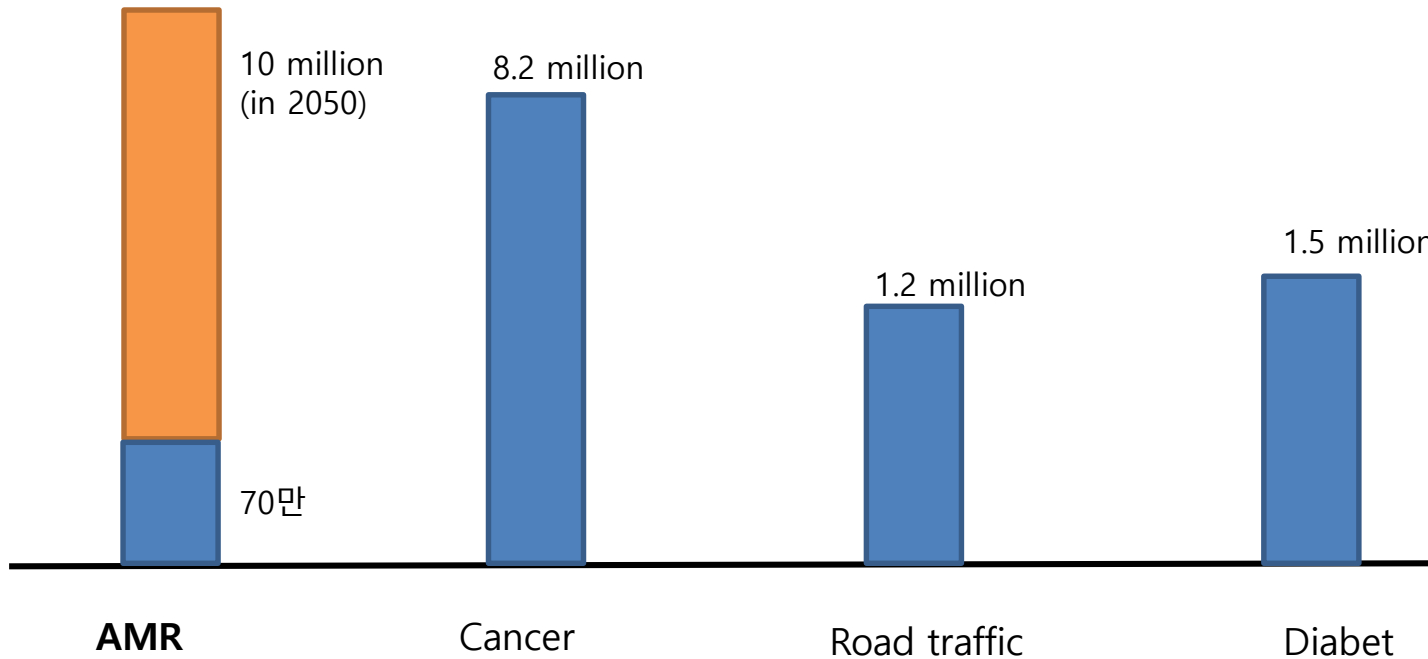
World Health Organization

World Health Day 2011



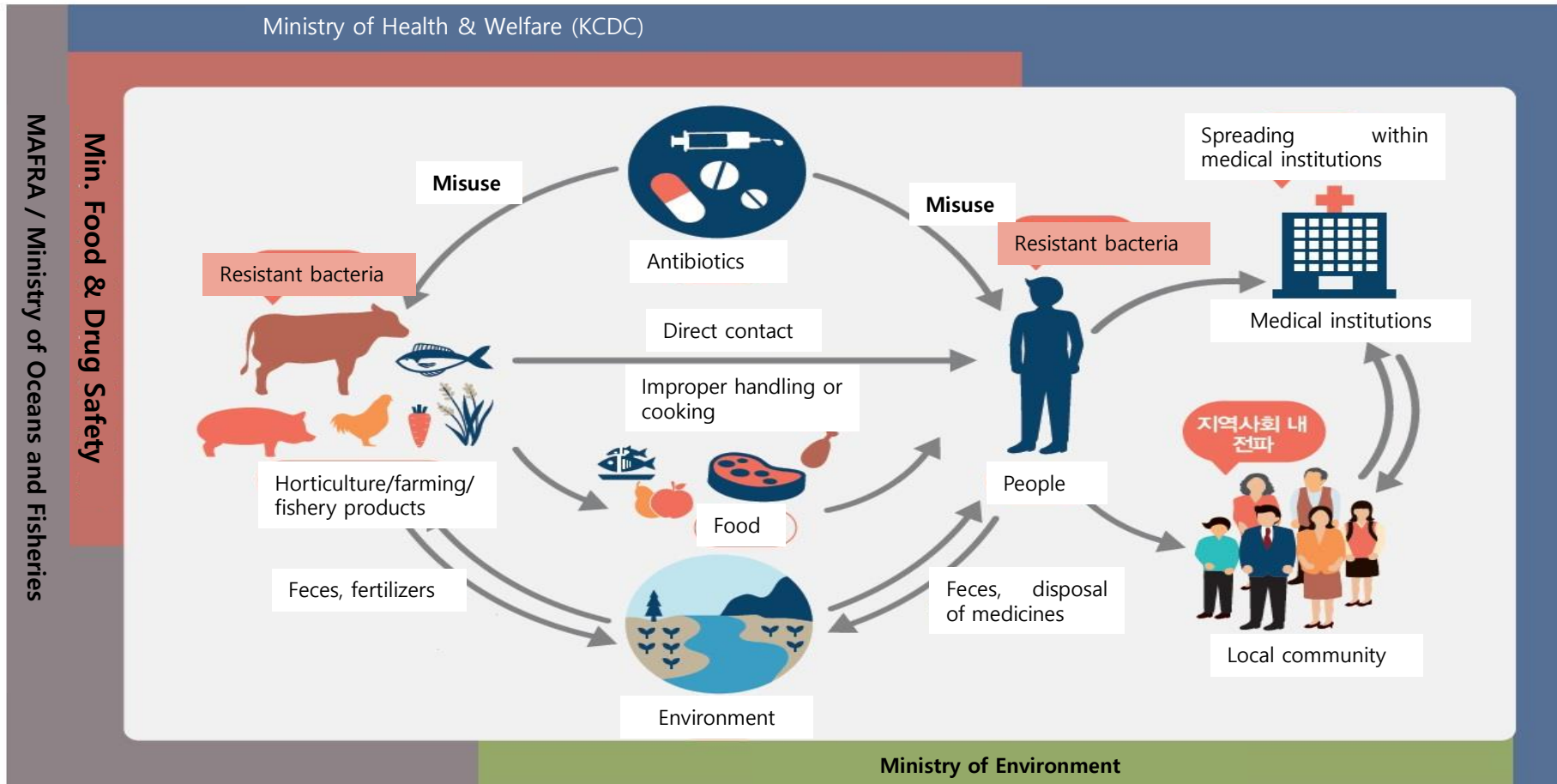
Threats of AMR

- Deaths attributable to AMR every year
 - It is estimated that the burden of deaths from AMR is growing into 10 million lives each year by 2050, unless action is taken.



Threats of AMR

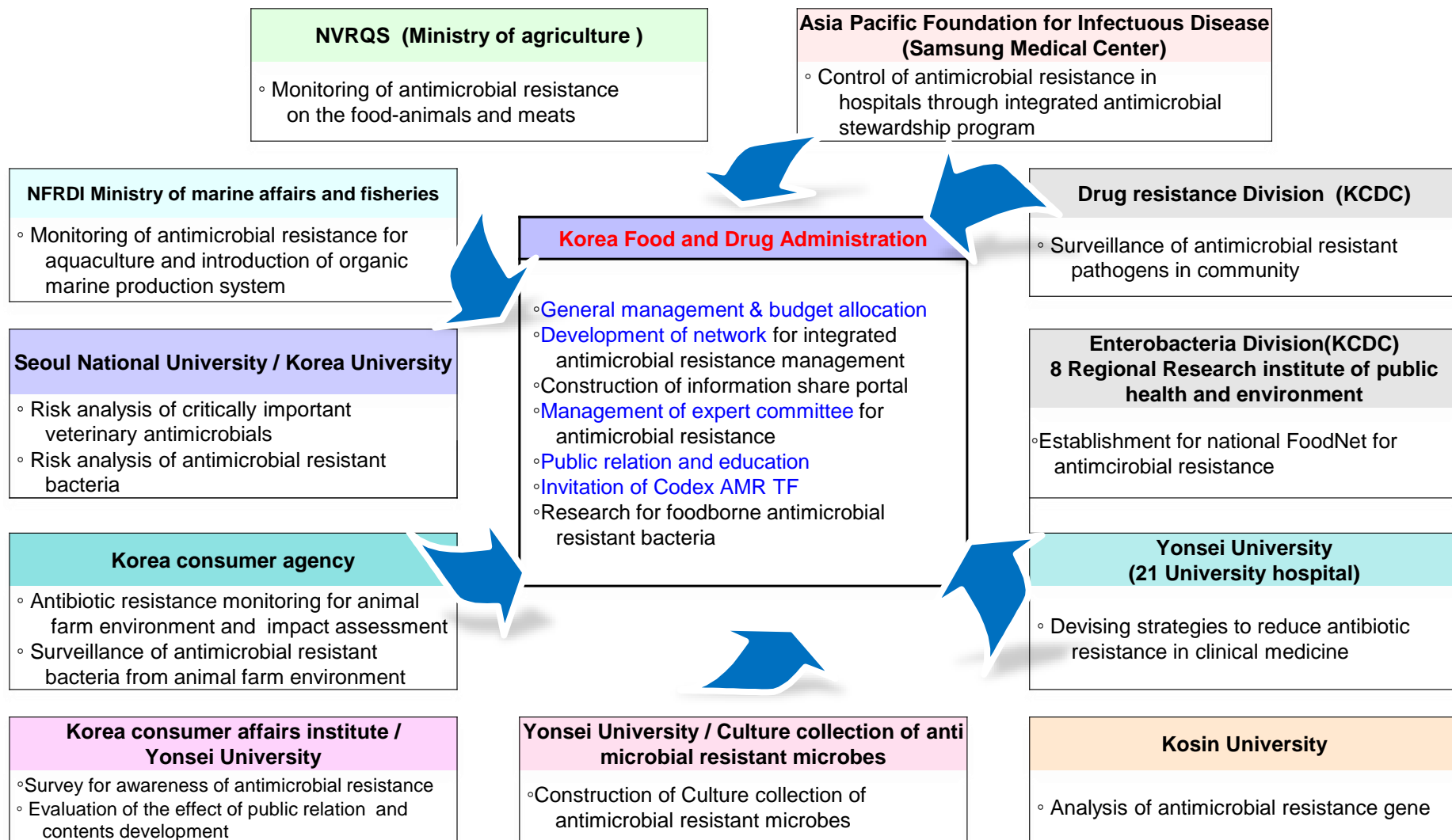
Origins and channels of contagion





History of the national AMR management program

National Antimicrobial-resistance Management Program (2003-2007)



National Antimicrobial-resistance Management Program (2008-2012)

Clinical field

Non-clinical field

Prime Minister's Office

Mediation & evaluation of tasks of governmental departments

Ministry of Health and Welfare

Revision of regulations
Public relation & Education

Korea Food and Drug Administration

Invitation of CODEX TFAMR
Consumer education

Center for Disease Control & Prevention

Antimicrobial resistance management
Hospital infection management

Health Insurance Review & Assessment service

Monitoring antibiotics prescribing rate & amount of hospitals

Ministry of Environment

Management of residual drugs in environment
Collection of used drugs in household

Ministry for Food, Agriculture, Forestry and Fisheries(Livestock)

Trace system of antimicrobials for animal
Mandatory system of prescription for animal
HACCP for livestock

Ministry for Food, Agriculture, Forestry and Fisheries(Aquaculture)

HACCP for aquaculture
Diffusion of vaccine
Guideline of using antimicrobials

Hospital, Medical college, Academic society
Regional research institute of public health and env.

Management & surveillance on antibiotic resistance
Management & surveillance on nosocomial infection

National Institute of Environmental Research

Monitoring of residual drugs in environment

Animal, plant & fisheries quarantine & inspection agency

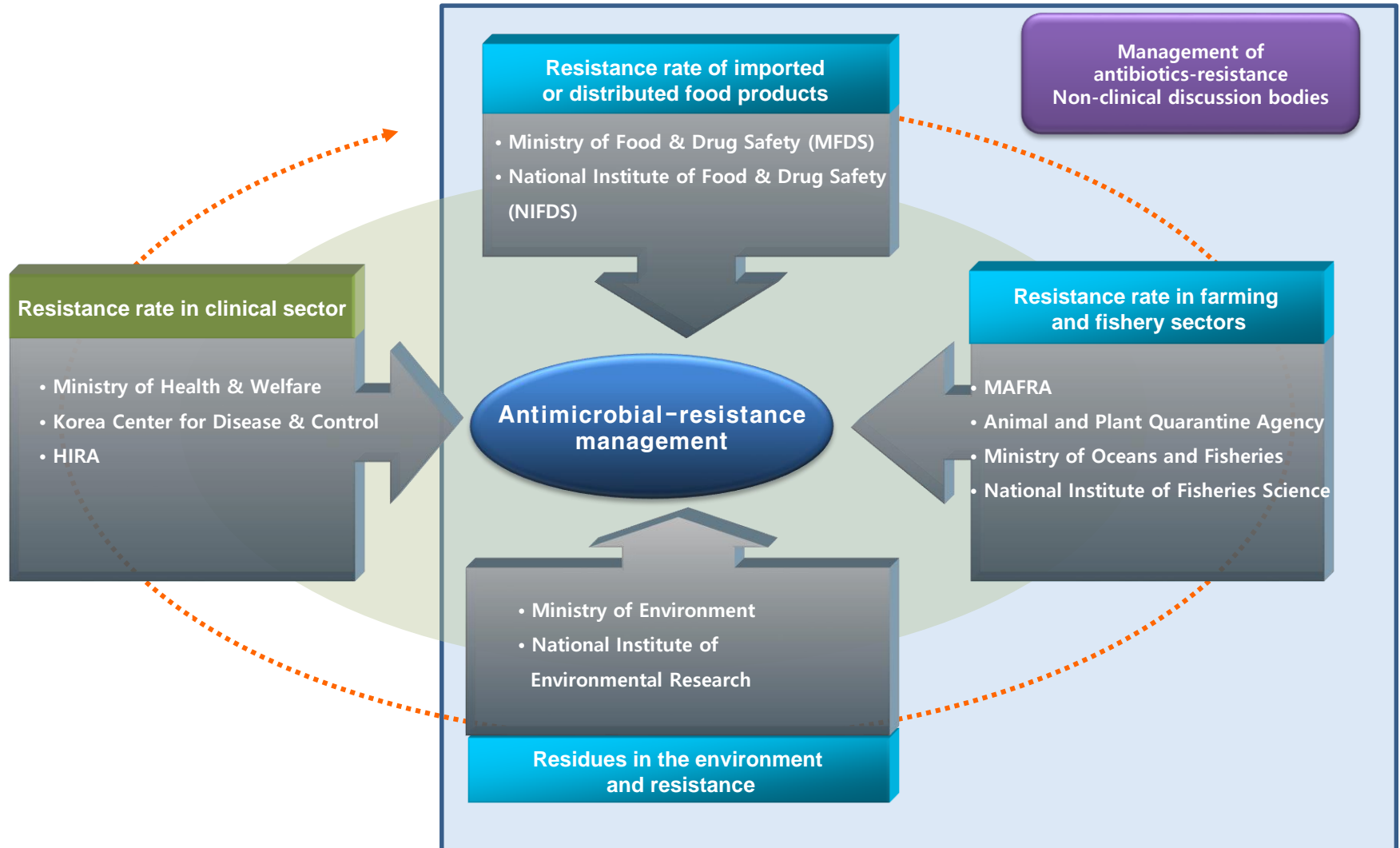
Monitoring of antimicrobial resistant bacteria & amount of antimicrobials used

National Fisheries Research & Development Institute

Monitoring of antimicrobial resistant bacteria & amount of antimicrobials used

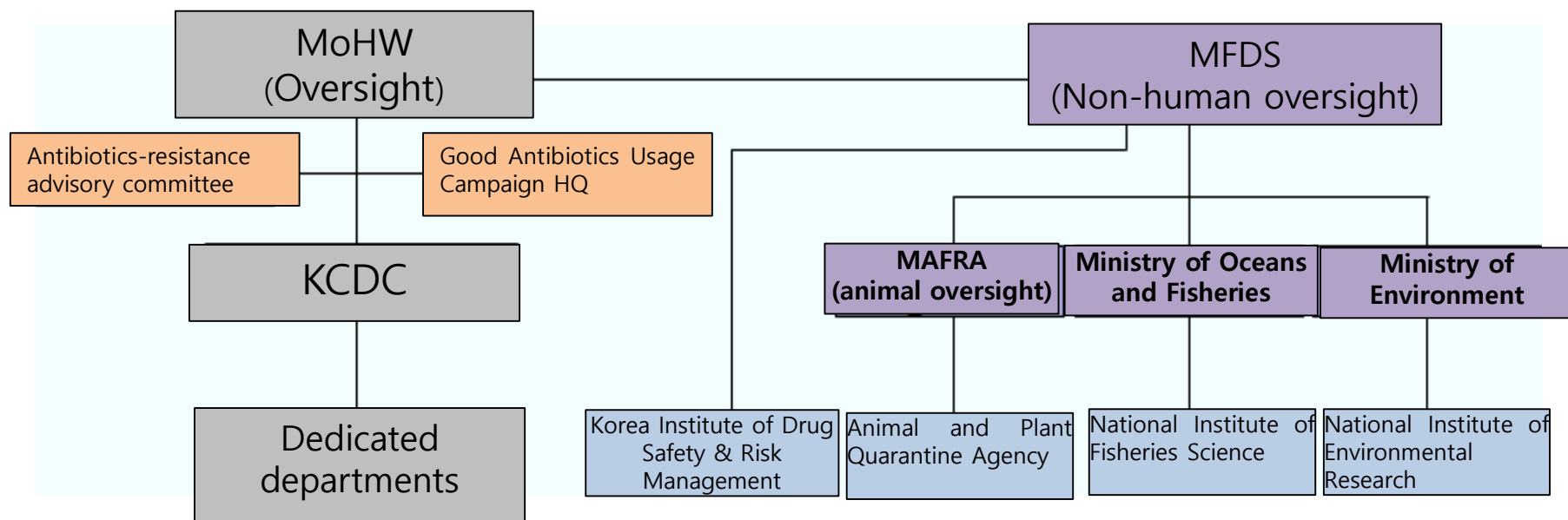
Non-clinical discussion bodies (2013~2016)

- Monitoring of antimicrobial-resistance in each sector after the end of “National Antibiotics-resistance Safety Management Program”

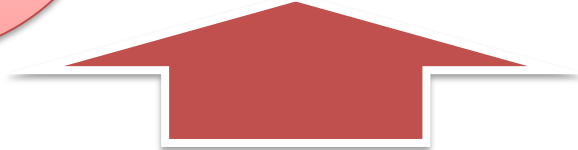
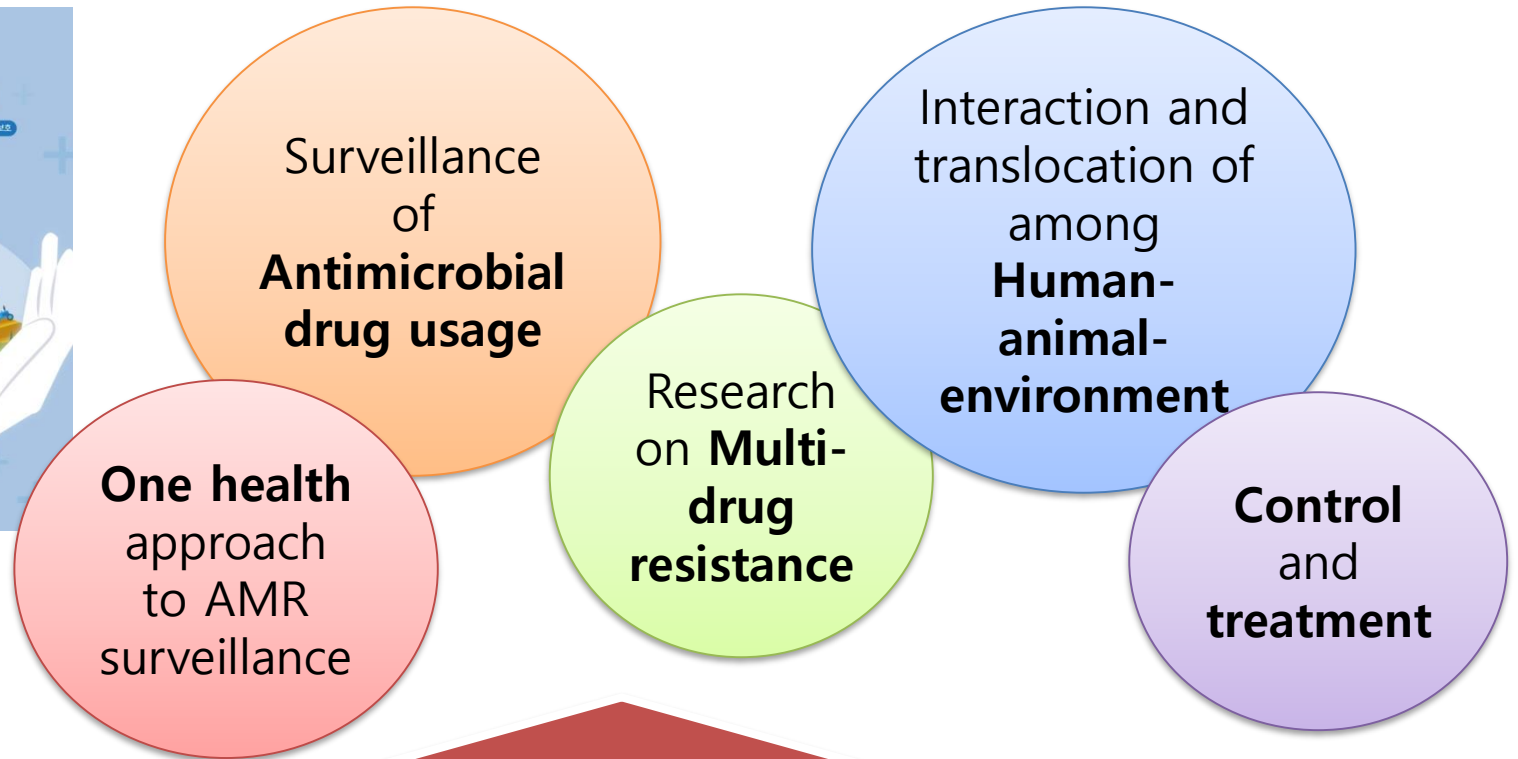


National action plan of Korea (2016~)

- WHO presented a **global action plan** and urged national-level actions (2015).
- Developed and implemented the **National Action Plan on AMR**



One health approach fight AMR (2017~)



- Ministry of Environment
- Ministry of Health & Welfare
- Ministry of Science & ICT
- Ministry of Oceans & Fisheries
- Ministry of Food & Drug Safety
- Ministry of Agriculture, Food & Rural Affairs

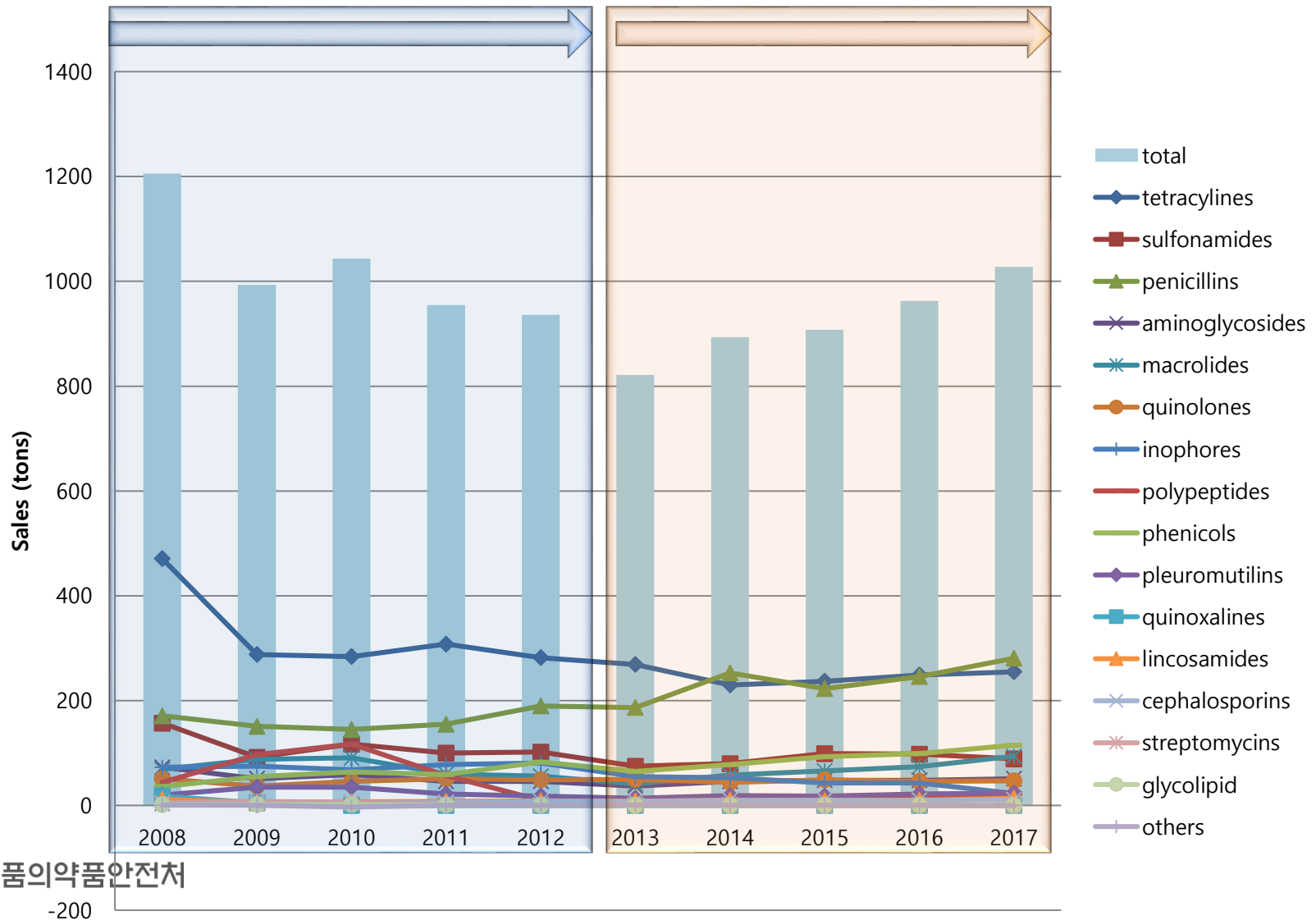


Major **outcomes** of national AMR management programs

Major outcomes of National programs

- **Ban** of adding antimicrobials in **animal feed** (*MAFRA*, 2011)
- Provide **government subsidies** for **organic** live stock farms (2008)
- Expansion of **HACCP** certified farms
- Adoption of **seafood traceability** system
(*Ministry of Oceans and Fisheries*, 2008)
- Adoption of **mandatory prescription by veterinarians** (*MAFRA*, 2013)
- **Public relation and education** (2003~)
- Medicinal waste recovery system (*MoE*, 2010)

Major outcomes of National programs



Major outcomes of public relation & education

- Guidelines for public education



- Educations on animal and aqua farms for prudent use of antimicrobials

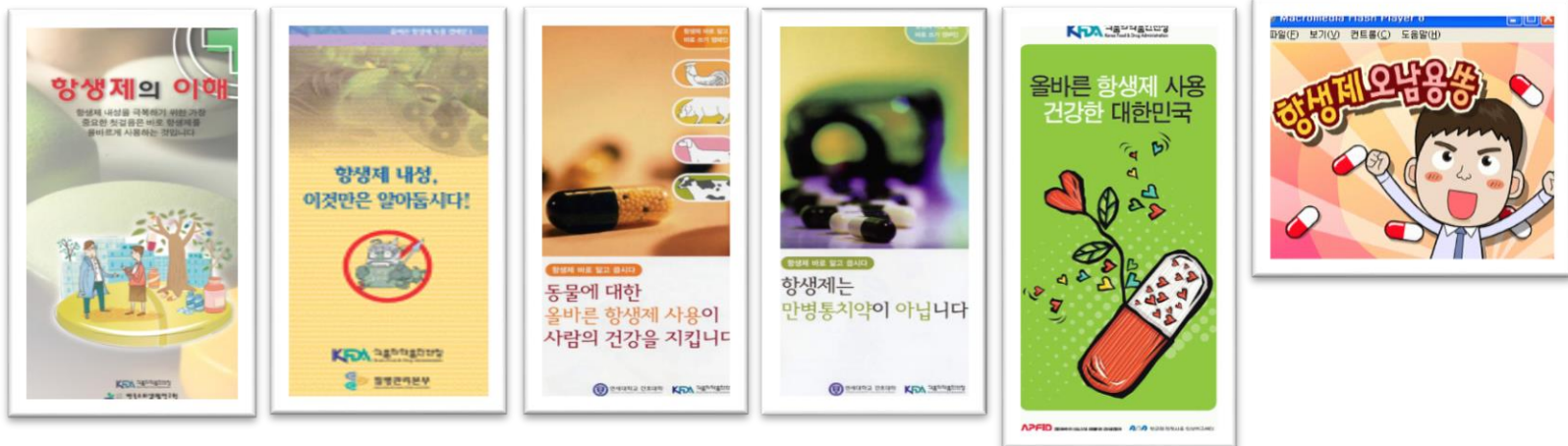


Major outcomes of public relation & education

- Public educations (TV shows)

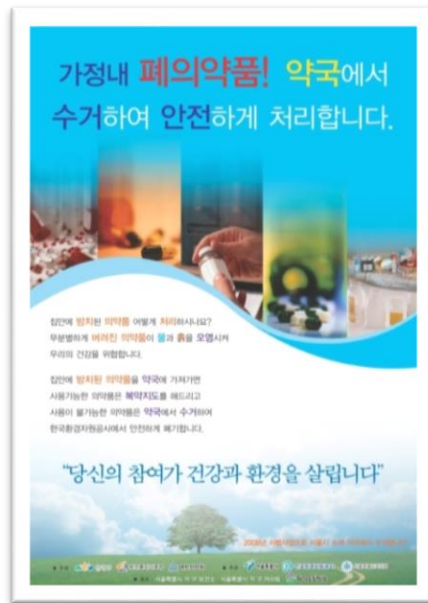


- Public educations (leaflets)



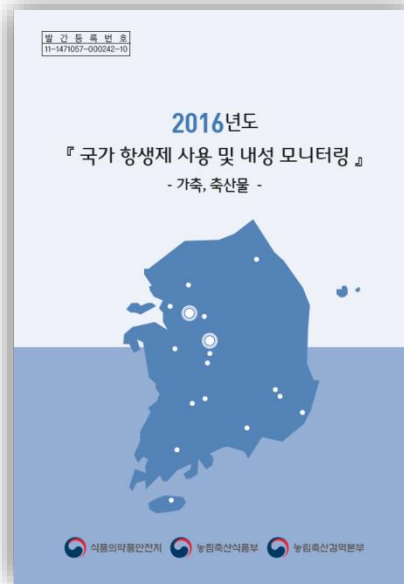
Major outcomes of public relation & education

- Collection and dispose of unused drugs



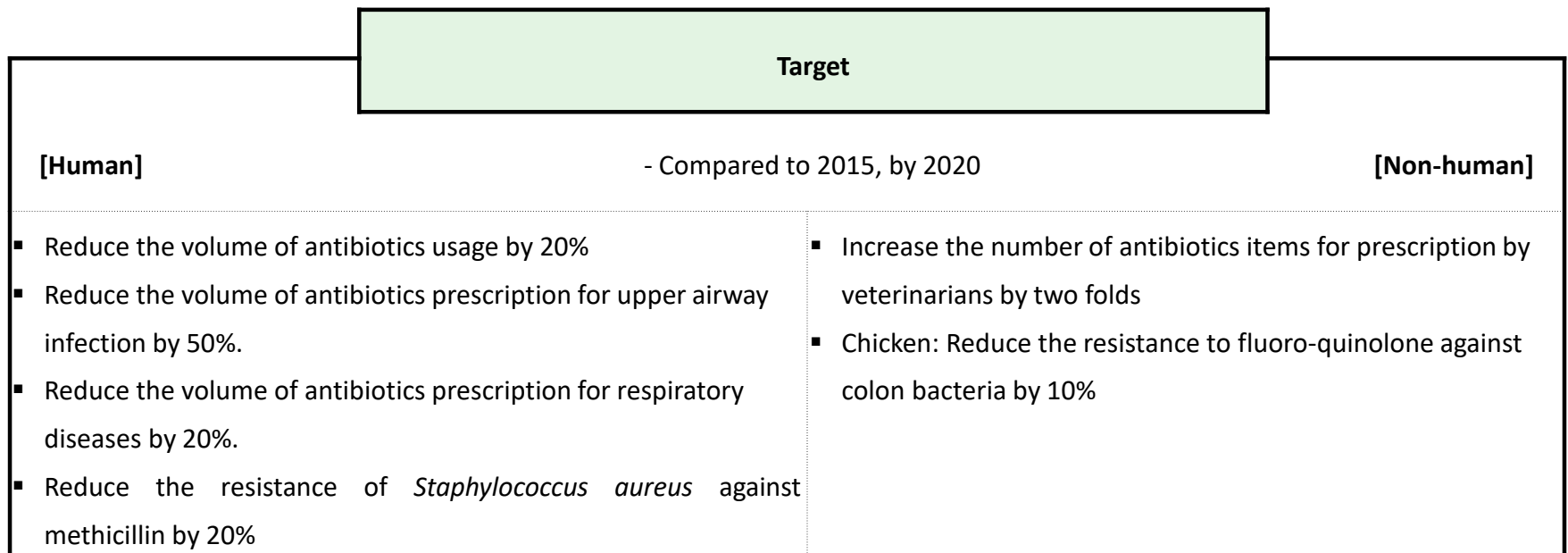
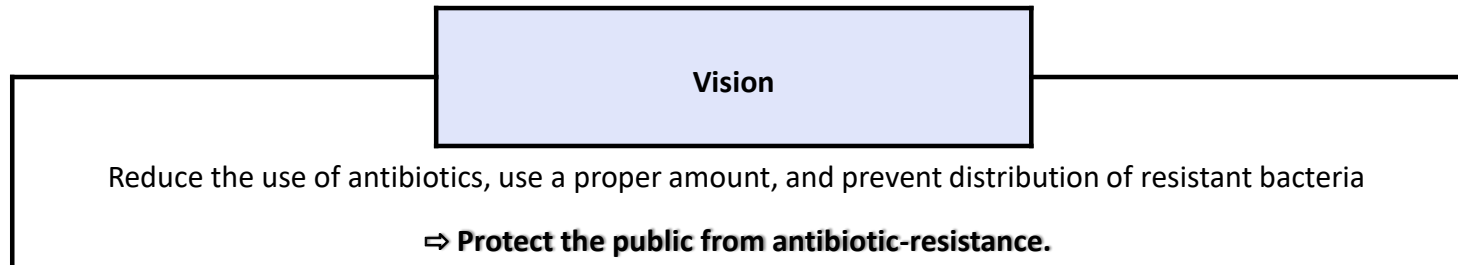
Monitoring outcome reporting

- Published integrated, non-clinical national antibiotics usage and resistance statistics report (livestock, farm products, and fishery products)
- Published *via* the website (www.mfds.go.kr)



Future directions

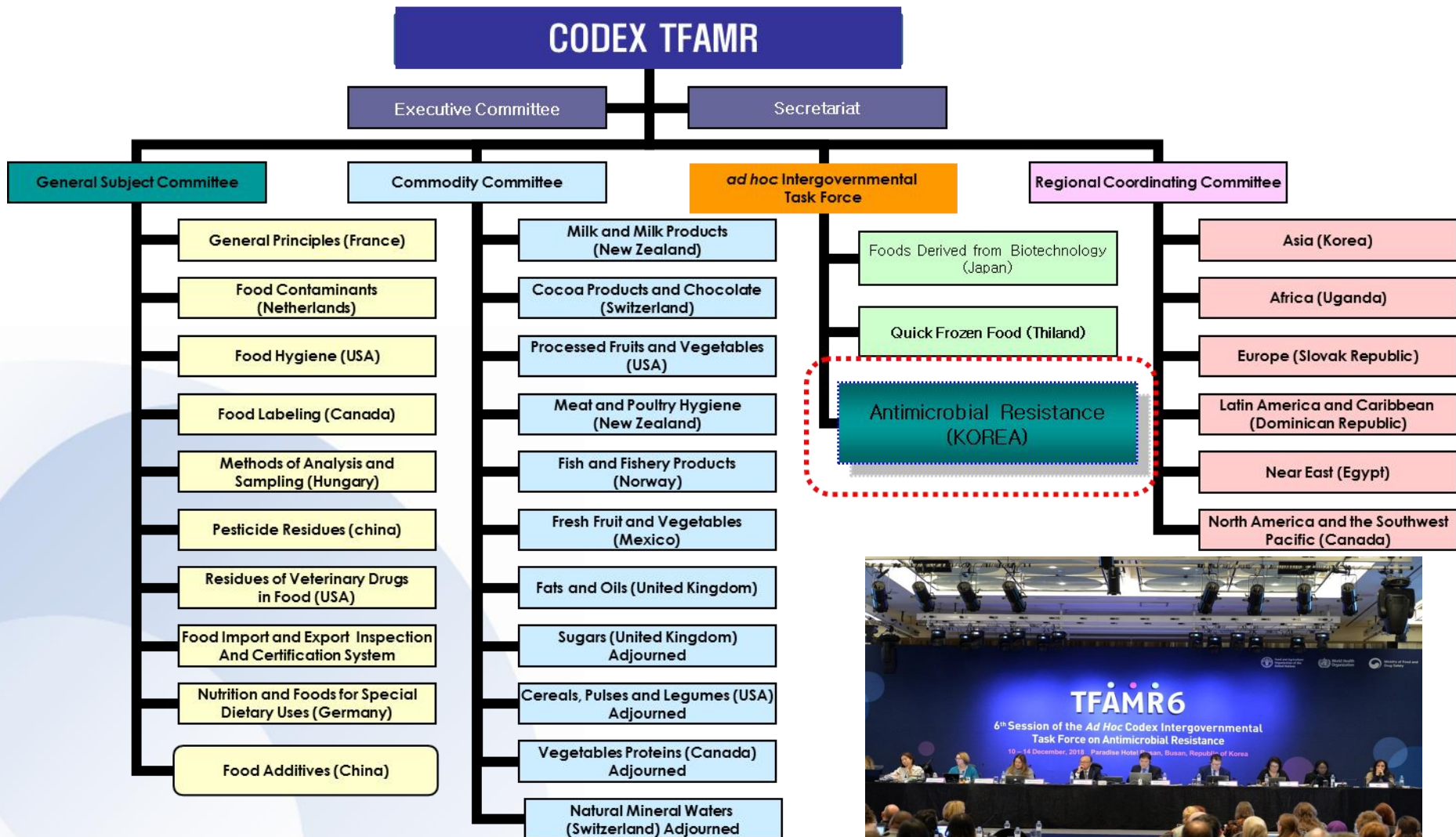
- Establish and implement national antibiotics- resistance management action plan(2016~)



CODEX *ad hoc* TF AMR

- The Codex *ad hoc* Intergovernmental Task Force on **Antimicrobial Resistance (TFAMR)** established in the Codex Alimentarius Commission (CAC) in 2006
- The **1st through 4th Codex TFAMR** held in Korea (2007~2010)
 - Guidelines on **risk assessment of foodborne antimicrobial resistance**
- The **5th Codex TFAMR** holding in Jeju, Korea in 2017
- The **6th Codex TFAMR** holding in Busan, Korea in 2018
 - Revision of **the Code of Practice to Minimize and Contain Antimicrobial Resistance** (CAC-PCP 61-2005)
 - Propose draft **Guidelines on integrated surveillance of antimicrobial resistance**

CODEX *ad hoc* TF AMR





Characteristics of ESBL- producing *Salmonella* from food samples

Salmonella Virchow isolated from human

- *Salmonella* Virchow strains from human feces samples had been gradually increasing during 2010-2014

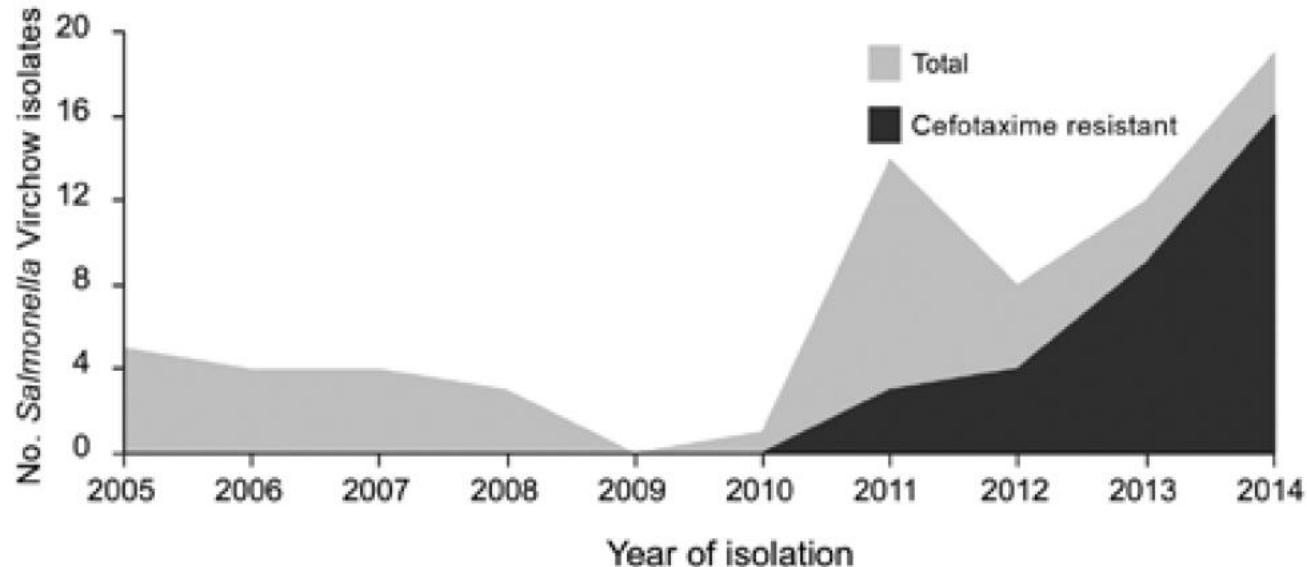
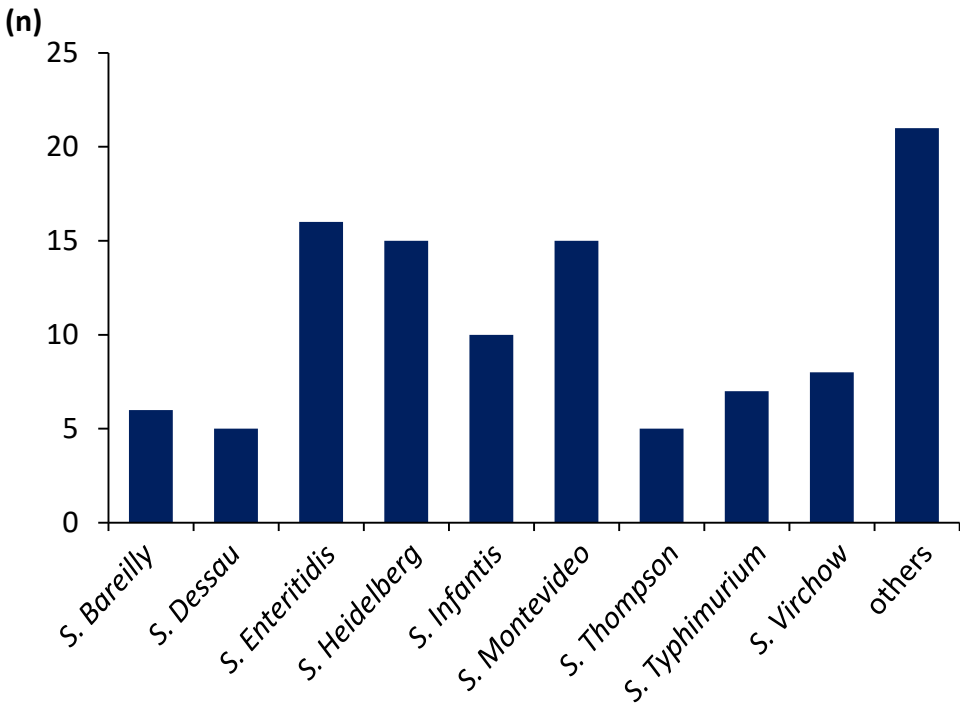


Figure. Temporal distribution of *Salmonella enterica* serotype Virchow isolates in South Korea, 2005–2014.

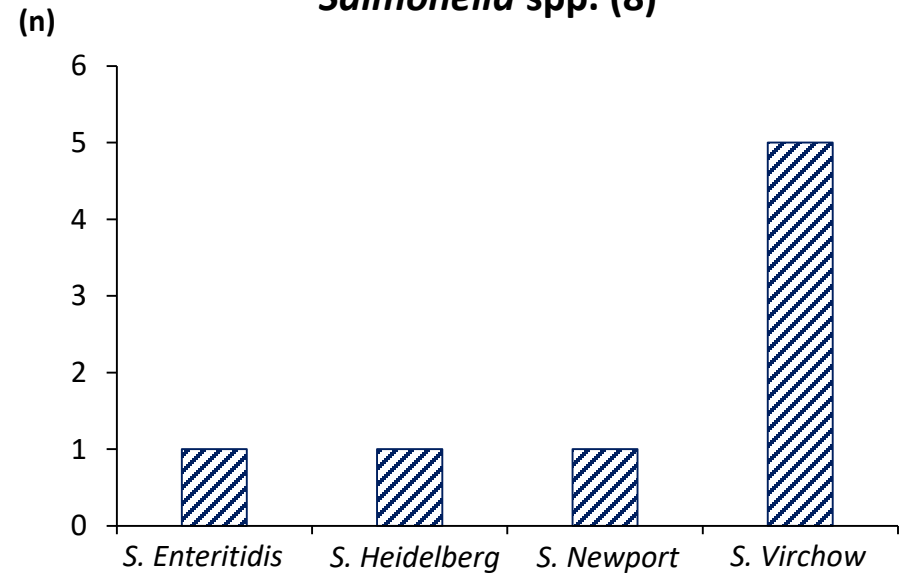
Distribution of *Salmonella* serotype

- Salmonella* spp. isolated from food samples During 2014 - 2017

***Salmonella* spp. (108)**



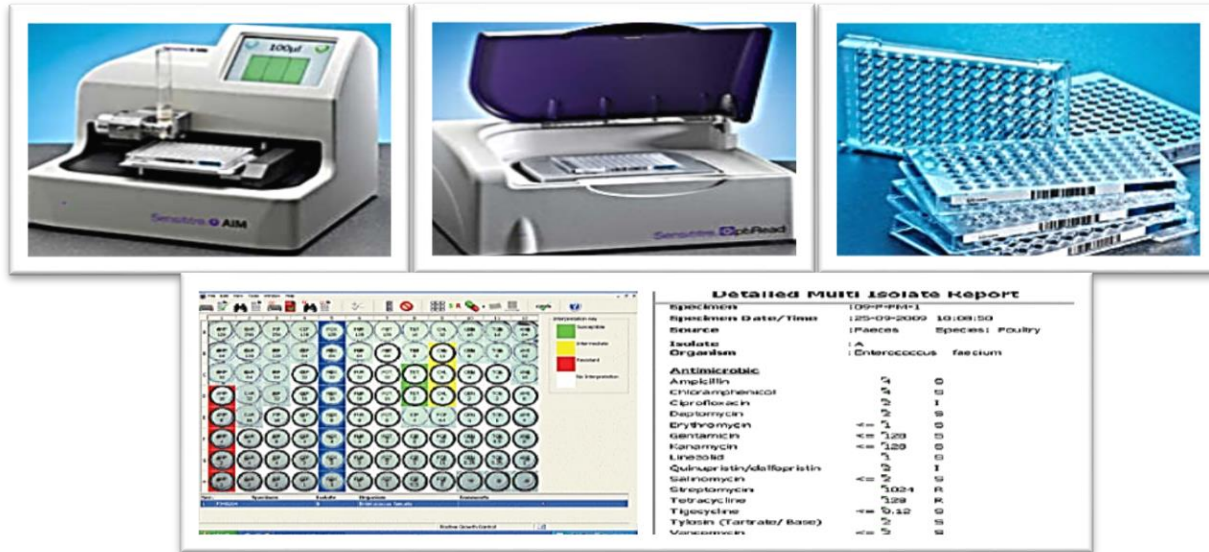
ESBL-producing *Salmonella* spp. (8)



*others (19) : *S. Augustenborg* (1), *S. Braenderup* (3), *S. Coeln* (1), *S. Derby* (2), *S. Edinburg* (1), *S. I 4,[5],12:i:-* (1), *S. Livingstone*(4), *S. Newport* (2), *S. Ohio* (1), *S. Richmond*(1), *S. Sandiego*(1), *S. Schwarzengrund*(1)

AMR analysis and genotyping tools(1)

- Antimicrobial resistance test : automated MIC determination (Trek Sensititre)

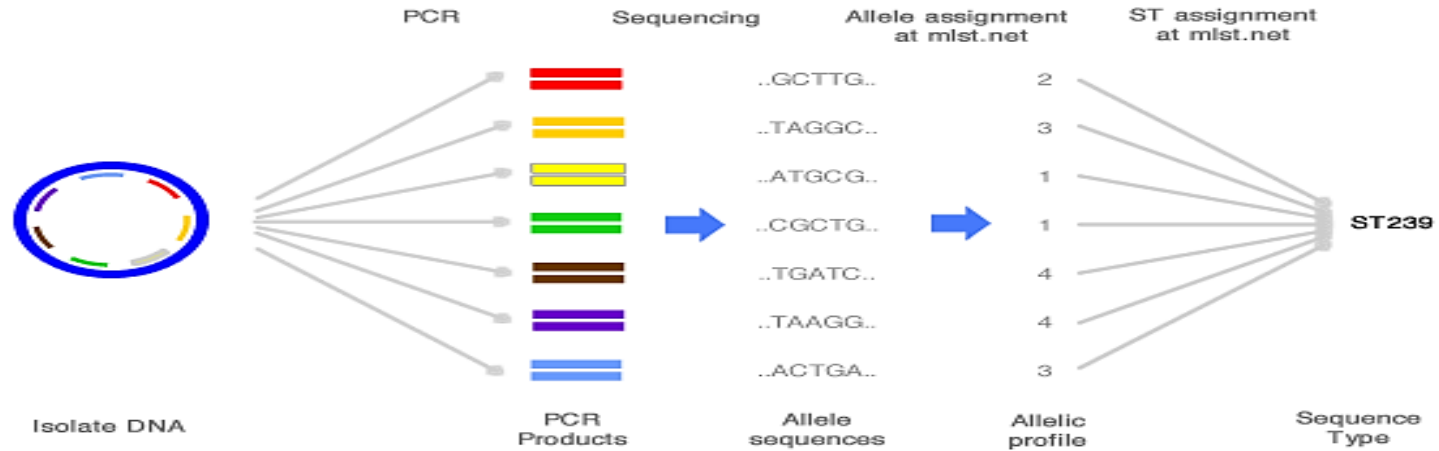


- Conventional PCR : identified antimicrobial genes

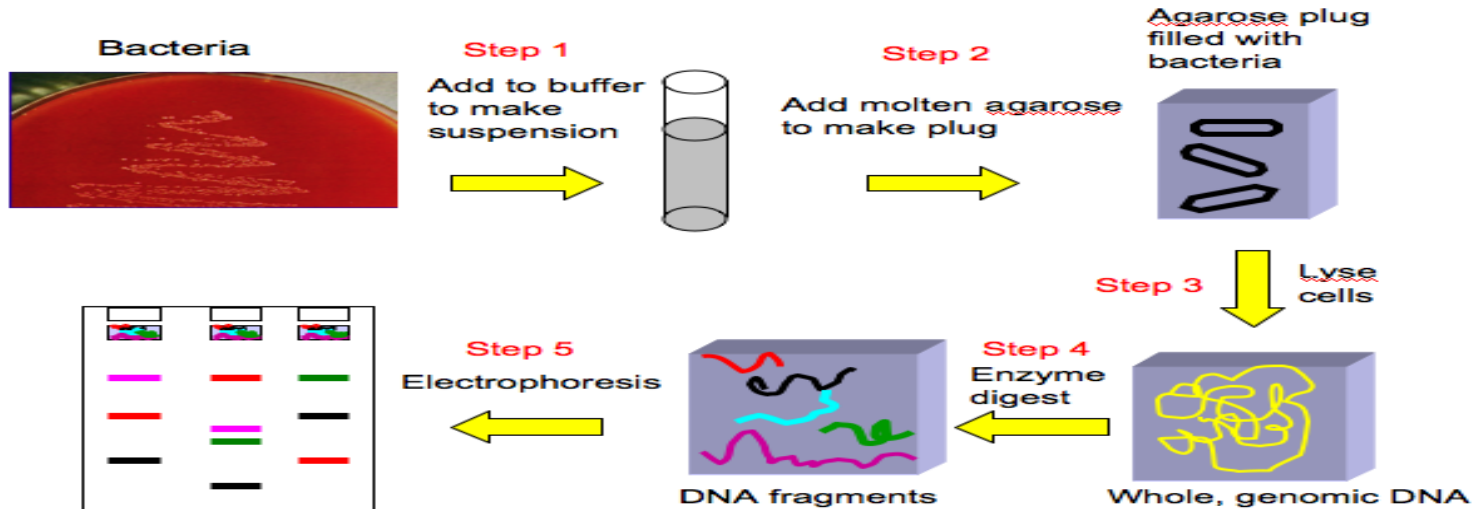


AMR analysis and genotyping tools(2)

- MLST(Multi Locus Sequence Typing)



- PFGE(Pulsed Field Gel Electrophoresis)



Illumina Miseq Sequencing



NexteraXT index kit with V2 chemical

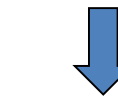
Removing adapter sequences using Trimmomatic

Aligned reads

```
ACGCGATTTCAGGTTACCACG
GCGATTTCAGGTTACCACGCG
GATTTCAGGTTACCACGCGTA
TTCAGGTTACCACGCGTAGC
CAGGTTACCACGCGTAGCGC
GGTTACCACGCGTAGCGCAT
TTACCACGCGTAGCGCATT
ACCACGCGTAGCGCATTACA
CACGCGTAGCGCATTACACA
CGCGTAGCGCATTACACAGA
CGTAGCGCATTACACAGATT
TAGCGCATTACACAGATTAG
```

Consensus contig

```
ACGCGATTTCAGGTTACCACGCGTAGCGCATTACACAGATTAG
```

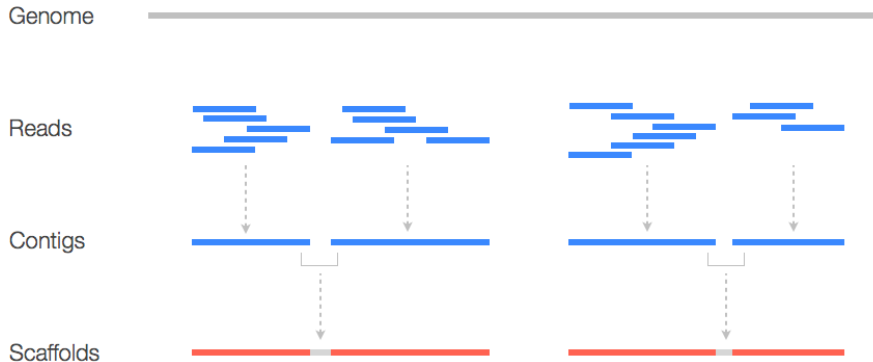


Sequencing reads



De novo assembly
SPAdes3.12.0
for *De novo* assembly

Assembled sequences (contigs)



Quality control and annotation



Apply different bioinformatic pipelines
to characterize the genome

Bioinformatic tools

Center for Genomic Epidemiology

Home Services Datasets

Overview of Services

Workflows

- Bacterial Analysis Pipeline (Batch Upload)

Phenotyping

- ResFinder
- KmerResistance
- PathogenFinder
- VmulenceFinder
- Restriction-ModificationFinder

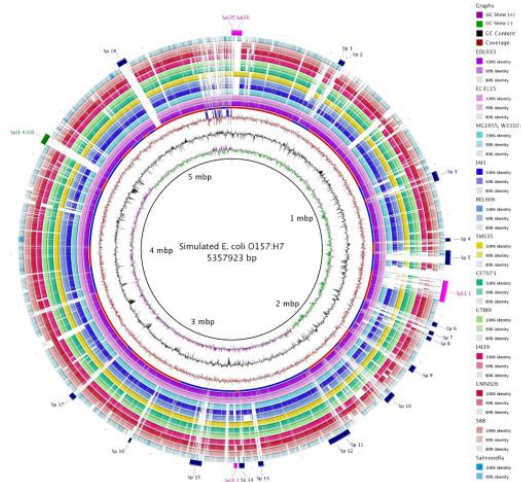
Typing

- KmerFinder
- SpeciesFinder
- MLST
- PlasmidFinder
- pMLST
- SerotypeFinder
- FirmTyper
- CHTyper
- spaTyper
- PAST
- SCCmecFinder

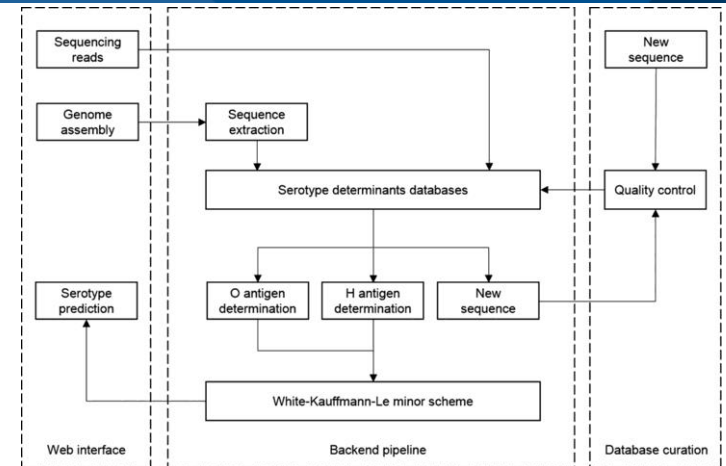
Phylogeny

- CSI Phylogeny
- NDTree

- *ResFinder*
- *PlasmidFinder*
- *MLST*
- *ISFinder*



• *BRIG*



• *SeqSero* : Predicting *Salmonella* serotype

Scope tools by selecting genome sets via workspace, global search, finders, browsing & phylogeny

Workspace Global Search Specialized Finders Browse by Taxon Browse by Phylogeny

Protein Family Analysis of Genomes Selected via Metadata

Sort, filter and select genomes by metadata

Comparative Pathway Tool

View subsystem conservation across genomes

Transcriptomics Data Analysis using Expression Filters and Heatmaps

Sort, filter and select experiments by metadata

Create gene lists from selected experiments

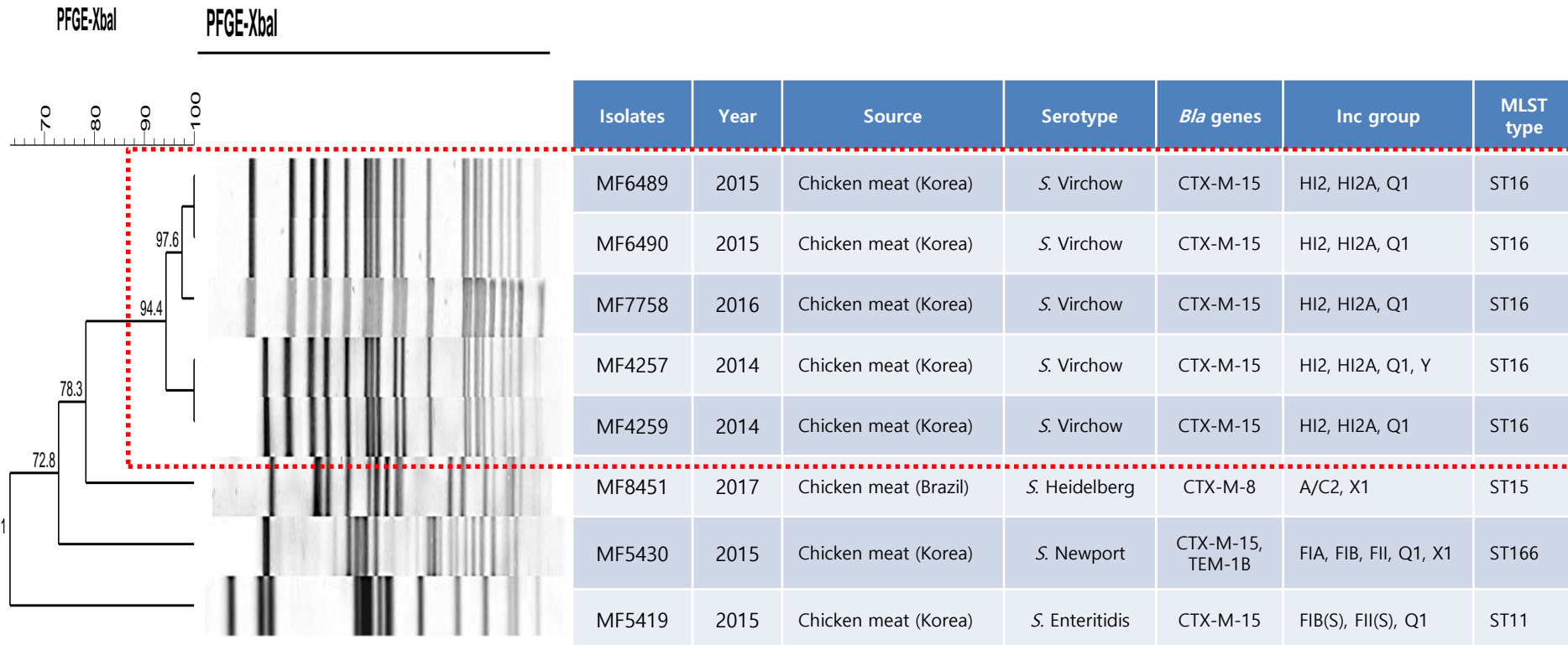
Cluster heatmap showing gene regulation

Create New Workspace Groups for Subsequent Analyses

• *PATRIC* • *Rast*

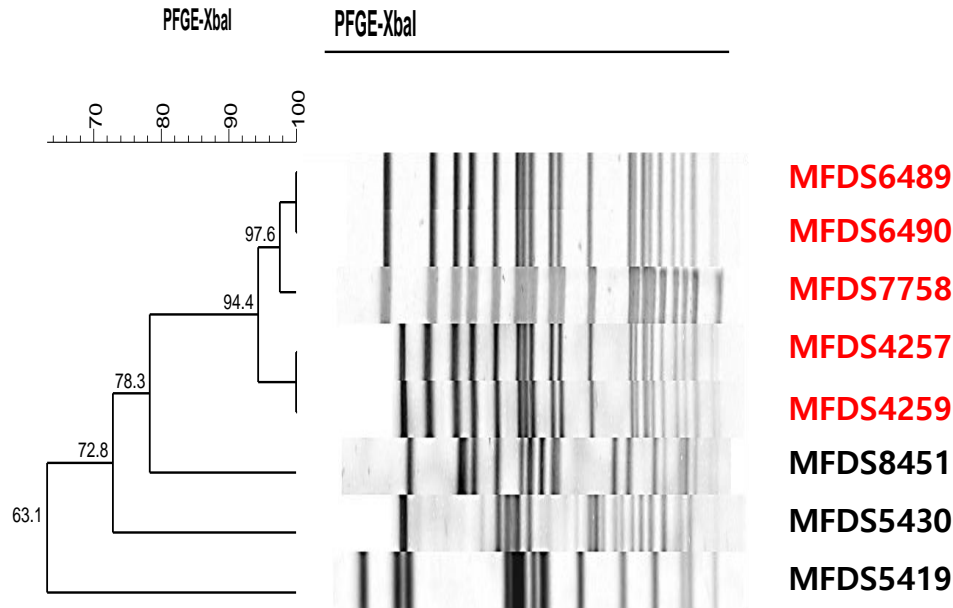
Genetic relation among ESBL-producing *Salmonella*

- Salmonella* Virchow isolated from chicken meat during 2014-2016 showed very similar PFGE patterns, the same clonal sequence type (ST16)

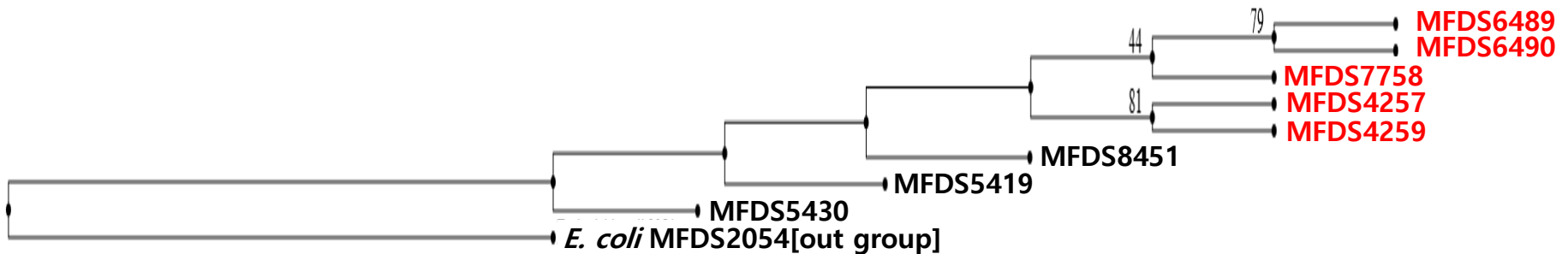


Genetic relation among ESBL-producing Salmonella

- Genetic relation of ESBL-producing Salmonella by PFGE

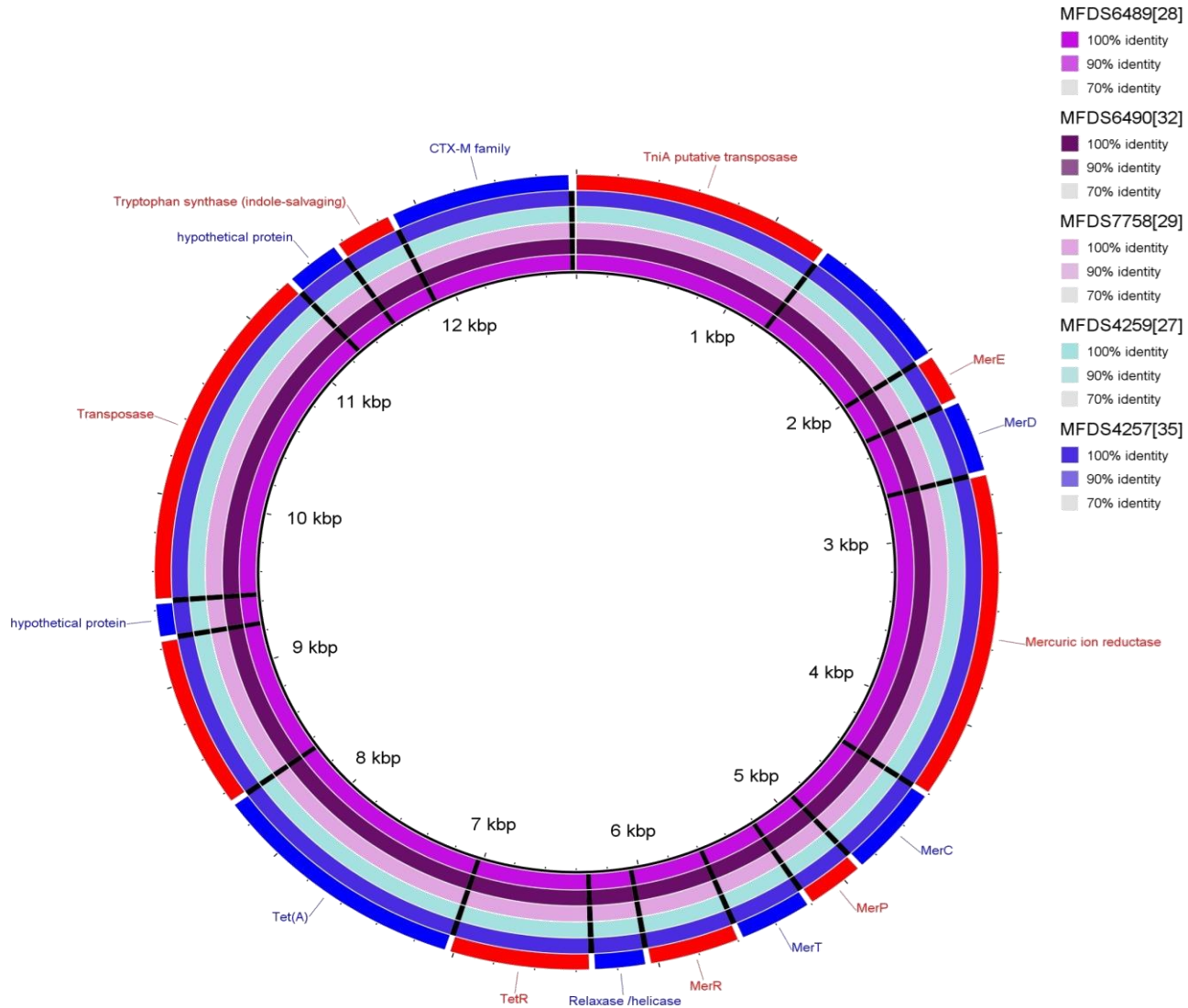


- Genetic relation of ESBL-producing Salmonella by FastTree method on PATRIC



Genetic characteristic

- bla*_{CTX-M-15} carrying contigs of *Salmonella* Virchow were compared by BRIG



One health approach

- *PFGE Comparison between Salmonella Virchow isolates from human and food samples*
 - *which dose it prefer clonal spread or horizontal transfer*

Conclusion

- Korean government tried to slow down the spread of resistance by “**national antimicrobial-resistance management program**” started since 2003.
- **National Action Plan on Antimicrobial Resistance** in accordance with **WHO’s global action plan** propositions since 2016 engaged in clinical and non-clinical national programs as part of the **ONE-HEALTH** approach
- Major outcomes of last 15 yrs of National AMR management Programs include **banning addition of antibiotics to animal feeds** and introduction of **mandatory prescription by vets**.
- Due to the ban on mixing in the feed, which resulted in a significant reduction in the usage of **tetracycline**, it turned out that the resistance against this drug reduced significantly.
- MFDS (NIFDS) is planning to continue its role of AMR management, including overseeing non-clinical areas such as **livestock, fishery, environment, and foods**, to reduce the AMR and ensure proper use of antibiotics.



Thank you!

