

EXHIBIT W

TO DECLARATION OF JENNIFER A. SORENSON

Letter from CDC Director Thomas R. Frieden (2010)



July 13, 2010

The Honorable Frank Pallone, Jr.
Chairman
Subcommittee on Health
House Committee on Energy and Commerce
Washington, D.C. 20515

Dear Chairman Pallone:

Please find attached written responses to questions for the record from the Subcommittee's April 28 hearing on antimicrobial resistance. These responses provide additional detail on the strong scientific evidence of a link between antibiotic use in food animals and antibiotic resistance in humans.

There are multiple North American studies describing how:

- Use of antibiotics in animals results in resistant bacteria in food animals
- Resistant bacteria are present in the food supply and transmitted to humans
- Resistant bacteria result in adverse human health consequences (such as increased hospitalizations)

In addition, a strong body of evidence from Europe demonstrates that antibiotic use in animals is linked with antibiotic resistance in humans. Multiple studies looked at the effects of the Danish ban on non-therapeutic use of antibiotics in food animals. We have thoroughly reviewed these studies and have found them to be well-designed and rigorous, and to establish a clear link between antibiotic use in animals and antibiotic resistance in humans.

I appreciate this opportunity to restate my conclusions from the April hearing, and provide you additional detail. This opportunity is particularly important because some discussion at the hearing has been mischaracterized. To be clear, the Centers for Disease Control and Prevention (CDC) finds that there is a compelling body of evidence to demonstrate this link, as summarized above, in my April testimony, and in the attached responses to questions for the record. I am pleased that the Subcommittee is holding another hearing in its series on this important issue, and that Dr. Ali Khan will be able to represent CDC to further elaborate on this evidence regarding the relationship between antibiotic use in food animals and antibiotic resistance in humans.

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CDC remains committed to working with Congress and our colleagues at the Department of Health and Human Services and the U.S. Department of Agriculture to identify the best ways to address the health risks posed by antibiotic resistance.

Sincerely,

A handwritten signature in black ink that reads "Thomas R. Frieden". The signature is written in a cursive style with a large initial 'T'.

Thomas R. Frieden, M.D., M.P.H.
Director, CDC, and
Administrator, Agency for Toxic Substances
and Disease Registry

Cc: Rep. John Shimkus, Ranking Member
Anthony Fauci, NIH
Margaret Hamburg, FDA
Josh Sharfstein, FDA
Ali Khan, CDC

**QUESTIONS SUBMITTED FOR THE RECORD
HEARING ENTITLED,
“ANTIBIOTIC RESISTANCE AND THE THREAT TO PUBLIC HEALTH”
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
UNITED STATES HOUSE OF REPRESENTATIVES
APRIL 28, 2010**

**Thomas Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services**

Representative Henry A. Waxman

Q1. You mentioned data from Europe demonstrating the link between animal antibiotic use and antibiotic-resistant microbes in people, in particular the example of avoparcin and vancomycin-resistant enterococcus. You also mentioned the data from Denmark, where antibiotics were banned for growth promotion uses for animals. Please evaluate the lessons from these European data and provide your views on any relevant lessons for the United States.

A. The Danish studies have focused on non-therapeutic use of antimicrobial agents in food-producing animals, particularly swine and broiler chickens. Non-therapeutic uses include promoting growth and improving feed efficiency; drugs for these purposes are typically given in feed.

- In 1995, the Danish government banned the non-therapeutic use of avoparcin for growth promotion in Denmark. In 1997, the commission of the European Union (EU) countries adopted the same ban for all of its member states.
- In 1998, Denmark banned use of virginiamycin for growth promotion. Also in 1998, the agriculture ministers in the EU voted to ban use of virginiamycin, bacitracin, tylosin, and spiramycin for growth promotion; this ban became effective for EU member states in 1999.
- The Danish cattle and broiler industries voluntarily stopped the non-therapeutic use of all antibiotics for growth promotion in February 1998.
- The Danish swine industry through voluntary and regulatory action stopped all non-therapeutic use of antibiotics for growth promotion in swine above 35 kg by February 1998 and for all age groups by December 1999.
- In 2002, the EU voted to phase out all non-therapeutic use of antibiotics for growth promotion (AGPs, i.e., all non-prescription use) beginning in 2006.

Effect of these actions^{1, 2, 3, 4, 5, 6}

¹ World Health Organization. 2003. Impacts of antimicrobial growth promoter termination in Denmark: The WHO international review panel's evaluation of the termination of the use of antimicrobial growth promoters in Denmark. Available at: <http://www.who.int/salmsurv/en/Expertsreportgrowthpromoterdenmark.pdf>.

² DANMAP. 2008. *Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark*. Available at: http://www.danmap.org/pdfFiles/Danmap_2008.pdf.

- While there has been an increase in therapeutic use of antimicrobials in animals, total antimicrobial consumption in animals in Denmark has decreased by over 50%. From 1998 to 2008, total antimicrobial consumption reduced from 100 to 49 milligrams of antimicrobials per kilogram of meat produced.
- Stopping the use of various non-therapeutic antibiotic growth promoters (e.g., avilamycin, avoparcin, spiramycin, tylosin, virginiamycin) has resulted in a major reduction in antimicrobial resistance as measured among several different bacterial species in food animals and food. This has been thoroughly documented in scientific publications from Denmark.
- Denmark measured total consumption of antimicrobial agents by food animals and resistance to those drugs among *Enterococcus* isolated from food animals and the foods derived from them.
- Resistance to these drugs among *Enterococcus* isolated from broilers, swine, and the meat from these animals decreased after AGPs were discontinued. However, in 2003, the World Health Organization (WHO) could not determine the ban's direct and total effect on antimicrobial resistance in humans because of limited data. Newer monitoring data available since then show that human resistance trends appear to be mirroring the decline in on-farm use of antibiotics; however, newer monitoring data on human resistance must be considered carefully. The trend must first be determined to be sustainable. Second, although the trend may mirror decreases in resistance in animals, more needs to be known about the potential causes for decrease in humans. If present, the trend toward decreased resistance is likely due to many factors including those aimed specifically at human antimicrobial usage and transmission of resistant bacteria.
- Weaner (swine) mortality increased several years before as well as a few years after non-therapeutic use stopped, but has drastically decreased in recent years, indicating that the termination had no effect on swine mortality.
- Production and economic impacts are described in a 2003 WHO report. The WHO reports that: "Overall, total volume of pork production in Denmark continued to increase in the period following the termination of antimicrobial growth promoters... The net costs associated with productivity losses incurred by removing antimicrobial growth promoters from pig and poultry production were estimated at 7.75 DKK (1.04 €) per pig produced

³ Aarestrup, F.M., A.M. Seyfarth, H.D. Emborg, K. Pedersen, R.S. Hendriksen, and F. Bager. July 2001. "Effect of Abolishment of the Use of Antimicrobial Agents for Growth Promotion on Occurrence of Antimicrobial Resistance in Fecal Enterococci from Food Animals in Denmark," *Antimicrobial Agents and Chemotherapy* 45(7): 2054-2059. Available at: <http://aac.asm.org/cgi/reprint/45/7/2054>.

⁴ Boerlin, P., A. Wissing, F. M. Aarestrup, J. Frey, and J. Nicolet. 2001. "Antimicrobial Growth Promoter Ban and Resistance to Macrolides and Vancomycin in Enterococci from Pigs," *Journal of Clinical Microbiology* 39(11): 4193–4195. Available at: <http://jcm.asm.org/cgi/reprint/39/11/4193>.

⁵ Evans, M.C. and H.C. Wegener. 2003. "Antimicrobial Growth Promoters and Salmonella spp., Campylobacter spp. In Poultry and Swine, Denmark," *Emerging Infectious Diseases* 9(4): 489-492. Available at: <http://www.cdc.gov/ncidod/eid/vol9no4/pdfs/02-0325.pdf>

⁶ Gravea, K., V.F. Jensen, K. Odensvik, M. Wierup, and M. Bangen. 2006. "Usage of veterinary therapeutic antimicrobials in Denmark, Norway and Sweden following termination of antimicrobial growth promoter use," *Preventive Veterinary Medicine* 75(1-2): 123-132.

and no net cost for poultry. This translates into an increase in pig production costs of just over 1%.”⁷

In general, subtherapeutic use has been shown to lead to an increase in resistant strains in animals. The European experience demonstrates that it is possible to stop these uses, reduce overall use of antibiotics in animals, reduce resistant circulating bacteria that can infect humans, and not have industry or consumers affected by decreased production or increased costs. Additional information, such as reliable data on quantities of antibiotics used in animals for various purposes and comprehensive on-farm studies of the relationship between use and resistance, would be needed to study the same effects in the United States.

Q2. The rates of foodborne illnesses—particularly those generated by antibiotic resistant organisms—have risen in this country. Ms. Capps asked about the National Antimicrobial Resistance Monitoring System data and suggested that much of the nation’s meat and poultry products are tainted with some kind of antibiotic resistant bacteria. There are a number of studies, both in Europe and in the United States, suggesting a link between the use of certain antibiotics in animals and bacteria resistant to those antibiotics in food products and humans. For example, a study in Minnesota and Wisconsin found evidence indicating that antibiotic-resistant E. coli in people were likely to have come from poultry, while antibiotic-sensitive E. coli in people likely did not come from poultry (J.R. Johnson et al., *Antimicrobial Drug-Resistant Escherichia coli from Humans and Poultry Products, Minnesota and Wisconsin, 2002-2004*, *Emerging Infectious Diseases* (June 2007) (online at <http://www.cdc.gov/EID/content/13/6/838.htm>). Can you expand on this information, and comment on whether CDC believes such antibiotic resistant bacteria from animals and their meat have been transmitted to people?

A.

- CDC is familiar with the J.R.Johnson article referenced and concurs with the conclusions described in the study. Johnson et al analyzed the distribution and virulence genotypes of drug-susceptible and drug-resistant E. coli isolates from human volunteers and poultry products. They found that drug resistant E coli isolates from humans were more similar to drug resistant isolates from poultry than they were from drug susceptible isolates from humans. This work as well as other work from Johnson’s group has contributed to the evidence that drug resistant E coli found in humans is most similar to that found in poultry.
- The National Antimicrobial Resistance Monitoring System (NARMS)⁸ has demonstrated a steady and statistically significant increase in the prevalence of resistance to the two

⁷ World Health Organization. 2003. Impacts of antimicrobial growth promoter termination in Denmark: The WHO international review panel’s evaluation of the termination of the use of antimicrobial growth promoters in Denmark. Available at: <http://www.who.int/salmsurv/en/Expertsreportgrowthpromoterdenmark.pdf>.

⁸ NARMS is a collaboration among CDC (human samples), FDA’s Center for Veterinary Medicine (retail meats and animal feeds), and USDA’s Food Safety and Inspection Service and Agricultural Research Services (animal samples). Participating health departments forward every twentieth non-Typhi Salmonella isolate, every Salmonella Typhi, every twentieth Shigella isolate, and every twentieth E. coli O157 isolate received at their public health laboratories to CDC for susceptibility testing. NARMS investigates outbreaks involving these bacteria and conducts research on resistance mechanisms.

most clinically important antimicrobial agents, ciprofloxacin and ceftriaxone, in *Salmonella* strains isolated from ill humans in the United States.

- A multidrug resistant (MDR) *Salmonella* Typhimurium emerged in the 1990s in cattle and in people, and has persisted since then (associated with ground beef).
- MDR *Salmonella* Newport emerged in 1998 in cattle and humans and has persisted since then (associated with ground beef).
- Resistance to ciprofloxacin in *Campylobacter* in poultry and people emerged in the late 1990s and steadily increased (associated with chicken and turkey).
- In 2005, FDA withdrew approval for fluoroquinolone use in poultry due to evidence it might be associated with resistant human infections.
- Although it has not been demonstrated conclusively in a single study that use of antimicrobial agents in food animals results in adverse human health consequences, numerous studies have demonstrated the movement of resistant pathogens through the food supply. Studies related to *Salmonella*, including many studies in the United States, have demonstrated that (1) use of antimicrobial agents in food animals results in antimicrobial resistance in food animals, (2) resistance strains are present in the food supply and commonly transmitted to humans, and (3) increases in resistant strains results in adverse human health consequences (e.g., increased hospitalization).^{9, 10}

Q3. Mr. Dingell asked that you provide the level of your request for financial support for antimicrobial programs in the President's budget, the amount CDC has been given for these programs during each of the last 3 years, and the amount anticipated for the next 3 years. Please provide such information, including your professional judgment budget for the appropriate level of funding for antibiotic resistance programs at CDC.

A.

- In FY 2008, FY 2009, and FY 2010, antimicrobial resistance was funded (\$16.9 million per year), either through specific Congressional appropriations or agency allocations.
- The FY 2011 President's Budget includes \$8.7 million available to fund AR activities. The FY 2011 Budget also includes an increase of \$19.6 million for the Emerging Infections program, which supports antimicrobial resistance activities, such as surveillance, technical assistance, and epidemiological and laboratory support.

CDC is committed to maintaining a strong AR program and is exploring the high value investments moving forward. CDC will work to prioritize funding through the Emerging infections program and antimicrobial resistance program to combat AR.

In CDC's professional judgment, to fully combat the growing problem of antimicrobial resistance, and to fully implement the CDC-coordinated sections of the Federal Inter-Agency Task Force on Antimicrobial Resistance *Action Plan* (surveillance, prevention and control), CDC requires an annual budget of \$50 million phased in over a three year period (i.e. \$30 million in FY 2012, \$40 million in FY 2013, and \$50 million in FY 2014). An incremental increase in the annual budget will allow for a stepwise expansion of surveillance, prevention and control

⁹ Dutil et al., Emerg Infect Dis 2010

¹⁰ Folster et al., Foodborne Pathog Dis 2010 and Zhao et al., Appl Environ Microbiol 2008.

activities described in the *Action Plan*. This does not include funding of antimicrobial resistance activities for specific diseases (such as tuberculosis and gonorrhea) funded through other CDC budget lines. This represents the professional judgment estimates of CDC staff on the size and scope of the AR activities, and is provided without regard to the competing priorities that the agency, the President, must consider to develop the Budget.

CDC would use this increase in funding to continue its antimicrobial resistance activities and add new applied research grants and demonstration projects; 75% of the division projects would be funded extramurally (both domestic and international) and 100% of the applied research grants and demonstration projects would be funded extramurally to domestic grantees. This increase in funding would also allow states via the Emerging Infections Program (EIP) and the Epidemiology and Laboratory Capacity (ELC) program to expand surveillance activities (e.g., to include antimicrobial resistance in healthcare-associated infections) and to increase state laboratory capacity to detect new and emerging resistance. CDC would also hire personnel to coordinate new surveillance activities and coordinate projects at state levels. This professional judgment budget also includes funding for capital expenses to reinforce select CDC reference laboratories and to develop and implement rapid diagnostic methods to determine the susceptibility of select microorganisms to new anti-infective agents. Funding would support an expansion of current databases of both antimicrobial use and antimicrobial resistance patterns, and expand web based reporting capabilities. Finally, the increase in funding would provide continued support for the Antimicrobial Resistance Task Force and allow CDC to plan and hold an antimicrobial resistance conference that will bring together scientists and consultants to update the Action Plan and discuss the latest scientific trends and developments in the field of antimicrobial resistance.

Professional Judgment Annual Budget for Antimicrobial Resistance Activities

Category	Explanation	Cost (in millions)		
		FY12	FY13	FY14
Continuing & new division projects	75% extramural, both domestic and international, Interagency Agreements	\$7	\$10	\$12
Continuing & new research grants	100% extramural applied research grants and demonstration projects; educational activities	\$5.5	\$8.5	\$15.5
Ongoing and new State-based AR activities	EIP and ELC funding to increase State-level capacity for surveillance, prevention activities, and reference laboratory services	\$9	\$10	\$12
CDC Support for on-going and new AR	CDC funding for FTEs, laboratory supplies,	\$8	\$11	\$10

activities	laboratory equipment, and software			
Task Force Support	Antimicrobial Resistance meeting, conference planning, Antimicrobial Resistance Task Force, consultants' meetings	\$0.5	\$0.5	\$0.5
Total		\$30	\$40	\$50

Q4. Your testimony before the Committee cited the theoretical risk of the use of antibiotics in animal feed. You also stated that you supported further action to ensure judicious use of antibiotics. Do you consider the use of antibiotics in animal feed for growth promotion or feed efficiency a judicious use of antibiotics, given these risks to public health?

A. CDC believes that the use of antimicrobials should be limited to protecting human and animal health. Purposes other than for the advancement of animal or human health should not be considered judicious use.

Q5. You spoke in your testimony about the need to judiciously prescribe antibiotics for humans. All antibiotics for humans in this country are prescribed under the oversight of a physician. In your view, should antibiotics used for animals be under the oversight of a veterinarian?

A. Yes, the use of medications for the prevention, treatment, and control of disease in animals should be under the supervision of a veterinarian. CDC supports the WHO's principles on containment of antimicrobial resistance in animals intended for food. Veterinarian oversight is a key principle in the "WHO Global Principles for Containment of Antimicrobial Resistance in Animals intended for Food" which is available at

http://whqlibdoc.who.int/hq/2000/WHO_CDS_CSRAPH_2000.4.pdf

Q6. I understand that the CDC's National Nosocomial Infections Surveillance (NNIS) does not track infections in long term care facilities or ambulatory surgical centers.

Can you explain why that is? In your view, would it be useful for the system to encompass long term care facilities and ambulatory surgical centers?

A. CDC agrees that it would be useful to expand healthcare-associated infection (HAI) surveillance and prevention activities to non-hospital settings. The National Healthcare Safety Network (NHSN – formerly NNIS) is successfully used by healthcare facilities in all 50 states (with 21 states using NHSN to fulfill their public reporting mandates) to collect and use HAI data for prevention activities, determine which practices help prevent HAIs, and to share data with other facilities within a healthcare system and/or public health agencies for collaborative prevention activities. Participation in NHSN has grown significantly in the past few years. As of March 20, 2009, over half of the approximately 5,000 U.S. hospitals are enrolled in and utilizing NHSN. Some states are already using NHSN for HAI surveillance and prevention activities in non-hospital settings. In October 2008, Colorado used American Recovery and Reinvestment Act funds awarded by CDC to extend its NHSN reporting of HAIs from ambulatory surgical centers. Additionally, there are 122 long-term acute care facilities, 51 outpatient surgical centers, and 109 hemodialysis facilities enrolled in NHSN.

Nationally, there are about 26,000 non-hospital facilities, including ambulatory surgical centers, dialysis centers, and long term care facilities where complex procedures are increasingly performed. CDC does currently have surveillance in these settings, though only a small portion of these non-hospital facilities are enrolled in NHSN because we are still refining the best way to capture surveillance data and modifying surveillance definitions for use in these settings. Currently, CDC's long-term care work group is using and modifying existing long-term care infection surveillance definitions in order to decrease surveillance burden on facilities. The FY 2011 Budget included an increase of \$12.3 million for NHSN to support the expansion to 2,500 additional hospitals, and facilitate the implementation of prevention activities to achieve HHS HAI goals and targets.

Representative Jim Matheson

Q1. It is my understanding that in December 2007, the federal Interagency Task Force on Antimicrobial Resistance held a consultation in Atlanta bringing in 60 external consultants to help the task force revise the 2001 Action Plan on Antimicrobial Resistance. A draft revision was promised in 2008. We are now in 2010 and are waiting to see a product. a. Can you provide the committee with an update on the status of this action plan? Will this revised action plan contain benchmarks, as would be required by legislation that I introduced –the STAAR Act– to measure progress including for CDC, FDA and NIH? b. If no, then why not?

A. The *Action Plan* is currently under development and is expected to be released this year. This *Action Plan* includes benchmarks and timelines and will be made available for public comments upon release when it is published in the *Federal Register*. The *Action Plan* identifies four focused areas and each one has an agency coordinator and timeline:

- Surveillance: CDC is coordinating most action items
- Prevention and Control: CDC is coordinating most action items
- Research: NIH is coordinating most action items
- Product Development: FDA is coordinating most action items

CDC plans to regularly update the *Action Plan* with specific project and implementation steps at least every 2 years so that it becomes an even more informative and useful document.

Q2. In November of last year, President Obama, along with our European partners, announced the creation of a Transatlantic Task Force on Antibiotic Resistance to strengthen the antibiotic pipeline, develop interventions to address resistant infections in hospitals and communities, and opportunities to eliminate inappropriate uses in human and veterinary medicine. I am aware that it takes time to set up such an entity, but we are approaching 6 months from the announcement and I am not aware of word from the Administration on how this group is going to operate, what its charge will be, and whether it will include nongovernment experts. Including external experts to advise the government is a critical component of the Strategies to Address Antimicrobial Resistance (STAAR) Act, which I sponsored. a. What is the status of this international group and what is the charge of the transatlantic task force? b. Please provide the Committee with the list of participants, both domestic and international.

A. The Transatlantic Task Force on Antibiotic Resistance (Task Force) EU-US planning group has had a series of videoconferences and a kickoff meeting of the Task Force is scheduled for

June 2010. The Task Force will develop an action plan focused on the areas defined by the 2009 EU-US Summit declaration:

- Developing appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities
- Preventing both healthcare- and community-associated drug-resistant infections
- Developing strategies to improve the pipeline of new antimicrobial drugs

The Task Force is composed of experts and officials from the European Union and the United States. The United States is represented by the following individuals and agencies of the Department of Health and Human Services:

US Department of Health and Human Services (HHS), Office of the Secretary

Nils Daulaire, Director, Office of Global Health Affairs

Mary Lisa Madell, Director, Europe and Eurasia, Office of Global Health Affairs

Centers for Disease Control and Prevention (CDC)

Denise Cardo, Director, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases (proposed)

J. Todd Weber, CDC Liaison to the European Centre for Disease Prevention and Control, National Center for Immunization and Respiratory Diseases

Jean Patel, Deputy Director, Office of Antimicrobial Resistance

National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health

Dennis Dixon, Chief, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Disease

Jane Knisely, Scientific Program Analyst, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Disease

Food and Drug Administration

Edward Cox, Director, Office of Antimicrobial Products, CDER Drug Shortage Coordinator

Linda Tollefson, Director, FDA Europe Office

The European Union will be represented as follows:

European Commission (EC)

Andrzej Rye, Public Health Director, Directorate General Health and Consumers

Martinus Nagtzaam, Policy Officer, Directorate General Health and Consumers

Anna Lonroth Sjoden, Deputy Head of Unit, Directorate General Research, Health-Infectious Diseases

European Centre for Disease Prevention and Control (ECDC)

Dominique Monnet, Senior Expert and Programme Coordinator, Scientific Advice Unit

European Medicines Agency (EMA)

David Mackay, Head of Unit, Veterinary Medicines and Product Data Management

European Food Safety Authority (EFSA)

Marta Hugas, Scientific Coordinator, Head of Unit, Biological Hazard

Council of the European Union will be represented by the TRIO Presidency: Spain, Belgium, and Hungary

Jose Campos, Head of Unit, Antibiotic Laboratory, Instituto de Salud Carlos III

Nathalie Denecker, Clinical Assessor, Federal Agency for Medicines and Health Products

Karolina Borocz, Head of Department, National Centre for Epidemiology

Q3. In the STAAR Act, I have suggested a holistic approach to the problem of antibiotic resistance and establish a network of experts across the country to conduct regional monitoring of resistant organisms as they occur—which would be like a real time snapshot to pick up on problems early. Would you agree that there is importance in augmenting CDC’s current surveillance system with some sort of expert surveillance network system?

A: CDC thinks it is important that legislative provisions enhance and complement CDC’s existing surveillance systems, research and prevention efforts in order to avoid duplication of efforts. Surveillance is part of CDC’s core mission and CDC agrees surveillance of resistant organisms is important. CDC’s current surveillance system for antimicrobial resistance, the Emerging Infections Program (EIP), is a network of 10 state health departments working with collaborators in laboratories, healthcare facilities, and academic institutions to conduct population-based surveillance. Through this surveillance system, CDC provides national estimates of disease burden and tracks changes in disease burden over time for both resistant community-associated and healthcare-associated bacterial infections.

CDC also has other surveillance networks for bacterial resistance because surveillance strategies, goals and objectives vary for different problems: the National Healthcare Safety Network (NHSN) and the National Antimicrobial Resistance Monitoring System (NARMS). These surveillance systems complement EIP and are used to assess and monitor the scope, magnitude and trends of the antibiotic resistance problems and also to drive and direct prevention efforts, determine treatment recommendations, guide new drug development, and evaluate the effectiveness of prevention programs.

The National Healthcare Surveillance Network (NHSN) is a web-based surveillance tool for hospitals and state health departments to monitor healthcare-associated infection (HAI) rates, such as those caused by MRSA, *Clostridium difficile*, and multi-drug resistant gram-negative bacteria. Approximately half of U.S. hospitals (over 2,500) are currently enrolled in NHSN. The National Antimicrobial Resistance Monitoring System (NARMS) is a lab-based surveillance system between CDC, the Food and Drug Administration (FDA), the U.S. Department of Agriculture (USDA), and all 50 states. NARMS is used to detect resistance in enteric bacteria that are commonly transmitted from animals to humans through food, such as *Salmonella*, *Campylobacter*, and *E. coli* and monitors trends in the prevalence of resistance among bacteria isolated from humans, retail meats, and livestock.

CDC is taking steps to connect these systems including developing and launching networks of acute care facilities reporting HAI data through NHSN within the EIP, building an infrastructure to link pathogen-based evaluation, developing innovative surveillance methodologies, and translating surveillance data between population-based and hospital-based systems.

Q4. In your written testimony (p. 7) you reference that the VA reduced their rate of MRSA infections by 60% in part by implementing universal screening of all ICU and high-risk patients for MRSA (VA MRSA Initiative 2007). As part of the recommended test methods to identify patients colonized with resistant bacteria to prevent transmission, would CDC consider studying the effectiveness of rapid pre-surgical screening?

A. The subject of pre-surgical screening has been studied in the past and a recently published, well-conducted trial suggested that this may be an effective approach in select settings and for select surgical procedures (Bode LGM, Kluytmans JAJW, Wertheim HFL, et al. Preventing surgical site infections in nasal carriers of *Staphylococcus aureus*. *New England Journal of Medicine* 2010;362:9-17). CDC agrees that prevention research is needed to define the optimal strategy for using rapid pre-surgical screening, and we have much to offer in making sure such research is aligned with public health goals. CDC is currently providing technical assistance for a national survey of infectious disease physicians to assess the prevalence of pre-surgical *S. aureus* screening in the US.

CDC guidelines recommend that hospitals tailor their MRSA prevention strategies to their individual institution. CDC recommends that hospitals consider active surveillance as part of a comprehensive strategy to reduce MRSA infections if initial measures are not effective in reducing MRSA infections. CDC guidelines point out that the current science shows that active surveillance for MRSA might have an impact in reducing MRSA infections but only as part of a comprehensive strategy. What matters are the steps a hospital takes after it has identified colonized or infected patients and what subsequent prevention measure it uses. CDC guidelines recommend that hospitals achieve a reduction in MRSA using a comprehensive approach to prevention. For hospitals not showing a reduction using CDC's initial or first tier recommendations, CDC directs them to add additional measures, including screening of high risk patients for MRSA colonization, until success is demonstrated.

Q5. As you may know, The Infectious Diseases Society of America (IDSA) has urged the Administration and Congress to adopt the goal of developing 10 new antibiotics by 2020. Obviously, this is a large undertaking considering how few novel antibiotics there are currently in the pipeline. Has the Administration reviewed IDSA's 10 x '20 Initiative? What policies do you think this Committee should take into consideration to spur antibiotic development – especially for gram negative bacteria which has little, if anything in the pipeline?

[Please note that the response to this question was prepared by the National Institutes of Health, in response to the same question. We defer to NIH's expertise on this particular issue.]

The National Institute of Allergy and Infectious Diseases (NIAID), the lead component of the National Institutes of Health (NIH) for research on infectious diseases, is aware of the IDSA's initiative and supports its intent of bringing attention to the need for new antibiotic drug development. While there may be a number of policies that may provide incentives for the pharmaceutical and biotechnology industries to further engage in antibiotic drug development, the key to spurring antibiotic drug development is continued support of the drug development pipeline from the earliest stages through advanced development. NIAID recognizes the need to develop new antibiotic drugs and has a longstanding commitment to facilitate such development.

NIAID plays a critical role in the federal government's comprehensive efforts to combat the problem of antimicrobial resistance, with a particular emphasis on the issue of drug development. NIAID conducts and supports basic research to identify new antimicrobial targets and translational research to apply this information to the development of therapeutics; to advance the development of new and improved diagnostic tools for infections; and to create safe and effective vaccines to control infectious diseases and thereby limit the need for antimicrobial drugs. NIAID supports research and development of diverse products through a variety of mechanisms, including grants and contracts to academic laboratories, non-profit organizations, and small and large companies. Research and development of novel agents with activity against Gram-negative pathogens is being supported via all of these mechanisms.

Since 2002, NIAID has supported translational research efforts through its Challenge Grant/Partnerships Program, which was created to stimulate collaborative efforts and multidisciplinary approaches to rapidly advance promising candidate products for infectious diseases through the product development pathway. This program has uniquely fostered many new research collaborations between experts from different disciplines of academia and industry and has significantly accelerated the development of numerous new or improved countermeasures against many pathogens and toxins. Each year, the initiative targets different pathogens based on scientific needs and priorities, and selected Gram-negative pathogens have frequently been the focus of this program. Drug-resistant Gram-negative pathogens of concern were specifically targeted in the 2009 initiative.

To complement these collaborative research efforts, NIAID provides a broad array of pre-clinical and clinical research resources and services to researchers in academia and industry designed to facilitate the movement of a product from bench to bedside. By providing these critical services to the research community, NIAID can help to bridge gaps in the product development pipeline and lower the financial risks incurred by industry to develop novel antimicrobials. Importantly, development activities for several therapeutics with activity against Gram-negative bacteria are being carried out through these mechanisms.

Through an initiative initially introduced in 2007, NIAID has made a sustained effort to support clinical trials aimed at prolonging the effectiveness of currently available antibacterial drugs. The contracts awarded under this initiative support studies designed to help answer key questions about proper antimicrobial dose, treatment duration and whether antimicrobial treatment is necessary in all cases. The contracts provide for the design and conduct of Phase III and/or Phase IV clinical trials to test different therapeutic approaches and regimens that will reduce overexposure to antimicrobial drugs, thereby decreasing the likelihood of antimicrobial drug resistance and preserving the effectiveness of existing antimicrobials. For example, one of these clinical trials is focused on evaluating the optimal duration of therapy for urinary tract infections in children. Since urinary tract infections are caused primarily by Gram-negative organisms, the potential to decrease antibiotic use in this area would help to alleviate the selective pressure that drives the development of resistance in Gram-negative bacteria. This initiative will continue with new trials this year aimed at *pneumonia*, Gram-negative *bacteremia*, *acute otitis media* and *pulmonary tuberculosis*.

In late July, NIAID will co-sponsor, along with IDSA and FDA, a public workshop on antibiotic resistance. Topics for discussion will include an overview of the scale of the current bacterial resistance problem; the current understanding of the science and mechanisms of bacterial

resistance; the use of rapid diagnostics in diagnosis and management of bacterial infections; and the science of antibacterial drug development.

Representative Marsha Blackburn

Q1. On November 3rd of last year, President Obama, along with our European partners, announced the creation of a Transatlantic Task Force on Antibiotic Resistance [to strengthen the antibiotic pipeline, develop interventions to address resistant infections in hospitals and communities, and find opportunities to eliminate inappropriate uses in human and veterinary medicine]. Obviously, it takes time to set up such an entity, but now 6 months later, there has been no word from the Administration on how this group is going to operate, what its charge will be, and whether it will include non-government experts. Can you give us the status of this international group? Also, can you please provide the Committee with the list of participants, both domestic and international?

A. The Transatlantic Task Force on Antibiotic Resistance (Task Force) EU-US planning group has had a series of videoconferences and a kickoff meeting of the Task Force is scheduled for June 2010. The Task Force will develop an action plan focused on the areas defined by the 2009 EU-US Summit declaration:

- Developing appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities
- Preventing both healthcare- and community-associated drug-resistant infections
- Developing strategies to improve the pipeline of new antimicrobial drugs

The Task Force is composed of experts and officials from the European Union and the United States. The United States is represented by the following individuals and agencies of the Department of Health and Human Services:

US Department of Health and Human Services (HHS), Office of the Secretary

Nils Daulaire, Director, Office of Global Health Affairs

Mary Lisa Madell, Director, Europe and Eurasia, Office of Global Health Affairs

Centers for Disease Control and Prevention (CDC)

Denise Cardo, Director, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases (proposed)

J. Todd Weber, CDC Liaison to the European Centre for Disease Prevention and Control, National Center for Immunization and Respiratory Diseases

Jean Patel, Deputy Director, Office of Antimicrobial Resistance

National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health

Dennis Dixon, Chief, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Disease

Jane Knisely, Scientific Program Analyst, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Disease

Food and Drug Administration

Edward Cox, Director, Office of Antimicrobial Products, CDER Drug Shortage Coordinator

Linda Tollefson, Director, FDA Europe Office

The European Union will be represented as follows:

European Commission (EC)

Andrzej Rye, Public Health Director, Directorate General Health and Consumers
Martinue Nagtzaam, Policy Officer, Directorate General Health and Consumers
Anna Lonroth Sjoden, Deputy Head of Unit, Directorate General Research, Health-Infectious Diseases

European Centre for Disease Prevention and Control (ECDC)

Dominique Monnet, Senior Expert and Programme Coordinator, Scientific Advice Unit

European Medicines Agency (EMA)

David Mackay, Head of Unit, Veterinary Medicines and Product Data Management

European Food Safety Authority (EFSA)

Marta Hugas, Scientific Coordinator, Head of Unit, Biological Hazard

Council of the European Union will be represented by the TRIO Presidency: Spain, Belgium, and Hungary

Jose Campos, Head of Unit, Antibiotic Laboratory, Instituto de Salud Carlos III
Nathalie Denecker, Clinical Assessor, Federal Agency for Medicines and Health Products
Karolina Borocz, Head of Department, National Centre for Epidemiology

Q2. In its Fiscal Year 2011 Congressional Justification, CDC calls antimicrobial resistance “one of the world's most pressing public health problems.” However, within the Preparedness, Detection, and Control of Infectious Diseases program’s proposed budget, CDC’s already severely strapped Antimicrobial Resistance budget would be cut dramatically by \$8.6 million—just over 50 percent! The FY2011 budget would allow only 20 state/local health departments and health care systems to be funded for surveillance, prevention, and control of antimicrobial resistance, down from 48 this past year. Can you tell us which states will no longer receive funding under the Antimicrobial Resistance program at CDC?

A. The FY2011 budget request would allow 20 state/local health departments and health care systems to be funded for surveillance, prevention, and control of antimicrobial resistance. It is not possible at this time to determine which states would receive funding. Its possible that more state and local health departments could be funded through the \$ 19 .6 million increase in the emerging infections program.

Q3. Additionally, in the budget justification, CDC states that the number of states to receive funds under the Get Smart in the Community program will go from 12 to zero. Can you give us the rationale for your decision to cut back so drastically on this important program given the dire health implications of antimicrobial resistance?

A.. The program has contributed to a 25 percent reduction in antimicrobial use per outpatient visit for presumed viral infections. In addition, more than 959 campaign partners and 166 funded state-based programs collaborate with the Get Smart campaign. Given competing priorities, CDC is looking for ways to efficiently use funding and make difficult decisions based

on available funds. Activities will continue on a prioritized basis, as funding exists through the Emerging Infections program.

Q4. For the past 18 months or more, there has been no full-time director for the Antimicrobial Resistance program, since the departure of the most recent permanent director. What is the status of appointing a new director to oversee the Antimicrobial Resistance programs at CDC?

A. CDC's Director of the Office of Antimicrobial Resistance (OAR) retired in April 2010. An acting director has been appointed and will remain in place until CDC hires a new permanent director. CDC is conducting a national search for an individual who is a recognized leader in the field of infectious diseases and antimicrobial resistance.