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Development and Implementation of a Surface Water Pilot Study Within the National Antimicrobial Resistance Monitoring System (NARMS)

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"Following the NARMS Review Subcommittee recommendations to incorporate the three major domains of the One Health model (humans, animals, environment), an important theme of this strategic plan is the expansion of testing to examine resistance in animal pathogens and the environment. For environmental monitoring, what constitutes the best sampling points will be refined over time. Surface waters as confluence points of ecosystems differentially affected by built environments is a starting point."

From the intro of the new NARMS Strategic Plan

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Outline

- Review background/rationale for NARMS Surface Water Pilot Project
- Status and process for developing the plan
- Next Steps

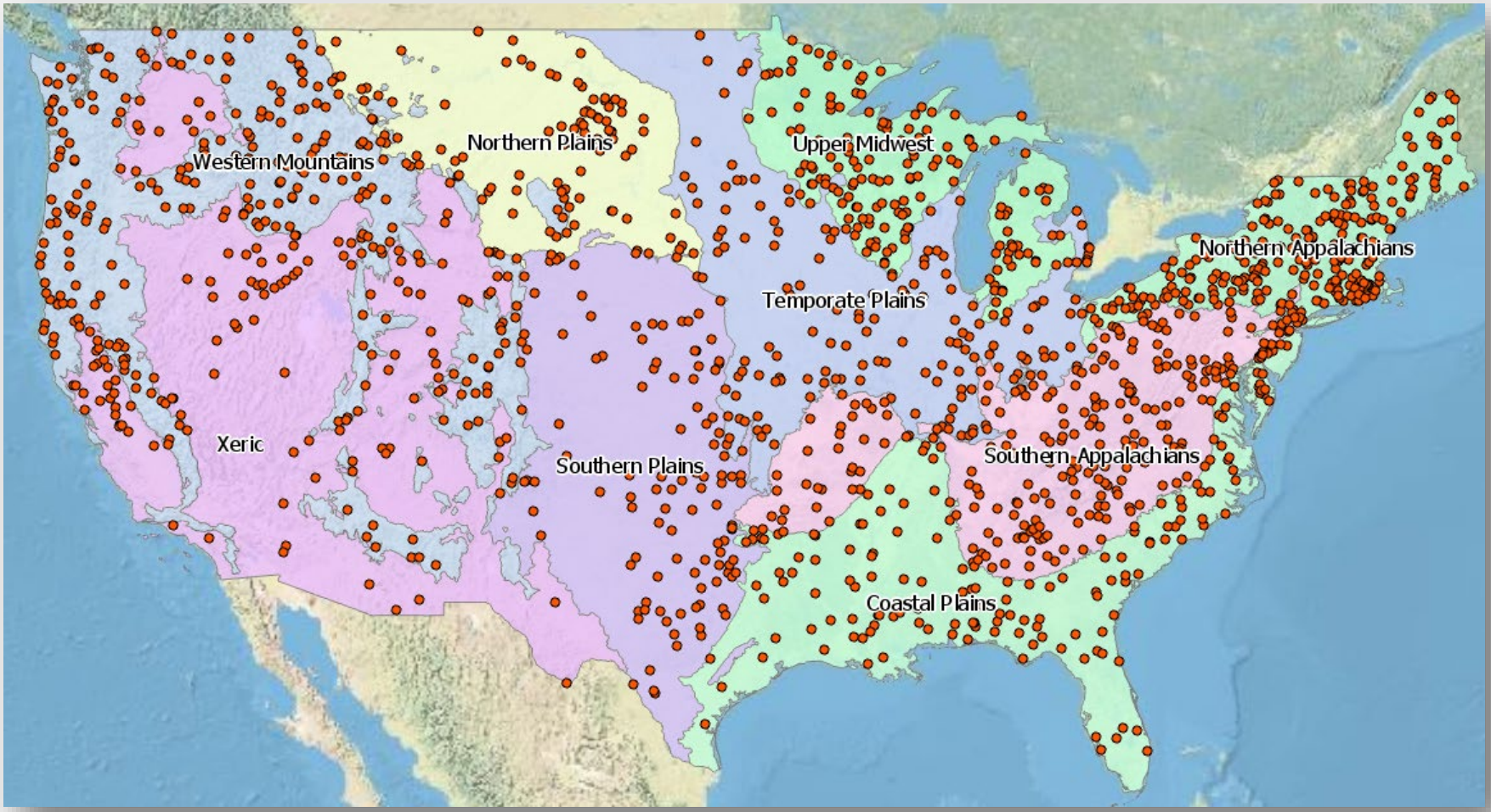
Initiatives for Addressing Antibiotic Resistance in the Environment*: Current Situation and Challenges*

- **One of the report out areas was on assessing Environmental Waters**
  - Geospatial distribution of resistant microbes in environmental waters needed to better understand risk
  - Focused studies to understand sources & selective pressures for amplification and transmission
  - Evaluate sampling strategies & testing methods to identify & standardize best practices

Group of international experts in the field of AMR drafted white paper and met to discuss at International forum in Vancouver April 2018

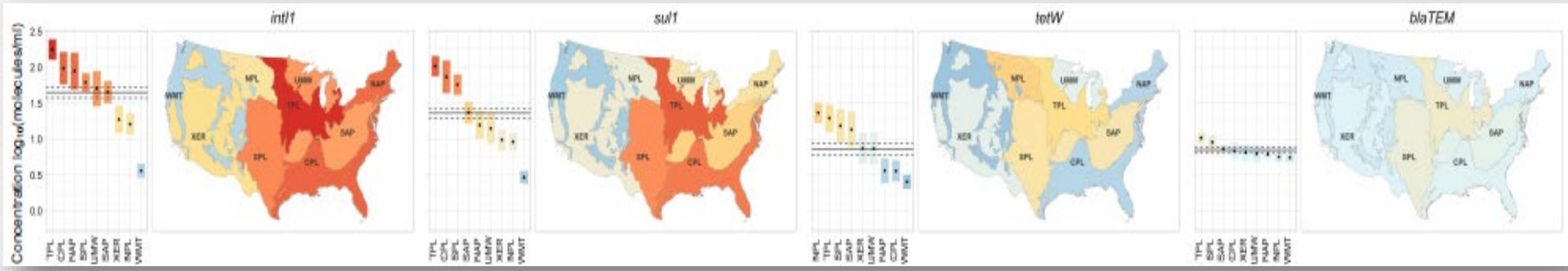
Sponsored by US CDC, UK Science & Innovation Network, and Wellcome Trust

Leveraging EPA Programs

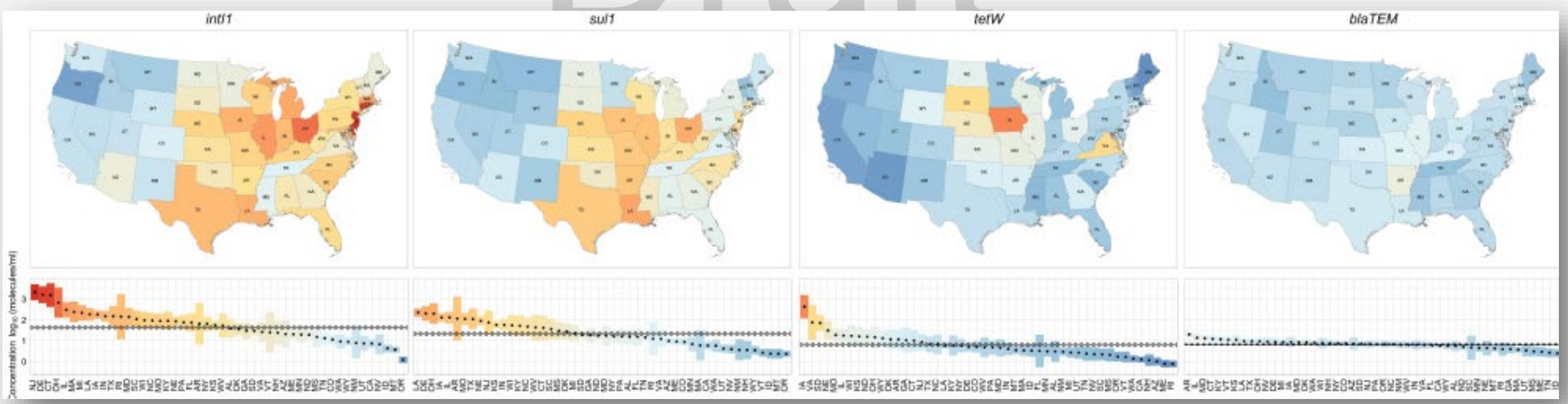


Map of National Rivers and Streams Assessment (ECO9 Regions Shown)

Geospatial Analysis of AMR Genes



Draft



Activities to Date

- IAA between FDA and EPA finalized for FY20, annual agreements planned for coming years

- Environmental Working Group with cross agency participation began meeting in May
  - Concurrence on project objectives
  - Developed a process for developing the project plan
    - Targeted work groups within 2 areas (design, analytical methods)

NARMS-SWAM Objectives

- A pilot environmental effort within a One Health focused NARMS

- Develop a national-scale, quantitative assessment of AMR within surface water:
  A. Standardized measure (and library of samples) to monitor trends as part of NARMS
  B. Input to models of AMR risks for various end uses of water (recreational, drinking, agricultural, water reuse).
  C. Help quantify drivers of occurrence and selective pressures for potential amplification
  D. Identify critical control points and assess current and new mitigation strategies

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A Hybrid Approach to Addressing the Different Objectives?

- Large scale, national surveys to define baseline and evaluate trends
  - Similar (or identical) design as NARS?
  - Goal of augmenting the 2023-2024 NRSA sampling to include expanded, standardized approaches for AMR analysis?
- More geographically focused, high frequency samples to address other objectives?

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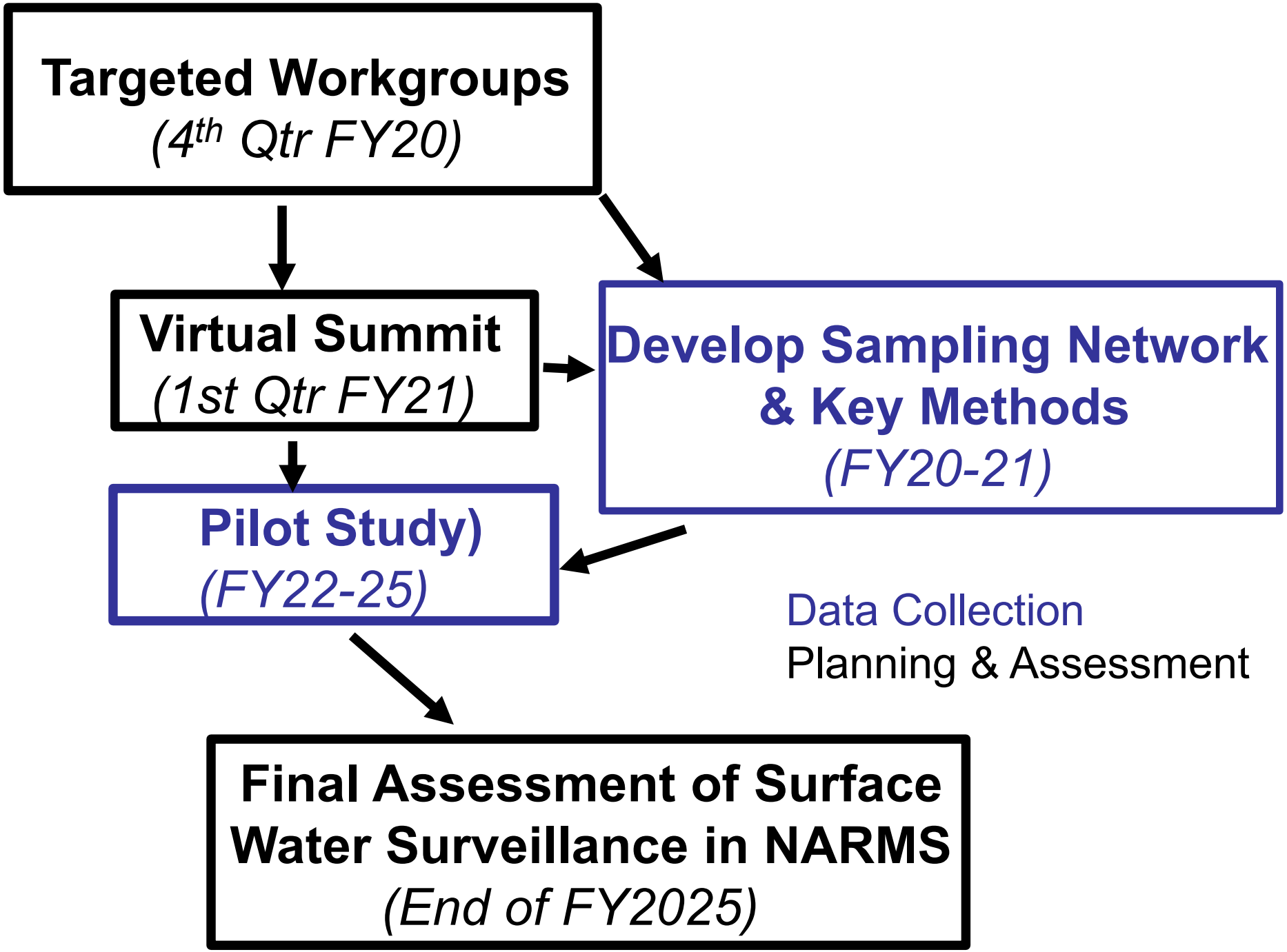
General Project Activities

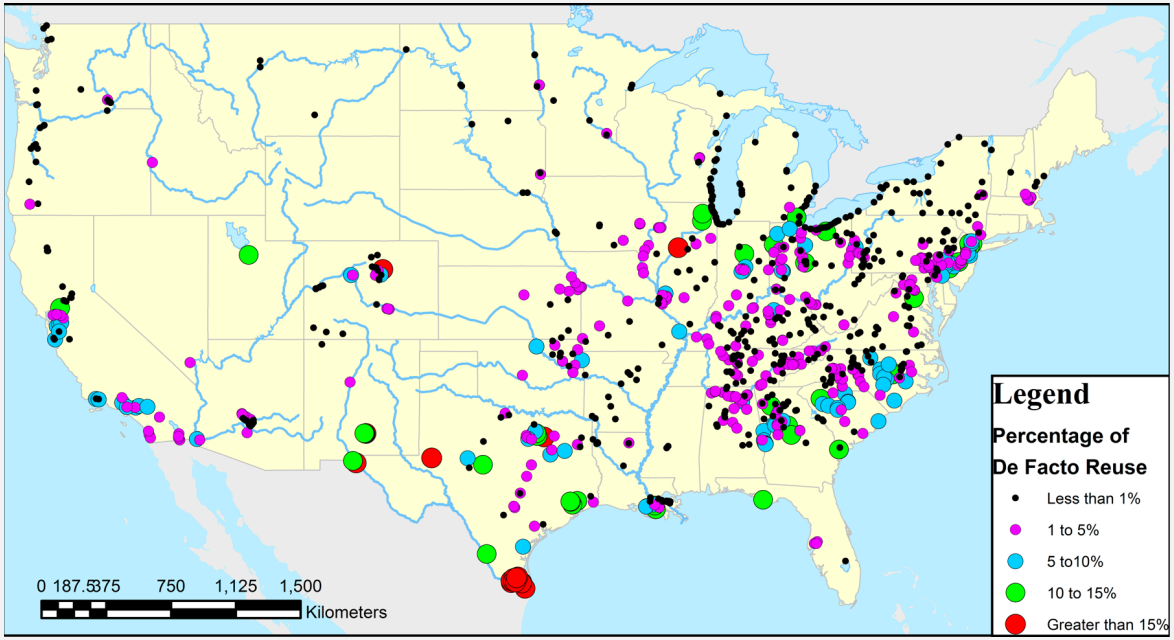
- FY20-21 Address key methodological issues and developing network
- FY22-25, Full pilot effort
- EPA has primary responsibility for collecting water samples, shipping filters to Cincinnati labs, extracting nucleic acids, culturing, targeted gene analysis
  - FDA/NARMS responsible for whole genome sequencing of isolates and metagenomic analysis of samples
- EPA, CDC, FDA, USDA conduct joint research studies to develop/evaluate methods and mine data for information about critical control points and effective mitigation strategies


Targeted Workgroups
(4th Qtr FY20)
Virtual Summit
(1st Qtr FY21)
Develop Sampling Network & Key Methods
(FY20-21)
Pilot Study)
(FY22-25)
Data Collection
Planning & Assessment
Final Assessment of Surface Water Surveillance in NARMS
(End of FY2025)

Targeted Working Groups

- **Design Area**
  - –Statistically valid study design(s) for
    - Quantitative, national-scale estimation of baseline AMR levels in surface water and as a function of both human and agricultural impacts
    - Addresses spatial and temporal intensity of sampling
  - –End Use of the Data
    - Integration with existing NARMS reporting structures
    - What insight does the environmental perspective provide? How is it linked to other components?
    - Use of data in development of risk models
  - –Development of appropriate metadata

Selecting Sites Based on Human Wastewater Impact

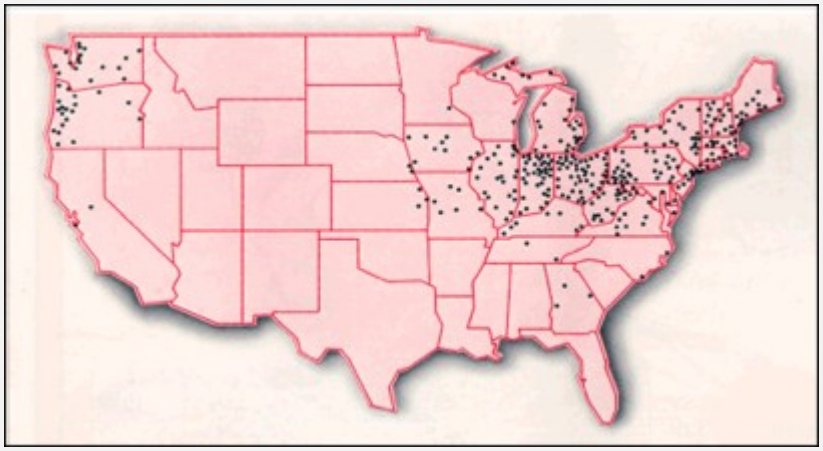


1210 of 1292 DWTP which use surface water and serve >10,000 people

WWTP discharges from 2008

Does not include combined sewer overflows (CSO), wet weather bypasses, or leakage

Rice J. and P. Westerhoff. 2015. Spatial and temporal variation in de facto Wastewater reuse in drinking water systems across the USA ES&T 49, 982



Combined sewers in US

Designing the Study: Analytical Targets

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- **Drivers**
  - Direct detection of resistant pathogens to build risk models & provide attribution/epidemiology
  - Quantifying concentration of targets is preferred to help build risk models
  - Link to existing data streams within NARMS to leverage resources and improve One Health data linkages
  - Standardization of methods (both for the pilot and as a model for other work)
- **Suggested approach**
  - Suite of culture based and molecular targets

There is a need for rigorous QA/QC in data collection, as well as agreement in the community regarding standardized methods and reporting. Until priority monitoring targets are agreed on, analysis of a suite of culture-based and molecular based indicators is logical

Pruden et al. 2018 *Environmental science and engineering framework for combating antimicrobial resistance*

Targeted Working Groups (cont'd)

- **Laboratory/Analytics Area**
  - Field Sampling Methods
    - Best approaches for collecting field samples
    - Emphasis on near term work both comparing methods & building sampling networks
  - Culturing
    - Define and prioritize targets for isolate based work
  - Targeted gene quantification
    - Define standardized set of targets
  - Metagenomics
    - Standardized approach including development of reference materials
  - Bioinformatics

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Working Group Charge

- Prepare an assessment of the targeted questions
  - What are the Key Drivers?
  - What is the consensus approach?
  - Are there key data gaps/questions to be resolved?
    - Suggested approach to addressing prior to FY20
- Report out to other working groups during virtual

Virtual Summit Charge

- November 16-17
- Review detailed recommendations from working groups
- Provide an integrated definition of the work, including where/what data will be collected and how it will be used, including both risk modeling and uses in the broader One Health surveillance program
- Define the specific goals of the pilot study plan, including prioritized list of data gaps/ questions to be addressed in the short term (i.e., FY21)

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Next Steps

- Review draft study plan with relevant stakeholders
- Work across agencies to implement

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Ancillary Slides

Working Group Membership

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NARMS Environmental Working Group

- Jay Garland, Scott Keely, Mark Bagley (EPA ORD)
- Amy Kirby, Dawn Sievert, Sue Gerber, Jason Folster, Andrew Huang, Beth Karp (CDC)
- Kim Cook, Lisa Durso (USDA-ARS) Kathy Bjork (USDA-APHIS)
- Daniel Tadesse, Heather Harbottle , Andrea Ottesen, Wesley Hunter (FDA Vet Center) Jie Zheng (FDA CFSAN)
- McDermott, FDA Vet Center (NARMS lead)

Design Area Sub-Groups

Statistical Design

- **Mark Bagley (EPA)**
- Heather Tate (FDA)
- Wesley Hunter (FDA)
- **Jim Wells (USDA)**
- Clinton Williams (USDA)
- Kim Cook (USDA)
- Kathe Bjork (USDA)
- Michael Jahne (EPA)
- Roy Martin (EPA)
- Scott Keely (EPA)
- Susan Gerber (CDC)
- Amy Kirby (CDC)
- Beth Karp (CDC)

End Use of Data

Interface with NARMS / Risk Modeling

- **Heather Tate (FDA)**
- Daniel Tadesse (FDA)
- Pat McDermott (FDA)
- Wesley Hunter (FDA)
- Heather Harbottle (FDA)
- Jonathan Frye (USDA)
- Clinton Williams (USDA)
- Kim Cook (USDA)
- Kathe Bjork (USDA)
- **Michael Jahne (EPA)**
- Alison Franklin (EPA)
- Susan Gerber (CDC)
- Amy Kirby (CDC)
- Beth Karp (CDC)

Metadata

- Heather Tate (FDA)
- **Christopher Grim (FDA)**
- Mark Ibekwe (USDA)
- Manan Sharma (USDA)
- Clinton Williams (USDA)
- Kim Cook (USDA)
- Michael Jahne (EPA)
- **Alison Franklin (EPA)**
- Susan Gerber (CDC)
- Amy Kirby (CDC)
- Beth Karp (CDC)

Laboratory/Analytical Sub-Groups

Field Sampling

Near Term Effort

- **Alison Franklin (EPA)**
- **Lisa Durso (USDA)**
- Daniel Tadesse (FDA)
- Andrea Ottesen (FDA)
- Pat McDermott (FDA)
- Jie Zheng (FDA)
- Jonathan Frye (USDA)
- Mark Ibekwe (USDA)
- Manan Sharma (USDA)
- Jim Wells (USDA)
- Clinton Williams (USDA)
- Kim Cook (USDA)
- Roy Martin (EPA)
- Jay Garland (EPA)
- Laura Boczek (EPA)
- Andrew Huang (CDC)
- Jason Folster (CDC)

Culturing

- Jie Zheng (FDA)
- Jon**athan Frye (USDA)**
- Mark Ibekwe (USDA)
- **Manan Sharma (USDA)**
- Jim Wells (USDA)
- Lisa Durso (USDA)
- Alison Franklin (EPA)
- Laura Boczek (EPA)
- Andrew Huang (CDC)
- Jason Folster (CDC)
- Amy Kirby (CDC)

Targeted Gene Analysis

- **Scott Keely (EPA)**
- Daniel Tadesse (FDA)
- Andrea Ottesen (FDA)
- **Mark Ibekwe (USDA**)
- Manan Sharma (USDA)
- Jim Wells (USDA)
- Lisa Durso (USDA)
- Alison Franklin (EPA)
- Andrew Huang (CDC)
- Jason Folster (CDC)

Laboratory/Analytical Sub-Groups

Metagenomics

- **Daniel Tadesse (FDA)**
- Andrea Ottesen (FDA)
- Christopher Grim (FDA)
- Padmini Ramachandran (FDA)
- Mark Ibekwe (USDA)
- Manan Sharma (USDA)
- Kim Cook (USDA)
- Lisa Durso (USDA)
- Scott Keely (EPA)
- Andrew Huang (CDC)
- Jason Folster (CDC)

Bioinformatics

- Daniel Tadesse (FDA)
- Andrea Ottesen (FDA)
- Ruth Timme (FDA)
- Mark Ibekwe (USDA)
- Lisa Durso (USDA)
- Scott Keely (EPA)
- Andrew Huang (CDC)
- Jason Folster (CDC)