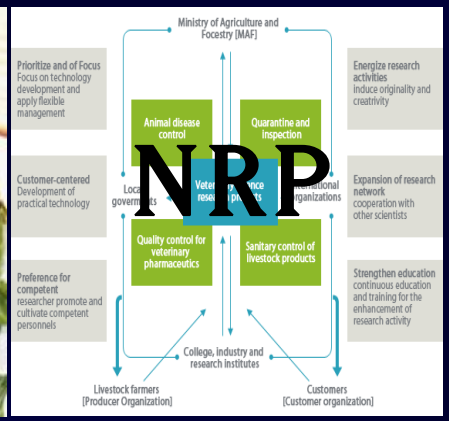
# The Korean National Residue Program for Veterinary Drugs and Contaminant Residues in Food of Animal Origin





Residue Chemistry & Toxicology Division

National Veterinary Research & Quarantine Service/MIFAFF

## Residues

- veterinary drugs
- pesticides
- its metabolites

## Contaminants

- substances not intentionally added
  - heavy metals
  - dioxins
  - mycotoxin (AF $M_1$)

  etc.

# Risk of Chemical Residues

- Veterinary Drugs


- Environmental contaminants

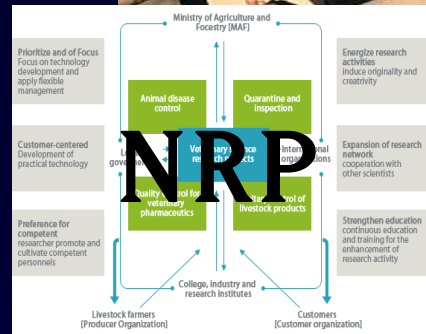
- antibiotic resistance
- hypersensitivity
- chronic poisoning
- endocrine disruption
- carcinogenesis

  etc.

# The Korean National Residue program (NRP)

- **1989.3.** Established chemical residue testing program for pork to be exported to Japan
  - 1988, found sulfamethazine in pork
    MRL: < 0.1 ppm

- Established MRLs & analytical methods (1989.5)
- Implemented National Residue Survey (1989-1995)
- **1996** Established the Korean NRP



NRP

- **Aim to** ensuring the safety of livestock products by providing guidance for effective implementation of testing and control of harmful chemical residues in meats.

- **Focus on** public health protection by safe foods
  - Assesses human exposure
  - Deterrent against slaughter & processing of adulterated animals
  - Identify violative product to remove from the food supply
  - Verifies HACCP system on slaughtering and processing

NRP

- **Obtain** national data on occurrence of chemical residues to support risk assessment, enforcement and educational activities

*** The national data provide**

- structures process of identifying and evaluating compounds of health concern
- capability to analyze for compounds of concern
- appropriate regulatory follow-up of reports of violative tissues residues
- collection, statistical analysis, reporting of the results, background information for the next activities and plans

# NRP Design

***Domestic vs. Import Sampling***

- Sampling components are similar for residue tests
- Functions are different
  - domestic: prevention of residue occurrence on farm
  - import: verification of exporting countries' residue control program

# Components of Domestic NRP

1. **Monitoring Plan**
   (national information gathering)
   - Statistical random sampling of animals that have passed antemortem inspection
   - Indicate national prevalence data
   - Evaluate residue trends
   - Identify correctable problems in the industry
   - Identify problem producers of unsafe animals

# Components of Domestic NRP

2. **Surveillance & Enforcement Testing** (condemnation)
   - Investigate and control the occurrence of residue violations in animal populations
   - Targeted sampling plans
   - Identify and remove violative animal food products
   - Focus on individual animals or lots that do not appear healthy
     - Emphasis on populations with high prevalence of residue violations
     - Follow-up on producers and others with a non-compliant history
     - Verify if an establishment's HACCP system effectively controls violative residues

# Components of Domestic NRP

## 3. Exploratory Projects

- Studies of the occurrence of residues without safe limits
- Evaluate new methods and approaches to residue monitoring
- Provide supplemental information used in considering a compound for NRP monitoring

# Sampling & Testing Procedures

- **Monitoring Plan** : samples are submitted randomly from slaughterhouse to PVS lab. (screen & confirm)
- **Surveillance & Individual Enforcement Testing**: previous residue-violated farm animal and residue-suspected animal samples are submitted from slaughterhouse to PVS lab

  - Inspector hold the carcass until outcome of lab testing, the carcass of exceeding of MRL is condemned

- **Exploratory projects** : PVSs send randomly the samples to NVRQS under the annual plan

# Korean MRL established for Veterinary Drugs and Contaminants in animal products upto Sep 2008

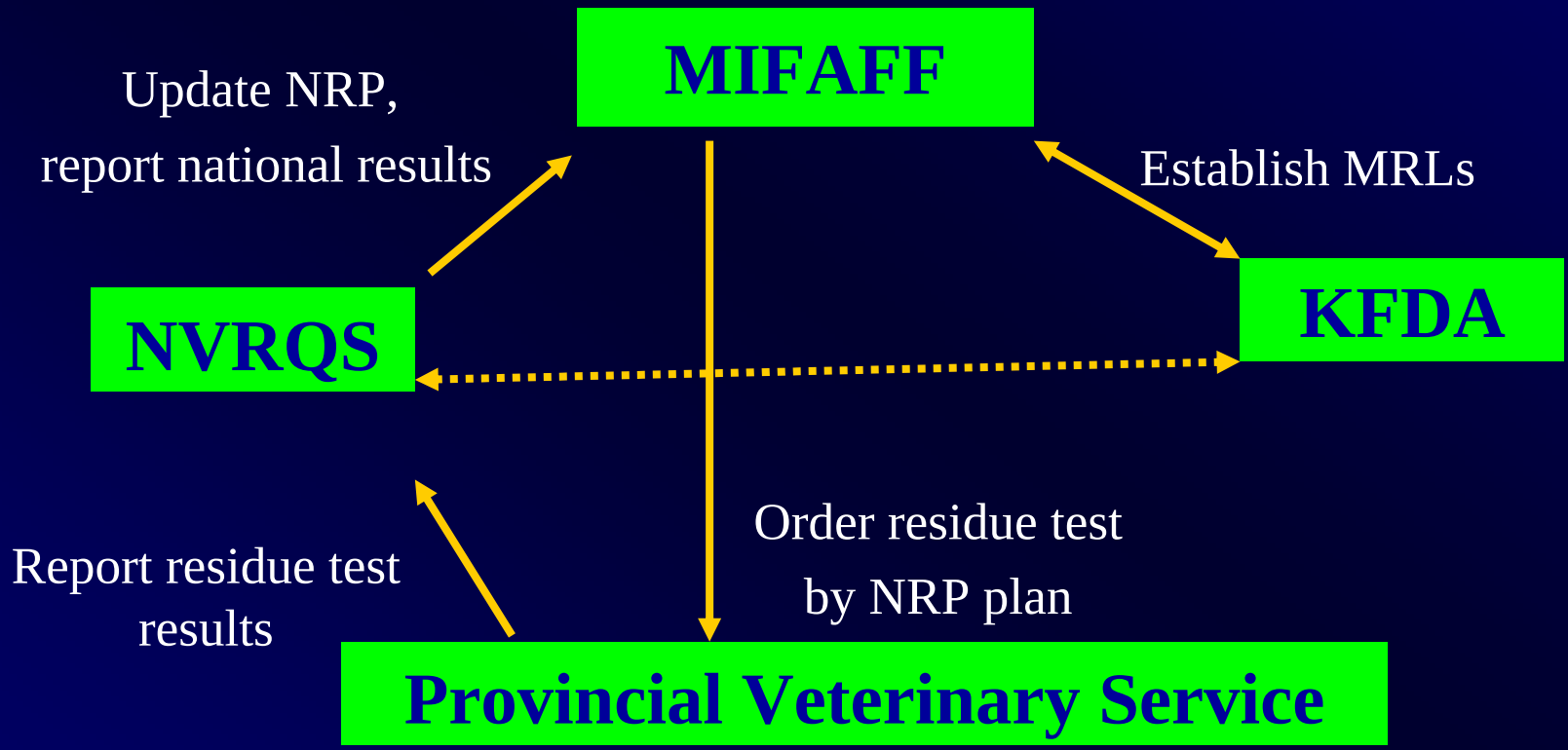
| Class | Established | In process | Total |
|---|---|---|---|
| Veterinary Drugs | 81 | 79 | 160 |
| Pesticides, etc. | 90 | 28 | 118 |
| Total | 171 | 107 | 278 |

❖ Codex : 143 substances, Japan : 548 substances(Positive list)

# List of Negative Substances in Food ( zero tolerance )

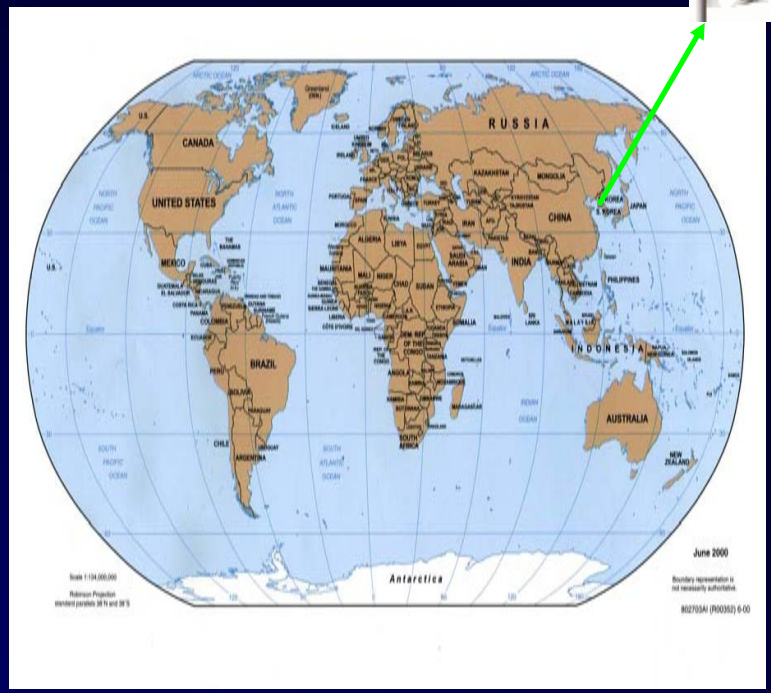
| | |
|---|---|
| 1 | Nitrofurans(Furazolidone, Furaltadone, Nitrofurazone, Nitrofurantoine, Nitrovin, etc.) and their metabolites |
| 2 | Chloramphenicol |
| 3 | Malachite green and its metabolite |
| 4 | Diethylstilbestrol(DES) |
| 5 | Dimetridazole |
| 6 | Clenbuterol |
| 7 | Vancomycin |
| 8 | Chlorpromazine |
| 9 | Thiouracil |
| 10 | Colchicine |
| 11 | Pyrimethamine |
| 12 | Medroxyprogesterone acetate( MPA) |

# Agencies involved in NRP System




**MIFAFF: Ministry of Food, Agricultural, Forestry & Fisheries**
**KFDA: Korean Food & Drugs Administration**
**NVRQS: National Vetrinary Research & Quarantine Service**

# Provicial Veterinary Service in Korea




# 2008 NRP - domestic Sampling Plan

| Program | Species | Compounds | Samples (heads) |
|---|---|---|---|
| Monitoring | Cattle, pig, chicken, duck, goat, horse | 94* | 91,990 |
| Surveillance & Enforcement | Cattle, pig, chicken, duck, goat, horse | 11+α | 18,010 |
| Exploratory | Pig, chicken | BFR/POPs** | 130 |

***Antibiotics (25), Synthetic antimicrobials (38), Hormones (2), Pesticides (29)**

****BFR/POPs : brominated flame retardants / persistent organic pollutants**

# Major Testing Veterinary Drug Residues - antibiotocs

- Beta-lactams
  - Penicillins: penicillin G, ampicillin, amoxicillin, etc.
  - Cephalosporins: ceftiofur, etc.
- Tetracyclines
  - Chlortetracycline(CTC), oxytetracycline(OTC), etc.
- Aminoglycosides
  - Gentamicin, streptomycin/DSM, neomycin, etc.
- Macrolides
  - Erythromycin, tylosin, tilmicosin, etc.
- Amphenicols
  - Chloramphenicol, thiamphenicol, etc.

# Major Testing Veterinary Drug Residues - antibiotocs

- Sulfonamides
  - Sulfamethazine(SMT), sulfadimethoxine(SDM), sulfamonomethoxine(SMM), etc.
- Quinolones
  - Enrofloxacin, ciprofloxacin, danofloxacin, sarafloxacin, ofloxacin, etc.
- Nitrofurans
  - Furazolidone, furaltadone, nitrofurazone, etc.

# Analytical Methods of Residues

- Screening & Qualification
  : Bioassay, TLC , ELISA, etc

- Confirmation & Quantification
  : HPLC, LC-MS, LC-MS-MS, etc

# Residue Violation Follow-up Actions

- In case of occurrence of violative residues, Provincial Veterinary Services (PVSs) notifies warning letters to a producer and other parties involved in offering animals that are found to contain violative residues
- Violators are posted on the NVRQS website with addresses for 6 months
- Competent PVSs make on-site educational visits to farms and investigate the source of violation

# Residue Violation Farm List

➤ (www.nvrqs.go.kr)


| No | Name | Farm address | Species | Substances of violation | Enforcement period | Slaughter house |
|---|---|---|---|---|---|---|
| 1 | K Y Kim | 1000 Haemang-dong, Gunsan-si, Jeollabuk-do | Pig | Oxytetracycline Chlortetracycine | 08. 1. 19 ~ 08. 7. 18 | JB05 |
| 2 | B Y Kim | 566 Manho-ri, Poseung-Myeon, Pyeongtaek-si, Gyeonggi-do | Chicken | Enrfloxacin | 08. 1. 21 ~ 08. 7. 20 | GG17 |

# Analysis of Residues in Animal Products

## Antibiotics

- **Screening Method**
  Bioassay, Immunoassay,
  Charm II assay, TLC .....

- **Confirmatory & Quantitative Method**
  HPLC, LC/MS, GC, GC/MS ……

# ❑ Confirmatory & Quantitative Method

Sample preparation

↓

Extraction of analytes from matrix

↓

Clean-up using SPE, etc.

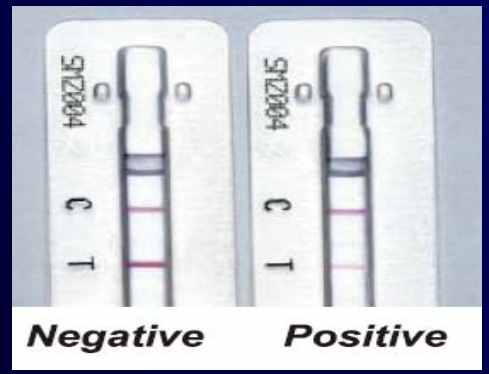
↓

Confirmation & Quantatification

# Analysis of Residues in Animal Products

## Hormones & Pesticides

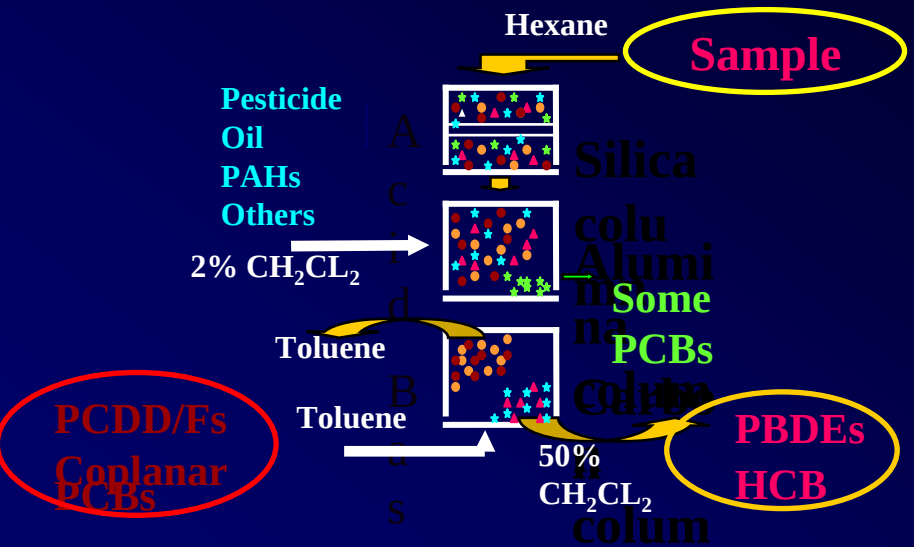
- **Screening Method**
  Immunoassay ……
- **Confirmatory & Quantitative Method**
  HPLC, LC/MS, GC, GC/MS ……




# Analysis of Residues in Animal Products

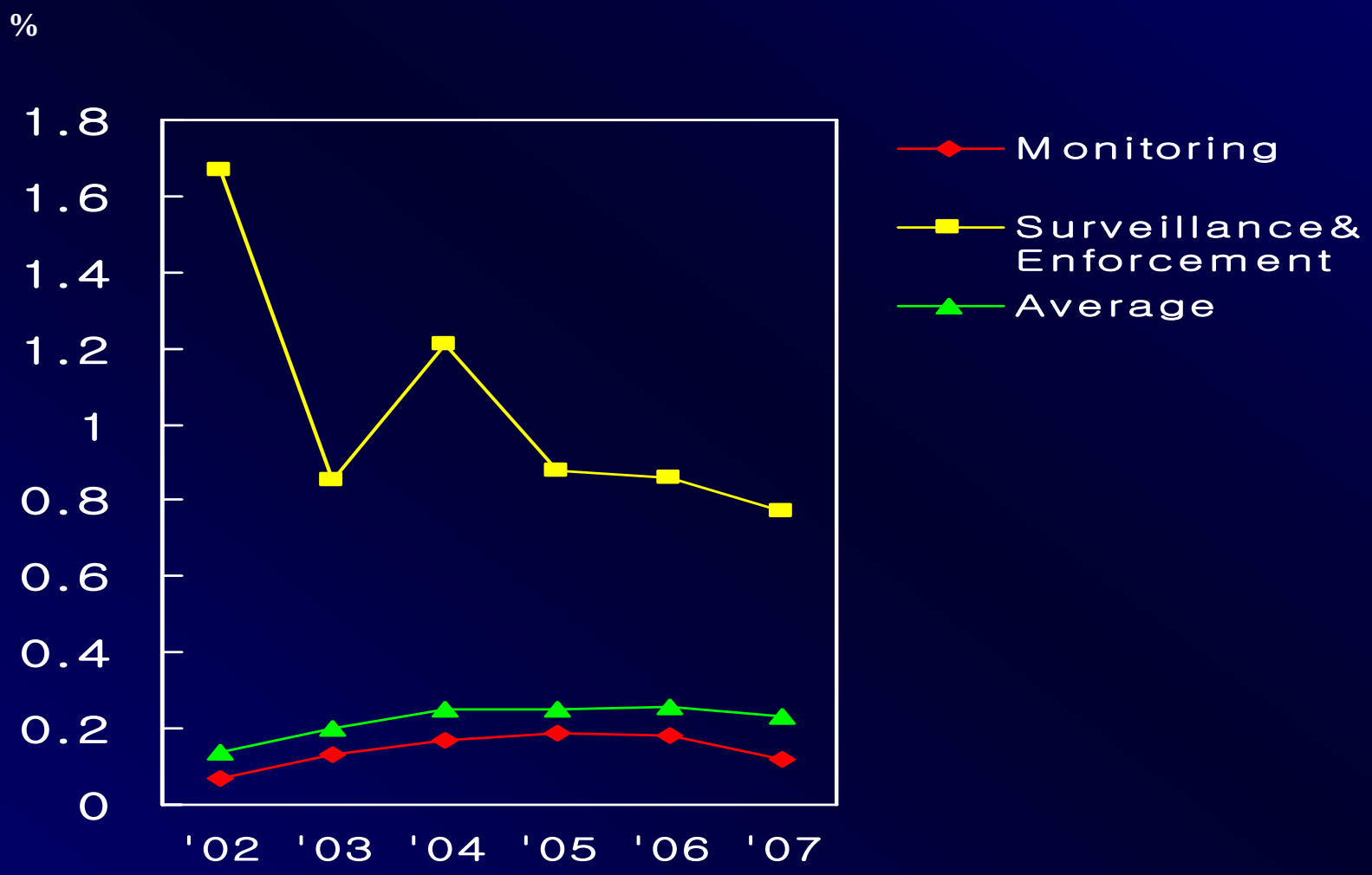
## Dioxins

- **Screening Method**
  Immunoassay
- **Confirmatory & Quantitative Method**
  Isotope dilution method & High resolution GC/MS



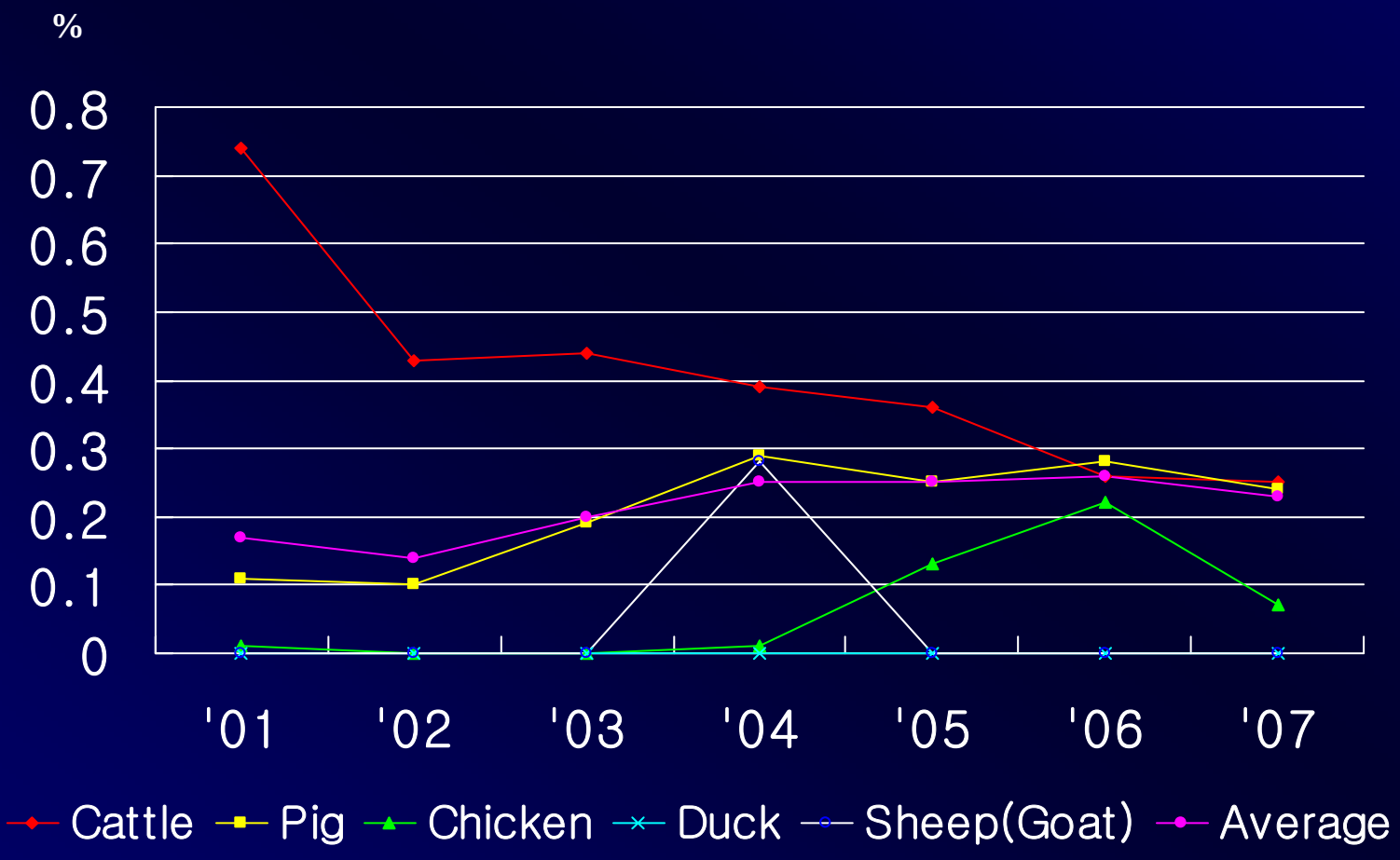

# NRP Results

## - Violation Rates in Korea -



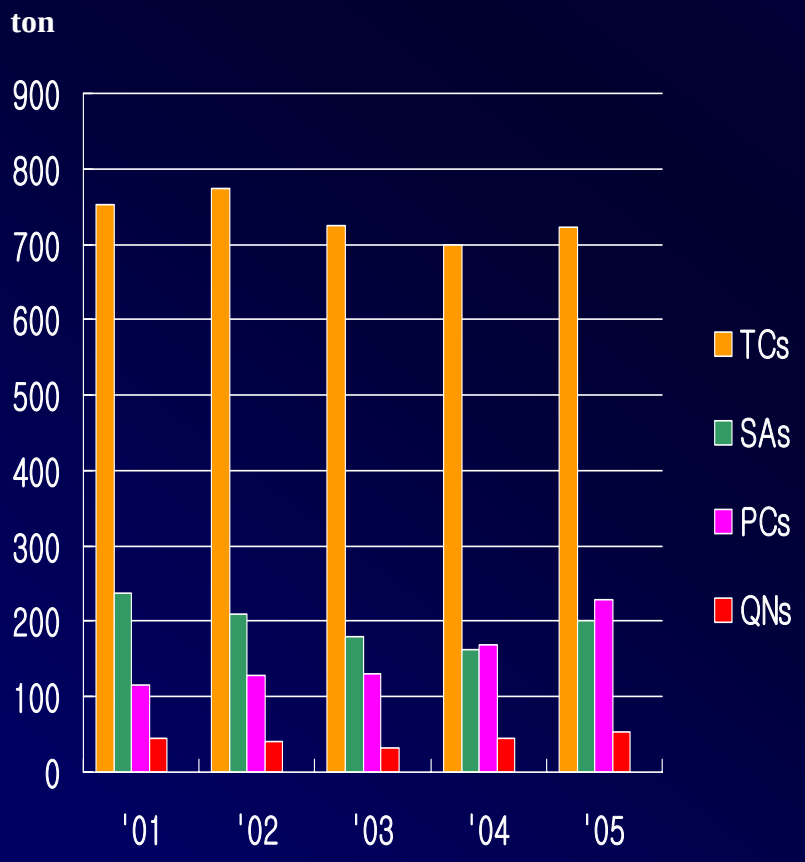
# NRP Results of Domestic Samples

## - Violation Rates of Animal Species -

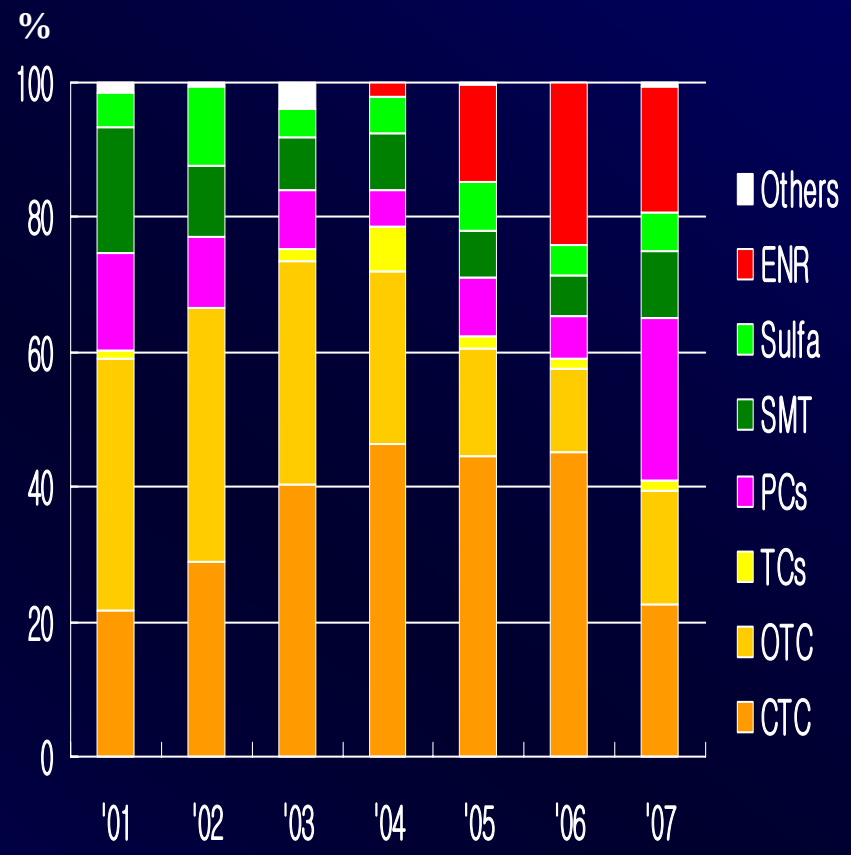


# NRP Results of Domestic Samples

## - Correlation between the Usage and Residue Violation Rates of Antimicrobials in meat products -




<Usage in Korea>

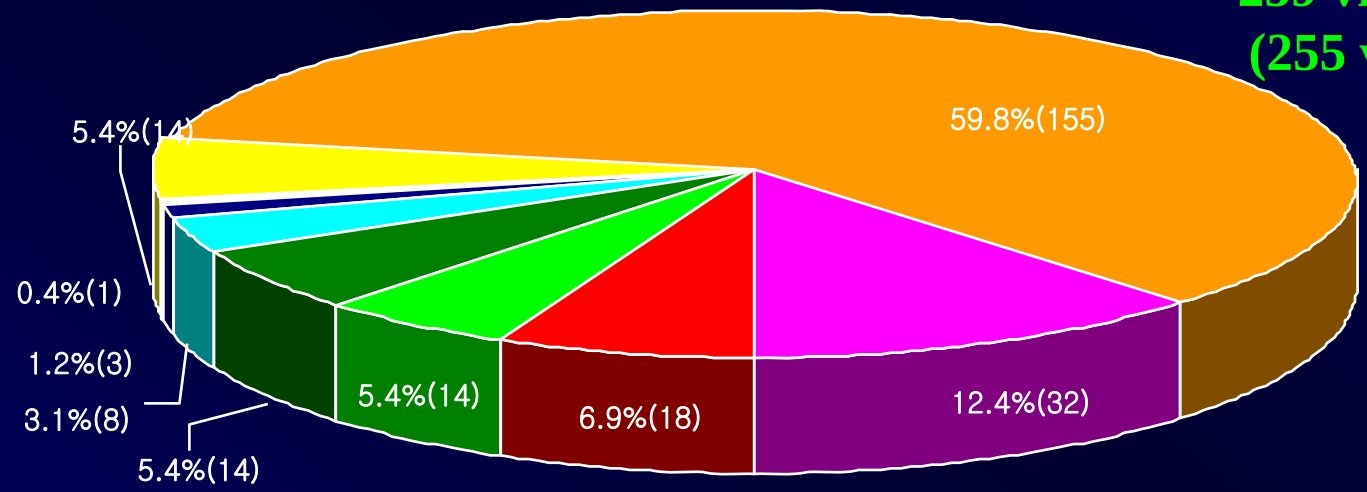



<Residue Violation Rates>

# NRP Results of Domestic Samples

## - The Causes for Residue Violation in 2007 -

**259 violative animals**
**(255 violative farms)**




- Inobservance of withdrawal period
- Inadequate feeding at finishing period
- Insufficient record of administration
- Contamination of non-medicated feed
- Feeding of medicated feeds
- Inadequate isolation or identification of medicated animals
- Overdose
- Contamination of the water system by mismanagement
- The others

# Pathways of Medicated Veterinary Drugs

Absorption

↓

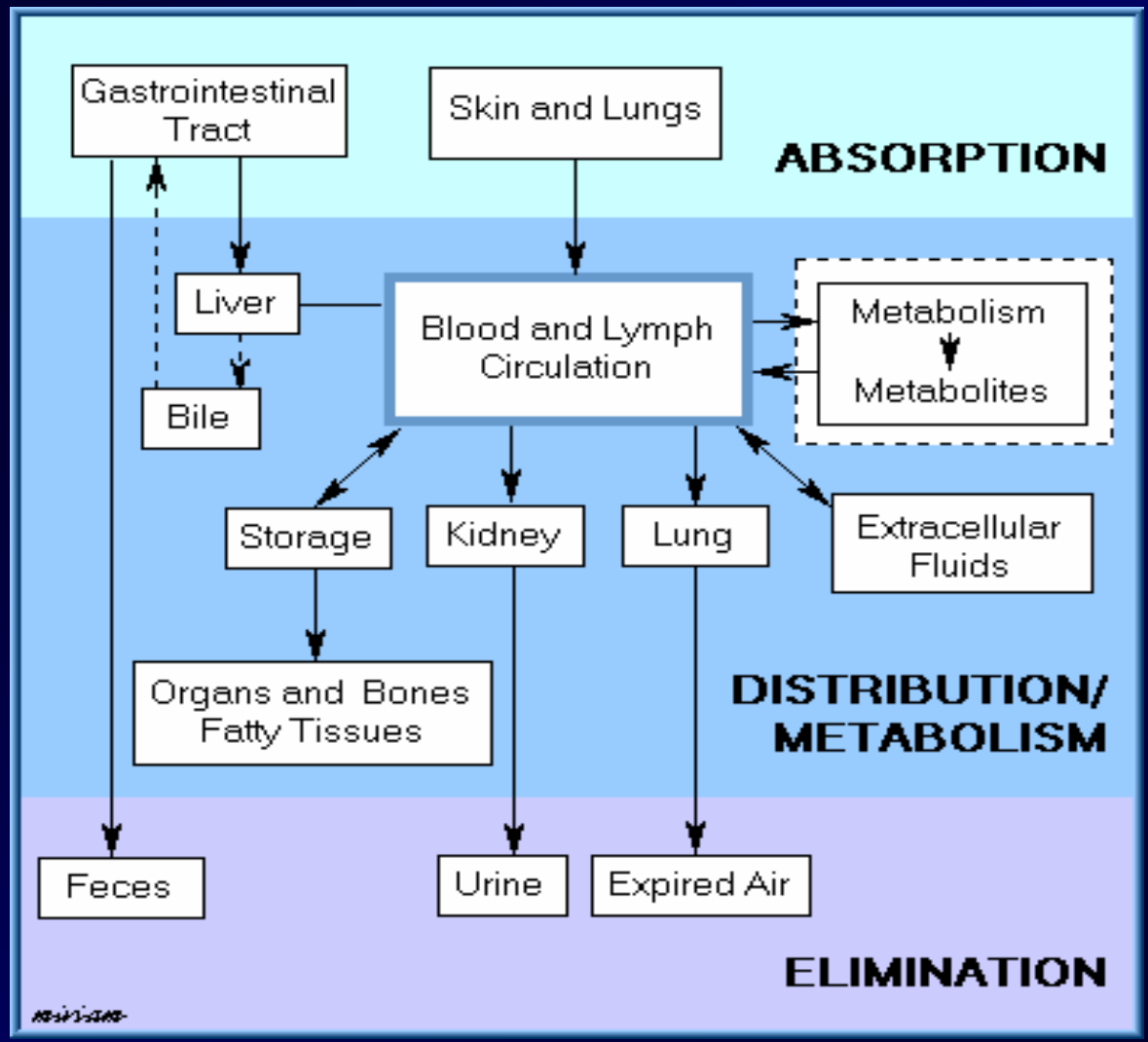
Distribution

↓

Metabolism

↓

Elimination



# Withdrawal Time?

* Terminal elimination phase of tissue residues closest to the tolerance (MRL) in medicated animals.

* Established the 99th percentile statistical tolerance limit with 95% confidence.

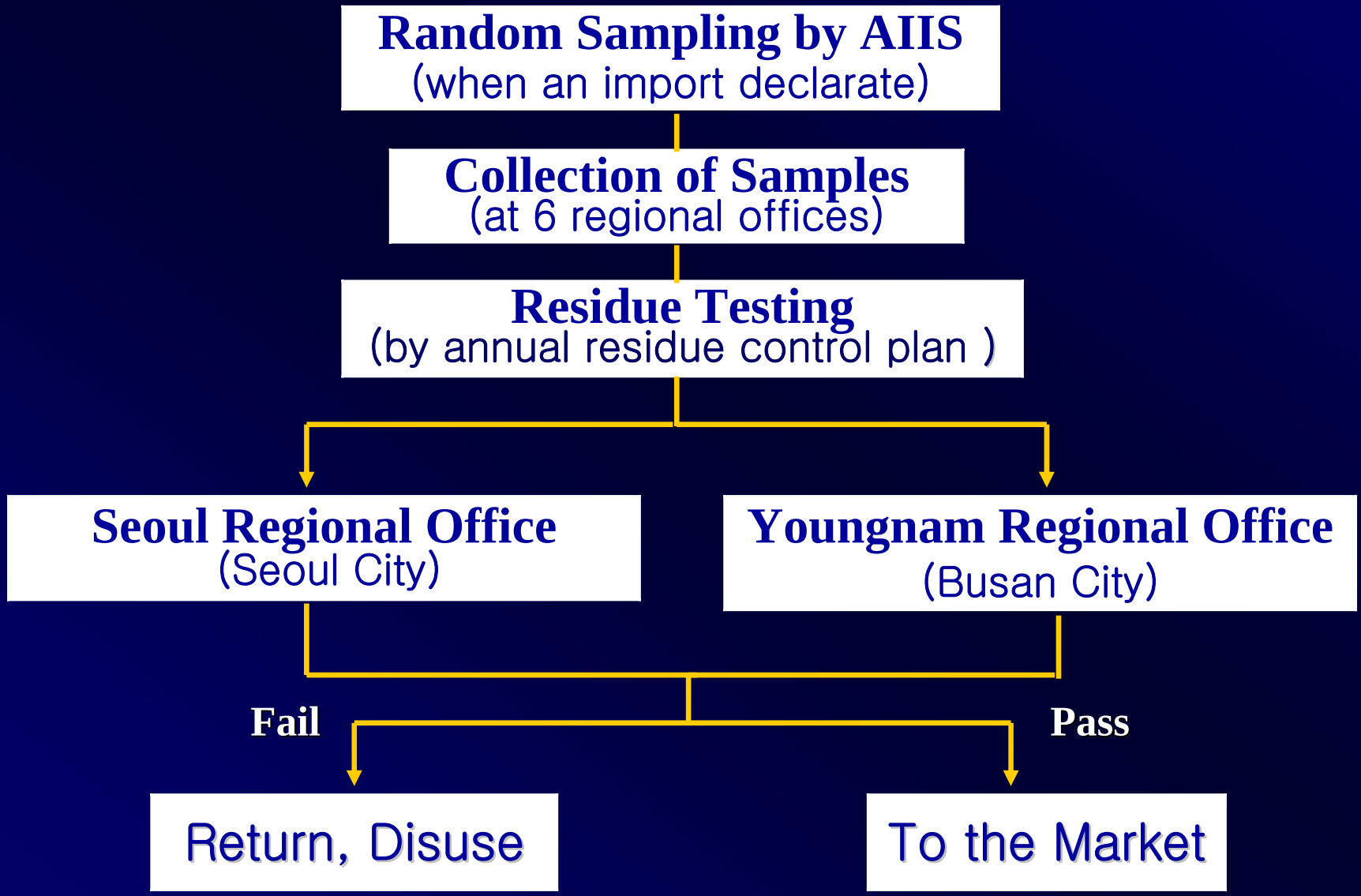
If a farmer follows the withdrawal times of drug, the eatable food from treated animals are Safe .



# Components of Import NRP

- **Monitoring** - statistically based random sampling and testing of imports
- **Surveillance & Enforcement testing** - follow-up when violative residues are suspected in a product from an exporting country
- **Exploratory testing** - follows identification of a need to study specific imported product or compound

# Import Residue Testing System



# Import Residue Testing Plan

- **Monitoring :** samples submitted randomly to NVRQS regional office laboratories
  – about 5,000 cases (15,000 samples) per year

- **Surveillance & Enforcement Testing:** samples submitted directly to NVRQS regional office laboratories
  – about 150 cases per year

- **Exploratory :** samples submitted randomly to NVRQS a headquarter laboratory
  – specific imported products or compounds

# NRP Results of Imported Samples

## - Major Residue Violations in Animal Products -

1999 Endosulfan in beef (Australia), PCBs in pork (Belgium)

2000 Sulfaquinoxine in duck (Thailand)

2001 Oxytetracycline in bovine product (Canada)

2002 Chlortetracycline in swine product (USA)

2003 Dioxins in pork (Chile),
Nitrofuran metabolites (AOZ) in egg products (India)

2004 Chlortetracycline in swine product (USA)

2005 Nitrofuran metabolites(AOZ/AMOZ) in pork (Mexico)
Enrofloxacin in pork (Spain), Endosulfan in beef (New Zealand)

2006 Dioxins in beef (USA)

2007 Sulfamethazine in pork (Spain, USA)

2008 Chloramphenicol in egg products (China), Dioxins in pork (Chile),
Endosulfan in bovine products (New Zealand)

# Future Issues of NVRQS NRP

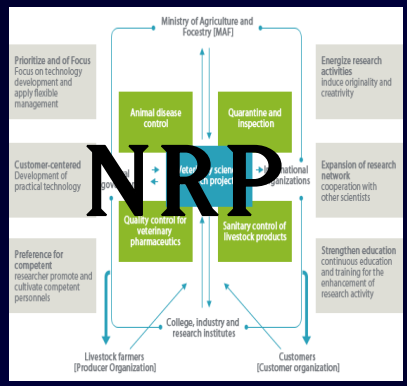
- Improve sampling system for domestic monitoring, surveillance & enforcement testing program
  - target tissue, marker residue
- Improve analytical methodology
- Enhance exploratory program for anti-infammatory agents and other banned veterinary drugs
- Enhance the management of residue violators
  - on-site education, increase imposing penalty

# Need for Residue Avoidance

- **To supply safe and wholesome animal products to domestic & foreign consumers**
  - Livestock farmer
  - Feed & veterinary drug manufacturer
  - Related producer association
  - Slaughtering & processing plant
  - Government (MIFAFF, NVQRS, PVS)


**→ should be involved in a national residue control program.**

# Thank you for your attention!




NRP