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Finding the Right Playground and the Perfect Toy

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The main point of my presentation is that all of us need to find the right “toy” or technology for what we want to detect or quantify and for that technology to be useful in the area we are researching. We have lots of “toys” or technologies. We’re really dazzled by the emerging technology and I am amazed at the new information that we can garner from this. But, I also think we must not lose sight of the fact that perhaps a simple detection method might give us the answers we seek. I mention playground for several reasons. One reason is the even though this meeting is on food protection and defense, there is a lot of overlap with food safety research and even infectious disease research. So we really do have a common playground on which to move forward. Then the other reason is that the term “playgrounds” conjures up images of playing in school years and learning to play nice with others. In order to move forward and accomplish some of our goals, we have to collaborate with each other not only among different disciplines, such as microbiologists, epidemiologists, and virologists but also among different centers and different networks.

Everyone in research provides an ultimate wish list for the ideal method. Most of us would agree to these qualities. Detection and diagnosis must meet the overall challenge which is to be able to sample and detect an agent or diagnose a disease. You know very well the realities and barriers that we have not only in finding detection methods but which affect the whole food defense and food safety research. We have a global food supply that is distributed widely and is complicated. We can talk about farm to fork and yet there are so many different facets of this food production chain as well as the consumption of raw products. Laboratories present more complexity in that their missions may be diverse, they are geographically scattered and don’t always communicate with each other.

I think the challenges in microbiology are well known. How do we detect low levels of contamination? How do we find a very small amount of a particular organism in a diverse background of other organisms and in foods where there is no uniformity among the pathogen distribution? I think this is one of the biggest challenges in microbiology and in food safety research. This challenge also feeds into another big challenge: detection of organisms in complex matrices like food. For example, biosensor research has been done for the last several years and there are biosensors available for some products. Yet, ground beef provides even more complexities while trying to determine pathogen levels. So if you are a microbiologist you are probably looking at all of these challenges and barriers and thinking, my gosh, it’s like looking

at a plate of ground beef. There are so many different organisms and so many different places, where do we start? I think through these difficult questions, microbiology has evolved. We’ve gone from culture-based methods to nucleate acid based methods, and then to microarrays and biosensors. Each method provides more data and is more efficient. So where does the evolution of microbiology go from here? Microbiologists continue to be leaders in this evolution.

Epidemiology, I think, has also evolved due to food safety and food defense research. We have gone from outbreak investigations to community based studies and case control studies. Mathematical modeling and risk assessment are fairly new fields that involve numerous disciplines, not just epidemiology. But I think it’s important for epidemiologists also to evolve with microbiologists in the pursuit of food defense and protection. Sciences have evolved- from infectious diseases to food safety and then food defense, and new emerging infectious diseases. With the evolving of science we’ve also evolved a little bit with funding. If you are talking about USDA and NIH and some other federal agencies, we have moved from single investigators, small awards to pushing for multidisciplinary, multi-institutional centers networks and larger awards. It is too early to decide if this is a good way of funding research.

I just want to talk just briefly about some of the funded centers and networks. Not all of them are listed for the National Institute of Health, but I have just listed the ones that are at veterinary schools. When the National Institute of Health funded these large networks, other Federal agencies did the same. The Dept. of Homeland Security, while this is not a complete list, funded two that involve veterinary schools, the Center for Food Protection and the Center for Foreign Animal Disease. The Dept. of Agriculture’s, Cooperative State Research Education and Extension Service, also followed this initiative and funded several large coordinated agriculture programs.

One of them was an avian influenza program that was funded last year. We also funded one related to food safety which is the Food Safety Research and Response Network. The lead institution is North Carolina State and compared to NIH and Homeland Security monies, the grant is small. It is five million for four years but we are encouraged about the potential. To date, there over 17 universities and more are being added. It’s not exclusive. Part of the reason we funded this network was for it to be responsive to emerging issues and flexible. For example, if there was an emerging need or event, this network could find the necessary expertise quickly. Within the project management plan, there is a microbial core and an epidemiology core. The

microbial core involves microbiologists that are willing to advise other people within the network on method development or cross train researchers and graduate students. This core is also trying to standardize some of the methods among the different universities. The epidemiology core involves epidemiologists that can give advice on statistics, epidemiology design. They are also developing standardized criteria for population based studies.

So where do we go from here? I listed a couple of areas that are related to science and to funding. How do we advance the evolution of microbiology to provide an impact? I mention an impact on food defense. How do we measure what we're doing and what impact it has on food defense and protection and food safety? How do we creatively use the disciplines that are already being involved and how do we bring in new disciplines like biologists for some important emerging issues? How do we utilize what we have, given that we may not have more funding? Then how do we leverage what resources we have? When I looked at these questions I feel like I'm looking at a petri dish. I'm not sure which way to go! The future for microbiology is many of the issues we have mentioned before pathogen detection in complex matrices. The future for epidemiology is providing necessary sampling strategies for the microbiologists trying to do the detection. Challenges in the food process include streamlining, validation, and standardization. There are also challenges with large networks or centers. The management is difficult, particularly with a large number of researchers. I think the potential for benefits is extraordinary. We can cross train researchers and graduate students; we can attempt to standardize among several labs. There is the potential for community projects, particularly if provided funding to maintain sample repositories and databases. We have the potential for extension and communication

programs, and leverage our resources. If you look at the different funding agencies, you'll see the missions are very similar. Yet, your research must address the specific mission. Sometimes to get funding, you need to be creative. There is potential for collaborations among agencies. For example, the USDA network has collaborated with the Dept. of Homeland Security Food Defense Network. I think all the networks and various researchers can benefit from this. I think that the centers and networks can work with other agencies. The potential is there so I'm just going to leave you with some challenges.

I think your challenge is to decide either as a researcher or as part of a center or network, what is your priority? What is the ultimate question that we need to answer before we can move forward? How do you become more visible either in participating in the different centers or networks or among your own peers and how do we keep the interaction going? It is important for us, as Federal agencies, and for you as researchers to be able to measure the impact of your research or funded program. I'm not sure any of us have solved this question.

As for future directions, I think it's important to continue and strengthen collaborations among different disciplines. I think somehow we need to enhance communication and define a few reachable goals. How do we define a goal that can show impact now? After telling you to collaborate, I must also mention that we must consider the phrase "divide and conquer". That is, all the centers should not be doing the same research and activities. We should coordinate, for example, when it comes to pathogen detection, can the food safety network work on the methodology of pathogen detection and the Department of Homeland Security network work on validating the methodology. Examine your unique strengths and collaborate with others to reach a certain goal.

Finding the right playground and the perfect toy

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USDA, CSREES

The Ultimate Wish List

- Easy
- Inexpensive and universal
- Applicable to multiple systems
- Real-time
- Robust and portable
- Quantitative



Overall Challenge

Sampling and detecting the agent (or diagnosing the disease) in question in the event of an attack (or outbreak) and...

Going beyond the source to attribute strains to a biocrime (intentional or differentiate from unintentional)

Realities/Barriers

- **Global food supply**
- **Complicated, multi-factorial**
- **Consumption of raw products**
- **Wide, effective distribution system**
- **Chemical, biological organisms**
- **Scattered, diverse laboratories**

Challenges in microbiology

Low levels of contamination

“Zero”-tolerance regulations

Non-uniform distribution of pathogens

Large sample sizes to assure representation

Detection of sublethally injured cells

High levels of background microflora

Application to Complex Sample Matrices

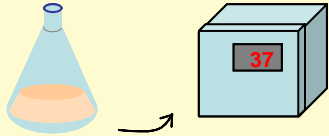

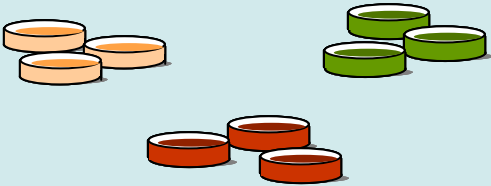
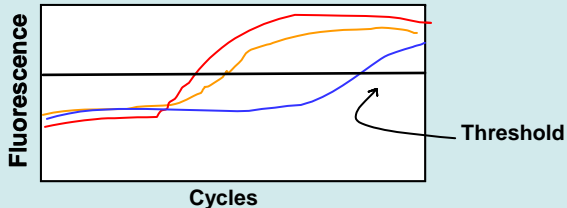
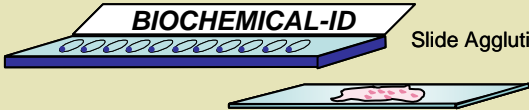
- ✧ **Feces**
- ✧ **Dairy Products**
 - ◆ Cheddar cheese
 - ◆ Yogurt
- ✧ **Produce Items**
- ✧ **Meats**



Evolution of Microbiology

- Culture-based methods
- Nucleic-acid based methods, immunoassays, molecular methods
- Microarrays
- Biosensors
- ????????????



A Comparison of Traditional and “Rapid” Detection Methods	
<p>Amplification</p>  <p>Cultural Enrichment: 24-48 hours</p>	<p>Amplification</p>  <p>Nucleic Acid Extraction: 1-2 hours Amplification: 1-4 hours</p>
<p>Detection</p>  <p>Selective/Differential Plating: 24-48 hours</p>	<p>Detection</p>  <p>Fluorescent Reading: “Real time”</p>
<p>Confirmation</p> <p>Testing Kits</p>  <p>Slide Agglutination</p> <p>Serotyping/Incubation: 12-48 hours</p>	<p>Confirmation</p> <p>Not necessary</p>
TOTAL 2-6 DAYS	TOTAL 2-6 HOURS

Courtesy of C.M.Moore



Challenges for Epidemiology

- **Sampling**
- **Impact of the environment (air and water)**
- **Sensitivity/specificity- predictive value**

Evolution of Epidemiology

- **Outbreak investigations**
- **More rigorous research in conjunction with microbiologists- community-based studies, case-controls**
- **Surveillance**
- **Mathematical modeling**
- **Risk assessment**

Evolution of the Science

- Infectious diseases
- Food Safety
- Food Defense and Protection
- Infectious Diseases

- Single-investigators, small awards
- Multi-disciplinary, multi-institutional Centers/Networks, large awards

Funded Centers/Networks

- **National Institute of Health Networks**
 - 2 Zoonosis research units (Cornell, WSU)
 - 1 Microbiology research unit (Michigan state)
 - 1 Microbiology and botulism research unit (Tufts)

Networks/Centers

- **Department of Homeland Security**
 - **Center for Food Protection and Defense (University of Minnesota)**
 - **Center for Foreign Animal Disease and Zoonotic Disease Defense (Texas A&M)**



Food Safety Research and Response Network

- **USDA CSREES Cooperative State Research
Education and Extension Service (CSREES)**
- **National Research Initiative**
- **Food Safety- CAP**
- **\$ 5 million for 4 years**
- **Lead institution, N.C State Univ.**





FSRRN

Food Safety Research & Response Network

17 Universities
50+ Food Safety Researchers
and Support Specialists

Cornell Univ.

Iowa State Univ.

McMasters Univ.

Mississippi State Univ.

N. Dakota State Univ.

The Ohio State Univ.

Tuskegee Univ.

Univ. of Arizona

Univ. of Calif. Davis

Univ. of Calif. Berkley

Univ. of Florida

Univ. of Illinois

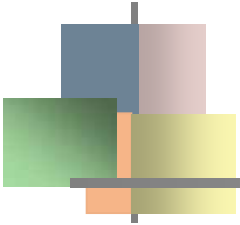
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Univ. of Minnesota

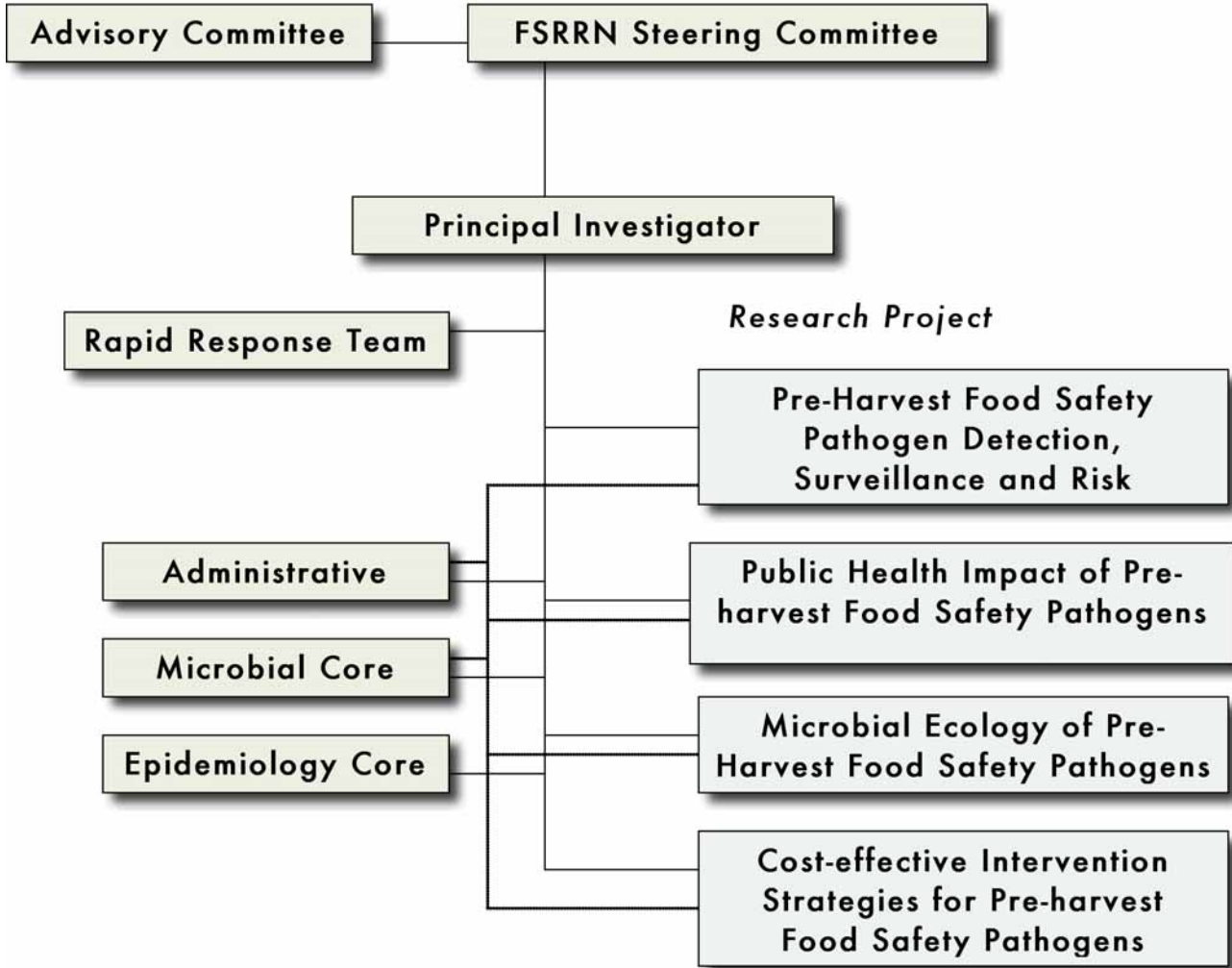
Univ. of Montreal

Washington State Univ.

West Texas A&M Univ.

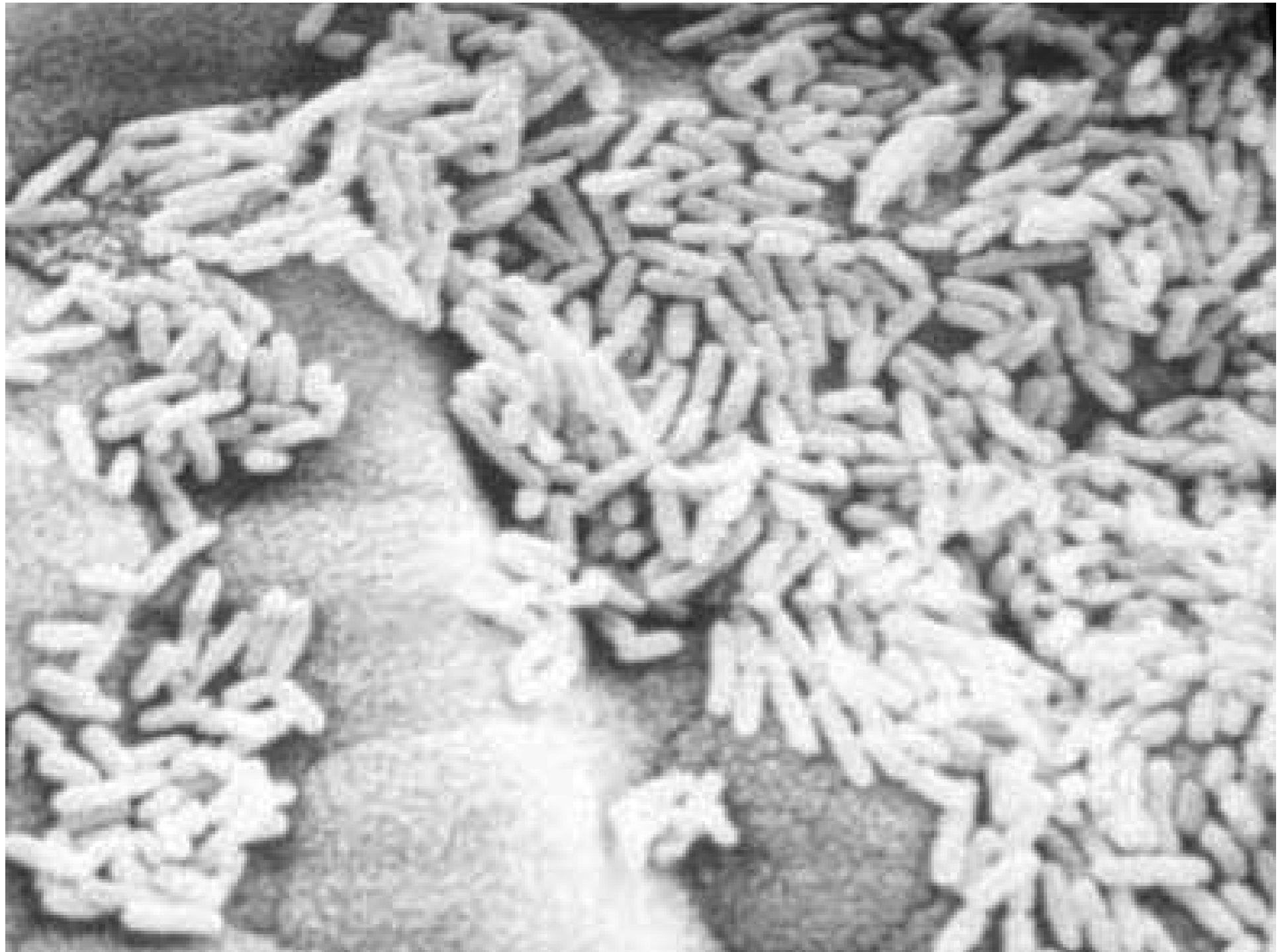


**Food Safety Research and Response Network (FSRRN)
Project Management Plan**



Where do we go from here?

- How do we advance the evolution of microbiology to provide an impact on food defense?
- How do we creatively use multiple disciplines effectively?
- How can we utilize the Centers/Networks current activities/infrastructure to get where we want to go?
- How do we leverage resources?



Future for microbiology

- Pathogen separation and concentration from matrix
- Real time detection
- More sensitive nucleic-based methods
- Improved biosensors
- New or combined methods

Future for both

- **Sound sampling strategies** (sensitivity for micro, for epi)
- **Combination methods** (serial or parallel) (to get best sensitivity, specificity, rapid)
- **Standardization and validation** (stand between labs for comparability) (validation for new tests)

Challenges in “process”

- Streamlining the process
- Validation of the methods
- Standardization of the Methods

Networks and Centers

Difficulties-

- Counter to academia and govt cultures
- Management
 - Organization and process
- Focus of people, projects
 - Collaborations
 - Goals
- Communication
 - Timely, inclusive
 - Confidentiality, trust

Networks and Centers

Benefits-

- **Cross-training and standardization**
- **“Community” projects**
 - *Sample repositories and databases*
 - *Extension and communication programs*

Networks and Centers

Benefits-

- **Piloting the implementation of new disease control strategies and tools**
- **Intangibles such as marketability and creativity**
- **Leveraging of resources**
- **Broader “coverage” of questions**

Missions

- **CSREES**- to identify and assess organisms, pathogens, toxins, and chemicals causing foodborne disease
- **NIH**-causes of allergenic, immunologic, and infectious disease and identify better means of preventing, diagnosing and treating illnesses
- **DHS**- research capability to address scientific and technology issues (food defense)

Baby steps

- **DHS and USDA**
- **USDA and NIH**
- **Centers/Networks with other agencies**

YOUR Challenge

■ Direction

- How do you decide what is a priority?
- How do you become more visible? More interactive?

■ Impact

- What is the measurement of your consortium and its funding in 5 years?

Future Directions

- **Continue and Strengthen collaborations among disciplines (e.g. micro and epi)**
- **Enhance communications in order to focus on a couple of reachable goals now**
- **Divide and conquer**