

APPENDIX N PILOT UPDATE

2018 UPDATE

ROGER HOOI – APPENDIX N MODIFICATION STUDY COMMITTEE CHAIR

APPENDIX N – REMINDER ON TASKS

- 2019 NCIMS Report (2015 NCIMS Proposal 211)
- The Appendix N Modification Committee is charged to develop a pilot program, establishing a regulatory framework by which testing raw milk for veterinary drugs would be *required for drugs other than beta-lactams*.
 - **Veterinary drugs required to be tested**
 - **Testing methodology required to be used**
 - **Availability of suitable test methods**
 - **Number of samples to be collected and assayed**
 - **Reduction of required Beta-Lactam testing**
 - **National Milk Drug Residue Database**
 - **Report of challenges of program implementation**

TETRACYCLINE PILOT

START UP

- Minimal issues, smooth launch
- Initial learning curve
- Sufficient communications?

TETRACYCLINE PILOT

- Stakeholders
- Plan ahead
- Patience
- Panic

TETRACYCLINE PILOT

- Bulk Milk Tankers
- 1/15 (6.7%) loads per quarter
- NCIMS Appendix N Accepted Tests
- Appendix N Beta-lactam Approved Labs
- Launched July 2017

REGULATORY PROGRAM

- Funding – None from FDA
- NCIMS method and Procedures
- 2400 Forms
- M-I and directions

REGULATORY PROGRAM

NEVER GIVE AN ORDER THAT CAN'T BE OBEYED. DM

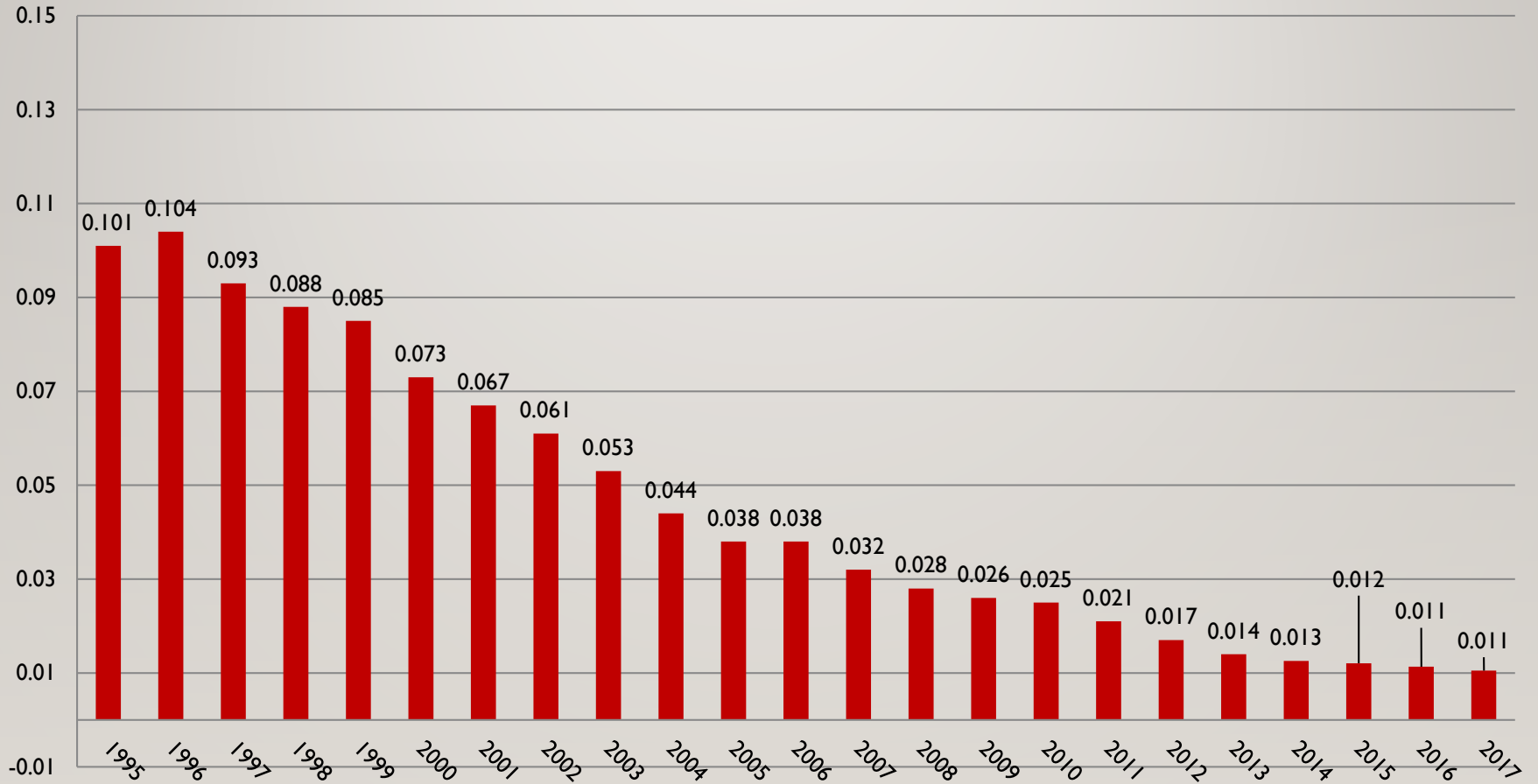
- Q&A on Tet Pilot
- Drug Residue Monitoring Database
- What does success look like?

ANIMAL DRUGS 1994 - 2017

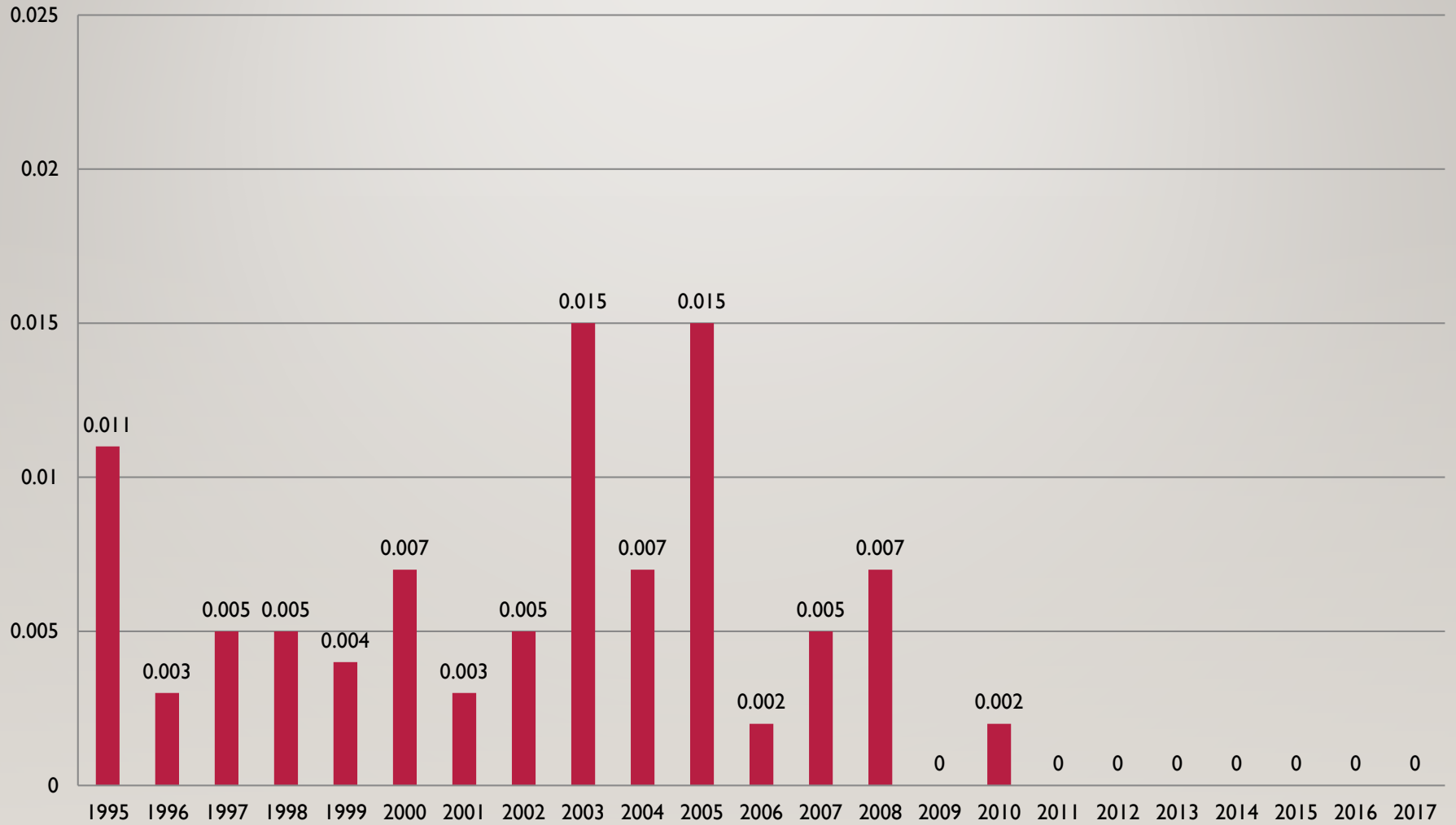
Drug Family	Total Tests	Total Positive	%
Aminoglycosides (Gentamicin)	25691	20	0.08
Amphenicol (Florfenicol, Chloramphenicol)	270	0	0.00
Avermectins (antiparasitics)			
Beta-lactams	76936306	35673	0.05
Fluoroquinolone - Enrofloxacin (Baytril)	50693	10	0.02
Macrolides	12457	3	0.02
NSAID (Flunixin)	2054*	0*	
Sulfonamides	2089905	405	0.02
Tetracyclines	1413179	711	0.05

* Internal data, 1 unconfirmed positive

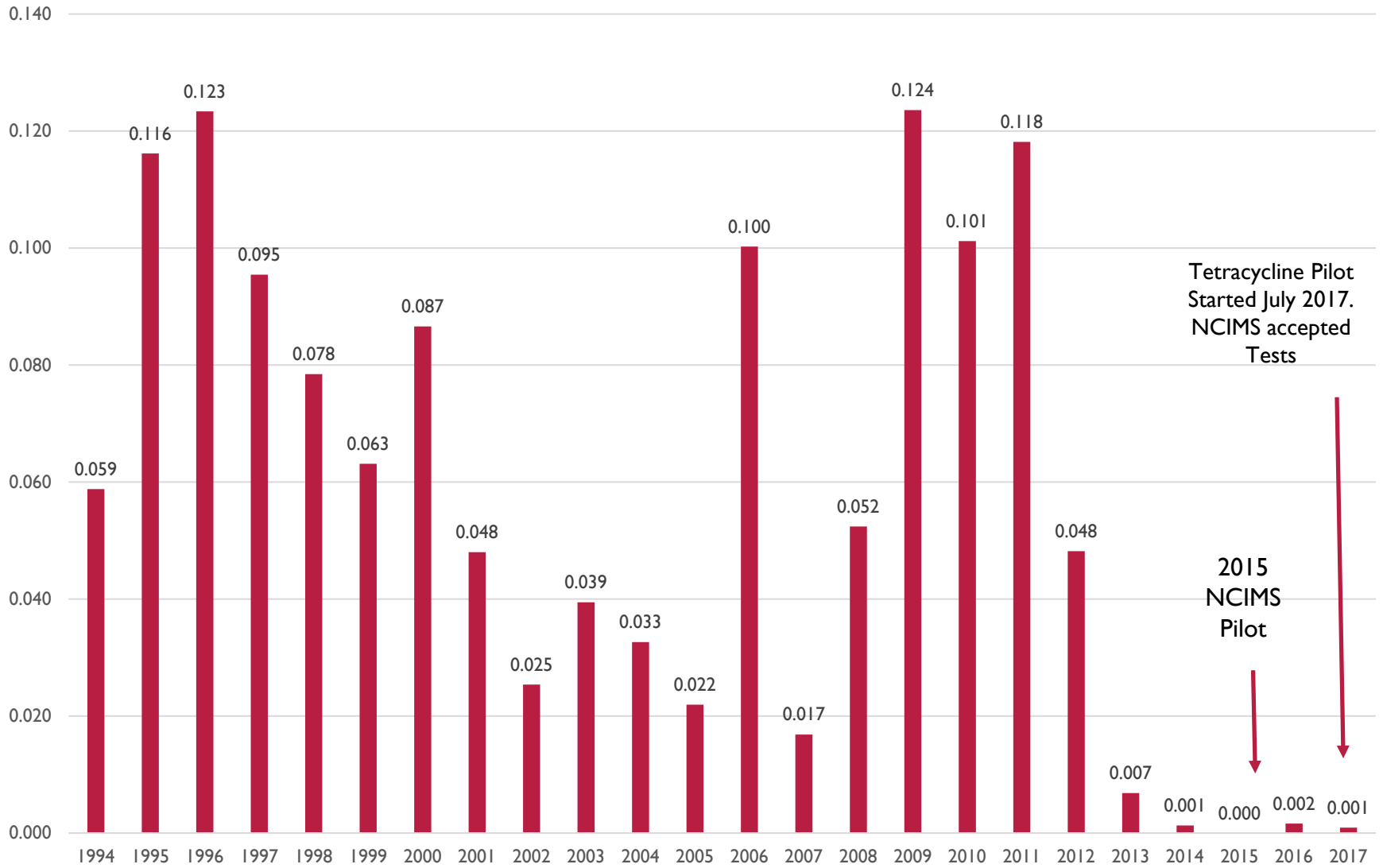
Bulk Milk Pick Up Tanker Appendix N Beta-lactam



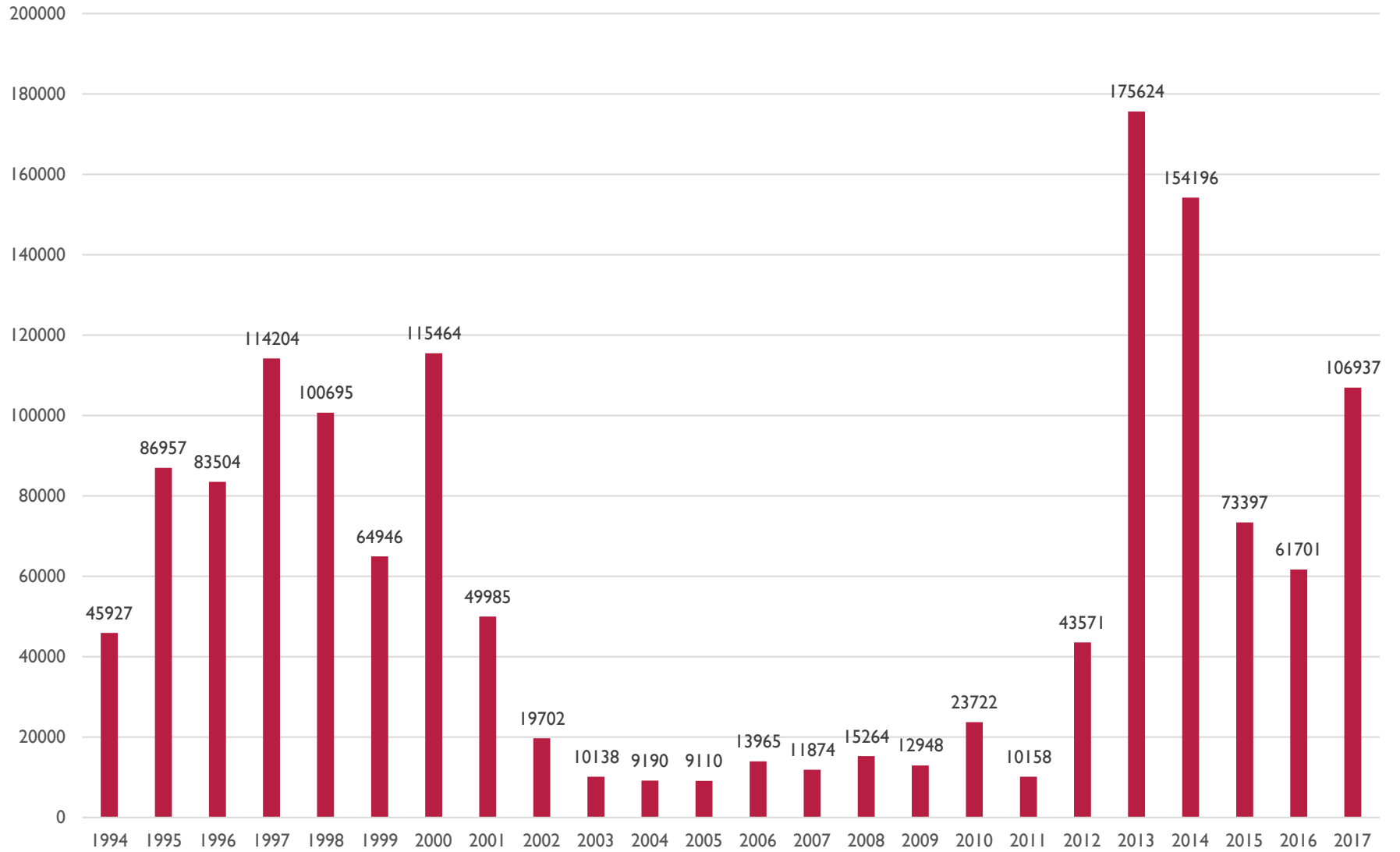
Pasteurized Milk and Milk Products % Positive



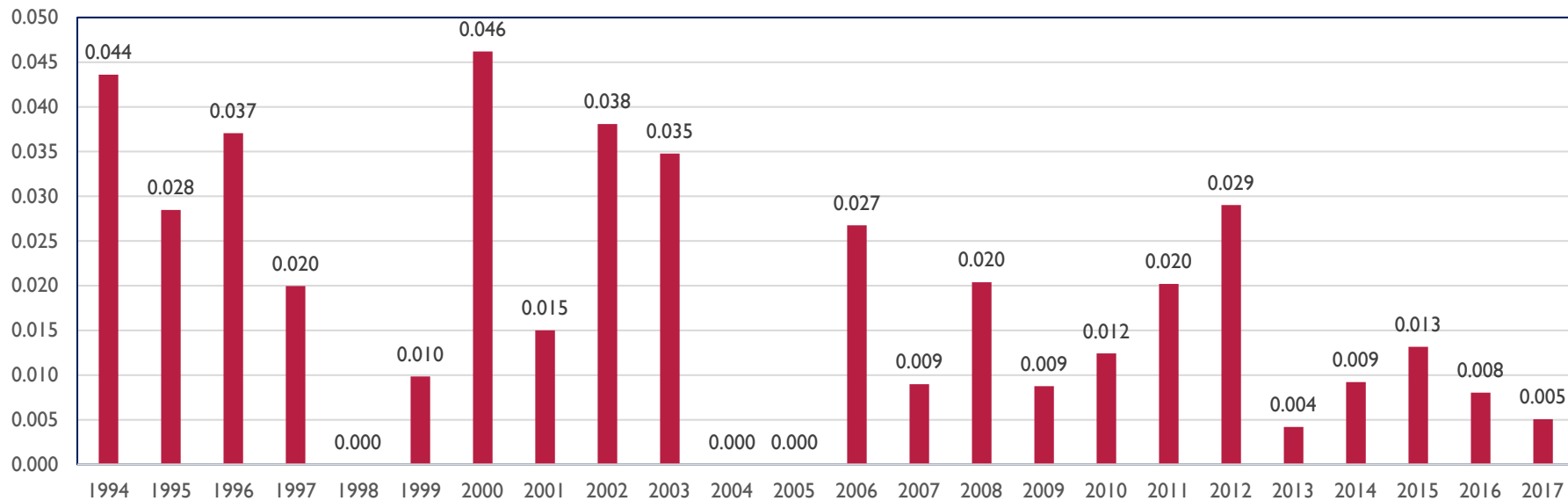
% Positive Tetracycline Family of Drugs Positives



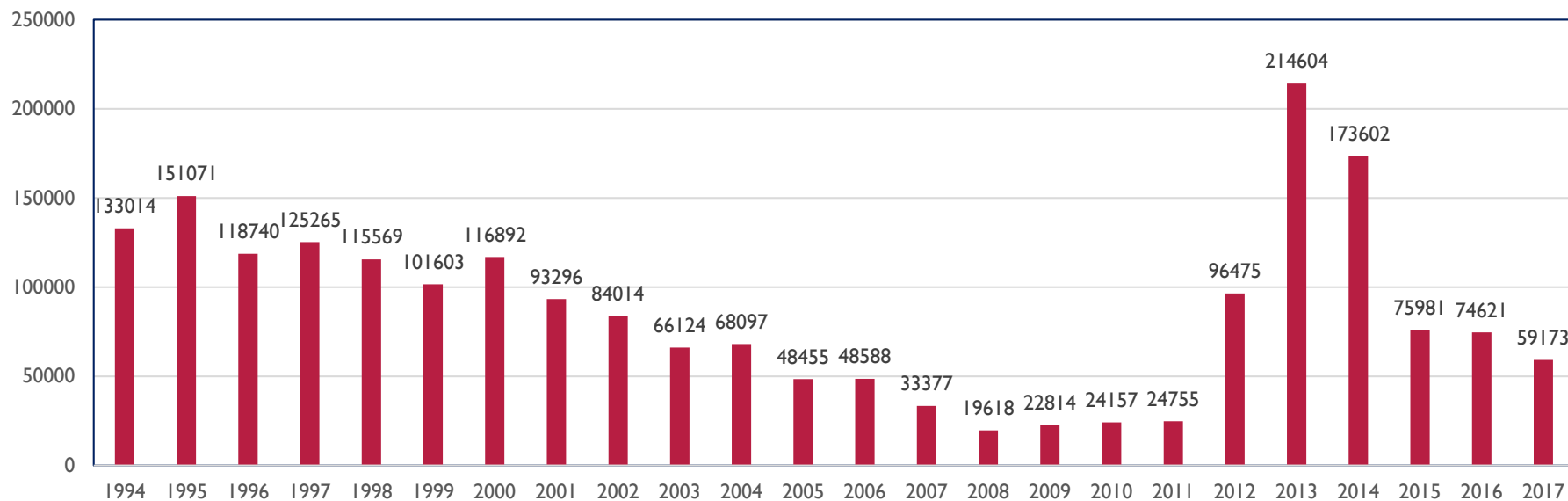
of Tetracycline Tests



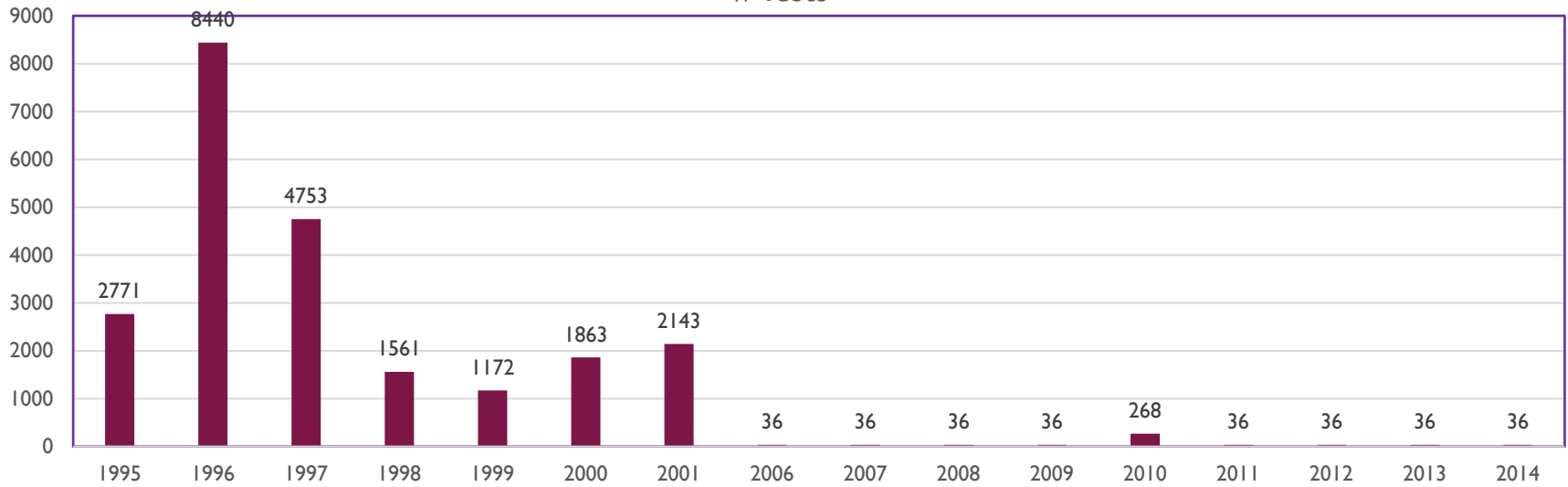
% Positive Sulfonamides



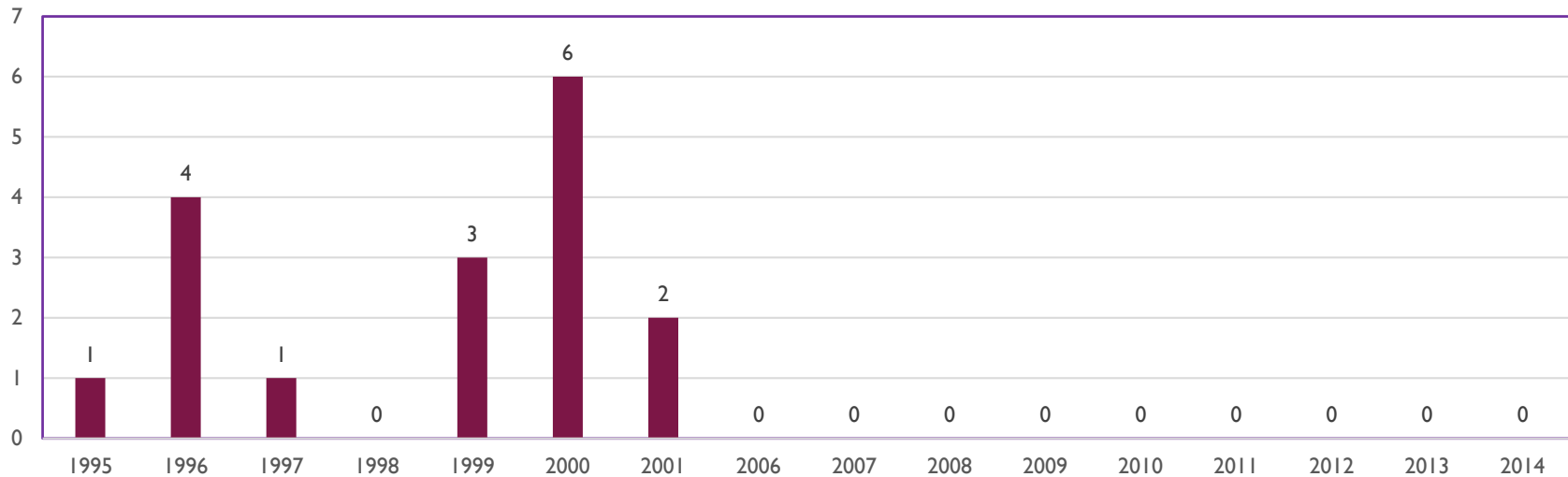
of Sulfonamides Tests



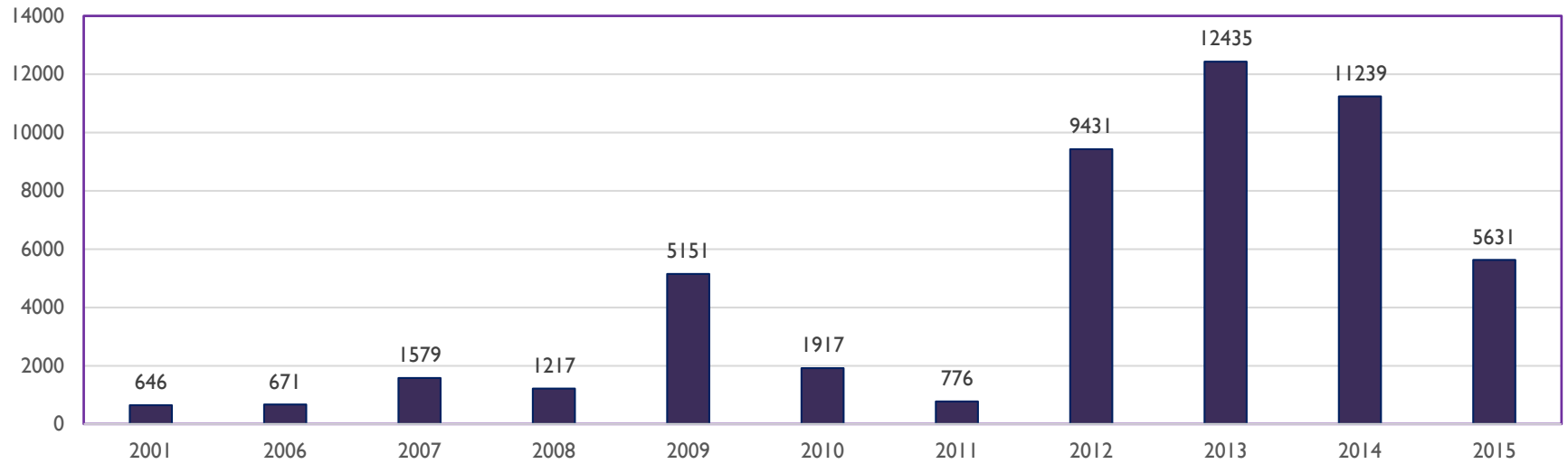
Aminoglycosides # Tests



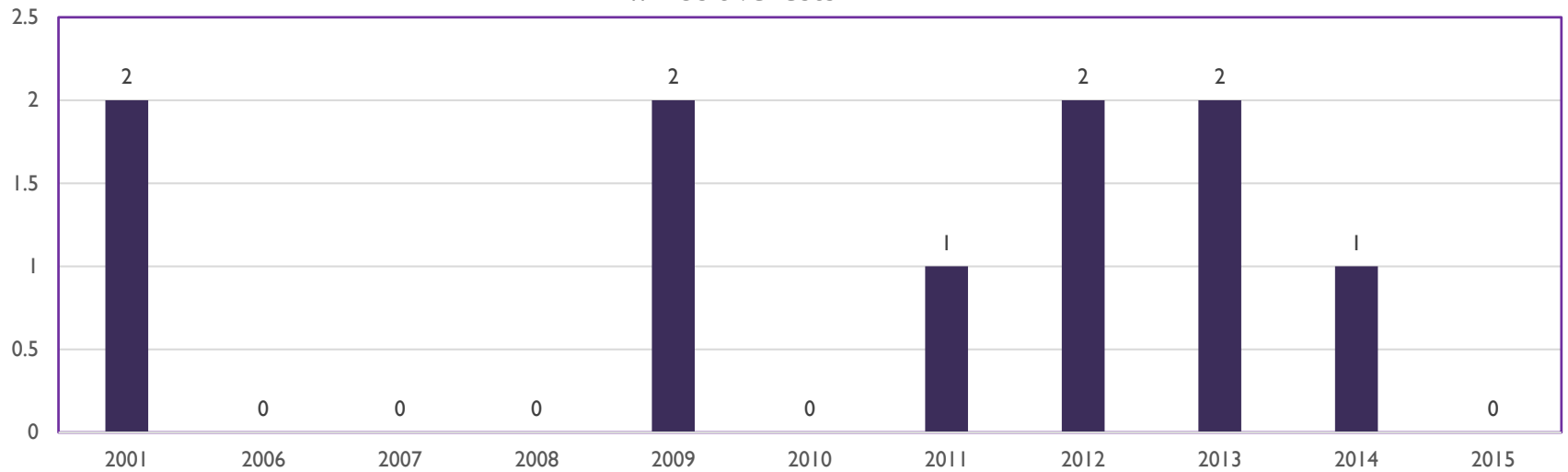
Aminoglycosides # Positive Tests



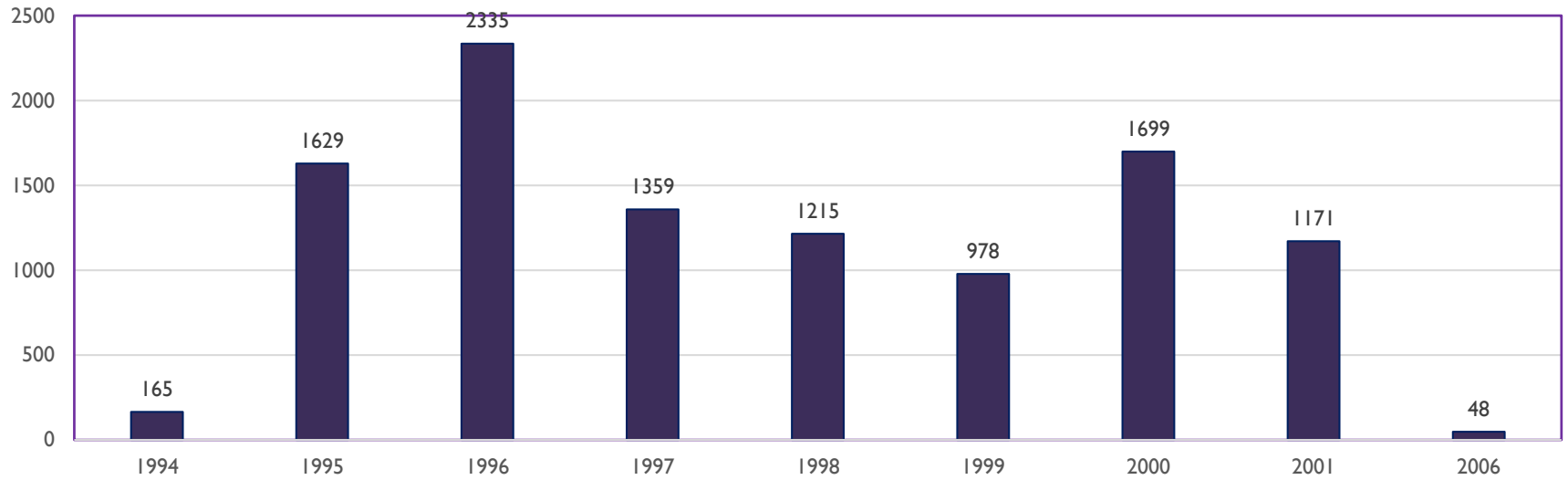
Enrofloxacin # Tests



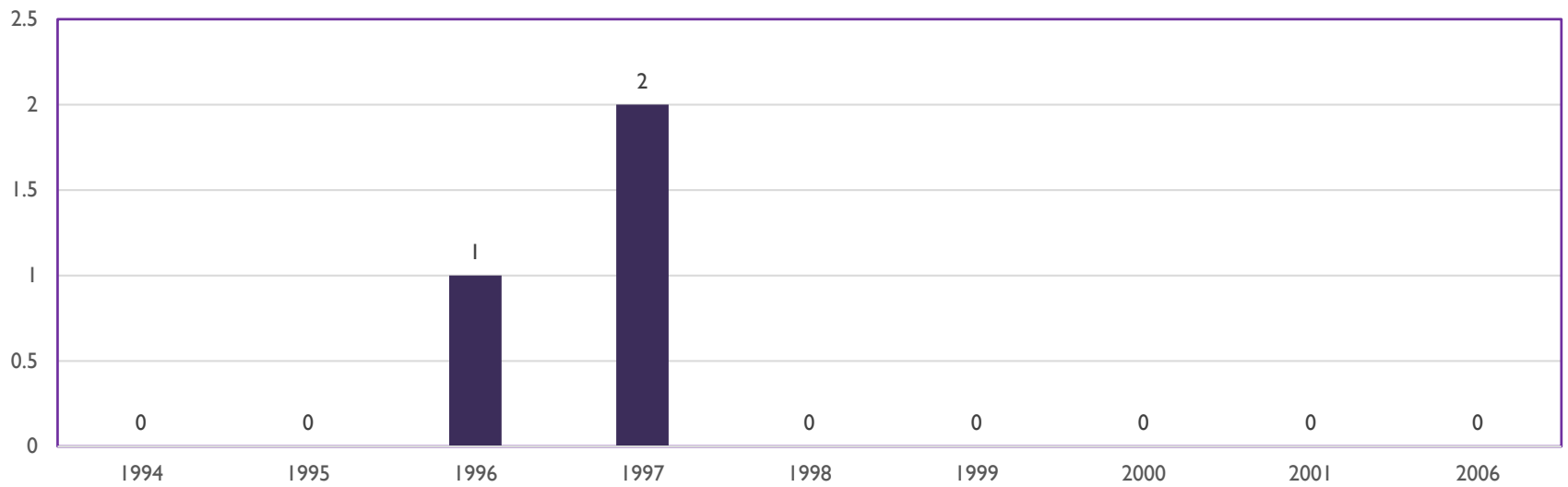
Enrofloxacin # Positive Tests



Macrolides # Tests



Macrolides # Positive Tests



WHAT ARE THE LATEST UPDATES?



HURDLES



WHAT ARE SOME OF THE HURDLES?

- Time and Cost
- Test Protocols
- Reporting
- Funding - Lack of Federal Funding
- Multi-drug, multi-analyte platforms
- State and Industry Participation
- Testing cannot commence until test methods are available, protocols established, NCIMS accepted, forms developed, and communicated.

APPENDIX N UPDATE

COMMITTEE ACTIONS

- April 10 – 12, 2018, DMI, Chicago
- Discussion committee on Other Inhibitor Testing.
 - Individual State program on OI test results in Section 6
- Q&A Version 7 – (10/18)
- Suspension of the Tetracycline (portion of the) Pilot December 31, 2018 (10/18)
- Drug Residue Database Review with FDA - Planned

APPENDIX N LATEST UPDATE

COMMITTEE ACTIONS

- Report to the NCIMS Board on status of Tetracycline Pilot - Draft
- 2019 NCIMS Report on the Pilot
- Permission and interpretation from NCIMS Board (10/18)
- Planning for the next drug
- NCIMS, St Louis, MO

2019 NCIMS: APRIL 26 – MAY 1, 2019

- **2018 December 15-21 - Initial mailing to all on distribution list**
- **2019 January 11 - Notification to Commissioners/Secretaries of state regulatory agencies.**
- **February 1 Deadline for receipt of all proposals**
- **February 11th week Program Committee meeting and Exec Board**
- **March 4 – 12 - Proposals mailed to registrants**
- **March 27 - Deadline for submission of pre-registration fees**
- **April 26 - First Day of Conference (Lab committee & FDA meetings April 25) Hyatt Regency St. Louis at the Arch, St. Louis, Missouri**

A REGULATORY FRAMEWORK

Don't tell people how to do things, tell them what to do and let them surprise you with their results. GP

WHAT'S NEW

In view, on the horizon, coming at us?

NEW TECHNOLOGIES



PROCESSING TECHNOLOGIES

- UV
- High Pressure
- Low Pressure (differential) Processing
- Pulsed Light
- E Beam
- Microwave
- Ohmic
- LED, Micro HTST, Electric, ...

DRUG RESIDUES ESTABLISHED METHODS

CURRENT COMMONLY USED

- Inhibition – Delvo, Charm
- Receptor Assay – Charm
- ELISA Methods – Charm, Neogen, IDEXX

ELISA

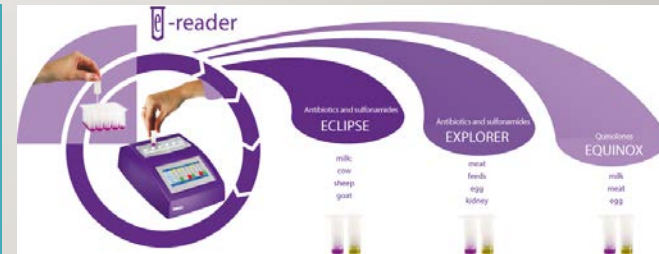
- Other Elisa Methods

- Microtiter well

- Eclipse, MilkGuard

- Lateral Flow

- Assuro, Auroflow, Ballrya, MDB (Milk Doctor Beta)
- Nankai, Green Spring, RingBio



Typical antibiotics Detection Limits	
- Penicillin	3ppb
- Cefazolin	3ppb
- Nafcillin	5ppb
- Cefoxime	5ppb
- Enoxacin	20ppb
- Cefuroxime	5ppb
- Cefotaxime	3ppb
- Cloxacillin	20ppb
- Cloxacillin	4ppb
- Cefquinom	20ppb

Operating Procedure	
Collect milk samples	Add milk samples
Collect milk samples	Dislodge test paper and wait at room temperature

Example of result	
Negative	Positive
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
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26	26
27	27
28	28
29	29
30	30

BIOSENSOR, SPECTROSCOPY, MULTIANALYTE ASSAY

- LC-MS/MS (AB SCIEX™), Multi-residue, multi matrix (product)
- Randox – Biochip, Multidrug, multiple assay throughput, 45-60 samples



Evidence Investigator

750 (H) x 480 (D) x 420 (W) mm

- Semi automated system
- Consolidation of testing delivers multiple test results from a single sample
- Fast analysis of up to 45 samples in under 2 hours (96 samples in 2 hours 30 minutes)
- Ideal for centralised laboratories



Evidence Evolution

1320 (H) x 1200 (D) x 1675 (W) mm

- Fully automated technology enables random and continuous access, STAT loading and batch mode
- Running up to 60 samples per hour with up to 2640 results, 36 minutes to the first result and results every minute thereafter
- Ideal for medium/high throughput labs

“EMERGING RAPID” METHODS

- Biosensors – Immobilized enzymes on bio-reactive surfaces (quartz, metals, semiconductors...)
- Spectroscopy - FTIR, NMR
- Molecular Methods - PCR, WGS, NGS, DNA/RNA, Biome testing
- Rapid Coliform, SPC, ...



“EMERGING RAPID” METHODS

- Testing within the “Matrix”
- What is the “new” Standard
- Measures of Accuracy, and Precision
- Rapid
- Easy to use
- Cost effective?

WHEN COMMON SENSE IS THE ONLY SENSE
DON'T SEEK ANOTHER SENSE!



QUESTIONS?

