

ANTIBIOTIC RESISTANCE AND THE THREAT TO PUBLIC HEALTH

HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED ELEVENTH CONGRESS SECOND SESSION

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ANTIBIOTIC RESISTANCE AND THE THREAT TO PUBLIC HEALTH

WEDNESDAY, APRIL 28, 2010

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 3:50 p.m., in Room 2123, Rayburn House Office Building, Hon. Frank Pallone, Jr., [chairman of the subcommittee] presiding.

Present: Representatives Pallone, Dingell (ex officio), Green, Capps, Schakowsky, Matheson, Christensen, Castor, Space, Waxman (ex officio), Whitfield, Shimkus, Blunt, Pitts, Burgess, and Blackburn.

Staff Present: Ruth Katz, Chief Public Health Counsel; Sarah Despres, Counsel; Rachel Sher, Counsel; Elana Stair, Policy Advisor; Katie Campbell, Professional Staff Member; Stephen Cha, Professional Staff Member; Virgil Miller, Professional Staff Member; Anne Morris, Professional Staff Member; Allison Corr, Special Assistant; Eric Flamm, FDA Detailee; Andre Bindman, Fellow; Clay Alspach, Minority Counsel, Health; Ryan Long, Minority Chief Counsel, Health; and Lyn Walker, Minority Coordinator, Admin/Human Resources.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. The hearing of the subcommittee is called to order.

Today we are having a hearing on antibiotic resistance and the threat to public health. And I will first recognize myself for an opening statement.

This is a very serious public health concern, and I know it is an issue of great interest to many Members of the House of Representatives. Antibiotics are among the most impactful medical innovations of the 20th century. When they were first discovered in the late 1920s, antibiotics became part of routine treatment to combat bacterial infections in the 1940s and were one of the main contributors in the decline of infectious diseases. Illnesses that had been widespread and often fatal prior to the development of antibiotics were suddenly curable with the administration of these new wonder drugs. In fact, the CDC lists control over infectious disease as one of their Top 10 Great Public Health Achievements of the last century and mentions antimicrobials as crucial to that accomplishment.

But bacteria, as we know, are living organisms, and as such, they can and will mutate with time to be able to resist the drugs that have been developed to combat them. And we now find ourselves in a situation where our triumph over infectious disease is in jeopardy.

More and more bacteria are proving to be resistant to the antibiotics currently on the market. Unfortunately, these resistant diseases are among the most predominant illnesses in the population, including respiratory diseases, such as pneumonia; food-related diseases, including E. Coli and salmonella; and hospital-acquired infections such as Methicillin-Resistant Staphylococcus Aureus, more commonly known as MRSA. And I should point out that MRSA in particular is now migrating out of the health care setting and can also be found in the community posing a new threat to Americans.

Newspapers across the Nation report on the danger and prevalence of these bacteria. In my State of New Jersey, we had a number of schools close a few years ago after children were diagnosed with MRSA. Some were even hospitalized for weeks. And I am sure everyone here remembers the scare we had not long ago in the House of Representatives when MRSA was found in the House staff gym.

The consequences of these antibiotic-resistant bacteria are dangerous, expensive, and at times deadly. In 2005, the CDC estimated that roughly 94,000 Americans contracted MRSA, and over 18,000 died as a result of that disease, including young and otherwise healthy patients.

And many in the medical community believe that MRSA might not be as big of a threat as some of the other antibiotic-resistant diseases, as fortunately there still are some drugs that can treat MRSA.

For other diseases, like Acinetobacter, there are very few options. As articles in the press have highlighted, Acinetobacter was of particular concern among the wounded troops in Iraq: 35 percent of those infections responded to only one antibiotic on the market today, and 4 percent were resistant to all of our current drugs. It is pretty horrifying to me to think that our soldiers could survive a war only to then succumb to a bacterial infection we are powerless to treat.

In treating these highly resistant infections, physicians often have to prescribe more expensive, older, and less commonly used antibiotics that can cause serious side effects, including nerve and kidney damage. Patients end up hospitalized for longer periods of time and often suffer recurring infections that send them back to the doctor time and time again. And not surprisingly, these illnesses tend to be very expensive, not to mention the threat that they pose to all who come in contact with these patients, and that is why this hearing is important today.

I am very eager to hear from our witnesses about the problems we experience with antibiotic-resistant bacteria, but also about the work that they are doing to address these problems. And I know that both of you are engaged in some very exciting research that will hopefully help us attack antibiotic resistance in the most effective way possible.

I want to welcome you both to the committee. I apologize for the fact that we had to start so late. I know that one or both of you mentioned catching a plane. I don't know what the situation is with that.

But for now, I will recognize our ranking member, Mr. Shimkus, for an opening statement.

OPENING STATEMENT OF HON. JOHN SHIMKUS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Mr. SHIMKUS. Thank you, Mr. Chairman.

Antimicrobial drugs are a life-saving tool when used correctly. We know that microbes, including bacteria, can quickly evolve and become resistant to drugs, and resistance is already a concern in our communities, particularly in the hospital setting, where numerous deaths occur each year as a result of a resistance.

I am glad we have a panel before us from the CDC and NIH here today to discuss the role the Federal Government has played, particularly with the U.S. Inter-Agency Task Force on Antibiotic Resistance. I look in order to the hearing more on the progress made and what we might expect from the task force's updated action plan expected to be released later this year.

I have always believed a crucial component in this fight is providing industry incentives and regulatory framework that encourages the development of more antimicrobial drugs. Many manufacturers have turned away from the R&D of new antimicrobials because of increase incentives to develop drugs in other therapeutic areas and the uncertainty of the marketplace.

As members of this committee, we should work hard to break down the barriers encouraging the marketplace incentives, like extended patent exclusivity for new antibiotics and new economic incentives, such as an R&D tax credit.

Unfortunately, I believe that the \$27 billion tax on the drug industry in the health reform law will have a negative effect and will only serve to stifle, not encourage more, development of antibiotic drugs. Perhaps that is not the case, but this is another example of why we must hold hearings on the new health reform law.

Last week I raised issues we already knew were problems: pre-existing conditions coverage for children; individuals who do not qualify for the new high-risk pools; families being forced into Medicaid; premiums going to rise on average of \$2,100 for those in the individual market; and being able to drop coverage and avoid penalties after 3 months and 1 day.

And this week we already have new questions. The majority repeatedly said health care spending will decrease. The President even pledged to the American people costs would go down, not up, as a result of health reform.

Yet CMS released a report by actuary Richard Foster last week saying national health care expenditures will increase by \$311 billion, making health care 21 percent of the GDP.

Should we believe the CMS actuary expert or the majority and their bill, now law? Are the \$575.1 billion in cuts in Medicare unrealistic and unsustainable as the report claims? Will the cuts drive 15 percent of hospitals in the red and force them to close their

doors? How would this jeopardize access to care for seniors? What does the hospital community say about this?

Are 50 percent of seniors really going to lose their Medicare Advantage plans? Can 14 million low-wage working Americans have their employer insurance dropped, forcing them into Medicaid? How will the State Medicaid plans handle these new populations and costs?

These are the questions being raised and the real concerns and fears coming from the public. This committee and this Congress cannot just bury our heads in the sand and pretend these problems don't exist in this massive health reform law.

Chairman Pallone, I asked before and I hope we—and Chairman Waxman is here—I hope we have hearings on the implementation of this law and address some of these problems that we should start moving to fix before they actually become problems. And I have identified quite a few of them.

And with that, Mr. Chairman, I yield back my time.

[The prepared statement of Mr. Shimkus follows:]

John Shimkus
Ranking Member
Subcommittee on Health
Hearing on Antibiotic Resistance
April 28, 2010

- Antimicrobial drugs are effective, often lifesaving tool when used correctly.
- We know that microbes, including bacteria, can quickly evolve and become resistant to drugs.
- This is already a concern in our communities particularly in the hospital setting where numerous deaths occur each year as a result of a resistance.
- I'm glad we have CDC and NIH here today to discuss the role the federal government has played particularly with the U.S. Interagency Task Force on Antibiotic Resistance.
- I look forward to hearing more on progress made and what we might expect from the task forces updated "action plan" expected to be released later this year.
- I've always believed a crucial component in this fight is providing industry the incentives and regulatory frame work that encourages the development of more antimicrobial drugs.
- Many manufacturers have turned away from R&D of new antimicrobials because of increased incentives to develop drugs in other therapeutic areas and the uncertainty of the antimicrobial marketplace.
- As members of this committee we should work to break down barriers and encouraging marketplace incentives, like extended patent exclusivity or priority review vouchers to economic incentives, such as an R&D tax credit.
- Unfortunately, I believe the \$27 billion tax on the drug industry in the health reform law will have a negative effect and only serve to stifle, not encourage more development of antibiotic drugs.
- Perhaps this isn't the case. But this is another example of why we must hold hearings on this health reform law.
- Last week I raised issues we already knew were problems.
 - Pre-existing condition coverage for children.
 - Individuals who won't qualifying for the new high risk pools.
 - Families being forced into Medicaid.
 - Premiums going to rise on average of \$2100 for those in the individual market.
 - And being able to drop coverage and avoid penalties after 3 months and 1 day.
- And this week we already have new questions.

- Is CRS correct that newly elected Members and their staff will not have FEHBP available to them? What will they do for insurance?
- The majority repeatedly said health care spending would decrease. The President even pledged to the American people costs would go down, not up, as a result of health reform.
- Yet, CMS released a report by actuary Rick Foster's last week saying national health care expenditures will increase by \$311 billion making health care 21% of GDP.
- Should we believe the CMS actuary expert or the President and the Democrat majority?
- Are the \$575.1 billion in cuts to Medicare unrealistic and unsustainable as the report claims?
- Will the cuts drive 15% of hospitals in the red and force them to close their doors?
 - How would this jeopardize access to care for seniors?
 - What does the hospital community say about this?
- Are 50% of Seniors really going to lose their Medicare Advantage Plans?
- Can 14 million low wage working Americans have their employer insurance dropped forcing them into Medicaid?
 - How will the state Medicaid plans handle these new populations and costs?
- These are the questions being raised and the real concerns and fears coming from the public.
- This committee and this Congress cannot just bury our heads in the sand and pretend problems don't exist in this massive health reform law.
- Chairman Pallone, I want to work with you to hold hearings so we can start to sift out concerns and address what is real.
- Mr. Chairman, will you commit to holding hearings on the health reform legislation?

Mr. PALLONE. Thank you.

Chairman Waxman is recognized for an opening statement.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you very much Mr. Chairman.

We need to debate the health care bill and review its implementation. But we ought to be able to chew gum and walk at the same time. Because it is not going to make much difference if you have health insurance or not if you are going to die from something that could have been prevented from an antibiotic.

And we are seeing more and more antibiotic resistance. The revolution of antibiotics starting with penicillin in 1927 has been a major accomplishment in the health care world and has led to many people surviving things that in the past might have cost them their lives. Before we had antibiotics, common skin infections could turn fatal; child birth could be a death sentence for both mother and baby; and superficial wounds could deteriorate rapidly, often resulting in amputation.

Antibiotics changed all of that, and with the discovery of these medicines, doctors could regularly treat infections and literally save lives. The modern age of medicine was launched.

Some 80 years later, this medical miracle is still saving lives, and without antibiotics, many of today's cancer protocols would be nearly impossible to use because the immune system, when it becomes compromised by the treatments, would quickly leave people to die from opportunistic infections without antibiotics.

So, in brief, we cannot do 21st century medicine without antibiotics, whether you like the provisions of the health care bill or not. We need to have antibiotics available, and shockingly, experts, which I understand is supposed to be the reason for this hearing, are telling us that we are on the precipice of losing the power of many of today's antibiotics. As a greater number of bacteria become more resistant to them for reasons that we will explore this afternoon, antibiotics in turn become less effective, making infections far more hazardous to health.

This is not an exaggeration or hyperbole or even the stuff of some hypothetical computer model. This is not propaganda, which we hear a lot about in these committee sessions when people are campaigning for the November election and not looking at the issues that we have to deal with. Too many Americans have already succumbed to our inability to treat infections, and the numbers are staggering.

Today we will learn about the impact of antibiotic resistance on human health from two of the Nation's leading experts on infectious diseases: Dr. Tom Frieden, director of the Centers for Disease Control and Prevention; and Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases at NIH.

As we do, I hope we can start to understand and appreciate the severity of the problem that we face and together work toward a public-private plan of attack. I don't know what we need to do. Obviously, research. That is our default and most important answer to any problem like this. But it is going to take a strong multi-

faceted yet coordinated strategy to get the job done. I think we have to think about things that have not been on the agenda for a while because of the pressure from some of the special interests.

What is the impact of using antibiotics without a medical need when it is applied to large numbers of animals? Is this resulting in more drug-resistant antibiotics? What will it take to get the pharmaceutical companies to do more work in this area? I met with a group yesterday who told me they need this, they need that, and they need the other thing, but they don't want to work on the antibiotics because it is not profitable enough. Well, let's look at that problem.

Let's look at whatever it is going to take and keep our eye on the objective. We cannot afford to live in a world where antibiotics don't work anymore. And I think the numbers are just so staggering: 90,000 Americans die each year of deadly hospital-acquired infections, which are predominantly caused by antibiotic resistant bugs. Over 18,000 Americans, including healthy young people, die annually from Methicillin-Resistant *Staphylococcus Aureus*, known as MRSA. We have seen soldiers defeat deadly enemies in Iraq only to return home with an epidemic of deadly antibiotic-resistant *Acinetobacter*.

And we need more hearings so we can say these words correctly, because these are infections that we want to stop with antibiotics.

Thank you very much, Mr. Chairman. I look forward to the testimony.

[The prepared statement of Mr. Waxman follows:]

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ONE HUNDRED ELEVENTH CONGRESS

Congress of the United States House of Representatives

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Opening Statement of Rep. Henry A. Waxman Chairman, Committee on Energy and Commerce Antibiotic Resistance and the Threat to Public Health Subcommittee on Health April 28, 2010

Mr. Chairman, thank you for holding this hearing on one of the most pressing public health issues we face today – the rising tide of antibiotic resistance.

From hospitals at home to battlefields in Iraq and Afghanistan, Americans are more vulnerable than ever to infection because of the growing resistance to critical antibiotics.

Antibiotics irrevocably changed public health for the better.

From the discovery of penicillin in 1927 by Dr. Alexander Fleming, antibiotics forged a revolution in public health.

Before we had antibiotics, common skin infections could turn fatal. Childbirth could be a death sentence for both mother and baby. And a superficial wound could deteriorate rapidly, often resulting in amputation.

Antibiotics changed all that. With the discovery of these medicines, doctors could readily treat infection and literally, save lives. The modern age of medicine was launched.

Some 80 years later, this medical miracle is still saving lives. Without antibiotics, many of today's cancer protocols would be nearly impossible to use – patients whose immune systems are severely compromised by the treatments would quickly die from opportunistic infections without these medications. Tuberculosis and other respiratory infections would be killing young and old alike. And surgeries that are now commonplace – procedures such as hip replacements or angioplasty – would be much more dangerous because of the possibility of the development of an untreatable infection. In brief, we cannot do 21st century medicine without antibiotics as an effective component within our collective medical toolkit.

Shockingly, experts tell us we are on the precipice of losing the power of many of today's antibiotics. As greater numbers of bacteria become more resistant to them – for reasons we will explore this afternoon – antibiotics, in turn, become less effective, making infection far more hazardous to health. Indeed, public health officials are increasingly warning that the escalation in antibiotic resistance is threatening to return us to the days before Dr. Fleming's discovery.

This is not exaggeration or hyperbole – or even the stuff of some hypothetical computer model. Too many Americans have already succumbed to our inability to treat infections. The numbers are staggering:

- Over 90,000 Americans die each year of deadly hospital-acquired infections, which are predominantly caused by antibiotic resistant bugs.
- Over 18,000 Americans, including healthy young people, die annually of methicillin-resistant staphylococcus aureus, also known as MRSA.
- We've seen soldiers defeat deadly enemies in Iraq, only to return home with an epidemic of deadly antibiotic-resistant acinetobacter, an infection that is extraordinarily difficult to remedy.

Today, we will learn about the impact of antibiotic resistance on human health from two of the nation's leading experts on infectious diseases: Dr. Tom Frieden, Director of the Centers for Disease Control and Prevention, and Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases at NIH.

As we do, I hope we can start to understand and appreciate the severity of the problem we face and together, work toward a public-private plan of attack. Because the status quo simply cannot be an option. To accept that as our standard of care would risk setting American medicine back to a time long gone. Instead, it will take a strong, multi-faceted, yet coordinated strategy to get the job done. I hope today's hearing will begin to set us on that path.

I consider this to be one of the most important public health issues we confront today.

I thank the witnesses for coming today and look forward to their testimony.

Mr. PALLONE. Thank you, Chairman Waxman.
The gentleman from Kentucky, Mr. Whitfield.

OPENING STATEMENT OF HON. ED WHITFIELD, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF KENTUCKY

Mr. WHITFIELD. Mr. Chairman, thank you very much.

We look forward to this very important hearing and certainly appreciate our two witnesses being here today.

I would, however, like to reiterate the importance and necessity, in my view, of holding hearings regarding the implementation of this massive and far-reaching change to our health delivery system.

As Chairman Waxman noted about hospital infections, according to the Centers for Disease Control and Prevention, 2 million people acquire bacterial infections in hospitals each year. And of that, around 90,000 people die because of these infections. And according to the information given to me, 70 percent of the hospital-acquired infections are caused by bacteria that are resistant to at least one of the drugs most commonly used to treat them.

I also do believe that we must explore incentives and other options to encourage pharmaceutical companies to continue their research and coming up with new medicines to deal with this problem. I look forward to the testimony of our witnesses today, and yield back the balance of my time.

Mr. PALLONE. Thank you.

The gentlewoman from the Virgin Islands, Mrs. Christensen.

OPENING STATEMENT OF HON. DONNA M. CHRISTENSEN, A REPRESENTATIVE IN CONGRESS FROM THE VIRGIN ISLANDS

Mrs. CHRISTENSEN. Thank you, Chairman Pallone.

And thank you, Dr. Fauci and Dr. Frieden, for being here, and it is good to see you again.

The hard facts and data about the prevalence of antimicrobial resistance are nothing short of astounding. Because of repeated and widespread improper antibiotic use, almost every type of bacteria has become stronger and less responsive to antibiotic treatment. Between 5 and 10 percent of all hospital patients—that is roughly 2 million people—will develop an infection, and 90,000 of these patients die. This trend is related to the fact that more than 70 percent of bacteria that cause these infections are resistant to at least one of the antibiotics that is most commonly used to treat them.

Though the full economic impact is difficult to determine, the estimated costs are somewhere in the vicinity of \$5 billion a year. What is so disturbing is that because of this resistance, we are facing the prospect of reverting to times in health care where we are only able to offer a hand to hold. Not only may antibiotics be priced out of reach, but we may see cases where there are none that are effective in a given infection, and that is unacceptable.

As a physician, I know the pressures that we are always under to prescribe antibiotics. I made it a point not to use them unless I thought they were indicated, either for my patients or my family. And I thank GW and Howard for that.

As I see it, the resistance horse is out of the barn. The only way to contain it is to fence it in by the National Institute developing the vaccines, as they did with Pneumococcus, which had as one of its goals the spurring the development of new antibiotics, and by the CDC campaigns that are directed at providers, including hospitals and the public, especially including the public.

None are easy but have to become a priority because this country and the world cannot revert to the dark days of medicine.

Thank you, Chairman Pallone and Ranking Member Shimkus, for holding this hearing.

Dr. Fauci and Dr. Frieden, I look forward to your testimony.

I yield back.

Mr. PALLONE. The gentleman from Pennsylvania, Mr. Pitts.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. PITTS. Thank you, Mr. Chairman.

Antimicrobial drugs have saved countless lives over the last half century and enhanced the quality of life for many more people. Unfortunately, we are observing a growing amount of bacterial resistance to antibiotics, and many infectious disease are becoming increasingly difficult to treat as a result.

There are multiple reasons for microbes becoming drug-resistant, including inappropriate use by physicians, inadequate diagnostics, hospital use, and agricultural use. I was pleased to see that in the majority's memo for this hearing they noted that, "The National Institute of Allergy and Infectious Diseases acknowledges there is debate about the public health impact," of antimicrobial use in animal agriculture, particularly in animal feed.

Because I believe that the legitimate and the judicious use of antibiotics in animal agriculture has been unfairly attacked and demonized in recent years. FDA puts these drugs through a rigorous approval process with many newer antibiotics having been extensively reviewed specifically to assess any risk to humans as a result of drug resistance. Treatment, prevention, control and growth promotion, feed efficiency are all FDA-approved uses for antibiotics. FDA also conducts post-approval monitoring, and multiple public and private surveillance systems monitor for any sign of antibiotic resistance.

While every possible cause of antibiotic resistance should be studied and explored, I would hope that this series of hearings would focus more on areas where the science has told us there is cause for concern, and that is not the antibiotic use in animals.

I look forward to hearing from our witnesses, and I thank you, Mr. Chairman, for scheduling this hearing.

Mr. PALLONE. Thank you.

Chairman Dingell?

Mr. DINGELL. Mr. Chairman, I thank you.

I have a splendid statement. I know that everybody will benefit by reading it. I ask unanimous consent to insert it into the record.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Dingell follows:]

**Statement of
The Honorable John D. Dingell
Subcommittee on Health Hearing on
“Antibiotic Resistance”
April 26, 2010**

Mr. Chairman, thank you for holding today’s important hearing. Alexander Flemming’s discovery of Penicillin in 1928 was one of modern medicine’s greatest achievements. However, over time antibiotic resistance has increased dramatically, and now many bacterial infections are resistant to the most commonly prescribed antibiotic treatments. This poses a very real public health threat to our country.

If we do not seriously begin addressing this issue, we could be headed for a world in which antibiotic resistance is so bad that we have very few interventions for infections. This problem may sound like something out of a science fiction novel, but even now there are strains of VRE that have become resistant to medicines of last resort. Across the globe there has been a resurgence of malaria and tuberculosis because the new strains are multidrug resistant.

I am grateful for our two witnesses – Dr. Thomas Frieden, director of the Centers for Disease Control and Prevention and Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases – have joined us today. It is my hope that we can learn more about this issue so that we have a better idea how we can all collectively respond.

Successfully addressing antibiotic resistance will require a multifaceted approach. First, we must work to prevent infectious diseases that require antibiotic treatments. We have made great strides in the area of vaccinations that do just that. We must also continue to work with our partners at the Department of Health and Human Services and hospitals across the country to prevent the spread of healthcare-associated infections. I am pleased that the President's budget makes a real commitment to reduce these HAIs. I am also proud of the work currently being done by the Michigan Health & Hospital Association through the Michigan Keystone ICU Project. This project, by working to ensure clinicians used a simple checklist when inserting catheters into ICU patients, helped dramatically reduce the number of health care associated infections in Michigan, saving over 1,500 lives and \$200 million.

Second, we must educate physicians, healthcare practitioners and patients on how to become better stewards of antibiotic use. I am pleased with CDC's educational campaign, Get Smart: Know When Antibiotics Work. This type of public and private partnership is crucial to changing the culture around appropriate antibiotic use.

Finally, we must create incentives that lead to the development of new antibiotics and antimicrobial drugs. In Dr. Fauci's written statement, he describes the market failures that have lead to a decrease of new antibiotic developments. We must find ways to fix these market imbalances and spur the pipeline of antimicrobial drugs that can address resistant strains of infections and diseases.

Again, I want to thank the witnesses for joining us today. I hope that your testimonies and the question and answer period will serve as a guide for how we respond to this growing crisis.

Thank you, I yield back the balance of my time.

Mr. PALLONE. Without objection, so ordered.

The gentleman from Texas, Mr. Burgess.

Mr. BURGESS. Thank you, Mr. Chairman.

And due to the high-octane witnesses we have, I am going to waive an opening statement and submit for the record and reserve time for questions.

[The prepared statement of Mr. Burgess was unavailable at the time of printing.]

Mr. PALLONE. Without objection, so ordered.

Did you have a statement? Oh, submit it for the record.

Let me just say all statements will be submitted for the record. Thank you.

The gentlewoman from Illinois, Ms. Schakowsky.

Ms. SCHAKOWSKY. I will put my full statement in the record, but I do have a couple of comments.

In my home State, the Illinois Department of Health has stated that in just 4 years, the incidence of MRSA has increased 57 percent to over 10,000 cases. As we are going to hear from the CDC and the National Institutes of Allergy and Infectious Diseases, antibiotics become less effective as humans are increasingly and often unnecessarily exposed to them. This can happen when they are overprescribed.

But it also happens through other types of exposure. It is for this reason I find the rampant use of antibiotics for nontherapeutic purposes in livestock populations alarming. Many factory farms give cows, chickens, and pigs antibiotics in their daily feed. They are not treating any known diseases. They are promoting growth and compensating for bad sanitation. When antibiotics are used in livestock populations, it gets into our food systems and into our water supply. Using highly potent medications for this type of use continues to contribute to the increasing prevalence of antibiotic-resistant infections.

I applaud by good friend, Representative Louise Slaughter, for introducing, The Preservation of Antibiotics for Medical Treatment Act, which would take needed steps to protect the effectiveness of antibiotics. I am a cosponsor of this legislation.

And I look forward to Dr. Frieden's and Dr. Fauci's testimony on this issue.

I hope you will address this as well.

And I yield back. Thank you.

[The prepared statement of Ms. Schakowsky was unavailable at the time of printing.]

Mr. PALLONE. Thank you.

The gentlewoman from Tennessee, Mrs. Blackburn.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mrs. BLACKBURN. Thank you, Mr. Chairman.

And Dr. Frieden and Dr. Fauci, thank you for being with us today.

I will have to say that this is a hearing that I have waited a long time for us to have.

I first wrote you, Mr. Chairman, in October 2007 with my concerns about MRSA and the fact that we needed to look into this. I find it astounding, when you look the at 2005 stats, that there are more people that die from MRSA-caused infections than those that die from AIDS, Parkinson's, emphysema, or homicide each year. And I do think that this is something that has to be addressed.

I was surprised, as I looked at the issue first in 2007, to find out from our Tennessee Department of Health that there is not a national standard on a way to report MRSA issues. And that is of concern to me. It is something that I want to address with both of you as we move through the hearing.

I do have a full statement that I want to submit for the record, but I thank you for the hearing and look forward to our witnesses.

[The prepared statement of Mrs. Blackburn follows:]

Congressman Marsha Blackburn
Opening Statement for Energy and Commerce
Health Subcommittee Hearing
"Antibiotic Resistance and the
Threat to Human Health"
April 28, 2010

Mr. Chairman, about two and a half years ago, the CDC released a study that established the first national baseline to assess future trends of drug-resistant staph infections commonly known as MRSA (methicillin-resistant *Staphylococcus aureus*), in our nation's communities. The study focused on MRSA cases from nine communities around the country, including Davidson County, Tennessee.

At the time, the CDC reported that MRSA caused more than 94,000 life-threatening infections and nearly 19,000 deaths in the United States in 2005. According to these statistics, MRSA causes more deaths than AIDS, Parkinson's disease, emphysema or homicide each year.

Unfortunately, while MRSA remains the most common source of hospital infections, the incidence of antibiotic resistant infections is increasing worldwide. The CDC estimates that roughly 1.7 million hospital-associated infections cause or contribute to almost 100,000 deaths per year. Surprisingly, the Tennessee Department of Health reports that no national standard exists on the most meaningful way to report rates of resistant organism, such as MRSA, by individual healthcare facilities.

A looming public health crisis is staring us in the face – rising incidence of drug-resistant bacteria and stagnant research and development of new therapies to treat these infections. It is

alarming that medical professionals have very few resources to treat infected patients, as demand far outpaces supply of antimicrobials. While prevention is key, not every infection is preventable.

I am concerned that only a small number of private companies are investing research and development funds into new antimicrobials. It is difficult to hit a moving target - as antimicrobial pathogens constantly mutate - and it makes economic sense for companies to invest in the development of long-term therapies for prevalent diseases as opposed to new antimicrobial drugs.

Congress should focus on potential solutions to align private-sector investment in antimicrobials with incentives to do so. Incentives will go a long way to increase the supply chain of antimicrobial drugs, and more importantly – save lives.

Mr. PALLONE. And the full statement will be entered into the record. Thank you.

Our vice chair Ms. Capps, the gentlewoman from California.

OPENING STATEMENT OF HON. LOIS CAPPS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mrs. CAPPS. Thank you, Mr. Chairman, I will be very brief.

But I thank you for holding the hearing and thank our witnesses for coming today and for their testimony.

I have to give a special thanks to Dr. Fauci, who gave a stirring commencement speech for someone named Amy Fisher, who is now my medical health specialist on my staff. So you must have said just the right things when she graduated from Emory. Thank you very much.

This issue of antibiotic resistance is of extreme importance to both the health and the economic well-being of all Americans. Resistant strains of bacteria are harder to treat, often requiring longer and more difficult courses of treatment. And the longer an individual must spend fighting an illness, the greater the loss of valuable time at work and at home with families.

But there is also an economic consequence to the Nation as a whole. These infections cost the health care system, through extended hospital stays, more expensive treatments, nearly \$5 billion in annual costs associated with hospital-acquired infections.

For many years, we have taken for granted that when we are sick, we can go to our doctor, take a week's worth of medicine, and be well again. But now we must face the fact that we need a more comprehensive approach to treating bacterial infection. Perhaps more concerning is that there are a broad range of potential causes for the antibiotic resistance that affects us today: Individual factors, like when and what medicines a doctor prescribes and how well a patient adheres to treatment, combined with health-care-associated infections, agricultural antibiotic use, and a lack of new antibiotic treatments, all of these have contributed to the current state of antibiotic resistance.

I look forward to our witnesses' thoughts on how to employ evidence-based strategies to combat antibiotic resistance and the multiple factors that contribute to it in a coordinated approach. Thank you for being here, and I yield back.

Mr. PALLONE. Thank you.

Next, the gentleman from Utah, Mr. Matheson.

OPENING STATEMENT OF HON. JIM MATHESON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF UTAH

Mr. MATHESON. Thank you, Mr. Chairman.

I have a full statement I will submit for the record, but I will make just one brief comment.

I just want to point out that on this important issue, I have once again reintroduced in this Congress H.R. 2400, the Strategies to Address Antimicrobial Resistance Act, or the STAAR Act. I believe this is a comprehensive piece of legislation to strengthen our country's response to pathogens that are increasingly becoming resistant to antibiotics.

Senators Sherrod Brown and Orrin Hatch will be introducing a companion bill in the Senate in the coming weeks. I encourage this hearing and others to move forward to, and I hope that piece of legislation, the STAAR Act, can contribute to this debate and offer opportunities for us to make progress.

And with that, I yield back.

[The prepared statement of Mr. Matheson follows:]

Opening Statement

Rep Jim Matheson (UT-02)

April 28, 2010

Thank you, Chairman Pallone for holding this hearing today. Thank you to the panel of expert witnesses for their insight into this important issue and their participation in today's hearing. I also want to thank Chairman Waxman for his commitment to these issues.

As you are aware, I have reintroduced legislation this Congress –HR 2400-The Strategies to Address Antimicrobial Resistance Act, which I believe is a comprehensive piece of legislation to strengthen our nation's response to pathogens that are increasingly becoming resistant to antibiotics. Senators Sherrod Brown and Orrin Hatch will introduce the companion bill in the coming weeks.

My legislation, the STAAR Act, provides a comprehensive approach to the antimicrobial resistance crisis and is supported by a broad range of health groups. H.R. 2400 provides strategies and authorizes critically needed funding to strengthen federal antimicrobial resistance surveillance, prevention and control, and research efforts. It also strengthens coordination within Department of Health and Human Services agencies as well as across other federal departments that are important to addressing antimicrobial resistance, and considers opportunities to address this issue globally. The STAAR Act provides a rare opportunity to bring multiple partners together to protect public health from antimicrobial-resistant bad bugs. This legislation, developed with input from infectious diseases experts and leaders in public health, provides authority for the federal government to combat antimicrobial resistance by:

- 1) Reauthorizing the Antimicrobial Resistance Task Force, establishing an Advisory Board of outside experts and an Antimicrobial Resistance Office reporting to the Secretary of Health and Human Services whose director will coordinate government efforts to combat antimicrobial resistance;

- 2) Creating an antimicrobial resistance strategic research plan, as well as establish the Antimicrobial Resistance Surveillance and Research Network;
- 3) Collecting available and relevant data to allow government to better assess the antimicrobial resistance problem; and
- 4) Establishing demonstration projects to encourage more appropriate use of existing antibiotics.

Mr. Chairman, as you are aware, our Committee has had a critical role in establishing the foundation for work on this issue. Our Chairman Emeritus Mr Dingell requested a report on the impact of antibiotic resistant bacteria in the 103th Congress. In the 106th Congress, Chairman Stupak introduced legislation to direct the Secretary of Health and Human Services to establish the Antimicrobial Resistance Task Force. In the 107th Congress, several members of this Committee joined Senator Sherrod Brown, then a Representative, to introduce legislation to provide funding for the top priority action items of the public health action plan.

Mr. Chairman, I provide a brief snapshot of this history for my colleagues to show that while some work has been accomplished, the war against resistance infections looms large for our nation's public health. And to be clear for my colleagues on both sides of the aisle, this is a public health emergency that in the year 2007 alone infected more than 94,000 people, kills nearly 19,000 annually, and is estimated to have cost our health care system millions of dollars.

Physicians, hospitals, researchers, and patients are becoming increasingly frustrated by the rise in life-threatening drug-resistant infections but also on the toll on the availability of antibiotics to treat these mutating bacteria. This is our opportunity to develop effective strategies and interventions to limit the emergence of resistance. Our committee needs to focus on strengthening our antimicrobial pipeline, improving our country's coordination to better monitor,

treat, and most important prevent the transmission of drug resistant microbes. I believe the STAAR Act provides that appropriate, balanced set of measures to achieve these goals. I urge the Committee to move this legislation and continue our Committee's legacy of important work in this arena.

Thank you.

Mr. PALLONE. Thank you.
The gentleman from Ohio, Mr. Space.

**OPENING STATEMENT OF HON. ZACHARY T. SPACE, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF OHIO**

Mr. SPACE. Thank you, Mr. Chairman, for holding this hearing.
I would like to thank the witnesses for their attendance today.

I think we have all as a Nation kind of taken it for granted that antibiotics were there. And certainly, as a parent, I have not thought much about the consequences if they hadn't been there.

And it is a little unnerving now to see that, in combating some forms of bacteria, we can now say that antibiotics are less effective. In the words of Chairman Waxman, that this would be a very frightening world if it was a world without antibiotics, ring true.

I am pleased that the CDC and FDA and other agencies have begun to take some basic steps to combat the problem. I think public awareness is certainly a big part of it. I think this Congress and other agencies have an obligation to advance research into the issue.

My only hope is that if this Congress this term decides to take legislative action, that we do so with a sense of moderation, to the extent that that can be done. The concern always is that we may be overreaching. I certainly don't want to see that.

So researching and developing a solution to this problem is very important, but ensuring access to antibiotics for all Americans is equally important during the process.

With that, Mr. Chairman, I yield back.

Mr. PALLONE. Thank you.

The gentlewoman from Florida, Ms. Castor.

**OPENING STATEMENT OF HON. KATHY CASTOR, A REP-
RESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA**

Ms. CASTOR. Thank you, Mr. Chairman, for holding this afternoon's hearing on human resistance to antibiotic drugs.

Welcome to our witnesses.

This is a critical and rather frightening issue that we must work to resolve. Particularly the findings of the recently released Agency for Health Care Research and Quality Report are alarming. Post-operative blood infections increased by 8 percent. Catheter-related urinary tract infections increased by 3.6 percent. There are more statistics like that, and the numbers should be going down, not up.

I thought it was also disturbing that the report found that Blacks, Hispanics, Asians, and Native American patients were less likely than whites to receive preventative antibiotics before surgery in a timely manner. So we still have those disparities in health care. And all of these infections cause nearly 100,000 deaths each year and account for up to \$26 billion a year in additional costs.

Many of these infections are resistant to some of the strongest antibiotics, causing some patients to be in the hospital for weeks or months. In Florida, drug-resistant MRSA infections are growing and are infecting healthy adults and children. The number of cases in Florida from outpatient facilities increased more than four times in the 3-year period from 2003 to 2005.

Drug-resistant gram-negative infections, different from MRSA, are also on the rise. These infections are primarily acquired in hospitals or long-term care settings. They have a high death rate and are resistant to antibiotics usually known as the last line of defense.

According to the CDC, the antimicrobial resistance problem is a major looming public health crisis. Researchers that I have heard from have highlighted to me the lack of resources coming from NIH for this particular issue. They have highlighted the lack of resources on the State level to detect, monitor, and control antimicrobial resistance in public health laboratories. Other States do not have the technical capability to detect and categorize resistance patterns quickly.

So, gentlemen, you have your work cut out for you. We need your help in tackling this crisis. I look forward to your testimony.

Thank you, Mr. Chairman.

Mr. PALLONE. Thank you.

I think everyone has had a chance to give an opening statement, so we will now turn to our panel.

We have our two witnesses today. I want to welcome you. Let me introduce, on my left, Dr. Thomas R. Frieden, who is director of the Centers for Disease Control and Prevention; and to my right is Dr. Anthony S. Fauci, who is director of the National Institutes of Allergy and Infectious Diseases.

Thank you for being with us today. Sorry, again, you had to wait. You know that we have 5-minute opening statements that are made part of the record, and you can submit additional statements or comments after, and we may also follow up with some written questions.

STATEMENTS OF THOMAS FRIEDEN, M.D., M.P.H., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. PALLONE. So we will start with Dr. Frieden.

Thank you.

STATEMENT OF THOMAS FRIEDEN, M.D., M.P.H.

Dr. FRIEDEN. Thank you, Chairman Pallone, Chairman Emeritus Dingell, Ranking Member Shimkus and members of the subcommittee for your interest in this topic and for holding this hearing.

As an infectious disease physician myself and having worked as a tuberculosis control officer, health commissioner for more than 20 years I have seen the growing problem of drug resistance and also the potential to prevent and reverse drug resistance with effective public health action.

I appreciate the opportunity to speak with you today about the public health threat of antibiotic resistance and the role that CDC plays in preventing, detecting, better understanding, and responding to the problem.

I would like to share several slides to illustrate the problem. The first one shows the increase in drug resistance in two different organisms, *Staphylococcus aureus*, resistant to penicillin. Something that emerged almost immediately after penicillin became available. Early on, tiny doses of penicillin were able to cure severe infections with *Staph aureus*. Those resistant organisms first emerged in the hospital and then, after a gap of a decade or so, in the community.

That same pattern has existed with MRSA, Methicillin-Resistant *Staph Aureus*, which first emerged in hospitals in the late 1970s, early 1980s, and over the past decade, we have seen increasingly in the community.

Antibiotic resistance is an increasing public health problem. Resistance occurs virtually wherever antibiotics are used. Many bacteria become resistant to more than one class or type of antibiotics, and doctors and nurses are now all too often faced with treating infections with antibiotic options that are limited or in some cases nonexistent. As resistance increases, both the risk of death and health care costs increase.

Addressing each antibiotic-resistant pathogen requires a balanced portfolio, a multifaceted approach that would reduce inappropriate use of antibiotics, prevent the spread of resistant organisms, and develop new antibiotics for the future.

Dr. Fauci will speak about the need to continue and accelerate our efforts to develop new antibiotics, but unless we improve our monitoring and use of antibiotics through effective public health action, we will steadily lose the ability to use both current and future drugs.

The next slide shows our approach to combating antimicrobial resistance. It starts with surveillance, understanding what is happening. Surveillance is key to assessing and monitoring the scope and magnitude and trends of antibiotic resistance. Surveillance data can drive and direct prevention efforts, and determine treatment recommendations, guide new drug developments, and evaluate whether our prevention efforts are working.

We need to detect and respond, including through more effective laboratory facilities in hospitals, in State and local health departments, and throughout the Federal system.

We need to develop and implement prevention strategies. An example of this: CDC working with the Veterans Administration hospital in Pittsburgh documented a 60 percent decline in MRSA infections. That same approach was rolled out to the VA system nationally and then to many other health systems nationally.

And although drug resistance is a growing problem, we have had some good news in that there has been a documented decline in MRSA nationally by about half and of Methicillin-susceptible infections in hospitals by about 70 percent, according to the hospitals that we track over time in the National Healthcare Safety Network.

And finally, to rigorously evaluate the impact to see what is working and what is not.

In my written statement, I highlighted several high-priority antibiotic infection and prevention strategies, and my next slide outlines some of those. MRSA, gram-negative rods, gonococcus, gonorrheal infections are becoming increasingly resistant in the U.S. and

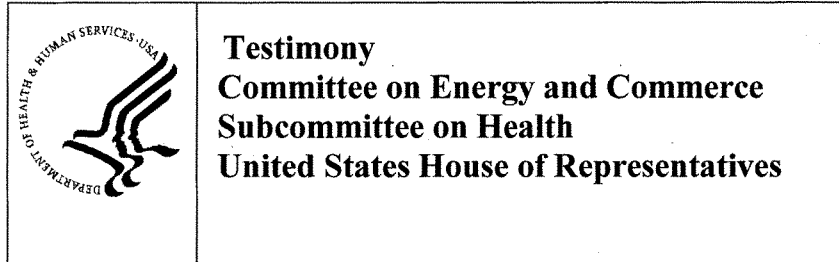
around the world; tuberculosis, where infections increase the risk of death and the cost of treatment.

Generally, we work to improve antibiotic use; facilitate rapid and accurate diagnosis; improve treatment of infections, and we have seen significant progress in reducing inappropriate antibiotic use among pediatricians; improve infection control; and wherever possible, create and distribute vaccines, for example, to prevent pneumococcal infections, a vaccine which has prevented about 10,000 deaths and saved more than \$300 million in direct medical costs each year over the past decade.

We speak of the pre-antibiotic and antibiotic eras. But if we don't improve our response to the public health problem of antibiotic resistance, we may enter a post-antibiotic world, in which we will have few or no clinical interventions for some infections.

We are working closely with our colleagues across HHS on this important issue. We very much appreciate the committee's interest and welcome your questions.

[The prepared statement of Dr. Frieden follows:]



**Antibiotic Resistance and the Threat to
Public Health**

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



For Release on Delivery
Expected at 2 p.m.
April 28, 2010

Good morning, Chairman Pallone and other distinguished members of the subcommittee. I am Dr. Thomas Frieden, Director of the Centers for Disease Control and Prevention (CDC), an agency of the Department of Health and Human Services, and I appreciate the opportunity to talk to you today about the public health threat of antibiotic resistance and the important role CDC plays in detecting, responding to and preventing this problem.

Introduction

Antimicrobials¹ are used to treat infections by different disease-causing microorganisms, including bacteria, mycobacteria, viruses, parasites and fungi. In the vast majority of cases where antimicrobials are used, the microorganisms have found a way to evade or resist the antimicrobial agent. Resistance occurs wherever antimicrobials are used -- in the community, on the farm, and in healthcare. Antimicrobial resistance is a global problem, and some of our most significant global threats are multi-drug resistant tuberculosis and drug-resistant malaria. Today, however, I will focus on domestic issues and antibiotic-resistant bacteria.

Antibiotic resistance is a public health problem of increasing magnitude, and finding effective solutions to address this problem is a critical focus of CDC activities. Infections with resistant bacteria were first reported over 60 years ago², but early on the problem was often overlooked, because if one antibiotic did not treat the infection another was usually available. Since then, infections with resistant bacteria have become more common in healthcare and community settings, and many bacteria have become resistant to more than one type or class of antibiotics. Consequently, doctors and nurses today are faced with treating infections where antibiotic options are very limited, and in some cases, where no effective antibiotics exist. When treatment options

¹ Antimicrobial is a general term for the drugs, chemicals, or other substances that either kill or slow the growth of microbes. Among the antimicrobial agents in use today are antibiotic drugs (which kill bacteria), antiviral agents (which kill viruses), antifungal agents (which kill fungi), and antiparasitic drugs (which kill parasites). An antibiotic is a type of antimicrobial agent made from a mold or a bacterium that kills, or slows the growth of other microbes, specifically bacteria. Examples include penicillin and streptomycin.

² Barber M. Staphylococcal infections due to penicillin-resistant strains. *British Medical Journal*. 1947.

are limited, healthcare providers might need to use antibiotics that are more expensive or more toxic to the patient. When no antibiotic is effective, healthcare providers may be limited to providing supportive care rather than directly treating an infection -- similar to how medicine was practiced before antibiotics were discovered. As resistance increases, the patient's risk of dying from infection also increases. Moreover, resistance is not just a problem for the patient who is infected. When an infection is not effectively treated because of resistance, the microorganisms will persist and potentially spread to others, further extending the resistance problem.

Antibiotics kill or inhibit bacteria that are susceptible to that antibiotic. Bacteria that are intrinsically resistant or that can acquire resistance will survive and replace the drug-susceptible bacteria. Thus, any antibiotic use will provide a selective pressure³ that perpetuates resistant bacteria. The more that antibiotics are used, the greater the selective pressure. Antibiotics are the most important tool we have to control many life-threatening bacterial diseases once infection has occurred, yet increasing levels of resistance are compromising the effectiveness of these antibiotics. Bacteria have developed multiple ways of becoming resistant to antibiotics; the more often bacteria are exposed to antibiotics, the more likely they are to survive through one of these mechanisms. Antibiotics are used widely to treat persons in the community and in healthcare settings, and are also used to treat animals in agricultural settings. It is imperative that we assess the use of antibiotics carefully -- regardless of setting -- and use them only when necessary, to avoid promoting the development of resistance among bacteria.

Antibiotic resistance is also an economic burden on the healthcare system. Resistant infections not only cost more to treat, but also can prolong healthcare use. In a 2008 study of attributable medical costs for antibiotic resistant infections, it was estimated that infections in 188 patients from

³ Selective pressure means that use of antibiotics will kill susceptible bacteria, but also "enrich" resistant bacteria. Resistant bacteria are "enriched" by the lack of susceptible bacteria to compete with for space, resources, hosts, etc. Thus, those resistant organisms can often thrive and multiply, passing on their resistant genes to the next generation.

a single healthcare institution cost between \$13.35 and \$18.75 million dollars.⁴ Unfortunately, infections caused by antibiotic resistant bacteria are an everyday occurrence in healthcare settings.

Overview of CDC's Antibiotic Resistance Programs

Without continuing to improve on our response to the public health problem of antibiotic resistance, we are potentially headed for a post-antibiotic world in which we will have few or no clinical interventions for some infections. Addressing antibiotic resistance requires a multifaceted approach to reduce inappropriate use, prevent disease transmission, and develop new antibiotic agents. CDC's activities in this area are focused on two goals: preventing the emergence and spread of resistant organisms, and improving antibiotic use to reduce resistance. Many of these activities are conducted in collaboration with partners including other federal agencies, state and local public health departments, academic centers, and international organizations.

Disease Surveillance and Response

Disease surveillance is a core CDC activity. CDC uses surveillance systems to assess and monitor the scope, magnitude and trends of the antibiotic resistance problem. Surveillance data are used not only to monitor resistance rates but are also used to drive and direct prevention efforts, determine treatment recommendations, guide new drug development, and evaluate the effectiveness of prevention programs.

Several different surveillance tools have been developed for bacterial resistance because surveillance strategies and objectives vary for different problems. One of CDC's most important surveillance platforms is the Emerging Infections Programs (EIPs), a network of 10 state health

⁴ Roberts, RR, Hota B, Ahmad I, Scott RD II, Foster SD, Abbasi F, Schabowski S, Kampe LM, Ciavarella GG, Supino M, Naples J, Cordell R, Levy SB, Weinstein, RA. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. *Clin. Infect. Dis.* 2009; 49:1175-84.

departments working with collaborators in laboratories, healthcare facilities, and academic institutions to conduct population-based surveillance. Through population-based surveillance, CDC is able to provide national estimates of disease burden and to track changes in disease burden over time. Through this network, CDC conducts surveillance for both resistant community-associated and healthcare-associated bacterial infections. Incidentally, the EIP network has been invaluable in our response to H1N1 influenza.

Another component of CDC's antibiotic resistance surveillance system is the National Healthcare Safety Network (NHSN). This web-based surveillance tool for hospitals and state health departments monitors healthcare-associated infections (HAIs), such as those caused by methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile*, and multi-drug resistant gram-negative bacteria. Over 2,500 U.S. hospitals (approximately half) are currently enrolled in NHSN, and the President's budget request for FY 2011 seeks to expand that enrollment by another 2,500 hospitals. Data from this network are used to monitor HAI rates and the prevalence of resistance among the bacteria causing infection.

The CDC, the Food and Drug Administration (FDA), and the Department of Agriculture (USDA) also work in collaboration with participating state and local health departments to operate the National Antimicrobial Resistance Monitoring System (NARMS). NARMS is a lab-based surveillance system in all 50 states that detects resistance in enteric bacteria (microorganisms that inhabit the intestines) that are commonly transmitted from animals to humans through food, such as *Salmonella*, *Campylobacter*, and *E. coli*. NARMS monitors trends in the prevalence of resistance among bacteria isolated from humans, retail meats, and livestock.

Prevention and Control of Antibiotic Resistance in the Community and in Healthcare

Preventing resistant infections provides the greatest opportunity to limit resistance. Strategies to prevent and control resistant bacteria vary by the pathogen and the setting in which the infection is acquired. For some diseases, like *Streptococcus pneumoniae*, there are vaccines to prevent infections. For others, CDC works collaboratively to develop infection control and treatment guidelines. Prevention of HAIs, such as MRSA, resistant gram-negative bacteria,⁵ and *C. difficile*, can require different interventions than those infections that are community-associated, such as tuberculosis and pneumococcal pneumonia. In all cases, surveillance data are used to monitor the effectiveness of prevention efforts.

CDC works with state and local public health authorities to detect and respond to the emergence of new resistant bacteria. Part of these efforts includes providing reference laboratory services for state and local public health departments to confirm and characterize unusual antibiotic resistance. New resistance patterns often require the development of new laboratory tools for detection. CDC develops these new laboratory tools and then distributes them widely to monitor resistance at the local level.

CDC also provides epidemiologic assistance in outbreak responses. Outbreaks caused by resistant bacteria can occur in community settings where people are concentrated, such as athletic teams, childcare centers, and prisons, or in healthcare settings, including hospitals, long-term care facilities, and ambulatory care facilities. In all of our investigations, CDC works cooperatively with state and local health authorities to learn from each outbreak and use the lessons learned to develop best practice recommendations to prevent similar outbreaks from occurring in the future.

High Priority Antibiotic Resistant Infections

⁵ There are several types of gram-negative bacteria that cause healthcare-associated infections. Some of the more common bacteria belong to the *Enterobacteriaceae* family, such as *Klebsiella* spp., and *Escherichia coli*. Other important bacteria are *Acinetobacter* spp. and *Pseudomonas aeruginosa*.

Healthcare Associated Multi-Drug Resistant Gram-Negative Bacterial Infections

The newest resistance challenge in the healthcare setting is multi-drug resistant gram-negative bacteria. Particularly concerning are the carbapenemase-producing bacteria, such as bacteria of the *Klebsiella* species, among others. Bacteria with the carbapenemase-resistance trait are resistant to a class of drugs that were considered the “last resort” for treating serious infections caused by these bacteria. The antibiotic resistant traits are often located on mobile genetic elements, called plasmids. That means that resistance can be readily transferred from one bacterium to another, facilitating the spread of resistance between bacteria.

Most recently, CDC has collaborated with state health departments in New York, Illinois, Florida, California, and Arizona to address outbreaks of carbapenemase-producing *Klebsiella*. In addition to these outbreaks, our reference lab has confirmed carbapenemase-producing *Klebsiella* for 32 other States. Preventing the spread of these resistant bacteria is difficult because patients may harbor the resistant bacteria in their intestinal tracts, but this goes unrecognized because it does not make the patients sick. This is called “asymptomatic colonization.” Outbreak investigations, such as the one CDC helped with at an Illinois long-term care facility, found that up to 50 percent of a patient population can harbor the resistant bacteria while only a few patients may have an active infection. Patients with asymptomatic colonization can be infectious without being sick themselves. There is no efficient method to identify all potential types of colonization; furthermore, many of these organisms are part of normal human bacteria, and simply eradicating them could harm a patient.

CDC has responded to this new public health threat by working with laboratory standard-setting institutions to identify and recommend tests for the accurate detection of carbapenemase-mediated resistance. CDC has also worked with our Healthcare Infection Control Practices Advisory

Committee (HICPAC) to recommend methods to identify patients colonized with the resistant bacteria so that infection control precautions can be implemented to prevent further spread.

Acinetobacter is another species of gram-negative bacteria that causes infections in hospitalized patients and often becomes resistant to many antibiotics. Infected patients are usually the individuals with the most compromised health, such as those receiving intensive care. *Acinetobacter* has also caused a large number of infections among U.S. service members injured in the Middle East. CDC investigations of *Acinetobacter* have led to some important discoveries. First, these resistant bacteria can spread rapidly within a healthcare institution and between healthcare institutions within a community. Second, contamination of the hospital environment is often a significant contributor to the spread of the resistant bacteria. In turn, these discoveries have led to the development of aggressive infection control strategies for *Acinetobacter*. Fortunately, consistent application of rigorous infection control precautions and environmental cleaning practices can prevent the transmission of *Acinetobacter*.

MRSA Infections

MRSA infections are transmitted primarily in the healthcare setting. These infections were first encountered in healthcare settings in the 1980s, and the rate of infections has continued to rise. Reducing MRSA infection rates in U.S. hospitals is the focus of several local, regional, and national interventions. For example, the Veterans Affairs Pittsburgh Healthcare System, in collaboration with CDC, achieved a 60 percent reduction in the rate of MRSA infections after it implemented a series of infection control procedures based on evidence-based guidelines designed to decrease the transmission of MRSA in hospitals. The measures included strict attention to hand hygiene, enhanced surveillance for infections, effective use of isolation rooms, and behavior modification techniques for healthcare workers to emphasize the importance of the new procedures. These

interventions were subsequently implemented in Department of Veterans Affairs (VA) medical centers nationwide and in multiple other healthcare systems.

National data from the NHSN show that there has been a significant drop in the incidence of both MRSA and methicillin-susceptible *S. aureus* (MSSA) central line-associated bloodstream infections among intensive care unit patients in U.S. hospitals over the last five years. The incidence of MRSA bloodstream infections per 1,000 central line days (i.e. a measurement of infection burden derived from the number of patients who have a central line, or catheter, whether infected or not) decreased by 50 percent, while the incidence of central line-associated MSSA infections decreased even more substantially, by 70 percent. Serious MRSA infections are also monitored using the Active Bacterial Core Surveillance (ABCs) system; a surveillance system conducted in the EIP network. MRSA ABCs data for 2005-2008 also show a decrease in hospital-onset and healthcare-associated MRSA infections, confirming a downward trend. Thus, it appears that these practical efforts to reduce the transmission of MRSA in hospitals are working, thereby reducing the need for antibiotic usage.

Most serious MRSA infections, an estimated 85%, are associated with a healthcare exposure, but nearly 14% of the infections are community-associated. Although progress in controlling MRSA in hospitals is being made, CDC ABCs data indicate that community-associated MRSA infections are not decreasing. Most of these are skin infections, but severe and sometimes fatal cases of necrotizing pneumonia continue to be reported among otherwise healthy people in the community with no links to the healthcare system. Controlling MRSA in community settings is a new challenge, and CDC is continuing to evaluate evidence-based methods to reduce these infections in community settings. While progress continues to be made, more can be done, and CDC wants every healthcare institution to move toward elimination of MRSA and all other HAIs.

Clostridium difficile

C. difficile infections can be an adverse consequence of antibiotic use. *C. difficile* bacteria can live in the intestinal tract without causing disease because its numbers are kept low by competing with healthy intestinal bacteria for nutrients. However, antibiotics can disrupt this balance by killing off healthy intestinal bacteria, whereas *C. difficile*, which is intrinsically resistant to many commonly used antibiotics, flourish and multiply. *C. difficile* disease can range from mild diarrhea to life-threatening infections. Since 2000, the United States has seen a rapid increase in the number and severity of *C. difficile* infections, primarily in hospitalized patients. Studies done in collaboration with CDC have demonstrated that modifying antibiotic usage in healthcare facilities can decrease *C. difficile* disease rates. Other studies have shown that daily cleaning of hospital rooms will also significantly decrease *C. difficile* infection rates.

Gonorrhea

Over time, *Neisseria gonorrhoeae* (gonorrhea) has become resistant to every antibiotic that has been used to treat it. During the 1970s and 1980s, resistance to penicillin and tetracycline increased significantly, leading CDC to stop recommending those antibiotics for therapy. Over the past decade, fluoroquinolone-resistant gonorrhea spread from the Far East and Western Pacific to the United States, leaving only one class of antibiotics still recommended for effective gonorrhea treatment, the cephalosporins.

It is expected that gonorrhea will also acquire resistance to the cephalosporins. Strains with decreased susceptibilities to cephalosporins identified in laboratory testing and some treatment failures following therapy with oral cephalosporins have been reported from several countries in Asia. Cephalosporin resistance has not yet been reported in the United States and has not been detected by CDC. With over 330,000 cases reported each year in the US, even small changes in

the treatment of gonorrhea (e.g., the need for multi-dose or multi-drug therapy) could significantly impact the cost and effectiveness of control efforts for this infection.

CDC is collaborating with the World Health Organization (WHO) to maintain and strengthen its regional gonococcal resistance surveillance programs and to strengthen the laboratory and epidemiological capacity of countries, particularly in the Far East and Western Pacific regions where resistance has emerged in the past.

Foodborne bacterial infections

Non-typhoid *Salmonella* causes approximately 1.4 million cases of disease in humans in the United States each year. Patients with complicated or severe infections are treated with fluoroquinolones or cephalosporins, and of these two drug classes, only cephalosporins are approved for treatment of children with these infections. Since NARMS began surveillance in 1996, cephalosporin resistance among *Salmonella* isolated from humans has increased significantly, and resistance to this class of drugs has also been found among *Salmonella* isolated from the livestock and retail meats for which NARMS conducts surveillance. In many cases, the same types of bacteria and genetic mechanisms of resistance are found in both human and animal sources. Studies have shown that use of cephalosporins in food animals can select for antibiotic resistant bacteria, and, in some cases, specific uses of this class of drugs in food animals are associated with higher rates of resistance among human *Salmonella* infections. In order to successfully manage resistance, it is important to understand antibiotic resistant human infections in the context of specific antibiotic use patterns, including use patterns in food animals.

Campylobacter is one of the leading causes of culture-confirmed foodborne bacterial disease in humans in the United States, and consumption of poultry has been shown to be an important risk factor for *Campylobacter* infection. Fluoroquinolones and macrolides are the drug classes of

choice for treating *Campylobacter* infections. Following the approval of fluoroquinolones for use in poultry, rate of resistance to this class of drugs among human *Campylobacter* isolates rose sharply, to more than 20 percent. FDA has since withdrawn approval of this drug class for use in poultry, and NARMS continues to monitor *Campylobacter* from humans, retail meats and food animals for fluoroquinolone resistance. Studies are also underway to understand domestic and foreign travel-associated sources of fluoroquinolone-resistant *Campylobacter*.

Tuberculosis

Treatment of drug-susceptible tuberculosis (TB) requires 6-9 months of therapy, while drug resistant cases require 18-24 months of therapy with drugs that are less effective, more toxic, and far more costly. TB bacilli become resistant to antibiotics through inappropriate or inconsistently taken therapy; therefore, programs that fail to assure appropriate prescription and direct observation of treatment regimens, drug susceptibility testing, uninterrupted drug supplies, and patient support throughout duration of therapy can contribute to the development of drug resistance. This was the scenario in the United States from 1985 to 1993. Due to a combination of program neglect, the HIV epidemic, and outbreaks in congregate settings, the United States experienced 52,100 more TB cases than otherwise would have been expected during this period. An influx of emergency funds enabled CDC to build capacity in state, local, and territorial health departments to implement Directly Observed Therapy, where healthcare or outreach workers observe the taking of each dose of anti-TB medication and monitor patients' response.

As a result, TB incidence in the United States has declined from 25,107 cases in 1993 to a preliminary count of 11,540 in 2009, with proportional decreases in drug-resistant TB cases. In 2008, 1.1 percent of U.S. TB cases were drug resistant as compared with rates exceeding 20

percent in other parts of the world.⁶ However, the epidemiology of drug-resistant TB in the United States has changed, reflecting global patterns. In 1993, 26 percent of multi-drug resistant TB cases occurred in foreign-born persons, whereas in 2008 this was 78 percent.⁷ CDC monitors for drug resistance in the United States and, globally, collaborates with the United States Agency for International Development and WHO to provide technical assistance to national TB programs to monitor and prevent drug resistance and implement infection control practices in congregate settings, for example, in waiting rooms in HIV antiretroviral therapy clinics. CDC is also conducting research to develop shorter, more effective regimens for treating TB, drug-resistant strains, and TB in HIV-coinfected persons and children.

Pneumococcal Infections

Vaccination is effective in preventing pneumococcal infections. Penicillin-resistant pneumococcal infections became common during the 1990s. In 2000, a new pneumococcal conjugate vaccine became available for children in the United States, and CDC began tracking the vaccine's impact on resistant pneumococcal infections with the ABCs project. Since the vaccine was introduced into the routine childhood immunization program in the United States, penicillin-resistant pneumococcal infections have declined by 35 percent. Not only has the vaccine been shown to prevent antibiotic-resistant infections, it has been shown to reduce the need for prescribing antibiotics for children with pneumococcal infection in the first place. CDC data also show that adults are getting fewer resistant pneumococcal infections because the vaccine is preventing spread of pneumococci from infected children to adults. It is estimated that since 2001, 170,000 severe pneumococcal infections and 10,000 deaths have been prevented by vaccine use and that the vaccine is highly cost-effective, saving an estimated \$310 million in direct medical costs each year.

⁶ MMWR, March 19, 2010/59(10), 289-294 and Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. WHO/HTM/TB/2010.3

⁷ CDC. Reported Tuberculosis in the United States, 2008. (<http://www.cdc.gov/tb>)

Despite the success of this vaccine, CDC's surveillance has identified the emergence of infections caused by a new multidrug-resistant strain of pneumococcus called serotype 19A. In a sense, the vaccine has provided selective pressure benefiting strains not covered by the vaccine. In February of this year, a new version of the vaccine, which includes protection against strain 19A, was approved for use. CDC will continue to use its surveillance systems to evaluate the impact of this new version of the vaccine.

Improving Antibiotic Use

Antibiotic use often provides lifesaving therapy to those who have a serious bacterial infection. Antibiotic use also provides the selective pressure for new resistance to develop. In order to minimize the selective pressure of antibiotics, it is important to make sure that when antibiotics are used, they are used appropriately. CDC's educational campaign ***Get Smart: Know When Antibiotics Work*** teaches both the provider and the patient when antibiotics should be used.

The ***Get Smart: Know When Antibiotics Work*** program is a comprehensive and multi-faceted public health effort to help reduce the rise of antibiotic resistance. Partnerships with public and private health care providers, pharmacists, a variety of retail outlets, and the media result in broad distribution of the campaign's multi-cultural/multi-lingual health education materials for the public and health care providers. Through ***Get Smart***, CDC develops clinical guidance and principles for appropriate antibiotic use to prevent and control antibiotic-resistant upper respiratory infections. ***Get Smart*** targets five respiratory conditions that account for most of office-based antibiotic prescribing, including: otitis media, sinusitis, pharyngitis, bronchitis, and the common cold. Data from the National Ambulatory Medical Care Survey confirm the campaign's impact on reducing antibiotic use for acute respiratory tract infections among both children and adults. There has been a 20 percent decrease in prescribing for upper respiratory infections (In 1997 the prescription rate for otitis media in children less than 5 years of age was 69 prescriptions per 100 children compared

to 47.5 per 100 children in 2007.) and a 13 percent decrease in prescribing overall for all office visits (Overall antibiotic prescribing dropped from 13.8 prescriptions per 100 office visits to 12.0 prescriptions per 100 office visits, comparing 1997-98 to 2005-06)⁸. The ***Get Smart: Know When Antibiotics Work*** campaign contributed to surpassing the Healthy People 2010 target goal to reduce the number of antibiotics prescribed for ear infections in children under age 5.

Following the success of this campaign, two new ***Get Smart*** campaigns have been launched: ***Get Smart in Healthcare Settings*** and ***Get Smart on the Farm***. ***Get Smart in Healthcare Settings*** will focus on improving antibiotic use for the in-patient population. One of the initial activities will be to launch a website that will provide healthcare providers with materials to design, implement, and evaluate antibiotic stewardship interventions locally. These materials will include best practices from established and successful hospital antibiotic stewardship programs.

Antibiotics are also used in veterinary medicine and animal agriculture. Antibiotic use in animals has lead to the emergence of resistant bacteria, and sometimes these resistant bacteria can be transferred from animals to humans by direct contact or by handling and/or consuming contaminated food. ***Get Smart: Know When Antibiotics Work on the Farm*** is an educational campaign with the purpose of promoting appropriate antibiotic use in veterinary medicine and animal agriculture. CDC funds and provides technical assistance for several state-based efforts to educate veterinarians and food producers, including those in the dairy and beef industries.

There are several CDC initiatives to improve surveillance of antibiotic use to measure how much and where antibiotics are used. One initiative is an enhancement of the NHSN to accept antibiotic use data from healthcare facilities through electronic medical records. This capability is expected

⁸ Unpublished data from the National Ambulatory Medical Care Survey, National Center for Health Statistics, 2009; <http://www.cdc.gov/nchs/ahcd.htm>

to be available in the next year. The second is a point prevalence survey of antibiotic use in selected healthcare facilities from around the U.S. This survey will be conducted through our EIP network, and it is expected to give us a snapshot of antibiotic use in the U.S. Antibiotic use data from both initiatives will provide much-needed information for implementing more targeted strategies to improve antibiotic use nationwide.

Antibiotic Resistance Requires a Coordinated Response

Since the impact of resistance is extensive, the Interagency Task Force on Antimicrobial Resistance was created to plan and coordinate federal government activities. The Task Force is finalizing an update of "A Public Health Action Plan to Combat Antimicrobial Resistance", which was first released in 2001. The Action Plan will focus on:

- reducing inappropriate antimicrobial use;
- reducing the spread of antimicrobial resistant microorganisms in institutions, communities, and agriculture;
- encouraging the development of new anti-infective products, vaccines, and adjunct therapies; and
- supporting basic research on antimicrobial resistance.

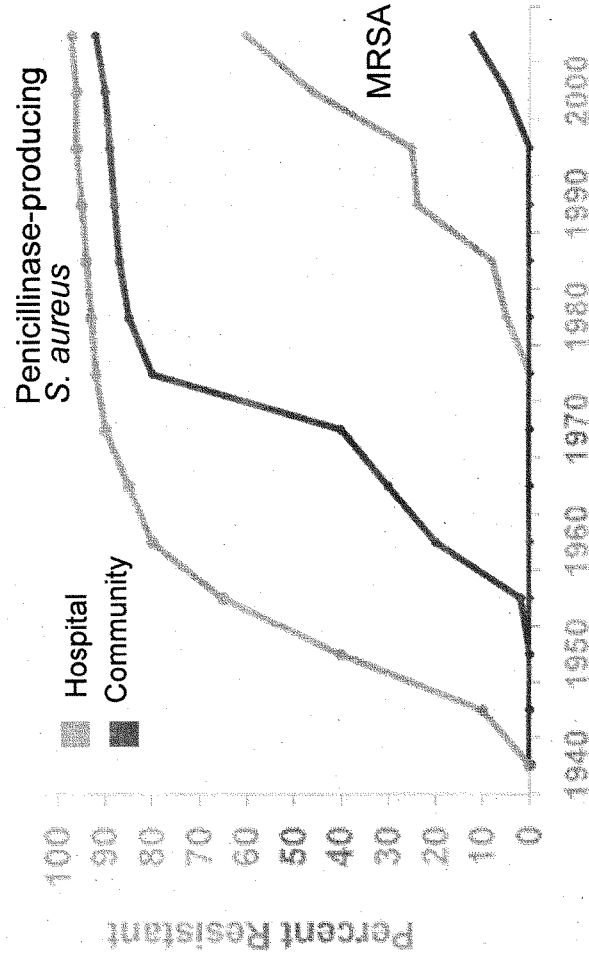
The Task Force is co-chaired by CDC, FDA, and the National Institutes of Health and includes seven other federal agencies (Agency for Healthcare Research and Quality, Centers for Medicare and Medicaid Services, USDA, Department of Defense, VA, Environmental Protection Agency, and Healthcare Resources and Services Administration).

Conclusion

With the growing development of antibiotic resistance, it is imperative that we no longer take the availability of effective antibiotics for granted. As a nation, we must respond to this growing problem, and our response needs to be multifactorial and multidisciplinary. CDC will continue to

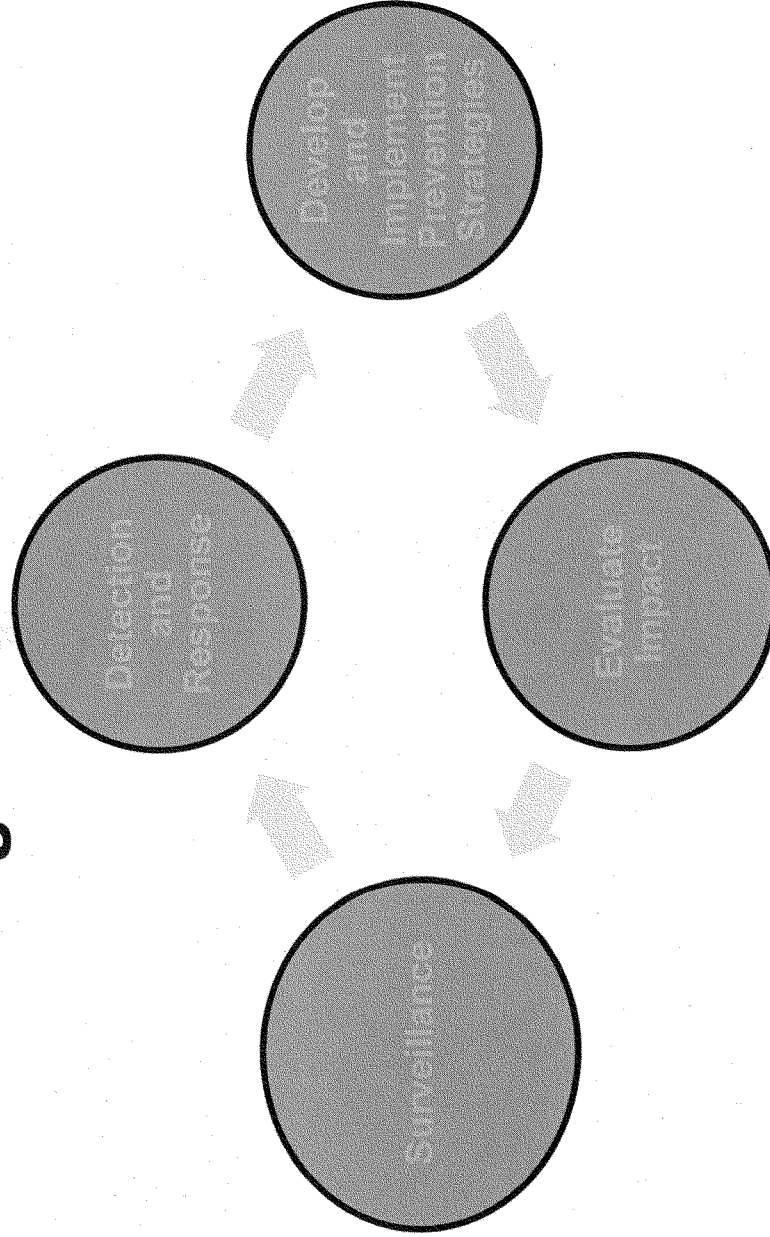
develop improved diagnostics to detect resistance rapidly and accurately. With the increased investments under the President's budget, we will enhance our surveillance systems, such as NHSN, with electronic laboratory data and electronic medical records data, which will facilitate surveillance at the healthcare level and thereby increase surveillance capacity. It will also result in real-time reporting, which means that there will be greater opportunities for a rapid prevention and control response. Healthcare institutions need robust infection control programs and antibiotic stewardship programs to prevent transmission of resistant bacteria and to decrease the selective pressure for resistance. CDC will continue its support of new and effective vaccines, like the pneumococcal vaccine, to prevent infections caused by some of the most serious infections such as MRSA and *C. difficile*. By building on our current efforts, we can extend the life of current antibiotics and develop future antibiotic therapies to protect us from current and future disease threats.

A problem in and then out of the hospital



Chambers H., The changing Epidemiology of *Staphylococcus aureus*? Emerging Infectious Diseases 2001; 7: 178-182.

Combating Antibiotic Resistance



Infection	Resistance Problem	Primary Prevention Strategies
Multidrug resistant gram-negative bacterial infections	Healthcare infections with limited treatment options	Improve antibiotic use Rapid and accurate diagnosis
MRSA Infections	Healthcare and community infections with limited treatment options	Effective treatment of infections Infection control
Pneumococcal infections	Emergence of resistant strain not covered by the old vaccine	New vaccine Improve antibiotic use
Tuberculosis	Infections with MDR or XDR TB with limited treatment options	Effective program management including: - Accurate, rapid diagnostic tests - Directly observed therapy - Infection control
Food-borne bacterial infections	Potentially severe diarrheal disease with limited treatment options	Improve antibiotic use Improve food-handling

Mr. PALLONE. Thank you, Dr. Frieden.
Dr. Fauci.

STATEMENT OF ANTHONY S. FAUCI, M.D.

Dr. FAUCI. Mr. Chairman, Ranking Member Shimkus, Mr. Dingell, members of the committee, thank you for calling this hearing, and thank you for giving me the opportunity to discuss with you for a couple of minutes here the role of the biomedical research endeavor in the comprehensive strategy to address antimicrobial resistance.

As shown on the slide on the screen, as pointed out so well by Dr. Frieden, the strategy to address antimicrobial resistance includes surveillance, infection control, and the promotion by various means of the rational use of antimicrobials.

An important component of that strategy is the biomedical research endeavor fundamentally to understand the mechanisms of resistance and to do the basic and clinical research to develop the countermeasures that are needed against microbial resistance.

On the next slide is a picture of a journal in which we have published the research agenda of the National Institute of Allergy and Infectious Diseases which has three major pillars to it: basic fundamental research, clinical research, and transnational research leading to product development.

On the next slide, I want to very briefly address the issue of basic research. Fundamental to the basic research approach is the study of the microbe itself. We have been enormously put at an advantage over the last decade by the striking, if not stunning, advances in the ability to sequence and annotate the genomes of microbes.

Just to give you an example, in 1996, when the first microbe, haemophilus influenzae, was sequenced, it took about year and about a million dollars. In the year 2000, you could sequence a bacteria for about \$50,000, and it would take about 4 days. Today, you can sequence a bacteria for \$1, and it takes just several hours.

So we have the capability right now to do sequencing, mass sequencing, of microbes as they evolve into their resistant form. This gives us the opportunity of what we are pursuing very aggressively in our research to determine the molecular mechanisms of resistance and use that to target both diagnostic vaccines but, importantly, the targets for new pipelines of antimicrobials.

In addition, we study the host pathogen interaction, namely how the microbe, be it a virus or bacteria, interacts with the host and what the body's immune response is in the form of immunological response.

On the next slide, we also do clinical research activities. And as Dr. Frieden has pointed out, we focus on some of the problematic organisms, in this case obviously one that was mentioned several times already this afternoon, Methicillin-Resistant Staph Aureus. In addition, the escape organisms, which are also prone to resistance, are on our top priority.

What do we do with clinical trials? Besides testing new drugs, we determine under certain circumstances, is treatment even needed, such as in some of the infections that turn out actually to be viral

infections that for which the use of antibiotics might not be appropriate?

We also need to know how much antibiotics we should use and for how long. The appropriate duration of therapy for different types of infections has still not been fully worked out.

And importantly, we are looking for new uses for older off-patent drugs. Drugs that have fallen into disuse because of the more modern antibiotics might actually be brought back if into the ball game to treat multiple drug-resistant microbes.

On the next slide, it is a scheme that goes from left to right. I think this is a very important slide that I would like to just spend a minute on, because it is the scheme of what happens when you develop products for antimicrobials, in this case those that are resistant. On the far left is what the NIH, NIAID in particular, does best and does more intensively, and that is the fundamental research to develop the concepts to ultimately, on the far righthand side of the slide, to develop countermeasures. These could be diagnostics which are critical in addressing microbial resistance because you want to know if you are dealing with a resistant microbe. The other is a vaccine, which some of you have mentioned, to prevent some of the infections in the first place, and finally the development of new antimicrobial drugs.

As you go from left to right, industry plays more and more of a role. As we have seen, the incentive for industry to get involved in the development of new antimicrobials is not very great. And I heard several of you mention in your opening statements, we need to address some of the incentives that we might partner with them in getting them involved in a very important public health problem that they don't have as an economic incentive something that is really a great drive on their force to get involved. And this is something that we generally use when we deal with emerging microbes for which there really are not any countermeasures. I believe this is something that we should address when we are dealing with addressing of older microbes that have developed resistance.

Finally, just to go back to my first slide, on the next slide, to reiterate that there are multiple strategies and multiple components of strategies to develop the issue of antimicrobial resistance. And in conclusion, I want to say that we will continue to pursue the biomedical research approach as an important part of that comprehensive strategy.

Thank you, Mr. Chairman, I will be happy to answer questions.
[The prepared statement of Dr. Fauci follows:]



**Testimony
Before the
Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives**

**The Role of NIH Research in
Addressing Antimicrobial
Resistance**

Statement of

Anthony S. Fauci, M.D.

Director

National Institute of Allergy and Infectious Diseases

National Institutes of Health

U.S. Department of Health and Human Services



**For Release on Delivery
Expected at 2:00 p.m.
April 28, 2010**

Mr. Chairman and members of the Committee, thank you for the opportunity to discuss the serious public health challenge posed by antimicrobial resistance and the research being conducted and supported by the National Institutes of Health (NIH), an agency within the Department of Health and Human Services (HHS), to address this challenge. I am the Director of the National Institute of Allergy and Infectious Diseases (NIAID), the lead component of NIH for research relating to infectious diseases including research on antimicrobial resistance.

NIAID plays a critical role in the federal government's comprehensive efforts to combat the problem of antimicrobial resistance. NIAID oversees a major effort built upon a foundation of basic research to understand the biology of microbial pathogens, the interactions between these pathogens and their human hosts, and the biological mechanisms by which pathogens develop resistance to antimicrobial drugs. In addition, NIAID is committed to basic and translational research to identify new antimicrobial targets and to translate this information into 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. Finally, NIAID is conducting studies to inform the rational use of existing antimicrobial drugs or alternative therapies to help limit the development of antimicrobial resistance.

OVERVIEW

Microbes are living organisms that multiply frequently and spread rapidly, efficiently increasing their numbers. Microbes include bacteria (e.g., *Staphylococcus aureus*), viruses (e.g., influenza and HIV), fungi (e.g., *Candida albicans*, which causes some yeast infections), and parasites (e.g., *Plasmodium falciparum*, which causes malaria). Some microbes are pathogenic; that is, they cause disease in their hosts. Others exist in the host without causing harm and may, in fact, be beneficial.

In 1928, while working with *Staphylococcus* bacteria, Scottish scientist Alexander Fleming noticed a “halo” of inhibited bacterial growth surrounding a type of mold growing by accident on a laboratory plate. The substance secreted by the mold, which Fleming called penicillin, later became one of the world’s first antibiotic drugs. Though not widely prescribed until the 1940s, antibiotics and other antimicrobial drugs (a general term given to medicines that kill or slow the growth of a microbe) have saved countless lives and blunted serious complications of many diseases and infections. The success of antimicrobials against disease-causing microbes is among modern medicine’s great achievements.

Yet, for all of the success that antimicrobial drugs brought to the fight against infectious diseases, microbes continuously are developing ways to circumvent these powerful medical tools. Antimicrobial resistance refers to the ability of a microbe to grow in the presence of an antimicrobial drug that would normally kill

it or limit its growth. The practical consequence of antimicrobial resistance is that the effectiveness of existing antimicrobial drugs is declining and that strains of pathogens that defy treatment with commonly available therapeutics are emerging. The emergence and increasing prevalence of these drug-resistant strains has become a global public health issue.

To illustrate this point, consider that in the United States in 2005, CDC estimated that 94,360 individuals developed an invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infection—most acquired in healthcare settings—and 18,650 patients died.¹ In recent years, there has been a markedly increased rate of infections caused by community-acquired MRSA (CA-MRSA).² The majority of CA-MRSA infections are skin and soft-tissue infections; however, CA-MRSA increasingly has been associated with severe invasive disease.³ *Acinetobacter* infections are a significant concern among wounded soldiers returning from the Middle East. Among these soldiers, CDC reports that 35% of *Acinetobacter* isolates are susceptible to only one commonly used antimicrobial drug; 4% of isolates are resistant to all commonly used drugs.⁴ Moreover, antimicrobial resistance is not solely a domestic health issue. The emergence of chloroquine-resistant malaria has contributed to the resurgence of malaria

¹ Klevens, RM et al. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States. *JAMA*. 2007; 298:1763-1771.

² Klevens, 1763.

³ Klevens, 1769.

⁴ *Acinetobacter baumannii* Infections Among Patients at Military Medical Facilities Treating Injured U.S. Service Members, 2002—2004. *MMWR*. 2004;53(45):1063-1066.

throughout the world, and resistance to second-line artemisinin-based therapies also has begun to emerge. Further, the World Health Organization (WHO) estimates that 3.6% of all tuberculosis (TB) cases are multidrug-resistant (MDR) TB, or resistant to at least two first-line TB drugs; 440,000 new MDR-TB cases arose in 2008.⁵ In some regions of Eastern Europe and Asia, the incidence is far worse; for example, in Baku, Azerbaijan, nearly a quarter of all new TB cases (22.3%) were reported as MDR-TB.⁶ An estimated 5.4% of MDR-TB cases are extensively drug-resistant (XDR), or resistant to second-line TB drugs.⁷ Viruses also develop resistance. Antiretroviral therapy (ART) has revolutionized the treatment of people with HIV infection, but as ART becomes accessible to more people around the world, concerns about the widespread emergence of drug-resistant HIV increase. Finally, while the pandemic 2009 H1N1 influenza strain is usually sensitive to the antiviral drug oseltamivir, strains of the virus resistant to oseltamivir have emerged sporadically around the world. Resistance developed to other classes of influenza drugs as well. For example, NIAID scientists recently identified a case of 2009 H1N1 influenza that rapidly developed resistance to the experimental antiviral drug peramivir.⁸ To deal with this

⁵ World Health Organization. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 Global Report on Surveillance and Response. 2010:1. Available at http://www.who.int/tb/features_archive/world_tb_day_2010/en/index.html.

⁶ WHO, 7.

⁷ WHO, 2.

⁸ Memoli et al. Rapid Selection of Oseltamivir- and Peramivir-Resistant Pandemic H1N1 Virus during Therapy in 2 Immunocompromised Hosts. *Clinical Infectious Diseases* 2010;50:1252–1255.

increasing threat, we need a better understanding of how drug resistance arises and how it can be prevented and managed.

Antimicrobial resistance occurs universally in microorganisms as a natural and unavoidable manifestation of their ability to evolve and adapt to their environment. Microbes acquire the ability to resist antimicrobial drugs by undergoing genetic changes—either by mutation or gene transfer within or between species—that allow microbes to defend themselves against the onslaught of antimicrobial drugs. For example, these genetic changes may alter bacterial cell membranes so that drugs cannot enter the cells, modify the microbial proteins with which the drugs normally interfere, or enhance the microbe's ability to degrade or pump antimicrobial drugs out of the cell. The use of antimicrobial drugs can exert a selective pressure on a population of resistant and susceptible microbes, allowing resistant microbes to multiply and emerge unharmed as the predominant strains in a population.

While even the appropriate use of antimicrobial drugs creates a selective pressure for resistant organisms, there are additional societal factors that act to accelerate the emergence of antimicrobial resistance. For example, physicians may inappropriately prescribe antibacterial drugs to patients with viral infections because the patients expect—or demand—such treatment. Also, physicians must often use incomplete or imperfect information to diagnose an infection and thus prescribe an antimicrobial “just in case” an infection is present or prescribe a

broad-spectrum antimicrobial for a known infection when a specific antibiotic may have been sufficient. Once patients have antimicrobial drugs in hand, they may take the drugs incorrectly or fail to complete a treatment course such as by stopping the drugs once symptoms have been relieved. These situations contribute to selective pressure and accelerate the development of antimicrobial resistance. In hospital settings, critically ill patients often are given antimicrobial drugs because these individuals are more susceptible to infections. However, the use of antimicrobials in these patients can exacerbate the problem by selecting for antimicrobial-resistant pathogens. The extensive use of antimicrobials and close contact among sick patients in hospitals or other health care facilities creates a fertile environment for the spread of antimicrobial-resistant microbes. Lastly, the practice of adding antibiotics to agricultural feed is thought to promote drug resistance. More than half of the antibiotics produced in the United States are used for agricultural purposes; however, there is much debate about whether drug-resistant microbes in animals pose a significant human health burden.

Success against the emergence of antimicrobial resistance will require a multifaceted approach that includes increased surveillance, more judicious use of antimicrobial drugs, and increased research on the biology of the microbes, mechanisms of resistance, host responses, vaccines, diagnostics, and therapeutics. Antimicrobial resistance is a long-standing research focus of NIAID, and the Institute has engaged in important partnership efforts to further

basic and applied research and support public health efforts to manage antimicrobial resistance, including participation in the federal government's Interagency Task Force on Antimicrobial Resistance. NIH, through NIAID, co-chairs this task force, which is implementing an action plan to address the consequences of antimicrobial resistance, including rising health care costs and increasing morbidity and mortality from certain infections.⁹ The task force comprises representatives from NIH, the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Agency for Healthcare Research and Quality, the Department of Agriculture, the Department of Defense, the Department of Veterans Affairs, the Environmental Protection Agency, the Centers for Medicare and Medicaid Services, and the Health Resources and Services Administration. NIAID also participates in the Transatlantic Task Force on Antimicrobial Resistance (TATFAR), established in 2009 by presidential declaration. The main goals of TATFAR are to enhance communication and cooperation in antimicrobial stewardship, to promote prevention and control of antimicrobial resistance, and to enrich the antimicrobial drug development pipeline through research and regulatory strategies. The U.S. representatives are HHS, CDC, FDA, and NIH.

⁹ US Interagency Task Force on Antimicrobial Resistance. A Public Health Action Plan to Combat Antimicrobial Resistance. 2001. Available at <http://www.cdc.gov/drugresistance/actionplan/html/index.htm>.

NIAID RESEARCH

The problem of antimicrobial resistance requires a multi-pronged research strategy. NIAID supports and conducts research on many aspects of antimicrobial resistance, including basic research on how microbes develop resistance, as well as clinical trials that translate research from laboratory findings into potential treatments. NIAID works in concert with other federal agencies and partners with industry and nonprofit organizations to develop comprehensive programs aimed at controlling antimicrobial resistance.

Basic Research

NIAID supports basic research on pathogens, host-pathogen interactions, mechanisms of drug resistance, and identification of new antimicrobial targets and therapeutics. NIAID-supported researchers are studying how microbes cause disease, including how they colonize and invade the host, the toxins they produce, and how they avoid or overcome an attack by the host's immune defenses, as well as the mechanisms used by microbes to block antimicrobial drugs. For example, NIAID scientists have shown that genetic factors that enhance the ability of *Staphylococcus* to cause disease and those that enable drug resistance both can be transferred from one strain to another in a single event.¹⁰ This suggests that, in some cases, *Staphylococcus* strains that acquire

¹⁰ S Queck *et al.* Mobile genetic element-encoded cytotoxin connects virulence to methicillin resistance in MRSA. *PLoS Pathogens*. 2009;5(7):e1000533:1-12.

genes for antimicrobial resistance may simultaneously acquire the ability to cause more severe disease.

Knowledge of the nucleic acid sequences of a microbe's genes can bolster our understanding of antimicrobial resistance, reveal vulnerable areas in a microbe's genome that could be potential drug targets, and aid in the development of better diagnostic tests. By isolating the same species of microbe from different geographic locations or from different human populations and comparing their genetic characteristics, it is sometimes possible to identify when and where drug resistance first emerged in these species and what mechanisms of resistance these microbes are using. NIAID supports such efforts to understand microbial genomes through its biological resource centers and genomic sequencing services. Biological resource centers offer the research community a centralized and reliable source of a wide range of strains of microbes and reagents. Since 2000, NIAID has supported a resource center for *Staphylococcus aureus* that has been particularly useful for studies of antimicrobial resistance. The Institute's extensive genomics program has sequenced more than 750 bacterial pathogens that infect humans (including multiple strains of some pathogens); nearly all key drug-resistant species have been sequenced. Examples include bacteria that cause XDR-TB; several species of *Staphylococcus*; and several species of *Streptococcus*, including one that causes so-called "flesh-eating" disease. These resources not only serve basic microbial research but also facilitate the translation of basic findings into products with clinical applications.

NIAID-supported basic research not only helps elucidate the mechanisms of antimicrobial resistance but also facilitates the identification of potential targets for new antimicrobial drugs. Some of these targets have been licensed for further development. For example, resistance to the antimicrobial drug tetracycline is mediated by a protein "pump" that eliminates tetracycline from the bacterial cell. Through basic research, NIAID-supported scientists determined the crystal structure of this protein pump and identified the bacterial genes that encode for these proteins.¹¹ This knowledge has enabled private-sector partners to develop new drug candidates that block this pump.

Translational and Applied Research

Building on this foundation of basic research, NIAID supports research to advance the development of new and improved therapeutics, diagnostic tools, and safe and effective vaccines to control infectious diseases and limit the use of antimicrobial drugs. Before discussing NIAID's activities in this area, however, it is important to understand the current landscape of the pharmaceutical and biotechnology industries and the challenges that we face in developing new antimicrobial drugs and other products for clinical use.

In recent years, the number of large pharmaceutical companies that are involved

¹¹ Levy SB. Active efflux, a common mechanism for biocide and antibiotic resistance. *J Appl Microbiol* 2002; 92(Suppl):65S–71S.

in antimicrobial drug development has dwindled. Drug development is an expensive process, costing hundreds of millions of dollars to bring a product from concept to market. When it is evident that a given pharmaceutical product has a potential to make a profit, the large pharmaceutical companies are willing to engage in the economically risky research and development process and feed the “pipeline” of drugs. However, companies generally will not embark on this development effort if there is no guarantee of a return on investment. This frequently is the case with antimicrobial drugs. Large companies may be unwilling to invest scarce resources to develop a drug that may be used in a relatively small number of patients for short (10-day to two-week) treatment courses. Yet, we desperately need to develop new classes of antimicrobial drugs to ensure that we have viable treatment options for newly emerging resistant strains.

NIAID has engaged smaller companies and academic investigators who are working to identify new leads for vaccines, therapeutics, and diagnostics. Yet this community, by and large, lacks the resources to move a candidate antimicrobial drug all the way from preclinical testing through advanced development. NIAID continues to provide a comprehensive set of services for researchers to facilitate the efficient progression of a basic research concept to product development, including preclinical resources that are capable of reducing the risk to drug development entities at each key point in the drug development

process. These preclinical services include quality-controlled research reagents, animal models and clinical specimens to accelerate the rate of discovery.

In addition to these research resources, NIAID supports a broad portfolio of research to develop new antimicrobial drugs. These projects span the research and development spectrum from target identification through preclinical development and evaluation. For example, the Institute supports the discovery of new drugs for such novel targets as those involved in quorum sensing, a biological process that allows bacteria to group together into complex, difficult-to-treat communities called biofilms. NIAID-supported academic and small business researchers are also engaged in the development of new broad-spectrum antibiotics targeting both well-characterized and novel bacterial pathways. In addition, NIAID-supported researchers are actively pursuing alternative treatment approaches, such as therapeutic monoclonal antibodies, for many drug-resistant pathogens of concern, including *Staphylococcus aureus*.

NIAID also is supporting the development of rapid diagnostic methods to identify infectious microbes and the drugs that may be active against these microbes. These new and improved tools will facilitate targeted treatment with specific antimicrobial drugs and reduction in the use of broad-spectrum antibiotics, and also reduce the inappropriate use of antibiotics for viral infections. For example, researchers are working to speed the development of techniques to rapidly detect the microbes most often responsible for life-threatening sepsis and

community-acquired pneumonia. Also, a promising new TB diagnostic test developed with NIAID support is being evaluated in advanced-stage clinical studies. In addition, a new program will assist in developing rapid diagnostics for a number of healthcare-associated bacterial infections that are showing signs of increased drug resistance, including *Clostridium difficile*, *Pseudomonas*, *Acinetobacter*, *Enterobacter*, and *Klebsiella*.

Effective vaccines against drug-resistant microbes would also reduce the occurrence of antimicrobial resistance and alleviate the need for new antimicrobials. For example, vaccines against *Streptococcus pneumoniae* have reduced the rate of invasive pneumococcal disease among vaccinated children under the age of five by 94% in the United States.¹² A similarly effective vaccine against staphylococcal infections would reduce the need for new antimicrobial drugs. Several groups of NIAID-supported researchers have been developing and assessing candidate *Staphylococcus* vaccines, including those targeted at surface proteins and surface polysaccharides. Several of these candidate vaccines have been shown to be protective against staphylococcal infection in animal models.¹³ Academic and government researchers have become partners in this endeavor, and NIAID will continue to encourage and support their efforts.

¹² US Department of Health and Human Services. The Jordan Report: Accelerated Development of Vaccines. 2007:109. Available at <http://www.niaid.nih.gov/about/organization/dmid/Documents/jordan2007.pdf>.

¹³ McKenney, D. *et al.*, Broadly Protective Vaccine for *Staphylococcus aureus* Based on an in Vivo-Expressed Antigen. *Science*. 1999 May 28;284(5419):1523-7; and Stranger-Jones, YK *et al.*, Vaccine assembly from surface proteins of *Staphylococcus aureus*. *PNAS*. 2006 Nov 7;103(45):16942-7.

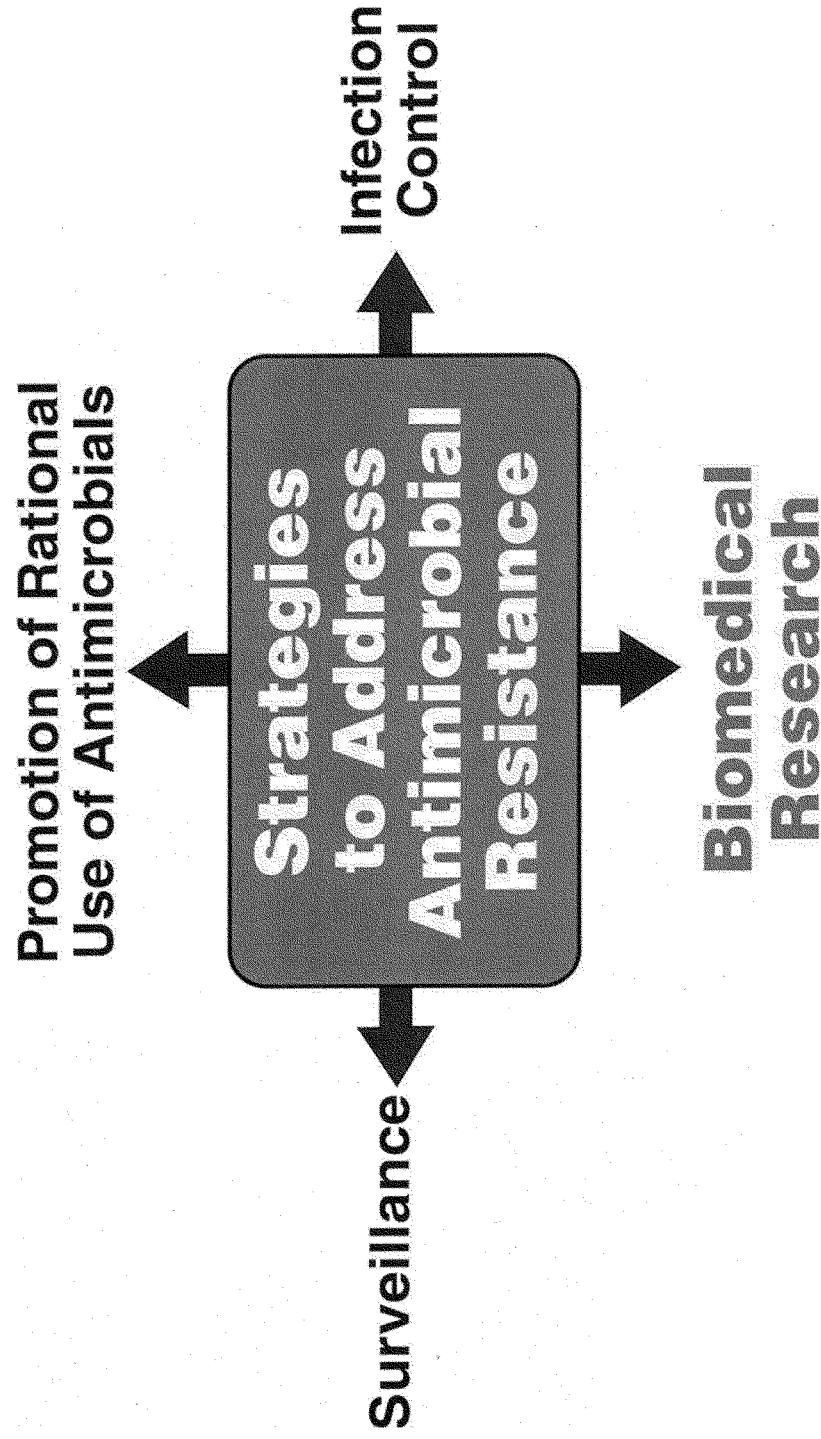
Another important area of translational research for NIAID is the evaluation of effective treatment strategies for endemic and emerging infectious diseases using existing drugs. Such treatment strategies are needed to limit the development of antimicrobial resistance. Well-designed and executed clinical trials that address standard-of-care antimicrobial treatment versus shorter durations of therapy or no antimicrobial therapy at all are crucial to the rational use of antimicrobials. Because pharmaceutical companies have little incentive to conduct clinical trials using generic drugs, NIAID plays a key role in ensuring that the value of each potentially active drug is fully realized by organizing and supporting such studies. If generic antimicrobial drugs can be effective front-line agents, newer antimicrobials can be held in reserve for more serious drug-resistant infections.

In an example of such an effort, NIAID in 2008 launched a new initiative, *Targeted Clinical Trials to Reduce the Risk of Antimicrobial Resistance*, to target disease areas in which there is a risk of developing antimicrobial resistance. This solicited research program supports the design and conduct of clinical protocols that test the safety and effectiveness of different therapeutic approaches and regimens. The ultimate goal of the studies is to provide data for the most prudent use of existing antibiotics in order to reduce the probability of the emergence of drug resistance by minimizing unnecessary drug exposure. NIAID plans to support additional clinical trials of strategies aimed at reducing

antimicrobial resistance in a similar initiative in FY 2011. NIAID also continues to support two contracts under the *Clinical Trials for Community-Acquired Methicillin-Resistant Staphylococcus aureus (CA-MRSA)* initiative. These contracts support clinical trials to determine the optimal treatment of uncomplicated cases of skin and soft tissue infections caused by CA-MRSA using existing off-patent antibiotics.

CONCLUSION

Antimicrobial resistance is a perpetual challenge in our attempts to maintain the upper hand in the perpetual battle between microbes and the human species. NIAID is addressing the problem of antimicrobial resistance by offering tools and resources to the scientific community to facilitate the highest-quality research and provide a flexible infrastructure to respond to emerging needs; supporting basic and translational research likely to lead to clinical applications that will reduce the prevalence of antimicrobial resistance; encouraging development of broad-based vaccines and therapeutics that are effective against multiple pathogens; and supporting the development of diagnostic tools that will enable clinicians to make informed treatment choices. The efforts of NIAID and our partners from the public health, research, medical, and pharmaceutical communities are critical to addressing this daunting challenge.



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The Research Agenda of the National Institute of Allergy and Infectious Diseases for Antimicrobial Resistance

N. Kent Peters, Dennis M. Dixon,
Steven M. Holland, and Anthony S. Fauci

■ Basic Research

■ Clinical Research

■ Translational
Research/Product
Development

Basic Research Activities

■ **Studies of the microbe**

- Genetics and genomics
- Mechanisms of resistance
- Target identification

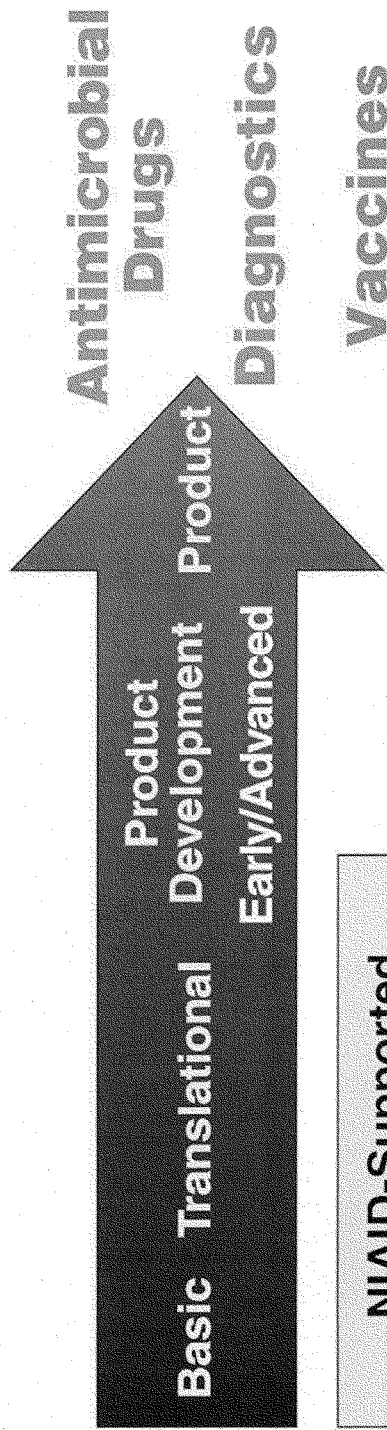
■ **Studies of host-pathogen interaction**

- Pathogenesis
- Immunology

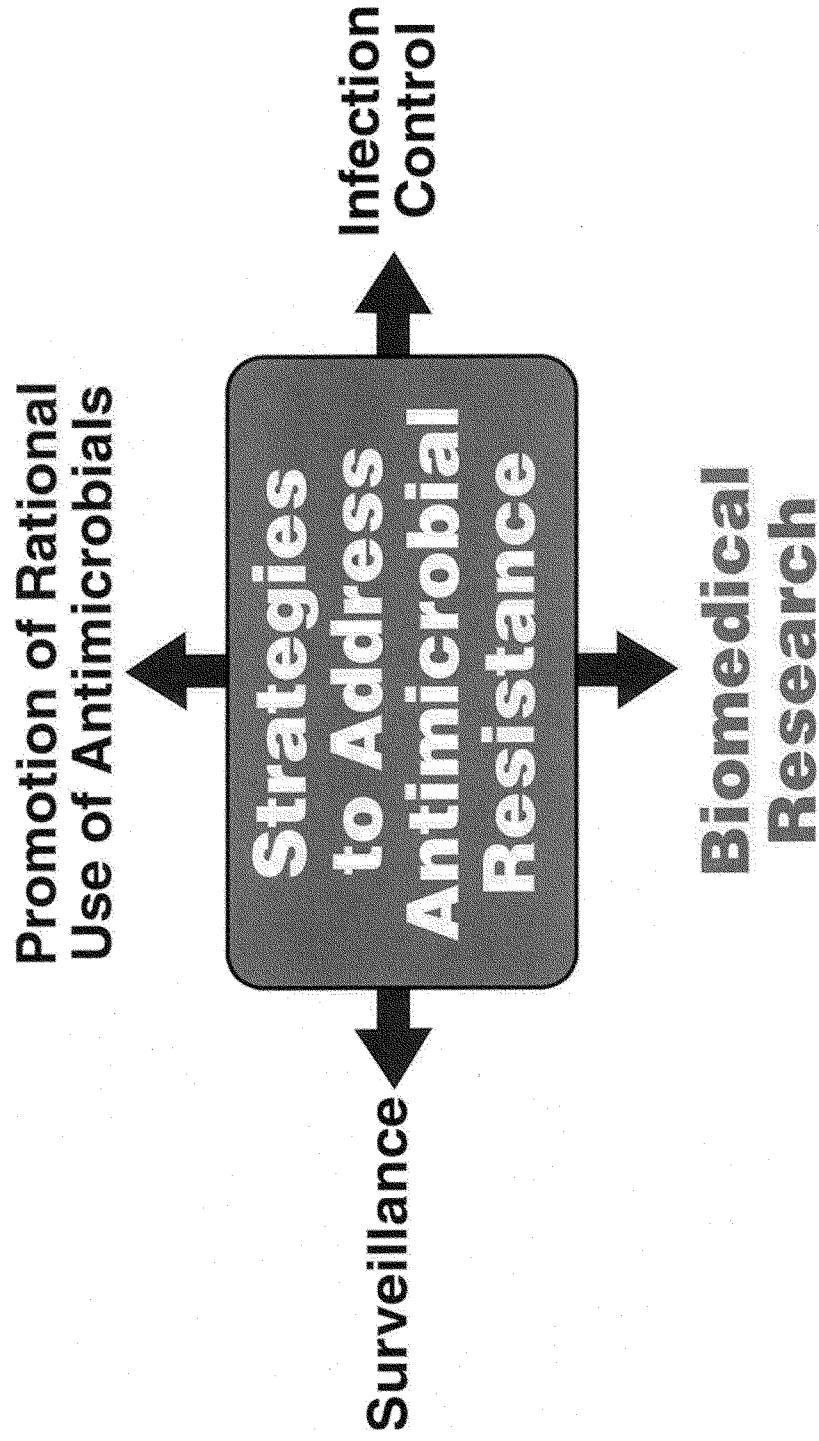
Clinical Research Activities

- **Focus on problematic pathogens, e.g., MRSA**
- **Improve treatment practices**
 - Is treatment even needed?
 - How much?
 - How long?
- **New uses for older, 'off patent' drugs**

Antimicrobial Product Development



NIAID-Supported
Research and
Research Resources



Mr. PALLONE. Thank you, Doctor.

Now we will have questions, 5 minutes, or in some cases 8 for some people who waived their opening statements.

I will start with myself for 5 minutes. I guess I am really addressing this to both of you, because both of you agree that resistance occurs wherever antimicrobials are used, whether they be in the community, on the farm, or in health care. I don't have time to explore all of these, so I am going to concentrate on resistance in the community and hope that my colleagues will talk about farm use or use in other, in health care settings.

Let me focus on the community. You both describe ways in which antibiotics are prescribed in the community, and to be clear, when say use in the community, I mean outside of the hospital. Dr. Fauci's testimony describes the fact that physicians often prescribe antibiotics to patients who have viral infections, not bacterial infections, simply because patients have come to expect or even demand treatment with antibiotics, even when they can't help. So my question is, how concerned should we be about these practices? Or I guess to put a bluntly, are doctors using antibiotics inappropriately and too frequently, and if that is true, what can we do about it? Either one.

Dr. FRIEDEN. Thank you very much. The Centers for Disease Control has a survey called the National Ambulatory Medical Care Survey, or NAMCS. This is one of our main instruments for determining what doctors' practices are and allows us to check over time what happens in clinical encounters. It is one of the few systems we have that is nationwide and allows us to monitor the quality of health care.

In these surveys, we have seen an improvement in that there has been a smaller proportion of patients who come in with, for example, upper respiratory infections, who leave with antibiotics, which they shouldn't leave with.

It still remains too common a practice. The challenge is educating physicians and then having a monitoring system in place to give feedback to clinicians.

One of the things that will greatly facilitate that work is the expansion of electronic health records where clinical decisions support systems can remind doctors that this isn't a good use of antibiotics or can track and give feedback on what the behavior of individual clinicians are. So we need to both have the monitoring; we need to intervene by educating better; and we need to put into the process of health care automatic ways of telling doctors or helping doctors to make the right decisions.

I don't know, Dr. Fauci.

Mr. PALLONE. I have to say, it is hard for me to relate to these questions because I never want to go to the doctor, and when I go, I always try to avoid having them give me anything, but I know it is a common practice.

Go ahead, Dr. Fauci.

Dr. FAUCI. Actually, I would agree completely with Dr. Frieden.

Also, it is an issue of getting better, sensitive point-of-care type of diagnostics, where you could really underscore and confirm, because sometimes, when it physician a talking to a family member and they say, you have got to put my child or my husband or what-

ever on antibiotics because I know they either have an infection or are going to get one, and if you could in the office show immediately that that person doesn't have a bacterial infection, I think it would go a long way to convince the person that the decision the physician is making is the appropriate decision.

Mr. PALLONE. Well, what is the Get Smart campaign that the CDC has been working on, Dr. Frieden? Do you want to talk about that? And I guess you haven't recommended that it continue in the budget, so do you want to say why, or what it is and why you are not recommending that we fund it again?

Dr. FRIEDEN. The Get Smart campaign is an educational intervention that works with physicians to try to reduce unnecessary or injudicious use of antibiotics. We are faced with significant budget constraints. We are not able to continue or expand all the programs which we would like to continue or expend, and we are committed to maintaining and strengthening work to reduce antimicrobial resistance in every way that we can within our budgetary limitations.

Mr. PALLONE. So it is not that, the reason you haven't recommended continuing it, it is not because it isn't a good thing. But just it is not that important compared to other priorities. Is that fair to say?

Dr. FRIEDEN. We believe the program is effective, but we are not able to include it in the current budget request.

Mr. PALLONE. So the answer is yes, right?

I want you to reflect that you said yes, not me.

The gentleman from Illinois, Mr. Shimkus.

Mr. SHIMKUS. Thank you, Mr. Chairman. I am trying to get my handles around this, I think, conjecture that is making the claim that antibiotic use in animals is translated in changing the resistance in humans, which in one of the testimony didn't—just kind of said that casually. There are assumptions made on the other side. Is there any peer-reviewed CDC study that shows a direct correlation to support that assumption?

Dr. FRIEDEN. It is clear that any antimicrobial use will result, virtually any antimicrobial use, will result in emergence, persistence and spread of antimicrobial-resistant organisms, so the use of antibiotics in farm animals will generate the development and spread and persistence of antimicrobial resistance among the farm animals.

Your question relates to whether there is evidence that that resistance has spread to humans. We do know there are many interconnections between human and animal health. There is experience from the several countries in Europe where prescription of an antibiotic that is related to Vancomycin was shown to be associated with an increase in Vancomycin resistance among humans. That was experienced in the European Union countries. That antibiotic was banned in the European Union, and the resistance levels then declined.

There is no scientific doubt about the theoretical possibility of transfer of parts of viruses, transpose onto other ways that you could spread antibiotic resistance from animals to people. There also are many outbreaks of—

Mr. SHIMKUS. I only have a limited amount of time.

But the question is, do you have peer-reviewed scientific research that shows this connection? Do you, the CDC?

Dr. FRIEDEN. So what I said is there is peer-reviewed research in Europe.

Mr. SHIMKUS. I am talking about in—

Dr. FRIEDEN. In the United States, it has not been, to knowledge, documented as having occurred.

Mr. SHIMKUS. Thank you.

My point is this, and I use this across the board in this committee, that running on emotions is running on emotions; running on science and fact, peer-reviewed replication is critical if we are going to move public policy. And we don't seem to want to do that here in Washington.

Do you know the Danish study? Have you followed the Danish example of banning antibiotic use in livestock?

Dr. FRIEDEN. I am not familiar with the specific study.

Mr. SHIMKUS. Well, what they did—not study—they actually did, they actually banned antibiotic use in livestock, and what they found is a couple of things: Antibiotic resistance, even though it was banned, increased in humans, issue one. Issue two was antibiotic use increased in the use of animals because it was then used therapeutically. So then the other question that has to be asked is, would we rather have in the livestock consumption industry antibiotic use for healthy animals, or would we rather be using antibiotic use treating sick animals that then eventually go in the food chain?

So these are all part of this debate, and I just want to caution people to make this jump on this without scientific research, peer-reviewed study that really makes a direct correlation, and I think, again, my friends would want to do this.

One of the issues of this is the industry; how do we get industry, in one of these charts, to develop that? And we have done that with different types of drugs. And Chairman Waxman has been very good PDUFA and stuff. How do you get industry to market in areas we want to do?

I will tell you one thing you don't do, you don't add an additional \$27 billion tax to an industry you are trying to incentivize to create life-saving antibiotics, which we just did in the health reform bill.

And I am concerned that if we go and take antibiotic use out of livestock, if you believe in economics 101, supply and demand, you reduce another supply avenue for selling antibiotics. Then you limit the ability of a return on investment on those companies that are producing it to begin with.

So this is an important hearing, and there are a lot of scientific aspects of this. But I would just plead that we make sure that any action we do is not based upon emotion, but we do peer-reviewed science.

With that, Mr. Chairman, I yield back my time.

Mr. PALLONE. Thank you, Chairman Waxman.

Mr. WAXMAN. I am trying to understand the science. It seems to me, from what I have understood, that when you use an antibiotic over and over and over again inappropriately—by inappropriately I mean not to deal with the bacterial infection but for other reasons—whether it is used on an animal or on people, it increases the

chance of resistance to the antibiotic. Is that the correct statement of the science, whichever of you would like to say?

Dr. FAUCI. Yes, it is. That is just the nature of how organisms are involved. You put any pressure on them, they will select for survival, and survival is resistance. It is just a natural phenomena of the interaction of a microbe with a pressure you put on the microbe. That is the scientific reality.

Mr. WAXMAN. So to avoid antibacterial-resistant microbes, we should be sure that we are using the antibiotics where it is necessary and not using it where it doesn't have a therapeutic purpose. Does that make sense?

Dr. FAUCI. Correct.

Mr. WAXMAN. You are both answering yes.

Dr. FRIEDEN. There is no disagreement about the use of antibiotics to treat infections, nor is there disagreement about the theoretical risk of promotion of drug resistance through the widespread use of antibiotics.

Mr. WAXMAN. Now, I don't know of anybody who would argue that we shouldn't give an antibiotic to an animal that has an infection, because it is for a legitimate therapeutic purpose. I haven't heard anybody argue that we shouldn't give an antibiotic to a person who has a bacterial infection if that antibiotic could stop that bacterial infection.

But if you give it to large numbers of animals for nontherapeutic purposes, let's say as a preventative, and if you give it to kids who may have a virus and not a bacterial infection, aren't we running a greater risk of resistance?

Dr. FRIEDEN. Yes, our basic principle is to promote judicious use of antibiotics. The Institute of Medicine has called for the phasing out—

Mr. WAXMAN. Is this from science from Europe, or is this science that is accepted here in the United States?

Dr. FRIEDEN. Public health authorities, including the Institute of Medicine, have called for phasing out of uses to promote growth. There is no disagreement, as you note, about use for treatment or evidence-based prevention of infections.

Mr. WAXMAN. Now, Dr. Fauci, I think you particularly raised the question that we don't have companies making new products where we need new breakthroughs in antimicrobials. And it appears to be a market failure.

Now I don't accept the idea that if we used it in a more widespread way, that that would encourage the drug companies to make more antimicrobials. It sounds to me like we are running a risk of making more bacterial-resistant diseases. It might make them more money, but I am not even sure then, because the product won't work after a while.

We have had market failures in the past, and you and I were in this room many years ago when we first heard about the AIDS epidemic, and we are trying to deal with it. And there was a small patient population. We didn't know what resources we had to treat them. In this room, we had many hearings on people with rare diseases, and it didn't offer profit potential for a lot of the companies to put efforts into drugs for people with—a small number of people, in effect, for diseases.

We came up with the Orphan Drug Act. We have tried to give other incentives for research and development. We have a patent law. We have removal of time that is lost at FDA to help the producers. Do you have any other ideas on how we can correct what appears to be a market failure? Is it because it is just not profitable to produce these antimicrobials, because it is just too few seldom used and not widespread enough?

Dr. FAUCI. Well, certainly, that is, Mr. Waxman, one of the major reasons why not. Pharmaceutical companies, who do great things, are driven by the profit margin and what they have to answer to, to their boards. And if a company has a choice in making a major investment, to develop a new product, a new drug, it is several hundreds of millions of dollars, an average of around \$700 million, which includes a risk that they take in the development of the product. So if they are going to make a choice of making a product that a lot of people are going to take every day for the rest of their lives, a lipid-lowering agent or whatever you have, they are going to lean towards that rather than to make a new product that a relatively small proportion of the population will use maybe 10 days to 2 weeks out of the year and then, because it happens naturally, that after a period of time, there is going to be resistance against that antimicrobial.

So from the interactions that I have had with industry, we need to work with them in partnership to figure out what incentives that we can do. We at the NIH, I showed that slide, we fundamentally do basic and clinical research, but what we are doing now is offering some of our research resources, our animal model capabilities, our reagent repositories, and even our clinical trial capabilities to lessen the risk of an investment on industry to give them more of an incentive to get involved. And I am sure there are other types of financial incentives that can be worked out in an appropriate way. But I really do think we need to push the envelop a bit in getting rid of some of disincentives for getting them involved.

Mr. WAXMAN. Just one last question, Mr. Chairman.

I assume this was a problem even before the health insurance bill was passed last month?

Dr. FAUCI. Yes, sir.

Mr. SHIMKUS. It is probably a bigger problem now though. I yield back.

Mr. PALLONE. Thank you, Chairman Waxman.

The gentleman from Texas, Mr. Burgess.

Mr. BURGESS. I am struggling to keep from taking the bait.

Let me depart from what I was going to do for just a moment, because the whole issue of profitability—penicillin, a truly wonderful discovery. Sir Alexander Fleming, appropriately knighted by the king or the queen, appropriately honored with a statue erected by the bull fighters in Spain, but really it was an American manufacturing company, I think it was Pfizer, in the Second World War, that changed penicillin from kind of a parlor trick that inhibited the bacterial growth on an agar plate to one of clinical utility for thousands and indeed hundreds of thousands of people because of the ability to create a lot of it in the manufacturing process that they developed in the Second World War.

You argue from purely a profit motive, they would have kept the numbers of doses of antibiotics low and kept the price high. But they went with the mass production, and as a consequence, soldiers during D-Day were spared life and limb because that they had readily available, abundant, cheap penicillin, which you alluded to on your slide worked well until that darn bacteria figured out that they could chew up that beta-lactam ring and survive quite nicely with their cell wall intact in spite of the penicillin. So it is not always a profit motive.

I am telling you stuff that you know better than I. This was a seminal event in American medicine. It fundamentally changed the way all of them and subsequently all of us were trained and practiced in the generations that followed. I mean, it truly was a life-altering event.

But let's think for just a minute, Dr. Fauci, the new molecular entities for broad-spectrum antibiotics that have been introduced by the FDA in the last 10 years, do we have an idea of how many new drugs have been produced?

Dr. FAUCI. Very few.

Mr. BURGESS. Broad-spectrum antibiotics.

Dr. FAUCI. New antibiotics, very few; I mean, handfuls.

Mr. BURGESS. I have a list of 10. Does that sound right?

Dr. FAUCI. That sounds about right.

Mr. BURGESS. But I have got, my staff has gotten me about 25 pages of antibacterials that have been approved for new indications, and you referenced that in your slide; new chores for old drugs that we might find. But these older drugs are not necessarily helping us fight the war against resistance; they are just an antibiotic that was found to have an indication for something else.

So the problem is, if there are only 2—I mean 10 truly new antibiotics produced in the last decade, and then another document that tracks \$92 million in Federal research at your institute, Dr. Fauci, in fiscal year 2009 alone on antibiotics research—does that sound like a fair figure?

Dr. FAUCI. No, actually, on antimicrobials research, we do about \$790 million of research; on resistance specifically, we do about 200-plus.

Mr. BURGESS. OK. So my numbers were low.

Dr. FAUCI. Right.

Mr. BURGESS. So taxpayers are pumping in a lot into the pipeline, and we are getting out at the other end approximately the average of one new antibiotic a year? Is that—am I making a correct—

Dr. FAUCI. Now—

Mr. BURGESS. Well, I would just ask the question, do we have a problem with—it sounds like we have a problem with the pipeline, so where in the pipeline is the problem? Is it the dollars we are pumping in? Is it the research we are putting into it? Is it the FDA? Where is the problem in the pipeline?

Dr. FAUCI. Well, I think, Mr. Burgess, the problem in the pipeline is right in the middle of that arrow that I showed in one of my slides, and that is that the pharmaceutical companies, as much as we can do research, we can sequence now, as I mentioned—I mentioned that for a reason. We can sequence a thousand microbes

for a reasonable price really, really quickly. We can pinpoint all the different targets that could serve as a target for the development of a drug. There is not an overwhelming incentive on the part of companies to get involved in developing a new antimicrobial.

That is why, in answer to the question of Mr. Waxman, I emphasized that there are a lot of issues that go into why we don't have a lot more drugs for the amount of fundamental research money that we put in, but one that is really paramount is to get the companies involved and incentivized into wanting to make them. And I don't have the complete answer for that. We are trying the things that I mentioned in response to Mr. Waxman's question, but we need to do better than that.

Mr. BURGESS. Yes, I do not want to cut you off, because I know your position in the scientific world and mine, but I need to ask you this, so market incentives, are those always dollars? Or are there changes we can make at the regulatory level that would help the environment?

Dr. FAUCI. The FDA right now is putting a considerable effort in pushing what is referred to now as regulatory science; in other words, to get them involved in developing bioassays, biomarkers, new clinical trial designs that would facilitate the development of any product, including a product that is geared against a resistant microbe. So there is something we could do at the regulatory level, and the FDA is really trying very hard to push that agenda.

Mr. BURGESS. Well, I am going to ask Mr. Shimkus this question, because I can't help myself. We put \$27 billion new tax on to the industry under the health bill, so is that likely to have a positive or negative effect on the pipeline problem that we have?

OK, we will go to the next question. Does your institute track how much of their research invested has translated into applications and approvals at the FDA? So what kind of data does the National Institute of Allergy and Infectious Diseases have that could be shared with this subcommittee?

Dr. FAUCI. When you say information, everything we do is transparent. You can get any information that you want. But I think you were asking—

Mr. BURGESS. The applications and approvals that then go over—the applications that go over to the Food and Drug Administration, and the approval of those applications that come out at the other end.

Dr. FAUCI. As a product?

Mr. BURGESS. As a product.

Dr. FAUCI. See, that is a question that is difficult if not impossible for me to answer because we don't control the concept to product. We do fundamental research that might develop the concept that can be pushed to the pre-clinical, but if we were solely responsible for soup to nuts, I could give you an exact answer.

Mr. BURGESS. All right.

Dr. FAUCI. But we are not. We have to punt it to the pharmaceutical companies. That is the point.

Mr. BURGESS. But on the slide that one of you showed with the Methicillin-Resistant Staph Aureus and the numbers going up and now community-acquired. I think it is a huge problem in jails, and it is a huge problem in dormitories and homeless shelters. It seems

like the market is being created, and none of the companies are interested in being the first one to cross the finish line with the silver bullet that wipes out MRSA? Where is the Paul Ehrlich of our generation?

Dr. FAUCI. I would think, personally, that a company would be very interested in getting in it. They balance the risk for the benefit. And as I mentioned, there is a considerable risk for a company to put several hundreds of millions of dollars to develop a product. And what I would be proposing is that somehow we in the Federal Government help alleviate that risk by doing some of the things that I mentioned we can do, but we are not the only player in this.

Mr. BURGESS. Let me just ask you a quick question on hospital-acquired infection. My epidemiologist that I rely upon a lot back in Dallas is Bob Haley, and he told me early on that in order to fix something, you have got to be able to measure it; in order to measure it, you have to drive out fear. You can't have people frightened to report data to you, or you will never have the accurate data to measure. Is that a valid observation?

Dr. FRIEDEN. Yes. In fact, we have expanding reporting of hospital-associated infections. Already 28 States report mandatorily, and about half of all hospitals in the country.

Mr. BURGESS. Just briefly, to the point, what is the best approach here? I have always felt that of the 28 States that report, you know, find the best practice or set some floor, perhaps at the Federal level. Let you guys deal with the de-identified and aggregate data so you are not getting into patients' privacy issues, so that you have the data to study, as opposed to what we seem to see here at this committee sometimes looks very, very punitive. I will just tell you, as someone who practiced medicine for years, if you make it punitive on the doctors, we will find a way to obscure things for you, so you don't pin it on us. I am over-simplifying, but really, that drive-out-fear concept is one I think we need to embrace, CMS needs to embrace, and I would encourage you to continue to work along that line. I think that is where the ultimate answer for this problem lies.

Thank you, Mr. Chairman, for your indulgence. I will yield back.

Mr. PALLONE. Sure.

Chairman Dingell.

Mr. DINGELL. Thank you, Mr. Chairman.

Gentlemen, welcome to the committee.

I am curious, has there ever been a definitive study on the impact on microbes and other similar creatures to define what the impact on them might be in terms of resistance to antibiotics by reason of using these antibiotics in animal feed and for other similar uses?

Dr. FRIEDEN. There are clear studies that show that use of antibiotics in animal feed increases resistance among animals.

Mr. DINGELL. Among animals or amongst bacteria?

Dr. FRIEDEN. Resistance in the bacteria that resident within animals.

Mr. DINGELL. Would such a study be useful? I mean, a thorough-going analysis of the matter as opposed to just bits and pieces.

Dr. FRIEDEN. There is an increasing body of evidence that looks at where antibiotic resistance emerges and how it spreads. An ad-

ditional evaluation of that to understand the spread from animals to community I think is something that many groups are working on. There is not right now definitive evidence. There is a clear understanding that the more judiciously we use antibiotics, the longer we will be able to continue to use them effectively.

Mr. DINGELL. Now has ever any work been done to define what is efficient use of antibiotics in animal feed? In other words, how much is necessary? How much is too much? How much doesn't work? How much we could do without, and what would be the benefits of the different steps? Has there been any study of this kind?

Dr. FRIEDEN. As the director of the Centers for Disease Control and Prevention, I would have to defer to my colleagues at the FDA and USDA on those questions.

Mr. DINGELL. Who else? I don't see the FDA here in the room. Who has authority to do this kind of research or to fix this level of tolerance or content or the time at which these antibiotics are fed or inserted into animal feed?

Dr. FAUCI. Mr. Dingell, I would imagine that the most appropriate venue to do that would be through the U.S. Department of Agriculture.

I mean, that is an obvious question of great importance for people who—

Mr. DINGELL. Do they have the authority to fix this or not?

Dr. FAUCI. I don't know if I could answer that definitively. I cannot imagine that they don't have the authority to do a study if they would want to do it.

Mr. DINGELL. I can imagine, A, that they don't have authority and, B, that they don't use it if they do.

Now let me go into some other questions. CDC's overall budget would see a 5 percent cut, and the antimicrobial resistance program would receive a cut of more than 50 percent.

Gentlemen, do you think these cuts would negatively impact the work you are doing related to antibiotic resistance, especially support for State and local surveillance, prevention and control efforts and the Get Smart campaign?

Dr. FRIEDEN. Mr. Dingell, we are committed to doing as much as we can.

Mr. DINGELL. That is not an answer to my question. Is that level of cut going to hurt what you are doing?

Dr. FRIEDEN. It will be difficult for us to continue current programs at that level.

Mr. DINGELL. Would you tell us, would you submit for the record the level of your request for financial support for these programs in the budget? And also submit the amount that you have been given for the last 3 years and for the coming 3 years.

Dr. FRIEDEN. We will provide that information.

Mr. DINGELL. All right.

Now, you have addressed this slightly, but I would like a little more on it. There appears to be much debate over whether the practice of adding antibiotics to agricultural feed is sought to promote drug resistance. What does current science and surveillance tell us on this point? Is there a direct link, and what is it?

Dr. FRIEDEN. I think we know that theoretically there is a risk. The literature that we have reviewed outlines a problem that clear-

ly emerged in Europe. I am not aware of evidence in this country that has documented the spread from animals to humans, feed animals to humans, we have of course seen spread from animal to humans in a wide variety of infections. But we know that the more antibiotics that are in the environment, given to animals and people, the higher the selective—

Mr. DINGELL. Let me try, sir, to try to reduce this. I am getting the impression from what you two gentlemen are telling us here is that we really don't know what the nexus between the feed is and the feed with antibiotics is, and when there is a point of danger, and what is the level of danger, and what research is going on? What comment do you make on that statement?

Dr. FAUCI. From your questions, Mr. Dingell, and the questions we have from the other members, there is no doubt in anyone's mind that if you give antibiotics to anybody, any animal, and you do it chronically, that resistance to microbes will evolve.

I think the question that Mr. Shimkus brought up and that others is that, what is the evidence that if you give it to an animal for feed and resistance develops in microbes in that animal, that that resistant microbe will then spread to a human? And I think—

Mr. DINGELL. It might spread to other microbes, or it might spread to humans.

Dr. FAUCI. Right.

Mr. DINGELL. Rather than coming to the conclusion, you don't have much information on that account.

Let me get to this, because time is limited here. The Food and Drug Administration withdrew its approval for the use of fluoroquinolone antibiotics, that is FQs, in poultry. Are there any preliminary, any RMS surveillance reports that would indicate the impact of FDA's decision? Yes or no.

Well, would you—

Dr. FRIEDEN. We would have to get back to you on that to give you the most recent information.

Mr. DINGELL. Would you submit that for the record?

Dr. FRIEDEN. Absolutely.

Mr. DINGELL. Dr. Fauci, in addition to the work that your agency is currently engaged in with the smaller manufacturers, what additional steps can or should be taken to incentivize participation of industry, both large and small manufacturers, in developing new effective therapies for these drugs-resistant infections?

Dr. FAUCI. There are several things that can be done, Mr. Dingell. One is to make available to the company some of the assets and capabilities that we have in the government, including in my own institute, and that is various assays, reagent repositories, animal models and clinical trial capabilities; and then also to reach out and partner with them on the risk for the advanced development, something that that they generally do themselves. If we could diminish somewhat the risk they take, I think there will be much more of an incentive for them to get involved.

Mr. DINGELL. Is this question raised at any point in the government regulatory structure when you address the questions of whether or not or how much antibiotics should be used in animal feed? And if so, who has authority to do that?

Dr. FAUCI. Well, we certainly, that is not something that we as a research institution get involved in.

Mr. DINGELL. Here is the purpose of for my question, if they are putting too much in the animal feed and not using it wisely and don't have any particular constraints on its use, we are obviously increasing a risk if a risk there is; is that right? Clearly, the answer to that is yes.

Dr. FAUCI. Well, I am not sure what—

Mr. DINGELL. Would you say there is no risk in this?

Dr. FRIEDEN. Certainly—

Dr. FAUCI. If—

Mr. DINGELL. So we agree. Doctor, my time is limited, and I am trying to get this through here. So who has the responsibility for defining the level of risk and defining what ought to be done to protect the American public and the world against runaway infections caused by antibiotics that no longer work on drug-resistant bacteria? Does anybody have this authority or not?

Dr. FRIEDEN. Both the FDA and the USDA.

Mr. DINGELL. They do?

Dr. FAUCI. Yes.

Mr. DINGELL. The Orphan Drug Act was written in 1983 to encourage pharmaceutical companies to develop drugs for diseases that have a small market. This was done through a series of incentives. FDAAA, the 2007 reauthorization of the FDA user fee programs included provisions intended to strengthen the antibiotic pipeline through the orphan drug program. How effective has the orphan drug program been in your research and development work related to drug-resistant bacteria? And what cooperation has it induced on the part of manufacturers, feed manufacturers, or antibiotic producers or farm organizations?

Dr. FAUCI. Certainly, the Orphan Drug Act has incentivized the development of drugs of various types.

Mr. DINGELL. Now you have said that this is incentivized. What particular incentive has it produced to do research and development work related to drug-resistant bacteria?

Dr. FAUCI. The basic research that we do feeds into a company wanting to develop a drug for a, quote, orphan disease, a disease that is a relatively rare disease.

Mr. DINGELL. Do you make it available to them automatically? Is it made available to them by the FDA, or is it available by the Department of Agriculture or just sort of catch as catch can, and we hope they learn about it in some way so that they can do something about it? And who is in charge of that?

Mr. PALLONE. Mr. Chairman, that has to be the last question. He can answer this, and we will move on.

Dr. FAUCI. When we provide the assets that we have, we essentially make it available for anyone who needs it or has a reasonable project.

Mr. DINGELL. So if they think they need it, they come by and see you.

Dr. FAUCI. They do.

Mr. DINGELL. If they don't think they need it or there is no incentive for them to come by, they don't come by.

Dr. FAUCI. Correct.

Mr. DINGELL. Well, Mr. Chairman, this is a very interesting subject. I commend you for the hearing. I think we have to have some more, got to learn a little more.

I don't want our two very fine panel members to think that I have in any way been trying to demean them. I think that we need a great deal more knowledge on this before I am going to feel comfortable on the subject.

Mr. PALLONE. Thank you.

Gentleman from Missouri, Mr. Blunt.

Mr. BLUNT. Thank you, Mr. Chairman.

I agree with the chairman emeritus; this is a good hearing. I may take a different tact on this same topic.

Several questions came to mind as Chairman Dingell asked his question, and one would be do, we know that the food chain, the animal food chain, doesn't get less safe if you don't put certain antibiotics in the food, in the system; how do we know that? I mean, there are veterinary guidelines on these antibiotics, so how do we know that it doesn't have the opposite effect?

Dr. FAUCI. Mr. Blunt, if you don't mind, I would like to finish the answer to a question that might feed into what you were saying. The issue is, if you give antibiotics to anybody, an animal, a human, or whatever, you will unequivocally ultimately induce the recurrence of a resistant microbe. The real question—

Mr. BLUNT. Isn't it true that antibiotics to animals, you don't have much of a chain of lifespan here in animals.

I agree with you, if you and I took a antibiotic for 30 years or 3 years, it might make a difference. But we both know that that is the not the processing system for animal, but let's not go there, that you are going to induce in the individual animal itself an antibiotic reaction because they have had antibiotics for a long time, because the process just doesn't go that long.

Dr. FAUCI. With all due respect you, can—I can have an upper respiratory tract infection, and I can take an antibiotic that is sub-optimum or not the right antibiotic, and in 10 days or less, I could have a resistant microbe.

Mr. BLUNT. Does that mean you shouldn't take any antibiotics?

Dr. FAUCI. No, I am not saying that.

Mr. BLUNT. I think you are answering Mr. Dingell's question instead of mine. Aren't there American veterinary guidelines on antibiotics to animals?

Dr. FAUCI. That is not my area of expertise of antibiotics to animals.

Mr. BLUNT. Then why wouldn't that be something you would look at as you look at this Get Smart, know when antibiotics work on the farm program; why wouldn't you look at the veterinary medical association's guidelines on judicious use of antibiotics if it is not your area of expertise?

Dr. FAUCI. No, actually, Mr. Blunt, that is actually more of a CDC issue than—no, it is. I am not trying to pass it off.

Mr. BLUNT. Dr. Frieden may answer the question.

Dr. FRIEDEN. Thank you.

The basic question is, we know that there is no disagreement about certain things, so we should start with those. First, we know that no one disagrees with the need to treat infections in humans

and animals that are responsive to those infections. Second, there are evidence-based preventive antibiotics that are sometimes needed in the situation of outbreaks or other similar situations. Third, there is a clear theoretical risk of—well, there is a known fact that the more antibiotics you give, the more resistance you will have.

The theoretical risk is whether those resistant organisms that emerge in animals and persistent in animals will cause human disease. And on that, there is some evidence, as I have indicated several times, that it occurred in Europe, and there is less evidence in this country.

Mr. BLUNT. But, Doctor, aren't there animal antibiotic guidelines? Am I wrong? Isn't the relative processing life of most food animals pretty short? So the more you give in a short period of time, I would think the veterinary medicine guidelines would have more impact there than the more you would give over a longer period of time. I mean, the processing time or the production time for animal agriculture is relatively short, and there are guidelines for the safety of animals. I guess another question would be, are you sure you don't make the food chain less safe by not giving the proper amounts of additives, including antibiotics, to animal feed prints is the question Mr. Dingell asked appropriately several times.

Dr. FRIEDEN. So two questions, two key points to make, the is that, unfortunately for humans, microbes divide very rapidly. And as Dr. Fauci indicated, even the course of a 10 days antibiotic course, you can have emergence of resistance by a variety of molecular mechanisms. So even relatively short durations of treatment may in fact lead to widespread emergence of drug resistance.

Second, antibiotics are not an essential nutrient. They may increase—they do increase growth, but they are not an essential nutrient. And there are certainly ways to keep the food supply safe without using antibiotics to promote growth.

Mr. BLUNT. I believe Mr. Dingell asked you, does the USDA have the authority to look at animal antibiotics, and I believe you said you didn't know, or what was your answer to that?

Dr. FRIEDEN. Yes.

Dr. FAUCI. We said yes, I can't imagine they don't have the authority to do that. There would be no reason why any one would prohibit them from doing that.

Mr. BLUNT. Do you have the authority to look at animal antibiotics?

Dr. FAUCI. I have the authority but not the mandate; that is not what the mandate of my institute is it to look at animal antibiotics and the agricultural issues.

Mr. BLUNT. Not the mandate, but you think you do have the authority, but you don't have the mandate?

Dr. FAUCI. Well, it depends on what you mean by the authority. If someone comes in with the grant and wants to do that, it is likely it would get referred to a different agency.

Mr. BLUNT. But you believe the USDA does have the authority.

Dr. FAUCI. I do believe that, but I don't know for sure.

Mr. BLUNT. Thank you, Mr. Chairman.

Mr. PALLONE. Dr. Fauci, Mr. Shimkus and I are of the opinion that you wanted to answer a question that you couldn't, so would you just answer the question.

Mr. BLUNT. Is this an extension of my time?

Mr. PALLONE. Just answer.

Dr. FAUCI. I was almost going to get to the point that, as Dr. Frieden and I had said several times, that there is no doubt that if you give antibiotics to an animal, a cow, bull or whatever, you give them antibiotics in that animal, there is unquestionably going to be the evolution of antimicrobial resistance in that animal.

The critical question that Mr. Shimkus was getting at and that Dr. Frieden answered with regard to a European study is that the question that people are struggling with is that, if you develop the antibiotic-resistant microbe in an animal who is getting antibiotics as part of the feed, is that a danger to the health of humans by transferring of that microbe to the humans? And there is some data that says that that is the case; that is European data. To my knowledge and to Dr. Frieden's knowledge, I don't think any of those studies have been done in the United States. So that is still something that people argue about whether there is any significance to that.

Mr. PALLONE. OK. Thank you.

The Gentlewoman from the Virgin Islands, Ms. Christensen.

Mrs. CHRISTENSEN. Thank you, Mr Chairman.

Dr. Fauci, as you talk about your institute, it supports basic research, how much of that research is done at universities, and how many of the universities involved in basic research are minority-serving institutions? And do you have any—well, that question to begin with.

Dr. FAUCI. About 90 percent, 89 to 90 percent of all of the research funding that we do goes out to universities on the outside. We fund by grants and contracts virtually all of the primarily minority institutions. Whether or not they have grants in antimicrobial resistance, I would have to get back to you on that, but we readily fund primarily minority institutions in our portfolio.

Mrs. CHRISTENSEN. Another question. Last week at our Spring Health Braintrust with the Minority Health Forum, where you received the award last year, we had a discussion on the lack of adequate minority participation in clinical trials and the need for diversity. In the translational research that is being done in this area, is it diverse enough, because given the different environments, I would assume there are different exposures, maybe different immunities, and maybe possibly even different responses to antibiotics? So do you feel that in the translational research area that we have a good representation of minorities and women?

Dr. FAUCI. It really varies. If you look at the clinical trials that we do, for example, with HIV/AIDS, because of the disproportionate disparity of infection among African Americans and, to a lesser extent, Hispanics, we are over-representative relative to the population, but equitably represented with regard to the burden of disease. That is for a specific disease.

It really varies. There are some clinical trials where, as hard as we try, because of either of location of where the trial takes place or, quite frankly, of some of the mistrust that the minority community has—

Mrs. CHRISTENSEN. We are going to really make an effort through those two organizations and others to work on that.

Dr. Frieden, you mention in your testimony that 10 States make up the network for EIPs, it is a similar question, are these States that have diverse populations, so the information that you get is reflective of the country's demographics?

Dr. FRIEDEN. Yes, it is, they are, and it is. However, this is an area we feel we need to continue to develop to ensure we have adequate representation.

Mrs. CHRISTENSEN. Thank you.

And you talked about helping States respond to outbreaks, and CDC has been very helpful to the Virgin Islands in assisting and investigating some of our outbreaks. As far as the NHSN and the NARMS, are the territories included in that?

Dr. FRIEDEN. I would have to get back to you.

Mrs. CHRISTENSEN. If you find they are not, could you see what you could do to make sure that we are, if it is appropriate?

Dr. FRIEDEN. Absolutely.

Mrs. CHRISTENSEN. Thank you.

Now this question is a little different, because there is a certain concern that I have had, but in the Patient Protection and Affordable Care Act, which you have heard a lot about this afternoon, there are provisions that where hospital-acquired infections occur, the hospitals will not be reimbursed and the providers, I assume, would not be reimbursed for the care that is provided. And there are a lot of antimicrobial products on the market that are used to clean surfaces in the hospitals, and some questions have been raised and brought about whether they are effective.

And I think it is very important if we are going to penalize hospitals and providers to know that these antimicrobials that are being used in the facilities are effective. Do you have any information on whether—that would suggest that they are not? And do you think that it would be worthwhile for the oversight subcommittee or this subcommittee to take a look at that question, given the importance of it going forward with the new legislation?

Dr. FRIEDEN. This is a complex issue.

Mrs. CHRISTENSEN. I am asking both of you that question.

Dr. FRIEDEN. One of the things that the new legislation does is require reporting of hospital-associated infections, and this we presume will be done through the National Healthcare Safety Network. This is something that we believe is an essential first step in recognizing and addressing infections.

For some infections, like *Clostridium difficile*, cleaning, environmental cleaning, may be very important. It may be challenging because it can be hard on the equipment to do it regularly. But this is an area where we work with others, with the hospital systems, to identify effective strategies to prevent the spread of infection or to stop outbreaks once they have occurred.

Mrs. CHRISTENSEN. Dr. Fauci, did you have any?

Thank you, Mr. Chairman.

I yield back the balance of my time.

Mr. PALLONE. Thank you, the Gentlewoman from Illinois Ms. Schakowsky.

Ms. SCHAKOWSKY. I want to get back to the use of antibiotics in animals.

Both of you in your opening statements talked about and the reason we are here are, public health problems of increasing magnitude; serious public health challenge posed by antimicrobial resistance. Both of you have acknowledged this is a serious problem.

We know that most of the antibiotics that are used in the United States are used for animals, and most of that is used for nontherapeutic use, mainly for growth of animals. You know, we are dancing around this because there is a lot of opposition. This is a highly-charged political issue. And there are many forces who think that, you know, stay out of the farm, leave that alone. And I know that.

But I am trying to understand why we don't have an answer to that question. If all of this use of antibiotics is going on right now in what people are eating and we are facing a serious health threat in this country, explain to me why there has not been any research done in the United States that you can cite, why we don't have an answer to this question, and why, even if we don't have an answer to this question, why nontherapeutic use of antibiotics is so la-de-da if potentially it has this kind of negative effect, dangerous effect?

It feels to me like there is this threat out there; there are so many threats that we can't totally control, but here is one, if we know about it as a potential threat— I mean, how much money are we spending in the Defense Department and Homeland Security to defend against potential threats? This is a potential threat. At least don't you think we ought to find out if this is a real threat? Will both of you please answer.

Dr. FRIEDEN. I think there is no doubt, as I said before, that there is a potential risk of spread. There is also no doubt that this is not the only way that resistance gets into the community. We see widespread abuse—

Ms. SCHAKOWSKY. Why don't we try and find out whether or not this is a source of the problem? And are there any plans to do that? I am a cosponsor of Congresswoman Slaughter's bill. What you are saying is not responsive.

Dr. FRIEDEN. There are several ways to study this, what we can do is look in more detail what is currently happening, what are the potential additional ways to get more information on it?

Dr. Fauci.

Dr. FAUCI. The simplest way to find out, because antibiotics are used in feed for the reasons that you mentioned. We both spoke of the theoretical risk. The real unanswered question, definitively unanswered, is, what is the risk—

Ms. SCHAKOWSKY. That is correct. That is what I am asking.

Dr. FAUCI. So you are asking a very appropriate question, is that, how do we get the answer to that? It would seem, since there is widespread use of antibiotics in a nontherapeutic, nonprophylactic feed for animal growth, that the only way you can answer the question that you are posing is to stop doing it and see if antimicrobial resistance goes down.

Ms. SCHAKOWSKY. Yes, that is right. And are there no farms in which they are not using—

Dr. FAUCI. Yes.

Ms. SCHAKOWSKY. So is there not some sort—are you telling me that science cannot determine whether or not this is a risk to human beings? Is that what you are saying?

Dr. FAUCI. No, I am saying you can determine it by stopping the use of it and seeing if the antimicrobial resistance goes down.

Ms. SCHAKOWSKY. Is there is no laboratory way? There is no possible way to find out? I mean, I just don't believe that.

Dr. FAUCI. No, I understand your question, and I understand your dilemma. If the question is, if an animal is given antibiotic in the feed, will there be resistance? And I could tell you, we could do that study, but I can tell you what the answer is; it is going to be yes.

The question is, does that resistant microbe get out into the community and spread into the community. That is not a very easy thing to get the answer to unless you stop it completely and measure for years what happens.

Ms. SCHAKOWSKY. Oh, really?

Dr. FAUCI. Yes.

Ms. SCHAKOWSKY. No. If we are going to test whether or not the fact of resistant bacteria in an animal then can transfer to a human being—

Dr. FAUCI. Right.

Ms. SCHAKOWSKY. —I mean, you can't possibly do it without stopping—

Dr. FRIEDEN. There are at least several ways to do that.

Ms. SCHAKOWSKY. Thank you.

Dr. FRIEDEN. One of them is to look for the markers of resistance and see whether the specific way that resistance has emerged among animals is found in people in the community.

I can just give you a little more information. I mentioned several times the European experience with the drug called Avoparcin, which is related to Vancomycin, which is a very effective drug that has been used to treat severe infections in animals and people. It is the last line of defense for many organisms. So it is very important to preserve Vancomycin for use therapeutically.

It was used for growth promotion in food animals in Europe in the 1970s and was gradually phased out and banned by the European Union in 1997. It was found that community carriage of Vancomycin-resistant strains of one particular microbe, enterococci, which is a highly-resistant organism, was quite common before the ban and, after the ban, gradually did decline. That is why we can say there is strong evidence from Europe that suggests that there is spread between feed animals and people in that environment and that restricting the use in that environment for that antibiotic resulted in a reduction in the amount of resistant organisms in the community.

That type of study we would have to look more comprehensively to see what has been done in this country and what could be done by different means.

Ms. SCHAKOWSKY. Well, I certainly think that we ought to do that, given the amount of antibiotics that we are feeding to animals and therefore eating ourselves, given that we have this problem. It is shocking to me that this kind of work doesn't seem to even be on the table. Thank you.

Mr. PALLONE. Thank you.

The vice chair, the gentlewoman from California, Ms. Capps.

Mrs. CAPPS. Thank you.

This has been an interesting hearing. Thank you very much.

I have a couple of questions for you, Dr. Fauci, and one, if I have time, for Dr. Frieden.

In today's hearings, we are getting what can be perceived, I believe, by the public as mixed messages. One hand, there is overuse of antibiotics, but on the other hand, we do need greater production of antibiotics as antidotes to antibiotic-resistant strains of bacteria, new antibiotics. And of course, underneath it all, provider and consumer education plays a role in all of this.

How do you reconcile, this is messages for the public, how do you reconcile these messages? And how are CDC and NIH working to devise a comprehensive strategy to combat antibiotic resistance by educating consumers?

Dr. FAUCI. It is an excellent question, Mrs. Capps.

There are two fundamental issues. You are asking a question, if we are concerned about antibiotic resistance, why are we trying to make more antibiotics? Well, antibiotics are——

Mrs. CAPPS. Well, I understand why, but it is a mixed message.

Dr. FAUCI. I will try to explain. We can get away from the mixed messages by compartmentalizing it.

You try as best as you can to prevent the emergence of resistance by the public health measures that Dr. Frieden spoke about.

Unfortunately, we are in a position where there are resistant microbes out there that we are up to the last line of defense with one and at the most two antibiotics that are useful. So there is a clear need to fill, to feed into the pipeline for new antimicrobials.

So I look at it as not a mixed message; we need to do two things simultaneously. We need to put the lid on the evolution and the development of antimicrobial resistance; and then we have got to have a pipeline of drugs to take them. So the message is, we have to get more antibiotics, but we have got to prevent further evolution of resistance.

Mrs. CAPPS. Do you have a public message that you are putting out for the public on ways to not go and keep asking your doctor for something for a sore throat and so forth, that kind of thing? Is that being done? The PSAs and so forth? I will assume that is happening.

Now from the other side, because I want to get at the concern that has been raised about—you know, I appreciate the history of the story of the development of penicillin. But pharmacology, pharmaceutical companies are very much working from more of a profit motive today than perhaps they were when some of these initial antibiotics came on to the market, just because they were out of their way to be developed.

Dr. Fauci, can you elaborate on the pathway that you illustrated in your sides from basic research to private development? I would like to know how you are collaborating with private industry in this area, which you noted isn't necessarily the first area that private industry would like to invest in. In other words, you really want some antibiotics to fight these resistant—to fight the MRSA's

and other resistant diseases. How can you, how can we incentivize them to do this?

Dr. FAUCI. I can give you actually a concrete, real-time, real-life example of how we have done that with one particular finding. Since we are involved fundamentally in pursuing and supporting basic research for concept development, we have funded a group of investigators from several of our centers. And they have found a small molecule which has the capability of inhibiting essentially any virus that has a lipid component to its envelope or its outer coating, potentially a really, really important advance. They have no—

Mrs. CAPPS. Where did you do this, at NIH? You have done this?

Dr. FAUCI. We funded them at a university.

Mrs. CAPPS. OK. Great.

Dr. FAUCI. They made the discovery. So how we are partnering with industry and biotech is that we are providing the resource reagents, the animal models, the capabilities to do a phase one clinical trial for those investigators and hooking them up with biotech companies and then, ultimately, Pharma in order to take what was just a concept into something that might actually be a product. And when, I hope, this comes to fruition of a product, and if and when it does, we are going to provide the clinical trial capabilities to test it in people to see if it works.

So we are really forming a partnership that goes right from the investigator who makes the original observation and develops the concept, up through and including the translation of that through biotech and industry.

Mrs. CAPPS. And you have a commitment from biotech and industry, because they see the kind of research that you are incentivizing at the university level, if you will, and so they are committed already?

Dr. FAUCI. We hope they are committed and stay in the game. If we make—and that was the point I was making in answer to several questions. If we can facilitate that difficult process from concept to product by any way we can, by making our assets available, other things beyond our control, such as financial incentives, et cetera, it makes that transition from concept to product much easier. We play an important but not an exclusive role in that. There are other components that have to come in to do that.

Mrs. CAPPS. Thank you very much. That is helpful.

I have a question for you, Dr. Frieden, but I am out of time so we will wait for the next hearing. Thank you very much.

Mr. PALLONE. Thank you.

The gentlewoman from Florida, Ms. Castor.

Ms. CASTOR. Thank you, Mr. Chairman.

I am interested in whether or not you are able to accumulate enough data to track what is obviously a major public health issue, one that has deadly consequences for so many. When I look at the estimates, we have estimates in the number of antibiotic-resistant infections, and then we have estimates in the number of health-care-associated infections.

The CDC's most recent data is that, in the U.S., every year it is about 2 million hospital-related infections, and about 90,000 Americans die from that. And then the other one included in our mate-

rials, in America, there are annually about 94,000 cases of MRSA every year with 18,000 deaths from MRSA.

Doctors, do these figures sound about right for you? Is it fair from these figures to conclude that over 100,000 Americans die each year due to antibiotic resistant?

Dr. FRIEDEN. Large numbers. I think the estimate that you gave was 90,000, which is an estimate that has been used before.

As I indicated in my opening statement, there has been progress in MRSA where we have seen a decrease of about 50 percent in serious infections in the hospitals that participate in the National Healthcare Safety Network.

Ms. CASTOR. So how is the data collected for you to compile these numbers and estimates?

Dr. FRIEDEN. We have two major methods. The one that is more widespread is the National Healthcare Safety Network. This builds on really more than a decade of experience working with hospitals, working with infection-control practitioners, standardizing definitions, encouraging reporting. And now we have 28 States which mandate reporting; 21 of them use the NHSN infrastructure to report. And about half of all hospitals in the United States currently are on board, including many hospitals in States that don't require a reporting publicly yet. And that reporting we expect to see expand nationally over the next couple of years.

Mrs. CAPPS. Why would States not mandate that? And why would hospitals not?

Dr. FRIEDEN. It is a recent phenomenon. So 5, 10 years ago, no State mandated it. Again, in a few States, it has been gradually spreading. It is concerning to hospitals. They are worried about reporting from a reputational risk. And the approach has been to make clear that reporting is a good thing, because it helps us to identify problems and then address them.

Ms. CASTOR. So with the estimates that you have now, knowing that some is not reported and some States don't mandate it, do you extrapolate?

Dr. FRIEDEN. Yes. These are extrapolated from both NHSN and also a network called the ABCs, which allows us to monitor antibiotic resistance to a series of core infections in a representative sample across the country.

Ms. CASTOR. Should it now become a reportable disease?

Dr. FRIEDEN. Certain strains are mandatorily reportable. There are some that are so common that reporting probably wouldn't be worth the burden, and sampling may be more effective. But for many organisms, reporting—mandatory reporting is something that is recommended by the Council of State and Territorial Epidemiologists, and is done in most or all States.

Ms. CASTOR. It sounds like we can do a lot better. What are you working on or what recommendations do you have to improve reporting so that we are able to track with adequate data?

Dr. FRIEDEN. Thank you. All excellent questions.

One of the things that we have done is to try to use electronic health records to extract information which then is validated a human being but would allow us to ensure that infections are reported reliably or assess the completeness of reporting. One of the things that is essential to make that happen is electronic reporting.

So when a laboratory gets a result, it ends up in the medical record. If it is a reportable condition, it ends up with the authorities to which it should be reported.

We also fundamentally need to make better use of the information so that we implement the programs that we know work, and there are some programs that we know can drastically reduce central-line associated infections and other hospital-associated infections; and that we continue to generate knowledge so we can better prevent problems that we don't yet have good tools to prevent, such as community-associated Methicillin-resistant Staph aureus.

Ms. CASTOR. Doctor, do you want to comment on the data tracking?

Well, I wanted to say, in my district back home, we have a researcher that is working on the antibiotic resistance, and he—this is Dr. Tuross at the University of South Florida. And his research is MRSA-based, and he is particularly looking at the design and development of nanoparticle-based technology for drug delivery. But in his comments to me in advance of the hearing, he was right on point with what you all are saying of what happens from the basic research level, and then turning that into some kind of new antibiotic. So it is a real issue, along with the lack of funding at NIH, CDC, and DOD in this area. He says it is practically nonexistent, and we simply cannot get the private companies to take any interest.

Thank you very much.

Mr. PALLONE. Thank you.

Gentlemen, Mr. Shimkus wanted to ask an additional question. And then if anybody else does, I will allow it, because I don't want to have another round, but I know there is a great deal of interest here.

So I will recognize the gentleman from Illinois.

Mr. SHIMKUS. Thank you.

And we talked about the CDC, NIH, FDA, USDA. And then, through this hearing, I remembered that the copper industry had been working with the Department of Defense to test copper as an antimicrobial—however you say it—killer, antimicrobial killer. And so EPA has just certified—the Environmental Protection Agency approved the registration by the Copper Development Association for copper and copper alloys to make public health claims as being antimicrobial. These claims acknowledge the fact that copper is inherently capable of killing bacteria.

Have you guys done any look at that? And should you? Is that something that CDC or NIH—or is this the problem with—I mean, the Federal Government is huge, and we are doing different things.

Dr. FAUCI. Well, let me try to answer it. It may not be the direct answer that you are asking for, but there are a lot of elements that can have antimicrobial activity. The question is to get it into a drug that would not be toxic. That is the issue.

Mr. SHIMKUS. But this is making a claim that copper being used on surfaces kills microbes. This is what—and I think we have Federal dollars doing research in DOD through the Department of Defense. All I would say is, you know—

Mr. PALLONE. You want to get back to us?

Mr. SHIMKUS. That is out there. The EPA has said that they can make that claim.

Mr. PALLONE. Why don't you get back to us?

Dr. FAUCI. We will do.

Mr. PALLONE. Mrs. Capps, did you want to ask your additional question?

Mrs. CAPPS. And I don't want to keep you, because you have already waited most of the afternoon anyway. But my question, and it kind of ties in with before and it can come up in another hearing we might have as well. I was just curious, because, according to the National Antimicrobial Resistance Monitoring System Data, and that is a mouthful, at least 80 percent of meat and poultry products are tainted with some kind of antibiotic-resistant bacteria. At least that is a study that has been out there. Can I use that as a basis of fact then, that fact?

Dr. FRIEDEN. I am not familiar with that specific statistic.

Mrs. CAPPS. OK, well, maybe we will make the assumption, since this is a National Antimicrobial Resistance Monitoring System Data, and they did state that at least 80 percent of meat and poultry products are tainted with antibiotic-resistant bacteria. Tainted. I don't know what level.

My question was that, what bacteria are we testing for in our food? Are we doing any kind of antibiotic-resistant pathogens, like staph or like MRSA, Methicillin-Resistant Staph MRSA? Is it possible to test for any markers or any kind of fact that this might be in food products?

Dr. FRIEDEN. These are all relatively easily tested for in small quantities. If you want to test a large proportion of the food supply, there obviously are logistical and financial implications. This really is the territory of the FDA.

Mrs. CAPPS. I understand that. But just from the science point of view, and you don't have to agree with the study.

Dr. FRIEDEN. I am not disagreeing. I just don't know.

Mrs. CAPPS. We can just take that off the table. But supposing something like that is true, there is the science to be able to pick up the markers or tests within food products? And, again, I am not suggesting that we should, because I understand—and this belongs to another department. But there is concern about the spread of MRSA and whether or not it is there. And there is a possibility that some research in another department like Food and Drug Administration could do this.

Dr. FRIEDEN. Yes.

Dr. FAUCI. It is scientifically possible. It is a logistical issue. It is very difficult at FDA to test broadly, and they only have the capability and the logistical capability of taking a very small fraction.

Mrs. CAPPS. Exactly. Thank you very much. And that completes.

Mr. PALLONE. Thank you.

Dr. BURGESS, do I dare ask if you have another question?

Mr. BURGESS. Of course, you can.

I just would like to hear from one or both of you, just what are some of the things you see over the horizon, just very quickly, that this committee should be aware of?

Dr. FAUCI, you referenced a couple of things with genomics and being able to sequence things very rapidly. We didn't really get into

the diagnostics part of this. We only talked about the vaccine part of this. But just very briefly, what is over the horizon that you guys see on a daily basis that we wouldn't be aware of?

Dr. FRIEDEN. I think, in terms of practice, the first thing is to scale up the proven means of reducing hospital-associated infections and reducing inappropriate antibiotic use. This is something which we have made progress in, but we could make a lot more progress in.

And I have to say, because there has been a lot of discussion of antibiotics in animal feed and use for growth promotion and feed efficiency, that we do not consider use to promote growth an example of judicious use of antibiotics.

I think the directions we are going are, first, to apply the things we know well to reduce infections. And I think we have a lot farther to go there; and second, to continue to generate knowledge on how we can reduce infections through programs, such as hospital-associated programs, electronic health records, reminder systems, control systems that will support doctors in restricting use of antibiotics, and, as Dr. Fauci mentioned, point-of-care diagnostics, which are very important in helping a doctor know right there, if the kid doesn't have strep throat, you don't have to treat them for strep throat.

Mr. PALLONE. OK.

You know, we obviously may ask additional written questions. We will try to get them to you in the next 10 days or so, which is the normal routine.

But members are free to send more written questions or comments to you. So I just want you to be aware of that.

But I do thank you. I mean, this was a very good hearing. And obviously, members are very concerned about the issue, and the work that you are doing is very crucial.

Thank you very much for your participation. And, without objection, the meeting of the subcommittee is adjourned.

[Whereupon, at 5:50 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Statement of the Honorable Anna G. Eshoo
Committee on Energy and Commerce, Health Subcommittee
Hearing on “Antibiotic Resistance and the Threat to Public Health”
April 28, 2010

Thank you, Mr. Chairman for holding this hearing on antibiotic resistance which has been a growing concern for scientists, healthcare professionals, and even patients for decades.

Contrary to popular belief, animals often receive the same antibiotics that are prescribed to people. While it's important to prevent sick animals from reaching grocery store shelves and contaminating the nation's food supply, it's also important that these drugs are not overused in a way that encourages antibiotic resistance.

I was shocked to learn how often antibiotics are given to *healthy* livestock. According to the Union of Concerned Scientists, 70 percent of antibiotic use in animals is for non-therapeutic purposes. Instead of being used to cure sick animals, they're administered to prevent transmissible diseases caused by crowded and unsanitary conditions. This high rate of antibiotic use increases the chances that these diseases will build up immunity to these drugs.

In fact, the overuse of antibiotics in the food supply is a major contributing factor to antibiotic resistance. Nearly two million Americans are diagnosed with hospital acquired infections each year. 63,000 of those Americans die from those hospital acquired infections that are resistant to at least one powerful antibiotic.

In addition to the heartache of the human toll, this is an expensive problem. If ordinary antibiotics don't work, a patient is at risk of more severe bacterial infections, increasing the length and cost of treatment. Estimates of the additional costs of hospital-acquired infections range from \$5 billion to \$26 billion annually. The wide variance in these numbers suggests we don't have a good grasp on the problem.

We need to better understand the effects of using these drugs on animals, similar to the way we evaluate the effects of drugs on people. That's why I'm a cosponsor of the *Preservation of Antibiotics for Medical Treatment Act* which would direct the FDA to review the safety of non-therapeutic uses of important human antibiotics in animal agriculture, and to revoke the approvals for those that cannot be proven to be safe from a resistance standpoint.

Antibiotic resistance poses a serious threat to our country's health, its economy and the entire world. I look forward to hearing more from our witnesses about what we can do to prevent it.

Opening Statement
Honorable Ranking Member Joe Barton
Subcommittee on Health
Hearing on Antibiotic Resistance
Wednesday, April 28, 2010 – 2:00 PM

Mr. Chairman, I understand that today's hearing will focus on antibiotic resistance, and I would like to welcome the witnesses and thank them for testifying.

Antibiotics are 20th century miracle drugs that everybody in the 21st century takes for granted until they don't work. So I agree that the buildup of resistance to the current generation of very powerful antibiotics is an important public health issue.

A lot of people look at the problem and focus on how antibiotics are used, and how often. Those are legitimate questions, but I also believe we need to focus on what we are not doing to get newer, better antibiotics on the market.

My understanding is the flow of development and approval of new antibiotics has slowed to a trickle. I hope we can find out why and figure out a way to restore some pressure to the system. One thing that will not make more and better antibiotics available is the \$27 billion in new taxes that will be coerced from researchers and manufacturers by the new Democratic health care law. I would hope that we could all agree that heavy new taxes will not spur innovation and cures, but will have the opposite effect.

On Friday, the Administration's Chief Actuary of the Centers for Medicare and Medicaid Services released a report on Obamacare. When I read this report, it was pretty clear to me that President Obama and Speaker Pelosi cannot possibly keep many of the promises they made about their health care law.

According to the Administration's own Chief Actuary, over \$575 billion will be cut from Medicare between now and September 30, 2019. Because of these cuts, over half of our nation's seniors will lose their Medicare Advantage plans. Apparently, when the President said that the American people could keep their current plan if they liked it, he was not talking about our nation's seniors.

According to the Administration's Chief Actuary, the President's promise on keeping your plan if you like it also fails to apply to Americans who get their health insurance through their employers. The Actuary reported that 14 million Americans will likely lose the employer-sponsored health insurance that they currently hold because of Obamacare.

The Administration's Actuary also reported that Obamacare imposes an \$87 billion tax on employers from 2014-2019. Our country has an unemployment rate of almost 10 percent and yet the President and Speaker Pelosi decided to tax our employers. How is taxing our employers going to create jobs and put Americans back to work?

Finally, the President also promised that his legislation would lower health care costs. Well, the Administration's Chief Actuary reported that the President is wrong on that front too. Under Obamacare, our country's national health expenditures will increase from 17 percent of GDP to 21 percent under Obamacare.

As implementation of the new Democratic health care law goes ahead, here are some dates to mark on your calendar:

- Jan. 1, 2014 -- After then, families who don't buy government-approved health insurance become liable for a fine that starts at \$285 and goes to \$2,085 in three years.
- Jan. 1, 2011 -- That's the day 10 million senior citizens who enrolled in a Medicare Advantage plan begin losing their extra health benefits or their policies, altogether.
- September 30, 2015 -- The end of federal funding for the State Children's Health Insurance Program.

Mr. Chairman, we repeatedly asked for hearings on this big, bad law before it got enacted. I continue to ask for this hearing because of the information reported by the Administration's Chief Actuary is alarming. Before it gets too late, we need to hold hearings and figure out the true impact of these policies.

Thank you Mr. Chairman, I yield back the balance of my time.

STATEMENT FOR THE RECORD
REP. TIM MURPHY
Health Subcommittee Hearing, "Antibiotic Resistance and the Threat to Public Health,"
Wednesday, April 28, 2010

Thank you, Mr. Chairman, for holding this hearing today. It's an opportunity for a very timely discussion on the heels of healthcare reform. Members of this committee have spent many hours working to find ways to cut healthcare costs while preserving the highest quality of care. It is appropriate and necessary that we examine antibiotic resistance more closely and how it impacts not only human health, but also taxpayer-funded government-run healthcare programs and the healthcare system as a whole.

As you likely know, finding solutions to the growing epidemic of hospital infections has long been a focus of my work on healthcare reform. Healthcare-acquired infections lead to nearly 100,000 deaths in the U.S. every year and \$50 billion in medical costs. These infections complicate hospital stays, cause serious illness, and place a heavy burden on hospitals and long-term care facilities. Providers, policymakers, and the community must together aim for zero deaths because HAIs are largely preventable.

My bill, the Healthy Hospitals Act (H.R. 3104) would require public reporting of healthcare-associated infections data by hospitals and ambulatory surgical centers. A number of states require some level of reporting about HAIs, but the requirements differ from state to state. Some report to the Department of Health. Some report some diseases and not others. We need to make this uniform across the nation. With this data, the public can review, compare, and ultimately bring the market to bear on reducing infections and

associated costs. By studying the trends apparent in publicly-available data, hospitals and doctors would adopt the best strategies for eliminating the spread of bacteria and these infections. An ounce of prevention is better than dispensing a single antibiotic for treatment.

In addition to stopping the spread of bacteria and resultant difficult-to-treat infections, we must also consider why antibiotic resistance is proliferating. Today, just one antibiotic-resistant infection – MRSA (methicillin-resistant *Staphylococcus aureus*) – kills more people in the U.S. every year than HIV/AIDS. Although MRSA is resistant to several important antibiotics, it can still be treated. What would happen should it finally become resistant to the few remaining effective antibiotics? I am afraid we will see many more deaths.

If a person's immune system is compromised, or even sometimes when it is not, antibiotic-resistant bacteria can cause illness that is much more difficult to treat. This transforms normally treatable ailments, such as skin infections or salmonellosis, into costly and potentially life-threatening experiences. When antibiotic resistance becomes prevalent in a hospital setting, it means that normally routine surgeries can also become quite hazardous as antibiotics fail to keep infection at bay.

The Infectious Diseases Society of America estimates that about 70% of all healthcare-associated infections in the U.S. are resistant to at least one antibiotic. The number of

infections and incidence of drug resistance are on the rise, with no sign of abating. With few new antibiotics in the research pipeline, we are facing a crisis.

As Dr. Frieden, one of our witnesses here today once said, "If we're not careful with antibiotics and the programs to administer them, we're going to be in a post-antibiotic era." I urge my colleagues to imagine the implications.

Given the seriousness of the health threat we are facing, it is necessary to examine the many causes of antibiotic resistance. The hospital infection control and reporting measures I have focused on are part of the solution, but there are additional measures we can take to curtail the generation of resistant bacteria in the first place.

Any use of antibiotics anywhere can cause bacteria to select for resistance, but overuse and misuse of antibiotics simply makes bacteria much more likely to develop resistance and multiply.

If we really want to cut healthcare costs, save lives and preserve the effectiveness of these vital drugs, we should eliminate unnecessary antibiotic use everywhere we find it – in the hospitals, long-term care facilities, cancer treatment centers, the general community, and even on the farm - and monitor the emergence of antibiotic resistance from all corners.

This means we need to examine routine antibiotic use in food animals, too. Some estimates suggest that as much as 70% of all antibiotics in the U.S. are being given to

healthy food animals in order to promote growth, improve feed efficiency, and routinely prevent disease. I have been examining the scientific literature in this area and although there is still more to learn, it appears that the vast majority of evidence from the last three decades points to a linkage between routine, low-level antibiotic use in food animals and the transfer of antibiotic-resistant bacteria to people, often through the food supply. The risk is real enough that virtually all major medical and public health organizations, including the American Medical Association, the American Academy of Pediatrics, the American Public Health Association, the American Nurses Association, the American College of Preventive Medicine, and many other human health experts have called for a significant reduction in the amount of antibiotics we use in food animal production.

I hope this hearing today will serve as a clarion call to awaken our colleagues to the very real threat to public health posed by the declining effectiveness of antibiotics. We need a comprehensive approach to this looming crisis that addresses not only efforts to preserve our existing antibiotics by eliminating unnecessary use, but also works to encourage the development of new antibiotics to replace those which are no longer effective.

Mr. Chairman, thank you again for convening this hearing, and giving us all a chance to work together to ensure that our children and grandchildren can enjoy a future at least as healthy as that which we inherited.

I look forward to learning more from the witnesses today, and hope and encourage the chairman to hold additional hearings to examine this critical and timely topic.

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April 28, 2010
The Honorable Louise M. Slaughter
Statement for the Record
Submitted to the Health Subcommittee
Committee on Energy and Commerce

M. Chairman,

M. Chairman and Members of the Committee, thank you for taking the time to hold a hearing on this important subject, as well as for giving me the opportunity to contribute comments for the record.

Every year, two million Americans acquire bacterial infections during their hospital stay, and 90,000 will die from them. 70 percent of their infections will be resistant to the drugs commonly used to treat them.

Antibiotic resistance is a major food safety issue, disproportionately affecting children. The CDC reports that half of all *Campylobacter* infections are drug resistant. Furthermore, 20 percent of *Salmonella* infections are resistant to at least one drug. Food-borne illnesses, sadly, are more likely to impact children, with young children being five times more likely to get *Salmonella* than adults.

Drug resistance makes an illness more difficult to treat, as well as increasing the length, cost, and severity of the illness. The cost of these infections to our already strained health care system cannot be ignored.

In 1998, an Institute of Medicine study concluded that antibiotic resistant bacteria cost the hospital system an additional \$5 billion annually. A more recent study – based on exhaustive chart reviews in Cook County Hospital in Chicago – would lead to a current nationwide estimate of \$16.6 billion to \$26 billion in annual costs.

Antibiotic resistance is a major public health crisis, and yet antibiotics are used regularly and with little oversight in agriculture.

Currently, seven classes of antibiotics certified by the Food and Drug Administration (FDA) as "highly" or "critically" important in human medicine are used in agriculture as animal feed additives. Among them are penicillin, tetracyclines, macrolides, lincosamides, streptogramins, aminoglycosides, and sulfonamides. These classes of antibiotics are among the most critically important in our arsenal of defense against potentially fatal human diseases. Penicillins, for example, are used to treat infections ranging from strep throat to meningitis. Macrolides and

sulfonamides are used to prevent secondary infections in patients with AIDS and to treat pneumonia in HIV-infected patients. Tetracyclines are used to treat people potentially exposed to anthrax.

Despite their importance in human medicine, these drugs are added to animal feed as growth promotants and for routine disease prevention. Approximately 70 percent of antibiotics and related drugs produced in the US are given to cattle, pigs, and chicken to promote growth. The non-therapeutic use of antibiotics in poultry skyrocketed from two million pounds in 1985 to 10.5 million pounds in the late 1990s.

This kind of habitual, non-therapeutic use of antibiotics has been conclusively linked to a growing number of incidents of antimicrobial-resistant infections in humans, and may be contaminating ground water with resistant bacteria in rural areas. In fact, a *National Academy of Sciences* report states that, "a decrease in antimicrobial use in human medicine alone will have little effect on the current situation. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."

Resistant bacteria can be transferred from animals to humans in several ways. Perhaps most glaringly, antibiotic resistant bacteria can be found in the meat and poultry that we purchase in the grocery store. In fact, a *New England Journal of Medicine* study conducted in Washington, DC found that 20 percent of the meat sampled was contaminated with *Salmonella* and 84 percent of those bacteria were resistant to antibiotics used in human medicine and animal agriculture.

Bacteria can also be transferred from animals to humans via workers in the livestock industry who handle animals, feed, and manure. Farmers may then transfer the bacteria on to their family. Indeed, one study showed that poultry-workers are 32 times more likely than the general population to have antibiotic-resistant *E. coli*.

A third method is via the environment. Nearly two trillion pounds of manure generated in the US annually contaminate our groundwater, surface water, and soil. Because this manure contains resistant bacteria, the resistant bacteria can then be passed on to humans that come in contact with the water sources or soil.

The problem has been well documented.

A 2002 analysis of more than 500 scientific articles and published in the journal *Clinical Infectious Diseases* found that "many lines of evidence link antimicrobial resistant human infections to food-borne pathogens of animal origin."

The Institute of Medicine's 2003 report on *Microbial Threats to Health* concluded "Clearly, a decrease in the inappropriate use of antimicrobials in human medicine alone is not enough. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."

As the impact of MRSA continues to unfold, there is little doubt that antibiotic resistant diseases are a growing public health menace demanding a high priority response. Despite increased attention to the issue, the response has been inadequate. Part of the problem has been the FDA's failure to properly address the effect of the misuse of animal antibiotics on the efficacy of human drugs.

Although the FDA could withdraw its approval for these antibiotics, its record of reviewing currently approved drugs under existing procedures indicate that it would take nearly a century to get these medically important antibiotics out of the feed given to food producing animals. In October 2000, for example, the FDA began consideration of a proposal to withdraw its approval for the therapeutic use of fluoroquinolones in poultry. The review, and eventual withdraw of approval, took five years to complete. Under its current regulations, the FDA must review each class of antibiotics separately.

For this reason, I introduced H.R. 1549, the Preservation of Antibiotics for the Medical Treatment Act (PAMTA).

H.R. 1549 would phase out the use of the seven classes of medically significant antibiotics that are currently approved for non-therapeutic use in animal agriculture. Make no mistake, this bill would in no way infringe upon the use of these drugs to treat a sick animal. It simply proscribes their non-therapeutic use.

Addressing this critical issue is not only important for protecting the public's health, but also to ensure that United States livestock producers remain competitive in international markets. The European Union, New Zealand, Thailand, and Korea all have either banned or will begin banning antibiotic growth promoters in animal feed. Under World Trade Organization rules, trading partners who implement this ban will have the right to refuse imports that do not meet this standard. Consequently, if the United States continues to allow non-therapeutic use of antibiotics in livestock, there may be major trade and economic implications.

The Preservation of Antibiotics for Medical Treatment Act, therefore, is an urgent trade matter as well as an urgent public health matter.

When we go to the grocery store to pick up dinner, we should be able to buy our food without the worry that eating it will expose our family to potentially deadly bacteria that will no longer respond to our medical treatments. Unless we act now, we will unwittingly be permitting animals to serve as incubators for resistant bacteria.

It is time for Congress to stand with scientists, the World Health Organization, the American Medical Association, and the National Academy of Sciences and do something to address the spread of resistant bacteria. We cannot afford for our medicines to become obsolete.

M. Chairman, thank you for the opportunity to submit comments for the record, and I look forward to working with you and all the Members of this Committee, as well as any other interested parties, to protect the integrity of our antibiotics and the health of American families.

Louise Slaughter

The STAAR Act Coalition

May 18, 2009

The Honorable James Matheson
United States House of Representatives
Washington, DC 20515

RE: The "Strategies to Address Antimicrobial Resistance Act" (H.R. 2400)

Dear Representative Matheson:

The undersigned organizations represent physicians, hospitals, pharmacists, healthcare epidemiologists, infection prevention and control professionals, and public health experts and advocates. We write today to thank you for sponsoring H.R. 2400, the "Strategies to Address Antimicrobial Resistance (STAAR) Act." This critical legislation will help guide our country in developing proper responses to the extremely urgent problem of antimicrobial resistance.

Antimicrobial resistance is a serious patient safety, public health, and national security issue. The recent 2009 Influenza A H1N1 virus (also known as "swine-origin influenza virus") outbreak clearly illustrates why infectious diseases experts are concerned about drug resistance. Although this novel H1N1 virus currently appears to be susceptible (sensitive) to two available antiviral drugs, Tamiflu (oseltamivir) and Relenza (zanamivir), it is resistant to other important antivirals, including amantadine and rimantadine. Not only can influenza viruses develop drug resistance quickly, but the overuse of Tamiflu during the current outbreak may also hasten the process further. Should the virus mutate and become resistant to all classes in the coming months, the United States would be left extremely vulnerable.

Drug resistance also is a serious problem in the day-to-day treatment of bacterial infections. Although initially affecting ill people in hospitals, drug-resistant bacteria, such as multi drug-resistant *Staphylococcus aureus* (MRSA), are infecting an increasing number of people in community-settings, including healthy athletes and children. The resulting infections affect hundreds of thousands of Americans and cause tens of thousands of deaths each year. The infections are painful, difficult to treat, frequently recur and cost many billions of dollars to the U.S. health care system annually.

"The last decade has seen the inexorable proliferation of a host of antibiotic-resistant bacteria, or bad bugs, not just MRSA but other insidious players as well. ...For these bacteria, the pipeline of new antibiotics is verging on empty. 'What do you do when you're faced with an infection, with a very sick patient, and you get a lab report back and every single drug is listed as resistant?' asked Dr. Fred Tenover of the Centers for Disease Control and Prevention (CDC). 'This is a major blooming public health crisis.'" — July 18, 2008 *Science* magazine.

1300 Wilson Boulevard, Suite 300 Arlington, VA 22209

PAGE TWO -- STAAR Act Coalition letter to Rep. Matheson

A CDC-supported study published in the *Journal of the American Medical Association* (October 17, 2007) estimated that MRSA infects more than 94,000 people and kills nearly 19,000 annually around the country—more deaths than those caused by emphysema, HIV/AIDS, Parkinson's disease and homicide. Infectious diseases doctors and other physicians are concerned about MRSA infections, but they also are deeply concerned about other extensively resistant organisms, including *Escherichia coli* (*E. coli*), *Acinetobacter baumannii* (afflicting soldiers returning from Iraq and Afghanistan), resistant *Klebsiella species* (spreading across the East Coast and into the Midwest), extensively drug-resistant tuberculosis (XDR-TB), *Pseudomonas aeruginosa*, and *Enterococcus faecium*. New national surveillance data from CDC demonstrate that an incredible 80 percent of *E. faecium* infections associated with device-related healthcare-associated infections were resistant to vancomycin.

The 2009 Influenza A H1N1 virus outbreak further heightens concerns about MRSA and other bacteria that cause secondary bacterial pneumonia following influenza infection. Indeed, many thousands of deaths were caused by complications due to secondary bacterial infections during the 1918 influenza pandemic and not by the influenza virus itself. Without effective prevention and control strategies, robust biomedical and epidemiological research, and an adequate supply of antibacterial drugs, we could be left in a precarious situation should the novel H1N1 virus outbreak become more severe in the coming months.

In addition, a bacterium known as *Clostridium difficile* (*C. diff*) is spawning infections in hospitals and communities in the United States and abroad that can lead to severe diarrhea, ruptured colons, kidney failure, blood poisoning (sepsis) and death. *C. diff* is a common cause of antibiotic-associated diarrhea, accounting for 15-25% of all episodes. This organism is also resistant to most antibiotics. CDC estimates there are 500,000 cases of *C. diff* infection annually in the United States, contributing to between 15,000 and 30,000 deaths. Elderly hospitalized patients are at especially high risk and mortality in these patients may exceed 10%. Recurrence of infection rates range between 20-50% even when treated appropriately.

Physicians and other healthcare professionals are increasingly frustrated by the hurdles they face in caring for patients with life-threatening drug-resistant infections, and they are distraught about the toll it takes on their patients' lives and those of their families and friends. It is simply unacceptable to see children and adults die when society has the resources and the tools—but not the will—to reduce the impact of these diseases. Moreover, resistant organisms and the infections they cause pose a national security threat and contribute significantly to the spiraling cost of healthcare in our country.

We cannot stop the development of antimicrobial resistance—bacteria, viruses and fungi will continue to mutate in response to antimicrobial drug use. However, we can respond with new

PAGE THREE -- STAAR Act Coalition letter to Rep. Matheson

and effective strategies and interventions to limit the emergence of resistance. Outside of strengthening our antimicrobial drug pipeline, what we need most are improved U.S. coordination and specific actions designed to better monitor, treat, and most importantly prevent the development and transmission of drug resistant microbes that threaten the health of all Americans. The STAAR Act provides the appropriate, balanced set of measures to achieve these goals and address our concerns.

As medical, healthcare, and public health organizations dedicated to patient care and safety, as well as public health in general, we thank you for introducing the STAAR Act and hope you will work to secure its prompt passage. Should you have any questions, please contact Robert J. Guidos, JD, vice president of public policy and government relations for the Infectious Diseases Society of America, at 703-299-0202 or rguidos@idsociety.org.

Sincerely,

Alliance for the Prudent Use of Antibiotics (APUA)
 American Academy of Family Physicians (AAFP)
 American Academy of Pediatrics (AAP)
 American Association of Critical-Care Nurses (AACN)
 American Dental Association (ADA)
 American Medical Association (AMA)
 American Pharmacists Association (APhA)
 American Public Health Association (APHA)
 American Society of Health-System Pharmacists (ASHP)
 Association for Professionals in Infection Control and Epidemiology (APIC)
 Council of State and Territorial Epidemiologists (CSTE)
 Food Animal Concerns Trust (FACT)
 Infectious Diseases Society of America (IDSA)
 International Society of Microbial Resistance (ISMR)
 Michigan Antibiotic Resistance Reduction Coalition (MARR)
 National Association for Sport and Physical Education (NASPE)
 National Athletic Trainers Association (NATA)
 National Foundation for Infectious Diseases (NFID)
 National Parent-Teacher Association (PTA)
 Pediatric Infectious Diseases Society (PIDS)
 Premier, a healthcare alliance serving 2,100 nonprofit hospitals and 58,000 healthcare sites
 Society for Healthcare Epidemiology of America (SHEA)
 Society of Infectious Diseases Pharmacists (SIDP)
 Trust for America's Health (TFAH)
 Union of Concerned Scientists (UCS)



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

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)

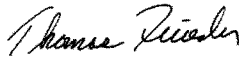
In addition, a strong body of evidence from Europe demonstrates that antibiotic use in animals is linked with antibiotic resistance in humans. Multiple studies looked at the effects of the Danish ban on non-therapeutic use of antibiotics in food animals. We have thoroughly reviewed these studies and 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.

Page 2 – The Honorable Frank Pallone Jr.

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, appearing to read "Thomas R. Frieden".

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 Lonnroth 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 Ryc, Public Health Director, Directorate General Health and Consumers

Martinus Nagtzaam, Policy Officer, Directorate General Health and Consumers

Anna Lonnroth 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. It is 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.

**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**

**Anthony S. Fauci, M.D.
Director, National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services**

The Honorable Jim Matheson

1. 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?

ANSWER

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.

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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.

The Honorable Marsha Blackburn

1. During the antibiotic resistance hearing on April 28th, in response to Representative Capps' question on how NIAID can incentivize industry to develop antibiotics against resistant bacterial infections, you responded that in addition to funding basic research for concept development, NIAID is partnering with industry and biotech to provide resource reagents, animal models, and clinical trial capabilities to test potential drug candidates. How much funding does NIAID anticipate will go into expanding NIAID's clinical trial infrastructure to study resistant bacterial infections, and what is the current status of this expansion?

ANSWER

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 oversees a major effort built upon a foundation of basic research to understand the biology of microbial pathogens,

the interactions between these pathogens and their human hosts, and the biological mechanisms by which pathogens develop resistance to antimicrobial drugs.

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. The number and types of available services have recently expanded, and include *in vitro* and *in vivo* screens to identify promising drugs, medicinal chemistry to improve drug activity, and the provision of difficult-to-obtain clinical samples to facilitate testing of drugs and diagnostics.

Through a research program originally started 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 through this initiative support studies designed to help answer key questions about proper antimicrobial dose, treatment duration, and the necessity for antimicrobial treatment in all cases. The contracts will 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. The first contract awards were made in 2007 to determine better treatments for skin and skin structure infections caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA); NIAID has committed to support up to \$14 million over five years to conduct this research. In 2009, NIAID made additional awards to study catheter-related bloodstream infections and urinary tract infections in children, with NIAID setting aside up to \$25 million over seven years for these research projects. NIAID also has two additional solicitations planned, one that will be awarded in the summer of 2010 and the second scheduled for 2011, that will target additional trials for pneumonia, bacteremia, acute otitis media and pulmonary tuberculosis. NIAID plans to set aside an additional \$110 million over six years to support the research projects awarded in 2010 and 2011.

NIAID's clinical infrastructure also includes the capacity to conduct clinical trials of promising new vaccine and therapeutics. Since the 1960s, the Vaccine and Treatment Evaluation Units have provided a ready resource for conducting Phase I through Phase IV clinical trials of new vaccines and treatments. The capacity of this network to rapidly mobilize to meet emerging needs was recently demonstrated during the 2009 H1N1 influenza pandemic. In addition, the Phase I Clinical Trial Units for Therapeutics, which were initiated in 2008, support studies to assess the safety of therapeutic products for viral, bacterial, parasitic, and fungal pathogens.

