

# Drug Residues in Animal Derived Foods



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# Compliance Program 7371.006-- Illegal Residues in Meat, Poultry, Aquacultured Seafood and other Animal Derived Foods



**Livestock Being Raised for Food Use are “Food” Under the Federal Food, Drug, and Cosmetic Act**



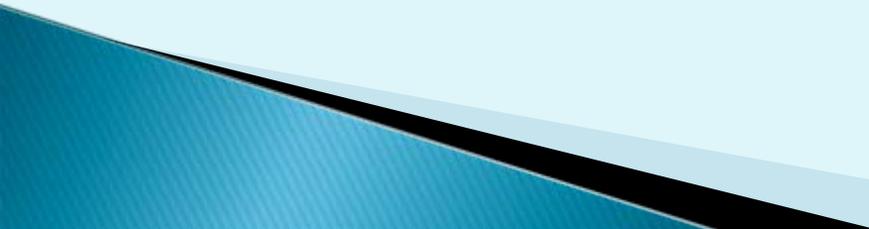


This Compliance program contains Center instructions to Field investigators on how to conduct inspections to follow up violative drug residues and how to develop appropriate administrative/enforcement responses.

# FDA Compliance Program Objectives

- ▶ To minimize consumer's exposure to food adulterated with illegal drug residues.
- ▶ To conduct inspections to determine the cause of illegal drug residues and prevent future violations.

# FDA Compliance Program Objectives

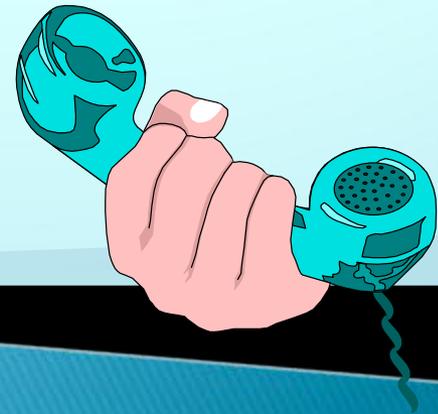
- ▶ To identify on-farm husbandry practices and animal drug use patterns leading to violative residues for program analysis, identification of educational needs, and policy and/or guidance development.
  - ▶ Obtain correction through voluntary and/or enforcement actions.
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# Memoranda of Understanding

- ▶ Food and Drug Administration (FDA)
- ▶ Food Safety and Inspection Service (FSIS)
- ▶ Environmental Protection Agency (EPA)



The Most Important Element of  
a Successful National Program  
is Communication

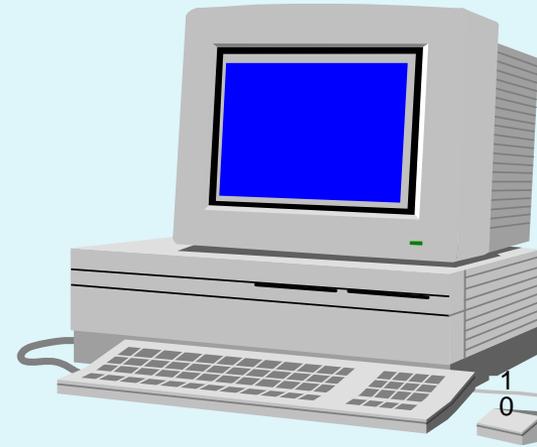


# Communication

- ▶ Interagency Residue Control Group (IRCG)
- ▶ Surveillance Advisory Team
- ▶ FSIS District Conferences
- ▶ Veterinary Field Committee
- ▶ Quarterly Conference Calls with District Program Monitors

# Databases

- ▶ Residue Violation Information System (RVIS) (Information on FSIS Sampling & Results)



# TISSUE RESIDUES IN DAIRY CATTLE – RVIS

| <b>DRUG</b>                | <b>2005</b> | <b>2006</b> | <b>2007</b> | <b>2008</b> | <b>Total</b> | <b>Percent</b> |
|----------------------------|-------------|-------------|-------------|-------------|--------------|----------------|
| <b>Amikacin</b>            | <b>4</b>    | <b>2</b>    | <b>0</b>    | <b>1</b>    | <b>7</b>     | <b>0.20%</b>   |
| <b>Ampicillin</b>          | <b>6</b>    | <b>10</b>   | <b>13</b>   | <b>8</b>    | <b>37</b>    | <b>1.04%</b>   |
| <b>Ceftiofur</b>           | <b>*</b>    | <b>*</b>    | <b>*</b>    | <b>71</b>   | <b>71</b>    | <b>1.99%</b>   |
| <b>Dihydrostreptomycin</b> | <b>14</b>   | <b>10</b>   | <b>8</b>    | <b>3</b>    | <b>35</b>    | <b>0.98%</b>   |
| <b>Florfenicol</b>         | <b>1</b>    | <b>0</b>    | <b>0</b>    | <b>0</b>    | <b>1</b>     | <b>0.03%</b>   |
| <b>Flunixin</b>            | <b>121</b>  | <b>133</b>  | <b>262</b>  | <b>233</b>  | <b>749</b>   | <b>20.99%</b>  |
| <b>Furazolidone</b>        | <b>1</b>    | <b>1</b>    | <b>0</b>    | <b>0</b>    | <b>2</b>     | <b>0.06%</b>   |
| <b>Gentamicin</b>          | <b>77</b>   | <b>95</b>   | <b>58</b>   | <b>50</b>   | <b>280</b>   | <b>7.85%</b>   |
| <b>Kanamycin</b>           | <b>2</b>    | <b>1</b>    | <b>0</b>    | <b>0</b>    | <b>3</b>     | <b>0.08%</b>   |
| <b>Lincomycin</b>          | <b>0</b>    | <b>0</b>    | <b>1</b>    | <b>0</b>    | <b>1</b>     | <b>0.03%</b>   |

# TISSUE RESIDUES IN DAIRY CATTLE - RVIS

| DRUG                        | 2005       | 2006       | 2007        | 2008       | Total       | Percent       |
|-----------------------------|------------|------------|-------------|------------|-------------|---------------|
| <b>Neomycin</b>             | <b>22</b>  | <b>28</b>  | <b>23</b>   | <b>21</b>  | <b>94</b>   | <b>2.63%</b>  |
| <b>Oxytetracycline</b>      | <b>31</b>  | <b>30</b>  | <b>21</b>   | <b>32</b>  | <b>114</b>  | <b>3.20%</b>  |
| <b>Penicillin</b>           | <b>301</b> | <b>358</b> | <b>413</b>  | <b>304</b> | <b>1376</b> | <b>38.57%</b> |
| <b>Phenylbutazone</b>       | <b>2</b>   | <b>0</b>   | <b>4</b>    | <b>3</b>   | <b>9</b>    | <b>0.25%</b>  |
| <b>Sulfachlorpyridazine</b> | <b>0</b>   | <b>1</b>   | <b>0</b>    | <b>0</b>   | <b>1</b>    | <b>0.03%</b>  |
| <b>Sulfadimethoxine</b>     | <b>102</b> | <b>158</b> | <b>159</b>  | <b>135</b> | <b>554</b>  | <b>15.53%</b> |
| <b>Sulfamethazine</b>       | <b>24</b>  | <b>33</b>  | <b>33</b>   | <b>22</b>  | <b>112</b>  | <b>3.14%</b>  |
| <b>Sulfathiazole</b>        | <b>1</b>   | <b>2</b>   | <b>0</b>    | <b>0</b>   | <b>3</b>    | <b>0.08%</b>  |
| <b>Tetracycline</b>         | <b>16</b>  | <b>16</b>  | <b>7</b>    | <b>15</b>  | <b>54</b>   | <b>1.51%</b>  |
| <b>Tilmicosin</b>           | <b>17</b>  | <b>27</b>  | <b>14</b>   | <b>4</b>   | <b>62</b>   | <b>1.74%</b>  |
| <b>Tylosin</b>              | <b>1</b>   | <b>0</b>   | <b>1</b>    | <b>1</b>   | <b>3</b>    | <b>0.08%</b>  |
|                             | <b>743</b> | <b>905</b> | <b>1017</b> | <b>903</b> | <b>3568</b> |               |

\* Prior to July 28, 2008 USDA could not quantitate Cefiofur

# Databases

- ▶ Tissue Residue Information Management System (TRIMS)  
(Information on Federal/State Investigational Findings)

# TRIMS

3/15/2011

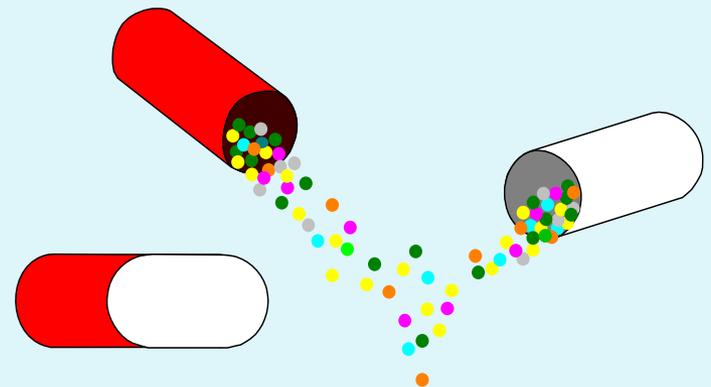
- ▶ An Interactive Database Containing Information Obtained During FDA/State Inspections of Firms Involved/Responsible for Tissue Residue Violations.
- ▶ Attachment C Ensures Consistent Data Collection by both Federal and State Investigators.
- ▶ Attachment C Data Entered into TRIMS



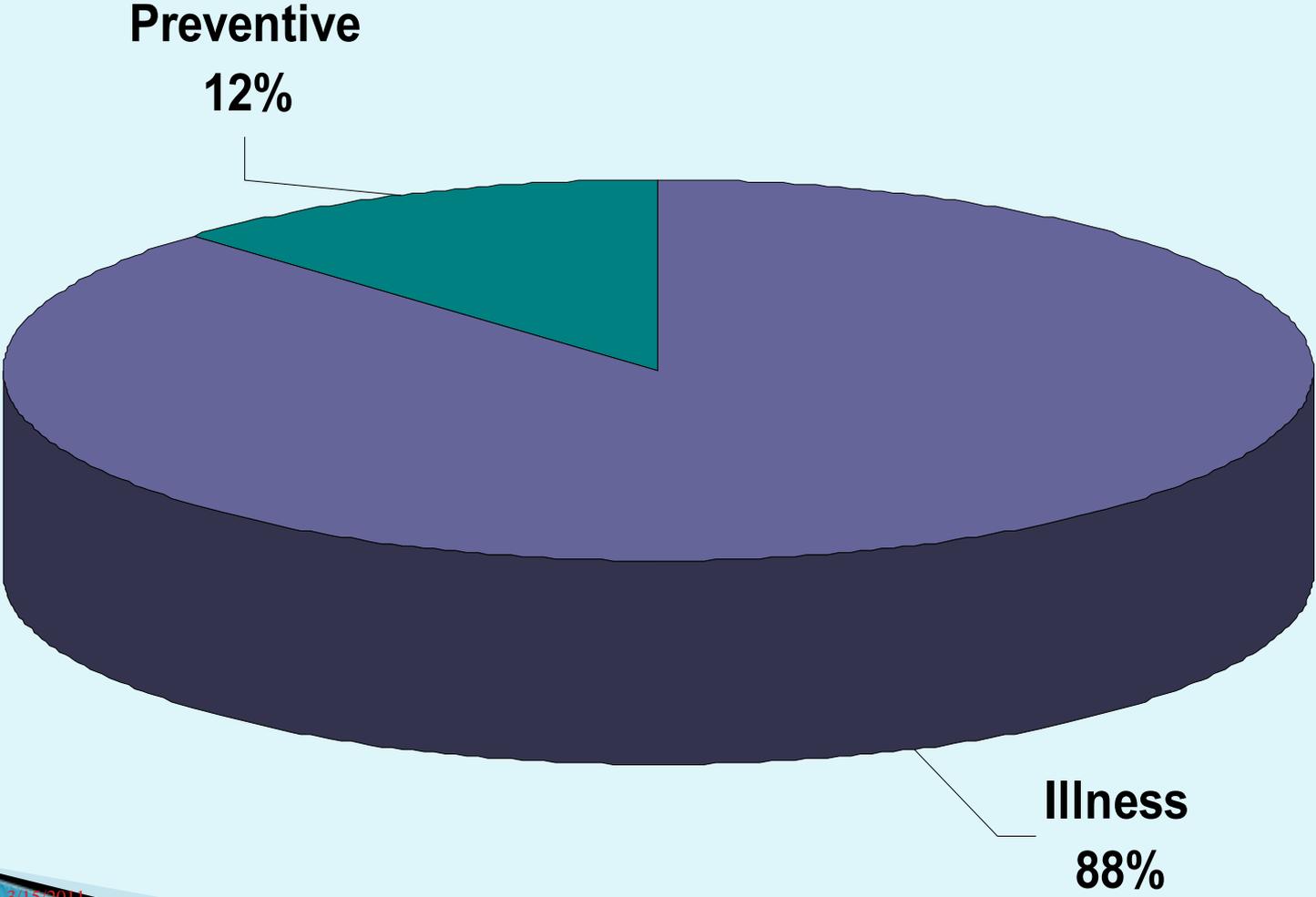
# TRIMS – Traditional Causes of Residues

3/15/2011

- ▶ Treatment Records Not Maintained
- ▶ Failure to Maintain Animal Id
- ▶ Withdrawal Time Not Followed
- ▶ Exceeded Approved Dose
- ▶ Extra Label Use by Laymen

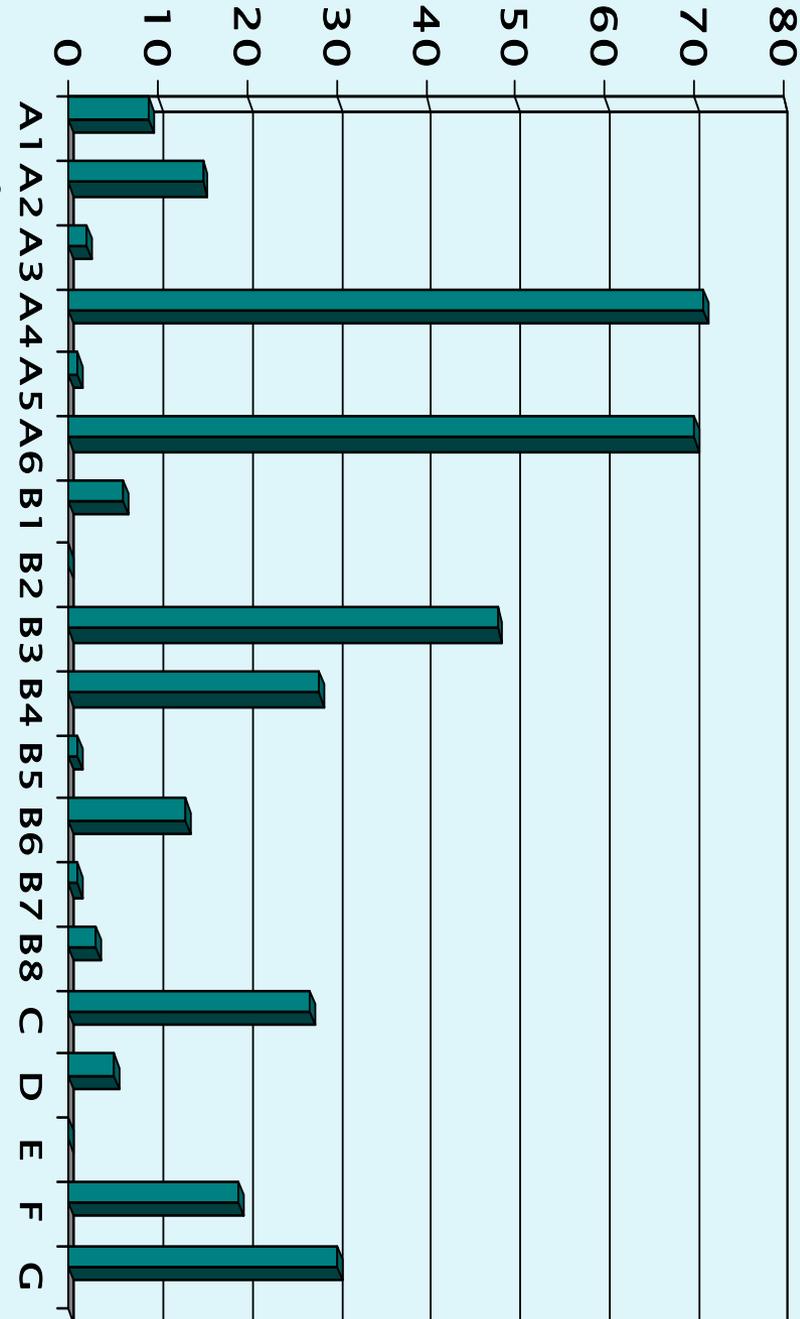


# Reason Drug Used - FY08

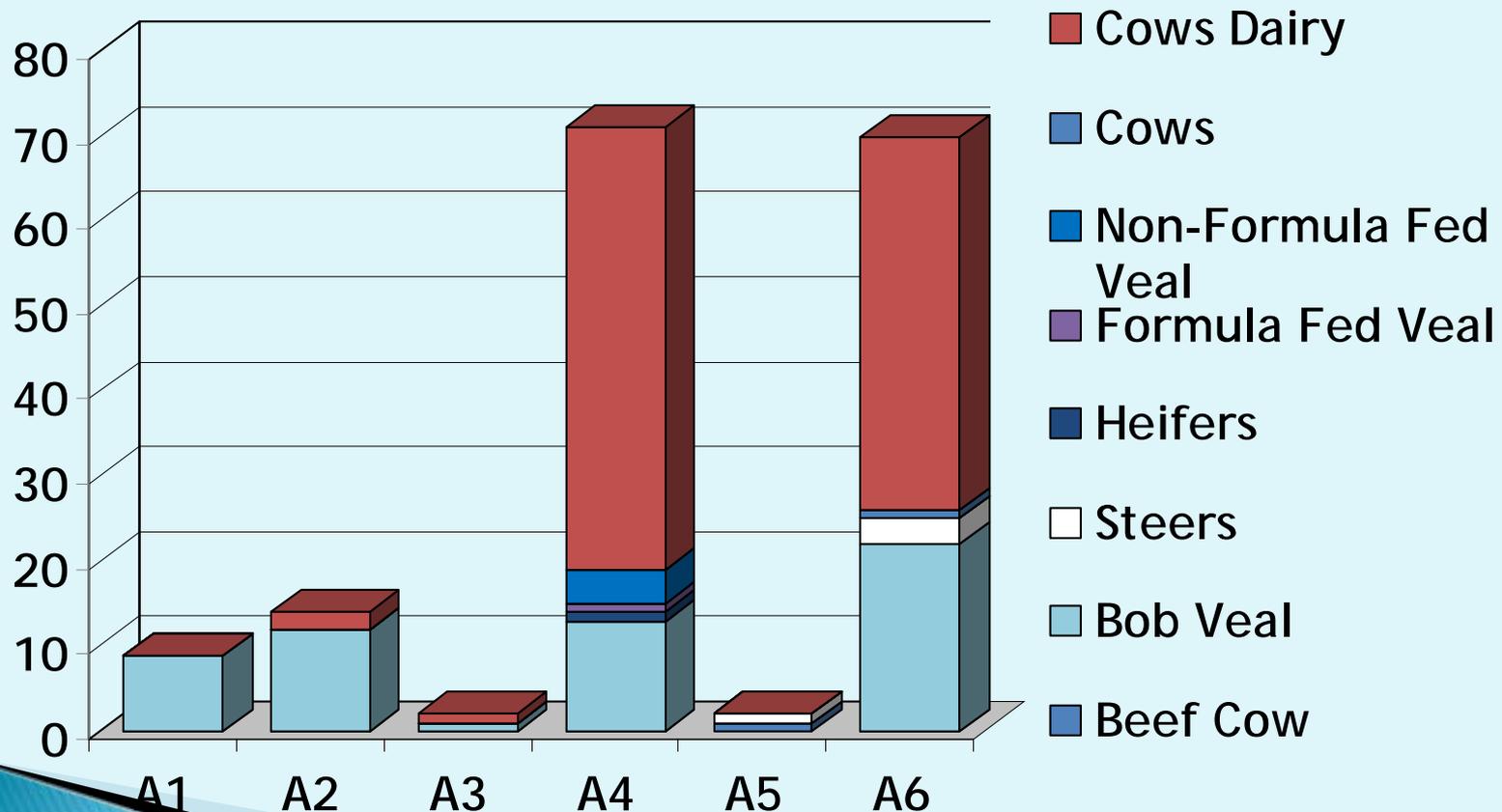


# Causes of Violative Residues FY08

- A1- Animal fed colostrum
- A2- Animal fed medicated feed by mistake
- A3- Drug given by mistake
- A4-Failure to maintain animal id & medication records
- A5- Inadequate animal segregation
- A6- Failure to follow withdrawal time
- A7- Feed manufacturing cGMPs
- B1- Vet's prescribed withdrawal time not followed
- B2- Vet's verbal withdrawal time not followed
- B3- Animal treated with higher dose
- B4- Labeled route of administration not followed
- B5- No withdrawal period prescribed
- B6- Drug not approved for species
- B7- Frequency different than labeled
- B8- Duration of treatment longer than labeled
- C- Could not Determine
- D- Drug not same as reported by FSIS
- E- Told purchaser that animal was medicated and it was later diverted
- F- All labeled directions followed and documented
- G. Miscellaneous other causes

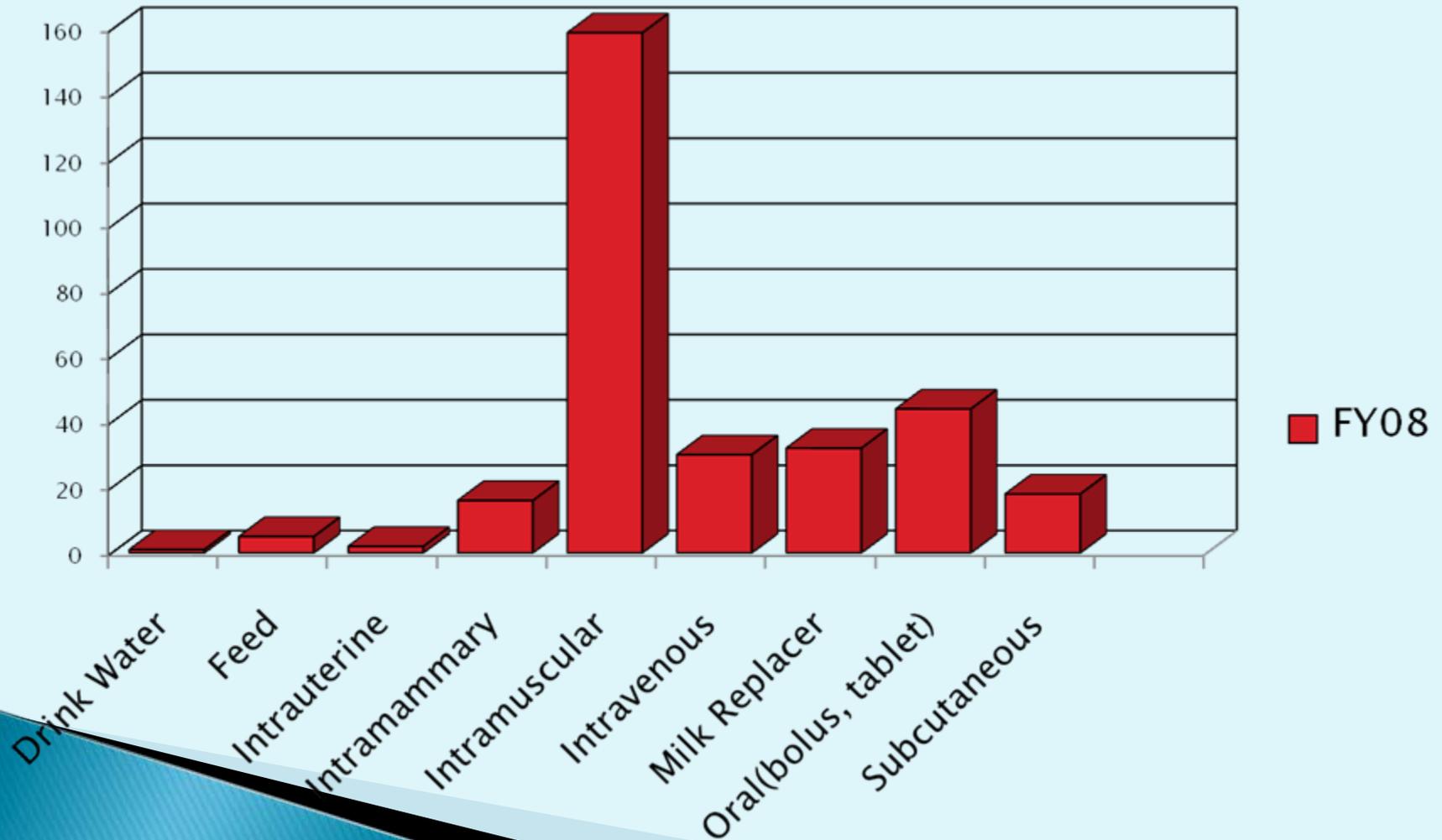


# Production Causes of Residues by Animal Slaughter Class for FY08

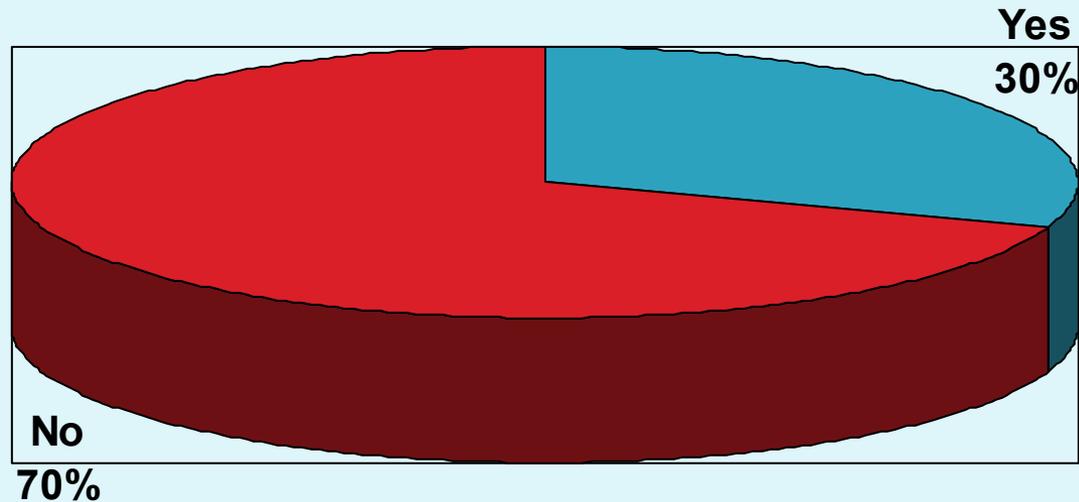


# Route of Administration for Drugs Causing Residues in FY08

3/15/2011



# Did they have a Valid VCPR for Use for FY08



## The Risk Question

*Which of the violators should I decide to inspect, given that my budget does not enable me to inspect all violators?*



From Deegan et al. 2003

# Risk Ranking

- ▶ Limited resources dictate that FDA conduct inspections/investigations for violations based on risk.
- ▶ CVM has developed a risk ranking system. The Risk Score will be between 1-3.
- ▶ The risk threshold will be calculated annually.

# Risk Analysis

- ▶ Hazard:
  - Residue Toxicity (RT)
    - Acceptable Daily Intake (ADI)
    - Drug Not approved for food animals
    - AMDUCA-prohibited drug
    - Human Carcinogen
- ▶ Likelihood of Exposure:
  - Firm Violation Frequency (VF)
- ▶ Exposure Level
  - Tolerance Exceedance (TE)

# RT/5 + VF/5 + TE/8 = RISK SCORE

|  | Low → High Risk                                |           |  |           |   |            |   |                 |   |  |
|--|--|-----------|--|-----------|---|------------|---|-----------------|---|--|
| <b>Hazard</b><br><br>Residue Toxicity                    | <b>1</b>                                       |           | <b>2</b>   |           | <b>3</b>  |            | <b>4</b>                                  |                 | <b>5</b>  |  |
|  | Residue with <u>high</u> ADI > 50 µg/kg/day    |           | 10 < ADI ≤ 50 µg/kg/day                          |           | 3 < ADI ≤ 10 µg/kg/day                              |            | 0.2 < ADI ≤ 3 µg/kg/day                   |                 | Residue with <u>low</u> ADI < 0.2 µg/kg/day<br>or<br>Drug not approved for food animals<br>or<br>AMDUCA-prohibited drug<br>or<br>Human Carcinogen |  |
| <b>Likelihood of Exposure</b><br><br>Violation Frequency | <b>1</b>                                       |           | <b>2</b>   |           | <b>3</b>  |            | <b>4</b>                                  |                 | <b>5</b>  |  |
|  | Current Violation: 1 animal; 1 residue /animal |           | Current Violations: >1 animal; 1 residue /animal |           | Current Violations: ≥ 1 animal; >1 residues /animal |            | Previous violation(s) prior to 1 year ago |                 | Previous regulatory action or Previous violation(s) within 1 year   |  |
| <b>Exposure Level</b><br><br>Tolerance Exceedance        | <b>1</b>                                       | <b>2</b>  | <b>3</b>   | <b>4</b>  | <b>5</b>  | <b>6</b>   | <b>7</b>                                  | <b>8</b>        |   |  |
|  | ≤ 10X  | 10X – 20X | 20X – 30X  | 30X – 40X | 40X – 50X   | 50X – 100X | 100X – 250X                               | >250X tolerance |   |  |

# Risk Ranking Cont.

- ▶ CVM issues an assignment to the appropriate District Office requesting an FDA on-site inspection/investigation be conducted when the risk score of the residue reported by FSIS exceeds the annually calculated FDA risk threshold.
- ▶ District Program Monitor will issue assignments to cooperating State Agencies for as many of the residues below the FDA risk threshold as cooperative agreements allow.

# HOW ARE ENFORCEMENT DECISIONS MADE?



- ▶ Jurisdiction – Interstate Commerce
- ▶ Document the violation
- ▶ Establish responsibility
- ▶ Size and scope of problem
- ▶ History of contact with FDA and prior notice of violations

# VOLUNTARY COMPLIANCE

- ▶ VAI Classification
- ▶ FDA investigator observations (FD 483);
- ▶ Educational handouts/materials
- ▶ Veterinarians
- ▶ Working with trade organizations.
- ▶ Provide clear guidance on requirements of FD&C Act;
- ▶ Correspondence with firm (Untitled Letter)

# OAI Inspections

- ▶ Obtain supervisory concurrence on recommendation
- ▶ Case sent to District Compliance Officer
- ▶ District Compliance Officer drafts charges
- ▶ Case sent to CVM Compliance Officer for review
- ▶ Case sent to OGC for final concurrence
- ▶ Action taken

# WARNING LETTER

- ▶ Written communication notifying firm of violations of the Act.
- ▶ Firm must respond with corrective actions within 30 days.
- ▶ Advisory, not considered a final agency enforcement action.

# INJUNCTION

- ▶ Injunction stops or prohibits a continuing violation.
- ▶ Consent Decrees are court orders signed by the defendants and judge.
- ▶ Contempt Actions

# Compliance Actions FY07-10 YTD

