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USA ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

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NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

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https://www.cdc.gov/drugresistance/pdf/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf



Development

The *National Action Plan* was developed in response to Executive Order 13676: Combating Antibiotic- Resistant Bacteria, which was issued by President Barack Obama in 2014. It called for a Task Force to create a five-year action plan that lays out steps and milestones for achieving the *Strategy's* goals and objectives.

The Task Force, was co-chaired by the Secretaries of Defense, Agriculture, and Health and Human Services.



Scope of the *National Action Plan*:

- “Antibiotic resistance” results from mutations or acquisition of new genes in bacteria that reduce or eliminate the effectiveness of antibiotics.
- “Antimicrobial resistance” is a broader term that encompasses resistance to drugs to treat infections caused by many different types of pathogens, including bacteria, viruses (e g , influenza and the human immunodeficiency virus (HIV)), parasites (e g , the parasitic protozoan that causes malaria), and fungi (e g , *Candida spp.*). While all of these pathogens are dangerous to human health, the *National Action Plan* focuses on resistance in bacteria that present an urgent or serious threat to public health.



The goals of the *National Action Plan* include:

- Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections
- Strengthen National One-Health Surveillance Efforts to Combat Resistance
- Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
- Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines
- Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control, and Antibiotic Research and Development



Milestones

- For each objective of each goal there are specific milestones (1 year, 3 year and 5 year) and federal agency responsibilities (some will be mentioned in this presentation but too many to cover)



Goal 1-Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

Objectives

- Implement public health programs and reporting policies that advance antibiotic-resistance prevention and foster antibiotic stewardship in healthcare settings and the community
- Eliminate the use of medically-important antibiotics for growth promotion in food producing animals and bring other agricultural uses of antibiotics, for treatment, control, and prevention of disease, under veterinary oversight
- Identify and implement measures to foster stewardship of antibiotics in animals



Accomplishments- FDA

- Regulation:
- FDA Guidance for Industry (GFI) #209—*The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*—is intended to limit medically important antimicrobial drugs to uses in animals that (1) are considered necessary for assuring animal health, and (2) include veterinary oversight or consultation
- FDA Guidance for Industry (GFI) #213—*New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*—calls for:
 - Revision of the FDA-approved use conditions on medically important antibiotics to remove growth promotion. **Done- never used for growth promotion in aquaculture**
 - Phased in veterinary oversight of all therapeutic uses of medically important antibiotics in feed or water. **In 2017 all antibiotic use in feed requires VFD. Aquaculture- Florfenicol (Aquaflor), oxytetracycline (Terramycin), sulfadimethoxine-ormetoprim (Romet)**
- FDA- seafood inspection- monitors banned substances in imported seafood- spot checking



Activities/Accomplishments- USDA

TRAINING

- APHIS-The National Veterinary Accreditation Program requires supplemental training every 3 years for renewal of accreditation. **Judicious use online training module for veterinarians has been added.**
- USDA/Ag Universities-Agricultural Cooperative Extension Service (ACES)- Local training of producers on proper use of Antimicrobials and alternative management strategies. Also training of consumers of food safety.



Goal 2-Strengthen National One-Health Surveillance Efforts to Combat Resistance

Objectives

- Create a regional public health laboratory network to strengthen national capacity to detect resistant bacterial strains and a specimen repository to facilitate development and evaluation of diagnostic tests and treatments
- Expand and strengthen the national infrastructure for public health surveillance and data reporting, and provide incentives for timely reporting of antibiotic-resistance and antibiotic use in all healthcare settings
- Develop, expand, and maintain capacity in State and Federal veterinary and food safety laboratories to conduct antibiotic susceptibility testing and characterize select zoonotic and animal pathogens
- Enhance monitoring of antibiotic-resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain for food animals and retail meat



Milestones

USDA and FDA -Accelerate and standardize antibiotic susceptibility testing and bacterial characterization for select zoonotic and animal health pathogens

- USDA and FDA will develop standardized protocols for assessing proficiency in susceptibility testing (year 1). Ten to twenty NAHLN and/or Vet-LIRN member laboratories will actively conduct antibiotic susceptibility testing using standardized methodologies (year 5)



Activities/Accomplishments- USDA

- U.S. National Residue Program, USDA's Food Safety and Inspection Service (FSIS)- samples meat and egg products for antibiotic residues as well as other drugs or chemicals, and FDA takes enforcement actions on FSIS-determined violations. **Catfish- now in inspection program- more intense than FDA seafood inspection.**
 - FSIS also monitors AMR at slaughter and verifies that establishments have food safety systems in place to minimize the level of pathogens that reach consumers. This is part of the National Antibiotic Resistance Monitoring System (NARMS)
- APHIS monitoring and surveillance to characterize health and management of livestock. The OIE competent authority. It maintains a network of approved laboratories (National Animal Health Laboratory Network-NAHLN) with defined diagnostic protocols that are evaluated by the national veterinary reference laboratory (NVSL). Surveillance is done by the National Animal Health Monitoring System (NAHMS), which includes sampling and producer surveys to evaluate management practices.



GOAL 3: Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Objectives

- Develop and validate new diagnostics—including tests that rapidly distinguish between viral and bacterial pathogens and tests that detect antibiotic-resistance—that can be implemented easily in a wide range of settings
- Expand availability and use of diagnostics to improve treatment of antibiotic-resistant infections, enhance infection control, and facilitate outbreak detection and response in healthcare and community settings



GOAL 4: Accelerate Research to Develop New Antibiotics, Other Therapeutics, Vaccines, and Diagnostics

Objectives

- Enhance understanding of environmental factors that facilitate the development of antibiotic-resistance and the spread of resistance genes
- Increase understanding the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease
- Develop new therapeutics and vaccines, first-in-class drugs, and new combination therapies for treatment of bacterial infections
- Develop non-traditional therapeutics and innovative strategies to minimize outbreaks caused by resistant bacteria
- Expand efforts to support the development of promising antibacterial drug candidates



Activities in Aquaculture

- USDA-ARS- research to reduce dependence on antibiotics
 - Genetic selection for disease resistance
 - Development of more effective vaccines for bacterial pathogens
 - Facilitating the use of Autogenous vaccines- efficacy testing
 - MDR isolate whole genome sequencing and R-plasmid sequencing, evaluating r-plasmid transfer between fish pathogens and mammalian pathogens. Characterizing the distribution of R-plasmids in aquaculture facilities- Research allows molecular tracing the development and dissemination of resistance.
 - Studies show *Y. ruckeri* R-plasmids are self transmissible and related to *Y. pestis*, *Salmonella* and *E. coli* MDR- plasmids (Welch et al 2007 PLOS ONE 3:309e)
 - Related plasmid from *E. ictaluri* was self-transmissible, conferring resistance to FFC, chloramphenicol, tetracycline, streptomycin, ampicillin, amoxicillin-clavulanic acid, ceftiofur, and cefoxitin, as well as decreased susceptibility to trimethoprim-sulfamethoxazole and ceftriaxone. (Welch et al 2009, Antimicrobial agents and chemotherapy 53: 845)
- USDA-NIFA- grants for research- Animal health, Special aquaculture grants, Small business Grants- Vaccines, management



GOAL 5: Improve international collaboration and capacities for prevention, surveillance and antibiotic research and development

overview

- The US will engage in international action with foreign ministries of health and agriculture, WHO, FAO, OIE, and other domestic and international stakeholders to strengthen national and international capacities to detect, monitor, analyze, and report antibiotic resistance, provide resources and incentives to spur the development of therapeutics and diagnostics for use in humans and animals, and strengthen regional networks and global partnerships that help prevent and control the emergence and spread of resistance.



GOAL 5: Improve international collaboration and capacities for prevention, surveillance and antibiotic research and development

Objectives

Surveillance

- Promote laboratory capability to identify at least 3 of the 7 WHO priority antimicrobial resistant (AMR) pathogens* using standardized, reliable detection assays.
- Collaborate with WHO, OIE, and other international efforts focused on the development of integrated, laboratory based surveillance to detect and monitor antibiotic-resistance in relevant animal and human foodborne pathogens.
- Develop a mechanism for international communication of critical events that may signify new resistance trends with global public and animal health implications.
- Promote the generation and dissemination of information needed to effectively address antibiotic-resistance.

*WHO priority AMR pathogens -a subset of the pathogens identified as urgent and serious threats:

- *Escherichia coli*: resistance to 3rd generation cephalosporins and to fluoroquinolones
- *Klebsiella pneumoniae*: resistance to 3rd generation cephalosporins and to carbapenems
- *Staphylococcus aureus*: methicillin resistance, or MRSA
- *Streptococcus pneumoniae*: resistance (non-susceptibility) to penicillin
- *Non-typhoidal Salmonella (NTS)*: resistance to fluoroquinolones
- *Shigella species*: resistance to fluoroquinolones
- *Neisseria gonorrhoeae*: reduced susceptibility to 3rd generation cephalosporins



GOAL 5: Improve international collaboration and capacities for prevention, surveillance and antibiotic research and development (Cont.)

Objectives

Research and development

Establish and promote international collaboration and partnerships to incentivize development of new therapeutics to counter antibiotic-resistance including new, next- generation, and other alternatives to antibiotics, vaccines, and affordable, rapidly deployable, point-of-need diagnostics



GOAL 5: Improve international collaboration and capacities for prevention, surveillance and antibiotic research and development (Cont.)

Objectives

Prevention and Control

- Support countries to develop and implement national plans to combat antibiotic-resistance and strategies to enhance antimicrobial stewardship
- Partner with other nations to promote quality, safety, and efficacy of antibiotics and strengthen their pharmaceutical supply chains
- Coordinate regulatory approaches by collaborating with international organizations such as FAO and OIE to harmonize international data submission requirements and risk assessment



Milestones

- U S will work with WHO, FAO, OIE, and other international partners to accelerate investment in research to develop point-of-care diagnostics, vaccines, and drugs to combat resistant bacteria, as well as to investigate the microbiomes of food animals For example, U S agencies and partners will work with TATFAR partners to advance collaborations with EU nations to facilitate research on tools to slow the emergence and spread of antimicrobial resistance. U S agencies will also explore collaborations with the New Drugs 4 Bad Bugs (ND4BB) programs of the Innovative Medicines Initiative
- FDA and USDA will contribute to and participate in global or regional cooperation with international organizations, including AGISAR, VICH, IICAB, and IMDRF, regarding development of vaccines, antibacterial drugs, and diagnostic tests for use in agriculture, and regarding risk assessments of the use of medically-important antibiotics in agriculture

Within three years:

- U S agencies and partners will establish or expand additional international partnerships to advance research to reduce antibacterial resistance through the development of point-of-care diagnostics, vaccines, and drugs
- USDA will establish or expand five collaborative international partnerships to facilitate research regarding development of alternatives to antibiotics, as well as vaccines and new antimicrobial drugs that are less likely to develop resistance
- U S agencies, led by USAID, will support country systems to enhance access to and appropriate use of quality-assured, safe, effective essential antibiotics through improved medicines, regulatory capacity and quality assurance systems, modern procurement practices, reliable and secure supply chains, and equitable pharmaceutical services in at least four LMICs



Future

- Current funding structure of agencies are in flux but AMR threats are recognized and goals remain a priority.
- Science demonstrates that one health is real (molecular evidence indicates widespread sharing of MDR-plasmids and antibiotic use of one drug can maintain these plasmids in the environment).
- FDA and USDA have implemented important regulatory changes to US aquaculture. Surveillance data will help use understand the impacts of these changes.



Resources

- USA NAP-
https://www.cdc.gov/drugresistance/pdf/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf
- USDA AMR plan (<https://www.usda.gov/sites/default/files/documents/usda-antimicrobial-resistance-action-plan.pdf>) developed as a result of a USDA workshop in 2012 (<https://www.fsis.usda.gov/wps/wcm/connect/9ddc0b9c-af04-4ed4-b959-b7799ddbfe11/USDA-Antibiotic-Resistance-Workshop-Summary.pdf?MOD=AJPERES>)
- FDA actions resource page-
<https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/#SalesData>

