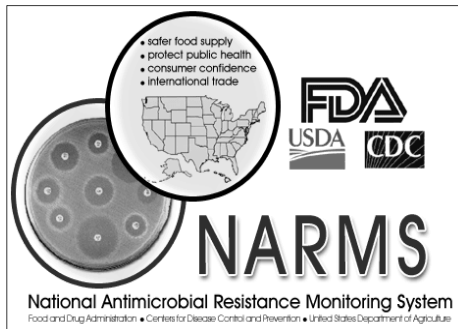


Response to the FDA Science Board Subcommittee on NARMS



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Director
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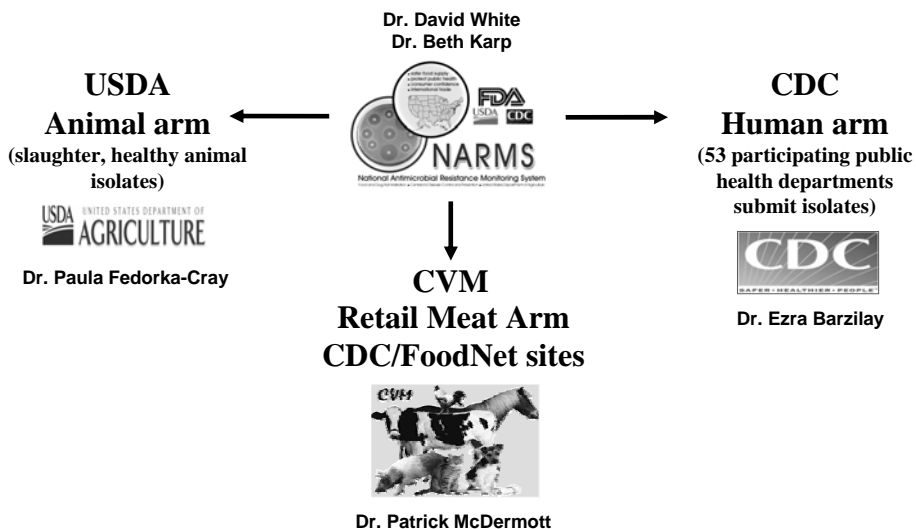
NARMS History

- **NARMS became operational in 1996**
 - *Salmonella* of animal & human origin was initial organism selected
- **Sources & types of isolates have expanded over time**
 - *Campylobacter* was added in 1998
 - *Enterococcus* & *E. coli* in 2000
 - Retail arm in 2002
- **Each year, samples are collected from numerous origins & tested to determine if there have been changes in the susceptibility/resistance of certain enteric bacteria to selected antimicrobial drugs**
- **The antimicrobial drugs tested annually are selected based on their importance in human & veterinary medicine**

Goals of NARMS Program

- Identify changes in antimicrobial resistance patterns in zoonotic foodborne bacterial pathogens & select commensal organisms
- Respond to unusual or high levels of bacterial drug resistance in humans, animals & retail meats in order to contain or mitigate resistance dissemination
- Assist the FDA in decision making on approving safe & effective drugs for humans & animals, as well as promote prudent & judicious use of antimicrobial drugs
- Design follow-up epidemiology & research studies to better understand the emergence & transfer of antimicrobial resistance

NARMS Components



Subcommittee Review of NARMS

- The FDA Science Board Advisory Committee established a subcommittee to evaluate the NARMS program & address 4 questions relevant to the continued success of the program:
 - Sampling strategies
 - Research studies
 - International activities
 - Data harmonization & reporting
- Subcommittee met on April 10-11, 2007 & heard presentations from NARMS partners & stakeholders
- Subcommittee report was presented on June 14 by Dr. Lonnie King, Chair

General Comments of Subcommittee

- NARMS has evolved into a mission-critical tool for FDA
- Commitment & dedication of NARMS team is laudable
- Outstanding progress & acceptance over last decade
- Suggest visioning, strategic, & business planning processes be adopted
- Suggest the program should evolve & become more predictive, responsive, & expansive
 - Underappreciated benefits for meeting needs of veterinary medicine & animal health
 - Need to keep the focus on the public health impact
- Endorse development of a 10-year plan with wide public involvement

NARMS Strategic Planning

- Strategic planning meeting with FDA, CDC, & USDA held in Atlanta on September 17-18, 2007
 - Discussed the recommendations in the report
 - Visioning/strategic planning processes initiated
 - Explored both short- & long-term goals
- Discussions have continued
 - Monthly interagency teleconferences
 - E-mails, other teleconferences
- Next NARMS strategic planning meeting is scheduled for March, following ICEID meeting

Sampling Strategies

Are there inherent biases in the sampling strategies employed in NARMS? If so, how can they be improved to ensure that the data and our interpretations are scientifically sound given current resources?

Human Sampling Strategies: Subcommittee Comments

- Intrastate/interstate variability in number & source of isolates submitted by clinical labs
- Variability in physician diagnostic (culture) practices
- National random sample of clinical isolates would be ideal, but may not be feasible
- Options within current sampling structure:
 - Stratify data when feasible
 - Periodic active sampling of clinical labs
- Encourage monitoring of commensals from healthy humans

Human Sampling Strategies: Program Response (1)

- Isolates in NARMS represent a random sample submitted to state laboratories
 - Random sampling of all clinical isolates is not feasible
 - Resources are not currently available for periodic active sampling of clinical labs
- Sampling in all states is frequency-based
- Continue to validate sampling scheme compliance & conduct data comparisons (e.g., NARMS vs. PHLIS)

Human Sampling Strategies: Program Response (2)

- Resources currently not available for targeted studies of physician diagnostic (culture) practices
 - Rely on other data sources
- NARMS data is not stratified in annual reports
 - Large number of sites
 - Small sample size for some sites
 - Lack of detailed demographic data at some sites
 - Article in development describing national distribution of clinically important MDR *Salmonella* isolates
- If more resources become available:
 - Expand *Campylobacter* geographic catchment area
 - Expand testing of commensal organisms from non-diarrheic humans

Retail Meat Sampling Strategies: Subcommittee Comments

- Extremely important data
- Samples are from a limited number of areas & a small number of products
- Lack of a national sampling strategy limits broader interpretation
 - May be more useful to adjust sampling strategy to answer specific, hypothesis-driven questions

Retail Meat Surveillance Strategies: Program Response (1)

- Agree that retail meat surveillance is very important
- Provides data on:
 - Prevalence of enteric bacteria in retail meats
 - Prevalence of resistance
- Data are used to:
 - Support safety evaluation of new animal drugs—GFI #152 (pre-approval)
 - Monitor resistance development (post-approval)
- Provides source of retail meat isolates
 - Can compare to human isolates to improve our understanding of the contribution of retail meats to enteric infections in humans

Retail Meat Surveillance Strategies: Program Response (2)

- Sampling is limited by availability of resources & personnel
 - Pennsylvania joined the program in July 2007
 - Maryland is rejoining the program in January 2008
 - May reduce testing of ground beef & pork chops due to relatively low yield of *Campylobacter* & *Salmonella*
- Pilot studies
 - Comparing different broiler meats (with & without skin & bone)
 - Other pathogens: *Clostridium difficile*, MRSA
 - Turkey parts
 - Seafood

Animal Sampling Strategies: Subcommittee Comments

- Samples from PR/HACCP monitoring are biased because processing plants are not randomly selected
 - May be more useful to adjust sampling strategy to help answer specific, hypothesis-driven questions
- Clinical diagnostic laboratory data are especially biased—limit to use as an early warning system for emerging resistance
- NAHMS & other on-farm data has potential utility but is limited because it is not representative of a national sample
 - Focus on answering specific, hypothesis-driven research questions where risk factors for resistance are the focus
- Encourage further pilots like Collaboration in Animal Health & Food Safety Epidemiology program (CAHFSE)

Animal Sampling Strategies: Program Response

- Samples from FSIS PR/HACCP provide for ongoing monitoring
 - In June 2006, FSIS moved to risk-based inspections
 - Focus on establishments with the most samples positive for *Salmonella* & the greatest number of samples with serotypes most frequently associated with human salmonellosis
- Periodic baseline studies provide ‘snapshots’ of national prevalence estimates
 - Raw Ground Beef Components Baseline Study: completed in 2007
 - Young Chicken (Broiler) Baseline Study: in progress
 - Young Turkey & Market Hog Baseline Studies: anticipated in 2008
- Will compare baseline data with PR/HACCP & retail meat data
- Ongoing discussions to explore alternate sampling strategies
 - Diagnostic vs. NAHMS vs. CAHFSE

Research Studies

Are there epidemiological and/or microbiological research studies that would better serve the goals of NARMS and the regulatory work of FDA?

Research Studies: Subcommittee Comments

- An active research program is critically important to the continued success of NARMS
- Suggest further expansion of research portfolio in:
 - Laboratory methods
 - Platform development
 - Pilot projects
- Expand hypothesis-driven research with an emphasis on assessing human risks
- Encourage more collaborations & partnerships
- Gain understanding of flow of resistance genes/bacteria across the farm-to-fork continuum

Research Studies: Program Response (1)

- NARMS is actively involved in research in the areas described:
 - Laboratory methods:
 - Standardize antimicrobial susceptibility testing (*e.g.*, *Campylobacter*)
 - Rapid isolate testing (*e.g.*, PCR, microarrays, molecular serotyping)
 - Platform development
 - Linking NARMS susceptibility data with CDC's PulseNet database
 - Sequencing 17 *Salmonella* genomes, including resistant strains, in partnership with the J. Craig Venter Institute
 - Ongoing studies to better understand cross-resistance, linked resistance & the transfer of resistance determinants in both pathogenic & commensal bacteria
 - Pilot projects to examine emergent issues in foodborne disease
 - MRSA, *C. difficile*, different commodities
 - *Enterococcus* strains in humans & local foods & farm animals
 - Targeted resistance profiling to help answer regulatory questions

Research Studies: Program Response (2)

- NARMS research projects are driven both by hypothesis testing & the need for new methods
 - Continued studies on burden of illness, risk factors, clinical outcomes for predominant or significant strain types
 - Examination of historical strain collections to document the emergence of resistance relative to new antimicrobial uses
 - Develop MLST strain characterization method to compare strains from humans & food
- Continue & enhance collaboration with NARMS partners, academia, & stakeholders
 - NARMS partners collaborate in comparing data & harmonizing methods
 - NARMS partners have numerous collaborations with academia examining various ecological aspects of resistant foodborne pathogens

International Activities

Are the current NARMS international activities adequate to address the worldwide spread of antimicrobial-resistant food-borne bacteria?

International Activities: Subcommittee Comments

- International activities are critical because resistance is a global problem
- Strongly endorse continuation & expansion of international activities, including training
- Need to improve coordination of NARMS components for international purposes & serve as a global model
- Continuing need to adopt new technologies & ensure quality data & timely reporting

International Activities: Program Response

- NARMS is committed to supporting international activities in the area of foodborne infections, as resources permit
- Continue to strengthen existing partnerships
 - WHO Global Salm-Surv support with trainers & materials
 - China a recent focus of training & support
 - Collaborations with ResistVet & CIPARS continue
- Enhance network development
 - INISAR (International Network of Integrated Surveillance for Antimicrobial Resistance in Enteric Bacteria) being developed as a forum for communication & harmonization

Data Harmonization and Reporting

Are our current plans for data harmonization and reporting appropriate? If not, what are the top priorities for advancing harmonized reporting?

Data Harmonization: Subcommittee Comments

- Critical needs:
 - Real-time, integrated database for all NARMS components
 - Database should be a dynamic, searchable tool
 - Timely reports
- Suggest data be more accessible to stakeholders

Data Harmonization: Program Response (1)

- We agree reports need to be more timely
- We are working to strengthen data reporting & harmonization
- Accomplishments:
 - Reports are becoming more timely
 - NARMS Coordinator position re-established this Summer
 - Implemented NARMS retail meat database application in CVM's Corporate Database Portal
 - Established NARMS IT Working Group
- Challenges:
 - Databases are currently completely separate
 - Will require significant resources & coordination to develop a combined data repository
 - Many technical issues to be addressed

Data Harmonization: Program Response (2)

- Short-term plan
 - Explore use of an interactive data visualization tool (Xcelsius) to supplement NARMS Executive Reports
- Long-term plan
 - Develop a “data cube” for each NARMS component
 - CDC has recently developed one for NARMS human data
 - Aggregate selected data from each agency into a centralized data repository
 - Develop a data cube for aggregate data
 - Contingent upon additional resources

NARMS Retail Meat Database Application in CVM’s Corporate Database Portal

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DP

Make your selection using:

- Sample/Isolate
- Isolate Query
- Resistance Gene
- Reporting
 - Percent positive samples
 - Number of bacterial species/serotype by year
 - Number of bacterial species/serotype by year/food
 - Antimicrobial susceptibility by bacterial genus
 - Antimicrobial susceptibility bacterial genus/food
 - Percent resistance by bacterial species
 - Multidrug resistance phenotypes
- NARMS User Guide

Database

Database

PORTAL

Center for Veterinary Medicine

Center for Veterinary Medicine

it Completed

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DP

Make your selection using the tool bar

Database

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Type a question for help

Courier

A1 PERCENT POSITIVE SAMPLES BY BACTERIAL GENUS AND FOOD TYPE

PERCENT POSITIVE SAMPLES BY BACTERIAL GENUS AND FOOD TYPE									
Genus Name	Meat Type	Year 2002			Year 2003			%Pos	
		# Sample	# Isolate	%Positive	# Sample	# Isolate	%Pos		
Campylobacter	Chicken Breast	616	288	46.80%	897	469			
	Ground Beef	642	0	0.00%	880	1			
	Ground Turkey	642	4	0.60%	857	5			
	Pork Chop	613	5	0.80%	899	4			
	Total		2513	297	11.80%	3533	479		
Enterococcus	Chicken Breast	390	381	97.70%	477	466			
	Ground Beef	399	383	96.00%	470	432			
	Ground Turkey	395	387	98.00%	447	418			
	Pork Chop	390	369	94.60%	479	426			
	Total		1574	1520	96.60%	1873	1742		
Escherichia	Chicken Breast	390	282	72.30%	477	396			

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Interactive Visualization of NARMS Data Using Crystal Xcelsius™

Salmonella (non-Typhi)
Percent Resistance Trends by Source

NARMS
CDC FDA USDA

Select Antimicrobial

Antimicrobials

- Aminoglycosides
- Aminopenicillins
- Beta-Lactam/Beta-Lactam Inhib
- Cephalosporins
- Cephamycins
- Folate Pathway Inhibitors
- Phenicol
- Quinolones
- Tetracyclines

Select Source(s)

Sources

Human

Retail Meats

- Chicken Breasts
- Ground Turkey
- Ground Beef
- Pork Chops

Animal Foods

- Chicken
- Turkey
- Cattle
- Swine

Number of Isolates Tested

	1996	1997	1998	1999	2000	2001	2002	2003
Humans	1324	1301	1460	1498	1377	1419	2008	1865
Chicken Breasts							60	83
Ground Turkey							74	114
Ground Beef							9	10
Pork Chops							10	5
Chicken		214	561	1438	1173	1307	1500	1158
Turkey		107	240	713	518	550	244	262
Cattle		29	284	1610	1388	893	1008	670
Swine		111	793	876	451	418	379	211

NARMS Summary (1)

- NARMS has evolved & matured since its inception in 1996 & has been characterized by continuous learning & improvement
- FDA Science Board review provided constructive recommendations with regard to key elements & future directions of the NARMS program
 - CVM has begun implementing several of these recommendations with partners, including strategic planning
- Sampling strategies continue to improve
 - Exploring long-term sampling strategies
 - Data needs to withstand scrutiny from both a scientific & regulatory perspective
 - Develop pilot projects where appropriate

NARMS Summary (2)

- NARMS research portfolio being further developed & expanded
 - Emphasis on hypothesis-driven & more collaborative research
 - Special emphasis on understanding the ecology of antimicrobial resistance across the farm-to-fork continuum & the resultant human health impact
- Working to strengthen data reporting & harmonization
 - Improving timeliness of annual reports
 - Looking at antimicrobial susceptibility trends among bacteria under surveillance by source, year, etc.
 - Ultimate goal is a central data repository that would permit generating both participant-specific & collective reports & analyses in a timely manner
- We will continue to update the Science Board on implementing both short- & long-term subcommittee recommendations