Inventory of Projects

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

June-05

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, FDA, NIH, 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. Through NARMS, CDC provided support to the Michigan Department of Health for a program on appropriate use of antimicrobial agents in agriculture. This will foster collaboration between the state public health department and state agriculture (veterinary diagnostic) laboratories. CDC is helping to develop a community-based program on appropriate use of antimicrobial drugs in animals.	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 in 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 3 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 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 1998-2003 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 were published in 2003. Data from 2004 will be available by Fall 2005. Location-specific (city, state, region) alerts and guidelines are regularly updated on the CDC's GISP website.
CDC, FDA	Surveillance Planning	Coordinate surveillance activities. Initial meeting was held with CDC April 2001. Interagency cooperation remains a high priority within the department. Information sharing and coordinated activities continue to increase between agencies.	Ongoing.
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.
CDC	Enhancing State-Based Surveillance for Drug-Resistant *Streptococcus 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 and 2) coordinate individual state-based surveillance programs into a national effort. 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 DRSP surveillance manual is available at www.cdc.gov/drspsurveillancetoolkit. Created list serves and DRSP contact lists to publicize DRSP events to state and local health departments. 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.

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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 2004, 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 module of the National Healthcare Safety Network (NHSN) which will replace the National Nosocomial Infections Surveillance (NNIS) System. 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 2005, TheraDoc software will be deployed at two additional pilot healthcare facilities. Also, the software tool developed at CDC will be modified to produce HL7 Version 3 messages containing pharmacy and ADT data.
CDC	Including AR surveillance in electronic laboratory-based reporting activities in the NEDSS	Develop, demonstrate, and implement automated, electronic reporting of susceptibility findings to health departments by using nationally-recognized data transmission and coding standards and sending the data through CDC's secure data network. The result of this project will enable various other AR surveillance activities to be used for this electronic communications medium. During 2002, beta-testing of a NEDSS based system with unique program area modules (PAM) began.	Ongoing. NEDSS continues to expand its capacity to report laboratory-based susceptibility findings.
CDC	Active Bacterial Core Surveillance (ABCs)	At Emerging Infections Program sites (EIPs), surveillance is conducted for invasive bacterial diseases due to pathogens of public health importance. For each case of invasive disease in the study population, a case report with basic demographic information is filed and, in most cases, bacterial isolates from a normally sterile site from patients are sent to CDC for laboratory study. System tracks emerging AR in isolates of *Streptococcus pneumoniae* , group A and group B streptococcus, *Neisseria meningitidis* and methicillin-resistant *Staphylococcus aureus* (MRSA). Data provide an infrastructure for further research, such as special studies aimed at identifying risk factors for disease, post licensure evaluation of vaccine efficacy, and monitoring effectiveness of prevention policies. Program remains one of the most accurate and comprehensive surveillance tools available.	Ongoing. ABCs produces yearly summaries on emerging resistance within the 10 EIPs (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee). An eleventh site, Texas, was added in 2004.
CDC	Translating lessons learned from ABCs to guide surveillance for drug-resistant *Streptococcus pneumoniae* (DRSP) in local and state health departments	A series of activities aimed at translating the lessons learned from ABCs for implementation in local and state health departments where information on DRSP is needed, but resources are limited and the goals of surveillance are more local in scope. A DRSP surveillance coordinator works with the Get Smart team to support surveillance associated with the state-based appropriate antibiotic use projects as well as surveillance programs in other states.	Ongoing. A surveillance coordinator was hired in March 2004. The coordinator assists in the development, implementation, and support of state-based AR surveillance programs, as well as facilitates communication and interaction between sites through web boards and listserves (starting spring 2005). Sections of the DRSP surveillance manual are available online now. A four day conference that includes AR education and surveillance presentations occurred in April 2005.

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CDC	The National Nosocomial Infections Surveillance (NNIS) System.	A cooperative effort between the CDC and >300 hospitals to create a national nosocomial infections database. The database is used to reveal the epidemiology of nosocomial infections and to show AR trends, among other purposes.	Ongoing. The data from the NNIS System are reported annually in the NNIS Report which appears on the NNIS Web page (http://www.cdc.gov/ncidod/hip/SURVEILL/NNIS.HTM) and in the December issue of the American Journal of Infection Control. This system was retired on 12/31/2004 and replaced by the National Healthcare Safety Network (NHSN). Similar data are collected under the NHSN.
CDC	Surveillance projects of HIV antiretroviral drug resistance	Surveillance for HIV antiretroviral drug resistance among different populations (adult, adolescent, and pediatric) and geographic areas in the U.S. using different methodologies, focusing on genotypic testing but also including phenotypic testing. Determine transmission of drug-resistant strains to previously uninfected persons and from mother to infant. Results support experts in deliberating potential recommendations for antiretroviral resistance testing before treating drug-naïve new patients. Results also provide information to guide regimens for post-exposure prophylaxis and prevention of mother to child transmission during pregnancy and delivery transmission. Could contribute to evaluation of success of risk prevention measures directed towards HIV-seropositive patients in treatment.	Ongoing. Funds awarded to participating state and local health departments.
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, 2003 , 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/surv2003/default.htm.
CDC	Estimate of the burden of MRSA disease in hospitalized adults	This project uses existing datasets to measure the annual incidence of MRSA disease in hospitalized adults.	In 1999-2000, there were 292,687 hospitalizations with diagnosis of *S. aureus* infection estimated annually, accounting for 0.8% of hospital discharges. The average methicillin resistance rate was 42.0%. 119,760 hospitalizations with diagnosis of MRSA infection were estimated annually, including 30,015 septicemias, 26,726 pneumonias, and 63,019 other infections, accounting for 0.3% of hospital discharges. Estimates in non-hospitalized persons are planned for 2003. Kuehnert MJ, Hill HA, Kupronis BA, Tokars JI, Solomon SL, Jernigan DB. Methicillin-resistant–Staphylococcus aureus Hospitalizations, United States. Emerg Infect Dis [serial on the Internet]. 2005 Jun. Available from http://www.cdc.gov/ncidod/EID/vol11no06/04-0831.htm

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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 seven major clonal lineages or pulsed-field types (PFTs) of MRSA in the U.S. Four PFTs are common among healthcare related strains, two PFTs are found primarily among community-acquired isolates, and one is found among strains from both healthcare and community-acquired strains. In 2004, two additional MRSA types among community MRSA strains have been identified.
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 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 or 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 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 2005, CDC has confirmed 13 VISAs and four VRSAs in the U.S. Updated guidance on appropriate testing was sent to State Health Departments in April, 2004 and updated laboratory testing information was available January 2005.
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. Are also having isolates from our historical collection analized for genetic relatedness, virulence factors and SCCmec typing to establish the genetic background for our ongoing surveillance. 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 C

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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.
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.

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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.	HARP conducts prospective, long-term monitoring of trends in AR to guide treatment regimens for *H. pylori* infections. Twelve academic medical centers throughout the United States submit *H. pylori* isolates and clinical and epidemiologic data from endoscopically-diagnosed patients monthly. Resistance is tested at CDC. Resistance and epidemiologic data are entered into a database at CDC for analysis of prevalence, risk factors and regional trends in rates of antimicrobial resistance in *H. pylori* strains. 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. A pilot study of the prevalence of *H. pylori* and dyspepsia symptoms was completed in the Republic of Georgia, and a grant application submitted for further research and disease control activities in that country.	Ongoing. Susceptibility testing methods established by FDA and National Committee on Clinical Laboratory Studies (NCCLS) for antimicrobial susceptibility testing of *H. pylori* were validated, and the minimum inhibitory concentration with quality control limits for antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, and tetracycline have been determined. Analysis of data from HARP show 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. The pilot study in the Republic of Georgia detected a 72% prevalence of *H. pylori* infection, and a 90% prevalence of dyspepsia. An external-source grant was obtain for *H. pylori* research, treatment and control activities in the Republic of Georgia.
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. Some worrisome trends were detected in small studies from a single or small number of hospitals. 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.	Evaluated and updated surveillance protocol and forms with a focus on improving completeness of case findings. MN submitted request to state to make *E. coli* reportable and began planning to implement surveillance (start: Jan., 2005) Reported 2000-2 surveillance trends (S. McCoy et al., ICEID, 2004), Began planning a new birth audit study (which will address risk factors for early onset GBS and other infections after implementation of 2002 guidelines, for births in 2003 and, published an analysis of data collected in 2003 from labs in the EIPs regarding susceptibility testing for GBS among penicillin allergic women (Centers for Disease Control and Prevention. Laboratory Practices for Prenatal Group B Streptococcal Disease. MMWR 2004; 53 (No.RR-23): 506-509).

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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. This system will target the population at greatest risk, systematically test isolates, further availability of these isolates for applied research studies, and allow further epidemiologic studies to identify risk factors and measures which can be used to develop effective prevention strategies in the population.	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). Set up Interagency Agreement with HRSA and received funding from HRSA to support stem-cell transplant activities of OTIP. Established steering committee with representation of CDC, IDSA, and OTIP sites, and held investigators meeting (November, 2004) at which time consensus towards project implementation was achieved.
CDC	Molecular tools for the control and epidemiology of head and body lice	Evaluate new molecular tools for monitoring louse populations and determining the role of insecticide resistance in louse infestations and re-infestations to design and implement appropriate control strategies. Characterize local populations of lice and the global relationships and movements of louse populations. Ascertain the genetic relationships of head, body, and pubic lice. When completed, the data generated will improve knowledge of the epidemiology of insecticide resistance in louse populations and improve prevention and control strategies.	Ongoing. In 2001, collected head and body lice from over ten states and seven countries, and sequenced over 700 clones from gene libraries. In 2002, the microsatellite markers developed through sequencing of head and body louse libraries were applied in field studies of head and body louse population biology and micro-epidemiology of insecticide resistance. In 2003, use of microsatellites developed at CDC were used in field studies in Nepal and Mongolia by collaborators at the University of Queensland, Australia to provide convincing evidence that head and body louse populations were, in fact, separate species. Moreover, pyrethroid resistance gene mutations were found in head louse samples submitted by our collaborators in Denmark and California. These studies are providing the data needed to assess the interaction of multiple resistance alleles and louse micro-epidemiology around the world, and will result in rapid increase in our understanding of louse resistance and micro-epidemiology.
CDC	Testing of drug-resistant *Trichomonas vaginalis*	Trichomoniasis is the most common curable STD in young, sexually active women. This project includes passive surveillance for *Trichomonas vaginalis* resistance among isolates from patients whose infection has not resolved after at least two courses of standard metronidazole therapy. Parasites are tested both aerobically and anaerobically for sensitivity to metronidazole and to tinidazole. These data will identify molecular markers of metronidazole-resistant strains, allow investigation of drug-resistance mechanisms, and will be utilized to identify alternative chemotherapeutic agents.	Ongoing. Testing is an ongoing service of CDC. In 2001, initiated testing on isolates obtained through the Grady Adolescent STD Project (GRASP) to determine the prevalence of metronidazole-resistant *T. vaginalis* isolates in an urban adolescent clinic. Isolate testing and data analysis is an ongoing process and results will prove useful in identifying alternate therapies.

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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 2004, surveillance for resistance to licensed drugs in human isolates from the US and other countries was continued. Viruses isolated in several Asian countries affected with the severe outbreaks of avian influenza A(H5N1) were analyzed for their sensitivity to adamantanes and neuraminidase inhibitors (NIs). It was shown that all human and many avian H5N1 isolates were resistant to adamantanes. All human and avian H5N1 viruses tested were sensitive to NIs. The M gene sequencing data obtained for recent human H1, H3 and H5 virus isolates were used to develop real-time PCR protocols for rapid identification of influenza viruses in clinical materials as well as for development of a pyrosequencing protocol for detection of influenza A viruses resistant to adamantanes. Analysis of different subtypes of influenza virus isolates resistant to licensed drugs did not reveal their antigenic difference from viruses sensitive to the drugs.
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 to develop a common plan for AR surveillance in the DoD.
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 4 DoD pilot sites, 3 in the US and 1 in Europe. Expansion to additional sites prepared and ongoing. Linkage of system into a DoD network (pilot sites plus DoD-GEIS) for information sharing and analysis of AR trends accomplished in 2004. Expansion of network and its evaluation planned 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.

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VA	a. Emerging Pathogens Initiative (EPI) b. Review of comercially available computer software to be used for infection prevention, control and containment	a. The Veterans Health Administration (VHA) currently has an ongoing and well-defined AR surveillance plan (the EPI, a laboratory-based automated surveillance system) b. VA is actively reviewing computer off-the-shelf software products to assist in infection control processes for prevention and control of infectious diseases including antimicrobial resistant organisms; computer-assisted decision support systems will be a key element in VA's choice of product.	Currently over 170 VHA facilities across the country transmit data to the EPI monthly. The data collected by the EPI are reviewed quarterly by the Infectious Diseases Program Office and reported to the Veterans Integrated Service Networks. Enhancements that acquire additional information on antimicrobial resistance of specified organisms were distributed to reporting stations in July 2004. b. Review to be completed by end of Federal Fiscal Year 2005.
VA	Emerging Pathogens Initiative (EPI)	The VHA uses standardized definitions and methods to set local parameters for surveillance in the EPI system. Currently EPI data regarding some AR organisms are returned to the Veterans Integrated Service Networks quarterly with reporting station specific data included. National quartiles are also provided for use at the Network and local level. Confidentiality is a key element in any activity undertaken by the VHA. Great effort has been put forth to maintain confidentiality of the Emerging Pathogens Initiative surveillance data set. Access is strictly limited for any data with unique identifiers.	Ongoing.
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*	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.
CDC	Grant Program: Applied Research on AR - Validation of National Committee for Clinical Laboratory Standards (NCCLS) 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 NCCLS 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 NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development.	Three three-year awards were made in 2002. Recipients include: University of Texas Medical Center, University of Pittsburgh, and University of Wisconsin Medical Center. Projects underway, results pending.

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FDA	Development of NCCLS testing standards	Campylobacter is one of the primary foodborne pathogens under surveillance in NARMS.	Developed quality control ranges for a broth microdilution susceptibility testing method for *Campylobacter* . QC ranges for 14 antimicrobials are established and will be incorporated into the upcoming CLSI (formerly NCCLS) performance standards. Developed the first standardized disk diffusion and broth dilution antimicrobial susceptibility testing methods for bacterial pathogens isolated from aquaculture foods. Two Proposed Guidelines, M42-P and M49-P have been submitted to the CLSI for publication in 2005. These guidelines contain standardized methods and quality control ranges for testing 10 antimicrobial agents commonly used in global aquaculture.
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. A yearly meeting is held to discuss and refine methodologies. Additionally, a new Campylobacter broth microdilution plate will be adopted in 2005. Test standards for Listeria are being explored. Bacterial Epidemiology and Antimicrobial Resistance Research Unit, ARS, Athens, GA.
Action Item #4: Address Additional Surveillance Issues Unique to AR.			
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
CDC	Monitoring Drug Resistance in Lymphatic Filariasis Elimination Programs	We will collect blood specimens from at least 20 microfilaria-positive persons in each of at least 10 filariasis-endemic countries in which mass treatment for LF has been implemented or is about to be implemented. Specimens will be collected to represent areas in which each of the three major elimination strategies are implemented (albendazole plus DEC; albendazole plus ivermectin; and DEC salt). Microfilariae will be preserved and made available to collaborators for testing for genes known to confer drug resistance to albendazole and ivermectin. This will allow us to compare the prevalence of resistant genotypes in different geographic and mass treatment settings. Microfilariae will also be preserved for later testing for DEC resistance (no tests are currently available for DEC resistance). Data will be collected on number of rounds of mass treatment and number of doses of antifilarial drugs taken by study subjects.	Funding for collaborators was not transferred until the end of FY04; nonetheless, in FY04, we contacted investigators working in Brazil, Tanzania, Haiti, Guyana, and Vanuatu to develop plans to collect microfilariae for the repository.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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	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 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.
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
**** TOP PRIORITY **** **Action Item #5: Develop and Implement Procedures for Monitoring Antimicrobial Use In Human Medicine, Agriculture, Veterinary Medicine, and Consumer Products.**			
CDC	AUR: component of the National Nosocomial Infections Surveillance (NNIS)	The AUR component of NNIS allows participating hospitals to collect data on select antimicrobial agents and cumulative susceptibility data on select organisms identified by the clinical microbiology laboratories, allowing the calculation of a national estimate of the prevalence of antimicrobial-resistant organisms in hospitals and the amounts of select antimicrobial agents used in these hospitals. These data allow select AR rates to be compared among hospitals and provide better understanding of the relative importance of antimicrobial drug use vs. other factors (i.e., cross-transmission, severity of illness) for development of antimicrobial-resistant infections by several key pathogens.	Ongoing. In 2001, implemented the AUR component and received data from fifteen hospitals. In 2002 twenty hospitals participated. A pilot system to electronically capture susceptibility testing results to simplify reporting was developed. Participation in 2003 and 2004 was stable. This aspect of the NNIS system was retired on 12/31/2004 and replaced by the National Healthcare Safety Network (NHSN). Similar data are collected under the NHSN.
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).
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

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.	One component of this project consisted of applying Toyota Production System (TPS) principles to MRSA prevention at units at VA hospital and Pittsburgh Medical Center (UPMC). In the VA hospital, a sustained 55% reduction in MRSA infection rates was observed, while the UPMC unit has experienced a sustained reduction of 90% in the MRSA infection rate. Fourteen additional hospitals have initiated prevention programs and are working collaboratively in an effort to duplicate the successful MRSA reductions seen in pilot hospitals. Current work is focusing on standardizing surveillance methods and definitions to allow interpretation of the regional impact on MRSA infection rates. Additional accomplishments: 1) completion a survey that demonstrates varying perceptions on how large the problem of MRSA is, what the main causes are, as well as priorities for prevention, 2) curriculum for medical students on control of antimicrobial resistance, 3) completion of hand hygiene studies demonstrating that adherence was lowest following brief patient encounters.
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. 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.
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).
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.
Action Item #6: Identify and Evaluate Methods for Collecting (e.g., Optimal Sampling Methods) and Disseminating the Surveillance Data on Antimicrobial Drug Use.			
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).
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
VA	a. Emerging Pathogens Initiative (EPI) b. Review of comercially available computer software to be used for infection prevention, control and containment	a. Resistance data are being gathered in the EPI, an automated surveillance system, at the reporting site level and can be used for comparisons based on geographic areas and can be linked to ICD-9-CM diagnostic codes. In addition, drug use data can be linked to laboratory testing and diagnoses for a significant emerging disease. b. VA is actively reviewing computer off-the-shelf software products to assist in infection control processes for prevention and control of infectious diseases including antimicrobial resistant organisms; computer-assisted decision support systems will be a key element in VA's choice of product.	a. This item is already underway in the VHA with reporting from facilities across the country. Enhancements that acquire additional information on antimicrobial resistance of specified organisms were distributed to reporting stations in July 2004. b. Commercially available software are being tested in clinical settings including some VA medical centers.
Action Item #7: Work With Accrediting Agencies To Address Antimicrobial Drug-Use As Part Of Quality Assurance In Health Care Delivery Systems.			
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 Public Comment period will run from February 22-March 22, 2005. After gathering the comments, NCQA's CPM will review the input and make a final decision in May on whether to include the measures for HEDIS 2006. HEDIS® 2004 is currently available online at: http://www.ncqa.org/Programs/HEDIS/HEDIS%202004%20Info.htm
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	Preventing Lab Errors: CD-ROM for susceptibility testing	New antimicrobial agents and new resistance patterns pose a challenge to clinical laboratories because testing methods vary with organism/antimicrobial agent combinations. NCCLS standards outline recommended procedures, but they are difficult for some laboratories to interpret. This CD shows laboratories how to apply NCCLS standards, demonstrates the modes of action of each group of antimicrobial agents and the mechanisms organisms develop to resist the agents, describes quality control procedures needed to verify accuracy of testing results, and demonstrates specific procedures laboratories must use to detect resistance in different organisms.	CD-ROM was completed in 2002 and has been distributed widely throughout the US and across the world. It is the backbone of the Washington State train-the-trainer workshops and has been give to over 1,000 participants in courses delivered by the NLTN on the subject of AST. An additional 15,000 have been mailed to laboratories by APHL. Available at: ast@aphl.org

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Multilevel Antimicrobial Susceptibility Testing Educational Resource (M.A.S.T.E.R.) Program	The M.A.S.T.E.R. program, is a 3-phase project to upgrade the accuracy of antimicrobial susceptibility testing and reporting in the U.S. Currently, the Web site has case studies, a Q and A section, hot papers, and a list of references.	Ongoing. The website has received over 209,000 hits from 50 countries. Material from the website has been used in numerous training courses on susceptibility testing and is frequently cited as a resource in medical technology classes. The CD-ROM based training course; "Antimicrobial Susceptibility Testing: A Self Study Guide" received the CDC Communications Roundtable Award. Outstanding Electronic Media Program award in 2003. http://www.phppo.cdc.gov/dls/master/aboutmaster.asp
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 2002 and June 2004, a total of 13,281 laboratorians received training on antimicrobial susceptibility testing (AST) using multiple modalities. The focus of these courses was the importance of using 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 several nationwide teleconferences on related topics. The teleconferences account for about 75% of the participants. These courses have been a major effort of the NLTN. One standard 5-hour program was presented at 31 locations in 24 states, and extensive evaluation of this course was conducted by CDC evaluators Posttest results demonstrated that substantial improvement occurred compared with pretest scores of individual participants. More than 450 laboratories were represented in the courses. Assessments of practices before and after the courses show that an increased number of laboratories adopted NCCLS standards.
CDC	National Healthcare Safety Network (NHSN)	The NHSN will be an Internet-based nationwide network that will monitor trends in adverse events associated with invasive devices, procedures, and medications used in the delivery of healthcare. Under the NHSN's Medication-associated Adverse Event Module, initial focus will be on use and resistance of antimicrobial agents and on establishing electronic reporting of antimicrobial use and resistance data to increase efficiency, timeliness, and accuracy of the monitoring effort. When implemented, the NHSN will significantly enhance the ability to monitor and track trends of usage and resistance of microbes to antimicrobial agents in a variety of healthcare delivery settings. These data can then be used to enhance patient safety by enabling healthcare workers to develop and deploy strategies to prevent overuse and inappropriate use of these agents, as well as strategies to prevent other pathogens from becoming resistant.	Initiated. In 2001-2003, gathered requirements for system, held joint application development sessions with current and potential users, and started work on data model, security, standard nomenclature for pathogens and antimicrobial agents, and detailed use cases that define system functionality. In addition, work has been ongoing to develop the messaging specifications for electronic reporting from hospitals of antimicrobial use (from pharmacy systems) and resistance (from microbiology systems). In 2003, efforts to design, develop, and deploy the NHSN (deployment of version 1.0 scheduled for January 2005) were started.

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 three vancomycin-resistant *Staphylococcus aureus* isolates in the United States.
CDC	*Mycobacterium tuberculosis* (Mtb) antimicrobial susceptibility testing program	Approximately 165 laboratories participate in this program designed to assess and enhance the ability of clinical laboratories to accurately test for AR. Most laboratories test for susceptibility to isoniazid, pyrazinamide, ethambutol and rifampicin, and streptomycin. Approximately 35 laboratories test nontuberculous mycobacteria in addition to susceptibility to other drugs. Laboratories can enter susceptibility test results through the online data entry system and view reports of results on a website address for each panel shipment for feedback.	Ongoing.
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 National Committee for Clinical Laboratory Standards (NCCLS), 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.	Coordinated the development of a NCCLS guidance document (M42-R) for standardizing an antimicrobial disk susceptibility test method for bacteria isolated from aquatic species. Also, see item #4 (Campylobacter quality control development).
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.
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.).			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Ongoing. Manuscript in press.
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)
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))
CDC	See Action Item #2 (Active Bacterial Core Surveillance (ABCs))	See Action Item #2 (Active Bacterial Core Surveillance (ABCs))	See Action Item #2 (Active Bacterial Core Surveillance (ABCs))

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 on *S. pyogenes* isolates collected from recruits at 9 military training centers and monitors for *S. pyogenes* resistance rates. As of September 2003, the rates detected were the following: erythromycin (13.5%), clindamycin (2.1%), tetracycline (4.6%), levofloxcin (1%) and 0% for penicillin and vancomycin. 2002 temporal trends in antibiotic resistance among *S. pyogenes* isolates demonstrated no discernible patterns, but increased resistance to erythromycin at 2 sites.	Reports of susceptibility test results and summary statements are being provided to primary care facilities, are accessible to DoD staff at www.geis.fhp.osd.mil and have been used in presentations at national meetings. Generated data show moderate AR rates as of 2003. National DoD surveillance data for antibiotic resistance and emm gene type of group A streptococcal isolates from eight basic-training military sites was recently published in the Journal of Clinical Microbiology, Vol 48, October 2003.
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. A pneumococcal isolate from a fatal case of meningitis was investigated using this technique, allowing the discovery of a non-vaccine serotype not commonly found among meningitis cases. During 2003 a conjunctivitis outbreak of *S. pneumoniae* was identified and analyzed. This work enabled the identification of a novel strain responsible for the outbreak and provided epidemiologic information on the causative isolate's resistance pattern. Further analyses of pneumococcal strains from Egypt is in process in hopes of providing valuable epidemiologic data for prevention and treatment options. Manuscripts of the above work have been submitted, and are under consideration for publication.
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* is established at 4 military training centers. Specimens are evaluated using PCR-based beacon probe. Standard culture, serology, and PCR results are compared to validate the accuracy of the PCR method.	Ongoing. As of March 2004, 360 specimen sets have been tested. Using culture, serology, and molecular testing, evidence of *B. pertussis* has been found in 10% of those enrolled.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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. MMWR article published on this investigation.
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.			
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 with the Veterans Affairs Medical Center in collaboration with Health Services Research and Development Service, Department of Veterans Affairs, and with hospitals in the Delaware Valley in collaboration with NIAID.	In some communities resistance of pneumococci to penicillin or other drugs recommended by national treatment guidelines raises the possibility that these guidelines may no longer be applicable nationwide (Metlay JP et al. Emerg Infect Dis 2004;10:54-9).
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 three-year awards were made in 2004. Recipients include: Duke University , Washington University, Minnesota Department of Health.
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.			
FDA	Antimicrobial resistant bacteria in feed ingredients	Assess the prevalence of antimicrobial resistant bacteria in feed ingredients , primarily rendered product. This work will be done in conjunction with FDA field personnel when they inspect suppliers for compliance with the bovine spongiform encephalopathy (BSE) regulation. Results will be incorporated into NARMS. Expand NARMS into retail foods of animal origin.	Ongoing. Initial surveys (1 year) of rendered products and plant based proteins completed. Also, see item #2. In addition, see item #17, with regards to antimicrobial resistance bacteria from produce surveys. FDA is also collaborating with USDA to characterize antimicrobial resistance profiles of Salmonella and *E. coli* obtained from their annual produce survey.
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.			
FDA	Antimicrobial resistant bacteria in sentinel human populations	Evaluate abattoir workers for carriage of antimicrobial resistant bacterial pathogens.	Ongoing. Pilot study 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.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations	Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment.	Data published: Enzo R. Campagnolo, et. al. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. The Science of The Total Environment, Volume 299, Issues 1-3, Pages 89-95, November 2002.
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.	Sampling delayed. Second & final round of sampling in Cape Fear and Pamlico Rivers completed in Spring '05. Samples to be analyzed & data provided to CDC in Fall '05
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.	Preliminary results presented at CDC CAFO workshop, Feb 2004. This project is completed. North Carolina has moved into a Phase II of this project being supported by CDC funding.
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.
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.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Latino and Asian parents were both 17% more likely to report that antibiotics were either definitely or probably necessary than non-Hispanic white parents. Physicians correctly perceived that Asian parents expected antibiotics more often than non-Hispanic white parents but underestimated the greater expectations of Latino parents for antibiotics. Physicians also correctly perceived that parents of children with ear pain or who were very worried about their child's condition were significantly more likely to expect antibiotics. Physicians were 7% more likely to make a bacterial diagnosis and 21% more likely to prescribe antibiotics when they perceived that antibiotics were expected (Mangione-Smith R. Pediatrics 2004;113:385-94).
AHRQ	Research Program Project (P01): Understanding and eliminating health disparities in blacks, project 2	Economic access to antiretroviral (ARV) prescription drugs and adherence to ARV guidelines for African- American Medicaid enrollees with AIDS or HIV disease in South Carolina.	The completed Medicaid data analysis have identified HIV-service regions with the low uptake of highly-active antiretroviral therapy. Barriers to the use of HAART may include physicians' values, knowledge, and cultural competence; stigma surrounding HIV; comorbidities and social problems; mistrust; and patients' religious beliefs. Ongoing activity includes intervention to change provider behavior and continuation of a comprehensive educational strategy.
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 will assess methods to avoid mistimed administration of preoperative antimicrobial agents. 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. In the past year, the TRAPE Project collected baseline data from 44 hospitals regarding their surgical antimicrobial prophylaxis process, including the timing of prophylaxis administration, the duration of prophylaxis drug use, and the drug selected for the administration of prophylaxis. The data were used to provide comparative feedback on prophylaxis performance to all 44 hospitals. All hospitals are currently remeasuring the prophylaxis process to evaluate the effectiveness of the group process intervention. 2. Median C-reactive protein levels were significantly higher for patients with pneumonia than in the other patients with acute cough. The area under the receiver operating characteristic curve for C-reactive protein level as a predictor of pneumonia was 0.83. C-reactive protein level and a clinical prediction rule were independently associated with pneumonia, yielding a combined area under the ROC curve of 0.93 (Flanders SA et al. Am J Med 2004;116:529-35). 3. Awarded May 2004.
AHRQ	Research demonstration and dissemination project (R18): HIV treatment error reduction using a genotype database	This project is evaluating a computerized decision- support system that integrates HIV genotypic testing results with corresponding patient medication data within an electronic medical record system to reduce antiretroviral prescribing errors and improve antiretroviral drug selection. A second aim is to assess the efficacy and usability of this system in a community-based, outpatient setting serving a predominantly urban, minority, and low-income population.	HIV drug resistance test results were provided within an electronic medical record system, increasing availability of these results to HIV clinicians. The scope and significance of the problem of suboptimal resistance test result utilization were also characterized in a national, multi-center prospective clinical database.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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, where little is known about management practices, and surveillance is rarely performed.	The data collection tool is now operational, and the recruitment of all nursing home patients is complete. Data collection and analysis are in progress.
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 children.	To assess trends in second-generation macrolide use among children treated as outpatients in 9 US health plans, claims data were sampled for 25,000 children in each of 9 US health plans. From 1995-1996 to 1999-2000, although overall antibiotic use decreased from 1.15 to 0.91 dispensings per person-year, second-generation macrolide use increased from 0.022 to 0.063 dispensings per person-year. Use as a proportion of all antibiotic dispensings increased from 1.9% to 6.9%, and use as initial therapy increased from 1.4% to 6%. For children <6 years of age, second-generation macrolide use as initial therapy increased from 0.9% to 5.0% for otitis media and from 5.2% to 24.0% for pneumonia. Despite recent trends toward decreased antibiotic use among children, the use of second-generation macrolides among children has increased dramatically, even among younger children, for whom use for initial treatment of illness is not recommended (Stille CJ et al. Pediatrics 2004;114:1206-11).
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	Recent accomplishments include demonstrating the impact of a multi-faceted hand hygiene program that resulted in sustained high hand hygiene adherence, and this was associated with decrease in MRSA and VRE incidence in one CARP facility. Demonstrated significant decrease in VRE transmission with use of daily chlorhexidine baths in the ICU setting. Developed and evaluated a method for using electronic data to identify inappropriate antimicrobial use, resulting in significant decrease in inappropriate use of two or more redundant agents. Using the same method, established that over 50% of vancomycin courses were needlessly prolonged; interventions were effective in discontinuing the drug in at least 54% of these cases. Currently conducting 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.
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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)
VA	Appropriate use of antimicrobials	The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federal agencies and other partners (including the private sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems.	Ongoing. Infectious Diseases Field Advisory Committee has representation on the national Antimicrobial Medical Advisory Panel (MAP) for pharmacy.
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	Evaluation of routine cycling of antimicrobial agents	Routine cycling in the choice of empiric antimicrobial agents has been proposed as a means of limiting development of AR mutants in hospitalized patients. This study in medical intensive care units at 3 institutions evaluates changes in prevalence of resistant target pathogens and patient outcomes during cycling interventions compared to baseline. The results will indicate whether cycling interventions have a protective effect on infection or colonization with resistant target pathogens and the impact of specific cycling periods on adequate therapy for suspected infections, length of hospital stay, and mortality rates.	This project has been completed. Results suggest that cycling of antimicrobial agents is not effective in reducing targeted resistance among gram-negative isolates. Two manuscripts have been published which summarize the data: Merz LR, Warren DK, Kollef MH, Fraser VJ. The Effects of an Antibiotic Cycling Program on Antibiotic Prescribing Practices in an Intensive Care Unit. Antimicrobial Agents and Chemotherapy 2004; 48:2861-5 and Warren DK, Hill HA, Merz LR, Kollef MH, Hayden MK, Fraser VJ, Fridkin SK. Cycling empirical antimicrobial agents to prevent emergence of antimicrobial-resistant Gram-negative bacteria among intensive care unit patients. Crit Care Med. 2004 32:2450-6.
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).
VA	a. Appropriate use of antimicrobials b. Surgical Site Infection Antibiotic Prophylaxis plan	a. The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federal agencies and other partners (including the private sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems. b. VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide. These performance measures constitute 50% of the annual evaluation for Executive Career Field (ECF) performance plans for VHA regional directors.	a. Ongoing. Infectious Diseases Field Advisory Committee has representation on the national Antimicrobial Medical Advisory Panel (MAP) for pharmacy b. For Federal Fiscal Year 2005, VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide
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).
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).
VA	a. Emerging Pathogens Initiative (EPI) b. AHRQ 1 UC1 HS014237 Toward a Safety Culture: Reducing Nosocomial Infections	a. Data on antimicrobial resistance with quartile rankings in the VHA nationwide are provided to the Networks, including reporting site-specific data by using the EPI, an automated surveillance system. This will be an ongoing initiative since it is not entirely clear what the best method for AR feedback will be in the final analysis b. VA personnel are leading a regional research study sponsored by AHRQ designed to look at rapid-cycle implementation strategies of evidence-based practices that are known to reduce health care associated infections.	a. Ongoing at VA sites across the country. Enhancements that acquire additional information on antimicrobial resistance of specified organisms were distributed to reporting stations in July 2004 b. Ongoing
**** TOP PRIORITY ****			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			
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 18,442 in January 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 develop 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 will be completed by 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.	2004 activities: Conducted 5 focus groups with Emory-affiliated hospital faculty and housestaff to determine knowledge, attitudes and beliefs about antimicrobial use. Utilized information from focus groups to inform interventions to optimize piperacillin/tazobactam use. Began interventions to optimize piperacillin/tazobactam use. Interventions include education sessions with pre- and post-tests, pocket cards with appropriate use criteria, antimicrobial utilization teams (3 facilities), and computer-order entry screen featuring recommended empiric antibiotic choices (at one facility). Conducted pre-intervention chart reviews, pre- and post-intervention antibiotic use review, collected microbiologic data. From pre-intervention to post-intervention, piperacillin/tazobactam use has decreased at 3 of the 4 hospitals, by an average of 23.7 defined daily doses in the MICUs.
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).
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).

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 Set, 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 Set will assess its effectiveness in deceasing antimicrobial prescribing in primary care practices.	In 2002 fluoroquinolones became the most commonly prescribed class of antimicrobials for adults. Much fluoroquinolone prescribing appeared inappropriate (Linder JA et al. Am J Med 2005;118:259-68). Physicians prescribed apparently inappropriate antimicrobials to 26% of patients diagnosed with influenza (Linder JA et al. Pharmacoepidemiol Drug Safety 2005; in press). The recipient has submitted a manuscript on usability testing of the ARI Smart Set with multiple participants and also an informatics-oriented abstract about the architectural requirements of Smart Forms to a journal. A pilot test with the ARI Smart Form will begin in May and a full randomized controlled trial in some 24 practices will start in October.
CDC	Combating Antimicrobial Resistance Through Hospitalist Education: Implementation of one strategy of the Campaign to Prevent Antimicrobial Resistance in Healthcare Settings	This project will produce a toolkit for Hospitalists on the topic of antimicrobial resistance, including Internet-based resources, a notebook of references, slides, and guidance on how to do a quality improvement project in a hospital setting. Hospitalists will receive training on use of the toolkit during educational workshops and local chapter meetings. Evaluation of the exposure, impact, and lessons learned will be conducted.	Revised the workshop, toolkit, and various resources (both online and in print) based on the experience of the presenter at an April 2004 training. Evaluation was begun via analyzing the pre and post tests from participants at the April training. Meetings were held to discuss a more comprehensive evaluation of the workshop and toolkit, and expansion of the workshop to include another step from the CDC's Campaign to Prevent Antimicrobial Resistance.
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. Expect to complete, print and distribute the manual by spring of 2005.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Campaign to prevent antimicrobial resistance in healthcare settings	The Campaign to Prevent Antimicrobial Resistance in Healthcare Settings was launched in March 2002. The Campaign's overall goal is to reduce 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.	2004 activities include: Collaborated with the Society for Healthcare Epidemiology of America (SHEA) to identify and feature during the Annual SHEA Conference three success stories related to implementation of the 12 Step Program for Hospitalized Adults. Completed phase II of the Antibiotic Management Program (AMP) Reporter Project at the Johns Hopkins Hospital; the AMP Reporter is a unique post-prescription intervention using an automated data system that combines pharmacy and microbiology. Two additional antiimicrobial use feedback methods, text pages and notes affixed to patient charts, were found to be as effective as traditional phone contact. Developed and pilot tested a standardized tool to monitor adherence to recommended central venous catheter (CVC) insertion practices and thereby reduce infections.
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.	Ongoing in twenty-six states and one county. Smart campaign maintains a comprehensive website 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. The Get Smart campaign is developing an evaluation manual for state partners as a guide for developing and implementing impact and/or outcome, which will be released in 2005. In June 2004, Get Smart hosted its fifth annual national conference. The conference brought together over 225 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.	Continued projects in twenty-six organizations, with 131 million members in 2002. Implemented CME certification programs for healthcare personnel participating in educational programs. In collaboration with the Council for Affordable Quality Healthcare the Get Smart campaign implemented an online CME certification program for healthcare personnel. Since September 2004 over 900 healthcare personnel have completed the program.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Get Smart: A medical curriculum promoting appropriate use of antibiotics	Developing and promoting appropriate antibiotic use curricula for providers: 1. 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. 2. Curriculum for primary care residents on appropriate antibiotic use based on the medical school curriculum. 3. Curriculum for family practice and pediatric residents for diagnosing otitis media.	Ongoing. 1. Medical school curriculum: 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 will be sent to 25 medical schools to incorporate into their overall curriculum. A meeting will be held in September 2005 for medical educators and deans to discuss the curriculum. 2, 3. Primary care residents curriculum and otitis media curriculum: In 2004 two new awards were granted for provider curricula; one to Oregon Health and Science University and the other to the Children's Hospital of Pittsburgh. Both curricula are being developed in collaboration with AAMC. Oregon Health and Science University is currently developing the primary care residency curriculum based on the medical school curriculum.
CDC	Reporting antimicrobial susceptibility data to clinicians	Assist NCCLS 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. Developed guidelines in 2001. Multicenter study showed significant problems in reporting of antimicrobial susceptibility testing results of positive blood cultures. Educational programs to improve reporting practices are now in progress in multiple healthcare institutions
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.
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) .
VA	a. Prudent use of antibiotics interventions b. Review of commercially available computer software to be used for infection prevention, control and containment	a. The VHA is already involved in many of these activities with particular emphasis on educational activities and training for prescribers at all levels, including physicians, nurse practitioners, and others who are involved with the direct care of patients. Particularly, the VHA provides a strong role in education for health professions students, medical and nursing trainees, and others critical to the provision of care to patients such as social workers, psychologists, and advanced role nurses. In addition, the VHA has produced guidelines, including those that relate to antimicrobial drug use. Therefore, the VHA is well underway for this action item. b. VA is actively reviewing computer off-the-shelf software products to assist in infection control processes for prevention and control of infectious diseases including antimicrobial resistant organisms; computer-assisted decision support systems will be a key element in VA's choice of product.	a. Ongoing b. Commercially available software are being tested in clinical settings including some VA medical centers.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			
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.			
Action Item #29: Periodically Review and Update Antimicrobial Drug Susceptibility Information Including In Drug Labeling, with Input from Stakeholders and Other Experts, e.g., the National Committee for Clinical Laboratory Standards (NCCLS) 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.	The meeting was convened in July, 2004, and included a panel of experts representing academia, clinicians, clinical microbiologists, professional societies, and public health practitioners.
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	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-
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
VA	Appropriate use of antimicrobials	The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federal agencies and other partners (including the private sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems.	Ongoing. Infectious Diseases Field Advisory Committee has representation on the national Antimicrobial Medical Advisory Panel (MAP) for pharmacy
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			
VA	Surgical Site Infection Antibiotic Prophylaxis plan	VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide. These performance measures constitute 50% of the annual evaluation for Executive Career Field (ECF) performance plans for VHA regional directors. The particular performance measures relative to surgical site infection antibiotic prophylaxis include percent of the cases the drug began timely, percent of the cases the appropriate drug was given, and percent of the cases the drug was discontinued timely.	For Federal Fiscal Year 2005, VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide
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.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research career award (K08): randomized trial of sinus CT for acute sinusitis.	This investigator at the University of Washington will develop and implement of a randomized controlled study assessing the impact of sinus CT on the use of antibiotics for patients with acute sinusitis. She will also develop and validate clinical prediction rules through the randomized clinical trial.	Awarded April 2004.
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.	Ongoing. Continued patient enrollment in 2003. Samples have been collected and stored to determine strain transmission. Genetic analysis of samples is underway with results expected in 2004.
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.			
VA	Laboratory accreditation	The VHA currently participates in surveys by the College of American Pathologists and all VHA laboratories are appropriately credentialed.	Ongoing.
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.			
CDC	National laboratory system demonstration projects	These projects promote linkages and coordination between State Public Health and clinical microbiology laboratories to optimize laboratory practice, in collaboration with medical societies and other stakeholders. AR is one focus area. In one project, the State of Washington developed and distributed a survey of laboratory practices related to antimicrobial susceptibility testing (AST) and has provided training to approximately 2,000 laboratorians in a dozen states in quality control for AST testing through a teleconference and a train-the trainer program on using an interactive CD-ROM program on the NCCLS AST laboratory guidelines. The survey was subsequently re-administered to measure changes in practice and use of the guidelines. An increase in use of guidelines was demonstrated.	Ongoing. CDC-funded demonstration projects are underway in numerous states.
CDC	Grant Program: Applied Research on Antimicrobial Resistance - Validation of National Committee for Clinical Laboratory Standards (NCCLS) 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 NCCLS 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 NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development.	Three three-year awards were made in 2002. Recipients include: University of Texas Medical Center, University of Pittsburgh, and University of Wisconsin Medical Center. Projects underway, results pending.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			
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: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use	Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings.	Four three-year awards were made in 2001. Recipients include University of Utah, University of Pennsylvania, Marsfield Epidemiological Research Center, and William Beaumont Hospital.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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).
VA	Long term care infection surveillance	A national VA taskforce has developed a CDC NNIS hospital prototype web-based point prevalence survey using CDC definitions of infections that will improve infection surveillance of VHA nursing homes.	Alpha testing of web-based tool complete; beta testing in process. Rollout to all 134 VA nursing homes after beta testing complete.
**** 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.**			
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	2004 activities include: 1) performed a multi-center intervention using post-prescription review as a method of promoting rational antimicrobial use, and demonstrated that 1/3 of broad spectrum antimicrobial use was unjustified at 48-72 hours; providers responded to suggested antibiotic changes in over ½ of cases. These results suggest that post-prescription review can enhance appropriate antimicrobial use. 2) Performed a multi-center study to determined baseline incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE) transmission in 12 intensive care units (ICUs) in 5 hospitals. Demonstrated that active surveillance cultures significantly increase detection of MRSA and VRE colonization in ICUs. 3) Intiated multicenter study to evaluate impact of daily chlorhexidine baths on transmission of MRSA and VRE in ICUs.
CDC	Impact of Chlorhexidine Bathing on Transmission of Antimicrobial Resistant Organisms in Long-term Care Facilities	We propose a study to examine the impact of chlorhexidine bathing on the rate of transmission of antimicrobial-resistant organisms of epidemiologic significance among patients in long term care facilities.	The Atlanta VA was identified as the collaborative partner, and funds were awarded late in FY2004. Based upon the resources needs, the project will focus on long term care. Work thus far has included protocol development and recruitment of study personnel. IRB approval is pending.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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)
VA	A. Six Sigma™ process to promote hand hygiene in VA medical facilities. B. Antibiotic Resistance Patterns for Streptococcus pneumoniae in VA. C. Antibiotic Resistance and Extended Spectrum Beta-lactamase (ESBL) Activity in VA: A Two-year Review. D. AHRQ 1 UC1 HS014237 Toward a Safety Culture: Reducing Nosocomial Infections E. Toyota Production System (TPS) process to reduce infection	A. National VA effort to use the Six Sigma™ process in the hand hygiene promotion effort. Pilot project at 3 VA medical facilities, with products from the testing to be distributed nationwide to all VA medical facilities. B. *S. pneumoniae* laboratory data collected nationwide from VA medical facilities to identify antibiotic resistance patterns. C. Antibiotic resistance and ESBL activity data collected from VA medical facilities nationwide. D. VA personnel are leading a regional research study sponsored by AHRQ designed to look at rapid-cycle implementation strategies of evidence-based practices that are known to reduce health care associated infections E. Through a demonstration project sponsored by CDC, VA facilities in Pittsburgh along with other health care institutions in the region participated in evaluation of a methodology (Toyota Production System process) for implementing change in infection control practices.	A. Six Sigma process regarding hand hygiene being tested at 3 VA medical facilities. B. Abstract presented at the Annual Conference on Antimicrobial Resistance, June 23-25, 2003, Bethesda, MD. Authors: G Roselle, A Kelly, L Danko, L Simbartl, S Kralovic. C. Abstract presented at the International Conference on Emerging Infectious Diseases, 2004, Feb 29-Mar 3, 2004, Atlanta, GA. Authors: GA Roselle, SM Kralovic, LH Danko, LA Simbartl, LB Rice. D. Ongoing E. Ongoing
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).	In development.
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.	Seminar held on December 3-4, 2001.
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
VA	a. Required Hand Hygiene Practices Directive VHA Directive 2005-002 b. Six Sigma ™ Process to promote hand hygiene in VA medical facilties	a. National directive which provides guidance for establishing the basic requirements for hand hygiene practices in VHA facilities. A hand hygiene policy (conforming to the Category IA, IB, and IC recommendations presented in the CDC Guideline for Hand-Hygiene in Health-Care Settings [2002]) was developed. b. Six Sigma ™ process was tested in VA facilties.	a. Distributed to VA field facilities on 1/13/05, with implementation to be accomplished in VA facilities nationwide by March 1, 2005 b. Further development of Six Sigma ™ defined strategies for implementation is ongoing.
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.	2004 activities: 1) Observations completed, and preliminary analysis reveals significant gaps between recommended and observed practices. Analysis to determine associations between practice and infection rate are ongoing. 2) Observations are being used to develop an intervention toolkit that can be utilized by dialysis centers for preventing catheter-associated bloodstream infections
VA	Educational activities since January 2001: A. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August 8, 2001. B. Emerging Pathogens Satellite Broadcast, September 5, 2001 C. Infomercials taped and aired on VA Knowledge Network. Viewed by VHA employees. D. Infection: Prevention and Containment Conference, such as handouts and responses to questions posed by attendees. E. Memorandum "CDC Hand Hygiene Recommendations and JCAHO Patient Safety Goal 7 for 2004" from VA Under Secretary for Health F. National Center for Health Promotion Monthly Topics	Conference Speakers/Topics: A. Employee Health: Vaccine and PPD Issues. Speaker: Gary A. Roselle, M.D. Emerging Infectious Diseases. Speaker: Stephen M. Kralovic, M.D. B. Part 1 – Tuberculosis. Part II – Implementation Thoughts and the Future. Presenter: Gary A. Roselle, M.D. C. 2-3 minute "infomercials" covering issues relating to influenza, PPD's and bloodborne pathogens D. Conference Speakers for Infection: Prevention and Containment Conference included Gary A. Roselle, M.D., Stephen M. Kralovic, M.D., Robert Gaynes, M.D., Louis Rice, M.D., Robert Muder, M.D., Lynne Sehulster, PhD. E. The memorandum addressed the VA expectations concerning hand hygiene in VA medical facilities F. Some of the monthly topics address specific diseases and some address specific infectious diseases preventive measures	The VHA is currently in the forefront of infection control programs in the healthcare settings in the U.S. This includes national guidance, educational activities, and current financial support of the program nationwide. It is anticipated that such activities will continue, particularly because of the more recent emphasis on patient safety and infection control as part of an overall safety program to prevent excess infections in the healthcare setting. D. Infection: Prevention and Containment Conference was held May 4-6, 2004. E. VA Under Secretary for Health Memorandum pertaining to hand hygiene was issued to VA medial facilities nationwide 12/15/03. F. Information on the following, STDs/AIDS (April 2003), Immunizations (August 2003), and Tuberculosis (March 2004) were issued to VA facilities nationwide

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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 will use 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.	Ongoing. Mendenhall, Utah State University. Funded through CSREES, National Integrated Food Safety Initiative.
Action Item #46: Educate the Public About the Merits and Safety of Irradiation as One Tool To Reduce Bacterial Contamination of Food.			
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	There are 52 QIO projects focused on underserved populations and the elimination of healthcare disparities, including increasing pneumonia and influenza vaccinations in adults.	Ongoing effort and is in the current QIO scope of work. Numerous ongoing projects to support community based programs that promote adult vaccinations.
VA	a. 2002-2003 Influenza/Pneumococcal Vaccine Toolkit, 2003-2004 Influenza/Pneumococcal Vaccine Toolkit, and 2004-2005 Influenza/Pneumococcal Vaccine Toolkit b. Pneumococcal and Influenza Vaccination as Performance Measures	a. Influenza/Pneumococcal Vaccine Toolkits were developed to enhance local influenza/pneumococcal immunization programs throughout VA, and contain promotional items along with directive containing most recent influenza vaccine recommendations b. For many years VHA has included the delivery of both influenza vaccination and pneumococcal vaccination to at-risk populations (based on CDC recommendations) as a key performance measure for patient care. Performance measures constitute 50% of the annual evaluation for Executive Career Field (ECF) performance plans for VHA regional directors.	a. Updated toolkits are sent to VA facilities nationwide in the fall of each year b. Ongoing
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.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae* , licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. 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.	Data collection began in 2002. Completed enrollment for children <2 years in 2003 and finished enrollment of children 2-4 years for a total of 3470 children enrolled. Analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. ABCs surveillance is ongoing indicates that by 2003 disease due to penicllin-resistant strains had dropped by over half. (Whitney CG, et al. N Engl J Med 2003 May 1;348(18):1737-46). In Anchorage, 4 consecutive carriage studies have been completed. 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. Impact of a conjugate vaccine on community-wide carriage of nonsusceptible Streptococcus pneumoniae in Alaska. J Infect Dis. 2004;190:2031-8.).
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. 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.	Ongoing. Completed enrollment of children 24-59 months, for a total of 3471 children enrolled in the study, and presented preliminary results at the International Symposium on Pneumococci and Pneumococci Diseases in May 2004, at ACIP, and during several meetings with ministries of health for other countries considering adopting the vaccine. Enrolled 40 cases into the study of risk factors for flouroquinolone-resistant infections for a total of 78 cases. Performed serotyping on >3000 pneumococcal isolates.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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 Application.	Ongoing. Several licensed vaccines. Continued vaccine supply essential to maintaining the near elimination of resistant *H. influenzae* disease in the U.S.
FDA	Pneumococcal vaccine	Monitoring and guidance provided to current manufacturer of a seven-valent conjugate vaccine. Ongoing. One licensed conjugate vaccine for the prevention of invasive disease and acute otitis media in infants and small children. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants. One licensed multivalent polysaccharide vaccine for the elderly.Facilitating clinical development of a more immunogenic vaccine for the elderly.	Ongoing. One licensed polysaccharide and one licensed conjugate vaccine for the prevention of invasive disease and acute otitis media. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants. One licensed multivalent polysaccharide vaccine for the elderly.
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 res eqrch and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND).
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 population.	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).	Ongoing: 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.
FDA	Staphylococcal vaccine	Fast-Track designation granted for prevention of invasive *S. aureus* infections in patients receiving renal dialysis.	Clinical development ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
VA	Improve use of vaccines related to prudent use of antibiotics	Department of Veterans Affairs, Veterans Health Administration Directive 2001-053. Influenza Vaccine – Recommendations for 2001-2002. Published and placed on VA Intranet website August 28, 2001. Infomercials were aired on VA Knowledge Network regarding influenza vaccine. Performance Measurement Program, 2001 and 2002 VHA Performance Measurement System Technical Manuals list Influenza Immunization and Pneumococcal Immunization as Preventive Care Quality Performance Measures, with specific recommendations for these immunizations for Nursing Home Care Units within the VHA system. Influenza Vaccine - Recommendations for 2002-2003, VHA Directive 2002-044, Published on 7/29/02. Influenza Vaccine Recommendations for 2003-2004, VHA Directive 2003-058, published 10/7/03, Influenza Vaccine Recommendations for 2004-2005 VHA Directive 2004-052 published 9/29/04. Performance Measurement System Technical manual (See #24).	The VHA is already in the forefront of immunization practices as is evidenced by the pneumococcal and influenza vaccine usage rates compared to the national averages. In addition, influenza vaccine use increases each year in the VHA as emphasis on this program continues. Therefore, this action item is already under way and will continue to be an area of emphasis area for the VA.
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).
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 #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 and cattle, develop alternatives to the use of antimicrobial drugs as growth promotants, and evaluate new practices to reduce resistant bacteria in food animals.	Ongoing. A new program, 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 April 2005 and to the greater Get Smart campaign.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			
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 . Report of findings being composed.
CDC	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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). G. Lonergan, West Texas A&M. Funded by CSREES, NRI's 32.1 Epidemiologic Approaches to Food Safety.
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 among foods of animal origin.	NARMS retail was initiated in 2002, as of 2005, 10 of 11 FoodNet sites are participating. The first NARMS retail meat annual report (2002 data) was published and can be found at http://www.fda.gov/cvm/index/narms/2002retailmeat/coversheet.htm . FDA is currently involved in publishing the 2003 annual report.
Action Item #54: Identify and Evaluate New Food Pasteurization Strategies.			
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	Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations	Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment.	Enzo R. Campagnolo, et. al. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. The Science of The Total Environment, Volume 299, Issues 1-3, Pages 89-95, November 2002.
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.	Sampling delayed. Second & final round of sampling in Cape Fear and Pamlico Rivers completed in Spring '05. Samples to be analyzed & data provided to CDC in Fall '05

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Preliminary results presented at CDC CAFO workshop, Feb 2004. This project is finished. North Carolina has moved into a Phase II of this project being supported by CDC funding.
FDA	Animal production studies	Determine dynamics of resistance development in naïve animal populations exposed to antimicrobial agents.	Completed animal studies focusing on the development and persistence of bacteria resistance after exposure to specific antimicrobials. Two studies have been completed in poultry: the first focused on fluoroquinolone resistance development in *Campylobacter* after exposure to veterinary approved fluoroquinolones, while the second concentrated on the emergence and carriage of streptogramin resistance in enterococci exposed to the veterinary streptogramin, virginamycin.
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.			
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, 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.
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. Subject matter experts have reviewed the first module of the curriculum – a background module. A dairy specific module has been written and other experts are being sought out to write additional species specific modules. It is expected to have the background module completed and in use by Fall 2005.
FDA	Education/outreach materials	Develop outreach material on judicious use targeted to veterinarians.	Ongoing activity.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.

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.	Ongoing. An approach for ranking antimicrobial drugs as to their importance for human medicine was developed by CDER and incorporated into CVM's draft guidance published in November 2002. Comments on the approach were obtained from the CDER Anti-infective Advisory Committee in January 2003 and incorporated into the final guidance that published in October 2003.
FDA	Fluoroquinolones	Withdraw approval of fluoroquinolones for use in poultry	Sarafloxacin voluntarily withdrawn April 30, 2001; hearing requested for Bayer's enrofloxacin. Legal proceedings ongoing. Both sides have filed narrative statements, written direct testimonies, and detailed proposed findings of fact. Oral cross examination took place between April 28 and May 9, 2003. Final briefs and reply briefs were filed in July and August, 2003. On March 16, 2004, Administrative Law Judge Daniel Davidson issued an initial decision, ordering the approval of the NADA for that drug for use in poultry be withdrawn, effective on the date the initial decision becomes final. Pursuant to 21 CFR 12.120(e) this initial decision will become the final decision of the Commissioner by operation of law in the absence of the timely filing of exceptions under 21 CFR 12.125(a) or the filing of a notice pursuant to 21 CFR 12.125(f) that the Commissioner intends to review the decision.
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 will be analyzed and risk assessment revised.
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.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Based on the information developed for veterinarians, FDA developed and printed booklets for swine producers and poultry producers, written with less technical language. Have contracted with specialists to write booklets for dairy and beef producers. These booklets have been printed and distributed.
FDA	AR use by veterinarians	Develop a Web-based decision support system for use by veterinarians to select and use antimicrobial agents appropriately.	Provided funding for development of Veterinary Antimicrobial Decision Support System; five year contract awarded late 2001.
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.			
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.
CDC	Board of Scientific Counselors, National Center for Infectious Diseases	Discussion of CDC activities to address AR at Board meetings, including extended discussion in breakout group in 2002.	Ongoing. Meetings occur twice yearly.
**** 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.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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. WARN also co-sponsored a conference on infectious disease issues in long-term care with the University of Wisconsin. 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.
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	Recent accomplishments include demonstrating the impact of a multi-faceted hand hygiene program that resulted in sustained high hand hygiene adherence, and this was associated with decrease in MRSA and VRE incidence in one CARP facility. Demonstrated significant decrease in VRE transmission with use of daily chlorhexidine baths in the ICU setting. Developed and evaluated a method for using electronic data to identify inappropriate antimicrobial use, resulting in significant decrease in inappropriate use of two or more redundant agents. Using the same method, established that over 50% of vancomycin courses were needlessly prolonged; interventions were effective in discontinuing the drug in at least 54% of these cases. Currently conducting 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.
CDC	IMPART (Inter-Mountain Project on Antimicrobial Resistance and Therapy)	A project to implement and evaluate a comprehensive approach in rural Utah and Idaho communities (in both inpatient and outpatient settings) for surveillance of AR, to improve antimicrobial prescribing, to assess the environmental impact of antimicrobial drug use in agriculture and aquaculture and to evaluate potential routes of transmission of resistant bacteria to humans, and to identify novel biotherapeutic approaches to AR that have applicability to the rural setting.	Three year grant awarded in 2001. During the first year of this study a comprehensive surveillance system has been established to monitor AR and assess the impact of antimicrobial drug use in agriculture and aquaculture. Multiple publications have resulted from this work.

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. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System (TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies.	Ongoing. Initiated pilot testing of the interventions in two hospitals within the network (University of Pittsburgh Medical Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital) during 2001. Follow-up observations show significant improvement in compliance across all occupations. Problems hindering compliance which continue to be targeted include unreliable delivery of isolation materials, inconsistent identification of patients requiring isolation, and time consuming inefficiencies in the delivery of patient care services such as medication administration. In addition, an assessment of policy, perception, and practice regarding MRSA control has been initiated. In 2003 we conducted a survey of knowledge, attitudes, and practices in facilities, and evaluated TPS in an inpatient surgical unit at PRHI which measured a decline of 54% in healthcare associated -MRSA infections.
VA	A. Six Sigma™ process to promote hand hygiene in VA medical facilities. B. AHRQ 1 UC1 HS014237 Toward a Safety Culture: Reducing Nosocomial Infections C. Toyota Production System (TPS) process to reduce infection	A. National VA effort to use the Six Sigma™ process in the hand hygiene promotion effort. Pilot project at 3 VA medical facilities, with products from the testing to be distributed nationwide to all VA medical facilities. B. VA personnel are leading a regional research study sponsored by AHRQ designed to look at rapid-cycle implementation strategies of evidence-based practices that are known to reduce health care associated infections C. Through a demonstration project sponsored by CDC, VA facilities in Pittsburgh along with other health care institutions in the region participated in evaluation of a methodology (Toyota Production System process) for implementing change in infection control practices	A. Six Sigma™ process regarding hand hygiene being tested at 3 VA medical facilities. B. Ongoing C. Ongoing
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.			
VA	A. Six Sigma™ process to promote hand hygiene in VA medical facilities. B. AHRQ 1 UC1 HS014237 Toward a Safety Culture: Reducing Nosocomial Infections C. Toyota Production System (TPS) process to reduce infection D. Surgical Site Infection Antibiotic Prophylaxis plan E. Influenza and Pneumococcal Vaccinations as Performance Measures	A. National VA effort to use the Six Sigma™ process in the hand hygiene promotion effort. Pilot project at 3 VA medical facilities, with products from the testing to be distributed nationwide to all VA medical facilities. B. VA personnel are leading a regional research study sponsored by AHRQ designed to look at rapid-cycle implementation strategies of evidence-based practices that are known to reduce health care associated infections C. VA facilities in Pittsburgh along with other health care institutions in the region participated in evaluation of a methodology for implementing change in infection control practices D. VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide. These performance measures constitute 50% of the annual evaluation for Executive Career Field (ECF) performance plans for VHA regional directors. E. VHA has included the delivery of both influenza vaccination and pneumococcal vaccination to at-risk populations as a key performance measure for patient care.	A. Six Sigma™ process regarding hand hygiene being tested at 3 VA medical facilities. B. Ongoing C. Ongoing D. For Federal Fiscal Year 2005, VHA has introduced surgical site antibiotic prophylaxis as a performance measure for VHA systems nationwide E. Ongoing

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			
VA	Quality assurance programs	The Office of Quality and Performance's Performance Measurement Program, which supports the VHA Strategic Plan, serves as a vehicle for effecting change in a balanced fashion. The Performance Plan operationalizes the premise that better quality, access, and satisfaction are often more efficient. For example, improved rates of inexpensive pneumococcal vaccinations may result in decreased antibiotic use. Immunization rates are assessed through a contract chart review system and are part of managers' performance standards, and, therefore, are used as part of the VHA quality-monitoring program. Excellent immunization rates in the VHA have resulted from this program. JCAHO Safety Goal #7 - Hand Hygiene to reduce healthcare-associated infections were addressed in a memorandum by VA Under Secretary for Health. AHRQ StudyToward a Safety Culture: Reducing Nosocomial Infections.	Ongoing. The VA Under Secretary for Health's hand hygiene memorandum was issued to VA medical facilities nationwide on 12/15/03. The study "Toward a Safety Culture" is in process.
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.			
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.
CDC	Grant Program for Applied Research on Antimicrobial Resistance: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use	Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings.	Four three-year awards were made in 2001. Recipients include University of Utah, University of Pennsylvania, Marsfield Epidemiological Research Center, and William Beaumont Hospital. Projects ongoing, results pending.
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 Unveristy. Projects underway, results pending.

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.
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. Described in Cebula, T.A., Levy, D.D. and LeClerc, J.E. Mutator bacteria and resistance development. In Antibiotic Resistence and Antibiotic Development (Eds. D. Hughes and D. Anderson) Harwood Academic Publishers, Amsterdam, pp. 107-116 (2000).	Ongoing.
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	Antibiotic resistance in vibrio	Investigate emergence of antimicrobial resistance in Vibrio species.	Ongoing.
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.	21 FQ resistant campylobacter were isolated from chicken liver samples and characterized by PCR-RFLP and Pulsed field gel electrophoresis (PFGE). Seventy-eight campylobacters were isolated from turkey litter samples and characterized for the presence of galE gene, PCR-RFLP and PFGE. Quinolone resistance determining regions (QRDR) from campylobacters and *E. coli* were PCR amplified and sequenced for the detection of silent mismatched mutations. The FQ resistant *E. coil* strains isolated from chicken and turkey litter were typed by ribotyping. Completed in vivo studies examining the development of fluoroquinolone resistance among Campylobacter from chickens administered approved fluoroquinolones. Continue to characterize at the molecular level, resistant Salmonella, Campylobacter and *E. coli* as part of the NARMS retail program.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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	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-02-038) Recently funded a project under this PA entitled "Novel Antibiotics: Site-Specific Recombination Inhibitor." Replaced with Program Announcement (PA-03-108), which was released on April 18, 2003; expiration date: April 18, 2006.
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: "Novel Inhibitors of Poxvirus Replication," "Combination Chemotherapy For Pandemic Influenza," "Novel Azole Resistance Mechanisms in Candida albicans," "Reservoirs of Drug-Resistant HIV-1," "Synthesis and Mechanistic Studies of Peptide Antibiotics," "New Antimalarials From Plant-Pathogenic Fungi" and "Novel Methods for Discovery of Anti-Microbials."
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: "N ovel antibiotics that trap Holliday Junctions," "Novel Ribostamycins and SAR Study of Ring III Aminosugar," "Combatting Quinolone Antimicrobial Resistance," and "Mechanism and Spread of Qnr-Mediated Resistance."
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: "Ceftiofur use in cattle: a Public Health Concern?," "Isolation of New Antibiotics From Soil Microorganisms," and "Anti-Trypanosomal Agents From a Neotropical Cloudforest."
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.	Ongoing. Recent awards include: "Development of DAM Inhibitors as Novel Antibiotics," "Novel Therapeutics for Biodefense," "Dual Purpose β-Lactamase Inhibitors," "Potentiating Compounds For Aminoglycoside Antibiotics," "Macrolide Discovery Through Glycosylation," "Development of Antifungals of Clinical Importance" and "Small Molecule Inhibitor of Quorum Sensing."

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 multiples pathogens"
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: i) 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. ii) Retrospective study of the emergence of AR Salmonella enteritidis. iii) Two additional studies focused on the emergence and transmission of AR zoonotic bacteria.
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.	Multiple awards made in 2004, including "BD Probe Tec ET for Diagnosis of Influenza and SARS," "Diagnostics for Bacterial/Viral Pathogens Including SARS" and "Advancing a new TB Drug Through Early Clinical Trials."
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 eradicated diseases.	PA-03-080; http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html. Expires March 2006. Recent awards made under this initiative include: "Novel Diagnostics and Therapeutics for Caliciviruses," "IMPDH as a Drug Target in Cryptosporidium," and "Mycothiol Biosynthesis and Metabolism as TB Drug Targets."
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
Action Item #68: Conduct Further Government-Wide Assessments with External Input on the Scope and Composition of AR Research To Identify Research Opportunities.			
NIH	Antimicrobial strategies and cardiothoracic surgery working group	Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery, including complications relating to the development of AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures.	Meeting held April 4-5, 2002 in Bethesda, MD., collaborative clinical trials and research initiatives under development.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Prevention and Treatment of *Staphylococcus aureus* Infections after Cardiac Surgery Request for Information	A Request for Information was released on October 15, 2003 to obtain information from the academic and industrial communities as to the availability and current development status of immunologic products to prevent and treat *S. aureus* infections.	Information was received from over 20 academic and industrial groups indicating the availability and current status of their products to prevent and treat *S.aureus* infections. The results are under discussion.
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 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 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, second meeting in October of 2004 and the third in March of 2005.

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.	Ongoing.
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 24 in FY2004. 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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Sequencing of whole pathogen genomes	NIAID has made a 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 FY2004, NIAID supported approximately 40 large scale DNA sequencing genome projects for microbial pathogens and invertebrate vectors of infectious diseases, including new projects for Burkholderia mallei, Burkholderia pseudomallei, Culex pipiens, Francisella tularensis, Histoplasma capsulatum, Influenza, Ixodes scapularis, Mycobacterium tuberculosis, Vibrio cholerae, and Yersinia pestis.Genome sequencing projects for bacteria Bacillus anthracis (4 strains), Bacillus cereus, Clostridium perfringens (SM101), Mycobacterium smegmatis, Legionella pneumophila, were completed. Genome sequencing data is available on publicly accessible web sites, and genome sequences for Bacillus anthracis, Bacillus cereus (ATCC 10987 and G9241), Burkholderia mallei, Crypotsporidium parvum (bovine), Legionella pneumophila, and Wolbachia have been published in FY2004.
NIH	Influenza Genome Sequencing Project	This project was launched in 2004 and will put influenza sequence data rapidly in 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	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. www.niaid.nih.gov/dmid/genomes/
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 FY2004, NIAID continued to participate in two 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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) contract	The network includes approximately 140 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 repository now includes a representative panel of clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from a variety of disease conditions, research isolates, genome sequenced isolates, virulence and toxin-producing strains, and a broader representation of drug-resistant strains. NARSA has also sponsored a staphylococcal annotation meeting in collaboration with the Institute for Genomic Research (TIGR) and a community MRSA meeting in collaboration with CDC. Plasmid sequence and annotation of the Michigan VRSA is now available through the TIGR CMR site on the NARSA homepage. Information concerning NARSA can be found at: www.narsa.net.
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 will include examining host response to immunization against smallpox and Bacillus anthracis.
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 proteins from TB. The structural and functional information is publicly available through web-based databases: http://www.doe-mbi.ucla.edu/TB/.
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.	One component of this contract is the "STEC Center Repository" (http://www.shigatox.net/cgi-bin/stec/index), which provides strains and genomic information to the scientific community.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Ongoing.
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.	Ongoing.
NIH	NIAID Microbial Sequencing Centers	The Microbial Genome Sequencing Centers (MGSCs) 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.	In FY2004, NIAID supported new genome sequencing projects for additional strains of Burkholderia mallei, Burkholderia pseudomallei, Coronaviruses, pathogenic Escherichia coli, Francisella tularensis, Influenza, Mycobacterium tuberculosis, Shigella, Vibrio cholerae, and Yersinia pestis. In addition, NIAID approved sequencing projects for invertebrate vectors of infectious diseases, Aedes aegypti, Culex pipiens and Ixodes scapularis. 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.
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).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.

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. In addition, DARPA provides funds for the Poxvirus Bioinformatics Resource Center (http://www.poxvirus.org). 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. It also serves as a repository of well-documented viral strains.
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.	Ongoing
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.
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 24 in FY2004.	Ongoing.
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/
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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."
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	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.
VA	Proposal Regarding Antibiotic Resistance Fellowship	The Infectious Diseases Program Office proposed the initiation of a two-year VA Special Fellowship in the area of antibiotic resistance at six sites. The proposal required trainees to have completed internal medicine and infectious diseases specialty and subspecialty residency training, and would have required scientific emphasis on antibiotic resistance.	The proposal was rewritten and restructured to focus on training leaders in Terrorism Response for the Future with emphasis on antibiotic resistance. A portion of the training was to include biologic threat agents (including pandemic influenza).
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, and 2005.

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)
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.
NIH, CDC, FDA	Gordon Conference on Tuberculosis Drug Development	Scientific conference co-sponsored by the Global Alliance for Tuberculosis Drug Development (GATB), the NIAID, and others. The meeting focused on all aspects of new drug development including analyses of the genomic sequences available for mycobacteria, criteria for selection of appropriate drug targets, review of compounds being synthesized, and planning for the development of clinical trial protocols. Investigators involved in all phases of TB drug development from many countries participated in stimulating sessions. In attendance were representatives from the pharmaceutical industry, NIAID, CDC, infectious disease physicians, x-ray crystallographers, chemists, and NIAID-supported research investigators.	Meeting held August 31-September 4, 2003 in Oxford, U.K. This conference is held during the Fall of every other year.
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/

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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	Program staff consult and serve as liaison members to national groups, including the Advisory Council for the Elimination of Tuberculosis (ACET) and the CDC TB Clinical Trials and Epidemiology Consortia. International activities include participation on WHO's TB Vaccine Initiative Advisory Committee (TBVIAC), STOP TB Coordinating Board, and the STOP TB Vaccine, Drug and Diagnostic Working Groups. NIAID staff also serves on the Scientific Advisory Committee of the Global Alliance for TB drug Development (GATB).	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	Annual meeting of the U.S.-Japan Cooperative Medical Sciences Program, TB and Leprosy Panel	A meeting celebrating the 40th anniversary of the US-Japan Cooperative Medical Sciences Program was convened in Kyoto, Japan on December 7-10, 2004. At this meeting, all ten scientific panels and boards met at one location. The goal of the US-Japan Program is to foster an exchange of ideas and stimulate international collaborations among U.S., Japanese and other Asian researchers. For more information about the US-Japan program: www.niaid.nih.gov/OGA/usjapan/default.htm	Ongoing. The 2005 meeting will be held in Seattle, WA (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 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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** 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.**			
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.
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.
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.	Protocols under development include: (1) "Infection control strategies to reduce colonization and infection caused by antimicrobial-resistant bacteria in an adult intensive care unit;" planned to begin in March 2005; and (2) "Randomized, multicenter, comparative trial of short-course course antibiotic therapy vs. standard intensive care unit;" enrollment planned for Aug 2005 (3) "Derivation of a Clinical Prediction Rule for Bacterial Pulmonary Infection in Mechanically Ventilated Children;" enrollment planned for June 2005.

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 early FY2005.
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 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.
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.
VA	VA research update	VA investigators have a rather extensive portfolio in antibiotic resistance research that for fiscal year 2000 identifies twenty-three separate funded proposals in AR. For 2001, there are twenty-nine funded projects related to AR by VA investigators. These funded research grants cover a wide spectrum of AR issues. In addition, these do not include large clinical trials that may have impact on AR such as collaboration with the NIH-funded HIV ACTG's and pharmaceutical corporate-related research that is widespread throughout the VHA. A specific area of emphasis is transmission of resistance among organisms and spread of these organisms from person to person. Such topics as spread of resistance in nursing homes, the relationship of resistance to staffing levels, and work practices (organization) as they relate to antibiotic resistance are all part of VA investigators' portfolios and are topics unlikely to be studied in the private sector. VA investigators continue to have an extensive and expanding portfolio in antimicrobial resistance research.	Ongoing. In 2001, twenty-eight projects related to bacterial resistance were underway, an increase of over 300% from 1997. Ongoing. In 2002, VA provided an increase in funding for projects related to AR of approximately 62% when compared to 2001. The number of studies receiving VA-funded financing increased by 80% when comparing 2002 to 2001. VA funding for bacterial antimicrobial resistance related research increased by 90.6% when comparing 2003 to 2001. For FY 2004, Medical Service Research funding for antimicrobial resistance decreased by 13.x% compared to the previous year. Overall Research funding within VA fell during this same period. The depth and breadth of research remains varied, despite this decline. Even though the total number of Medical Research Service funded projects was less, the number of individual VA medical centers supporting this research remained unchanged.
**** 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
CDC	*C. trachomatis* resistance	Chlamydia trachomatis causes a sexually transmitted infection in an estimated 3 million Americans annually; untreated women can develop pelvic inflammatory disease, which can lead to chronic pelvic pain, infertility, and potentially fatal ectopic pregnancy. Several methodologies are used to assess antimicrobial susceptibility among C. trachomatis isolates, and this project will compare those that are currently used in an attempt to better understand the relationship	A report on a meeting of external consultants was published in the Journal of Infectious Diseases (2005;191:917-923).
FDA	Test kit evaluation	Work to develop streamlined mechanisms for evaluating rapid diagnostic test kits for identifying microbes and for determining 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 the clinical setting.	Cleared/approved in 2004:1)QuantiFERON® -TB Gold aids in in-vitro laboratory diagnostic testing as an indirect test for *M. tuberculosis* complex infection; 2)Immunetics® QuickELISA™ Anthrax-PA Kit is intented for use in the qualitative detection of antibodies to the Protective Antigen (PA) protein of *B. anthracis* in human serum as an aid in the diagnosis of anthrax; 3) Glucatell assay for the qualitative detection of beta-D-Glucan in the serum of patients with symptoms of, or medical conditions predisposing the patient to invasive fungal infection. IDE for SARS approved for CDC PCR assay-active IDE. Ongoing:1) Development 2 international documents for an international reference AST method w/ISO/TC 212 WG(document in final review stage); and for the evaluation of performance of AST devices(in development stages);2)Collaborative work w/CDER on antibiotic breakpoint disparities that exist and the resulting public health impact. Includes efforts w/pharmaceutical industry, device manufacturers, CLSI, CMS, FDA.
FDA	Rapid diagnostic methods to detect multi drug resistant TB (MDRTB) strains	Research: development of rapid diagnostic methods for detecting MDRTB based on the microarray technology.	Collaboration of CDRH with CBER.
FDA	New rapid diagnostic methods	Research: new rapid diagnostic methods for bacterial contamination of foods.	Collaborating with CFSAN research. Developed new detection method using antibodies attached to chip. Working to establish limits of detection and apply to variety of foodborne agents.
FDA	Surveillance activities	Coordinate surveillance activities with CDC.	Held initial meeting with CDC April 25, 2001; further discussions ongoing.
FDA	Nucleic Acid Tests (NAT) for detection of bacteria in donated blood products	Research: Development of nucleic acid tests (NAT) based on PCR-test, TaqMan assay and DNA microarray to detect transfusion induced sepsis causing gram positive and gram negative bacteria potentially present in donated blood products. This technology can be easily adapted to detect bloodborne antibiotic resistant bacteria.	Ongoing project: Awarded Director's Targeted Research Grant, CBER, FDA.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.	Awards will be made in early 2005. The initiative can be found at (http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-04-043.html).
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)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae* , licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. 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.	Data collection began in 2002. We completed enrollment for children <2 years in 2003 and finished enrollment of children 2-4 years for a total of 3470 children enrolled. Analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. ABCs surveillance is ongoing indicates that by 2003 disease due to penicllin-resistant strains had dropped by over half. (Whitney CG, et al. N Engl J Med 2003 May 1;348(18):1737-46). In Anchorage, 4 consecutive carriage studies have been completed. 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. Impact of a conjugate vaccine on community-wide carriage of nonsusceptible *Streptococcus pneumoniae* in Alaska. J Infect Dis. 2004;190:2031-8.).

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.	Ongoing. 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.
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.	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.
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.	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)
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH, USAID	Randomized, double-blinded, controlled Phase III efficacy trial of pneumococcal conjugate vaccine	NIAID is conducting 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 is 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 will be 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. Approximately 16,000 children will be recruited into the trial from shortly after birth over a period of three and a half years. Three doses of the DTP/Hib vaccine mixed with the 9-valent pneumococcal conjugate vaccine will be administered to half the children at two, three, and four months of age. The other half will receive just the DTP/Hib vaccine.	Preliminary efficacy and safety data are promising. Results published in: Cutts, FT, et al:Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial. 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 FY2004, more than 150 new TB vaccine candidates had been tested under the contract, one of which has recently entered human clinical trials with several others progressing through various stages of preclinical development.
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Phase I Malaria vaccine trial	NIAID, in collaboration with Walter Reed Army Institute of Research (WRAIR), GlaxoSmithKline Biologicals, USAID, the University of Maryland Center for Vaccine Development (UMd/CVD), and the University of Bamako, Mali, has just completed a Phase 1 trial in Mali of a novel candidate vaccine that targets the blood-stage of malaria parasites.	Data analysis is underway. A second trial with a different malaria vaccine candidate is underway.
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).	Results of this initial trial are expected to be available for analysis in mid 2005.
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 and immunogenicity of a combination ETEC vaccine."
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 several Phase 1 vaccine trials, including: "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" and "Shigella CVD 25000G: Shigella CVD 25000G: Safety and immunogenicity of CVD 1208S(pCFA/I-A2B), a prototype live, oral attenuated Shigella flexneri 2a vector vaccine expressing two putative protective antigens of enterotoxigenic Escherichia coli."
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 proteins from TB. The structural and functional information is publicly available through web-based databases: http://www.doe-mbi.ucla.edu/TB/

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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.
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; and (4) to provideinformation for selection of anti-mycobacterial drug candidates and for design of clinical studies.	Awards include “Drug Development for Opportunistic Infections-Mycobacterium avium Complex,” “Tuberculosis Drug Screening,” and “Animal Model Testing of TB Drugs,” among others.
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/.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.
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 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.

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.
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.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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 **** **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.	A clinically-relevant in vitro biofilm model was also established based on the CDC Biofilm Reactor system. The system has been set up and optimized for growing and quantifying *Candida* biofilms. To date, isolates from 3 of the 6 *Candida* species have been analyzed for biofilm formation using this in vitro model. The effects of incubation time, nutrient limitation, and flow-rate have been analyzed. Significant differences in biofilm formation under these 3 different conditions were not observed. Two different substrates have also been investigated in this model and include polycarbonate and glass. For all species tested, biofilm quantity was on the order of 10-fold less when glass was used as the substrate. Preliminary experiments using fluorescent microscopy to characterize biofilm architecture have been performed. Based on these early experiments, results of microscopy are consistent with results of the initial biofilm quantification assays using the 96-well plates in that *C. krusei* forms less dense biofilms compared to *C. albicans* and *C. parapsi*
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.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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
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
**** 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.
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
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)
FDA	New AR products	Development of Hyper-Immune Globulins	CBER role is to develop immunization protocols, assays and standards for such products.
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	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.	1)Presentation on regulatory requirements for tests of use in AR initiaties 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)CDRH assisted device manufacturers in the most efficient way to get an alternative method for detecting vancomycin resistance in *S. aureus* to market by offering protocol advice and providing an expedited review option; 3)preliminary stages of esubmission for AST devices to promote a faster more efficient means of presenting data for a 510(k) review process.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
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.			