Inventory of Projects

Progress Report: Implementation of
A Public Health Action Plan To Combat Antimicrobial Resistance (Part I: Domestic Issues)

June-06

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
		Focus Area I: Surveillance	
Action Item #1: Determine Which Organisms and Susceptibility to Specific Antimicrobial Drugs Should Be under Surveillance and Create a Mechanism for Periodic Updating of This List.			
CDC, USDA, FDA, DoD, VA	Public Health Surveillance	Organisms currently under public health surveillance for antimicrobial resistance include: Campylobacter, *E. coli* O157:H7, Gram negative and Gram positive organisms causing health care associated infections, group A Streptococcus, group B Streptococcus, *Haemophilis influenzae*, *Helicobacter pylori*, HIV, Influenza, Malaria, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pneumocystis carinii*, Salmonella, Shigella, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Trichomonas vaginalis*. Organisms are added to this list when resistance emerges as a public health problem, as tools are developed for detecting resistance, and when there is capacity at the appropriate level.	Ongoing.
****TOP PRIORITY**** **Action Item #2: With Partners, Design and Implement a National AR Surveillance Plan.**			
CDC	National molecular surveillance of antibiotic-resistant *Streptococcus pneumoniae*	The Respiratory Diseases Branch (RDB) and our collaborators at the Emory Rollins School of Public health will establish a national laboratory for the molecular surveillance of invasive *Streptococcus pneumoniae* (*Spn*). We will provide front-line information concerning established and newly emerging antibiotic resistance mechanisms, clonal types, and serotypes of ABCs *Spn* isolates. We will monitor effects of currently used vaccines and antibiotics on the emergence and distribution of antibiotic-resistant strains.	Ongoing.Emergence of multi-resistant strains not targeted by the pneumococcal conjugate vaccine: We have found that the increase in antibiotic resistance within the important vaccine serotype replacement serotype 19A is primarily due to emergence of serotype 19A capsular switch variants. Seven different penicillin resistant clonal lineages of serotype 19A were discovered among year 2005 ABCs isolates, four of which were highly related to internationally disseminated clones that are of PCV7 or PCV7-related serotypes.

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CDC	Enhancing state-based surveillance for drug-resistant S*treptococcus pneumoniae*	This project's goals are: 1) to improve surveillance methods used by persons conducting surveillance for drug-resistant *Streptococcus pneumoniae* (DRSP) in state health departments, 2) coordinate individual state-based surveillance programs into a national effort, and 3) translate lessons learned from CDC's Active Bacterial Core surveillance (ABCs) program. A CDC-based project coordinator will develop a family of measures to provide information to state health department personnel conducting surveillance or who are starting such a program, conduct site visits, host national meetings to provide training and facilitate interaction between state-based personnel conducting surveillance, assist with funding of surveillance programs through the ELC program, and gather, aggregate and disseminate information on DRSP from individual surveillance programs.	The coordinator has assisted in the development, implementation, and support of state-based AR surveillance programs and facilitated communication and interaction between sites through web boards and listserves. A four day conference that includes AR education and surveillance presentations occurred in April 2005. The DRSP surveillance manual is available at www.cdc.gov/drspsurveillancetoolkit. The coordinator has provided regular technical assistance to state and local health departments addressing DRSP surveillance-related questions such as how to implement antibiogram and lab based surveillance, methods that were evaluated through analyses of ABCs data and shown to be reasonable and efficient means for tracking resistant pneumococcal infections.
CDC	Antimicrobial resistant neonatal sepsis in the era of GBS prophylaxis	Major reductions in neonatal sepsis caused by group B streptococcus have been documented over the past decade, but a potentially alarming increase has been detected in ampicillin resistance among selected other neonatal pathogens, especially in the low birth weight or preterm newborn. Because higher mortality is associated with ampicillin resistant gram negative infections, preliminary data on these trends raised alarms. CDC's Emerging Infections Program network, through ABCs, provides an opportunity to monitor longer term, wider-spread trends in sepsis in the first week of live and correlate ampicillin resistant E. coli infections with maternal receipt of intrapartum antibiotics. Enhancement of the neonatal sepsis surveillance activities in four EIPs can also address the impact of recent recommendations for use of vancomycin in the setting of penicillin allergy among women who carry group B streptococcus resistant to clindamycin.	Updated surveillance protocol and forms with a focus on improving completeness of case findings. MN implemented surveillance in Jan., 2006. CA, CT and GA expanded collection of intrapartum antibiotic exposure din 2005. ABCs launched a new multistate labor and delivery reocord review of births in 2003 and 2004 to characterize use of intrapartum antibiotics and perinatal infection prevention practices in the era of universal prenatal GBS screening recommendations. Publications/presentations: CDC. Laboratory Practices for Prenatal Group B Streptococcal Disease. MMWR 2004; 53 (No.RR-23): 506-509); CDC. 2005. Early-Onset and Late-Onset Neonatal Group B Streptococcal Disease --- United States, 1996—2004. MMWR 54: 1205-8; 2000-2 neonatal sepsis surveillance trends (S. McCoy et al., ICEID, 2004); Association between intrapartum antibiotics and early-onset E. coli sepsis (S. Schrag, ICWID, 2006); Schrag, SJ and Schuchat, A. 2005. Prevention of Neonatal Sepsis.

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CDC	The epidemiology of MRSA strains in the U.S., using PulseNet	PulseNet is an innovative, laboratory-based national surveillance program that tracks the pulse-field gel electrophoresis (PFGE) profiles of selected bacteria. In collaboration with state health departments, MRSA strain types and their AR profiles in the U.S. are monitored through PulseNet to determine similarity with MRSA strains throughout the country, the prevalence of MRSA strain types from which vancomycin-intermediate strains of MRSA are derived, and similarity of U.S. epidemic strains of MRSA to those known to cause outbreaks and epidemics in Europe, Canada, and the Far East.	Ongoing. Data from this nationwide system have already been used to begin to understand the spread of specific MRSA strains among certain groups of patients in hospitals and in the community and will provide a clearer picture of the pathogenicity of *S. aureus* and the spread of AR among staphylococci. Recent PFGE data have been extremely useful for monitoring the spread of MRSA isolates in the United States. PFGE data have indicated the presence of 11 major clonal lineages or pulsed-field types (PFTs) of MRSA in the U.S. Four PFTs are common among healthcare related strains, four PFTs are found primarily among community-acquired isolates, and three are found among strains from both healthcare and community-acquired strains. In 2005, a novel lineage of MRSA, USA300, became the major cause of skin and soft tissue infections in the United States. The strain is now becoming common in hospitals even as a cause of healthcare associated infections.
CDC	Surveillance for Emerging Antimicrobial Resistance Connected to Healthcare (SEARCH)	The appearance of MRSA with reduced susceptibility to vancomycin (vancomycin-intermediate *Staphylococcus aureus* [VISA]), and resistance (vancomycin-resistant *Staphylococcus aureus* [VRSA]) is concerning and may be a warning that more strains resistant to vancomycin could soon appear. SEARCH is a network of voluntary participants (i.e., hospitals, private industries, professional organizations, and state health departments) which have joined together to report the isolation of *Staphylococcus aureus* with reduced susceptibility to vancomycin. All U.S. healthcare organizations and practitioners are encouraged to report such isolates to SEARCH and, after notifying their state health department, to send the isolates to CDC for confirmatory testing. SEARCH enhances the ability to detect these pathogens, which have a high public health and clinical importance but are difficult to detect through traditional surveillance systems, and provides confirmatory diagnostic and expedited susceptibility testing for these isolates when local testing is not feasible.	Ongoing. As of April 2006, CDC has confirmed 16 VISAs and six VRSAs in the U.S. Updated guidance on appropriate laboratory testing was sent to clinical laboratories and posted on the CDC website in April, 2006.

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CDC	MRSA disease in Alaska	In recent years, several community outbreaks of MRSA skin infections have occurred among Alaska Natives and in some areas 85% of all Staphylococcus aureus isolated are methicillin-resistant. Risk factors for disease include recent antimicrobial use, having a household member with a skin infection, use of sauna which has *S. aureus* isolated from it, and use of a crowded sauna. Current activities include establishing laboratory surveillance for MRSA, identifying patients with severe disease education about MRSA risk factors and prevention.	Ongoing. Currently collecting isolates for surveillance for CAMRSA from regional hospital in southwest Alaska where the outbreak occurred. Have obtained tribal approval to enroll cases of severe *Staphylococcu aureus* disease in the case series, and are in the final steps of approval for collecting surveillance data on CAMRSA. Have obtained approval to collect surveillance isolates and enroll severe S. aureus cases at the Alaska Native Medical Center. Baggett HC et al. Community-onset methicillin-resistant Staphylococcus aureus associated with antibiotic use and the cytotoxin Panton-Valentine leukocidin during a furunculosis outbreak in rural Alaska. Journal of Infectious Diseases. 189(9):1565-73;2004. Baggett HC et al. An outbreak of community-onset methicillin-resistant Staphylococcus aureus skin infections in southwestern Alaska. Infection Control & Hospital Epidemiology. 24(6):397-402;2003
CDC	Sentinel surveillance for antimicrobial resistance among *Helicobacter pylori* infections in Alaska	Surveillance for antimicrobial resistance among clinically identified *H. pylori* isolates is conducted at 5 hospitals in Alaska. Gastric biopsies obtained for clinical reasons are sent in for culture and antimicrobial susceptibility testing. Drugs tested include: clarithromycin, metronidazole, amoxicillin, tetracycline, and levofloxacin. The goal is to provide data on the prevalence of drug resistance and to aid clinical decisions regarding empiric therapy and retreatment of patients where initial therapy was unsuccessful.	Since 1999, over 1000 biopsies have been received; over 51% were positive for *H. pylori* by culture. Metronidazole resistance (MtzR) was demonstrated in isolates from 44% persons, clarithromycin resistance (ClaR) was found in 31% persons, amoxicillin resistance in 3% persons and no persons were infected with isolates resistant to tetracycline. Females were more likely than males to show MtzR (54% vs. 32%, OR=2.5, $p < .01$) and ClaR (35% vs. 25%, OR=1.6, $p = .05$). Resistance to metronidazole and clarithromycin is more common among *H. pylori* isolates from Alaska Native person when compared with the rest of the United States. These data have been reported back to clinicians who contribute to the surveillance and to other clinical providers in Alaska who treat patients with *H. pylori* infections. Publication titled “Alaska Sentinel Surveillance for Antimicrobial Resistance in *Helicobacter pylori* isolates from Alaska Native Persons, 1999-2003” submitted to Emerging Infectious Diseases.

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CDC	Trends in antimicrobial prescribing for children and adolescents at Alaska Native Medical Center, 1992 - 2004	Although national data indicate a decrease in antimicrobial prescription rates for children in recent years, no data have been available to assess the trends among the Alaska Native Health Services. Traditionally, infectious disease rates for pneumonia and otitis media have been high among Alaska Native children prompting speculation that prescribing rates have driven a trend towards increasing drug resistance seen among pneumococci and other common pathogens. Local speculation indicates that campaigns to promote judicious antimicrobial use have not had sufficient impact on prescribing practices. To address this need, we queried the electronic pharmacy records of the Alaska Native Medical Center in Anchorage for prescriptions giving to children as outpatients in the past 12 years.	The visit-based annual rate per 1000 persons < 18 remained stable from 101 (1992) to 109 (2004) (p = .672). Overall, visit-based prescription rates in AN/AIs were lower (range 100-150) than those previously reported in US children < 15 years old (250-340). Penicillins comprised >50% of all antimicrobials prescribed. The overall visit-based prescribing rate of oral antimicrobials in AN/AIs <18 was lower than rates reported from a similar age group in US and these rates remained stable from 1992 to 2004. These data indicate that prescribing rates for Alaska Native children are not higher than for the rest of the US and have not increased over time. Presentation of these data is planned at a national meeting and for dissemination to local providers. We propose to employ this methodology statewide in Alaska to provide local data for healthcare providers in rural communities and to establish ongoing monitoring of antimicrobial prescribing practices for benchmarking purposes.
CDC	An analysis of molecular epidemiology of multi-drug resistant *M. tuberculosis* in the United States	The purpose of this research project is to develop a comprehensive national tuberculosis (TB) genotyping registry for TB case-patients with multidrug-resistant *M. tuberculosis* (MDR-TB) and to assess the molecular epidemiology of MDR-TB in the United States (U.S.). Through this investigation, the Division of TB Elimination (DTBE) at the Centers for Disease Control and Prevention (CDC) will work with 14 selected U.S. TB Epidemiologic Studies Consortium (TBESC) sites to collect epidemiologic and genotyping data from all MDR-TB case-patients in the U.S. This will be a five-year cross-sectional population based study design where recruitment and data collection are handled prospectively starting on October 1, 2005 through 2010.	Project is currently in a piloting phase with 4 of 14 sites enrolling patients.
CDC, FDA, USDA	Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria	NARMS is a collaboration among CDC, FDA (Center for Veterinary Medicine) and U.S. Department of Agriculture. Fifty state and four local public health department laboratories forward every 20th non-Typhi Salmonella, Shigella, and *E. coli* O157 , and every Salmonella typhi, to the CDC NARMS laboratory for antimicrobial susceptibility testing. Additionally, ten state laboratories, who also participate in FoodNet, submit a proportion of Campylobacter isolates to the CDC NARMS laboratory. In 2001, NARMS launched the "Retail Food Study." Currently, ten participating states test grocery store meat products for enteric bacteria and resistance.	Ongoing. NARMS has been expanded to all 50 states, providing national surveillance for antimicrobial resistance among foodborne pathogens. Campylobacter sampling in the ten FoodNet states has been changed to allow for burden estimates and a plan for further expanding to more sites is underway. Five additional sites send enterococci and *E. coli* isolated from outpatient stools to CDC NARMS for resistance testing in order to monitor for changes in indicator bacteria. A third arm of NARMS testing retail grocery store meat samples has completed 4 years of surveillance and has expanded to a random sampling method. The third testing site is FDA's Center for Veterinary Medicine's Office of Research. The 10 Foodnet sites submit *Salmonella, Campylobacter,* Enterococci, and *E. coli* isolated from retail meat and poultry samples to the FDA -CVM Office of Research laboratory, where they are tested for susceptibility to a the NARMS panel of antimicrobial agents.

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CDC, DoD	Gonococcal Isolate Surveillance Project (GISP)	Sentinel surveillance system for monitoring AR of *Neisseria gonorrhoeae* in the United States established in 1986. Male urethral gonococcal isolates together with clinical and demographic patient data are submitted for susceptibility testing each month from STD clinics in approximately twenty-eight cities in the United States. GISP data demonstrate the ongoing spread of fluoroquinolone-resistance and the emergence of *N. gonorrhoeae* with decreased susceptibility to azithromycin in the U.S. GISP data are published in an annual report and periodically in the MMWR. (http://www.cdc.gov/std/gisp) contains GISP annual reports from 1998-2004 as well as important reference and link resources.	Ongoing. GISP data were used to revise the latest version of CDC's Sexually Transmitted Diseases Treatment Guidelines which will be published in 2006. Finalized data from 2005 will be available by Fall 2006. Location-specific (city, state, region) alerts and guidelines are regularly updated on the CDC's GISP website.
CDC	Enhanced collection and electronic transfer of data on Antimicrobial Use and Resistance (AUR)	A cooperative study of enhanced collection, compilation, and transmission of data on antimicrobial use and resistance from automated laboratory instrumentation systems in healthcare settings to CDC and other public health systems using architecture fully compatible with NEDSS. This will create a database that will facilitate benchmarking and performance feedback to promote local AR improvement efforts; development of regional, state, and national data about patterns of use and resistance; and evaluation of prevention programs.	Ongoing. During 2005, TheraDoc software was modified to successfully create HL7 Version 3 messages containing microbiology, pharmacy and admission/discharge/transfer (ADT) data from a pilot healthcare facility. This data complies with the AUR option in the medications-associated module of the National Healthcare Safety Network (NHSN) which began early in 2005. Additionally, a software tool was developed at CDC that allows pilot healthcare facilities who have not purchased TheraDoc software to successfully create HL7 Version 3 messages containing microbiology data to be sent to CDC. During 2006, TheraDoc software was deployed at one additional pilot healthcare facility. Also, the software tool developed at CDC was modified to produce HL7 Version 3 messages containing pharmacy and ADT data. In addition, this tool was updated to create messages with much greater efficiency which minimizes processing time. Additional advancements were implemented for processing received messages.
CDC	National Tuberculosis Surveillance System (NTSS)	Ongoing collection, analysis, and communication of national tuberculosis surveillance information; expanded in 1993 to include the frequency and type of AR, enabling strategically focused tuberculosis control and elimination efforts. The expanded national TB surveillance system has proven its usefulness in assisting in the evaluation of the success of TB control efforts and monitoring the status of the epidemic, particularly through the collection of data on initial drug susceptibility. Information on the use of initial regimens of four first-line drugs, directly observed therapy, and completion of therapy in one year or less have been used as measures to evaluate program success. As future efforts towards TB elimination increase, both existing and new surveillance systems at the national, state, and local levels will become even more critical to monitor the burden and impact of TB, evaluate the success of control and prevention efforts, and direct planning and policy development.	Ongoing. Data collection and analysis are gathered on a continuous basis. Since 1993, when the case report was expanded to include drug susceptibility results, the proportion of patients with primary MDR TB decreased from 2.5% to 1.0% each year during 1998-2001. After an increase to 1.2% in 2002, the proportion decreased to 0.9% in 2003. In 2003 , the percentage of U.S.-born persons with MDR TB decreased, from 0.7 % in 2002 to 0.6 %. Of the total number of reported MDR TB cases, the proportion occurring in foreign-born persons increased from 31% in 1993 to 74 % in 2003 . Tables 10, 11, and 36 of the CDC annual TB surveillance report, Reported Tuberculosis in the United States, 2004 , provide detailed summaries of anti-TB drug resistance from the national surveillance data. This report and other publications and recommendations based on these data are available on the internet http://www.cdc.gov/nchstp/tb/surv/surv2004/default.htm.

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CDC	Surveillance for drug resistant invasive bacterial diseases in Alaska	AIP conducts statewide laboratory-based surveillance for invasive *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, and Groups A and B Streptococcus. Surveillance for invasive *H. influenzae* began in 1980, *S. pneumoniae* in 1986, and the other organisms in 1998. The population under surveillance is the State of Alaska, a total of 626,932 persons (Census 2000). Case detection occurs year-round as participating laboratories from all hospitals throughout the state send isolates recovered from sterile sites to the AIP lab in Anchorage, accompanied by basic demographic and clinical information on the cases. Materials and forms for isolate shipment and data collection are provided to each lab by AIP. Staff from AIP complete a surveillance form for each case and collect clinical and sociodemographic information. At year-end, AIP asks that each laboratory review their records and provide information on any cases that may have been overlooked.	Evaluated regional outbreak of invasive disease due to serotype 12F S*treptococcus pneumoniae* with reduced susceptibility to trimethoprim /sulfa. Determined most cases were among persons who had medical indications for receipt of pneumococcal polysaccharide vaccine and had sought care for acute illnesses but were not vaccinated. Worked with regional health care system to encourage development of standing orders for administering vaccine to persons in this category. Determined that the mechanism of erythromycin-resistance among invasive Streptococcus pneumoniae isolates collected was due to mefE (85%) and ermB (11%), 2% with both genes present and 2% with neither. Prevalence of invasive isolates with macrolide resistance has declined since introduction of PCV7. Recent increase in invasive disease due to serotype 19A is showing increased resistance to trimethoprim-sulfa and is intermediate to penicillin.
CDC	Antimicrobial resistant early-onset sepsis and maternal intrapartum antibiotic use	Increased use of antibiotic prophylaxis during labor and delivery to prevent perinatal group B streptococcal (GBS) disease has decreased the rate of early-onset GBS infections by 81%. As more antimicrobial drugs are used in the labor and delivery setting to prevent mother-to-child transmission of group B streptococcus, the risk of newborns acquiring infections with other perinatal pathogens, such as *E. coli* drug resistant infections might increase. The objectives of this project are to monitor trends in early-onset infections with non-GBS pathogens including drug resistant *E. coli* in selected areas, to evaluate whether antimicrobial drug use during labor and delivery is associated with an increased risk of drug resistant E. coli, and to assess the impact of a penicillin G shortage on prophylactic use of penicillin, ampicillin, and other agents during labor and delivery.	Surveillance for non-GBS sepsis is ongoing in the Active Bacterial Core Surveillance (ABCs) with a new surveillance area, MN, starting case finding in 2005 . To date surveillance has led to two publications summarizing data from CT , GA, and CA ; recent data were presented at the International Conference on Emerging Infectious Diseases, 2004. Evidence that the rate of resistant *E. coli* infections increased among preterm infants, particularly among very low birthweight infants from 1998-2000, raised concern. A review of an apparent increase in non-GBS sepsis rates in 2003 revealed variation in case finding methods across sites that led us to implement more standardized prospective case finding methods and 6 monthly laboratory audits in 2005. Additionally, a review of a random sample of births in 2003 and 2004 is planned for these surveillance areas to evaluate antibiotic agents used for GBS prophylaxis, with a particular focus on use of vancomycin and on the impact of a new penicillin G shortage in 2004.
CDC	The *Helicobacter pylori* Antibiotic Resistance Program (HARP) and antimicrobial resistance in *Helicobacter pylori* in Alaska and *H. pylori* research activities in the Republic of Georgia.	A three-year project for defnining the epidemiology of H. pylori infection and associated diseases, for introdcution of diangnosis and treatment into standard medical practice, and for development of a national control strategy has been initiated in the Republic of Georgia, where a pilot study in 2003 had shown high prevalence of infection. A sentinel surveillance system for *H. pylori* has been established in Alaska to monitor antimicrobial resistance among Alaska Natives who have high rates of *H. pylori* infection; and where AR among *H. pylori* is high.	Ongoing. The objectives of the Republic of Georgia H. pylori project are: 1. Determine prevalence of infection and H. pylori associated illness 2. Identify risk factors for infection and clinical illness, 3. Introduce diagnosis and appropriate treatment in to regular medical care, and 4., based on study findings, develop a national control strategy. The HARP project has been terminated. Analysis of data from HARP showed that nearly 40% of isolates are resistant to one or more first-line antimicrobial agents. Clarithromycin resistance among *H. pylori* was associated with past antimicrobial use of macrolides and led to higher rates of treatment failure using clarithromycin-based regimens.

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CDC	Surveillance and detection of antimicrobial resistant invasive fungal infections among organ transplant recipients	Goals of this project are to detect and monitor trends in emerging antimicrobial resistance among invasive fungal infections, and develop a collection of such strains for applied research by CDC and other researchers. To accomplish these goals we will refine and maintain a provider-based sentinel network of organ transplant centers to collect surveillance data, and fungal isolates, related to invasive fungal infections among persons who have received stem cell or organ transplants. This will be accomplished through a new cooperative agreement. This population is at highest risk for anti-fungal resistant *Candida* spp. and mold infections. There is no current system to track emerging anti-fungal resistance among fungal infections nationally.	Awarded cooperative agreement through Office of Extramural Affairs by publishing a new Program Announcement "Organ Transplant Infection Detection and Prevention Program." Funded 2 applications which will support 3 transplant centers each: University of Pittsburgh (includes Pittsburgh, University of Toronto, Cleveland Clinic) and University of Alabama (includes Alabama, University of Michigan, and University of Pennsylvania). Held investigators meeting (November, 2004, September 2005) during which time protocol approvals, IT development, and SOPs were completed. Patient enrollment begins April 2006, anticipate 24 months of patient enrollment. Due to loss of internal funding sources, CDC Foundation support was sought and successful for FY 2006.
CDC	Testing of drug-resistant *Trichomonas vaginalis*	Trichomoniasis is the most common curable STD in young, sexually active women. Ongoing surveillance on metronidazole resistance among trichomonas infected patients has been established to determine associated risk factors for resistance and success rates for alternate drug therapy suggested. Practitioners send culture isolates for patients who have failed two standard courses of metronidazole therapy based on the CDC's Treatment Guidelines. Parasites are tested both aerobically and anaerobically for sensitivity to metronidazole and to tinidazole. These data should answer the following questions: Using isolates sent to the CDC for susceptibility testing, what percent of the isolates exhibiting clinical resistance to metronidazole are clinically resistant to tinidazole? How well does in vitro testing of sensitivity to tinidazole correlate with clinical resistance?	Ongoing. Testing is an ongoing service of CDC.
CDC	Enhanced surveillance of influenza viruses for resistance to licensed drugs and development of tests for rapid detection of drug-resistant strains with pandemic potential	Improved molecular tests for rapid diagnosis of mutants resistant to both the old and new drugs are needed for pandemic preparedness as well as for interpandemic control of influenza. This project studies avian influenza viruses of different subtypes, which will improve pandemic preparedness. In addition, it will evaluate existing biochemical tests and develop new molecular techniques for detecting influenza A and B mutants resistant to neuraminidase inhibitors (NIs), which will improve surveillance for drug-resistant variants among human influenza viruses.	In 2005, surveillance for resistance to licensed drugs (M2 blockers: amantadine and rimantadine) in human isolates from the US and other countries was continued. Concerning increase in the proportion of influenza A(H3N2) viruses resistant to amantadine/rimantadine circulating in many countries was revealed. In particular, it was shown that in the US the percentage of influenza A(H3N2) viruses resistant to amantadine/rimantadine was much higher (14%) than in previous years (~1%) published in The Lancet on September 22, 2005 [see Bright RA et al., The Lancet, 2005; 366: 1175-1181]. Continued analysis of different subtypes of influenza virus isolates resistant to amantadine/rimantadine did not reveal their antigenic difference from viruses sensitive to the drugs.

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CMS	Medicare Patient Safety Monitoring System (MPSMS)	A national project to identify the rates of adverse events in the Medicare population. In 2005 MPSMS added two relevant surveillance topics, inpatient MRSA and VRE, to the portfolio.	Currently in the first year of data collection for MRSA and VRE. The first year's accural for this data will end July 2006 and be available for the National Healthcare Quality and Data Reports as AHRQ sees fit.
DoD	Development of a DoD AR surveillance plan consistent with the national AR surveillance plan	Establish an overarching framework for facilitating the implementation, operation, and evaluation of activities in AR surveillance within DoD.	Ongoing. Leaders in infectious disease, laboratory, and preventive medicine in the three services are working on AR issues and related surveillance in the DoD. The Armed Forces Epidemiology Board published a recommendation, "Antimicrobial Resistance 2004-10" dated Dec 10, 2004 (http://www.ha.osd.mil/afeb/2004/2004-10.pdf). In this recommendation the AFEB recommends that antimicrobial-resistance monitoring becomes an integral component of military surveillance activities, and that system-wide data be routinely accessible to military health care institutions and providers. Ideally, these data should be correlated with antimicrobial use patterns and health care outcomes. Other items in this recommondation include related recommendations for deployed military settings, model policies for prudent use of antibiotics in the military and research, if undertaken, to focus on prevention of infectious diseases.

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DoD	DoD antimicrobial resistance surveillance network	Under a Cooperative Research and Development Agreement (CRADA) with private industry, developing a DoD-wide AR surveillance network for identifying AR occurrences and trends within the military population. The cornerstones of this mechanism are: 1) the provision of daily, independent quality-assurance review and feedback of a military laboratory's susceptibility test results by experts in the field, 2) the continuous generation of up-to-date antibiograms based on an individual medical facility's AR patterns, 3) access to validated information on antimicrobial resistance occurrences and trends in the facility's geographic region for evaluating their implications for military personnel, and 4) facilitation of DoD-wide monitoring of AR trends to improve evidence-based decision and policy making on antibiotic usage and patient care, and 5) to enhance DoD ability to identify and respond to AR events of military significance in a timely manner.	Ongoing. Electronic antimicrobial susceptibility testing quality assurance and analysis system is being used in three pilot sites. During 2004-2--5 a major DoD medical center located in Germany was added as a site. One existing site was located in a medical center severely impacted by Hurricane Katrina; that site's data flow ceased as a result; the future of that site is not yet known. Expansion to additional sites anticipated. Linkage of system into a DoD network for information sharing and analysis of AR trends initiated in 2004-2005. Expansion of network and its evaluation anticipated for the next 2 to 3 years.
FDA	Proposed Rule – Surveillance/Reporting	Publish proposed rule regarding surveillance and annual reporting (included with proposed rule "Safety Reporting for Human Drug and Biologic Products").	Assessing economic impact of the proposed regulation.
FDA	Guidance - Surveillance Planning	Develop guidance relating to surveillance and annual reporting (based upon proposed rule "Safety Reporting for Human Drug and Biologic Products").	Assessing economic impact of the proposed regulation.
Action Item #3: Develop Standards and Methodologies.			
CDC	Grant Program for applied research on antimicrobial resistance: characterization of strains of Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA)	This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus* (*S. aureus*) causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques.	Five three-year awards were made in 2003. Recipients include: Harbor-University of California Los Angeles Research & Education Institute, University of California at San Francisco, University of Chicago, William Beaumont Hospital, and Columbia Unversity. Projects underway, results pending. Funding cycle complete. Numberous publications resulted. "1) Genetic background affects stability of mecA in Staphylococcus aureus." J Clin Microbiol. 2005 May;43(5):2380-3. 2) "Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles." N Engl J Med. 2005 Apr 7;352(14):1445-53. 3) "Incidence of and risk factors for clinically significant methicillin-resistant Staphylococcus aureus infection in a cohort of HIV-infected adults." J Acquir Immune Defic Syndr. 2005 Oct 1;40(2):155-60.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Grant Program: Applied Research on AR - Validation of National Committee for Clinical Laboratory Standards (CLSI) Breakpoints for Bacterial Human Pathogens	The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of CLSI breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing CLSI methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing CLSI methods and quality control as a starting point for novel test development.	Funding cycle complete. Publications resulting: Reevaluation of Enterobacteriaceae MIC/disk diffusion zone diameter regression scattergrams for 9 B-lactams: adjustments of breakpoints for strains producing extended spectrum B-lactamases. Diagnostic Microbiology and Infectious Disease, Volume 52, Issue 3, Pages 235-246. In vitro susceptibilities of aerobic and facultative Gram-negative bacilli isolated from patients with intra-abdominal infections worldwide: the 2003 Study for Monitoring Antimicrobial Resistance Trends (SMART). J Antimicrob Chemother. 2005 Jun;55(6):965-73. Epub 2005 Apr 22.
FDA	Development of CLSI/NCCLS testing standards	*Campylobacter* is one of the primary foodborne pathogens under surveillance in NARMS.	Development & implemented 2 antimicrobial susceptibility testing methods for the fastidious bacterium *Campylobacter*. These methods are the agar dilution and the broth microdilution methods. Both methods are approved by CLSI (formerly NCCLS), the agar dilution in 2003 and the broth dilution in 2005. The broth dilution method is being incorporated into public health systems in Canada, Durope, Central and South America, and is being used in WHO training labs worldwide. This method enhances the quality of data and ensures intra- and inter-laboratory reproducibility among the 3 arms of NARMS and other surveillance systems worldwide. This information and interpretive criteria for select antimicrobials will be published in the CLSI proposed guideline M45-A "Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria" in 2006. Developed CLSI standardized methods for antimicrobial disk susceptibility and broth dilution susceptibility testing of bacteria isolated from aquatic animals in 2005.
USDA	Quantitative Measurement of Antimicrobial Resistance Gene Loads in Samples	The increasing rate of development of bacterial resistance to antimicrobials has been well-documented, and this has major consequences for human and animal health. The results of this study will improve our ability to relate antibiotic use to antibiotic resistance in an accurate manner. This will enable the development of rational approaches to antibiotic use policy.	CSREES Epidemiological Approaches for Food Safety, NRI -- University of Minnesota, Singer, R.S. -- Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Rapid detection, molecular characterization, and antimicrobial resistance of foodborne pathogens	CSREES Hatch grant. Rapid and sensitive detection methods with considerable ease of use and low cost are needed for biodefense purpose. The researchers will develop and validate a multi-analyte detection method for major foodborne pathogens, which could potentially be used for biodefense purposes. They will also gain valuable scientific data on the contamination level of multiple foodborne pathogens in the retail food supply in Louisiana, their genotypes, and the extent of antimicrobial resistance. This will be an invaluable source of information for analyzing population biology and trends of antibiotic resistance among these foodborne bacteria and the likelihood of human exposure more pertinent to our region.	CSREES Hatch Grant -- Louisianna State University (Ongoing) Characterizing antibiotic resistance in lactic acid bacteria contributes to testing the overall hypothesis that commensals serve as reservoirs for antimicrobial resistance genes. An understanding of resistance frequencies and resistance mechanisms present in Vibrio will provide information to facilitate quantitative risk assessment of the emergence of antibiotic resistance in Vibrio and ensure oysters safety. Both studies will benefit public health in an effort to preserve the effectiveness of antimicrobials agents and reduce the incidence and levels of antimicrobial resistance in human pathogens in the long run.
USDA	QC testing as a part of NARMS	Methodologies and standards for Salmonella, Campylobacter, E. coli and Enterococci have been developed and implemented as a part of NARMS.	Ongoing.
Action Item #4: Address Additional Surveillance Issues Unique to AR.			
CDC	Enhanced surveillance for *Salmonella* Paratyphi	Determine the susceptibility patterns for isolates of *S.* Paratyphi collected in the United States for a one year period and determine associated travel history, clinical syndrome, and drug use.	Ongoing: Through NARMS all 50 states are participating and sending *S. Paratyphi* isolates to CDC for testing. States are interviewing all cases for enhanced surveillance.
CDC	Specialized surveillance projects and treatment trials for drug-resistant tuberculosis	Information on the initial drug regimen prescribed, coupled with information on initial drug susceptibility results, allows a judgment about the adequacy of therapy and corrective action on individual cases of tuberculosis by public health officials and health care providers. To improve knowledge on treatment of drug susceptible and drug resistant tuberculosis, CDC's TB Trials Consortium conducts studies on new agents and regimens, including the treatment of HIV-related tuberculosis using a rifabutin-based regimen, a trial to determine the effectiveness of twice-weekly treatment for isoniazid-resistant tuberculosis, trials of shortened regimens relying on newer fluoroquinolones, and a trial of short-course treatment for latent TB infection. CDC also collaborates with MDR treatment programs globally and serves as the chair of WHO Green Light Committee (GLC).	Ongoing. The addition of several new international sites (Brazil, Uganda, South Africa) have expanded capacity to study both drug susceptible and drug resistant TB. TBTC works closely with private sector partners (e.g., Global Alliance for TB Drug Development; e.g., Foundation for Innovative New Diagnostics) to assure engagement of promising new diagnostics for drug resistance, and new therapies and agents. Results of these studies will inform recommendations for new treatment regimens. Current surveillance data can be obtained at: http://www.cdc.gov/nchstp/tb/surv/surv2002/default.htm Current TBTC information is available at: http://www.cdc.gov/nchstp/tb/tbtc

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Monitoring drug resistance in lymphatic filariasis elimination programs	Annual mass treatment with antifilarial drugs (albendazole plus either ivermectin or diethylcarbamazine) is the cornerstone of the global program to eliminate lymphatic filariasis (LF). Although the primary goal of the program is to interrupt transmission of LF, additional benefits also are expected because of the known anthelminthic properties of these drugs. Substantial reductions in the prevalence of intestinal helminth infections are associated with mass treatment for LF. Though encouraging, the results also raise questions about the intensity of selection for albendazole resistance. Genes for resistance to benzimidazoles are known to occur at a low frequency in all nematodes studied to date. Monitoring for drug resistance has not been done as part of the LF elimination program. We propose to develop tools and a surveillance strategy to monitor the development of albendazole resistance in the context of the LF Elimination Demonstration Project in Leogane, Haiti.	Stool collections in FY2005 were concentrated in 3 communities with a prevalence of hookworm infection of >20% prior to the implementation of mass drug administration (MDA) for lymphatic filariasis. From over 2000 persons tested, 11 persons were hookworm positive; thus, the prevalence of infection has declined more than 95% following MDA. Cases clustered in families and 7 of 11 cases reported inconsistent participation, if any, in previous rounds of MDA. Hookworm eggs from these persons were purified in the field and transferred to our collaborators at the University of Georgia. Following the MDA in October 2005 and only 2 persons had hookworm eggs detectable by stool exam, at reduced numbers compared to pre-treatment. There seems to be little clinical evidence of resistance to albendazole by hookworms at this point. Our collaborators at the College of Veterinary Medicine at the University of Georgia have focused on developing PCR assays for individual eggs and characterizing microsatellite markers that can be used for genetic comparisons.
CDC	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).
FDA	Antimicrobial surveillance plan	Development of a surveillance plan for antimicrobial drug resistance among clinical laboratory isolates.	Ongoing. A five year option contract was awarded to Focus Technologies in October 2002. Announcemnt of Focus Contract (http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=VANW_VA.story&STORY=/www/story/11-18-2002/0001843012&EDATE=Nove+18,+2002) FDA/CVM awarded a 3 year contract to the American Type Culture Collection in 2003 to use existing microbiological collections to examine the historical susceptibility of pathogens to antimicrobial agents, and to better understand the temporal trends of resistance development.
FDA	See Action Item #2 (Proposed Rule - Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule -Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).
USDA	Implementation of a dairy pilot program in the Midwest.	Prior to implementation of a dairy component of the CAHFSE program, and in addition to the RDQMA described above, APHIS and ARS have undertaken a pilot study on 5 dairy farms in the midwest for comparison to the RDQMA program. Currently, samples are being cultured for Salmonella, Campylobacter, E. coli and Enterococci, (zoonotic and commensal bacteria). Sera are being banked for future testing. Samples and health/management data are being collected from each farm monthly.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Implementation of the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE).	Collaboration in Animal Health, Food Safety, and Epidemiology (CAHFSE) is a comprehensive USDA program designed to address animal health and food safety issues, including antimicrobial resistance, utilizing continual tracking of the selected data points. This program includes on-farm sample collection and data and risk factor analysis (Animal and Plant Health Inspection Service (APHIS), research efforts with molecular and phenotypic characterization of isolates, pathogenesis and development of intervention strategies (Agricultural Research Service (ARS), and in-plant efforts for sample collection, data analysis and risk assessment (Food Safety and Inspection Service (FSIS). CAHFSE will enable USDA to reliably track both emerging animal diseases and zoonoses within the food animal population which may affect the food supply and impact public health.	Ongoing. CAHFSE commenced in July 2003. As of January 2004, fecal and blood samples are being collected quarterly from pigs on sentinel farms in five states, Missouri, Minnesota, Iowa, Texas, and North Carolina, which are representative of swine production within the industry. Herd health/management data are also being gathered. Currently, samples are being cultured for Salmonella, Campylobacter, E. coli and Enterococci, (zoonotic and commensal bacteria). However, once the sample is collected, culture of any bacterium or virus of concern is possible. Sera are being analyzed for antibody to Lawsonia intracellularis, the bacterium responsible for ileitis in growing swine as well as Porcine Respiratory and Reproductive Syndrome virus (PRRS). As with the fecal samples, banked serum samples could be tested to determine exposure to other pathogens or toxins. Samples and health/management data are being collected from each farm four times per year.
USDA	Participation in the Regional Dairy Quality Management Alliance (RDQMA).	The mission of the RDQMA is to assure a healthful and safe food supply by advocating the adoption of best management practices (BMPs), which promote animal health and welfare, imporve productivity and profitability of dairy farms and encourages environmental styewardship. The RDQMA utilizes the New York State Cattle Health Assurance Program (NYSCHAP) herd risk assessment model and this model has been adopted for use in all participating states. The USDA is responsible for addressing specific issues such as Johne's Disease, salmonellosis, antimicrobial resistance and mastitis/milk quality. The RDQMA is being considered as the pilot program prior to implementation of a dairy component of the CAHFSE program.	Ongoing. Blood, manure, weekly bulk milk tank samples, environmental samples, management data surveys, economic data, nutrient management data and carcass data are being gathered from 2 farms in the northeastern US. Samples are being analyzed for the presence of Mycobacterium avium spp. paratuberculosis, Salmonella spp., E. coli 0157:H7 and generic E. coli, Listeria monocytogenes, Campylobacter, and Enterococci. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
**** TOP PRIORITY **** **Action Item #5: Develop and Implement Procedures for Monitoring Antimicrobial Use In Human Medicine, Agriculture, Veterinary Medicine, and Consumer Products.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Monitoring antimicrobial use in the community and correlating usage with resistance patterns	Analysis of antimicrobial use databases has proven to be complex, requiring sophisticated statistical methods to adjust for the design of certain usage survey samples and requiring substantial medical consultation time to link drug use with appropriate clinical diagnosis codes and potentially with databases regarding resistant infections. This project will develop a core analytic team that will track antimicrobial drug use in the community and correlate results of use with drug-resistance patterns (using drug-resistant *Streptococcus pneumoniae* as the marker community-acquired respiratory organism) and with community intervention efforts. The team will review availability and appropriateness of antimicrobial use databases and focus on establishing baseline trends in prescribing for upper respiratory infections using the National Ambulatory Medical Care Survey (NAMCS), National Hospital Ambulatory Medical Care Survey (NHAMCS), Medicaid databases, Synergy, and other databases.	Ongoing. In 2001, analyzed and published trends in prescribing for respiratory conditions in the community during the 1990s by using NAMCS and NHAMCS, initiated development of standard programs and documentation for regular analyses of three national or regional databases for drug prescribing, and provided technical support to five intervention programs or partners. During 2002, completed and published analysis of national data on trends in antibiotic prescribing for children for upper respiratory infections (McCaig et al. JAMA June 2002), issued new recommendations for alternative antibiotics for group B streptococcal prophylaxis for penicillin allergic women. During 2003, published analysis of national data on trends in antibiotic prescribing in ambulatory care settings (McCaig et al. EID April 2003). Will present trends in antimicrobial prescribing in ambulatory care settings at the 2006 Annual Conference on Antimicrobial Resistance.
CDC	National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS)	NAMCS is an annual national survey that collects data on the utilization of ambulatory medical care services provided by office-based physicians in the United States. Findings are based on a sample of visits to nonfederally employed office-based physicians who are primarily engaged in direct patient care. NAMCS monitors trends in prescription of antimicrobial drugs in the physician office setting. NHAMCS is an annual national survey that collects data on the utilization of ambulatory medical care services provided by hospital emergency and outpatient departments in the United States. Findings are based on a sample of visits to emergency departments and outpatient clinics. NHAMCS monitors trends in prescription of antimicrobial drugs in hospital emergency and outpatient departments.	Ongoing. During 2002, completed and published analysis of national data on trends in antibiotic prescribing for children for upper respiratory infections (McCaig et al. JAMA June 2002), issued new recommendations for alternative antibiotics for group B streptococcal prophylaxis for penicillin allergic women. During 2003, published analysis of national data on trends in antibiotic prescribing in ambulatory care settings (McCaig et al. EID April 2003). Recent NAMCS and NHAMCS methodology, data, and reports are available on the internet: http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.html Will present trends in antimicrobial prescribing in ambulatory care settings at the 2006 Annual Conference on Antimicrobial Resistance.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* in healthcare facilities	This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania.	The success of the initial interventions in two area hospitals has attracted interest and participation from other healthcare facilities in the region, and the organization of the regional prevention initiative continues to mature. Milestones include: • 19 regional hospitals have committed to the MRSA prevention initiative, and the group has elected to use CDC's National Healthcare Safety Network (NHSN) for regional data collection. Pilot data submission has begun in two pilot hospitals, with plans to pilot in an additional 7 hospitals prior to expanding to all participants in the region. • Regional third party payor (has initiated an pilot, voluntary, pay-for-performance initiative among hospitals in the region regarding MRSA infection prevention. • Investigators in Southwestern Pennsylvania collaborated with Plexus Institute received a $290,000 grant from Robert Wood Johnson Foundation tp spread the initiative to hospitals in eastern Pennsylvania, Marlyand, and Montana.
DoD	Prescription databases	Use of the prescription database (PDTS) is being piloted for gastrointestinal and respiratory outbreak detections.	In 2001, DoD developed a prescription database as part of a patient safety program. This database is used principally to screen for drug-drug interactions resulting from patients filling their prescriptions in more than one medical treatment venue. A DoD syndromic surveillance system (ESSENCE) has piloted the use of this data as a potential early signal for disease outbreaks. Efforts are underway to broaden the use of ESSENCE as a surveillance system for general use, with DoD Health Affairs taking the lead for standardizing use of this framework across the military services' installations and treatment facilities. When DoD AR surveillance is more mature, further use of the database can be attempted for detecting AR trends in association with prescription practices and disease occurrences.
USDA	CAHFSE, RDQMA, and midwestern dairy pilot program	Antimicrobial use information at the farm level is being collected as part of CAHFSE, RDQMA, and the midwestern dairy pilot program. Additional information regarding disinfectant use will be inititated in-plant.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
FDA	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance). To date, there is no veterinary antimicrobial use monitoring system in the United States. Monitoring antimicrobial use in agriculture and veterinary medicine would most likely require statutory change and FDA has not made significant progress on this action item due to the press of other responsibilities.
Action Item #6: Identify and Evaluate Methods for Collecting (e.g., Optimal Sampling Methods) and Disseminating the Surveillance Data on Antimicrobial Drug Use.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance). To date, there is no veterinary antimicrobial use monitoring system in the United States. Monitoring antimicrobial use in agriculture and veterinary medicine would most likely require statutory change and FDA has not made significant progress on this action item due to the press of other responsibilities. However, in an attempt to gather more information on this subject, FDA/CVM has funded several grants focusing on quantifying the effect of common antimicrobial use practices on the development and dissemination of antimicrobial resistant bacteria among food animals. Project titles and final reports can be found on the FDA/CVM Web site.
USDA	CAHFSE, RDQMA, and midwestern dairy pilot program	As a component of each of the programs, methods are being evaluated and optimized.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
Action Item #7: Work With Accrediting Agencies To Address Antimicrobial Drug-Use As Part Of Quality Assurance In Health Care Delivery Systems.			
CDC	See Action Item #32 (Development and testing of Health Plan Employer Data and Information Set (HEDIS) measures for appropriate antibiotic use).	See Action Item #32 (Development and testing of Health Plan Employer Data and Information Set (HEDIS) measures for appropriate antibiotic use).	See Action Item #32 (Development and testing of Health Plan Employer Data and Information Set (HEDIS) measures for appropriate antibiotic use).
Action Item #8: Ensure That Clinical Laboratories That Provide Data for AR Surveillance Purposes Have Access to and Routinely Participate in Pertinent Training and Proficiency Testing Programs with Good Performance and Indicate AR Testing Methodologies in Their Surveillance Reports (e.g., Specific Automated Methods or Manual Techniques).			
CDC	The National Laboratory Training Network (NLTN)	The National Laboratory Training Network (NLTN) delivers training around the country on proper methods of antimicrobial susceptibility testing and reporting.	Between July 2004 and April 2006, a total of 23,576 laboratorians received training on antimicrobial susceptibility testing (AST) in 39 events using multiple modalities. The focus of these courses was the importance of using CLSI (formerly NCCLS) standards for testing and insuring that reports given to clinicians provide correct information for appropriate treatment. Most of the courses are 5-6 hours long, but the NLTN also presented ten nationwide teleconferences on related topics. The teleconferences account for about 90% of the participants. These courses have been a major effort of the NLTN. One standard 5-hour program was presented at 20 locations reaching 706 students. Five Web-Conferences attracted 855 participants, and Webcast on Demand remains available for other interested laboratorians. Additional training on this topic is available on CD-Rom. Data from this modality will be available at a later date.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	AR research and reference testing	CDC reference laboratory conducts ongoing research and provides selected reference services for susceptibility testing of numerous bacterial species.	Ongoing. Recent achievements include the description of new AR mechanisms, which has led to modification and improvement of the testing methods used in clinical microbiology laboratories to detect resistance, evaluations of NCCLS/CLSI methods completed and modifications made to improve accuracy, and evaluations of commercial susceptibility testing methods completed and problems noted to the manufacturers. Additional accomplishments include confirmation and investigation of phenotype and genotype of the first six vancomycin-resistant *Staphylococcus aureus* isolates in the United States. DHQP led an effort to modify the national vancomycin breakpoints for *Staphylococous aureus* to improve the accuracy of identifying *S. aureus* isolates that have decreased suscetibility to vancomycin.
FDA	Pertinent training	Continue to ensure validity of antimicrobial susceptibility information derived from NARMS.	Developed both an antimicrobial susceptibility testing quality control and quality assurance program for the three arms of NARMS, human, slaughter plants, and retail meat.
Action Item #9: Evaluate the Performance of Licensed, Automated AR Testing Devices in the Context of Changing Resistance Patterns and Update Their Labeling When Appropriate (e.g., Changes in Quantitative Resistance That May Make a Test Result Invalid).			
Action Item #10: Working with Partners, Including CLSI, Further Develop, Refine, and Promote Standardized Clinical, Epidemiologic, and Laboratory Methods for Documenting and Assessing the Significance of Drug Resistance Among Yeasts and Moulds, Parasites, and Viruses.			
FDA	In-vitro antimicrobial susceptibility testing	Develop quality control standards for the in-vitro antimicrobial susceptibility testing of bacterial pathogens isolated from aquaculture foods.	Developed and implemented 2 CLSI/NCCLS approved antimicrobial susceptibility testing methods for the fastidious bacterium *Campylobacter*. These methods are the agar dilution and the broth microdilution methods. This informaiton and interpretive criteria for select antimicrobials will be published in the CLSI proposed guideline M45-A "Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria" in 2006. Developed CLSI standardized methods for antimicrobial disk susceptibility and broth dilution susceptibility testing of bacteria isolated from aquatic animals in 2005. These methods were published in 2 proposed guidelines in 2005, M42-P "Methods of antimicrobial disk susceptibility testing of bacteria isolated from aquatic animals" and M49-P "Methods for broth dilution susceptibility testing of bacteria isolated from aquatic animals."
FDA	Devices containing antimicrobials guidance	Draft guidance document for industry: how the Center for Devices and Radiologic Health (CDRH) intends to regulate devices containing antimicrobial agents, and what information regarding efficacy and resistance CDRH wants to see in premarket applications (interim until rulemaking is completed).	In development.
FDA	HIV Drug Resistance Genotype Assay Guidance	Revised guidance on HIV Drug Resistance Genotype Assays.	Publication pending.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #11: Identify Ways To Overcome Economic, Legal, and Other Barriers To Appropriate AR Testing and to the Reporting of Results (e.g. Sufficient Human Resources, Cost Considerations, Empiric Treatment Recommendations, Managed-Care Practices, etc.).			
CDC	Economic modeling of diagnostic and treatment strategies for gonorrhea based on prevalence of AR	The increasingly widespread use of nonculture methods for gonorrhea diagnosis is a major challenge to monitoring AR in *N. gonorrhoeae*, especially in light of the emergence of ciprofloxacin-resistant gonococcal isolates from Hawaii (ciprofloxacin is first-line gonorrhea therapy). This project will examine which diagnostic and treatment strategies are more cost-effective when the proportion of *N. gonorrhoeae* that are ciprofloxacin-resistant is less than 5%: continue to use ciprofloxacin and implement more widespread susceptibility testing, or switch to a more expensive cephalosporin and not increase the scope of susceptibility testing. When completed, the results will help provide a rational basis for programmatic decisions both for selection of gonorrhea treatment and for use of laboratory resources.	Project complete. "Optimizing Treatment of Antimicrobial-resistant Neisseria gonorrhoeae." Kakoli Roy, Susan A. Wang, and Martin I. Meltzer. Emerging Infectious Diseases. Vol. 11, No. 8, August 2005
Action Item #12: Pursue Legal Mechanisms for Manufacturers To Provide Otherwise Unavailable Drugs to Government Reference Laboratories for the Sole Purpose Of Antimicrobial Drug Susceptibility Testing (as part of surveillance) with the Understanding That These Drugs Will Not Be Used for Drug Discovery Purposes.			
Action Item #13: With State Health and Agriculture Departments and Other Stakeholders, Define Needed Core Capacity (Human, Laboratory, and Electronic Resources) at the State and Local Level To Ensure That Basic AR Surveillance Is Conducted In These Jurisdictions. As Part of This Effort, Ensure That State Public Health and Veterinary Diagnostic Laboratories Maintain the Capacity To Test the Drug-Susceptibility Patterns of Resistant Organisms of Public Health Importance, Especially For Drug-Microorganism Combinations for Which Testing Mechanisms Are Not Routinely Available at Hospital and Commercial Laboratories.			
Action Item #14: Provide Resources To Assist In Meeting State and Local Core Capacity Needs for AR Surveillance. Strive To Provide Consistent Funding from Year to Year to State and Local Health and Veterinary Diagnostic Laboratories That Meet Quality Assurance Standards.			
CDC	Support for state AR surveillance	An AR coordinator enhances communication and coordination between states and thus assists states meet capacity needs for improved AR surveillance. Resources provided include: the online DRSP surveillance manual, intra-site communication tools, site consultations, and the Get Smart campaign. The surveillance coordinator provides technical assistance to funded sites and monitors surveillance activities on the state and local level, and coordinates communication between sites. Specific surveillance techniques are identified for each site according to available resources.	Ongoing. An AR surveillance conference is scheduled for April 2005 and will allow collaboration between many AR stakeholders. Sections of the DRSP surveillance manual are available online now. State health departments are surveyed to determine methods of AR surveillance. Communication tools such as web boards and list serves are in development and will be available Spring 2005.
Action Item #15: Provide an Accessible, Centralized Source of AR Data from Major Surveillance Systems Involving Animal and Human Populations. In Consultation with Stakeholders, Determine How To Report AR Data in a Way That Is Valid and Useful to Interested Parties (e.g., Clinicians, Public Health Officials, Veterinarians, and Researchers). Include Sufficient Detail in Surveillance Reports To Permit Local Analysis and Comparison with Trends in Drug Use and Medical and Agricultural Practices.			
CDC, FDA, NIH, USDA	See Action Item #3 (Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria)	See Action Item #3 (Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria)	See Action Item #3 (Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Surveillance for Streptococcus pyogenes among military trainees	Increasing resistance to macrolide antibiotics has been demonstrated for S. pyogenes isolates. Furthermore, during military-recruit training exercises, penicillin-allergic patients are often given erythromycin when mass prophylaxis is recommended. If resistant organisms are present or develop in this population, S. pyogenes infections (latent or overt) may not be treated effectively. Recruits could be reservoirs of resistant pathogens for military populations. This project conducts antimicrobial susceptibility and gene typing. As of October 2005, the rates detected were the following: erythromycin (14.4%), clindamycin (2.0%), tetracycline (5.0%), levofloxcin (1.2%) and 0% for penicillin and vancomycin. Temporal trends in antibiotic resistance among S. pyogenes isolates demonstrated no discernible patterns, however the emergence of emm-type 5 as a cause of outbreaks among recruits has been noted in 2005-06.	Reports of susceptibility test results and summary statements are being provided to primary care facilities, are accessible to DoD staff at www.geis.ha.osd.mil and have been used in presentations at national meetings. Generated data show moderate AR rates as of October 2005. Three manuscripts from this work have been published to date: 1. National Department of Defense surveillance for clinical group A streptococcal isolates, antibiotic resistance, and emm gene types from 8 basic training military sites. October 2003. Journal of Clinical Microbiology. Vol 48, No 10, pp 4808-4811. 2. Pneumonia outbreak associated with Group A Streptococcus at a military training facility. 2005. CID, Vol 40, pp 511-518. 3. Rapid identification and strain-typing of respiratory pathogens for epidemic surveillance. 2005. PNAS, Vol 102, No 22, pp 8012-8017.
DoD	Surveillance of antibiotic-resistant S. pneumoniae in military populations	Antibiotic resistance in S. pneumoniae has risen dramatically over the last decade, with varying levels of resistance found in different regions of the country. Similarly, S. pneumoniae causes significant morbidity among populations served by U.S. military medical centers. In this study, S. pneumoniae isolates from 7 U.S. military medical centers are serotyped, subtyped, and tested for antibiotic resistance. As of April 2006, full or partial penicillin resistance was found in 33% of the isolates, with 22% having resistance to three or more antibiotics. This represents no discernable change in rates from 2001. Most invasive serotypes found in this population are included in the current 23-valent vaccine.	Reports of resistance findings and trends continue to be shared with the contributing medical centers, and summary statements are available through the website http://www.geis.ha.osd.mil. Continued surveillance is warranted for determining AR and type distribution trends over time in these populations, including association of particular strains with more invasive disease. National DoD surveillance for invasive Streptococcus pneumoniae: Antibiotic resistance, serotype distribution, and arbitrarily primed polymerase chain reaction analyses was published in the Journal of Infectious Disease, 2001; 184:591-6.
DoD	Multilocus sequence analysis of Streptococcus pneumoniae isolates	DoD data from 1981 to 1991 suggest that S. pneumoniae may cause about 12% of military pneumonia hospitalizations. Multilocus sequence typing characterizes isolates of bacterial species using the sequences of internal fragments of 7 house-keeping genes. This highly discriminatory molecular typing method is used to track the global spread of virulence, to provide a direct comparison of isolates of multidrug-resistant S. pneumoniae, to define serotypes of isolates, estimate recombinational parameters, and identify discrete clonal complexes.	Ongoing. Three manuscripts have been published from this work to date: 1. An Outbreak of Conjunctivitis Due to a Novel Unencapsulated Streptococcus pneumoniae Among Military Trainees. 2004. CID, Vol 39, pp 1148-1154. 2. Antimicrobial Susceptibility and Serotype Distribution of Streptococcus pneumoniae Causing Meningitis in Egypt, 1998 – 2003. 2005, JAC, 55(6):958-64. 3. Fatal Meningitis in a Previously Healthy Young Adult Caused by Streptococcus pneumoniae Serotype 38: an Emerging Serotype? 2005. BMC-Inf Dis, 5(38).
DoD	Surveillance of Bordetella pertussis among military trainees and the evaluation of newly developed highly sensitive PCR-based beacon probe for the detection of B. pertussis	Whooping cough is a contagious respiratory disease caused by Bordetella pertussis. Studies indicate that it is on the rise in adolescents, adults, and within confined populations such as military trainees. Surveillance for B. pertussis was established at 4 military training centers. Specimens were evaluated using PCR based beacon probe. Standard culture, serology, and PCR results were compared to validate the accuracy of the PCR method.	Completed. Four-hundred and eight specimen sets were tested. Using culture, serology, and molecular testing, evidence of B. pertussis was found in 11% of those enrolled. A manuscript is being prepared.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Investigations of methicillin-resistant Staphylococcus aureus (MRSA) outbreaks occurring on military bases.	Hospital acquired MRSA outbreaks are well known, but recent reports have caused concern about community acquired MRSA infections. Investigations into this recent trend have been conducted at several military bases. Laboratory work has involved culture identification followed by antibiotic resistance testing. The presence of the panton valentine leukocidin gene which is a known virulence factor has been shown in many of these investigations. The multilocus sequence typing method has also been used to identify global virulent clones by characterizing the isolates with the sequencing of 7 house-keeping genes. Further molecular analyses have been utilized to discover the specific SCCmec type of these MRSAs, which is the mobile genetic element that mediates the methicillin resistance.	Ongoing. Capabilities are in-house when need arises. Historical samples from over the last decade are currently being analyzed. Trends in clones circulating before community acquired transmission was recognized are under investigation. Community acquired isolates are now being archived from various military settings. Two manuscripts have resulted to date: 1. Risk Factors for Community-Associated Methicillin-Resistant Staphylococcus aureus Infections in an Outbreak of Disease among Military Trainees in San Diego, California, in 2002. 2004. JCM, Vol 42, No 9, pp 4050-4053. 2. 15-Year retrospective study of the changing epidemiology of methicillin-resistant Staphylococcus aureus (MRSA). 2006. Am J Med. In Press.
DoD	Investigation of multi-drug resistant Acinetobacter baumanni in US service members	Acinetobacter baumannii is an opportunist, with pathogenicity usually associated with high infectious doses or contamination of deep or necrotic wounds. Its importance as an nosocomial agent is due to its high rate of multi-antibiotic resistance. A review of A. baumannii infection in wounded US service persons is underway to determine 1) the number and location of patients involved, 2) what risk factors are common to the patients (eg, military unit or geographic proximity before injury, type and site of wound causing hospitalization, specimen source, type and location of all medical and surgical treatment, exposure to other patients with A. baumannii infection), and 3) the phenotypic strain(s) of A. baumannii involved.	Ongoing. Results of investigations are shared with preventive medicine and infectious disease staffs for review and implementation of prevention and control measures. An article in MMWR described this outbreak Acinetobacter baumannii Infections Among Patients at Military Medical Facilities Treating Injured U.S. Service Members, 2002--2004. MMWR, Nov 19, 2004 / 53(45);1063-1066.
CDC, DoD	See Action Item #2 (Gonococcal Isolate Surveillance Project (GISP))	See Action Item #2 (Gonococcal Isolate Surveillance Project (GISP))	See Action Item #2 (Gonococcal Isolate Surveillance Project (GISP))
Action Item #16: Provide Healthcare System Administrators and Other Decision Makers with Data on the Impact of Drug-Resistant Organisms (e.g., Outcome, Treatment Costs) and on Effective Prevention and Control Measures.			
CDC	Grant program for applied research on antimicrobial resistance (AR): estimates of economic cost for antimicrobial resistant human pathogens of public health importance	This program will fund research for estimating the economic costs of antimicrobial resistance in human pathogens of public health importance and provide additional information needed to prevent and control AR. This will include: analysis of data on incidence, prevalence, and antimicrobial susceptibility of specific infectious diseases; development of methods to determine costs which are simple and reproducible for different antimicrobial resistant organisms; and calculation of economic costs (direct and indirect) of infections that are resistant to one or more antimicrobial agents compared with infections that are susceptible to those agents.	Three two-year awards were made in 2004. Recipients include: Duke University , Washington University, Minnesota Department of Health.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research.	The University of Pennsylvania Center for Education and Research on Therapeutics has undertaken studies on AR using the General Practice Research Database in the United Kingdom.	Concern exists about the extended use of antibiotics to treat acne. Of more than 118,000 persons aged 15 to 35 who were diagnosed with acne between 1987 and 2002, 72% received either topical or oral antibiotic treatment for their acne for more than 6 weeks, while 28 percent did not. Within the first year of observation, patients receiving antibiotics were twice as likely as other acne patients to develop an upper respiratory tract infection.
Action Item #17: Expand and Enhance Coordination of Surveillance for Drug-Resistance in Enteric Bacteria In Sick and Healthy Humans and in Sick and Healthy Animals on Farms, at Slaughter, and at Retail.			
CDC, FDA, USDA	Integrated (human, animal, retail) National Antibiotic Resistance Monitoring System for Enteric Bacteria (NARMS) report	An integrated summary of human, animal, and retail meat NARMS data will be developed for annual publication	Ongoing: The three arms of the NARMS program are enhancing the coordination of reporting of surveillance data. CDC collect isolates from sick and healthy humans, USDA from sick and healthy animals and FDA from healthy animals via retail meat. The three arms are working together to coordinate common data base management and reporting formats. An integrated report will be finalized and published in 2006.
CDC, FDA, USDA	FDA Science Board Review of the NARMS program	A scientific review designed to help the program identify how it can enhance the coordination among the three arms to provide a more comprehensive look at drug resistance in enteric bacteria has begun .This review will be conducted by the FDA Science Board and a panel of outside experts .	Ongoing: FDA's science board has received the documents for the review and has begun to select outside experts to serve on the external review panel.
FDA	Antimicrobial resistant bacteria in feed ingredients	Initate surveys of rendered feed products and plant based proteins for antimicrobial resistant foodborne bacteria.	CVM is currently conducting surveys in conjunction with FDA field personnel (ORA) examining the prevalence of antimicrobial resistant foodborne pathogens (*Salmonella* and *E.coli* O157:H7) in complete mixed feeds. FDA is also collaborating with USDA to characterize antimicrobial resistant patterns among *Salmonella* and *E.coli* obtained from their Microbiological Data Program (MDP). On going. Also, see item #2.
Action Item #18: Evaluate the Usefulness of Monitoring Sentinel Human Populations (e.g., Farm, Abattoir, Fruit and Vegetable, and Food Processing Plant Workers) and Persons in the General Community for Infection or Colonization with Resistant Enteric Bacteria.			
CDC	NARMS Enterococci and *E coli* surveillance study	Determine the susceptibility patterns for isolates of Enterococci and E coli isolated from stool samples of healthy persons or outpatients from the community. Determine the risk factors associated with resistant and susceptible bacteria.	Ongoing: Five states are sending isolates of enterococci and E. coli to NARMS CDC lab collected from stool of healthy volunteers or outpatients who report no hospitalization. Interviews are being conducted to determine specific environmental, medical, and food exposures previous to the culture.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Antimicrobial resistant bacteria in sentinel human populations	Evaluate abattoir workers for carriage of antimicrobial resistant bacterial pathogens.	FDA/CVM funded a cooperative research agreement to the University of Maryland to study antibiotic resistance bacteria in food animals, abattoir workers, and human referent groups. The initial pilot study is complete and current efforts are focusing on characterizing Enterococcus isolates from poultry farms, retail poultry meats, and humans. Research is ongoing and FDA will report the findings when complete.
Action Item #19: Conduct Pilot Studies To Assess the Extent of Environmental Contamination by Antimicrobial Drug Residues and Drug-Resistant Organisms That Enter the Soil or Water From Human and Animal Waste. If Contamination is Detected, Conduct Appropriate Surveillance in Waste, Surface and Ground Water, and Soil from Agricultural Areas in Which Waste Is Used for Fertilizer, and Conduct Studies To Determine Potential Impact on Human and Animal Health.			
CDC	Sampling for antibiotics in an agricultural river basin	Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities.	Final sampling was completed in winter of 2005-2006. Samples currently being analyzed by USGS laboratory. Expect sampling data and water sample results by June 2006.
CDC	Evaluation of the impact of flooding on water quality and human health indicators	Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water.	Results of human subject sampling did not indicate an association between water quality and incidence of antibiotic resistance in pathogenic microbial isolates from human subjects. This project is finished. Presentations and Publications include: Environmental and Occupational Risk Factors for Intestinal Colonization with Antibiotic Resistant *Escherichia coli* and Enterococcus sp: A Pilot Study in Rural North Carolina. C.A Ohl, V.A. Varela, K. Johnson, T. Morris, D. Campell, J. Tysmans, T. Karchmer, C Rubin, N. MacCormack. Abstract for presentation to American Society for Microbiology Detection and Occurrence of Antimicrobially Resistant Enteric Bacteria on or Near Swine Farms in Eastern North Carolina. 2003. Final Report. Mark D. Sobsey and Maren E. Anderson.
USDA	Enhance overall understanding of pathogens that pose a food-safety risk particularly from the environment.	In response to the increased recognition of the impact the environment plays in dissemination of bacteria, we have initiated a study to determine the contribution waterways play in moevment of bacteria originating from animal production facilities in particular.	On going: A mobile microbiology trailer has been designed and equipped. In the summer of 2005, collection will start in the southeastern US with the intent to visit all 50 states within the next 5 years. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Enhance overall understanding of pathogens that pose a food-safety risk and to routinely monitor critical diseases in food-animal production, and develop a model for future surveillance efforts on a national level.	CAHFSE will enable USDA to identify and implement mitigation strategies for animal health and food safety issues in a timely manner thereby averting adverse economic, animal well-being, and public health consequences. Further, it will provide comprehensive science based answers regarding animal health and public health, it will serve as a model for future surveillance efforts on a national level, and it will complement information obtained from both the National Antimicrobial Resistance Monitoring System (NARMS) and USDA VetNet programs. These data are being used by the swine industry to develop management recommendations for producers.	Ongoing: This program is being expanded to all commodities and has been endorsed by the Animal Ag Coalition and other commodity groups. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
Action Item #20: Gather Information on the Relationship Between Antimicrobial Pesticide and Herbicide Use and the Emergence of Drug-Resistance by Monitoring.			
Focus Area II: Prevention and Control			
Action Item #21: Identify Factors That Promote or Impede Appropriate Drug Use in Hospitals, Extended Care Facilities, and Outpatient Settings In Collaboration with Partners.			
CDC	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).
CDC	The Chicago Antimicrobial Resistance Program (CARP)	CARP is a 5-year demonstration program to determine the impact of antimicrobial use and infection control interventions on the reduction of antimicrobial resistance in a healthcare delivery system. Components include developing improved methodology for interhospital and intrahospital comparisons of AR rates, computer-based surveillance of antimicrobial drug use, and interventions to improve antimicrobial drug use and prevent emerging resistance	Recently completed a randomized controlled trial to compare prospectively the extent to which three approaches – provision of routine prescribing guidelines available at the time of ordering, intensive education of providers, and electronic surveillance with realtime intervention as needed by clinical pharmacists. Preliminary results presented at 2006 Annual Meeting of the Society for Healthcare Epidemiology of America.
AHRQ	Independent Scientist Award (K02): Doctor-parent communication and antibiotic over-prescribing	This study focuses on doctor-parent communication as a determinant of both inappropriate antibiotic prescribing and parent satisfaction with care. Parents presenting with their children who were suffering from cold symptoms were recruited for study participation. With informed consent, both physicians and parents were surveyed and their encounters were videotaped. The findings from this work will be used to develop a communication-based intervention to decrease antibiotic over-prescribing in the pediatric outpatient setting.	Pediatricians used two formats to recommend treatment: positive recommendations in which physicians explained what could be done for the child and negative recommendations in which physicians ruled out the need for antibiotics. Negative treatment recommendations increased the odds that parents would disagree with non-antibiotic treatment plans. When parents disagreed with the treatment plan, physician perceptions that the parent expected antibiotics increased significantly. When physicians perceived an expectation for antibiotics they were 22% more likely to prescribe them. Failure to receive expected antibiotics did not decrease parent satisfaction with care, however, failure to be given expected advice on how to make their child feel better did. Focusing treatment recommendations on what can be done to make a child feel better rather then on what is not needed, i.e., antibiotics, increases both acceptance of non-antibiotic treatment recommendations and satisfaction with care. (Mangione-Smith R et al. Pediatric Research. 2004;55:22A.).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Program Project (P01): Understanding and eliminating health disparities in blacks	Practices of antimicrobial drug importation and use of nonprescribed antimicrobial drugs among Latinos in South Carolina.	Adults were interviewed to assess health beliefs and past and present behaviors consistent with acquiring antimicrobial drugs without a prescription in the United States. Many (30.6%) believed that antimicrobial drugs should be available in the United States without a prescription, 16.4% had transported nonprescribed antimicrobial drugs into the United States, and 19.2% had acquired antimicrobial agents in the United States without a prescription (Mainous AG 3rd et al. Emerg Infect Dis. 2005;11:883-8.).
AHRQ	Research Projects (R01): 1. Trial to reduce antimicrobial prophylaxis errors (TRAPE). 2. Improving antibiotic use In acute care settings. 3. Implementing Evidence-Based Guidelines for Treating NHAP	1. The trial assesses whether an intervention based on a group-collaborative model and the feedback of comparative performance data improves the timing of preoperative antibiotic administration compared to comparative performance feedback alone. 2. Randomized controlled trial of a quality improvement program in urgent care clinics and emergency departments. 3. This quasi-experimental study is designed to test the translation of multidisciplinary guidelines on evaluating and treating nursing home-acquired pneumonia (NHAP) into practice in multiple nursing facilities.	1. The 44 TRAPE hospitals collected and reported data regarding their surgical antimicrobial prophylaxis process, including timing, duration, and drug selected. These data were fed back to the hospitals, after which 22 hospitals were randomized to participate in a 9-month group collaborative process aimed at facilitating process change. Preliminary analysis shows that both groups signficantly improved their antibiotic administration processes, but there was little evidence that participation in the group collaborative process led to additional improvement. 2. 4,538 outpatients with community-acquired pneumonia without coexisting conditions were studied. Fluoroquinolone use was common and increased from 2000 to 2002, while macrolide use decreased. Increased age correlated with increased fluoroquinolone use, but increased use of fluoroquinolones occurred in healthy young and old patients alike (MacDougall C et al. Emerging Infect Dis. 2005;11:380-4.). 3. The timeline for the first year has been completed, and the intervention is being implemented. The budget for the second year has been approved and funded.
AHRQ	Research demonstration and dissemination project (R18): HIV treatment error reduction using a genotype database	The investigators designed and implemented an automated decision support system for antiretroviral prescribing in conjunction with genotypic resistance test data and assessed the efficacy and usability of the system at the University of Illinois Medical Center in HIV primary care clinics utilizing an electronic medical record system. The prevalence of erroneous prescribing was measured in HIV Insight, a research database in which UIMC HIV patients are entered.	The system was designed and implemented as planned, but utilization was constrained by technical and usability limitations. There was a high rate of errors in antiretroviral prescribing in response to a genotype resistance test. 13% of patients were started on a drug after a resistant test result, and over 40% of patients who were on a resistant drug were kept on that drug for at least 6 months after the resistance test. These errors did not correlate with clinical outcomes as expected.
AHRQ	Mentored Clinical Scientist Development Award (K08): Antibiotic use and bacteriuria in the rural nursing home	The focus of this work is antimicrobial resistance among gram-negative urinary isolates and the management of catheter-associated bacteriuria and urinary tract infections in rural nursing homes, for which little is known about management and surveillance practices.	This project consists of two components: a surveillance study and an intervention study. The surveillance study includes a survey of infection control practices (completed), and an observational study of antibiotic resistance among gram-negative urinary isolates from residents of these nursing homes (ongoing). The intervention study is currently finishing up its piloting stage before full roll-out at nursing homes throughout rural Utah this summer.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The Harvard Pilgrim Healthcare CERT supports nine collaborating systems within an HMO Research Network to study antibiotic use in chilidren.	A survey of college students found an increase in pharyngeal pathogenic bacteria among students with acne, both those who were taking tetracycline antibiotics and those who were not. Children born with life-threatening congenital heart disease may develop medistinitis as a complication of surgery within the first few weeks of life. A CERTs study found an attack rate of 1.4%, similar to the rate of mediastinitis previously found in adults. However, one-third of the infants' infections were caused by gram-negative bacilli. This high proportion may be explained, at least in part, by peripartum exposure of infants to enteric bacteria. Delay in closing the sternum at the end of the operation (in order to have rapid access to the area in case of internal complications) was associated with an increased risk of infection in cases in which gram-negative bacteria were present. The use of common antimicrobials in childhood urinary tract infections increased the cost of care, the likelihood of treatment failure, and the number of subsequent illnesses and deaths.
FDA	Labeling Rule	The new labeling is intended to educate physicians and the public about the resistance problem and to encourage physicians to prescribe systemic antibacterial drugs only when clinically necessary.	The Final Labeling Rule was published in the Federal Register on February 6, 2003. The rule will go into affect February 6, 2004. Announcement of Labeling Rule (http://fda.gov/bbs/topics/NEWS/2003/NEW00869.html)
Action Item #22: Develop Appropriate Drug Use Policies and Evaluate the Impact (Including on Prescribing Patterns, Resistance Rates, Patient Outcomes, and Cost) of Implementing These Policies in Hospitals and Other Health Care Delivery Settings. Identify Ways To Increase Adherence to Appropriate Use Policies Proven To Be Beneficial in Collaboration with Partners.			
CDC	Get Smart: Know When Antibiotics Work (hand hygiene)	One strategy the Get Smart: Know When Antibiotics Work campaign utilizes to promote appropriate antibiotic use in the community is to provide funding to states and local communities to develop tailored campaigns. Although on a national level hand hygiene is currently not promoted, many of the state and local level sites have chosen to focus on preventing viral illnesses through proper hand hygiene. Campaigns in Michigan, Nevada, and Minnesota have developed educational materials and/or trainings on the basics of hand hygiene in various settings.	Hand washing campaigns on the state and local level to promote the transmission of viral illnesses are currently funded and being implemented in six sites.
CDC	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).
CDC	See Action Item #21 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Program (CARP).
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
FDA	Antimicrobial Safety Working Group	This working group will monitor antimicrobial drug products with a focus on examining significant trends that may affect antimicrobial resistance as well as examining adverse events that pose significant safety risk to the public health not reflected in current FDA labeling.	New Initiative
Action Item #23: Evaluate the Relationship Between Prescribing Behavior and Specific Antimicrobial Drug Marketing and Promotional Practices. Assess the Public Health Effects of These Practices in Collaboration with Partners.			
FDA	Direct to Consumer (DTC) Promotion	Review "Direct to Consumer" (DTC) promotion as applies to antimicrobials.	Ongoing.
Action Item #24: Help Individual Hospitals and Healthcare Systems Analyze How the Availability of AR Data and Computer-Assisted Decision Support Systems Influences Prescriber Behavior, Health Outcomes, and Costs. This Plan May Include the Provision of Computer Software and the Establishment of Projects That Involve the Medicare Peer Review Organizations (PROs).			
CDC	See Action Item #21 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Project (CARP).
**** TOP PRIORITY **** **Action Item #25: Conduct a Public Health Education Campaign To Promote Appropriate Antimicrobial Use as a National Health Priority. The Health Campaign Should Involve Many Partners.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC, FDA	"Get Smart: Know When Antibiotics Work" national ad campaign	This national media education campaign is being developed to promote appropriate antimicrobial drug use in the community for upper respiratory infections, e.g., to decrease patient requests for antibiotics for illnesses for which they offer no benefit. Target audiences are parents of young children and healthy adults. The campaign uses a variety of health communication materials based on concepts tested in focus groups, and its effectiveness will subsequently be evaluated.	Ogilvy Public Relations Worldwide was awarded the media contract in September 2001 to implement a three phase media plan. Phase I focused on research and development while Phase II culminated with a nationwide launch of the media campaign. The TV PSA received 86.5 million impressions; the radio PSA received 160 million impressions; the print ads were viewed by 185 million; and traffic to the Get Smart website substantially increased (unique visitors jumped from just 4,927 in August 2003 to 28,604 in December 2004). Phase III of the media plan involved continuing the outreach efforts implemented in Phase II. During the final phase of the media plan the campaign tested and developed appropriate antibiotic use messages and media for Spanish speaking parents of young children, English speaking healthy adults 21- 49, and American Indian/Native American groups, in an effort to expand the campaign's reach. This work was conducted during 2004 and was completed May 2005.
CDC	Optimizing antimicrobial use in Emory-affiliated hospitals	Four Emory University-affiliated hospitals began an intervention in 2003 to improve the use of piperacillin/tazobactam.	Four participating hospitals (VA, CLH, EUH, GMH) completed a study during which common interventions to decrease Piperacillin/Tazobactam (PTZ) use were implemented. Preliminary results showed the rate of PTZ use decreased between periods in two of the four hospitals' non-ICUs; VA non-ICU decreased by 13.4% (92.6 to 80.2 DDD/1000 pt-days, $p < 0.001$), and GMH non-ICU decreased by 20.6% (68.3 to 54.2 DDD/1000 pt-days, $p < 0.001$). CLH non-ICU showed no change (32.8 to 33.9 DDD/1000 pt-days, $p = 0.17$), while EUH non-ICU showed an increase (44.2 to 51.8 DDD/1000 pt-days, $p < 0.001$). In the SICUs and MICUs, no significant change in PTZ use occurred. Preliminary conclusions: Interventions may have had an effect on the rate of PTZ use in two of four non-ICU areas. These preliminary results will be used to guide further analysis to find which intervention may have had the most impact.
CDC	See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare).	See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare).	See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare).
CDC	Get Smart: Know When Antibiotics Work - multicultural outreach/diversity initiative	Several projects are in development or implementation stages to increase awareness of antibiotic resistance and appropriate antibiotic use among minority communities and those who do not speak English. Projects include: development of educational materials for Spanish-speakers and American Indian/Native American (AI/NA) communities, train-the-trainer sessions with Latino and AI/NA community members, speaking engagements, and development of partnerships to further develop and sustain the initiative.	This initiative and the Get Smart staff member are fully supported by grant funds and in-kind work. The Spanish and AI/NA materials were launched as part of the Phase III media release (see media campaign). The staff member has conducted numerous presentations and train-the trainer sessions with Latino interest associations and the Indian Health Service Community Health Representative members. A contest was conducted in early 2006 among the CHRs to distribute educational materials and appropriate antibiotic use messages to AI/NA audiences. Since early 2005, this initiative has developed 17 new partnerships.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Get Smart: Know When Antibiotics Work - pharmacy initiative	Several projects are in development or implementation stages to increase awareness among consumers about antibiotic adherence, and to educate pharmacists about counseling consumers/clients on appropriate antibiotic use. Projects include: hospital pharmacist CE program, development of adherence messages for consumers and message placement, statewide activity in Michigan focusing on medication adherence, development of partnerships to develop and sustain initiative.	Hospital Pharmacist CE**:** In FY05, Get Smart campaign partner, Society of Infectious Diseases, began development of a hospital pharmacists CE program to teach about the issue of antibiotic resistance and give tools to communicate with consumers. The program is being developed in collaboration with the online provider, Pharmacy Choice. Antibiotic Round-Up: Statewide activity was planned in 2005 and conducted in early 2006 with the assistance of CDC-funded state program Michigan (MARR), EPA, a midwest pharmacy chain, a PR company, and others. The activity began with a statewide media release to kick-off the collection of unused antibiotics.
FDA	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion). FDA/CVM has developed a series of booklets that explain prudent use principles in depth for beef, dairy, swine, polutry, and more recently aquatic veterinarian. CVM also produced a 9 minute animation explaining how antimicrobial resistance both emerges and proliferates among bacteria. It can be found on the CVM Web site http://www.fda.gov/cvm/antiresistvideo.htm. CVM/FDA also awarded a 5-year cooperative agreement (2001-2006) to develop a web-based decision support system (The Veterinary Antimicrobial Decision System, VADS) for use by veterinarians to select and use antimicrobial agents appropriately.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #26: In Collaboration with Many Partners, Develop and Facilitate the Implementation of Educational and Behavioral Interventions That Will Assist Clinicians in Appropriate Antimicrobial Prescribing.**			
AHRQ	Mentored Clinical Scientist Award (K08): Improving Care for Acute Respiratory Infection	The recipient is developing and implementing an electronic medical record-based template for acute respiratory infection (ARI) visits, the ARI Smart Form, to standardize documentation of care and give clinicians easy access to clinical information, on-line decision support, and patient-education materials. A randomized controlled trial of the ARI Smart Form is assessing its effectiveness in deceasing antimicrobial prescribing in primary care practices.	About 15% to 36% of children with sore throat will have streptococcal pharyngitis, the only common cause of sore throat warranting antibiotic treatment. Physicians in the United States from 1995 to 2003 prescribed antibiotics to 53% of children with a sore throat and performed streptococcal testing in only 51% of children who received antibiotics (Linder JA et al. JAMA. 2005;294:2315-22.). A manuscript on usability testing of the ARI Smart Set with multiple participants is in press (Linder JA et al. J Biomed Inform.). The ARI Smart Form was pilot tested in Spring 2006, and a full randomized controlled trial in some 24 practices took place during the 2005-2006 cold and influenza season.
CDC	Development and distribution of evaluation manual for programs promoting appropriate antibiotic use in the community	CDC distributes funds to state and local health departments to develop local campaigns to promote appropriate antibiotic use, and all funded sites are required to include an evaluation component. However, with limited resources, the vast majority of sites do not adequately evaluate the success of their work. In addition, our grantees have repeatedly requested assistance in planning and implementing these evaluations. Data gathered during evaluation enables managers and staff to create the best possible programs, identify lessons learned, make modifications as needed, monitor progress toward program goals, and judge the success of the program in achieving its short-term, intermediate, and long-term outcomes.	During FY 2004, meetings with the evaluation manual working group focused on reviewing manual content, coordinating writing styles, and planning for the completion and distribution of the manual. Completed drafts of two appropriate antibiotic use case studies, sent them to program coordinators of some of our funded sites to solicit feedback, and revised the case studies accordingly. The manual was finalized and cleared in fall 2005. The manual underwent final revisions and proofreading in early 2006 and was released to all CDC-funded state programs and other interested parties in April 2006 via electroinc message board, Epi X. The manual will be printed and distributed to funded sites and some conference attendees at the Get Smart national conference in May 2006.
CDC	Campaign to prevent antimicrobial resistance in healthcare settings	The Campaign to Prevent Antimicrobial Resistance in Healthcare Settings (the Campaign) was launched in March 2002. The Campaign's overall goal is to reduce antimicrobial resistance (AR) by decreasing inappropriate antimicrobial use and improving adherence to proven infection control precautions. Five 12-step Programs with evidence-based action steps have been developed to target physicians who provide care to the following populations: hospitalized adults, dialysis patients, surgical patients, hospitalized children, and long-term care residents. Didactic tools and materials also have been developed and tested and accompany each of the 12-step Programs to promote the implementation of the recommended steps. In addition, materials have been developed that focus on the prevention of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA).	Major FY 2005 activities: 1) Funded five states through the Epidemiology and Laboratory Capacity (ELC) mechanism to conduct educational activities to prevent AR in healthcare settings and CA-MRSA, 2) Collaborated with the Association for Professionals in Infection Control and Epidemiology to host a session that featured three institutions that successfully used the Campaign and to reduce catheter-associated infection rates, 3) Collaborated with the Society for Hospital Medicine to develop a toolkit and conduct three workshops (Boston, Denver, Portland) based on the Campaign. 4) Collaborated with the Society for Infectious Diseases Pharmacists to draft a continuing medical education module based on the Hospitalized Adults 12-step Program. 5) Translated educational materials for Hand Hygiene in healthcare settings into Spanish. 6) Assessed dermatologists' knowledge, attitudes, and practices regarding CA-MRSA. 7) Conducted eight focus groups (Atlanta, Houston, New Orleans, Phoenix) with the general public to assess their perceptions.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections	The campaign assists states in implementing broad-based multi-faceted health communication and behavioral interventions to promote appropriate antibiotic use for outpatient upper respiratory infections. State health departments develop broad-based coalitions (e.g., state medical societies, healthcare delivery organizations, healthcare purchasers, consumer groups), use CDC educational materials, develop materials of their own, launch campaigns targeting providers and the general public, and evaluate various aspects of their local campaigns and/or appropriate antibiotic use knowledge, behaviors, and attitudes. Controlled trials have demonstrated success of this program in decreasing inappropriate prescribing; also, nationwide antibiotic prescribing rates for children are declining.	In FY05, 31 local programs were funded (29 program, 2 travel-only). In FY06, 34 local programs were funded (25 program, 9 travel-only). The Get Smart campaign maintains a comprehensive website that funded sites can utilize to gain access to campaign resources and educational tools and to learn more about national campaign activities. The Get Smart campaign conducts regularly scheduled phone calls to provide technical assistance as well as document ongoing activities. In April 2005, Get Smart hosted its sixth annual national conference. The conference brought together over 250 participants including healthcare providers, public health professionals, and representatives from medical professional groups, the pharmaceutical industry, and consumer groups to discuss and share information regarding appropriate antibiotic use.
CDC	Partnerships with healthcare delivery organizations and insurers to promote the appropriate use of antibiotics for outpatient upper respiratory infections	Work with Coalition for Affordable Quality Healthcare to implement educational and behavioral interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections in managed care organizations.	In 2005, CAQH discontinued its domestic antibiotic reistance work, dissolving the Save Antibiotic Strength program. However, the online CME certification program for healthcare personnel, collaboratively developed by CAQH and Get Smart, continues. Between September 2004 and mid 2005, over 900 healthcare personnel have completed the program. Get Smart continues to work with the managed care groups under CAQH.
CDC	Get Smart: A medical curriculum promoting appropriate use of antibiotics: medical students	Developing and promoting three appropriate antibiotic use curricula for providers: Curriculum for medical students regarding appropriate antibiotic use. Topics include extent of antibiotic resistance, diagnostic techniques, and appropriate antibiotic use. Case studies focus on diagnosis, treatment, and provider-patient communication. This course is designed to meet the needs of a variety of medical schools with components that can be used separately or as a whole.	Medical school curriculum, ongoing: CDC and the University of California, San Diego developed and produced a multi-faceted educational curriculum in 2000-2001, which was then pilot tested during the 2002-2003 school year at six medical schools in collaboration with the Association of American Medical Colleges (AAMC). During 2004 the curriculum was updated and revised. In 2005 the revised draft of the curriculum was sent to 25 medical schools to incorporate into their overall curriculum. In order to distribute the curriculum nationwide, it has been cleared by CDC and is undergoing final revision by AAMC. THe curriculum is intented to be distributed nationally during summer 2006.
CDC	Get Smart: A medical curriculum promoting appropriate use of antibiotics: primary care residents	Curriculum for primary care residents on appropriate antibiotic use based on the medical school curriculum.	Primary care residents curriculum, ongoing: The Oregon Health and Science University developed a curriculum for primary care residents based on the medical school curriculum. The resident curriculum is in use in a few Oregon residency programs to pilot test it. After refinement, the curriculum will be used in additional Oregon programs, and later made available nationally.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Get Smart: A medical curriculum promoting appropriate use of antibiotics: family practice and pediatric care residents	Curriculum for family practice and pediatric residents for diagnosing otitis media.	Otitis media curriculum, ongoing: The Children's Hospital of Pittsburgh is developing a curriculum for family practice and pediatric residents to improve training in the diagnosis and treatment of otitis media. However, the development in on hold due to lack of second year funding.
CDC	Reporting antimicrobial susceptibility data to clinicians	Assist CLSI to produce guidelines for clinical microbiology labs on how to compile and report summaries of cumulative antimicrobial susceptibility data (antibiograms) in a standardized manner to aid in clinical decisions. When completed and evaluated, standard reports should improve empiric prescribing, based on data of antimicrobial susceptibility testing and allow comparisons of data among hospitals.	Ongoing. CDC worked with NCCLS/CLSI to developed better reporting guidelines in 2001 and updated these in 2005. Multicenter study showed significant problems in reporting of antimicrobial susceptibility testing results of positive blood cultures. Educational programs to improve reporting practices were conducted in multiple healthcare institutions and repeat proficiency testing to document improvement in practice in now ocurring.
CMS	Surgical Care Improvement Project	All 53 QIOs are working with volunteer hospitals in their jurisdiction and are partnering with Federal and non-Federal agencies and Professional Organizations to look at processes and outcomes involving timing, duration, proper drug selection, surgical site preparation, and post-op complications including pneumonia and surgical infection.	This project will continue into the QIOs next scope of work. The quality improvement project will soon have national, self-collected, hospital data on the proper selection and timing of prophylactic antibiotics for surgery. The other, less mature aspects of SSI reduction and ventlator associated pneumonia reduction are underway with data expected to be available in 2007.
FDA	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).
FDA	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) . FDA/CVM awarded a 5-year cooperative agreement (2001-2006) to develop a web-based decision support system (The Veterinary Antimicrobial Decision System, VADS) for use by veterinarians to select and use antimicrobial agents appropriately. The Veterinary Antimicrobial Decision System continues to be revised and improved. Feedback from users on the data used as well as modeling and interpretation methods are currently being solicited.
Action Item #27: Explore Ways To Integrate Appropriate Use Information into Antimicrobial Package Inserts and Promotional Materials, To Provide Such Information to Patients with Each Prescription, and To Provide Clear Guidance to Industry To Ensure That Promotion of Antimicrobials Directed Towards Consumers Encourages Appropriate Use and Discourages Inappropriate Use.			
CDC	Get Smart: Know When Antibiotics Work - pharmacy initiative: patient monograph project	In 2005, Get Smart developed a partnership with Catalina Health Resource, the largest distributer of prescription packaging advertising in the U.S. The antibiotic adherence message developed as part of the Pharmacy Initiative has and will be placed as ads with antibiotic prescriptions nationwide.	During fall 2005, the Get Smart adherence PSA ran for 6 weeks nationally, due to donations of space from Catalina Health Resource. 13,000 pharmacies were reached along with over 1.25 million people, valuing $1.4 million in advertising cost. A larger scale paid campaign will take place in fall 2006, from partner donations received through CDC Foundation.
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #28: Articulate Factors That Support the Current Approach of Requiring Prescription-Only Dispensing for All Systemic (e.g., Nontopical) Antimicrobial Drugs Used In Clinical Medicine.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #29: Periodically Review and Update Antimicrobial Drug Susceptibility Information Including In Drug Labeling, with Input from Stakeholders and Other Experts, e.g., CLSI and CDC.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #30: Convene an Advisory Panel or Other Expert Group in Involving Stakeholders and Partners To Consider Issues Related to Resistant Pathogens That Cause Serious Infections for Which Available Treatments Options Are Very Limited or Nonexistent.			
FDA, CDC, NIH	Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP)	Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues.	Workshop held April 15-16, 2004. Discussed the use of pharmacodynamic information in appropriate dose selection in clinical trials of anti-infective agents, and summarized the issues with developing antimicrobial drugs by allowing data from one serious disease to be supportive of data in another less serious disease such that sponsors would only have to perform one trial instead of two in the less serious disease. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)
CDC	Experts Meeting: community-onset methicillin-resistant *Staphylococcus aureus*: implications for antimicrobial therapy and potential prevention strategies	These funds will be used to convene a two day meeting of approximately 20-25 experts and stakeholders to discuss issues surrounding the diagnosis, treatment, and prevention of community-associated MRSA infections (CA-MRSA). Participants will include clinical experts and epidemiologists from academic institutions and public health agencies with expertise in community associated MRSA and other Staphylococcal infections, as well as representatives from relevant professional societies (e.g. IDSA, Pediatric ID Society) and potentially representatives from other stakeholder organizations (schools, daycare, athletic associations). Expected products resulting from the meeting include proceedings and plans for guidance documents for clinicians and others on diagnosis, treatment, and prevention strategies for CA-MRSA infections.	A detailed summary of strategies for the clinical management of MRSA in the community, based on discussions held at this meeting, in conjunction with additional data available as of January 2006, is available in pdf format on the CDC website: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca_04meeting.html
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
FDA	Otitis Media Advisory Committee	Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population).	Meeting held on July 11, 2002. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder02.htm#Anti-Infective
FDA	FDA/PhRMA Co-Sponsored Workshop	Discussion of statistical issues in clinical trials including trials related to resistant pathogens.	Meeting held on November 9, 2002.
FDA	FDA/IDSA/PhRMA Co-Sponsored Public Workshop	Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical Research and Manufacturers of America, and U.S. academic institutions along with representatives from CDC and NIH to address current topics of interest associated with AR and antimicrobial drug development.	Meeting held on November 19-20, 2002. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to macrolide-resistant Streptococcus pneumoniae *(* MRSP).	Meeting held on January 24, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to AR in *Streptococcus pneumoniae*.	Meeting held on March 4, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant pathogens.	Meeting held on May 5, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	FDA/NIAID Co-Sponsored Public Workshop	Coordinated a public workshop with the National Institute of Allergy and Infectious Diseases, which brought together top scientists to discuss issues affecting antifungal drug development for febrile neutropenia and combination antifungal therapy.	Meeting held on September 4, 2003.
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of clinical trial design issues for demonstrating the safety and efficacy of antibacterials in the treatment of diabetic foot infections.	Meeting held on October 28, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of clinical trial design issues for studies in acute bacterial sinusitis.	Meeting held on October 29, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Nonprescription Drugs Advisory Committee (NDAC)	Discussion of the microbiologic surrogate endpoints utilized in demonstrating effectiveness of antiseptic products in various healthcare settings.	Meeting held on March 24, 2005. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4099T1.pdf.
FDA	Nonprescription Drugs Advisory Committee (NDAC)	Discussion of the benefits and risks of antiseptic products marketed for consumer use.	Meeting held on October 20, 2005. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4184T1.pdf
Action Item #31: Convene A Working Group To Examine the Impact of Federal Reimbursement Policies for Home Parental Antimicrobial Treatment, Appropriate Antimicrobial Use, and Appropriate Use of Antimicrobial Susceptibility Testing. Where Needed, the Working Group Will Make Recommendations for Modifying These Policies.			
Action Item #32: Develop and Submit Measures for Appropriate Antimicrobial Use to the National Committee for Quality Assurance for Inclusion in Health Plan Employer Data and Information Set (HEDIS), Which Provides Comparative Data on Managed Care Organizations			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Development and testing of Health Plan Employer Data and Information Set (HEDIS) measures for appropriate antibiotic use	HEDIS is a performance measurement tool used by purchasers and consumers to compare many of the nation's leading health plans. In this project, CDC epidemiologists collaborate with experts in the development and testing of HEDIS measures to develop and test one or more measures of appropriate antimicrobial use in children. Measures include rate of prescribing antimicrobial drugs for acute upper respiratory infections and bronchitis; rate of prescribing antimicrobial drugs for pharyngitis where no throat culture or rapid streptococcal antigen test was performed; and episodes of otitis media treated with a recommended first-line agent. When the measure is incorporated into HEDIS, the measure and its impact on physician and patient awareness of appropriate antimicrobial use will be evaluated. Additionally, two new measures were developed and tested during 2004 for adults; the treatment of acute bronchitis and all upper respiratory infections.	In 2002, National Center for Quality Assurance (NCQA) was presented with specifications for two potential measures relating to Appropriate Antibiotic Prescribing for Respiratory Infections for Children. Two measures for children were agreed upon, developed and tested following NCQA's specifications. In 2003 these two measures; one on pharyngitis and one on upper respiratory infections were pilot tested. NCQA reviewed and accepted these measures and they were incorporated into the 2004 HEDIS set. NCQA's Committee on Performance Measurement (CPM) unanimously approved both the adult bronchitis and antibiotic utilization measures for Public Comment. The two adult measures were included in the HEDIS set beginning in 2006. See http://www.ncqa.org/Programs/HEDIS/HEDIS%202004%20Info.htm for more information.
Action Item #33: Evaluate The Potential Impact Of Improved Diagnostic Tests, Including Rapid Point-of-Care Tests on Antimicrobial Drug Use and Patient Care, and Assess Their Financial Implications. Take into Account Tests That Distinguish Between Bacterial and Viral Infections, Tests That Identify Resistant Pathogens, and Tests That Distinguish Common Clinical Entities such as Bacterial Sinusitis and Acute Bacterial Otitis Media from Illnesses with Similar Manifestations for Which Antimicrobials Are Not Beneficial.			
AHRQ	Research career award (K08): randomized trial of sinus CT for acute sinusitis.	This investigator at the University of Washington will develop and implement a randomized controlled study assessing the impact of sinus CT on the use of antibiotics for patients with acute sinusitis. She will also assess clinical outcomes as well as downstream costs related to acute sinusitis. She will develop and validate clinical prediction rules through the randomized clinical trial.	In order to speed enrollment into the study, two additional recruitment sites, the Emergency Department and Student Health at the University of Washington have been added. At the end of April enrollment stood at 34 patients. Opening the follow-up outcome data and cost data await completion of the randomized controlled trial.
CDC	Rapid detection of MRSA colonization to reduce spread within hospitals	This project's focus has been revised to study the dynamics of MRSA transmission in the ICU setting. This information will the be used to institute appropriate infection control measures to decrease the spread of MRSA in high-risk hospital areas.	This projected was completed in 2004. A publication was completed by Warren et al entitled "Detection of Methicillin-Resistant *Staphylococcus aureus* Directly from Nasal Swab Specimens by a Real-Time PCR Assay". This and other related information has been instrumental in supporting efforts for rapid screening for MRSA and for commercial availability of rapid diagnostic tests from manufacturers.
Action Item #34: Identify Economic and Other Barriers in the Health Care System (e.g., Reimbursement Policies by Third Party Payers, Managed Care Practices, Cost Considerations, Empiric Treatment Recommendations, etc.) to Diagnostic Testing That Promotes Appropriate Use of Antimicrobials. Develop Recommendations That Remove Disincentives or Promote Incentives to Such Testing.			
Action Item #35: In Collaboration With Professional Societies, Industry, Health Departments, And Other Stakeholders And Partners, Develop Guidelines for Clinicians And Clinical Microbiology Laboratories To Address Appropriate Specimen Collection, Interpretation, And Reporting Of Susceptibility Tests, And Use Of In-Office Tests For Infection.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Grant Program: Applied Research on Antimicrobial Resistance - Validation of CLSI Breakpoints for Bacterial Human Pathogens	The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of CLSI breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing CLSI methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing CLSI methods and quality control as a starting point for novel test development.	Funding cycle complete. Publications resulting: Reevaluation of Enterobacteriaceae MIC/disk diffusion zone diameter regression scattergrams for 9 B-lactams: adjustments of breakpoints for strains producing extended spectrum B-lactamases. Diagnostic Microbiology and Infectious Disease, Volume 52, Issue 3, Pages 235-246. In vitro susceptibilities of aerobic and facultative Gram-negative bacilli isolated from patients with intra-abdominal infections worldwide: the 2003 Study for Monitoring Antimicrobial Resistance Trends (SMART). J Antimicrob Chemother. 2005 Jun;55(6):965-73. Epub 2005 Apr 22.
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).
CMS	Memo to Proficiency Testing (PT) Providers	In an April 7, 2004 letter to Proficiency Testing (PT) Providers, CMS is requesting all PT providers offering bacteriology to include educational material discussing antimicrobial selection and testing for 2004. During 2005, labs are asked to identify antimicrobial agents and laboratory tests or reports that are inappropriate by NCCLS guidelines, with no penalty attached. Beginning in 2006, inappropriate drug choices will be graded as incorrect results. The PT programs are to use the NCCLS guidelines (M100-S14 Performance Standards for Antimicrobial Susceptibility Testing: Fourteenth Informational Supplement) regarding proper selection of antimicrobial agents for testing and reporting.	Letter distributed 4/7/2004.
Action Item #36: In Collaboration with Professional Societies, Industry, Health Departments, and Other Stakeholders, Develop Guidelines That Address the Use of Clinical Microbiology Laboratories for Use by Health Care Delivery Organizations.			
Action Item #37: Promote the Increased Performance of Direct Examination of Microbiological Specimens (e.g., by Gram Stain or Other Rapid Method) in Circumstances Where Appropriate, Clinically Relevant, and Reliable Information Can Be Garnered, as Readily Available Point-of-Care Diagnostic Test. This Step Will Require Working Within the Framework of the Clinical Laboratory Improvement Amendment (CLIA) Regulations and Involving Medical Education And Health Care Delivery Organizations.			
Action Item #38: Identify Factors That Promote Transmission of Drug-Resistant Pathogens in Healthcare Facilities, in Extended Care Facilities, and in Community Settings, Including Daycare Centers in the Community at Large. These May Include Characteristics of the Facilities and of the Populations They Serve.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Assessing transmission and prevention of community-associated MRSA infection among children, family members and close contacts	We propose a study to a) characterize transmission of CA-MRSA among family members and close contacts of children infected with CA-MRSA, and b) determine effectiveness of different interventions in controlling and preventing CA-MRSA among family members and close contacts of children infected with CA-MRSA. The information gained from this study will help determine interventions that are effective for controlling and preventing spread of CA-MRSA in families and settings where children are at risk for acquiring CA-MRSA (e.g., day care centers). Many health departments are currently receiving requests from parents and day care centers for guidance on controlling and preventing MRSA infections. We anticipate the proposed study can be implemented through existing response and notification activities at a state or local health department.	The Minnesota Department of Health (MDOH) was selected as project site in September 2004. DHQP personnel conducted a site visit to MDOH in September 2004 to meet with MDOH investigators and collaborate on development of protocol.
CDC	Grant program for applied research on antimicrobial resistance: Characterization of strains of Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA)	This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus (S. aureus)* causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques.	Five three-year awards were made in 2003. Recipients include Harbor-University of California Los Angeles Research & Education Institute, University of California at San Francisco, University of Chicago, William Beaumont Hospital, and Columbia University. Funding cycle complete. Numberous publications resulted. "1) Genetic background affects stability of mecA in Staphylococcus aureus." J Clin Microbiol. 2005 May;43(5):2380-3. 2) "Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles." N Engl J Med. 2005 Apr 7;352(14):1445-53. 3) "Incidence of and risk factors for clinically significant methicillin-resistant Staphylococcus aureus infection in a cohort of HIV-infected adults." J Acquir Immune Defic Syndr. 2005 Oct 1;40(2):155-60.
CDC	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).
CDC	See Action Item #21 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #21 (The Chicago Antimicrobial Resistance Project CARP).
CDC	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).

**** TOP PRIORITY ****

Action Item #39: Evaluate the Effectiveness (Including Cost-Effectiveness) of Current and Novel Infection-Control Practices for Health Care and Extended Care Settings and in the Community. Promote Adherence to Practices Proven To Be Effective.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Centers of Excellence in Healthcare Epidemiology (Prevention Epicenters)	Academic medical centers conduct research to improve infection control practices. Current projects address improving antimicrobial use in acute care facilities, the epidemiology of transmission of resistant organisms in the ICU setting, and exploring novel approaches to preventing transmission	Recent activities include: 1) completed a multi-center evaluation of the use of novel approaches to routine skin antisepsis (daily chlorhexidine baths) to reduce transmission of antimicrobial resistant organisms among patients in intensive care units. Data analysis not yet complete.2) Completed a multi-center intervention using post-prescription review as a method of promoting rational antimicrobial use. Preliminay results presented in 2005, final analysis and manuscript preparation pending. 3) Completed a multi-center study that determined baseline incidence of methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE) transmission in 12 intensive care units (ICUs) in five hospitals. The study demonstrated that active surveillance cultures increase detection of MRSA and VRE colonization in ICUs by up to 49%. Manuscripts have been submitted for publication. 3) CDC recently completed competitive renewal of the Prevention Epicenter Program, and the new Prevention Epicenters began their work in February 2006.
CDC	See Action Item #63 (Comprehensive Demonstration Project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities)	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities)	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities)
Action Item #40: Evaluate the Cost-Effectiveness and Impact on Patient Care and Drug Resistance of Medical Devices That Incorporate Anti-Infective Compounds To Prevent Infection (e.g., Anti-Infective Urinary Catheters and Prosthetic Heart Valves). Where Appropriate (e.g., Shown To Be Effective and Not Induce Resistance), Encourage the Clinical Use of These Devices.			
FDA	Devices containing antimicrobials – draft guidance	Draft guidance document for industry: how CDRH intends to regulate devices containing antimicrobial drugs, and what information regarding efficacy and resistance CDRH wants to see in premarket applications (interim until rulemaking is completed).	CDRH is developing a draft guidance document for industry on how CDRH intends to regulate devices containing antimicrobials, and what information regarding efficacy and resistance CDRH wants to see in premarket applications. The issuance of this draft guidance is considered a high priority for CDRH with a projected issuance this fiscal year.
FDA	Standards development seminar	Standards development: seminar to gather information from experts on developing test methods that should/could be used to demonstrate efficacy of antimicrobial agents on devices for use in guidance and rulemaking.	CDRH continues to work with stakehlders outside the Center to develop laboratory methods that will be useful in predicting whether the use of antimicrobials on devices is effective in reducing device related infections.
Action Item #41: Encourage the Development and Implementation of Clinical Alternatives to Those Invasive Medical Procedures That Increase the Risk of Infection in Hospitals and Other Health Care Settings, e.g., Substitutions of Transcutaneous Monitoring of Blood Oxygen Levels of Indwelling Catheters.			
Action Item #42: Evaluate the Benefits and Risks of Incorporating Antimicrobial, Disinfectant, or Antiseptic Chemicals into Consumer Products (e.g., Soap, Toys, Kitchen Utensils, Clothes, Paints, Plastics, and Film Preservatives) and of Applying Disinfectants and Sanitizers to Hard, Non-porous Surfaces such as Food-Contact Surfaces, Hospital Premises, Bathrooms, etc. Consider Whether They Have Any Efficacy in Reducing and/or May Play a Role in Promoting Drug Resistance.			
Action Item #43: Conduct a Public Health Campaign To Promote Hand Hygiene and Other Hygienic Practices, as well as Other Behaviors That Prevent the Transmission of Infectious Organisms, in Collaboration with Professional Societies and Stakeholders. This Campaign May Be Coordinated with the Public Health Education Strategy To Promote Appropriate Antimicrobial Use Described in Action Item #25: Prevention and Control.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Get Smart: Know When Antibiotics Work (hand hygiene)	One strategy the Get Smart: Know When Antibiotics Work campaign utilizes to promote appropriate antibiotic use in the community is to provide funding to states and local communities to develop tailored campaigns. Although on a national level hand hygiene is currently not promoted, many of the state and local level sites have chosen to focus on preventing viral illnesses through proper hand hygiene. Campaigns in Michigan, Nevada, and Minnesota have developed educational materials and/or trainings on the basics of hand hygiene in various settings.	Hand washing campaigns on the state and local level to promote the transmission of viral illnesses are currently funded and being implemented in six sites.
CDC	"It's a SNAP" handwashing campaign	CDC is collaborating with the Soap and Detergent Association to launch the second year of an education-based effort for middle level school communities to improve health by making hand cleaning an integral part of the school day.	Ongoing. Vist SNAP at: http://www.itsasnap.org/index.asp
Action Item #44: Facilitate and Support the Activities of Infection Control Programs in Health Care Settings as a Component of Medical Care. Promote Infection Control Education at all Stages of Training and Practice for all Health Care Workers Who Have Contact with Patients.			
CDC	Dialysis best practices project	This study was designed to identify prevention practices that are effective at preventing dialysis catheter-associated bloodstream infection rates. Participants were recruited from the Dialysis Surveillance Network, a network of > 60 dialysis centers reporting bloodstream infection rates to CDC. Onsite observations of adherence to recommended prevention practices were performed in over 20 dialysis centers, with the intention of correlating observed prevention practices with reported infection rates.	The project has been completed. The information was used to create an intervention toolkit that can be utilized by dialysis centers for preventing catheter-associated bloodstream infections. Manuscripts desribing gaps between recommended and observed practices and policies in preparation.
Action Item #45: Support Ongoing Public Health Education Campaigns on Food Safety, such as FDA and USDA's Fight BAC Program, Whose Aims Are To Educate Food Producers, Retailers, and Consumers About Food Safety Practices That Reduce Foodborne Infections (Including AR Infections).			
CDC, USDA, FDA	Children Fight BAC!: A Scientific, Interactive Food Safety Instruction Program	Utah State University used instructional computer simulation modules to teach students about the science behind the USDA's Fight BAC! public education program, while encouraging them to adopt recommended food safety behaviors.	Terminated. Funded through CSREES, National Integrated Food Safety Initiative. The Children Fight BAC! instructional modules were evaluated for functionality and instructional capability in six, sixth grade Technology, Life, and Careers classes. One hundred and thirty students participated in the classroom evaluation. Three classes learned about food safety using the modules with a teacher-led instruction, the other three classes learned about food safety using the modules through student-led exploration. The program evaluation included a pre-test and food handling observation, observation during program use, a post-test and food handling observation, and a one-month post test. Results show that teacher-led and student-led uses of the modules are equally effective instructional methods. One month after using the modules, sixth grade students had a 24% increase in retained food safety knowledge and an 80% increase in time spent washing hands during in-class food preparation activities.
Action Item #46: Educate the Public About the Merits and Safety of Irradiation as One Tool To Reduce Bacterial Contamination of Food.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Food Irradiation Education	CDC has produced a FAQ document on the promising benefits of food irradiation. Designed to education the public and discredit any myths about the process.	Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/foodirradiation.htm
Action Item #47: Support Community-Based Programs That Promote and Facilitate Availability of Recommended Vaccinations for Adults and Children.			
CDC	National Immunization Program (NIP)	NIP's mission is to reduce disease and disability from diseases that can be prevented through immunization.	Numerous ongoing projects support state and community-based programs that promote vaccination and provide vaccines.
CMS	Reduction of Healthcare Disparities Initiative	Quality Improvement Organizations (QIOs) at the Statewide level, are working to improve clinical performance measure results for the six clinical quality indicators in the area of diabetes, mammography, and adult immunization (increasing pneumonia and influenza vaccinations in adults) for underserved racial/ethnic populations.	Ongoing effort and is in the current QIO scope of work. Numerous ongoing projects to support community based programs that promote adult vaccinations.
Action Item #48: Identify Vaccines Useful in Preventing Drug-Resistant Infections and Reducing Antimicrobial Drug Use and Evaluate Novel Methods For Improving Coverage with These Vaccines.			
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	Four CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in nine Emerging Infections Program areas in which population-based active surveillance is conducted. Second, ongoing active surveillance in these areas will track any change in the amount of invasive disease due to drug resistant strains. The third project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The fourth is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees.	Completed reports have been either submitted or published for all four projects. The case-control study enrolled 782 cases and 2512 controls. Effectiveness for ≥1 dose against vaccine serotypes was 96% among healthy children and 81% among children with comorbid conditions; effectiveness was 76% against penicillin-nonsusceptible infections (Whitney et al, submitted). ABCs surveillance is ongoing indicates that by 2004 disease due to penicllin-resistant strains had dropped by over half (Kyaw M et al N Engl J Med 2006). In Anchorage, carriage study results suggest that introduction of PCV7 into the routine infant immunization schedule in a community with a high prevalence of resistant pneumococci appears to reduce transmission of PCV7 vaccine serotypes and COT-NS pneumococci but has no impact on overall carriage of pneumococci.(Moore MR et al J Infect Dis. 2004). Alaska surveillance data also show a reduction in invasive infections caused by resistant strains (Hennessy TW et al Vaccine 2005).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Drug resistant *Streptococcus pneumoniae* in rural Alaska villages: impact of PCV7	This project is designed to evaluate the impact of the new infant vaccine for *Streptococcus pneumoniae* (PCV7, Prevnar7) on nasal colonization of children living in 8 villages in rural Alaska. The vaccine is expected to reduce nasal colonization of vaccine-type bacteria which, in turn, may reduce colonization of drug-resistant bacteria since vaccine-types are most likely to be drug-resistant. Thus, the vaccine may prevent serious disease (meningitis, blood stream infections) and may also help prevent drug-resistant infection, a growing problem among pneumococci.	Completed pneumococcal colonization survey of 2,870 persons living in 8 rural Alaska villages. Annual surveys done 1998-2004. Data included microbiologic characterization of colonizing pneumococci including antimicrobial susceptibility, antibiotic use and PCV7 vaccine use. Key findings are: 1) Overall colonization with pneumococci similar to 2003 (41%) PCV7 uptake remains high with 80% of children < 5 years old age appropriately vaccinated. 2) Colonization with vaccine serotypes has continued to decline and is now at the lowest point since the project began in 1998. Only 5% of colonized persons of all ages carried one of the vaccine types as compared with 41% of persons during 1998-2000 ($P < 0.001$). 3) Colonization with antibiotic resistant pneumococci has continued to decline for isolates non-susceptible to ceftriaxone, tetracycline and erythromycin. 4) Observed a decline in colonization of isolates fully resistant to penicillin (-58%) since introduction of PCV7.
CDC	ABCs special projects on pneumococcal resistance: prevention using vaccine and risk factors for fluoroquinolone resistance	This proposal seeks funding to complete two ongoing case-control studies being conducted in ABCs areas. The purpose of the first project is to evaluate the effectiveness of pneumococcal conjugate vaccine in children 3-59 months of age. The study began enrolling in FY 2001 and by the end of FY 2003 had enrolled 3031 children in eight ABCs areas; in FY 2004, study personnel will be enrolling children 24-59 months of age for one additional year to meet an objective of assessing effectiveness specifically for that age group. The purpose of the second project is to identify risk factors for invasive disease in adults caused by fluoroquinolone-resistant pneumococci. Cases are adults with invasive pneumococcal disease caused by a fluoroquinolone-resistant strain; 2 controls are selected for each case from subsequent cases caused by susceptible strains in adults. This study is ongoing in 9 ABCs areas and, based on our sample size estimates, will continue until Spring 2005.	Nearly complete. The vaccine effectiveness study has been completed and a manuscript submitted (see #98). A total of 91 cases with matching controls were enrolled into the study of risk factors for flouroquinolone-resistant infections. In multivariate analysis, nursing home residence and exposure to fluoroquinolones in the 3 months prior to disease were risk factors for infection with fluoroquinolone-resistant disease (Kyaw et al ICAAC 2005 abstract). A manuscript is in preparation.
FDA	New and licensed vaccines of AR importance	Maintaining supply of currently licensed vaccines and facilitating the development and licensure of new vaccines of AR importance.	Approved numerous supplements to BLAs for vaccines and therapeutics against diseases such as pneumococcus, diphtheria, tuberculosis (BCG), typhoid, Haemophilus influenzae, pertussis, and influenza. These approvals allow for the continued manufacture of these vaccines. Conducted review of information regarding safety and efficacy of novel vaccines and therapeutics for infectious diseases with AR importance, i.e. staphylococcus, pneumococcus, mycobacteria, shigella, meningococcus and other Neisseria sp., malaria, influenza, RSV, HIV, HSV (approximately 100 active INDs.
FDA	*H. influenzae* type B (HIB) vaccine	Monitoring of polysaccharide conjugated vaccines, including regular inspections of the production facilities, review and conduct of Lot Release studies, and review of amendments to the current Biologic License Applications.	Several licensed vaccines. Continued vaccine supply essential to maintaining the near eliination of resistance *H. influenzae* disease in the U.S.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Pneumococcal vaccine	Monitoring and guidance provided to current manufacturer of a seven-valent conjugate vaccine. One licensed multivalent polysaccharide vaccine for the elderly. Facilitating clinical development of a more immunogenic vaccine for the elderly. Facilitating availability of new vaccines and continued availability of licensed vaccines through IND and BLA review, and research leading to imporved process, identification of surrogate endpoints, product and assay validation	One licensed polysaccharide and one licensed conjugate vaccine for the prevention of invasive disease and accute otitis media. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants. Since Prevnar's introduction in 1999, the vaccine is proving to be highly effective in reducing the burden of pneumococcal disease in children, with accompanying evidence of a decrease in the antibiotic resistant strains causing disease. For example, the proportion of resistant strains of pneumococcus has fallen from 59.8% to 30.4% in Tennessee (Talbot, TR, et.al., CID 2004:39, 641-648). And, the use of the conjugate vaccine in children has substantially benefited older adults, resulting in a 28% decrease in invasive pneumococcal disease in adults >50 years (Lexau, CA, et. al., JAMA, 294(16)2043-2051).
FDA	Influenza vaccine	Regulatory and research support of annual trivalent inactivated and live intranasal influenza vaccine development, production and licensure, including additional manufacturers and novel technologies. Facilitating expanding indication to additional age groups and select immunocompromised populations.	Ongoing regulatory review, research support and guidance for both current vaccines and those vaccines under IND, including vaccines against avian influenza.
FDA	Pertussis vaccine	Regulatory and research support for expanding the use of pertussis vaccine into additional age groups (ie: adolescent/adult use and possibly neonatal use).	Approval for adolescent and adult use. Participated in First International Neonatal Vaccination Workshop in March 2004. Also, participating in collaborative study with FDA, CDC and Vanderbilt University to establish a serologic diagnostic cut-off point for pertussis infection in adolescent/adults (NHNES study). Pending approval for adolescent and adult use.
FDA	Shigella vaccine	Developing a prototype live-vectored oral vaccine containing protective antigen genes from Shigella. Goal is to construct a single vaccine for protection against all major serotypes of Shigella.	Ongoing.
USDA	See action item #4 (Implementation of the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE)).	See action item #4 (Implementation of the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE)).	See action item #4 (Implementation of the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE)).
USDA	Comparison of antimicrobial resistance in Salmonella, E. coli, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia	The epidemiology of Salmonella, Campylobacter, Enterococcus and E.coli on swine farms using three different antimicrobial regimens was assessed. Results indicated that more resistance was identified in bacteria isolated from the farm using antimicrobials both sub-therapeutically and therapeutically. However, resistant bacteria were found to persist on the farm that has not used antimicrobials for the past 30 years.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
Action Item #49: Evaluate the Nature and Magnitude of the Impact of Using Various Antimicrobial Drugs as Growth Promotants in Different Species, Using Current Animal Husbandry Practices. Use This Information To Assist in Risk-Benefit Assessments of Such Use.			
CDC	See Action Item #50 (Reducing resistant bacteria in food animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #50: Conduct Additional Research To Further Define the Effects Of Using Various Veterinary Drugs on the Emergence of Resistant Bacteria That Infect or Colonize Food Animals of Different Species, Using Various Animal Husbandry Practices. Identify Risk Factors and Preventive Measures to Humans.			
CDC, FDA	Reducing resistant bacteria in food animals	Projects assess the impact of antibiotic use in swine, cattle, and diary cattle to develop alternatives to the use of antimicrobial drugs as growth promotants, and evaluate new practices to reduce resistant bacteria in food animals.	Ongoing. Get Smart: Know When Antibiotics Work on the Farm was developed under the greater Get Smart: Know when Antibiotics Work Campaign. We are currently engaging health departments across the country to design antimicrobial resistance education projects they can implement in their own state. Monies received from grants and from industry partners will be used to help fund state and federal projects. Get Smart: Know When Antibiotics Work on the Farm will be a contributing member to the Get Smart conference in May 2006 and to the greater Get Smart campaign.
USDA	Dethroning the King of the Gut: The impact of first choice microbials on E. coli resistance phenotype	This project examines the impact of the most popular animal antibiotics on developing resistance in a sentinel organism, E. coli. The methods described will serve as a foundation for future methods that examine issues relevant to both human and animal health. These include the impact on developing resistance of: other clinically important antimicrobials drugs, non-antimicrobial drugs (ie, anticancer drugs), patient factors which increase the risk of developing resistance (ie, immunosuppression, stress, etc) mechanisms by which developing resistance might be muted (ie, combination antimicrobial therapy, probiotic therapy).	New CSREES grant. Awarded to Auburn University, D. Boothe
USDA	Antimicrobial Drug Use and the Development of Resistant Enteric Bacteria in Dairy Cattle	Antimicrobial drugs are commonly used in food animal production for the treatment of disease adn the enhancement of animal production. Recently, this use has been implicated as a potential cause for emergence of antimicrobial-restistant bacteria of public health concern. The purpose of this study is to determine the effect of antimicrobial treatment on the development of resistance in bacteria present in cattle, develop and apply prudent antimicrobial-use guidelines specific for dairy cattle and to disseminate these guidelines to dairy producers and their veterinarians.	CSREES grant awarded to Ohio State University, Wittum, T.E. through the National Integrated Food Safety Initiative Program.
USDA	See Action Item #49 (Comparison of antimicrobial resistance in Salmonella, E. coli, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)	See Action Item #49 (Comparison of antimicrobial resistance in Salmonella, E. coli, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)	See Action Item #49(Comparison of antimicrobial resistance in Salmonella, E. coli, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)
Action Item #51: Conduct Epidemiologic And Laboratory Studies To Assess the Risk of Development and Transfer of Resistance Related to The Use of Antimicrobial Drugs in Food and Non-Food Plants, and Identify Risk Factors and Potential Preventive Measures.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Antibiotics used as pesticides in orchards	Apple and pear orchard farmers have used streptomycin to control the plant disease fireblight, a bacterial infection caused by *Erwinia amylovora*, since the 1950s. After years of streptomycin use, streptomycin-resistant strains of *E. amylovora* developed. Farmers now use oxytetracycline in *E. amylovora* resistant areas to control fireblight. In this pilot study involving 4 orchards in 3 states, fruit is tested to determine whether human pathogens, including antimicrobial-resistant organisms, are present in orchards and whether antibiotic residues are potentially reaching the food supply.	Completed specimen and laboratory testing . Manuscript draft completed awaiting editorial review and clearance.
CDC	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).
CDC	See Action Item #55 (Evaluation of the impact of flooding on water quality and human health indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).
USDA	To characterize Salmonella serotypes on their ability to cause disease in animals and to acquire and disseminate antimicrobial resistance genes.	Although there are over 2,400 different serotypes of Salmonella, they differ in their ability to cause disease in humans and animals, acquire resistant attributes, and colonize and persist with the host and environment. Salmonella serotypes were first characterized by their antimicrobial resistant pattern followed by molecular characterization in which mechanisms of resistance and genetic relatedness among other isolates of the same serotype were determined. These data demonstrated that Salmonella serotypes differ in their ability to persist within the host and environment and have determined that both integrons (mobile genetic elements) and plasmids, play a role in dissemination of resistance genes.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA. Poultry Processing and Meat Quality Research Unit, Poultry Microbiology Safety Research Unit, and the Eastern Regional Research Center in Philadelphia.
USDA	Study the prevalence of resistant in Mexico in E. coli populations	The prevalence of and risk factors for, fecal quinolone-resistant E.coli (QREC) in children from Yucatan, Mexico. WREC was higher in children with recent Salmonella infection than in children with diarrhea or healthy children. Recent hospitalization of a family member and carriage of Salmonella were identified as independent risk factors. These data indicate that novel strategies are required to measure the significance of these findings and that QREC should be closely monitored.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Feedlot Practices and their Impact on pre- and post- harvest antimicrobial susceptibility patterns of enteric bacteria.	This study will evaluate the effect of both subtherapeutic and therapeutic antimicrobial use in feedlot cattle on antimicrobial resistance and pathogen load in animals and on their carcasses.	Awarded 2004 (3 year grant -- Ongoing). G. Lonergan, West Texas A&M. Funded by CSREES, NRI's 32.1 Epidemiologic Approaches to Food Safety. This research will provide a scientific evaluation of the impact of antimicrobial drugs in feedlot production. It will also determine the sources of bacterial contamination of carcasses in relation to bacterial carriage by cattle entering plants. The data generated to date provide an estimate of bacterial load across time and entering packing plants.
Action Item #52: Develop Rapid Tests For Inspecting Fresh Commodities Like Fruit For Evidence Of Contamination With Bacteria That Are Resistant To Antibiotics.			
FDA	Rapid methods development	Validated culture methods for foodborne pathogens in animal feeds.	Extramural contract with University of Tennessee completed. Final report being prepared. Collaboration with USDA-Agricultural Marketing Service to determine antimicrobial susceptibilities among Salmonella and *E. coli* isolates recovered from produce obtained from the microbiological data program plan.
FDA	Rapid methods development	Development of rapid diagnostic methods to detect biological contamination of foods. Have developed and evaluated several microarray-based assays for detection of resistence genes for Streptococcus and Staphylococcus species.	Ongoing
Action Item #53: Evaluate the Effect of Current Food Processing and Distribution Methods on the Emergence and Spread of Drug-Resistant Organisms.			
FDA	NARMS retail food	Monitor prevalence of antimicrobial resistant zoonotic pathogens and commensal organisms among foods of animal origin.	NARMS retail was initiated in 2002, as of 2005, 10 of 11 FoodNet sites are participating. NARMS retail meat annual reports have been published and can be found on the NARMS website http://www.fda.gov/cvm/narms_pg.html. FDA is currently involved in publishing the 2004 annual report. FDA is also collaborating with USDA to characterize antimicrobial resistant patterns among Salmonella and E. coli obtained from their Microbiological Data Program (MDP). Also, see comments to action items # 2 & 17.
Action Item #54: Identify and Evaluate New Food Pasteurization Strategies.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Strategic Planning Meeting for Emerging Food Processing Technologies Workshop	National Program Leaders at CSREES coordinated an Emerging Food Processing Technologies workshop. The agenda included: "Historical Review of Development of Modern Food Processing Technologies by Daryl Lund from University of Wisconsin, Madison, "Commercialization of Emerging Technologies for Meal Solutions, by Ash Husain, from ConAgra, and "Predicting Microbial Inactivation Kinetics for Emerging Preservation Technologies -- Future Challenges" Dennis Heldman, Heldman Associates; High Hydrostatic Pressure: Daniel Farkas (Oregon State University); Ohmic Heating: Sudhir Sastry (Ohio State University); Ultrasound: "Power ultrasound", Hao Feng (Food Science and Human Nutrition, University of Illinois, Urbana-Champaign).	Terminated
USDA	A project directors meeting is scheduled to be held at CSREES headquarters for the NRI 71.1 Competitive Grants program, Improving Food Quality and Value where	Project directors will provide presentations and opportunities for discussion of "Thermal and electrical conductivity of selected foods under high pressure" being peformed at Ohio State University by V.M. Balasubramaniam and "Understanding Microwave Combination Heating through Modeling and Experiments" being conducted at Cornell University by Ashim Datta.	The CSREES project directors meetings are held annually and are a mandatory post award activity.
USDA	Pressure assisted thermal processing: Key engineering properties and process improvements.	The researchers propose to measure properties (thermal conductivity, specific heat, density, and electrical conductivity as function of pressure and temperature) of foods in-situ under high pressure processing, using a specialized, instrumented four-chamber pressure vessel. A further hurdle to development of PATP is the slow, cumbersome method of preheating products before loading into a pressure vessel. The researchers propose to address this issue by investigating three methods for preheating that may reduce thermal exposure - conventional heating, microwave preheat and an in-situ ohmic preheat. The study will provide an improved body of knowledge regarding thermal distributions during and contribute to the development of database on properties of food materials under pressure.	CSREES grant (FY 2005) awarded to Ohio State University, Balasubramaniam, V. M through the NRI 71.1 Improving Food Quality and Value Competitive Grants Program.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Models for Safety, Quality and Competitiveness in Food Processing: A workshop	The food industry currently benefits only minimally from the revolution in computer-based technologies. To increase the efficiency and competitiveness of product, process and equipment designs for value-added foods, computer-based technologies need to be more customized to food processing, integrated between several disciplines and thus appropriately developed. This customized development requires careful consideration of the specific needs of the food processing/distribution/storage sector. The objective of this workshop is to develop needs, direction, guidance and awareness leading to the enabling of simulation technology for predicting/forecasting safety of foods processed/stored/transported in various ways. Once developed, the user of such simulation technology would be able to check 'what if' scenarios to prevent/minimize health risks from pathogens and chemicals.	CSREES grant (FY 2005) awarded to Cornell University, Data, A. through the NRI 71.1 Improving Food Quality and Value Competitive Grants Program.
Action Item #55: Assess the Risk of AR Emergence and Spread due to Environmental Contamination by Antimicrobial Drugs or by Resistant Bacteria in Animal and Human Waste. Collect Information on Whether Environmental Contamination by Antimicrobial Drugs Can Lead to the Development of Resistance in Bacteria That Live in Soil or Water.			
CDC	Sampling for antibiotics in an agricultural river basin	Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities.	Final sampling was completed in winter of 2005-2006. Samples currently being analyzed by USGS laboratory. Expect sampling data and water sample results by June 2006.
CDC	Evaluation of the impact of flooding on water quality and human health indicators	Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water.	Results of human subject sampling did not indicate an association between water quality and incidence of antibiotic resistance in pathogenic microbial isolates from human subjects. This project is finished. Presentations and Publications include: Environmental and Occupational Risk Factors for Intestinal Colonization with Antibiotic Resistant *Escherichia coli* and Enterococcus sp: A Pilot Study in Rural North Carolina. C.A Ohl, V.A. Varela, K. Johnson, T. Morris, D. Campell, J. Tysmans, T. Karchmer, C Rubin, N. MacCormack. Abstract for presentation to American Society for Microbiology Detection and Occurrence of Antimicrobially Resistant Enteric Bacteria on or Near Swine Farms in Eastern North Carolina. 2003. Final Report. Mark D. Sobsey and Maren E. Anderson.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Animal production studies	Determine dynamics of resistance development in naïve animal populations exposed to antimicrobial agents.	FDA/CVM has completed two animal studies focusing on the dynamics of resistance development in naïve animal populations exposed to antimicrobial drugs. These two studies both used poultry models and examined either fluoroquinolone resistance development in Campylobacter after exposure to veterinary approved fluoroquinolones (McDermott et al. 2002. J. Infect. Dis. 185:837-840) and emergence and carriage of streptogramin resistance in enterococci exposed to the veterinary streptogramin, virginiamycin (McDermott et al. 2005. Appl. Environ. Microbiol. 71:4986-4991).
USDA	See Action Item #19. Enhance overall understanding of pathogens that pose a food-safety risk particularly from the environment.	See Action Item #19. Enhance overall understanding of pathogens that pose a food-safety risk particularly from the environment.	See Action Item #19. Enhance overall understanding of pathogens that pose a food-safety risk particularly from the environment. Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
Action Item #56: Assess the Impact of Antimicrobial Use in Companion Animals (Pets) on Colonization and Infection with Drug-Resistant Organisms in The Animals and Their Humans Household Contacts.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #57: Work with Veterinary and Agricultural Communities To Help Educate Users of Veterinary and Agriculture Antimicrobials About AR Issues, and Promote the Implementation and Evaluation of Guidelines That Address These Issues.			
CDC	Fund and develop state-based educational programs to promotoe appropriate antimicrobial drug use	Several states are developing state based education programs in collaboration with agricultural industry groups to educate veterinarians and animal producers on appropraite antimicrobial drug use. Funding for these projects is provided by the Get Smart: Know When Antibiotics Work on the Farm program.	Ongoing. Continuing development of educational materials with partners at Tacoma-Pierce County Health Department in Tacoma Washington. A KAP survey of dairy producers was completed and educational materials were distributed to all of the state's dairy producers. The project is now evaluating six dairy farms for antibiotic use best practices. All other state programs were discontinued due to lack of funds.
CDC	Development of model veterinary school curriculum to promote appropriate antimicrobial drug use	A curriculum is being developed in collaboration with partners that will be offered to veterinary schools. Completed curriculum will consist of Background Module and several Species Specific Modules (dairy cattle, small animal, poultry, etc.).	Ongoing. Continuing development of Web-based course material with partners at Michigan State University, College of Veterinary Medicine and the University of Minnesota, College of Veterinary Medicine. A background module is complete and is posted to the web. Subject matter experts have reviewed the several modules of the curriculum including an exotics module, a dairy modules, and an international module. A beef specific module has been written and a swine module and companion animal module are under development. Other experts are being sought out to write additional species specific modules. It is expected to have the background module and several species specific modules completed and in use by Fall 2006.
CDC, FDA, USDA	Liaison with American Veterinary Medical Association Steering Committee on Antimicrobial Resistance	Participate in committee activities, including development of prescribing principles and educational programs.	AVMA disbanded committee in 2005. The committee developed General Principles for Judicious Therapeutic Use of Antimicrobial (1998), which were then adapted by species groups for their membership, to date including swine (1999), poultry (2000), bovine (2000), feline (2001), and equine (2001). Implementation is promoted through educational programs and a computerized veterinary decision support system, which is under development.
USDA, FDA	Education programs to producers	University based programs to educate producers on the difference between A.R. and residues.	Finished. D. Moore, University of California. The educational materials have been distributed by web-based programs and CD-ROM.
FDA	Education/outreach materials	Develop outreach material on judicious use targeted to veterinarians.	Ongoing activity.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY ****			
Action Item #58: In Consultation with Stakeholders, Refine and Implement the Proposed FDA Framework for Approving New Antimicrobial Drugs for Use in Food-Animal Production and, When Appropriate, for Re-Evaluating Currently Approved Veterinary Antimicrobial Drugs.			
FDA	Drug categorization	Develop an approach for how to evaluate drugs as to their importance in human medicine for use in animal drug premarket application requirements for use in CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Pre-approval assessment of microbial safety is described in a final guidance for industry (GFI # 152), Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern. Appendix A of the guidance document 152, ranking of antimicrobial drugs with respect to human health importance, was developed by FDA Center for Drug Evaluation and Research and the FDA CDER Anti-Infective Drugs Advisory Committee. The final guidance was published on October 23, 2003, and presents a regulatory pathway sponsors can use in seeking approval of an antimicrobial in a food-producing animal. FDA also participated in a WHO consultation on developing criteria for the ranking of antimicrobial drugs based on their importance in human medicine held in Canberra, Australia in February 2005. FDA also participated in an OIE consultation on developing criteria for the ranking of veterinary critically important antimicrobials.
FDA	Fluoroquinolones	Withdraw approval of fluoroquinolones for use in poultry	Sarafloxacin voluntarily withdrawn April 30, 2001; hearing requested for Bayer's enrofloxacin. The Final Rule withdrawing approval of the antimicrobial drug enrofloxacin for the purpose of treating bacterial infections in poultry was effective on September 12, 2005.
FDA	Risk assessment	Risk assessment: Conduct an analysis of the relationship between emergence of streptogramin-resistant *Enterococcus faecium* (Synercid) in humans and use of streptogramins (virginiamycin) in food-producing animals.	Draft risk assessment published November 23, 2004; public comment period through February 25, 2005. Comments were received from a broad range of interested stakeholders, including representatives of consumer groups, the animal drug industry, veterinarians, and infectious disease physicians. The draft risk assessment is available at: http://www.fda.gov/cvm/Documents/SREF_RA_FinalDraft.pdf. FDA/CVM will revisit the risk assessment at a time dictated by the availability of new data and scientific developments in streptogramin resistance.
FDA	Pathogen load	Develop guidance relating to antimicrobial drug effects on pathogen load and incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Literature review published on CVM website May 2001. Veterinary Medicine Advisory Committee meeting held January 22-24, 2002. Based on the lack of scientific consensus on the issue, CVM has decided not to pursue guidance regarding pathogen load effects at this time.
FDA	Microbiological safety requirements	Develop pre-approval requirements for microbiologic safety regarding the use of antimicrobial agents in food-producing animals. Incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiologic effects on bacteria of human health concern.	Draft guidance for industry was published in September 2002. Public meeting was held in October 2002 to present guidance document and obtain public comment. Comment period from the guidance closed in November 2002 and an analysis of comments received has been completed. Final guidance was published in October 2003. Several drugs have been approved using the guidance.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Antimicrobial use in food-producing animals	Develop rulemaking relating to annual reports of use and quantity of antimicrobial drugs marketed for food animals	Participated in WHO expert consultation on monitoring drug use in September 2001. Developed draft proposed rule and guidance. FDA is holding proposed rule and guidance while assessing economic impact of the proposed regulation. No change.
FDA	Framework document	Refine the Framework Document and incorporate the concepts into guidance for industry on a strategy for assuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Comments from public meetings and submitted to the Framework Document have been incorporated into guidance; small, outreach meetings held with stakeholder groups throughout 2001 for additional input. Key concepts from the Framework Document have been incorporated into the draft guidance for industry published in November 2002. Final guidance was published in October 2003. http://www.fda.gov/cvm/VMAC/antimi18.html
Action Item #59: Strongly Encourage Involvement of Veterinarians in Decisions Regarding the Use of Systemic Antimicrobial Drugs in Animals, Regardless of the Distribution System Through Which the Drug Is Obtained (e.g., Regardless of Whether a Prescription Is Required To Obtain the Drug).			
FDA	Educational materials	Develop outreach materials on judicious use targeted to food animal producers.	In 2002, CVM published four booklets that explain prudent use principles in depth for beef, dairy, swine and poultry practitioners. AVMA provided CVM with the names, mailing addresses and types of practices of its members, so CVM was able to send the appropriate booklet to practitioners. CVM also produced two videotapes to be used at meetings to introduce practitioners and food animal producers to the prudent drug use principles. The Center also shipped copies of the tape to veterinary medical schools across the United States. In 2006, CVM in cooperation with AVMA, published a document on judicious use of antimicrobials in aquatic animals for veterinarians.
FDA	AR use by veterinarians	Develop a Web-based decision support system for use by veterinarians to select and use antimicrobial agents appropriately.	FDA/CVM awarded a 5-year cooperative agreement (2001-2006) to develop a web-based decision support system (The Veterinary Antimicrobial Decision System, VADS) for use by veterinarians to select and use antimicrobial agents appropriately. The Veterinary Antimicrobial Decision System continues to be revised and improved. Feedback from users on the data used as well as modeling and interpretation methods are currently being solicited.
Action Item #60: Evaluate the Potential Impact of Making All Systemic Veterinary Antimicrobial Drugs Available by Prescription Only.			
Action Item #61: Convene an Expert Group To Consider How To Incorporate AR Issues into Regulations Governing the Registration and Use of Antimicrobials and Antibiotic Pesticides. Invite External Experts, Stakeholders, and the Public To Provide Input.			
Action Item #62: Establish an Ongoing Mechanism To Obtain Periodic Input from External Experts on AR Issues. This Process Will Include Ensuring Input from Stakeholders and Partners (e.g., State and Local Health Agencies, the Private Sector, and the Public) in Developing and Reviewing Federal Efforts To Address Antimicrobial Resistance.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
ARHQ, CDC, CMS, DoD, HRSA, USAID, VA, EPA, FDA, NIH, USDA	Antibiotic resistance task force	Annual Progress Report and Public Meeting.	In 2004, progress report issued consisting of inventory of projects that address Action Plan items. Fourth annual public meeting June 29, 2005, Bethesda, MD. Convened consultants meeting to discuss issues relating to writing of Part II of the Action Plan (Global Issues), September 26, 2002, San Diego, CA. Sent Task Force Representative to World Health Organization to help WHO implement Global strategy on AR.
**** TOP PRIORITY **** **Action Item #63: Support Demonstration Projects To Evaluate Comprehensive Strategies That Use Multiple Interventions To Promote Appropriate Drug Use and Reduce Infection Rates.**			
CDC	Wisconsin Antibiotic Resistance Network (WARN)	The Wisconsin Antibiotic Resistance Network (WARN) is a statewide program to reduce antibiotic overuse and reduce the spread of resistant bacteria that cause upper respiratory illnesses. WARN is a partnership between the State Medical Society of Wisconsin, the Marshfield Medical Research Foundation, and the Wisconsin Division of Public Health. Activities include antimicrobial susceptibility testing; implementation and evaluation of educational interventions for the community, health departments, and health professionals, pharmacy outreach, and economic analyses to determine intervention costs.	The Coalition operates out of the Center for Community Outreach, Marshfield Clinic, Marshfield, Wisconsin. In addition, the WARN program continued activities intended to raise awareness and knowledge among parents and providers about appropriate antibiotic use. These activities resulted in approximately 12 CME presentations by members of the WARN Speakers Bureau, a revised and updated WARN Web site, informational mailings to over 5,000 day care providers and 9000 primary care providers, and the mailing of the new "Guidelines for Antibiotic Prescribing in Primary Care" brochure to 9000 clinicians and pharmacists. In addition, WARN developed policy statements for Telithromycin, Ciprofloxacin, and the judicious use of antibiotics during a Pertussis outbreak. Manuscripts on the WARN initiative were published in Preventive Medicine and Emerging Infectious Diseases. As of 2006, the WARN program is no longer receiving program support funds from CDC/Get Smart.
CDC	The Chicago Antimicrobial Resistance Program (CARP)	CARP is a 5-year demonstration program to determine the impact of antimicrobial use and infection control interventions on the reduction of antimicrobial resistance in a healthcare delivery system. Components include developing improved methodology for interhospital and intrahospital comparisons of AR rates, computer-based surveillance of antimicrobial drug use, and interventions to improve antimicrobial drug use and prevent emerging resistance	Recently completed a randomized controlled trial to compare prospectively the extent to which three approaches – provision of routine prescribing guidelines available at the time of ordering, intensive education of providers, and electronic surveillance with realtime intervention as needed by clinical pharmacists. Preliminary results presented at 2006 Annual Meeting of the Society for Healthcare Epidemiology of America.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities	This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania.	The success of the initial interventions in two area hospitals has attracted interest and participation from other healthcare facilities in the region, and the organization of the regional prevention initiative continues to mature. Milestones include: • 19 regional hospitals have committed to the MRSA prevention initiative, and the group has elected to use CDC's National Healthcare Safety Network (NHSN) for regional data collection. Pilot data submission has begun in two pilot hospitals, with plans to pilot in an additional 7 hospitals prior to expanding to all participants in the region. • Regional third party payor (has initiated an pilot, voluntary, pay-for-performance initiative among hospitals in the region regarding MRSA infection prevention. • Investigators in Southwestern Pennsylvania collaborated with Plexus Institute received a $290,000 grant from Robert Wood Johnson Foundation tp spread the initiative to hospitals in eastern Pennsylvania, Marlyand, and Montana.
Action Item #64: Utilize Federal Health Care Systems (e.g., DoD, VA) as Models for AR Surveillance and Prevention and Control Activities Involving Appropriate Drug Use, Optimized Diagnostic Testing, Infection Control, and Vaccination Practice.			
Action Item #65: For All Healthcare Systems for Which Federal Funds Are Provided, Identify and Promote Strategies To Establish AR Prevention and Control Activities as Part of Quality Monitoring Programs.			
Action Item #66: Encourage Nationally Recognized Accrediting Agencies such as The National Committee for Quality Assurance (NCQA), and the Joint Commission on Accreditation Standards That Promote Efforts To Prevent and Control AR, Including Appropriate Use, Infection Control, Vaccine Use, and Diagnostic Testing. These Standards May Draw on the Findings of Existing Data and Demonstration Programs and AHRQ Evidence-Based Practice Centers.			
Focus Area III: Research			
Action Item #67: Additional Research, Including High Risk and High Payoff Research in Nontraditional Fields, Is Needed.			
CDC	Grant program for applied research on antimicrobial resistance: characterization of strains of community-associated methicillin-resistant *Staphylococcus aureus*	This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus (S. aureus)* causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques.	Five three-year awards were made in 2003. Recipients include Harbor-University of California Los Angeles Research & Education Institute, University of California at San Francisco, University of Chicago, William Beaumont Hospital, and Columbia University. Funding cycle complete. Numberous publications resulted. "1) Genetic background affects stability of mecA in Staphylococcus aureus." J Clin Microbiol. 2005 May;43(5):2380-3. 2) "Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles." N Engl J Med. 2005 Apr 7;352(14):1445-53. 3) "Incidence of and risk factors for clinically significant methicillin-resistant Staphylococcus aureus infection in a cohort of HIV-infected adults." J Acquir Immune Defic Syndr. 2005 Oct 1;40(2):155-60.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	AR mechanisms of *S. pneumoniae* (Alaska)	Use of PCR methodologies to rapidly screen *S. pneumoniae* isolates for genetic determinants of resistance; monitoring the emergence, spread, persistence, and decline of multidrug-resistance organisms by molecular-based typing capabilities to include multilocus sequence typing (MLST).	Ongoing. In 2002, expanded surveillance methodologies to include the molecular typing techniques Pulse Field Gel Electrophoresis (PFGE) and Multi Locus Sequence Typing (MLST) which allow an enhanced understanding of the emergence and transfer of resistance genes among these Pneumococcal isolates. Began retrospectively screening previously collected multidrug resistant isolates using these molecular typing techniques.
NIH, DoD	Biotechnology Engagement Program (BTEP)	The BTEP Program is an attempt by the U.S. government to engage former Soviet Union scientists that conducted biowarfare research to refocus on issues of mutual benefit. DMID program staff oversee a U.S. – Russian Collaborative TB research project initiated in 2001 with Professor A. Llyichev of Vector in Novosibirsk entitled, "Drug resistant tuberculosis in Western Siberia." Staff oversee, "Molecular epidemiology and antibiotic resistance of bacterial infections in Georgia" in collaboration with Lela Bakanidze of the National Center for Disease Control of Georgia.	Ongoing.
FDA	Multi-drug resistant TB	Identified genetic mechanisms causing resistance in multi-drug resistant tuberculosis.	Ongoing.
FDA	Role(s) of mutators in natural populations	Conduct research on genetic diversity within populations of bacterial pathogens; Determine if mutator subpopulations of Salmonella enteritidis promote antibiotic resistance; Investigate role of bacterial persistence in emergence of AR.	Project Completed
FDA	DNA microarray profiling of antibiotic resistance genes.	Develop DNA microarray techniques and DNA chips for characterizing antibiotic resistance genes for multiple bacterial pathogens.	Ongoing. In conjunction with scientists at the University of Maryland, developed over 60 PCR primers to target genes associated with resistance in Salmonella and *E. coli* to 6 categories of antimicrobial agents, including B-lactams, aminoglycosides, phenicols, tetracyclines, and sulfonamides.
FDA	Genomic sequencing of antibiotic-resistant Salmonella serovars.	Whole genome sequencing of 16 clinical isolates of *Salmonella enterica* being carried out to compare paired antibiotic-susceptible and antibiotic-resistant serovars.	Ongoing. Project supported by NIAID and TIGR, in collaobration between CFSAN and CVM.
FDA	Antibiotic resistance in vibrio	Investigate emergence of antimicrobial resistance in Vibrio species.	Project discontinued
FDA	Studies on the Mechanism of fluoroquinolone (FQ) resistance and molecular screening for resistance determinants in Campylobacter, *E. coli*, and Salmonella	Isolate and characterize FQ resistant Campylobacter, *E. coli* and Salmonella from chicken and turkey farms.	Continue to characterize at the molecular level, resistant Salmonella, Campylobacter and *E. coli* as part of the NARMS retail program.
FDA	Development of a microarray chip for the detection of multiple antibiotic resistant genes.	An oligo based microarray chip is being developed to screen 131 antimibiotic resistant genes. The specificity of the probes is tested by Cy3/Cy5-labelled antisense probes.	The microarray chip is currently being validated.
FDA	Epidemiology of the occurrence of tetracycline-resistant genes in catfish and imported aquaculture samples.	Assess the prevalence of tetracycline-resistance and characterize the resistant genes in pathogenic bacteria such as *Aeromonas* spp., and *Pseudomonas* spp.. In aquaculture samples.	Molecular characterization of tetracycline-resistance in 81 Aeromonads from catfish has been completed and a manuscript is currently in review. The other aspects of the investigation is still in progress.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Molecular characterization of *Salmonella* spp. and *Vibrio* spp. from seafood and development of a microarray detection method.	A total of 204 *Salmonella* and 120 *Vibrio* spp. were isolated from imported seafood samples. The antibiotic resistant profile of these bacteria will be dtermined and the genes will be characterized by PCR-RFLP, PFGE, ribotyping, ERIC-PCR and RAPD. A rapid microarray chip will be developed to detect these pathogens and their resistance markers in imported seafood samples.	Ongoing.
FDA	Safety evaluation of colistin and other anibiotic residues in food on the human intestinal microflora.	All aspects of the drug metabolism such as absorption, distribution, biotransformation, toxicokinetics, and effects on animal intestinal microflora by colistin and other antibiotics approved for4 usage in food producing animals were examined by the Joint FAO/WHO Expert Committee on Food Additives in March 2006. Colistin is a priority drug of teh Codex Committee on Residues of Veterinary Drugs in Foods.	A guidance document by the committee will be issued shortly.
FDA	Assessment of membrane-associated antibiotic resistance mechanisms in bacteria.	Multidrug efflux mechanisms have emerged as the primary mechanism for drug therapy in both prokaryotes and eukaryotes. *E.coli* (AcrAB-TolC) is used as a model to better understand this mechanism because it offers greatest intrinsic drug resistance of any single genetic determinant.	Ongoing.
FDA	Elucidation of the Molecular Mechanisms of Fluoroquinolone Resistance in *Clostridium perfringens.*	The *in vitro* effects of various concentrations of fluoroquinolones of different structures, mutations in the target enzymes resulting in the resistance of this bacterium will be studied. Isolation of mutants capable of resisting high concentrations of various fluoroquinolones will be studied. The role of these mutations in the protection of the bacterium from these antibiotics will be determine.	Ongoing.
FDA/USDA	Molecular epidemiology and charaterization of antibiotic resistant *Salmonella* spp. from poultry and development of an oligo microarray chip for the detection of antibiotic resistant genes.	The antimicrobial susceptibility profiles of *Salmonella* serovars were tested by micro broth dilution assay using the SensiTitre system. A majority of *Salmonella* isolates were resistant to multiple antibiotics.	Ongoing.
FDA	Fate and degradation of antimicrobials, oxytetracycline (OTC) and sulfadimethoxine-ormetoprim (Romet 30) from aquaculture environmental samples	To isolate and characterize OTC and Romet 30 resistant Aeromonas spp., Pseudomonas, Citrobacter and *E. coli.* From aquaculture and catfish tissues.	30 OTC resistant *Aeromonas spp*. have been isolated. These isolates have been characterized by PFGE. These investigations are still in progress.
FDA	Develop a microarray chip for the detection of multiple antibiotic resistance markers	Oligonucleotide probes to detect resistance markers for 17 different antibiotics would be embedded in microarray slides. These would be hybridized with in vitro-labeled cDNA of the resistant bacteria isolated from farm animals or clinical samples. The microchip would help FDA efficiently monitor and track resistant markers and make regulatory decisions. It would also aid physicians for choosing appropriate antibacterial therapy.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Elucidation of the mechanism of resistance development in anaerobic bacteria from human intestinal tract	Evaluation of the effect of fluoroquinolones on the resistance development in the bacteria from the human intestinal tract and analysis of the fluoroquinolone resistance mechanism in anaerobic bacteria from the human intestinal tract.	Ongoing.
FDA	Biodegradation of fluoroquinolone antibiotics	The fungus Pestalotiopsis guepini metabolized the fluoroquinolone antimicrobial agent norfloxacin to 7 amino-1-ethyl-6-fluoro-4-oxo- 1,4 dihydroquinolone-3-carboxylic acid and three other metabolites during growth on rice hulls used as poultry litter, suggesting that fungi that grow on poultry litter may be able to metabolize residues of fluoroquinolone drugs. The intestinal bacterium Enterococcus durans degraded 1-phenylpiperazine to N-acetyl-1-phenylpiperazine, N-formylaminoethylaniline and 2-phenylaminoethanol, suggesting a potential role in the breakdown of other compounds, such as fluoroquinolone drugs, that contain a piperazinyl group.	Ongoing.
FDA	Blood borne pathogens	Develop rapid assays to identify blood borne pathogens using nucleic acid based tests (NAT) and a TaqMan assay to detect bacterial contamination in whole blood and platelets. The sequences used in these primer sets are conserved in 19 bacterial species.	Ongoing research to develop a DNA microarray based pathogen chip that could detect all pathogenic bacteria that contaminate blood and blood products.
NIH, DoD	Biotechnology Engagement Program (BTEP)	The BTEP Program is an attempt by the U.S. government to engage former Soviet Union scientists that conducted biowarfare research to refocus on issues of mutual benefit. DMID program staff oversee a U.S. – Russian Collaborative TB research project initiated in 2001 with Professor A. Llyichev of Vector in Novosibirsk entitled, "Drug resistant tuberculosis in Western Siberia." Staff oversee, "Molecular epidemiology and antibiotic resistance of bacterial infections in Georgia" in collaboration with Lela Bakanidze of the National Center for Disease Control of Georgia.	Ongoing.
NIH	NIH CRISP Database	CRISP <http://crisp.cit.nih.gov/> (Computer Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions. The database, maintained by the Office of Extramural Research at the National Institutes of Health (NIH), includes projects funded by NIH, Substance Abuse and Mental Health Services Administration (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), and Office of the Assistant Secretary of Health (OASH). Users, including the public, can use the CRISP interface to search for scientific concepts, emerging trends and techniques, or identify specific projects and/or investigators.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Innovative approaches for combating antimicrobial resistance	This initiative (RFA: AI02-009) was designed to stimulate novel and innovative research, including high risk and high payoff studies in nontraditional fields, to acquire a better understanding of the factors affecting the development of resistant pathogens and spread of resistance genes, in order to direct actions to diagnose, control, and treat AR.	Ongoing. 18 grants funded in early 2003. Projects include: "Using Genomics to Identify Antibiotic Sensitivity Genes," "Predicting Resistance: Validating Mathematical Models," "and "Ciprofloxacin resistance and compensatory mutations," among others.
NIH	Investigator-initiated small research grant award program announcement (R03)	The R03 award supports small research projects that can be carried out in a short period of time, with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	Program Announcement PA-03-108 was released on April 18, 2003; expiration date: April 18, 2006. Recently funded awards include: "Characterization of novel MurA inhibitors (TB)", "Structure of the multidrug efflux protein AcrA" and "Shaping antibody responses to small molecules by design."
NIH	NIH Exploratory/Developmental Research Grant Award (R21)	This announcement redefines the National Institutes of Health (NIH) Exploratory/Developmental Research Grant Award (R21) mechanism, and extends its use as an investigator-initiated mechanism to a variety of Institutes and Centers (ICs) listed in the announcements.	Ongoing. Examples of recent R21 NIAID awards include: "Towards drugs that prevent resistance to the HIV OI, TB" "Chromatin-based regulation of multidrug resistance gene" and "Molecular mechanism of antibiotic rifampicin action."
NIH	Investigator initiated grants mechanisms (R01)	NIH funds a diverse portfolio of grants to study AR in major viral, bacterial, fungal, and parasitic pathogens. Projects include basic research into the disease-causing mechanisms of pathogens, host-pathogen interactions, and the molecular mechanisms responsible for drug resistance, as well as applied research to develop and evaluate new or improved products for disease diagnosis, intervention, and prevention.	Ongoing. Examples of recent R01 awards include: "Fluoroquinolone resistance in M. tuberculosis","Discovering new Anti-Tuberculosis Drugs", "Innate immunity and bacterial quorum sensing", and "Targeting cofactor biosynthesis in biodefense pathogens."
NIH	NIH Academic Research Enhancement Award (AREA) Grants - (R15)	AREA grants support individual research projects in the biomedical and behavioral sciences conducted by faculty, and involving their undergraduate students, who are located in health professional schools and other academic components that have not been major recipients of NIH research grant funds.	Ongoing. Examples of recent R15 awards include: "Molecular evolution of flavivirus-resistance in mice", "Gene discovery and expression analysis using sAGE", "Ecology of large and small scale mosquito invasions", and "Microbial altruists: Helping cohorts survive lethal drugs."
NIH	Small Business Innovation Research and Technology Transfer Research Program (SBIR/STTR)	The SBIR/STTR program is an omnibus solicitation established under federal law that seeks to use small business to stimulate technological innovation, increase the participation of small business in federal R&D, and to increase private sector commercialization of technology development through Federal R&D. The annual set-aside for agencies with extramural research budgets over $100M is 2.5%.	Ongoing. Recent awards include: "Microarray detection of MDR-TB," "Treatment of latent TB and MDR-TB with FAS20013" , "Technology and database for antimicrobial identification" , and "Bacterial DNA helicases: Targets for novel antibiotics."
NIH	Cooperative Research for the Development of Vaccines, Adjuvants, Therapeutics, Immunotherapeutics & Diagnostics for Biodefense	To support discovery/design and development of vaccines, therapeutics, adjuvants, and diagnostics for biodefense. This program will help translate research from the target identification stage through target validation to early product development.	Recent awards include: "Peptide & antibodies as antidotes for superantigens", "Combination therapies to counteract anthrax toxin", "Novel vaccine adjuvants to counter bioterrorist threats" and "Inhibitors of poxvirus enzymes as novel drugs."

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN)	NIAID's FWDIRN network includes multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network includes Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network is supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism.	Ongoing, innovative projects that address this action item include: 1) Investigation of the effect of human immune system genetic polymorphisms on the response to Shigella vaccine components; results will contribute to the rational design of effective vaccines; 2) Retrospective study of the emergence of AR Salmonella enteritidis, and 3) Two additional studies focused on the emergence and transmission of AR zoonotic bacteria.
NIH	Challenge Grants: Biodefense Product Development	To facilitate collaborative partnerships between government and the private sector for further development of already identified products against NIAID Category A, B and C high priority pathogens and all stages of product development against Severe Acute Respiratory Syndrome (SARS), including vaccines, adjuvants, therapeutics, diagnostics and research resources.	Multiple awards made in 2005, including "Broad-spectrum antagonist of superantigen toxins", "Development & manufacture of an MDR tuberculosis vaccine", "Multivariate pathogen diagnostic products" and "Recombinant antigen mutiagent diagnostic assays."
NIH	NIAID Intramural Laboratory of Immunogenetics, TB Research Section	The Tuberculosis Research Section (TBRS) is an integrated group of chemists, clinicians, and microbiologists dedicated to improving the chemotherapy of tuberculosis.	Ongoing. Section scientists work to identify new strategies to improve therapy.
USDA	Develop a fundamental understanding of the process of antimicrobial resistance in order to prevent the spread of unwanted resistant factors among the microorganisms that live normally in the gut of swine and cattle	ARS used continuous culture models of gut bacteria to determine the effect of the drug vancomycin on bacteria within the continuous culture model and within the gut of animals. Although ARS previously demonstrated that growth of certain vancomycin-resistant microorganisms was prevented in the model by the bacterial mixture, ARS found that a sub-therapeutic concentration of vancomycin in the growth media will allow these microorganisms to survive in the culture. This information will be used to determine antimicrobial dose and duration regimens that are therapeutically effective but limit the spread of antibiotic resistant bacteria, and will ultimately lead to more appropriate approaches to using antibiotics in food animal agriculture.	Completed Poole, USDA-ARS: College Station, TX.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Determination of the persistence of antimicrobial resistant pathogens in the environment	The persistence of AR bacteria following the cessation of use of a given antibiotic is a problem for the development of effective intervention strategies to combat antimicrobial resistance. In collaboration with the FDA Center for Veterinary Medicine, ARS examined the antimicrobial resistance patterns of disease causing strains of Escherichia coli from newborn pigs experiencing diarrhea. ARS found that 53% of the isolates were resistant to chloramphenicol, a broad spectrum antibiotic that has been banned for use in food animals in the United States since the mid 1980s. This information will help to determine the factors that govern the persistence of resistance genes once an antibiotic is no longer used in animal agriculture.	Completed : Bischoff USDA-ARS College Station, TX.
USDA	Assessment of the effect of penta-resistant bacteria on virulence and/or colonization	ARS challenged broiler chicks on the day of hatch with either a sensitive or penta-resistant Salmonella typhimurium DT104 and determined that penta-resistant bacteria did not cause clinical illness in broiler chicks. However, ARS did observe a significant increase in the numbers of birds that were colonized in the penta-resistant group. In contrast to in vitro studies, these data indicate that acquisition of multiple resistance does affect colonization rates but may affect the numbers of bacteria that may reach the food chain.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Characterization of Salmonella serotypes on their ability to cause disease in animals and to acquire and disseminate AR genes	We determined that Salmonella serotypes differ in their ability to persist within the host and environment and have determined that both integrons (mobile genetic elements) and plasmids, play a role in dissemination of resistance genes.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	To evaluate the effect of media, temperature, and culture conditions on the species population and antimicrobial resistance of Enterococcus.	Although optimal growth conditions for Enterococcus are well-established, a paucity of information exists on the influences of growth conditions on the overall population or antimicrobial resistance of Enterococcus. In this study, the effect of temperature, culture media and enrichment period were examined. Data indicated that increased temperature favored the selection of E. faecium and E. hirae, while lower temperature (37oC) favored growth of E. faecalis, E. casseliflavus, and E. durans. In addition, significantly lower numbers of E. faecalis were isolated from Enterococcosel agar while higher numbers of E. faecium were isolated from Enterococcosel agar. For antimicrobial resistance, significant differences were found in the number of ciprofloxacin, linezolid or nitrofurantoin resistant E. faecalis and linezolid or Synercid resistant E. faecium due to media. Temperature influenced the number of bacitracin, flavomycin, gentamicin, nitrofurantoin, penicillin, streptomycin or tetracycline resistant E. faecalis and gentamicin, kanamycin.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Characterization of erythromycin resistance in enterococci isolated from swine farms using different regimens of tylosin	The effect of tylosin use on erythromycin resistant enterococci isolated from farms was investigated. Results from the study suggested that although resistance was higher on a farm where tylosin was used as a growth promotant, a few resistant enterococci also persisted on a farm where no antimicrobials were being used. Isolates from farms were analyzed for antimicrobial resistance gene content as well as genetic determinants for dissemination of resistance.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Evaluation of prevalence and antimicrobial susceptibility of E. coli isolated from fruits and vegetables	In collaboration with scientists from USDA-AMS, we are evaluating the prevalence and antimicrobial susceptibility of generic E. coli isolated from fruits and vegetables collected from different regions of the US. This information will be useful for determining the effect of antimicrobials on E. coli isolated from these sources and the potential impact that these bacteria may have on consumer health.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Establish a model for quantitative determination of rates of antimicrobial resistance acquisition	The objective of the study was to determine the frequency of spontaneous acquisition of resistance to select antibiotics by Salmonella typhimurium when grown in pure culture in a glucose limited continuous flow culture at slow (D= 0.025 h-1) or fast (D=0.27 h-1) dilution rates. Results suggest that spontaneous acquisition of resistance to the select antibiotics was highly unlikely regardless of growth rate or exposure to lethal or sublethal antibiotic concentrations. Future studies are underway to expand the model to a mixed microbial ecosystem containing transmissible genetic elements.	Completed Food and Feed Safety Research Unit, ARS, College Station, TX.
USDA	Investigate the effect of ionophore feeding (long-term) on pathogen populations and antimicrobial susceptibility in stocker cattle	A collaborative project with the USDA-ARS Dale Bumpers Small Farm Research Center is being conducted determine the effect of long-term ionophore feeding on pathogen populations and antimicrobial susceptibility in stocker cattle.	Completed Edrington Food and Feed Safety Research Unit, ARS, College Station, TX.
USDA	Surveillance of antibiotic resistance in normal enteric bacteria	The project goal is to determine tetracycline resistant genotypes, species identities, and resistance "baseline' levels of commensal bacteria in the swine intestinal tract. A survey was conducted of the resistant bacterial species present in swine under different environmental conditions and feeding regimes. Intestinal bacteria from feral swine had very low levels of tetracycline resistance compared to strains isolated from both organic and conventionally to strains isolated from both organic and conventionally reised swine. Novel mechanisms of tetracycline resistance were found. Intestinal species are how being characterized.	Ongoing. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa.
USDA	To assess the gene variability associated with resistant versus secceptible strains of Salmonella, Campylobacter, Enetrococci and E. coli	A microarray chip has been developed that can screen for over 100 known reistance genes among the four bacterial species as well as over 900 virulence and regulatory genes for Salmonella. Additional genes are being added for the other bacteria.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Assess the ability temperature has on survival of resistant versus sensitive bacteria.	A pan-susceptible and multiple-rsistant strains were compared for their ability to survive following challenge of poultry exposed to vaerious room temperatures.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Study the role of tetracycline resistance in Campylobacter species.	Tetracycline resistance appear to be common among bacteria particularly when multiple resistance is detected. Our goal is to study the presence of, and characterize, teracycline resistant genes among Campylobacter species.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Characterize mechanisms of resistance to extended spectrum b-lactams in Salmonella from animal sources	Recently, the numbers of Salmonella isolates resistant to the third generation cephalosporins have increased. To investigate the increase in resistance, a diverse group of Salmonella serotypes resistant to ceftiofur was selected. Those strains were analyzed for the presence of the CMY-2 AmpC type b-lactamase gene. The majority of strains contained the CMY-2 gene. Most of the strains also contained large plasmids and are being subjected to Southern analysis to determine the location of the CMY-2 gene. The strains were also analyzed for the presence of the integron 1 gene, intI1. Most strains positive for intI1 were Salmonella serotype Newport, Heidelberg, or Typhimurium.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Determine the effect of antimicrobial selective pressure on the rate of spread of Salmonella typhimurium in poultry	Salmonella strains have arisen that are resistant to multiple antimicrobials including 3rd generation cephalosporins. The ability of those strains to be transmitted between hosts and under antimicrobial selective pressure is presently unknown. Two Salmonella strains (one pan-susceptible and one resistant to 12 antimicrobials used in the NARMS program) were compared by a natural transmission study in chickens in the presence of MIC levels of chlortetracycline (tet). The percentage of positive cloacal swabs from birds exposed to the resistant strain indicated that more birds were positive when tet treatment was administered. Cloacal swabs from the susceptible strain exposed birds indicated that more birds were positive in the absence of tet treatment. The same results were observed for tissues at necropsy on D10. Results indicated that resistant strain did not transmit faster in the presence of tet, and suggested that use of tet had a protective effect on tissue colonization.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Develop an assay for the detection of horizontally acquired antimicrobial resistance genes in Salmonella and other bacteria	Previously, PCR techniques and Southern analysis have been used to identify specific resistance genes. In order to increase the speed, efficiency, and sensitivity and to broaden the applicability of these techniques, a DNA microarray to perform multiple simultaneous assays for a broad range of antimicrobial resistance genes is being designed to incorporate current PCR product probes as well as synthetic oligonucleotides. These microarrays will be able to assay the antimicrobial resistance gene content of any number of diverse bacterial species, especially those under NARMS surveillance. This information can be used by other scientists when they study mechanisms of resistance among bacterial species.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	To phenotypically and genotypically characterize Salmonella serotype Newport identified from NARMS 2000 and 2001 collection of isolates	Between 2000 and 2001, the animal arm of NARMS recovered a total of 241 Salmonella newport non-diagnostic (slaughter and on-farm) isolates. MDR S. newport isolates were recovered more frequently than pan-susceptible isolates and most of the MDR isolates were resistant to > nine antimicrobials. None of the Newport isolates contained Class 2, Class 3, or Class 4 integrons (intI2, intI3, or int4, respectively). However, Class I (intI1) integrons were identified in most of the animal species regardless of whether they were MDR or pan-susceptible. Large and small plasmids were identified mainly in the MDR Newport isolates. By PFGE analysis, Newport appears to be heterogeneous among multiple animal species, but homogeneous in a particular species. These data can be used for comparison with isolates obtained from human outbreaks to determine if a particular animal species served as the source of infection.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Exploring opportunities for technology transfer to the field of human medicine	The project goal is to determine if M. elsdenii is a normal bacterial inhabitant of the human GI tract and if this bacterium can be used as an indicator of enteric species in humans for antibiotic resistance status. Due to low population levels, M. elsdenii was found not to be suitable.	Completed. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Assess the occurrence of Salmonella serotype Typhimurium DT104 in retail ground beef	Salmonella was isolated from 3.5% of samples and eight serotypes were identified including Typhimurium. Phage typing indicated that they were DT104A, a subtype of DT104. Generic E. coli was also isolated from 25% of samples. Comparison of antimicrobial resistant profiles between Salmonella and E. coli did not indicate that genes were being transferred among isolates. These data indicate that DT104A can be isolated from ground beef but the significance is unknown. Further, these multi-resistant E. coli are infrequently found in ground beef. This information can be used by other scientists and the beef industry for designing and implementing reduction and control programs.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Evaluate the prevalence and antimicrobial susceptibility of E. coli isolated from fruits and vegetables	Although a number of studies have determined levels of resistant bacteria on meat items from grocery stores, few studies have been conducted on the prevalence of bacteria from fruits and vegetables. In collaboration with scientists from USDA-AMS, we evaluated the prevalence and antimicrobial susceptibility of generic E. coli isolated from fruits and vegetables collected from different regions of the US and determined that resistance to 17 different antimicrobials among these E. coli is low.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Determine the presence of E. coli 0157:H7 in swine	Data indicated that is was possible to isolate E. coli 0157:H7 from the colons of pigs presented at slaughter, although the recovery rate was low. Even though the recovery rate was low, the presence of 0157:H7 may have a significant impact on human health if contaminated meat is handled or consumed. Further studies are required to determine the true prevalence and risk of E. coli 0157:H7 in swine. This information can be used by other scientists and the swine industry for designing and implementing reduction and control programs.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA. and ERRC, Wyndmoor PA.
USDA	Assess the prevalence of E. coli 0157:H7 in downer cows	As a team member, the laboratory participated in a study to assess the prevalence of E. coli 0157:H7 in downer cows. Data indicated that 4.9% of downer cows versus 1.5% of health cows harbor E. coli 0157:H7 in their colons. Not all isolates were clonal, resistance to antimicrobials was low and very little multiple resistance was observed. These data implicate downer cows as having a higher prevalence of E. coli 0157:H7 than healthy cows and may affect the use of downer cows as sources of meat.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Determine the effect of three feed-based antimicrobials (apramycin, carbadox, and tetracycline) on the development of antimicrobial resistance in generic E. coli	Resistance to tetracycline in E. coli varied widely by sample, group, and trial. However, a significant increase in the percentage of resistant isolates was observed in piglets fed antimicrobials when compared to controls. Resistance to apramycin also increased in piglets when compared to controls. However, upon removal of apramycin, resistance in E. coli declined. Resistance to carbadox remained unchanged after feeding carbadox when compared to controls. Piglets fed low doses of antimicrobials demonstrated improved growth when compared to controls. These data are useful for veterinarians, pharmaceutical manufacturers, and scientists as they devise ways to limit the development of resistance to antimicrobials while maintaining animal health.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Characterize antimicrobial resistance, species, and genetic diversity of Campylobacter isolated from feedlot cattle	In collaboration with scientists from USDA-APHIS-VS-CEAH, antimicrobial resistance was examined in Campylobacter isolates from feedlot cattle as part of a NAHMS study. Results indicate that a majority of the isolates were susceptible to the antimicrobials that were tested and that there is significant genetic diversity among isolates. These data provided a significant overview of antibiotic resistance among Campylobacter from healthy beef cattle across the US. This work will be useful to beef producers, regulatory agencies and researchers in antimicrobial resistance.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	To increase recovery of Campylobacter from various sources	Because of the fastidious nature of Campylobacter, recovery from meat or other sources is difficult. We developed an enhanced methods for recovering Campylobacter from chicken carcass rinsates by employing a centrifugation step of the rinsate prior to enrichment in culture media. This resulted in a >50% increase in the recovery of Campylobacter. This is significant in that previous methods were leading to the isolation and under reporting of Campylobacter in samples. This work will be useful to scientists involved in Campylobacter research.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Determine the prevalence and level of Campylobacter in parents (breeders) and offspring (broilers) of commercially reared pigs	Studies were conducted to determine the prevalence and level of Campylobacter in parents (breeders) and offspring (broilers) of commercially reared pigs Prevalence of Campylobacter ranged from 42 to 100% positive in three broiler offspring flocks (90% of breeders were shedding).	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	To evaluate the prevalence and antimicrobial resistance of enterococci isolated from retail food items	In a study of retail food (meat, vegetables, and fruit) collected from grocery stores in NE Georgia, enterococci were isolated, identified to species, and tested for antimicrobial susceptibility. Results indicated that although enterococci were prevalent among food items, resistance to antimicrobials used in human medicine was very low (linezolid, gentamicin, ciprofloxacin) or nonexistent (vancomycin). This was the first study analyzing enterococci isolated not only from meats, but fruits and vegetables as well. This work will be useful to scientists involved in Enterococcus research as well as regulatory agencies and the industry as they develop and implement mitigation strategies.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Characterize erythromycin resistance in enterococci isolated from swine farms using different regimens of tylosin	The effect of tylosin use on erythromycin resistant enterococci isolated from farms was investigated. Results from the study suggested that although resistance was higher on a farm where tylosin was used as a growth promotant, a few resistant enterococci also persisted on a farm where no antimicrobials were being used. Isolates from farms were analyzed for antimicrobial resistance gene content as well as genetic determinants for dissemination of resistance. These data provide insight as to the development and persistence of resistance on-farm and will be useful to research and industry scientists as they develop and implement Enterococcus mitigation strategies.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Characterize aminoglycoside resistance among enterococci isolated from poultry	Aminoglycoside antimicrobials are of interest due to their use in both animals and humans. In this study, resistance to aminoglycosides in enterococci from poultry samples was examined. High-level gentamicin, kanamycin, and streptomycin resistance was found in 23%, 41%, and 19% of the isolates, respectively. Of the ten aminoglycoside resistance genes examined, five were identified in the isolates using PCR. Seven resistant E. faecalis isolates were negative for all genes tested suggesting that additional resistance genes may exist. Phylogenetic analysis revealed that the isolates were genetically different with little clonality. Data from this study suggest that enterococci from poultry are diverse and contain potentially unidentified aminoglycoside resistance genes. This work will be useful to scientists involved in Enterococcus research as well as the industry as they develop and implement mitigation strategies.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	To characterize 3rd generation cephalosporin resistant Salmonella from animal sources.	We characterized the strains and resistance mechanisms of 3rd generation cephalosporin resistant Salmonella in the United states and found that the CMY-2 gene is the most common mechanism by which salmonellae acquire this resistance in the US. This is in contrast to Europe where it is the Extended Spectrum Beta-Lactamase (ESBL). Furthermore, we found that isolates carrying the CMY-2 gene are significantly more likely to multiple drug resistant, and that certain Salmonella serotypes were more likely to carry the resistance. Third generation cephalosporins are important antimicrobials used to treat severe infections in both humans and animals. The research resulted in a predictive diagnostic test for multiple drug resistant Salmonella. Turkeys, horses, cats and dogs are significantly more likely to have these isolates than cattle, swine, chicken and exotics. The multiple drug resistance identified was found to be encoded on a large transferable plasmid.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	To monitor serotypes and development of resistance to Ciprofloxacin in Salmonella.	The first Salmonella isolate resistant to Ciprofloxacin (a fluoroquinolone) was identified and characterized. Salmonella serotype Niakhar is a rarely isolated serotype and only five isolates have been acquired as part of NARMS. These isolates originated either from a dog or cattle, and only one (cattle isolate) was resistant to Ciprofloxacin. The presence of a multiple resistance gene (MAR), integrons and transferable plasmids were identified. While resistance was localized to the plasmid, only two of the resistance genes were located within an integron. Molecular analysis of the isolates also indicated more heterogeneity between isolates and only two (but not the multiple resistant one) appeared to be related. Impact: Further characterization of this isolate, as well as continued monitoring for an increase in the number of S. Niakhar and other Ciprofloxacin resistant serotypes over time will be done.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	To study the ability of resistant strains to have a competitive persistance advantage	Recently, Salmonella strains have arisen that are resistant to multiple antimicrobials including 3rd generation cephalosporins. The ability of those strains to be transmitted between hosts and under antimicrobial selective pressure is presently unknown. Two Salmonella strains (one pan-susceptible and one resistant to 12 antimicrobials used in the NARMS program) were compared by a natural transmission study in chickens in the presence of MIC levels of chlortetracycline (tet). The percentage of positive cloacal swabs from birds exposed to the resistant strain indicated that more birds were positive when tet treatment was administered. Conversely, cloacal swabs from the susceptible strain exposed birds indicated that more birds were positive in the absence of tet treatment. The same results were observed for tissues at necropsy on D10. These results indicated that resistant strain did not have an increased transmissibility in the presence of tet and suggested that use of tet had a protective effect on tissue colonization.	Ongoing. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Evaluate the effect of media, temperature, and culture conditions on the species population and antimicrobial resistance of enterococci	Although optimal growth conditions for enterococci are well-established, a paucity of information exists on the influences of growth conditions on the overall population or antimicrobial resistance of enterococci. In this study, the effect of temperature, culture media and enrichment period was examined. Data indicated that increased temperature favored the selection of E. faecium and E. hirae, while lower temperature (37oC) favored growth of E. faecalis, E. casseliflavus, and E. durans. In addition, significantly lower numbers of E. faecalis were isolated from Enterococcosel agar while higher numbers of E. faecium were isolated from Enterococcosel agar. For antimicrobial resistance, significant differences were found in the number of ciprofloxacin, linezolid or nitrofurantoin resistant E. faecalis and linezolid or Synercid resistant E. faecium due to media. Temperature influenced the number of bacitracin, flavomycin, gentamicin, nitrofurantoin, penicillin, streptomycin or tetracycline resistant E. faecalis and gentamicin, kanamycin.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Quantitative measurement of antimicrobial resistance gene loads in samples	This study will optimize and evaluate real-time PCR in the quantitafication of a.r.genes in fecal samples. It will assess the accuracy and precision for quantifying the association between antimicrobial use and antimicrobial resistance.	Awarded in 2004 by CSREES, NRI's 32.1 Epidemiologic Approaches for Food Safety. R. Singer, University of Minnesota. (Ongoing) The technique has been applied to cattle fecal samples collected during a long-term ecological study of antimicrobial resistance on dairies. The established real-time PCR-based assay offers a quick, sensitive, efficient, and reliable approach to the detection and quantification of the studied antimicrobial resistance genes and may provide a more accurate indication of selection pressures than standard cultivation approaches.
Action Item #68: Conduct Further Government-Wide Assessments with External Input on the Scope and Composition of AR Research To Identify Research Opportunities.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Novel Therapeutics for Enteric Infections: A Workshop	Workshop to assess the opportunities for discovery and clinical development of novel therapeutics for enteric infections. Attendees included representatives from NHLBI, FDA, Institute for OneWorld Health, Industry and Academia.	Meeting held September 22, 2005, in Bethesda, Maryland. The current status and new opportunities were addressed by 18 invited experts. Several promising entities have been identified and some are now under preclinical development.
NIH	Emerging Clostridial Diseases Workshop	The CDC, FDA, and NIAID are planning a public workshop to develop a draft research agenda to better understand the virulence, pathogenesis, host factors, and non-antimicrobial risk factors contributing to reports of morbidity and mortality associated with Clostridium sordellii and Clostridium difficile. Additionally, our goals are to identify research needs and priorities that will enable rapid progress, as well as to develop and provide recommendations for detecting cases and conducting surveillance of diseases and organisms.	To be held May 11, 2006 in Atlanta, Georgia.
Action Item #69: Work with the Appropriate Peer Review Structures To Ensure That the Requisite Expertise Is Applied to the Review Process To Facilitate Funding of Quality AR Research.			
NIH	The Panel on Scientific Boundaries for Review has conducted a comprehensive examination of the organization and function of the review process that is carried out by the Center for Scientific Review (CSR) at NIH. The purpose of this evaluation is to position the CSR peer review system so that it fosters expanded research opportunities, as well as permits the review system to keep pace with the accelerating rate of change in the way that health-related research is performed. This examination is being carried out in two phases, with extensive involvement of the extramural research community. The Panel has proposed a set of Integrated Review Groups (clusters of scientifically related study sections, referred to as IRGs) and proposed	The Infectious Diseases and Microbiology IRG review by the Expert Working Group was conducted from May – August 2001 and developed a proposed set of guidelines and shared interests for new study sections. NIH's CSR has established a new Study Section, Drug Discovery and Mechanisms of Antimicrobial Resistance (DDR), within the new Infectious Diseases and Microbiology Integrated Review Group (IRG). It will review applications that are concerned with the identification of novel antimicrobial agents, including agents that could be used in bioterrorism, for the prevention and treatment of infectious diseases and the study of the evolution, mechanisms, and transmission of resistance.	NIH's CSR has established a new Study Section, Drug Discovery and Mechanisms of Antimicrobial Resistance (DDR), within the new Infectious Diseases and Microbiology Integrated Review Group (IRG). It will review applications that are concerned with the identification of novel antimicrobial agents, including agents that could be used in bioterrorism, for the prevention and treatment of infectious diseases and the study of the evolution , mechanisms, and transmission of resistance. DDR held its first meeting in June of 2004, and has met regularly thereafter.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #70: Provide To the Research Community Genomics and Other Powerful Technologies To Identify Targets in Critical Areas for the Development of New Rapid Diagnostics Methodologies, Novel Therapeutics, and Interventions To Prevent the Emergence and Spread of Resistant Pathogens. Examples Include Tools Such as Microbial Genome Sequences, Information on Comparative Genomics, DNA Chip Technology, Informatics, and Assistance in the Application and Use of These Tools.			
NIH, USDA, FDA, EPA, FDA	Microbe project interagency working group	NIAID staff is participating in the Microbe Project Interagency Working Group, which coordinates microbial genomics activities across Federal government agencies.	This working group continues to coordinate genomic activities across federal agencies, including those related to biodefense, and has also focused on issues related to genomic data release and usage, as well as on bioinformatics and microbial sequencing efforts.
FDA	Genomics and Proteomics	Research in support of the use of genomics, proteomics and other powerful technologies to identify targets in critical areas for the development of new rapid diagnostic methodologies, novel therapeutics, and interventions to prevent the emergence and spread of resistant pathogens.	Established microarray group and CBER core program (for producing and reading oligonucleotide microarray chips). Initiated several research projects related to vaccine development, AR, pathogen identification and detection. Developed a rapid typing method for Neisseria gonorrhoeae applicable to non-cultured specimens and the identification of ciprofloxacin resistant strains. Also developing rapid DNA assays to detect all four species of human malaria parasites. And developing microarray technology for detecting drug resistence among mycobacteria.
NIH	The tuberculosis research materials and vaccine testing contract (Colorado State University)	The contract was recompeted and awarded in September 2004. The contract will continue to provide TB research reagents to qualified investigators throughout the world, enabling them to work with consistent, high quality microbiological, immunological and genomic reagents, prepared from contagious and technically demanding mycobacterial pathogens.	At the end of FY2005, more than 150 new TB vaccine candidates have been tested under this contract, one of which has recently entered human clinical trials with several others progressing through various stages of preclinical development. Research reagents, including specialized post-genomic materials, continue to be provided to researchers worldwide and are being used for drug, vaccine and diagnostic development. Contract staff collaborates with the PFGRC for the production and dissemination of mycobacterial specific molecular reagents.
NIH	NIAID Pathogen Functional Genomics Resource Center (PFGRC)	The PFGRC was established in FY2001 to provide and distribute to the broader research community a wide range of genomic and related resources and technologies for the functional analysis of microbial pathogens and invertebrate vectors of infectious diseases. The number of organism-specific microarrays produced and distributed to the scientific community has increased to 25 in FY2005. In addition, the PFGRC was expanded to provide the research community with the needed resources and reagents to conduct both basic and applied research on microorganisms responsible for emerging and re-emerging infectious diseases and those considered agents of bioterrorism and organisms considered agents of bioterrorism.	Ongoing. See http://www.niaid.nih.gov/dmid/genomes/pfgrc/default.htm for details.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Sequencing of whole pathogen genomes	NIAID has made significant investment in large-scale projects to sequence the genomes of medically significant bacterial, fungal, and parasitic pathogens. In addition, NIAID collaborates with other funding agencies to sequence larger genomes of protozoan pathogens such as the organism that causes malaria. A listing of currently active pathogen genome sequencing projects is available at http://www.niaid.nih.gov/cgishl/genome/genome.cfm. The availability of microbial and human DNA sequences will open up new opportunities and allow scientists to examine functional analysis of genes and proteins in whole genomes and cells, as well as the host immune response and an individuals' genetic susceptibility to pathogens.	In FY2005, NIAID supported approximately 40 large scale genome sequencing projects for additional strains of viruses, bacteria, fungi, parasites, viruses and invertebrate vectors and include Hepatitis C, Coronaviruses, Bacillus anthracis, Bacillus cereus, Bartonella baciformis, Burkholderia cenopcepacia, Burkholderia dolosa, Camplyobacter, Coxiella burnetii, Escherichia coli, Listeria, Pseudomonas aeruginosa, Shigella, Vibrio paramaeolyticus, four strains of Aspergillus, additional strains of Entamoeba, Plasmodium falciparium, and Toxoplasma gondii, and additional sequencing of Plasmodium vivax and Trichomonas vaginalis,and one strain of Ricinus communis.
NIH	Influenza Genome Sequencing Project	This project was launched in 2004 and puts influenza sequence data rapidly into the public domain, enabling scientists to further study how influenza flu viruses evolve, spread, and cause disease and may ultimately lead to improved methods of treatment and prevention. This project is a collaborative effort among NIAID, NCBI/NLM, CDC, St. Jude Children's Research Hospital in Memphis and others, bringing together expertise in sequencing and bioinformatics, as well as expertise in human and avian influenza viruses to help NIAID prioritize, select and obtain strains.	Ongoing. See http://www.niaid.nih.gov/dmid/genomes/mscs/default.htm#influenza for details.
NIH	NIAID pathogen genomics website: www.niaid.nih.gov/dmid/genomes/	The NIAID genomics website serves as a focal point to disseminate to the scientific community current information about NIAID's microbial genomics research program and related activities, including information on funding opportunities, policies, application procedures, priorities for large-scale genome sequencing projects, press releases, and currently funded large-scale genome sequencing projects.	Currently available to the scientific community.
NIH	Bioengineering Consortium (BECON)	BECON is a trans-NIH committee composed of representatives from each of the NIH centers, institutes and divisions, including representatives from other federal agencies www.grants.nih.gov/grants/becon/becon.htm.	In FY2005, NIAID continued to participate in three BECON program announcements that support multi-disciplinary research with a focus on bioengineering to develop knowledge and/or methods to prevent, detect, diagnose or treat disease or to understand human health and behavior. These grants allow biomedical research scientists to partner with scientists from other disciplines including physics, mathematics, chemistry, computer sciences, and engineering to approach current complex biological problems (http://www.becon2.nih.gov/becon_funding.htm).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) contract	The network includes approximately 200 registered users including basic researchers, clinical laboratories and infectious disease clinicians involved in staphylococcal AR research. NARSA supports electronic sharing of information, a yearly investigator's meeting, and a case registry and repository of well-characterized staphylococcal isolates including the three newly emerged vancomycin resistant *Staphylococcus aureus* isolates.	The network includes approximately 73 core investigators, 201 affiliates, which include basic researchers, clinical laboratorians, epidemiologists, and infectious disease clinicians involved in staphylococcal and antimicrobial resistance research. NARSA supports electronic sharing of information and meetings, integrates with CDC's surveillance system on antibiotic resistance, and supports a case registry and extensive repository of staphylococcal clinical, research, resistant, and historical isolates. The seventh annual meeting of this group took place on March 6-7, 2006. The repository has available the three VRSA isolates noted above. A special application and approval is required to procure these isolates.www.narsa.net and http://www.niaid.nih.gov/dmid/antimicrob/.
NIH	Population Genetics Analysis Program: Immunity to Vaccines/Infections	The goal of this program is to identify associations between specific immune response gene polymorphisms/genetic variations and susceptibility to infection or response to vaccination with a focus on one or more of NIAID Category A-C pathogens.	NIAID awarded 6 Centers in 2004 and studies include examining host response to immunization against smallpox, anthrax, typhoid fever, and cholera. Additionally, the host genetics of infection susceptibility to encapsulated bacteria, influenza, and tuberculosis is being studied.
NIH	Research Center Grant, "Structural Organization and Proteomics of TB"	The goal of this global consortium, which involves over 70 laboratories in 12 countries, is to determine and analyze the structures of over 400 functionally relevant Mtb proteins.	To date, the consortium has determined the structures of over 60 biologically important proteins from Mtb. The structural and functional information is publicly available through web-based databases: http://www.doe-mbi.ucla.edu/TB/. This Center Grant will end in early FY 2006 and will be continued as a more scientifically targeted, collaborative program project grant.
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN)	NIAID's FWDIRN network includes multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network includes Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network is supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism.	The network currently funds: • Research and development of improved diagnostics for enteric pathogens • Vaccine research on tularemia vaccine strain LVS, Shigella, and S. typhi • Therapeutics research for botulinum neurotoxin intoxication and for infections with Shiga-toxin producing E. coli (STEC) • Research on diagnostics for botulism • Clinical study to improve response to S. typhi vaccination • Research on the molecular evolution and transmission of antibiotic-resistance genes in enteric pathogens • Animal model development for botulinum neurotoxins, STEC-mediated HUS, Campylobacter-mediated enteritis, and Crohn's disease • Strain repository for STEC
NIH	Structural Genomics of Pathogenic Protozoa	NIAID has cofunded the Structural Genomics of Pathogenic Protozoa (http://depts.washington.edu/sgpp/) to provide the three dimensional structure of many proteins deduced from the genome information of the trypanosomatid and Plasmodium species. This will be valuable information for future drug and vaccine discovery design, as well as information for the discovery of new protein folds and function.	In 2006, the focus of this project will continue to be structures of potential drug targets in pathogenic protozoa, including protozoan pathogens of potential Biodefense concern. However, a greater emphasis will be placed on aiding drug discovery efforts, including the structural basis for antimicrobial resistance in these pathogens.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Malaria Research and Reference Reagent Resource (MR4) Center	The MR4 continues to provide expanded access to quality controlled reagents for the international malaria research community. The website averages more than 5,000 visitors per month, and acquires and distributes more than 100 items per month to researchers worldwide. The MR4 has compiled a Laboratory handbook on "Methods in Malaria Research", available as a resource to scientists. Also, MR4 is acquiring standard sets of parasitized blood smears for diagnostic training to scientists particularly in endemic regions. A program is also in place for coordinating site(s) in African countries, with the vision of expanding availability of MR4 resources to endemic country scientists.	In FY 2005 the MR4 was recompeted, and a new award made to the American Type Culture Collection.
NIH	NIAID Microbial Sequencing Centers	The Microbial Genome Sequencing Centers address NIAID's need for sequencing of microorganism and invertebrate vectors of disease. The MGSCs provide rapid and cost efficient resources for production of high quality genome sequences of pathogens considered agents of bioterrorism (NIAID category A-C priority list), or causing emerging and re-emerging infectious diseases, their closely related organisms and clinical isolates and invertebrate vectors of disease.	These Centers have the capacity and are responding to scientific community and national and federal agencies' priorities for genome sequencing, filling in sequence gaps and therefore, providing genome sequencing data for multiple usages including understanding biology of microbe, forensic strain identification and identifying targets for drugs, vaccines and diagnostics. See http://www.niaid.nih.gov/dmid/genomes/mscs/default.htm.
NIH	Bioinformatics Resource Centers	NIAID Bioinformatics Resource Centers are designed to develop, populate, and maintain comprehensive, relational databases to collect, store, display, annotate, query, analyze genomic, functional genomic, structural and related data for microorganisms responsible for emerging and re-emerging infectious diseases and for those considered agents of bioterrorism. The center will also develop and provide software tools.	Eight Centers were funded in FY04 http://www.niaid.nih.gov/dmid/genomes/brc/default.htm. Publicly accessible individual BRC web sites were developed in FY05 and are available. BRCs are now providing long term maintenance of the genome sequence data and annotation released by the NIAID Microbial Sequencing Centers as well as by other national and international sequencing efforts.
NIH	Biodefense Proteomics Research Programs: Identifying Targets for Therapeutic Interventions Using Proteomic Technology	NIAID Proteomic Centers are intended to develop and enhance innovative proteomic technologies and methodologies and apply them to the understanding of the pathogen and/or host cell proteome for the discovery and identification of novel targets for the next generation of drugs, vaccines, diagnostics and immunotherapeutics against microorganisms considered agents of bioterrorism.	Seven Centers were funded in 2004 (http://www.niaid.nih.gov/dmid/genomes/prc/default.htm). In FY2005 more than 700 potential targets for vaccines, therapeutics and diagnostics have been generated.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Proteomic Profiling of Proteins from Staphylococcus aureus.	These studies demonstrate that proteomic profiling strategies are a useful tool to display, evaluate and select abundant proteins present in cell surface of microbial proteomes. Since extracellular and cell wall proteins in Gram-positive organisms such as Staphylococcus aureus are of interest in study of virulence and survival in bacterial infections, these identified proteins provide the scientific community with targets to further study in elucidating mechanisms of virulence and antibiotic resistance in microorganisms.	Published Results: Gatlin, CL, Pieper R, Huang ST, Mongodin E, Gebregeorgis E, Parmar PP, Clark DJ, Alami H, Papazisi L, Fleischmann RD, Gill SR, and Peterson SN. Proteomic Profiling of Cell Envelope-Associated Proteins from Staphylococcus aureus. Proteomics 2006 Feb 8;6(5):1530-1549.
NIH	Scientific Advance: Improve Detection of Diverse Anthrax Strains	Scientists at Northern Arizona University, the Translational Genomics Research Institute and NIAID PFGRC at The Institute for Genomic Research (TIGR) used a combination of whole genome sequencing, comparative genomics analysis and single nucleotide polymorphisms (SNPs) discovery to define detailed phylogenetic lineages of Bacillus anthracis and identify three major lineages (A,B, C) with the ancestral root located between A+B and C branches. This study provided new phylogenetic lineages of Bacillus anthracis and provided a model to be used for examining other biothreat organisms. More importantly, the study provides new DNA biosignatures that have the potential to be used in the development of more sensitive diagnostic assays for *Bacillus anthracis.*	Results are published in, Pearson T, Busch JD, Ravel J, Read TD, Rhoton SD, U'Ren JM, Simonson TS, Kachur SM, Leadem RR, Cardon ML, Van Ert MN, Huynh LY, Fraser CM and Keim P: Phylogenetic discovery bias in Bacillus anthracis using single nucleotide polymorphisms from whole genome sequencing. PNAS 101: 13536-13541, 2004.
USDA	The role of calf-adapted E.coli in maintenance of antibiotic resistance in dairy calves	This project will use a combination of in vitro and in vivo comparison studies to study the fittness differences between SSuT and non-SSuT strains. Gene knockout studies will also be conducted.	Awarded in 2004 by CSREES, NRI's 32.0 Ensuring Food Safety. D. Call, Washington State University.
USDA	The role of calf-adapted E.coli in maintenance of antibiotic resistance in dairy calves	This project will use a combination of in vitro and in vivo comparison studies to study the fittness differences between SSuT and non-SSuT strains. Gene knockout studies will also be conducted.	Awarded in 2003 by CSREES, NRI's 32.0 Ensuring Food Safety. D. Call, Washington State University. Ongoing. For the first experiments, the researchers selected two nalidixic acid resistant SSuT strains and used either a fusaric acid or nickel-chloride system to select against genotypes that express the tet(B) gene. In vitro and in vivo competition assays were undertaken to characterize the null mutants. Results from the in vitro experiments demonstrated that most ex-SSuT strains out-compete parental resistant SSuT strains and generic susceptible strains. The ex-SSuT strains that were competitive in vitro were also equally competitive as their parent resistant SSuT strains when the competition took place within the animal. It is clear from these experiments that the genes conferring the SSuT phenotype are not directly responsible for greater fitness in dairy calves, but the occasional loss of fitness with the absence of some or all of the SSuT genes supports the hypothesis that the gene(s) of interest are located proximally to the SSuT genes on the chromosome.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #71: Encourage Sharing of AR Data Between Industry and the Research Community, Including Genomics and Other Technologies.			
NIH/DoD	Collaboration on genomics technologies and resources	NIAID continued its agreement with the Defense Advanced Research Project Agency (DARPA) in support of genomics efforts targeted at pathogens of potential bioterrorist threat.	Through this collaboration with DARPA large-scale genome sequencing projects for Brucella suis and Coxiella burneti have been completed and are available at http://www.ncbi.nlm.nih.gov/genomes/lproks.cgi. Neither of these genomes included resistance markers. In addition, a joint NIAID-DHS funded project has funded the sequencing of a multidrug resistant strain of Yersinia pestis available at http://www.ncbi.nlm.nih.gov/genomes/lproks.cgi under the unfinished genome tab. The funding on the Poxvirus database is now through NIAID as part of the regional bioinformatics centers (http://www.brc-central.org/cgi-bin/brc-central/brc_central.cgi) and specifically at the web site http://www.biovirus.org/ as the Viral Bioinformatics Resource Center. This resource for the scientific community provides sequencing and functional comparisons of orthopox genes and the design and maintenance of a relational database to store, display, annotate, and query genome sequences, structural information, phenotypic data and bibliographic information.
FDA	Reagent development	Facilitation of research through reagent development for the scientific community: Pertussis, *H. influenzae,* TB, influenza.	collaborated with the World Health Organization and the Aeras Global Tuberculosis Foundation to prepare standard reagents for pre-clinical testing of new TB vaccines in preparation for human clinical trials. Reagents are stored at CBER and distributed to researchers throughout the world. CBER's influenza research group produces the reagents needed to standardize influenza vaccines, and tests and releases live and inactivated influenza vaccines to be used in the United States. The laboratory also produces reassortant influenza viruses with high growth characteristics to support large scale manufacturing, and conducts research on mechanisms for differences in growth and attenuation of influenza virus strains. Also participating in the pandemic influenza vaccine preparation by generating safer reference viruses for production of pandemic influenza vaccine, conducting collaborative research with CDC and WHO and contributed scientific expertise supporting the development of vaccines against influenza virus, including the H5NI strain.
FDA	See Action Item #30: (Anti-Infective Drugs Advisory Committee)	See Action Item #30: (Anti-Infective Drugs Advisory Committee)	See Action Item #30: (Anti-Infective Drugs Advisory Committee)
FDA	International Collaboration	Participated in and supported international efforts to develop improved vaccines and drugs to prevent multi-drug resistent tuberculosis. Research is being conducted in collaboration with American and Russian scientists. Participated in, led, and supported international efforts to speed and coordinate efforts to develop effective vaccines for prevention of H5N1 Avian Influenza.	Held and participated in multiple meetings and workshops in the USA and other countries to address and coordinate international efforts to prevent pandemic influenza.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Bioinformatics Resource Centers	NIAID Bioinformatics Resource Centers are designed to develop, populate, and maintain comprehensive, relational databases to collect, store, display, annotate, query, analyze genomic, functional genomic, structural and related data for microorganisms responsible for emerging and re-emerging infectious diseases and for those considered agents of bioterrorism and develop and provide software tools.	Eight Centers were funded in FY04 http://www.niaid.nih.gov/dmid/genomes/brc/default.htm. Publicly accessible individual BRC web sites were developed in FY05 and are available. BRCs are now providing long term maintenance of the genome sequence data and annotation released by the NIAID Microbial Sequencing Centers as well as by other national and international sequencing efforts.
NIH	NIAID Microbial Sequencing Centers	The Microbial Genome Sequencing Centers address NIAID's need for sequencing of microorganism and invertebrate vectors of disease. The MGSCs provide rapid and cost efficient resources for production of high quality genome sequences of pathogens considered agents of bioterrorism (NIAID category A-C priority list), or causing emerging and re-emerging infectious diseases, their closely related organisms and clinical isolates and invertebrate vectors of disease.	These Centers have the capacity and are responding to scientific community and national and federal agencies' priorities for genome sequencing, filling in sequence gaps and therefore, providing genome sequencing data for multiple usages including understanding biology of microbe, forensic strain identification and identifying targets for drugs, vaccines and diagnostics. See http://www.niaid.nih.gov/dmid/genomes/mscs/default.htm.
NIH	NIAID pathogen functional genomics resource center (PFGRC)	The PFGRC was established in FY2001 to provide and distribute to the broader research community a wide range of genomic and related resources and technologies for the functional analysis of microbial pathogens and invertebrate vectors of infectious diseases. The number of organism-specific microarrays produced and distributed to the scientific community increased to 25 in FY2005.	Ongoing. See website for additional details: http://www.niaid.nih.gov/dmid/genomes/pfgrc/default.htm.
Action Item #72: Bring New Researchers into the Field, by Utilizing Appropriate Strategies such as Training and Research Opportunities.			
FDA	Fellowship Program	Combined Pediatric Infectious Diseases Fellowship formed with Children's National Medical Center, Washington, D.C.	Ongoing: First fellow to complete the program is in June 2004.
NIH	Research Scholar Development Award (RSDA)(K22)	The RSDA will provide support for postdoctoral fellows who are moving to assistant professor positions in an academic institution. The purpose of the RSDA is to ease the transition to an academic position by enabling the recipient to focus on the establishment of his/her research laboratory prior to submitting applications for grant support. This is intended to establish new young investigators in needed fields, including AR.	(PAR-02-018) released November 15, 2001; remains active.
NIH	Other ongoing training and research fellowship awards	PA-00-003 Mentored Clinical Scientist Development Award (K08) PA-00-004 Mentored Patient Oriented Research Career Development Award (K23) PA-00-005 Mid-career Investigator Award in Patient Oriented Research (K24).	Important ongoing programs are fostering the development of young scientists and clinical investigators. Examples of recent awards include: "Defining Moxifloxacin as a First-line TB Drug," "Improving Antimicrobial Use," "Evaluation of MDR-TB Treatment Strategies in Lima, Peru" and "Molecular Epidemiology of Drug Resistant Malaria."

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	NIH Exploratory/Developmental Research Grant Award (R21)	This announcement redefines the National Institutes of Health (NIH) Exploratory/Developmental Research Grant Award (R21) mechanism, and extends its use as an investigator-initiated mechanism to a variety of Institutes and Centers (ICs) listed in the announcement. The R21 is intended to encourage exploratory and developmental research projects by providing support for the early and conceptual stages of these projects. This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	Ongoing.
NIH	MDR-TB Included on Category C Biodefense List	Multi-drug resistant TB is a re-emerging infectious disease that is included on NIAID's category C biodefense list. Grant applications for translational research or product development are responsive to biodefense initiatives that include category C agents.	Ongoing.
NIH	Investigator-initiated small research grant award program announcement (R03)	The R03 award supports small research projects that can be carried out in a short period of time, with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	Ongoing.
Action Item #73: Organize Conferences That Address Research Issues Relating to AR.			
CDC, EPA, FDA, NIH, USDA	National Foundation for Infectious Diseases Conference on Antimicrobial Resistance: Science, Prevention, Control	Scientific conference on Antimicrobial Resistance held annually in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA.	Organized conference in 2002, 2003, 2004, 2005, and 2006.
CDC, EPA, FDA, NIH, USDA	National Foundation for Infectious Diseases Conference on Antimicrobial Resistance: Science, Prevention, Control	Scientific conference on Antimicrobial Resistance held annually in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA.	Organized conference in 2002, 2003, 2004, and 2005.
USDA, FDA	American Society of Microbiology research colloquium on preharvest food safety and security	Session took place in December 2004, in Perthshire Scotland and brought together international experts in pre-harvest food safety. One issue that was discussed was Antimicrobial resistance.	Finished. Proceedings available on ASM web site.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	The NIAID Summit on the State of Anti-Infective Development	The meeting was a follow-up to the Summit on Development of Infectious Disease Therapeutics, hosted by NIAID in 2000. The August summit brought together leaders from government and the pharmaceutical industry to assess the current state of antimicrobial development. A major focus of the meeting was identifying perceived barriers to new anti-infective development and determining opportunities for NIAID to work with the public and private sector to help overcome those barriers.	Meeting held August 16-17, 2004. Meeting summary posted on NIAID website at: http://www.niaid.nih.gov/dmid/drug/
NIH	Division of Microbiology and Infectious Diseases Program staff serve as external consultants or liaison to a variety of national and international TB-related groups	NIAID program staff members serve as external consultants or liaison to a variety of national and international TB-related groups. These collaborative activities inform NIAID's strategic directions for the TB Program to assure maximum utilization of NIAID resources. National groups include the Advisory Council for the Elimination of Tuberculosis (ACET), CDC's TB Clinical Trials Consortium and TB Epidemiologic Studies Consortium, and the Infectious Disease Society of America. International groups include the STOP TB Vaccine Partnership' s Diagnostic, Vaccine, Drug Development and HIV/TB Working Groups, WHO's TDR, International Union against Tuberculosis and Lung Disease (IUATLD), the Global Alliance for TB Drug Development (GATB), and several European research consortia.	Ongoing.
NIH	Immune Mechanisms in Polymicrobial Infections Symposium	This symposium was part of the 2004 American Society for Microbiology general meeting. The goals and objectives of this workshop are consistent with program objectives to understand host factors associated with susceptibility to infections and with the research scope and objectives of recently released RFA A1 02-008 on "Impact of Microbial Interactions on Infectious Diseases".	ASM Meeting was held May 23-27, 2004. In follow up to this meeting, the IDSA is planning to feature a symposium entitled "New Insights into and Current Challenges Presented by Polymicrobial Diseases of the Respiratory Tract" October 5-9, 2005.
NIH	Novel Therapeutics for Enteric Infections: A Workshop	Workshop to assess the opportunities for discovery and clinical development of novel therapeutics for enteric infections. Attendees included representatives from NHLBI, FDA, Institute for OneWorld Health, Industry and Academia.	Meeting held September 22, 2005, in Bethesda, Maryland. The current status and new opportunities were addressed by 18 invited experts. Several promising entities have been identified and some are now under preclinical development.
NIH	Emerging Clostridial Diseases Workshop	The CDC, FDA, and NIAID are planning a public workshop to develop a draft research agenda to better understand the virulence, pathogenesis, host factors, and non-antimicrobial risk factors contributing to reports of morbidity and mortality associated with Clostridium sordellii and Clostridium difficile. Additionally, our goals are to identify research needs and priorities that will enable rapid progress, as well as to develop and provide recommendations for detecting cases and conducting surveillance of diseases and organisms.	To be held May 11, 2006 in Atlanta, Georgia.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Advanced Product Development for Multiplex Infectious Disease Diagnostics Workshop	Purpose of this workshop was to inform NIAID about the current status of multiplex infectious disease diagnostics, determine criteria to assess performance of multiplex instruments, and identify current and potential obstacles to developing and integrating this functionality into the clinical setting.	Workshop held June 2005; summary found at: http://www.niaid.nih.gov/dmid/meetings/adv_prod.pdf
NIH	Annual meeting of the U.S.-Japan Cooperative Medical Sciences Program, TB and Leprosy Panel	The U.S.-Japan Cooperative Medical Sciences Program's TB and Leprosy Panels will hold their annual meeting in Kagoshima, Japan on July 26-28, 2006 to foster an exchange of ideas and stimulate collaborative research among U.S., Japanese and other Asian Pacific Rim mycobacterial researchers. For more information about this program: http://www3.niaid.nih.gov/about/organization/odoffices/oga/usjapan/.	Ongoing. For more details: contact Gail Jacobs, gg6z@nih.gov.
USDA	Bilateral meetings between Canada and the US related to antimicrobial surveillance	Participated in a bilateral meeting in Quebec to discuss harmonization of NARMS program with the Canadian CIPARS program.	Completed.
Action Item #74: Explore the Need To Encourage Preclinical Studies on the Toxicology, Pharmacokinetics of Novel Therapeutic Agents for the Treatment of Multidrug-Resistant Pathogens And Facilitate the Transition of Potential Products from Preclinical to Clinical Studies Leading to Development by Industry of Novel Therapeutic Agents.			
NIH	Pharmacokinetics and pharmacodynamics animal model contract	This contract, awarded in June 2004, provides a resource to determine basic pharmacology and efficacy characteristics of new chemical entities in order to best evaluate candidate compounds as potential new drugs for tuberculosis and other infections. This contract will allow NIAID to provide critical support for investigator-initiated drug discovery, to stimulate private sector sponsorship of new drugs, to perform comparison (or confirmatory) studies from different sponsors, and to provide information for selection of antimicrobial drug candidates for design of clinical studies. This contract will serve as the central facility for evaluation of novel compounds for physical, pharmacokinetic, and pharmacodynamic properties.	Ongoing.
**** TOP PRIORITY **** **Action Item #75: In Consultation with Academia and the Private Sector, Identify and Conduct Human Clinical Studies Addressing AR Issues of Public Health Significance That Are Unlikely To Be Studied in the Private Sector.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA, CDC, NIH	Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP)	Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues.	Workshop held April 15-16, 2004. Discussed the use of pharmacodynamic information in appropriate dose selection in clinical trials of anti-infective agents, and summarized the issues with developing antimicrobial drugs by allowing data from one serious disease to be supportive of data in another less serious disease such that sponsors would only have to perform one trial instead of two in the less serious disease. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)
NIH, NIAID	Division of AIDS Clinical Trials	Numerous trials underway that are monitoring for resistance: R. Chaisson, Johns Hopkins University, "Novel TB Prevention Regimens for HIV-Infected Adults" in South Africa. C. Whalen, Case Western Reserve, "Randomized, Phase II Study of Punctuated Antiretroviral Therapy for HIV Infected Patients with Active Pulmonary Tuberculosis and CD4 count > 350 cells/mm3." S. Abdool Karim, University of Natal, South Africa "Collaborative AIDS Programme of Research in South Africa.	Ongoing. Additional study started in 2005: (1) Sok Thim, Cambodian Health Committee: U01-AI-061736 "A Cambodian Clinical Research Network for HIV/TB" (CIPRA). This study is currently enrolling and will determine if early initiation of antiretroviral therapy impacts tuberculosis cure, survival, relapse and control of HIV in urban and rural settings. It is jointly sponsored by the French National Agency for Research on AIDS and Viral Hepatitis (ANRS) – ANRS 1295 CAMELIA. Expected total enrollment: 660. Positive cultures will be assessed for resistant TB.
NIH	Tuberculosis Research Unit (TBRU)	The TBRU contract (N01-AI-95383, Case Western Reserve University) continues to make progress in developing surrogate markers of disease and human protective immunity and in conducting clinical trials of potential new TB therapeutic, preventive, and diagnostic strategies. Activities of the TBRU are coordinated with other major organizations involved in TB research, including the CDC, USAID, FDA, WHO, Global Alliance for TB Drug Development and IUATLD, and with interested industrial partners.	Information about on-going TBRU supported studies can be found at: http://www.tbresearchunit.org. The TBRU is currently undertaking a clinical trial to evaluate the potential of Fluoroquinolone drugs to be used as anti-TB agents. This contract is currently being recompeted and will continue to provide targeted clinial research in tuberculosis.
NIH	Bacteriology and Mycology Study Group (BAMSG) and Bacteriology and Mycology Biostatistical and Operations Unit (BAMBU)	The BAMSG and BAMBU continue to support clinical trials against fungal and resistant bacterial infections. The BAMSG was awarded to the University of Alabama in 2001. A reserve fund to support orphan studies that cannot be funded through industrial sponsors is available through the BAMSG contract.	Active and Planned Protocols include: BAMSG 3-01 A phase II randomized trial of amphotericin B alone or combined with fluconazole in the treatment of AIDS-associated cryptococcal meningitis" (8 US sites, 5 Thai sites); BAMSG 4-01 Strategies to Reduce Transmission of Antimicrobial Resistant Bacteria in Intensive Care Units (STAR*ICU Trial) (20 US sites); BAMSG 4-02 Randomized, Multi-Center, Comparative Trial of Short-Course Empiric Antibiotic Therapy versus Standard Antibiotic Therapy for Subjects with Pulmonary Infiltrates in the Intensive Care Unit (ICU) (12 US sites); and BAMSG 4-03 Derivation of a Clinical Prediction Rule for Bacterial Pulmonary Infection in Mechanically Ventilated Children (3 US sites)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Vaccine and Treatment Evaluation Units (VTEUs)	The VTEUs are a network of university research hospitals across the United States that conduct Phase I, II, and III clinical trials to test and evaluate vaccine and therapeutic candidates for infectious diseases. Through these sites, researchers can quickly carry out safety and efficacy studies of promising vaccines in children, adult, and specific high-risk populations. The results of these trials may have a profound effect on public health here and abroad. Through numerous studies at the VTEUs, researchers have tested and advanced vaccines for malaria, tuberculosis, pneumonia, cholera, and whooping cough. In the last 6 years alone, NIAID has supported more than 110 clinical trials through the VTEUs.	The VTEU is sponsoring "Phase I Studies of the Safety and Immunogenicity of Primary and Secondary BCG Vaccination Delivered Intradermally, Orally, and by Combined Routes of Administration in Healthy and Previously Immunologically Naïve Volunteers." Enrollment is expected to start in FY 2006.
NIH	Prevention of group B streptococcal (GBS) disease contract	NIAID continues to support research on the prevention of GBS disease through a five year multidisciplinary contract awarded late in 2002 to the Channing Laboratory, Brigham and Women's Hospital. This collaborative multidisciplinary effort is focused on clinical studies in selected populations to further understand GBS infection and on studies of the host immune response.	A clinical trial was recently initiated to evaluate the impact of a GBS vaccine on GBS colonization that had implications for reducing the amount of antibiotics administered to pregnant women during delivery. Ongoing.
NIH	Science Advance: Combining sulfadoxine pyrimethamine (SP) with other antimalarials – artesunate (AS) or amodiaquine (AQ) - reduces treatment failure rates	In this study, investigators used SP alone or combined with either AS or AQ to treat patients with uncomplicated malaria. The results indicated that the SP+AQ combination is more effective treatment than SP alone and may both impede the spread of drug-resistant parasites as well as prolong the therapeutic lifespan of current antimalarials.	Dorsey G, Viahos J, Kamya MR, Staedke SG, and Rosenthal PJ: Prevention of increasing rates of treatment failure by combining sulfadoxine-pyrimethamine with artesunate or amodiaquine for the sequential treatment of malaria. The Journal of Infectious Diseases 188: 1231-1238, October 2003.
NIH, NIAID	Treating Infectious Diseases in a Microbial World: New Classes of Antimicrobials	Workshop organized and corvine by the National of Academics of Sciences	Workshop held on May, 2005, summary can be found at: http://fermat.nap.edu/catalog/11471.html
NIH, NIAID	Treating Infectious Disease in a Microbial World: Immunomodulation	Workshop organized and corvine by the National of Academics of Sciences	Workshop held on May, 2005, summary can be found at: http://fermat.nap.edu/catalog/11471.html

**** TOP PRIORITY ****

Action Item #76: Identify, Develop, Test, and Evaluate New Rapid Diagnostic Methods for Human and Veterinary Uses with Partners, Including Academia and the Private Sector. Such methods Should Be Accurate, Affordable, and Easily Implemented in Routine Clinical Settings.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Test kit evaluation	Work to develop streamlined mechanisms for evaluating rapid diagnostic test kits for identifying microbes and for determine susceptibility to treatments. Work with academia and industry to produce guidance documents and reference methods that could be used in evaluating new rapid diagnostics for use in clinical settings.	**Cleared or approved:** CDRH cleared an IVD device, developed by CDC, designed to detect highly pathogenic influenza A/H5 viruses. CDC's test is called the Influenza A/H5 (Asian lineage) Virus Real-time RT-PCR Primer and Probe Set. **ONGOING:** 1) Development of 2 international documents for an international reference AST method with ISO/TC 212 WG (Doc in final stage); and for the evaluation of performance of AST devices (in first comment period); 2) Collaborative work with CDER on antibiotic breakpoint disparities that exist between CLSI and FDA and the resulting public health impact. Includes efforts with Pharmaceutical industry, device manufacturers, CLSI, CMS, and FDA. **COMPLETED:** Collaboration with CDC on inability of commerical devices to detect vancomycin resistance in S. aureus.
FDA	Foodborne pathogens	Rapid Diagnostics for foodborne pathogens	Development of rapid diagnostic methods to detect biological contamination of foods (FDA joint center project). During the past three years, researchers in CBER, CDRH, and CFSAN, have developed and evaluated several microarray-based assays for the reliable detection, discrimination, and multilocus typing of all Listeria species, four Campylobacter species (C. jejuni, C. coli, C. lari, and C. upsaliensis), Bacillus anthracis, enterotoxins of Staphylococcus spp., toxin genes of Clostridium perfringens, as well as the genes involved in bacterial drug resistance (Staphylococcus spp, and Streptococcus spp.). The results of this study have already been published in several articles in peer-reviewed scientific journal.
FDA	Bloodborne pathogens	Rapid Diagnostics for bloodborne pathogens.	**Development of rapid assays to identify blood born pathogens.** CBER scientists have developed nucleic-acid-based-tests (NAT) and a TaqMan assay to detect the potential bacterial contamination in whole blood and platelets. The sequences used in these primer sets are conserved in 19 bacterial species and it is anticipated that it will be possible to detect contamination with any of these bacteria in a single PCR-reaction. Addition, work is in progress to develop a DNA microarray based pathogen chip that could detect all pathogenic bacteria that contaminate blood and blood products. **Development of rapid assays to detect malaria parasites.** Scientists have developed NAT-based on a PCR-test, a TaqMan assay and DNA microarray test to detect of all four species of human malaria parasites. Results demonstrated this test could be used for the reliable species discrimination of the human PlasmodiumPotential for use as a tool for screening donors. Also working to develop an ELISA as a blood-screening test.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Biodefense and Emerging Infectious Diseases Research Opportunities	In response to growing concerns about the use of biological agents in acts of terrorism, NIAID has expanded its biodefense research program. The ultimate goal of that expansion is to develop effective diagnostics, vaccines and therapeutics to protect the public in the event of a biological attack or the sudden emergence of select rare or believed to be eradicated diseases.	Notice AI-02-023; http://grants1.nih.gov/grants/guide/notice-files/NOT-AI-02-023.html. In 2003 converted to PA-03-080; expires March 2006 http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html.
NIH	Challenge Grants: Biodefense and SARS Product Development	To facilitate collaborative partnerships between government and the private sector for further development of already identified products against NIAID Category A, B and C high priority pathogens and all stages of product development against Severe Acute Respiratory Syndrome (SARS), including vaccines, adjuvants, therapeutics, diagnostics and research resources.	Recent awards include: "Mass Tag PCR Detection of Respiratory Pathogens," "Diagnostics For Bacterial/Viral Pathogens Including SARS," and "Multiplexed Detection of Bioterror Agents."
NIH	Cooperative Research for the Development of Vaccines, Adjuvants, Therapeutics, Immunotherapeutics & Diagnostics for Biodefense	To support discovery/design and development of vaccines, therapeutics, adjuvants, and diagnostics for biodefense. This program will help translate research from the target identification stage through target validation to early product development.	Recent awards include: "A Multiplexed Diagnostic Platform for Bioagent Detection," "Therapeutic and Diagnostic Antibodies Against SARS," "Detection of Category A Pathogens by Gold Nanoparticles," and "Synthetic Peptide SARS Coronavirus Diagnostic Kit."
NIH	"Sepsis and CAP: Partnerships for Diagnostics Development"	This initiative was released in August 2004 with a receipt date of December 14, 2004 (RFA-AI-04-043). The purpose of the initiative is to support industry development of broad diagnostic technologies that provide early detection of select major causes of septicemia, bacteremia, candidemia, and community-acquired pneumonia.	Nine projects were funded in 2005. The purpose of the initiative is to support industry development of broad diagnostic technologies that provide early detection of select major causes of septicemia, bacteremia, candidemia, and community-acquired pneumonia.
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN)	NIAID's FWDIRN network includes multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network includes Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network will be supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism.	Several projects utilizing different methodologies, i.e., RT-PCR, ELISA, and antigen microarrays, are underway to develop rapid, sensitive clinical diagnostics. Targeted enteric pathogens include Salmonella, Shigella, Campylobacter, diarrheagenic Escherichia coli, Listeria, caliciviruses, hepatitis A, and Francisella tularensis.
NIH	Partnerships for Vaccines and Diagnostic Development	A Request for Applications (RFA 03-028) entitled “Partnerships for Vaccines and Diagnostic Development” was released on June 9, 2003. This RFA is focused on development of vaccines against GAS, GBS and Helicobacter pylori and point of care diagnostics for GAS and GBS. Cooperative agreements (U01s) will be used to support the research which must include substantive involvement by an industry partner.	In 2004, NIAID awarded 3 Group A Streptococcal and 1 Group B Streptococcal vaccine-related grants, as well as a grant focused on the development of an improved GBS diagnostic. The initiative can be found at (http://grants2.nih.gov/grants/guide/rfa-files/RFA-AI-03-028.html).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	New methods for the determination of AR in Campylobacter	Antimicrobial test methodologies for Campylobacter are technically difficult, costly and often difficult to compare to agar dilution which is considered the 'gold standard'. A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in Campylobacter species. This work will be presented to the National Committee for Clinical Laboratory Standards (NCCLS) for adoption as a recommended testing methodology. NCCLS determines the most accurate means of antimicrobial susceptibility testing and disseminates this information worldwide.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Identification of collagenase secreted by Salmonella typhimurium DT 104 and the development of a RT-PCR assay for collagenase expression	In a recent study, we identified a collagenase secreted by DT104. The collagenase identification was based on DNA sequence homology to an E. coli collagenase. Also, we could reconstitute the cytotoxic phenotype by introducing the collagenase gene into a collagenase(-) strain. This collagenase is expressed and secreted only under certain conditions that seem to be determined by the host. We have developed an RT-PCR assay for collagenase expression, and we will be using this assay to identify other strains that exhibit the cytotoxic phenotype. Collagenase expression appears to only occur in immunosuppressed veal calves.	Completed. NADC, Ames IA
USDA	Antibiotic resistance determinants and the protozoa-mediated upregulation of virulence in Salmonella	For certain multiresistant Salmonella, I.e., those strains possessing the integron structure in S. typhimurium DT 104, virulence is enhanced following growth within protozoa.	Ongoing NADC ARS Ames IA
USDA	Development of a rapid PCR assay for genus and species identification of enterococci	We developed a multiplex PCR procedure in conjunction with a colony PCR method that will identify the genus and the species of 25 Enterococcus strains that have been isolated and classified. Primers specific for the genus have been combined in 7 different reaction mixtures to primers for the different species and from bacterial culture to finish, the entire process requires approximately 3 ½ hours. The procedure is a cost-effective, rapid, and accurate method for identification of enterococci and an application for a patent is currently being pursued.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Factors affecting microbial ecology of pathogen colonization and AR acquisition	An automated ribotyping system is being used at the USDA/ARS FFSRU to identify, characterize and monitor gut bacteria isolated by us and others; information obtained from this use is being maintained in the Gastrointestinal Microflora Ribotype Database (GMRD). Molecular typing methods (e.g. ribotyping, denaturing-gradient gel electrophoresis (DGGE), and DNA sequencing) are being used to distinguish bacterial strains inhabiting the gastrointestinal tract with even greater precision and to determine genetic alterations occurring within these bacteria. This database is being used by scientists worldwide to develop a more thorough understanding of the effects of sub-therapeutic antibiotic administration and other stressors on the ecology of the gut microflora.	Ongoing. Sheffield Food and Feed Safety Research Unit, ARS, College Station, TX.
USDA	Evaluate a microbroth dilution assay for antimicrobial susceptibility testing of Campylobacter	A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in Campylobacter species. This assay provides an alternate means for testing large numbers of Campylobacter for resistance to a panel of antimicrobials. This work will be useful to scientists and clinicians involved in assessing antimicrobial resistance.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Develop a PCR assay for detection of mixed cultures in Campylobacter	Testing for antimicrobial resistance typically occurs on bacteria originating from one single colony. It is commonly assumed that this single colony arose from one bacterium. However, recent reports suggest that bacteria may aggregate, making selection of a single bacterium difficult. We developed a PCR assay which identifies mixed populations of Campylobacter. This PCR assay is ideal for applications with high throughput requirements, such as often occurs within our laboratories testing bacteria for resistance to antimicrobials. This work will be useful to scientists and clinicians involved in assessing antimicrobial resistance.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Develop a rapid PCR assay for genus and species identification of Enterococci	The current classification and identification scheme for Enterococcus is both tedious and laborious and is based upon phenotypic analysis and there is no procedure that will allow genus and species identification of enterococci in less than 24 hours. To this end, scientists in our Unit have developed a multiplex PCR procedure in conjunction with a colony PCR method that will identify the genus and the species of 25 Enterococcus strains that have been isolated and classified. Primers specific for the genus have been combined in 7 different reaction mixtures to primers for the different species and from bacterial culture to finish, the entire process requires approximately 3 ½ hours. The procedure is a cost-effective, rapid, and accurate method for identification of enterococci. This work will be useful to scientists involved in Enterococcus research.	Completed. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
USDA	Emergence of multiresistant Salmonella choleraesuis	Recently we isolated a multiresistant salmonella choleraesuis possessing the integron structure found in S. typhimurium DT 104. Ongoing studies are aimed at determining the pathogenicity and protozoa-mediated alteration in pathogenicity for this swine-adapted serotype.	Ongoing NADC ARS Ames IA
Action Item #77: Encourage Basic and Clinical Research in Support of the Development and Appropriate Use of Vaccines in Human and Veterinary Medicine in Partnership with Academia and the Private Sector.			
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	Four CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in nine Emerging Infections Program areas in which population-based active surveillance is conducted. Second, ongoing active surveillance in these areas will track any change in the amount of invasive disease due to drug resistant strains. The third project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The fourth is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees.	Completed reports have been either submitted or published for all four projects. The case-control study enrolled 782 cases and 2512 controls. Effectiveness for ≥1 dose against vaccine serotypes was 96% among healthy children and 81% among children with comorbid conditions; effectiveness was 76% against penicillin-nonsusceptible infections (Whitney et al, submitted). ABCs surveillance is ongoing indicates that by 2004 disease due to penicllin-resistant strains had dropped by over half (Kyaw M et al N Engl J Med 2006). In Anchorage, carriage study results suggest that introduction of PCV7 into the routine infant immunization schedule in a community with a high prevalence of resistant pneumococci appears to reduce transmission of PCV7 vaccine serotypes and COT-NS pneumococci but has no impact on overall carriage of pneumococci.(Moore MR et al J Infect Dis. 2004). Alaska surveillance data also show a reduction in invasive infections caused by resistant strains (Hennessy TW et al Vaccine 2005).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Double-blind placebo-controlled clinical effectiveness trial of the 23-valent pneumococcal vaccine	S. pneumoniae is a leading cause of morbidity in the U.S., causing an estimated 500,000 cases of pneumonia, 3,000 cases of meningitis, 50,000 cases of bacteremia, and 7,000,000 cases of otitis media annually. Data from 1981 to 1991 suggest that S. pneumoniae causes approximately 12% of pneumonia hospitalizations in the military or 9.5 admissions per 100,000 person-years. A 23-valent pneumococcal vaccine is being used at one military basic training facility and at military training facilities. This vaccine provides coverage for 85 - 90% of the serotypes causing bacteremia in the general population, but its clinical benefit needs to be more fully characterized before the impact of its use on the emergence or spread of S. pneumoniae resistance can be determined.	Enrollment was completed in June 2003, with a total of 152,765 recruits enrolled. Data analysis is ongoing. Preliminary results were presented at the 4th International Symposium on Pneumococci and Pneumococcal Diseases in May of 2004. Manuscript in preparation.
FDA	Pneumococcal conjugate vaccine	Identify mechanisms for establishing efficacy of additional pneumococcal conjugate vaccines with additional serotypes. Participated in multiple WHO Workshop held to discuss serologic correlates of protection. Also, provide regulatory review, conduct research and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND).	Research regarding serologic assessment of response to vaccines ongoing. (Lee, CJ, et.al., Crit Rev Microbiol 2003:29(4)"333-349; Mikolajczyk, MG, et.al., Clin Diagn Lab Immunol 2004; 11(6):1158-1164)Also, provide regulatory review, conduct reseqrch and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND). CBER scientists have worked with the WHO to derive a set of immunological response endpoints or measures to evaluate possible new higher valent pneumococcal conjugate vaccines
FDA	Enteric vaccines	Research to facilitate enteric vaccine development and licensure	Studies of multiple antibiotic resistant Salmonella typhimurium DT104 identified unique virulence attributes - cloned and patented 7 genetic promoters strongly upregulated during bacterial growth in human epithelial cells. Developed a prototype live-vectored Salmonella typhi-based oral vaccine containing key protective antigen genes from Shigella. Studying adaptive mutations in S. sonnei that allow this organism to become lactose-utilizing, - this high frequency mutational event is partially responsible for the spread of multiantibiotic resistant strains.
FDA	Vaccine research	Research in support of the development and appropriate use of vaccines in humans to: 1) prevent viral infections, i.e. influenza, RSV; 2) prevent common bacterial infections i.e. *S. pneumoniae*, non-typable *Haemophilus influenzae*, group B streptococcus, *N. gonorrhoeae, N. meningitidi*s. Regulatory and research support of annual trivalent inactivated and live intranasal influenza vaccine development, production and licensure, including additional manufacturers and novel technologies.	Twelve ongoing research projects support development of vaccines for the organisms listed 1) Completed study of protective levels of antibody against neonatal type 1a and 3 group B streptococcal infection (funded through interagency agreement with NICHD). 2) Ongoing research regarding correlates of protection against other common types of group B streptococcus. 3) Investigating correlates of protection against infection with *Streptococcus pneumonia*. 4) *N. gonorrhoeae*. Studying immunogenicity and pathogenicity of associated proteins, funded through the FDA Office of Women's Health. 5) Ongoing regulatory review, research support and guidance for both current vaccines and those vaccines under IND, including vaccines against avian influenza.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Vaccine development	Research in support of the development of vaccines to prevent colonization, infection, and transmission of tuberculosis	Current projects investigate the following vaccine candidates in mouse model of tuberculosis: combination DNA vaccines, multigene DNA constructs, attenuated live vaccines and subunit vaccines. These vaccines are also being tested using prime-boost strategies and post-exposure models. (Kamath AT, et.al., Vaccine 2005; 23(29):3753-3761)
FDA	Multidrug resistant TB	Research: mechanisms of resistance in multidrug resistant tuberculosis. Since there is evidence that TB patients who have been "cured" by antibiotic treatment can be re-infected with Mtb and since outbreaks of MDRTB in countries such as Peru have demonstrated that certain strains of DRMtb cannot be treated with currently available drugs, new preventive vaccines are critical for controlling the spread of tuberculosis.	Identified genetic mechanisms for multiple mechanisms of drug resistance in *M. tuberculosis*. (TangX, et.al., J Microbiol Methods 2005:May 2005, Devito JA, et.al., Antimicrob Agents Chemother 2003, 47(1):188-195) CBER/OVRR has a laboratory (Laboratory of Mycobacterial Diseases and Cellular Immunology (LOMDCI)) devoted to research on new TB vaccines including new antigen discovery and evaluation of new vaccines for safety, immunogenicity and effectiveness using a novel animal challenge model located in CBER's BL3 facilities. Scientists in LOMDCI are also collaborating with other institutes on the development of new drugs and diagnostics. These scientists have published >10 peer-reviewed papers on this topic since 2004.
FDA	Drug therapy	Research: novel targets for drug therapy (to avoid resistance).	Two ongoing projects that examine the mechanisms of development of HIV drug resistance.
NIH, USAID	Randomized, double-blinded, controlled Phase III efficacy trial of pneumococcal conjugate vaccine	NIAID conducted a randomized, double-blind, controlled Phase III efficacy trial in Gambia, West Africa, using a 9-valent pneumococcal conjugate vaccine manufactured by Wyeth-Lederle Vaccines and Pediatrics (WLVP). The trial was designed to determine the impact of the pneumococcal conjugate vaccine, when administered with DPT/Hib (TetramuneTM) in the same syringe, on childhood mortality due to invasive pneumococcal disease. The main endpoint was overall mortality; however, secondary endpoints will include the effect of the vaccine on mortality and on invasive pneumococcal disease caused by pneumococci of vaccine serotype.	The results of the trial indicated that among the group of children who received pneumococcal conjugate vaccine, there were: 1) 37% fewer cases of pneumonia (confirmed by chest X-ray); 2) 15% fewer hospital admissions; 3) 16% reduction in overall mortality; and 4) half the rate of laboratory-confirmed pneumococcal pneumonia, meningitis, and septicemia. Overall, the pneumococcal conjugate vaccine was shown to be highly effective against pneumonia and invasive pneumococcal disease and it can substantially reduce hospital admissions and improve child survival. The Lancet, Vol 365: 1139-1146, 2005.
NIH	Bacterial Respiratory Pathogen Research Unit (BRPRU)	This project supports bacterial pre-clinical and clinical studies for the diagnosis, prevention, and management of selected human bacterial respiratory pathogens. The contractor is currently pursuing clinical studies to evaluate a new pneumococcal surface protein vaccine and vaccines for non-typeable Haemophilus influenzae organisms using a human challenge model. Additional studies include the interaction of GAS with pharyngeal epithelial cells to better understand GAS colonization and infection.	Ongoing.
NIH	The tuberculosis research materials and vaccine testing contract (Colorado State University)	The contract provides exploratory and preclinical evaluation of promising new TB vaccine candidates in state of the art animal models and as such continues to provide critical resources for the interface between fundamental and applied science.	At the end of FY2005, more than 150 new TB vaccine candidates have been tested under this contract, one of which has recently entered human clinical trials with several others progressing through various stages of preclinical development.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Partnerships for Vaccines and Diagnostic Development	A Request for Applications (RFA 03-028) entitled “Partnerships for Vaccines and Diagnostic Development” was released on June 9, 2003. This RFA is focused on development of vaccines against GAS, GBS and Helicobacter pylori and point of care diagnostics for GAS and GBS. Cooperative agreements (U01s) will be used to support the research which must include substantive involvement by an industry partner.	In 2004, NIAID awarded three Group A Streptococcal and one Group B Streptococcal vaccine-related grants, as well as a grant focused on the development of an improved GBS diagnostic.
NIH	Vaccine Action Program(VAP)	The INDO-US Vaccine Action Program initiated in 1987 is a bilateral program that focuses on the development of safe and effective vaccines for major communicable diseases of interest to the two countries through joint research and development efforts.	Priorities under VAP include issues such as: acute respiratory illness, group A streptococci, hepatitis, diarrhea caused by Rotavirus, cholera and other infectious agents, leishmaniasis, typhoid, rabies, HIV/AIDS, tuberculosis, malaria, malnutrition and emerging and re-emerging infectious diseases.
NIH	Phase I Malaria vaccine trial	NIAID, in collaboration with Walter Reed Army Institute of Research (WRAIR), GlaxoSmithKline Biologicals, U.S. Agency for International Development (USAID), the University of Maryland School of Medicine Center for Vaccine Develoment (Md/CVD), and the University of Bamako, Mali, completed two Phase I trials in Mali of novel candidate vaccines that target the blood-stage of malaria parasites.	Under the initiative International Collaborations in Infectious Disease Research, an award was made to the University of Maryland Center for Vaccine Development and the University of Bamako to carry out additional clinical trials of promising candidate vaccines in Mali.
NIH	Phase I Malaria vaccine trial	In collaboration with Apovia, Inc., a biotechnology company, NIAID has undertaken a Phase 1 trial of a novel candidate malaria vaccine at the University of Maryland Center for Vaccine Development (UMd/CVD). This vaccine was developed with grant support from the SBIR Program administered at NIAID, and with additional support and collaboration from the Malaria Vaccine Initiative supported by the Program for Appropriate Technology (PATH).	Initial analysis of the serologic results indicated that the vaccine was poorly immunogenic. Analysis of cellular immune responses in this trial is expected later in 2006. In 2006 NIAID expects to launch Phase 1 trials of 2 other vaccine candidates.
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN)	NIAID's FWDIRN network includes multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network includes Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network is supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism.	On-going and/or planned clinical activities within the FWDIRN include: "Cell-mediated immunity studies from Salmonella typhi vaccine trials", "Sensitivity of TLR4 polymorphisms to Shigella LPS," "Immunogenicity of tularemia live vaccine strain in humans," "Prime-boost study of the immunogenicity of Vi polysaccharide typhoid vaccine after priming by oral Vi+ S. typhi strain," and "Safety of an anti-Shiga toxin type 2 monocolonal antibody."

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Vaccine Treatment and Evaluation Units (VTEUs)	The VTEUs are a network of university research hospitals across the United States that conduct Phase I, II, and III clinical trials to test and evaluate vaccine and therapeutic candidates for infectious diseases. Through these sites, researchers can quickly carry out safety and efficacy studies of promising vaccines in children, adult, and specific high-risk populations. The results of these trials may have a profound effect on public health here and abroad. Through numerous studies at the VTEUs, researchers have tested and advanced vaccines for malaria, tuberculosis, pneumonia, cholera, and whooping cough. In the last 6 years alone, NIAID has supported more than 110 clinical trials through the VTEUs.	The VTEU network is sponsoring: "A Randomized, Double-Blind, Placebo-Controlled, Dose Escalation, Inpatient Phase I/II Study to Determine the Safety and Immunogenicity of Ty800 [Salmonella typhi] in Healthy Adult Subjects."
NIH	Structural Organization and Proteomics of TB	This consortium is co-funded by NIGMS and NIAID and was initiated in 2000. The goal of this global consortium, which involves over 70 laboratories in 12 countries, is to determine and analyze the structures of over 400 functionally relevant Mtb proteins.	To date, the consortium has determined the structures of over 60 biologically important proteins from Mtb. The structural and functional information is publicly available through web-based databases: http://www.doe-mbi.ucla.edu/TB/. This Center Grant will end in early FY 2006 and will be continued as a more scientifically targeted, collaborative program project grant.
NIH	Science Advance: A tuberculosis subunit vaccine ready for testing in humans has shown promising results in two different animal models	NIAID funded scientists have now reported encouraging animal results with a new candidate TB subunit vaccine. The vaccine displayed potent immune response in mice and guinea pigs and protected the animals from challenge with a virulent strain of TB. In addition, the immune responses in the guinea pigs lasted for more than 1 year. This candidate vaccine has been approved for testing in humans that began early in 2004.	Results are published in: Skeiky YAW, Aldeson MR, Ovendale PJ, Guiderian JA, Brandt L, Dillon DC, Campos-Neto A, Lobet Y, Dalemans W, Orme, IM, and Reed, SG: Differential immune responses and protective efficacy induced by components of a Tuberculosis polyprotein vaccine, Mtb72F, delivered as naked DNA or recombinant protein: Journal of Immunology 172: 7618-7628, 2004. Recently, Aeras Global TB Vaccine Foundation has entered into an agreement with GSK to continue development of the Mtb72f vaccine.
Action Item #78: Encourage Basic and Clinical Research in Support of Novel Approaches to Preventing or Treating Infections with Resistant Organisms That Occur in Humans and Animals by Partnering with Academia and the Private Sector.			
CDC, NIH, USAID	Global Alliance for TB Drug Development	The Global Alliance for TB Drug Development is a new public/private partnership to stimulate new drug development against tuberculosis. NIAID is involved in this collaboration with private partners, who are contributing to the development of new drugs to shorten the treatment of TB and facilitate its control in the poorest countries. Over 30 organizations are stakeholders in this innovative public-private partnership, including the Bill & Melinda Gates Foundation, CDC, NIAID/NIH, Rockefeller Foundation, USAID, the World Bank, and WHO. For a comprehensive list, see: http://www.tballiance.org	Program staff assist the GATB in the process of soliciting requests for drug discovery and development proposals from the global research and development community and in the scientific peer review of the received proposals. As part of a broad search for new collaborations and new drug candidates, program staff and GATB representatives attended meetings with pharmaceutical companies with compounds or drugs showing promise as new TB drugs. Staff hold memberships and chair of the Scientific Advisory committee and NIAID TB contract resources contributed significantly to the pre-clinical development of a new TB drug candidate, PA-824.
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals	Working group formed; Draft document completed.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Cooperative Research for the Development of Vaccines, Adjuvants, Therapeutics, Immunotherapeutics & Diagnostics for Biodefense	To support discovery/design and development of vaccines, therapeutics, adjuvants, and diagnostics for biodefense. This program will help translate research from the target identification stage through target validation to early product development.	Recent awards include: "Novel Therapeutics for Pathogenic E. coli Diseases," "DNA Minor Groove-Binding Drugs and Food-borne Pathogens," and "HRF, an NFKB antagonist targeting multiple pathogens."
NIH	Anti-Infective Drug Development Contracts are testing new medicines	Research and development contracts are being used to actively test new candidate compounds for efficacy against infectious complications of AIDS in culture and in animals, a critical component in new drug development and approval. The contract resources will allow NIAID: (1) to support investigator-initiated drug discovery; (2) to stimulate private sector sponsorship of new drugs; (3) to perform comparison or confirmatory studies from different sponsors; (4) to provideinformation for selection of anti-mycobacterial drug candidates and for design of clinical studies; and (5) testing new candidate drugs against drug resistant strains of M. tuberculosis.	Awards include “Drug Development for Opportunistic Infections-Mycobacterium avium Complex,” “Tuberculosis Drug Screening,” and “Animal Model Testing of TB Drugs,” among others. These contracts are still active.
NIH	Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF)	This contract was established to acquire compounds for screening against virulent Mtb, maintain a computerized chemical database of compound structures, coordinate and distribute compounds for evaluation in vitro and in an animal model, and report data to suppliers. The TAACF has contacted over 3,500 chemists throughout the world seeking candidate anti-TB compounds.	Over 70,000 compounds have been received from academic and private sector investigators, principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites. The facility website is http://www.taacf.org/.
NIH	Submission of compounds for in vitro evaluation	Staff has selected for evaluation more than 10,000 compounds, based on their chemical structure, from the National Cancer Institute (NCI) chemical repository of over 500,000 compounds. Of these compounds, many have shown initial in vitro activity against a wild-type strain, and some have promising in vitro activity against isoniazid (INH)-resistant strains. A large part of this effort is conducted under an interagency agreement with the Health Resources and Services Administration at the National Hansen’s Disease Programs Center.	Ongoing. Of note, efficacy evaluations in animal models of TB are being conducted on selected compounds.
NIH	High-throughput screening contract with Southern Research Institute	This contract provides a high throughput screening capability to develop and implement biochemical, target-specific Mtb drug screening assays and to develop and implement Mtb metabolic stage-specific drug screening assays.	Ongoing. Selected molecular targets are being screened against large chemical libraries to identify new candidate antibiotics as potential additions to the combined regimen for treatment of tuberculosis, particularly to combat multidrug resistant strains.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Therapeutics Research on AIDS-Associated Opportunistic Infections and Malignancies	The goal of this program is to stimulate iterative preclinical research for novel therapeutic strategies against opportunistic infections (OIs), co-infections, and malignancies in people with HIV/AIDS. The PA is a joint sponsorship with the National Cancer Institute (NCI) and the National Institute of Dental and Craniofacial Research (NIDCR). The AIDS-associated infections emphasized by this PA are Mycobacterium tuberculosis, Pneumocystis carinii, Crypotsporidium parvum, and the microsporidia.	NIAID awarded two grants in FY 2004 [DAIDS]: "Menaquinone Biosynthesis in M. tuberculosis" and "Design/Syntheses/Studies/Novel Antituberculosis Agents"
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN)	NIAID's FWDIRN network includes multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network includes Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network will be supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism.	Basic research to support novel prevention and/or treatment of infections include projects that focus on: i) the development of small animal models that mimic human disease caused by Campylobacter and the life-threatening sequelae to infection by Shiga toxin-producing Escherichia coli, the hemolytic uremic syndrome (HUS); ii) comparison of the efficacy and potential side-effects of several antibiotics in the treatment of Shiga toxin-producing Escherichia coli; and iii) determination of the benefits and possible risk of monoclonal antibody therapy for HUS.
NIH	Pharmacokinetics and Pharmacodynamics of Antimicrobials in Animal Models	This contract, awarded in 2004, provides a resource to determine basic pharmacology and efficacy characteristics of new chemical entities in order to best evaluate candidate compounds as potential new drugs for tuberculosis and other infections. This contract will allow NIAID to provide critical support for investigator-initiated drug discovery, to stimulate private sector sponsorship of new drugs, to perform comparison (or confirmatory) studies from different sponsors, and to provide information for selection of antimicrobial drug candidates for design of clinical studies. This contract will serve as the central facility for evaluation of novel compounds for physical, pharmacokinetic, and pharmacodynamic properties.	Ongoing.
NIH	Challenge Grant: Development and Manufacture of an MDR-TB Tuberculosis vaccine	The goals of this program are to select the most suitable vaccine candidates that are active in animal models of infection with drug senstivive and MDR tuberculosis and to move the candidate which is most likely to provide protection in humans through preclinical development.	Awarded in 2005, ongoing.
NIH	Challenge Grant: Dihydrolipoamide Acyltransferase: Target for Chemotherapy	Dr. Carl Nathan (Weill Medical College of Cornell University) in collaboration with DeCode, Inc. is developing inhibitors to biochemical pathways of M. tuberculosis that are thought to be specifically active during infection in a host. The long term objective of this program is to conduct state of the art drug discovery, merging bioinformatics and laboratory approaches and to move promising drug candidates for TB through preclinical development.	Awarded in 2004; ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Grant: New Treatment for C. difficile-associated Diarrhea".	Under SBIR funding, NIAID is supporting a Phase II clinical trial of a promising therapy against Clostridium difficile. C. difficile is a significant problem in hospitals and long term care facilities. Current treatments have a high relapse rates. The Phase II trial will evaluate the efficacy of OPT-80, a novel antibiotic, against C. difficile in infected patients.	A protocol for the trial has been submitted to NIAID for review.
NIH	Grant: DNA gyrase and quinolone resistance in tuberculosis	The goals of this program are to understand how the quinolones act in mycobacteria and to discover ways to protect the compounds from the development of resistance.	Ongoing.
NIH	Grant: Drug Development for MDR-TB	Recent studies by Dr. James Dick (Johns Hopkins University) have demonstrated the antimycobacterial activity of the b-sulfonylcarboxamides to be the result of inhibition of a potentially unique pathway/target involved in central energy metabolism. The long-term objectives of this grant are to determine the molecular target and mechanism of action of this novel class of compounds, with subsequent optimization of drug structure, synthesis, and preclinical drug development.	Awarded in 2003; ongoing.
NIH	Grant: Inhaled Large Porous Particles for Treatment of MDR-TB	David Edwards, Harvard University, seeks to develop an aerosol delivery approach to more effectively treat and improve the control over transmission and outbreak of respiratory infectious diseases, specifically tuberculosis (TB) and multi-drug resistant TB (MDR-TB). His hypothesis is that direct, topical delivery of antibiotics to infected lungs results in relatively high local drug concentrations, which can more quickly eradicate active bacterial populations, thus sterilizing the lungs and reducing the duration of infectivity and the duration of chemotherapy necessary to achieve a durable cure in pulmonary tuberculosis relative to parenteral or oral dosing.	Awarded in 2004; ongoing with improvements in delivery technology for drugs against MDR-TB.
NIH	Malaria Grant Activities	NIAID also supported a Phase 1 clinical trial of a chloroquine-analog effective against chloroquine-resistant P. falciparum, as well as investigator-initiated research on preclinical development and evaluation of novel compounds. The Institute is also supporting preclinical and clinical studies of combination therapies for malaria, especially those including artesunate.	Based in part on data provided by NIAID supported studies, the chloroquine analog AQ-13 has been selected by the Medicines for Malaria Venture for further development as part of a combination therapy with other antimalarials. NIAID is also supporting research to examine alternative means to synthesize artemisinin, a key component of artemesinin combination treatment (ACT).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Science Advance: Tuberculosis Drug Resistance Protein Mimics DNA	NIAID-supported investigators have identified a novel Mtb protein that works through a completely new mechanism and helps the microbe resist damage from a class of drugs, called fluoroquinolones. This is the first antibiotic-resistance protein that binds to a drug's target, rather than working directly on the drug. These investigators speculate that this newly identified Mtb protein and mechanism may have a role in the basic regulation of bacterial growth, although its role is not yet proven. In addition to better understanding the role of this mechanism, future work could involve re-engineering the protein to kill, rather than protect, Mtb by providing a means to specifically target Mtb DNA and interfere with known DNA-binding proteins.	Results are published in: Hegde SS, Vetting MW, Roderick SL, Mitchenall LA, Maxwell A, Takiff HE, Blanchard JS: A Fluoroquinolone Resistance Protein from Mycobacterium tuberculosis that Mimics DNA. Science 308: 1480-1483, 2005.
NIH	Science Advance: A Potential New Immunotherapeutic Treatment for Tuberculosis.	Siderocalin (Lipocalin 2) binds to iron-scavenging molecules (siderophors) secreted by various pathogens and has been implicated in the innate immune response to gram-negative bacteria. An NIAID investigator has recently shown that human Siderocalin also binds to the siderophors produced by mycobacterium. This finding leads to the possibility of developing a new field of immunotherapeutics for the treatment of tuberculosis.	Results are published in: Holmes MA, Paulsene W, Jide X, Ratledge C, Strong RK: Siderocalin (Lcn 2) also binds carboxymycobactins, potentially defending against mycobacterial infections through iron sequestration. Structure (Camb). Jan. 13(1):29-41, 2005.
NIH	Science Advance: Moxifloxacin with rifampicin and pyrazinamide shortens treatment time in mice.	The addition of a new quinolone antibiotic (moxifloxacin) to a combination of two existing tuberculosis drugs reduced the treatment time needed to eradicate Mycobacterium tuberculosis from the lungs of infected mice when compared to the standard regimen of isoniazid, rifampin, and pyarzinamide. NIAID-supported scientists have shown improvement in bactericidal activity by replacing isoniaizid with a fluoroquinolone and improved sterilization. Using the accepted mouse model of infection, these findings suggest that this regimen has the potential to substantially shorten the duration of therapy needed to cure human tuberculosis.	Results are published in: Nuermberger EL, Yoshimatsu T, Tyagi S, O'Brien RJ, Vernon AN, Chaisson RE, Bishai WR, Grosset JH: Moxifloxacin-containing Regimen Greatly Reduces Time to Culture Conversion in Murine Tuberculosis. Am J Respir Crit Care Med 169: 421-426, 2004.
NIH	Scientific Advance: A Multidisciplinary Approach Identifies Potent New Inhibitors Active Against Tuberculosis	NIH-supported scientists have discovered the structural requirements for the design of potent new drugs that inhibit a key pathway by combining the properties of two other drugs into a single molecule based on elegant biochemical studies of their mechanisms of action, coupled with structural biology and molecular genetics. New compounds with 200-fold improved potency against the target pathway and 20-fold improved activity against M. tuberculosis were recently discovered by using these data to direct combinatorial chemical synthesis. This is an exceptional example of the power of using a multidisciplinary approach for discovery of new anti-tubercular drugs.	Results are published in: Rawat, R, Whitty, A, and Tonge, PJ: The isoniazid-NAD adduct is a slow, tight-binding inhibitor of InhA, the Mycobacterium tuberculosis enoyl reductase: Adduct affinity and drug resistance. Proceedings of the National Academy of Science 100: 13881–13886, 2003.
Focus Area IV: Product Development			
**** TOP PRIORITY ****			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #79: Create An Interagency AR Product Development Working Group To Identify and Publicize Priority Health Needs in Human and Animal Medicine for New AR Products (e.g., Innovative Drugs, Targeted Spectrum Antibiotics, Point-of-Care Diagnostics, Vaccines and Other Biologics, Anti-Infective Medical Devices, and Disinfectants).			
CDC	Characterization of biofilm formation among *Candida* species bloodstream isolates and evaluation of a novel antifungal drug catheter lock technique to eradicate or prevent catheter-associated *Candida* biofilms	To date, an antifungal lock technique has not been evaluated for Candida biofilms. Furthermore, the risk of inducing drug resistance in Candida cells colonizing the catheter and exposed to low concentrations of antifungal drug in the lock solution must be carefully studied. Recently, two new classes of antifungal agents, lipid-associated amphotericin B (L-AmB) and echinocandins (ECAN), have been shown to have some efficacy against Candida biofilms. Use of these agents in an antifungal lock solution could offer promise as a technique to prevent or reduce catheter-associated Candida BSI and should be analyzed. This project proposes to establish a laboratory model of living Candida biofilms to characterize biofilm formation among Candida spp. bloodstream isolates. An adaptation of the model will be designed to test the efficacy of an antifungal catheter lock technique and the potential to select for drug resistance in Candida cells within a catheter-associated biofilm.	This project will be completed April 30, 2006. The preliminary data collected in the first year of this two year project established the parameters used to grow *Candida* biofilms in a laboratory model of central venous catheter -associated fungal biofilms for the purpose of testing the efficacy of antifungal lock therapy. Results demonstrated that *Candida* biofilms readily formed on CVC tubing under the conditions tested which mimicked in vivo conditions as closely as possible. Results suggest that cells capable of resisting killing by amphotericin B are likely doing so via the extracellular matrix which acts as a physical barrier to the drug and not microbial resistance mechanisms. Key outcomes include establishment of laboratory capacity to study *Candida* biofilms and response to antifungal treatment, standard operating protocols to test antifungal drug susceptibility of fungal biofilms, and evidence to support further evaluation of antifungal lock therapy for treatment and prevention of *Candida* biofilms in vivo.
FDA	Nonprescription Drugs Advisory Committee (NDAC)	Discussion of the microbiologic surrogate endpoints utilized in demonstrating effectiveness of antiseptic products in various healthcare settings.	Meeting held on March 24, 2005. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4099T1.pdf.
FDA	Interagency AR product development working group	FDA has chosen to perform these cooperative activities using existing advisory committees with other agency and industry participation.	Initial AC meeting Feb 19-20, 2002. Docket available for additional comment.
FDA	Otitis Media Advisory Committee	Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population)	Meeting held on July 11, 2002. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder02.htm#Anti-Infective
FDA	FDA/PhRMA Co-Sponsored Workshop	Discussion of statistical issues in clinical trials including trials related to resistant pathogens.	Meeting held on November 9, 2002.
FDA	FDA/IDSA/PhRMA Co-Sponsored Public Workshop	Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical Research and Manufacturers of America, and U.S. academic institutions along with representatives from CDC and NIH to address current topics of interest associated with AR and antimicrobial drug development.	Meeting held on November 19-20, 2002. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to macrolide-resistant *Streptococcus pneumoniae* (MRSP)	Meeting held on January 24, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to AR in *Streptococcus pneumoniae*.	Meeting held on March 4, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant pathogens.	Meeting held on May 5, 2003. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/cder03.htm#Anti-Infective
FDA	Nonprescription Drugs Advisory Committee (NDAC)	Discussion of the microbiologic surrogate endpoints utilized in demonstrating effectiveness of antiseptic products in various healthcare settings.	Meeting held on March 24, 2005. CDER advisory committee transcripts http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4099T1.pdf.
**** TOP PRIORITY **** **Action Item #80: Identify Ways (e.g., Financial and/or Other Incentives or Investments) To Promote the Development and/or Appropriate Use of Priority AR Products, such as Novel Compounds and Approaches, for Human And Veterinary Medicine for Which Market Incentives Are Inadequate.**			
FDA	New AR products	Identify and publicize priority public health needs for new AR products; identify the kinds of products we would want to see developed.	Preliminary meeting has occurred; working group is forming; future action TBD CDER advisory committee held February 2, 2002. In 2005, FDA proposed implementing regulations for designation of new animal drugs for minor uses and minor species (MUMS). The Minor use and Minor Species Animal Health Act (MUMS) is designed to encourage the development of animal drugs that are currently unavailable to minor species (species other than cattle, horses, swine, chickens, turkeys, dogs, and cats) in the United States or to major species afflicted with uncommon diseases or conditions (minor uses). The MUMS act was enacted to provide incentives to develop new animal drugs for minor species and minor uses, while still ensuring appropriate safeguards for animal and human health.
FDA	Joint efficacy workshop and advisory committee meeting	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures of efficacy.	Completed February and March 2001. Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines held Spring 2002.
FDA	See Action Item #79 (Interagency AR Product Development Working Group)	See Action Item #79 (Interagency AR Product Development Working Group).	See Action Item #79 (Interagency AR Product Development Working Group).
FDA	Maternal immunization	Development of approaches for licensure of vaccines to prevent group B streptococcal infections. CDC, NIH, FDA meeting May 1998 regarding Maternal Immunization and NIAID, NIH Advisory meeting regarding serological assays.	Continued regulatory and research effort to remove barriers to product development under current funding.
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals.	Working group formed; Draft document completed.
FDA	Noval therapeutic approaches using immunoglobulin	Include a humanized monoclonal antibody and a respirator synctial virus human immune globulin indicated for prevention of serious lower respiratory tract diseases (caused by RSV) and sepsis.	Ongoing regulatory review and research.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Collaborations to facilitate vaccine development	Collaborations to facilitate vaccine development.	Participated in and supported international efforts to develop improved vaccines and drugs to prevent multi-drug resistant TB. For example, scientists from the LOMDCI have participated in a project (funded by the Biotechnology Engagement Program) that is focused on developing a new class of drugs against TB. This research is being conducted in collaboration with Russian scientists and chemists from the Southern Research Institute and investigators at the Albert Einstein College of Medicine, the Aeras Global Tuberculosis Foundation, and the NIH in evaluating the safety and effectiveness of new TB vaccines
Action Item #81: Consider, in Consultation with Academia and Industry, Whether Government Has a Constructive Role To Play in Discovery of Drugs and Other Products Targeted To Address Areas Where Market Incentives are Limited and Unmet Needs Exist (e.g., Novel Antimicrobial Drugs Targeted To Specific Resistant Organisms).			
FDA, CDC, NIH	Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP)	Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues.	Workshop held April 15-16, 2004. Discussed the use of pharmacodynamic information in appropriate dose selection in clinical trials of anti-infective agents, and summarized the issues with developing antimicrobial drugs by allowing data from one serious disease to be supportive of data in another less serious disease such that sponsors would only have to perform one trial instead of two in the less serious disease. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)
Action Item #82: Continue Ongoing Approaches that Streamline the Regulatory Process, Including Clinical Trials and Enhanced Pre-Clinical Studies (e.g., Use of Pharmacokinetics and Pharmacodynamics Data) To Help Bring AR Products (Including Drugs, Vaccines, Diagnostics and Devices) To Market as Efficiently and As Rapidly as Possible, While Still Assuring Their Safety and Efficacy.			
FDA, CDC, NIH	Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP)	Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues.	Workshop held April 15-16, 2004. Discussed the use of pharmacodynamic information in appropriate dose selection in clinical trials of anti-infective agents, and summarized the issues with developing antimicrobial drugs by allowing data from one serious disease to be supportive of data in another less serious disease such that sponsors would only have to perform one trial instead of two in the less serious disease. CDER resistance web site to access workshop transcripts (http://www.fda.gov/cder/drug/antimicrobial/default.htm)
FDA	Vaccines	Identify mechanisms for establishing efficacy of additional pneumococcal conjugate vaccines with additional serotypes. Participated in multiple WHO Workshop held to discuss serologic correlates of protection. Also, provide regulatory review, conduct research and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND).	Research regarding serologic assessment of response to vaccines ongoing. (Lee, CJ, et.al., Crit Rev Microbiol 2003:29(4)"333-349; Mikolajczyk, MG, et.al., Clin Diagn Lab Immunol 2004; 11(6):1158-1164)Also, provide regulatory review, conduct reseqrch and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Workshop and committee meeting on efficacy	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures of efficacy.	Completed February and March 2001 Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines was held in Spring 2002.
FDA	Meningitis Vaccine Project (MVP)	MVP is a combined WHO Program for Appropriate Technology in Health (PATH) project to develop affordable meningococcal conjugate vaccines for Africa.	Scientific panel met in March 2003. Consortium of public, private, and non-profit organizations, and a philathropic organization (the Gates Foundation) will develop a vaccine that is critically needed in Africa.
FDA	Regulatory requirements – industry and scientific community	Clarify FDA regulatory requirements to both industry and the scientific community.	**ONGOING:** 1)Presentation on regulatory requirements for tests of use in AR initiatives to the Professional IVD Roundtable (a group representing all major professional laboratory groups) twice yearly.Discussion on obstacles and issues which might exist in technology transfer; 2) preliminary stages of esubmission for AST devices to promote a faster more efficient means of presenting data for a 510k review process including bundling; 3) CDRH is participating in planning of a workshop for rapid diagnostics for infectious diseases that would bring together goverment, academia, and industry to develop technologies to provide useable IVD results as quickly as possible. **COMPLETED:** Demonstrated that the use of the expedited review process works when CDRH was able to prioritize and put on a accelerated approval schedule to approve the CDC's new test to detect avian influenza within 2 weeks of the time CDC submitted it. FDA's expedited review process is designed to ensure that new devices that have important public health benefits are available for use as quickly as possible.
FDA	Topical micobicides	CBER/CDER working group on Topical Microbicides.	Working group formed; Draft document completed.
FDA	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).
FDA	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).
FDA	HIV Drug Resistance Genotype Assay Guidance (See Action Item #10)	Revised guidance on HIV Drug Resistance Genotype Assays. Significantly reduces the extent of studies required for clearance.	Publication pending
FDA	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)
Action Item #83: In Consultation with Stakeholders and Expert Consultants, Identify Ways To Promote The Development of New and Alternative Veterinary Treatments and The Improved Use of Existing Therapies That Are Unlikely to Stimulate Resistance to Drugs in Human Medicine.			
Action Item #84: Streamline the Regulatory and Approval Process for Veterinary Antimicrobial Drugs and Related Products That Are Unlikely, Now or in the Future, To Result In Transfer of Antimicrobial Resistance To Humans.			