FDA's View on EMA Survey Results

Hesha J. Duggirala, PhD, MPH
Epidemiologist, Center for Veterinary Medicine
Chair, FDA Data Science Council

U.S. Food and Drug Administration

Use Cases for Discussion

Pharmacovigilance*

- "2.A To implement a solution which compares Signal Detection outcomes across Marketing Authorization Holders (MAHs) ensuring quality control and obtaining harmonized safety outcomes"

Antimicrobial Resistance*

- "3.A. To integrate antimicrobial use data with a variety of other data sources and develop data analytic methods"

*From 2022 EU survey results on proposed use cases for 2nd Veterinary Big Data forum

Pharmacovigilance 2.A: Challenges

- Signal management processes
- Variability across entities
- Things to keep in mind

FDA U.S. FOOD & DRUG ADMINISTRATION

Signal Management Processes: Under Development

- defining “signal”
- identifying potential safety signals as early as possible in a product’s lifecycle
- validating the signals
- further assessing and characterizing the signals
- determining whether a new risk has been identified or a change appears to have emerged for a known risk
- determining what actions may be needed to mitigate the risk
- enacting risk mitigation measures
- monitoring the effectiveness of those measures

U.S. FOOD & DRUG ADMINISTRATION

Variability across MAHs

- Expert knowledge, technical capacities, technologies, and data availability can vary
- Variability in the degree to which organizations can implement PV tools may create a potentially imbalanced system
- quantity of data available is often a function of the market size and the regulations governing adverse event reporting in different jurisdictions (although in EU all MAHs can and are legally obliged to query the data warehouse (DWH) of the Union Pharmacovigilance database)

FDA U.S. FOOD & DRUG ADMINISTRATION

PV considerations across MAHs

- Nature of the database
  - Large and diverse products vs. subset of product classes
- Type of disproportionality analysis
  - All products and events across all species vs. restricted by species
- At what VeDDRA level should the analysis be performed?
  - Preferred Term vs. Low Level Term
- Should concomitantly administered products be included or excluded?
- Is statistical signal detection appropriate for products that do not receive many AEs?

Further PV considerations across MAHs

- What is the appropriate statistic and associated threshold?
  - Is it same for all species? All product classes?
- Should cases reported from research studies be included in disproportionality analyses?
- Should AERs generated through active surveillance of non-MAH social networking websites, where users can post comments, be included in disproportionality analyses?
- Should lack of effectiveness, medication error, or product defect cases be excluded from disproportionality analyses?

Comparison of signal detection outcomes

- Veterinary-specific databases are even more complex than those in human medicine due to the number of species and variation in stage of production and production type.
- No set guidelines or standards to follow when using data mining approaches for signal detection in veterinary medicine
- Signal detection and management process should be as transparent as possible

Antimicrobial Resistance 3.A

"To integrate antimicrobial use data with a variety of other data sources and develop data analytic methods"

Big Data Analytics for AMR

FDA maintains a suite of dashboards that integrate next generation sequencing data with sample metadata and other laboratory-generated information (e.g. MIC values).
These include:

- Animal Pathogen AMR Data collected by Vet-LIRN and USDA-NAHLN
- NARMS Now: Integrated Data
- Resistome Tracker
- NARMS Strain Explorer

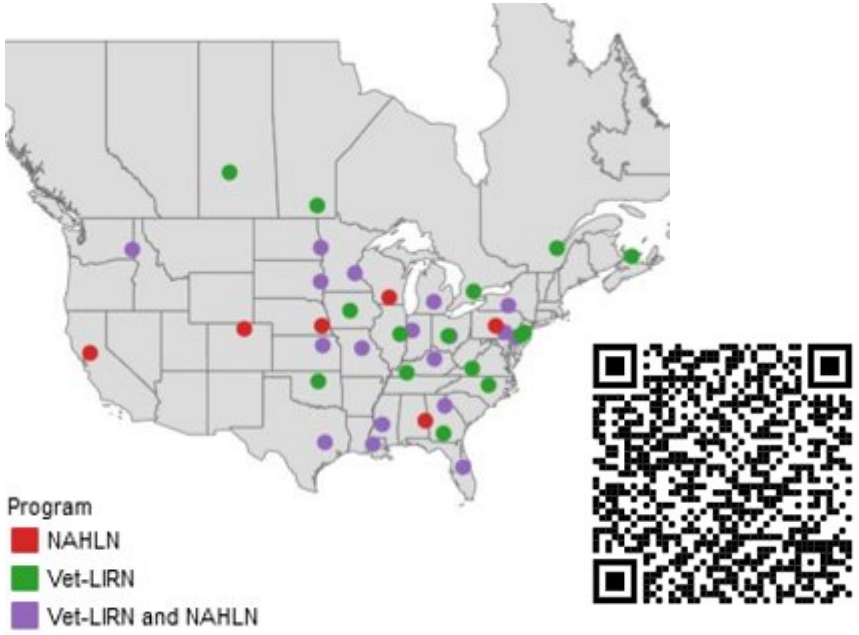
NARMS
National Antimicrobial Resistance Monitoring System

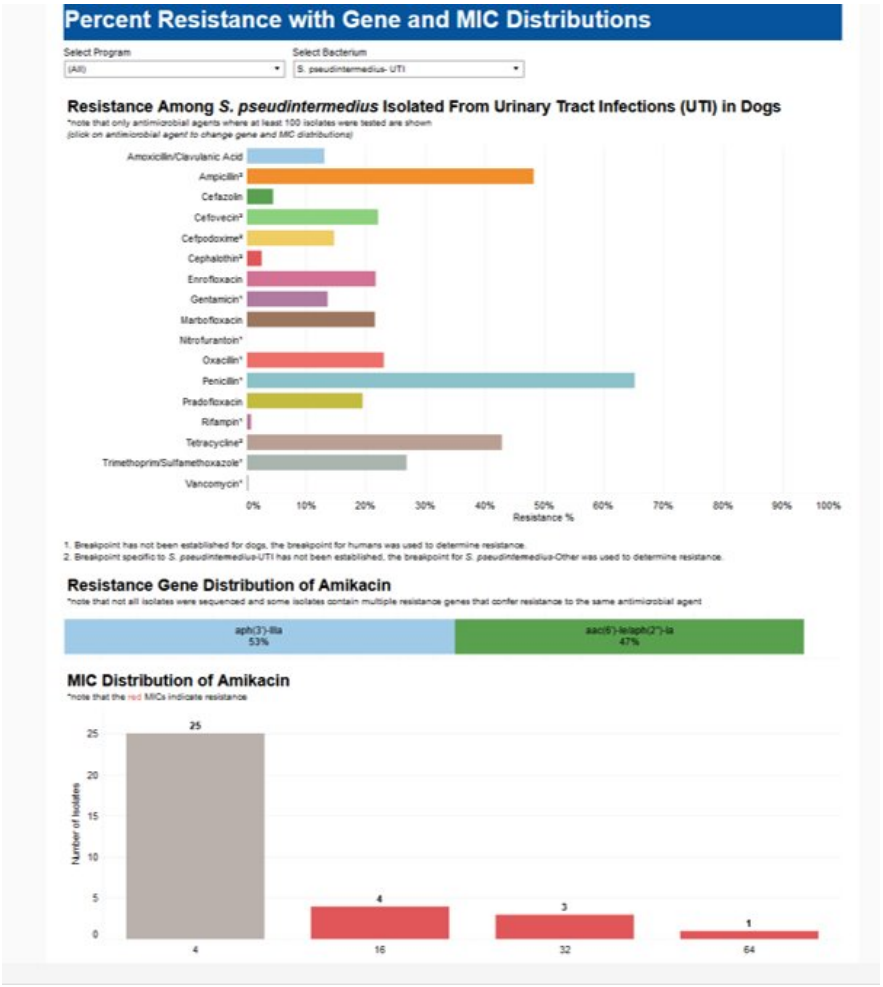
Vet-LIRN®

NAHLN
National Animal Health Laboratory Network

Vet-LIRN/NAHLN Integrated Animal Pathogen AMR Data

>40 Laboratories





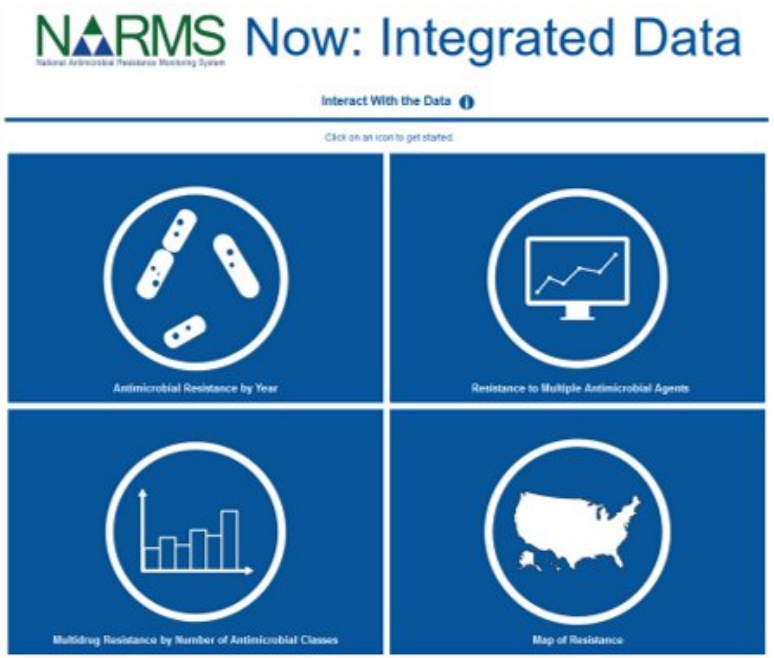
Users can view integrated AMR monitoring data from dogs, collected from FDA and USDA's networks. Dashboards include resistance mechanisms from genomics data, along with the percent resistance and MIC distributions

NARMS Now: Integrated Data

- Allows users to **explore trends in resistance** to specific antimicrobial agents using both real time genomic data and standard *in vitro* susceptibility testing methods

- Uses **NARMS data** in the NCBI Pathogen Detection data repository and AST data

- Updated weekly



RESISTOME TRACKER

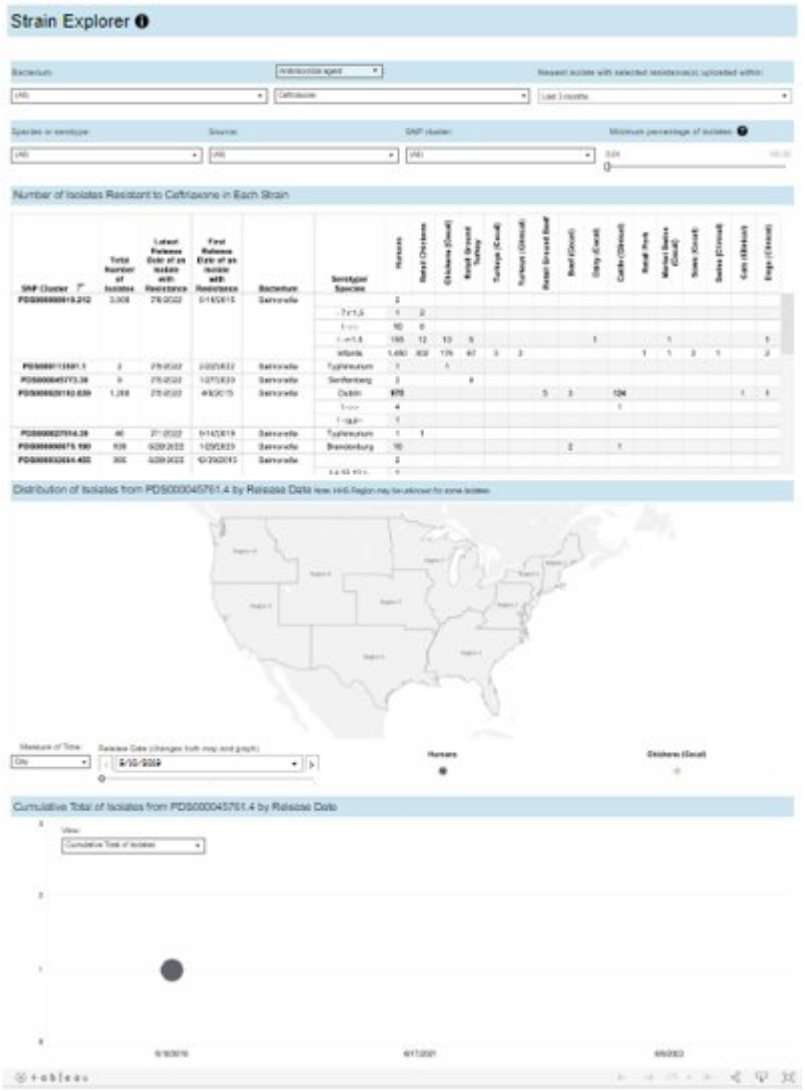
•Allows users to **track the appearance and spread of specific resistance genes** in nontyphoidal *Salmonella enterica*, *E. coli*, *Enterococcus*, *Campylobacter* spp. from different sources around the world

•Uses **all WGS data** in the NCBI Pathogen Detection data repository

•Updated weekly

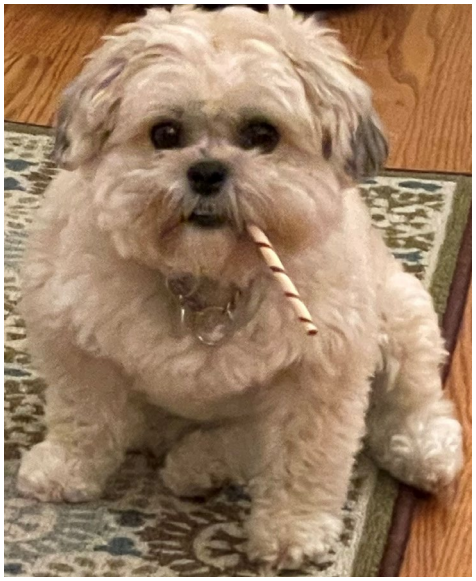
NARMS Strain Explorer

- Allows users to **track related NARMS isolates (SNP clusters) from different sources that confer resistance to one or more clinically important antimicrobial agents** (azithromycin, erythromycin, ciprofloxacin, ceftriaxone, meropenem and colistin, depending on the bacterium)
- Uses **NARMS data** in the NCBI Pathogen Detection data repository
- Updated weekly



Thank you for your attention.

Hesha.Duggirala@fda.hhs.gov




FDA
U.S. FOOD & DRUG
ADMINISTRATION