NABC Report 23

FOOD SECURITY

The Intersection of Sustainability, Safety and Defense

Edited by

Allan Eaglesham
F. Abel Ponce de León
&
Ralph W.F. Hardy

2011

National Agricultural Biotechnology Council Report

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Providing an open forum for exploring issues in agricultural biotechnology

NABC Report 23

Food Security: The Intersection of Sustainability, Safety and Defense

Proceedings of the twenty-third annual conference of the National Agricultural Biotechnology Council, hosted by the University of Minnesota, Minneapolis-St. Paul, June 15–17, 2011

Edited by
Allan Eaglesham, F. Abel de León and Ralph W.F. Hardy

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Food Security: The Intersection of Sustainability, Safety and Defense

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National Agricultural Biotechnology Council

Providing an open forum for exploring issues in agricultural biotechnology

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ACKNOWLEDGMENTS

NABC's twenty-third annual conference—*Food Security: The Intersection of Sustainability, Safety and Defense*—was hosted by Abel Ponce de León, senior associate dean for research and graduate programs at the College of Food, Agriculture and Natural Resource Science, University of Minnesota. We are grateful to Dr. Ponce de León and to his assistants, Jessica Weaver and Betty Davidson, for being chiefly responsible for a smoothly run, highly successful conference.

Thanks are due to the scientific advisory committee[1]—Frank Busta, Francisco Diez-Gonzalez, Richard Isaacson, Carol Ishimaru, Shaun Kennedy and Ted Labuzza—for designing the program and for selecting excellent speakers.

The conference's seamless operation resulted from the excellent efforts of the following:

Moderators: Frank Busta, Francisco Diez-Gonzalez, Richard Isaacson and Carol Ishimaru

Workshop Facilitators, Recorders and Reporters: Bonnie Anderson, Frank Busta, Deb Hamernick, Michael Kahn, Jozef Kokini, Graham Scoles, Steven Slack, Nancy Toedt and Lisa Wiley.

Student Voice Program Administrator: Susanne Lipari.

Student Voice Reporters: Caroline Anderson and Michele Martin.

And we are grateful to the following for organizational contributions before, during and after the conference: Sahar Angadjivand, Michael Balak, Becky Beyers, Paul Brady, Mary Buschette, Cynthia Cashman, Kay Ellingson, Lori Engstrom, Michael Herrick, Kris Igo, Holly Klinger, Maggie Kubak, Allen Levine, Cece Martin, Pat McKay, Kerry Muerhoff, Krystal Ringwelski, Sara Specht and Honey VanderVenter.

* * *

On behalf of NABC, we thank Bill McCutchen (Texas A&M University) for excellent leadership as NABC's chair, 2010–2011.

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NABC

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Executive Director
NABC

October 2011

[1]Dr. Ponce de León, RWFH and AE also served on the scientific advisory committee.

PREFACE

In 2002, NABC's fourteenth annual conference—hosted by the University of Minnesota—had the theme *Foods for Health*. The resulting proceedings volume, *NABC Report 14*, was titled *Integrating Agriculture, Medicine and Food for Future Health*. In similar vein, in 2009, NABC published *Food and Agricultural Research: Innovation to Transform Human Health*[1], a white paper proposing a 21st-century plan to make food and agriculture a full partner in the endeavor to improve human health. Building on the themes presented in *Food and Agricultural Research*, NABC's twenty-second conference, *Promoting Health by Linking Agriculture, Food, and Nutrition*, was convened at the University of California's Davis campus in 2010. In 2011, the twenty-third NABC conference was hosted again by the University of Minnesota, June 15–17, with food once more the underpinning issue. However, this time, diet was replaced by food security as the focus of discussion. *Food Security: The Intersection of Sustainability, Safety and Defense*, addressed the realities of a food-insecure world in the 21st century.

Under the weight of a burgeoning global population, changing climate, rising food prices, emerging pathogens, and concerns over environmental integrity and food safety, agriculture faces a period of transition as it is challenged to respond rapidly at local, regional, and global levels to the complex dimensions of food security. Agricultural biotechnology, as a promising way forward, looks to play a key role in the development of technologies that will help feed the world, yet substantial debate remains on how to best capitalize on its benefits while mitigating its risks.

To foster discussion on these issues, NABC 23 was organized around four topic areas:

- *Sustainability and Needs of 2050 Agriculture*;
- *Systems-Based Approaches to Food Protection and Safety*;
- *Preparing for Emerging and Unknown Threats*;
- *Emerging Biotechnologies to Promote Safety, Enable Defense, and Discourage Fraud.*

The focus on food security emphasized safety, chiefly from the perspectives of contamination and terrorism. There was less stress on global food adequacy by 2050. An excellent cross-section of interdisciplinary talks was presented[2] to 104 attendees by an impressive list of speakers—from academia, industry, federal agencies, CDC, and FAO—and at the conclusion of each session, the presenters convened for panel question-and-answer sessions, to reflect on the issues raised and to take comments and questions from the audience. As is traditional at NABC meetings, attendees had additional opportunities for discussion during breakout workshop sessions[3].

[1]http://nabc.cals.cornell.edu/pubs/AgFood_web.pdf.

[2]An overview of the presentations is provided on pages 3–11.

[3]Workshop discussions are summarized on pages 15–23.

Participants in the *Student Voice at NABC*[4] program attended the plenary sessions and breakout workshops, and then met as a group to identify current and emerging issues relevant to the conference subject matter[5].

This volume contains an overview of the conference, a summary of the breakout-workshop discussions, manuscripts provided by the speakers[6], and the *Student Voice* report. Transcripts of the Q&A sessions are included.

NABC's 2012 conference—on agriculture and water, hosted by the University of Arkansas[7]—will convene in Fayetteville, June 11–13.

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The figures in the printed version are in grayscale. Information may have been lost from those received from the speakers in color. Color versions are available at http://nabc.cals.cornell.edu/pubs/pubs_reports.cfm#nabc23.

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[4]The *Student Voice at NABC* program provides grants of up to $750 to graduate students at NABC-member institutions (one student per institution) to offset travel and lodging expenses. Also, registration fees are waived for grant winners.

[5]The *Student Voice* report is on pages 243–245. Information on the *Student Voice at NABC 24* will be available at http://nabc.cals.cornell.edu/studentvoice/.

[6]In some cases, edited transcripts replace speaker-written manuscripts.

[7]Further information may be accessed via http://nabc24.uark.edu.

CONTENTS

PART I—CONFERENCE OVERVIEW

Overview of NABC 23
Food Security: The intersection of Sustainability, Safety and Defense

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The National Agricultural Biotechnology Council's twenty-third annual conference took place in St. Paul, Minnesota, and was organized and hosted by the College of Food, Agricultural and Natural Resource Sciences (CFANS) at the University of Minnesota.

The world will have to double food production in a sustainable manner in the next 40 years if it is to support the nine billion people expected by 2050. The amount of food to be produced in this short lapse of time is almost equivalent to the total produced in the world up to this point in time. This challenging task has to be accomplished in the context of a global warming trend due to the accumulation of greenhouse gasses (GHGs) generated by human activity and resulting in climate change. To make matters more complicated, world energy demand has grown significantly, and agriculture is envisioned as one of the sustainable sources of renewable energy. In the context of this conference, food security does not only mean food availability, but also its protection from contamination, bioterrorism and fraud.

Daniel Gustafson (Food and Agriculture Organization) opened the conference with his keynote presentation, *The Importance of the Convergence of Sustainability, Safety and Defense for World Food Security.* He reminded us that the challenge at hand is no longer local, regional or continental, it is global. He further pointed out that

> *natural resource degradation, water scarcity, and climate change are raising concerns that we are nearing a tipping point where disaster may be imminent if we continue on the same unsustainable path…It is clear that decades of progress may be wiped out very quickly. The issues are now elevated, and rightly so, to be seen as threats to national security.*

These interconnected threads demand the convergence of disciplines, generation of integrated solutions, in sum to develop the

> *…concept of "climate smart" agriculture that has the objective of looking for solutions that simultaneously increase productivity, reduce vulnerability and increase resilience to change, reduce or remove GHG emissions, and contribute to food security and national-development goals.*

However, Gustafson acknowledged the

> *inherent difficulty in creating a shared understanding of the problems and shared commitment to solutions… It is very difficult to integrate science and society where values are in conflict, where experts from science or industry expect to dictate policy objectives or command conformity. There is, for better or worse, reduced faith in the ability of science to manage risks, coupled with increasing communication within communities of like-minded individuals who share strong beliefs and opinions regardless of the evidence.*

Even though the latter is a difficult task, the urgency to find win-win solutions requires that we pursue the convergence that Gustafson proposed, a tall order for all involved in moving forward global solutions.

Plenary Session 1. Sustainability and Needs of 2050 Agriculture

Jonathan Foley (University of Minnesota, *Solutions for a Cultivated Planet: Simultaneously Addressing the Food Security and Global Sustainability Challenges Facing the World*) stated that the magnitude of the challenge in doubling food production equals all of the six previous efforts in doubling food production in human history. He proposed six contributory approaches from a global-scale perspective:

- Slow the rate of agricultural land expansion into sensitive ecosystems because production and productivity returns do not justify the increase in detrimental environmental effects.
- Close agricultural yield gaps. For example, corn yields vary by a factor of 100 between high- and low-efficiency farmers.
- Raise crop-yield ceilings: A phase-in approach is needed in some of the poorly performing regions of the world with nutrients and water limitations addressed first and genetic improvements made later.
- Improve the efficiency of environmental resource use. This is explained as the need to improve crop productivity with less nitrogen, less phosphorus and less irrigation water.
- Diet modification. About 60% of global crop production is for food, 35% is for feed and 5% is for biofuels production. Changing to 100% of production for food would increase availability of food by 40% over the current level.

- Food-waste reduction. It is estimated that about a third of the food produced worldwide is wasted. In high-income countries, waste occurs at the consumer end, and in low-income countries at the production end due to crop failures and lack of infrastructure.

Taking all of these recommendations together, great strides towards a comprehensive solution can be made. Foley stated:

> *The task is to feed the world while sustaining the planet. Failure is not an option. Civilization depends on solving this problem literally. We have to get it right and we get only one try at it.*

Water is an issue that needs to be addressed at various geographical scales; however, it is widely recognized that changes/actions in water management and conservation need to start at the local level, with the understanding that it affects, in comparable measure, the regional and continental scales. Water is perhaps the most important natural resource and agriculture uses most of the available fresh water. It is becoming scarce in some regions of the world and it must be managed and preserved if food production is to be doubled sustainably.

Minnesota is at the headwaters of three of the largest North American river basins, which are replenished largely from rain and snow. Minnesotans are conscious of their water heritage and of their responsibility to care for their state's water resources and for effects on users downstream. Three years ago (2008) Minnesotans added the Clean Water, Land and Legacy Amendment to the state constitution and part of a small increase in the state's sales tax goes to the Clean Water Fund to protect and enhance water resources. In her presentation, *Looking Far into the Future: The Minnesota Water Sustainability Framework*, Deborah Swackhamer (University of Minnesota) described the Framework as providing

> *…a long-range plan that frames major water sustainability issues and provides strategies and recommendations for addressing them. It is not a specific spending plan for the Minnesota Clean Water Fund, nor should it be limited by the availability of Clean Water Funds; rather, it includes recommendations for investments that may come from sources beyond the Clean Water Fund (other state funds, private funds,* etc.*), as well as recommendations that require little or no investment by the state.*

The Framework is not a set of strategies and recommendations that are applicable across the globe because there are factors that affect different regions in different ways. However, it can serve as a model for other states in the Union and beyond.

Terry Stone (Syngenta, *Developed and Developing World Sustainability Perspectives*) presented several examples of progress achieved in developing countries by application of new technologies and also of continued stagnation and poor efficiencies caused by lack of infrastructure, poor resources and restrictions to adoption of modern technologies due to lack of information and low literacy. If the goal to double food production is to be achieved, then increases in agricultural productivity in both developing and developed nations are essential.

In the developed world, it will require sustaining gains in agricultural productivity through continued investment and implementation of advanced technologies, measuring agricultural productivity holistically and harnessing the market power of major players to create farm-to-fork incentives for sustainability. The most problematic barriers in the developed world will likely continue to be over-zealous, under-informed and unsynchronized regulatory strictures. Many of the catalysts that can help accelerate the evolution of smallholder, subsistence farmers into viable commercial farmers are likely to come in the form of new hybrids, new traits, new seed treatments and new crop-protection chemistries.

Development of extension services to educate the approximately 1.5 billion smallholders and subsistence farmers in the use of these technological advances is a must if sustainable increases in productivity are to be realized.

Plenary Session 2. Systems-Based Approaches to Food Protection and Security.

This session was opened by June Medford (Colorado State University) with a keynote presentation, *Detector Plants for Agriculture, Food and Environmental Monitoring*. Plants are being developed as sentinels to monitor human and natural environments for the presence of pollutants, chemical contaminants and explosives that are intentionally or unintentionally introduced. To achieve this,

. . . sentinel plants need to have a reporting system which is easily detectable, allows remote monitoring and is re-settable.

Medford's laboratory has engineered a synthetic de-greening system that causes rapid chlorophyll loss when sensing a specific input. The chlorophyll loss can be detected within hours by remote sensing by induction of a white plant phenotype that is easily recognizable.

The de-greening circuit functions via light-dependent damage to photosystem cores and the production of reactive oxygen species.

These de-greened plants are also able to re-green after removal of the inducer agent. Hence, it provides the first easily re-settable reporter system for plants and the capacity to make re-settable biosensors.

The second component of this system is based on the conserved histidine kinase (HK) signal-transduction system. The Medford laboratory demonstrated that

HK sequence conservation and cross talk can extend across kingdoms and can be exploited to produce a synthetic plant signal-transduction system.

Hence, in response to exogenous cytokinin, the HK-engineered system is activated and a bacterial response regulator is translocated to the nucleus and activates gene transcription. The last piece of this integrated system uses computationally designed periplasmic binding proteins that allow specific small-molecule ligand-sensing capabilities on plant-leaf receptors. When the HK signal-transduction system is activated by these proteins, it prompts the expression of a gene that in turn produces a protein that activates the de-greening circuit, previously described, and generates a visual white phenotype (chlorophyll loss) that can be remotely monitored. This is a very clever system that will, in due time, be applied to monitor the presence of environmental contaminants.

The second presentation in this session was by David Andow (University of Minnesota) who focused on *Risk and Vulnerability*. Andow's talk provided a series of examples of environmental risk assessment (ERA), their uses and acceptability to validate environmental policy. In general when ERA is carried out, the public is more likely to accept policy decisions. However, he pointed out that risk assessment is imperfect and highlighted some of the underlying reasons of why this is so. For instance, different risk-assessment frameworks exist in different countries. In Australia, agriculture has a separate ERA, whereas Europe considers agriculture as part of the environment and farming practices are part of risk assessment. Conversely, in the United States, only some aspects of agriculture are considered to be part of the environment. Therefore, many indirect effects may or may not be considered as part of the risk assessment of specific technologies, depending on the regulatory process of the country. Andow argued in favor of including cultural significance as part of ERA. His example for the latter was based on the public uproar due to possible negative effects of *Bt* corn on the monarch butterfly; the public reaction was linked to the cultural significance of monarch butterflies in the United states and Mexico. Other countries may also have "preferred" species that need special consideration for ERA analyses. In general, Andow pointed out that

> *…polarization of opinions results from the fact that some people see mostly benefits and some people see mostly risks and everyone balances risks and benefits differently. It's a social phenomenon with no agreement about how we weigh the factors involved and, therefore, it is impossible to reach consensus.*

Martin Duplessis (Health Canada, *Detection and Prevention*) explained the organization of the Canadian food-safety system and the several responsibilities of the institutions involved. He elaborated on the methodological approach used to identify foodborne pathogens, and emphasized the importance of sampling, sample preparation, pathogen enrichment, and methods for pathogen detection, isolation, identification and typing. Each of these steps has its own criteria and complications that need to be managed and overcome to deliver quick and accurate results. Microfluidic modules are being developed and are proving to be effective. Future technologies are focusing on more-rapid detection methods and miniaturization.

Detloff von Winterfeldt (International Institute for Applied Systems Analysis, *Systems and Risk Analysis for Food Protection and Security*) provided definitions for system analysis and risk analysis.

> *Systems analysis is a group of model-simulation analysis tools—applied mathematics if you will—specifically applicable to very complex systems that undergo dynamic changes and are fraught with uncertainty…[T]he analysis is problem-focused and solution-oriented.…The model is usually developed by a multidisciplinary team taking a holistic view of the problem.*

On the other hand, his definition of risk analysis

> *...is a combination of risk assessment and management that involves identifying the risks, quantifying them*—i.e. *quantifying the possibilities of events that could occur as well as quantifying their consequences—and then looking at decision-opportunities, intervention and risk reduction, and evaluating them.*

von Winterfeldt gave examples of systems and risk analysis for bioterrorism and food protection. His recommendation for food protection was

> *...to find risk-management options with large co-benefits that pay for themselves. For food defense, you might think in terms of strategies to prevent a terrorist tainting something that may be beneficial for other food-safety reasons. Equally, solutions that address regular safety issues by introducing new testing and inspection procedures may help prevent terrorism.*

In sum, he concluded:

> *The main challenge is how secure is secure enough? Clearly, we will never be completely safe from terrorism. Nor will we ever have a completely safe food supply.*

Plenary Session 3. Preparing for Emerging and Unknown Threats

In his presentation, *Preparing for Emerging and Unknown Threats: Public Health,* Robert Buchanan (University of Maryland) discussed factors affecting the emergence and re-emergence of foodborne diseases, research needs, and the role of biotechnology innovation in assessing and preventing foodborne diseases. The drivers that cause disease emergence are global demographics, global food chains, processing technologies, and gene transfer that causes pathogen variation. He identified research needs in the areas of anticipation and prevention of emergence of food pathogens, containing diseases before they become established, and disease eradication. Buchanan acknowledged the inherent difficulties of these research needs and their relative importance based on their effectiveness. Biotechnology may be helpful in determining the mechanisms of gene transfer and what selective pressures, if any, can prevent it. Many foodborne microorganisms show considerable diversity, *e.g.* 2,400 serotypes of *Salmonella enterica* have been identified; is it possible to identify a common factor that biotechnology can take advantage of to prevent foodborne outbreaks? Is it possible to reduce genetic variation in microorganisms? Biotechnology may also provide tools to assist in assessing sentinel populations like the very young, the elderly and immune-compromised individuals. Likewise, Buchanan identified long-standing research needs that have not been resolved: sample size and assessment of the immune status of individuals. In the former, as food-sample size becomes smaller, assay sensitivity is significantly reduced, and it is important to have rapid methods to determine the immune status of affected individuals to help in risk assessment and in determining what factors should be emphasized. In essence, he placed emphasis on the need for "just in time" research when responding to an emerging foodborne disease.

With *Recent Animal Disease Outbreaks and their Impact on Human Populations*, Jeff Bender (University of Minnesota) reminded the audience that there are very positive and strong connections between animals and humans, but that there are, as well, reasons for concern because about 61% of all human pathogens are zoonotic (acquired from animals); of 175 newly emerging pathogens in humans, 132 are zoonotic. The increase in new diseases, aside from the fact that humans are encroaching more and more on wild-animal habitats, is due to increases in world trade, animal translocation, ecological disruptions, climate change, adaptation of pathogens, and changes in the way we raise animals. Animal health and human health are intertwined, and we should be cognizant of the global consequences of international trade in animals and animal products and the impacts of human population growth on the environment. Early and rapid detection coupled with prompt intervention are the goals that will allow quick identification of exposed individuals for early treatment, isolation and containment of emerging diseases.

Jacqueline Fletcher (Oklahoma State University) presented a talk on *Preparing for Emerging and Unknown Threats in Crops*. Plant diseases have significant impact on food security. Our vulnerability resides principally on the fact that we grow, for the most part, monocultures that could be wiped out in a single season by a new pathogen. Fletcher provided the example of the potato famine in Ireland in 1880. A relatively new race, TTKS, of the wheat stem-rust pathogen, *Puccinia graminis* f. sp. *tritici*—commonly known as "Ug99" because it emerged in Uganda in 1999—has spread beyond its area of origin. Most currently grown wheat varieties lack resistance to Ug99. Accordingly, the task is to identify resistant varieties and incorporate that resistance into cultivated genotypes.

Plant-disease impacts on food security and social stability can be significant, and in the last few years plants have been the sources of foodborne diseases by consumption of contaminated fresh produce. Fletcher described for the audience the National Plant Disease Recovery System (NPDRS) that is the responsibility of the USDA Office of Pest Management Policy.

> *This initiative consists of the preparation of response plans for each of the APHIS plant pathogen select agents as well as a number of other threatening plant pathogens. The NPDRS's purpose is to ensure that the tools, infrastructure, communication networks, and capacity required to mitigate the impacts of high-consequence plant-disease outbreaks are such that a reasonable level of crop production is maintained in the United States.*

A second initiative established the National Plant Diagnostic Network (NPDN) after the September 11, 2001, attacks. This is a nationwide system of plant diagnostic laboratories that include USDA, land-grant universities, state Departments of Agriculture and private laboratories. Furthermore, in 2007, the National Institute for Microbial Forensics & Food and Agricultural Biosecurity (NIMFFAB) was established at Oklahoma State University. NIMFFAB's role is "to serve as a link between the plant-pathology community and law enforcement and security communities, policymakers, and funding agencies," *i.e.* a system to assess, characterize and respond to emerging plant diseases and reduce our crops' vulnerability to harmful intent.

Plenary Session 4. Emerging Biotechnologies to Promote Safety, Enable Defense, and Discourage Fraud

John Besser (Centers for Disease Control) began his presentation *Emerging Biotechnologies to Promote Safety* by indicating that "each year, one out of six American—48 million people—are thought to become sick with a foodborne illness, and 3,000 die." By this measure, foodborne illnesses are quite common, hence emphasis is being placed on prevention and surveillance. A national network of public-health and food-regulatory agency laboratories coordinated by the Centers for Disease Control and Prevention (CDC) has been developed. All collaborators perform standardized molecular fingerprinting of foodborne-disease-causing microorganisms by pulse field gel electrophoresis (PFGE). PFGE images are deposited in a centralized database at the CDC and are used to make comparisons and identify strains of microorganisms. The consortium and database are known as PulseNet USA. PulseNet collaborations and databases have been developed in Canada, Latin America and Caribbean countries and are integrated with PulseNet USA. PulseNet International includes 86 countries with the exception of Europe where it has been difficult to integrate the systems because some EU countries prefer to operate independently. Besser presented several examples of foodborne diseases for which the use of PulseNet information facilitated the identification of the origin and also reduced the time of detection and of recall of the contaminated food. Research in enhancing strain resolution for identification is necessary. At present, the system is limited to only the 30% of known foodborne-disease-causing pathogens. Use of metagenomics technology to assess unknown pathogen seems to have potential.

In his talk, *Emerging Food Systems Defense Risks and Technology Needs*, Shaun Kennedy (University of Minnesota) defined differences between food security, safety, defense and protection. Security may be defined as supply sufficiency, whereas safety implies system reliability. Defense, on the other hand, implies system resiliency and protection is defined as the continuum of safety and defense. Kennedy examined emerging intentional threats and technology needs in two areas:

- Food-system drivers—public-health surveillance systems; system complexity and globalization; and developing-world value-added agriculture—that generate concerns for intentional contamination, and
- Intentional-contamination drivers—economically motivated adulteration (EMA); disgruntled employees; criminals and deviants; and terrorists.

Essentially, surveillance systems require technologies for earlier detection of contamination. The complexity of food systems (the many components of any product delivered to consumers and the global origin of each component) make the task of identifying origin of contamination difficult and lengthy. It is obvious that new, fast and reliable technologies for traceability are needed. When developing countries move from commodity production to value-added production, although it contributes to the food supply, risks for food contamination and vulnerability increase, hence the need to develop better capability for assessment of systems-based risk and vulnerability.

Food Fraud: Public Health Threats and the Need for New Analytical Detection Approaches was the theme addressed by Jeffrey Moore (US Pharmacopeia), who focused largely on EMA of food products. A practical example is the adulteration of milk with water—when milk was sold by weight—to increase its value at sale. When milk was sold based on protein content, its adulteration with water was eliminated. However, in more recent times, it has been adulterated with melamine because protein content is often assayed with non-specific technologies like the Kjeldahl method, which measures total nitrogen. More-specific methods and/or method combinations can detect melamine adulteration and more precisely measure protein content. EMA examples are numerous: wheat can be extended with urea; turmeric powder can be extended with lead chromate; and olive oil can be diluted with hazelnut oil. Factors that motivate EMA are the rising prices of agricultural raw materials, the complexity of supply chains, and the complex compositions of food products. Many times, adulteration has had significant public-health consequences, *e.g.* fatalities from adulteration of baby formula with melamine. Moore provided examples of the significant advances achieved by the US Pharmacopeia[1] (USP) in collaboration with many institutions in establishing standards to detect EMA. However, he also pointed out that

> *...the nature of EMA and the paucity of analytical detection methods means that the safety of counterfeit foods is in the hands of fraudsters. A significant gap needs to be filled to develop analytical technologies to detect and deter EMA.*

[1]A global independent, not-for-profit, non-governmental, science-based, public-health, volunteer-based organization dedicated to the collection and establishment of standards for pharmaceuticals, medicines and dietary supplements. Since 1966 it has produced the Food Chemicals Codex, a compendium of internationally recognized standards for the purity and identity of food ingredients.

PART II—BREAKOUT SESSIONS

Workshop Summary

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Breakout sessions were held on days 2 and 3 of the conference, each comprising four parallel workshops. Oral reports on the first workshop were delivered on day 3 prior to the second breakout session, and written reports on the second workshop were prepared soon after the conference. The objective of the workshops was to provide all participants the opportunity to contribute verbally on the aspects of food security that had been discussed during the formal presentations and Q&A sessions.

To help initiate dialog during the breakout sessions, the facilitators posed these questions:

- *Breakout session 1:* Given what we have heard at the conference and the nature of food security, what would you propose should be the set of research actions necessary to start addressing food security at the local, regional and global scales?
- *Breakout session 2:* What research and policies do you think are required to overcome the challenges of water and land availability in our quest to double food production while minimizing environmental impact in the next 39 years?

[1]Recorder.
[2]Discussion facilitator.
[3]Oral Reporter.

The participants' responses did not necessarily address these questions. Instead, the facilitators allowed free-flowing discussions. This is not an exhaustive coverage of those discussions, but a synthesis of key points that emerged[4], under ten headings. Questions posed by participants may be interpreted as researchable issues.

Food Security

- A primary definition of food security is freedom from hunger. A broader definition is that food security comprises food safety, which is a consumer-level issue, and food supply, which is a crop-production/distribution issue. Food safety is relatively more important in developed countries and food supply is relatively more important in developing countries in which significant fractions of the population are concerned with where their next meal will come from. The global population is expected to increase by ~2.5 billion to ~9.5 billion by 2050, requiring a doubling of food availability in developing countries. In most of the world, food security is viewed chiefly as freedom from hunger.
- On the other hand, in developing countries, agricultural exports can be a source of cash that can lift people out of poverty, which then increases their food security.
- Food security is multidisciplinary in scope. The disciplines involved need to be defined to understand the social factors involved in policymaking that affects food security. Accordingly, national and international initiatives require taking local priorities into account. Each country has unique strengths and weaknesses; optimization of national strengths will be needed to feed 9.5 billion people by 2050.
- Food security is often used to refer to freedom from hunger. Food availability and accessibility are part of the definition, and quality, including protein content, should be included. It is not just about calories; calorie type is also important.
- Local preferences affect food security. For example, prejudice exists against rice that isn't white; many are reluctant to eat Golden Rice.
- How the general public reacts to policies adopted for improvement in food security depends, in large part, on the degree to which direct benefits are perceived. Approval of herbicide tolerance, for example, may be difficult to ensure because consumers are unaware of its popularity among farmers.

Food Safety

- As stated above, food security comprises food safety, which is a consumer-level issue, and food supply, which is a crop-production/distribution issue. Food safety is relatively more important in developed countries where food is plentiful and relatively inexpensive, but where several outbreaks of foodborne illness, affecting thousands of people, have occurred in recent years.

[4]As judged by AE.

- Research is needed to develop new ways of treating foods to prevent or eliminate contamination by pathogenic organisms and/or chemicals.
- Crop breeding focuses mainly on pre-harvest characteristics, *e.g.* susceptibility to insects and disease and to abiotic stresses. Post-harvest issues are often neglected. The only example where a pre-harvest trait created a post-harvest impact is *Bt* corn, *i.e.* in reducing mycotoxin production. More research is needed on preventing adverse changes during storage of harvested entities.
- Recent food-safety issues—*e.g.* the contamination of fresh foods by *E. coli* in Germany—have stimulated discussion of how national and international food systems are managed.
- Measures to keep food safe must be used at all stages in the value chain—from farm-gate to plate. However, many of the greatest risks result from inadequate hygiene in the home due to consumers being poorly informed on best practices for handling food.
- Scale is an issue. Research is needed to determine if the same inspection processes should be in place to assess safety for small-scale, locally produced food as for regional and national production systems.
- Although not as broad in its importance as food availability, if food-safety issues are not addressed, societal and political disruptions could be massive.
- Minnesota voters increased their tax burden to support water legislation. Research is needed on how to induce the general public to follow this model for food safety.

Food Supply

- What fraction of national resources is the United States willing to expend to produce food for other countries? Under some circumstances, when we export it is counterproductive to the long-term viability of agriculture in the importing countries. Doubling production may be possible for the United States and Canada, but the challenge is to get other countries, where the needs are greatest, to produce more food. Most countries have enough land and water and can produce sufficient food if it is priced right. An essential aspect is to get fertilizers to farmers who can't afford them, and can benefit most from them.
- Developing countries need to invest in food-production research with particular emphasis on addressing biotic and abiotic factors. To partner with developing countries to improve food production, the United States should provide more financial and logistical support via the international agricultural institutes. US public buy-in obviously will be needed here, particularly in these difficult financial times.
- The reason many developing countries are resisting genetically engineered crops is because they can't sell them in Europe, and often not in Asia, whether or not

they are safe. Cultural barriers can preclude acceptance of data produced by good science. Research is needed on how to close gaps between cultural concepts and science.

- The global economy will prosper best when all of its members are self-sufficient in food. The Gates Foundation provides a useful model for tackling problems affecting the developing world, and with US federal funds potentially significantly greater than those provided by Gates, better progress may be made.
- There is a grass-roots movement in the farming community to return to traditional methods of food production and sale. Concerned about the nutritional value of the food they produce, these farmers wish to contribute to their local economies. Extension programs are encouraging them, but are there sufficient economic incentives?
- In general, consumers understand local food-production systems and place value on locally produced food. With the qualifier "organic," there is a perception of greater healthfulness, albeit not verifiable. Research is needed into improving public understanding both of the risks and benefits of local systems.
- Research is needed to examine whether local food systems are "better" and conducive to food security. Are they more likely to provide environmentally beneficial solutions to current acute public-health issues, with opportunities for closer monitoring and rapid diagnoses of problems?
- Farm-Bill policies influence farmers regarding when and how to use their land. What incentives may be introduced via the Farm Bill to encourage maximum food production?
- The United States and Canada continue to enjoying cheap food, costing <10% of family income. However, agriculture does not operate in a vacuum; it has many impacts on the environment. These effects should be taken into account when placing a value on agricultural production.
- Research is needed in how to modify consumer eating habits to address the obesity epidemic. Food-production companies must change their model for making money; encouragement to eat more must be mitigated.
- Eliminating hunger while feeding 2.5 billion more people by 2050 will require efforts similar to the Manhattan project. At this time, this effort is hugely underfunded.

Animal Production

- Single cell protein—produced on non-arable land—represents a viable substitute for feed for animals that currently consume wheat and corn. It also represents a viable substitute for meat for human consumption.
- Further research is needed in the utilization of animal waste (*e.g.* for energy production).

- The minimization of loss of nutrients from animals is important, *e.g.* similar to the Enviropig® which digests phosphorus more efficiently.
- Nutrigenomics in animals has the potential to improve efficiency of utilization of feed.

Sustainability

- A broadly accepted definition of "sustainability" is needed. It still means different things to different people. In general, it is used effectively from a marketing standpoint. But it is important that we have a common basis to help make progress on an issue that is fundamentally important.
- There is a pressing need to gain better understanding of sustainability of water usage.
- To assess the sustainability of a food-production system requires 10+ years of experiments. Yet funding for such long-term research is seldom available. Funding longevity is usually no more than a third of this time-span.
- Assessing agricultural sustainability must include consideration of soil erosion, soil organic matter, soil moisture content, soil microbiology, soil salinity, and soil macronutrients and micronutrients. A major research need is the development of markers of sustainability, including carbon sequestration, water use and impacts on soil bacteria.
- Some importers in the EU and China are asking for sustainability certification, although there is no consensus on metrics. In the United States, sustainability-certification metrics are being developed at the Universities of Wisconsin and Illinois and at Purdue, with funding from the Soybean Foundation. It is hoped that the next Farm Bill will provide opportunities to further resolve such metrics.
- Importers requiring sustainability certification must be flexible in terms of time-frame, unless they have alternative sources of the commodities they need. It is hoped that, in time, standards will be improved to fulfill buyers' needs.

Water

- Is there a water shortage, or is water just not priced right? How well do we understand the cost of water? Research is needed to help producers make decisions on how much water is needed to maintain crop yields and to increase them. When we export grain and meat produced from that grain, we are, essentially, also exporting the water required to produce that grain, yet the cost of that water is not figured in.
- For water, the priority should be keeping chemicals out rather than developing means of detecting them once they are in. Processing procedures are available to decrease toxin levels, but more research is needed in this regard.

- Hydrological mapping, as in Minnesota, should be done in all states as an important priority.
- Hydraulic fracturing ("fracking") involves pumping large quantities of brine deep into shale in the ground (in the NE United States) to release natural gas. Some 20%–30% is lost and the water that's recovered contains a cocktail of chemicals. The cost of the water should be included in the cost of production of the energy.
- Climate-change effects on water usage, availability and aquifer depletion need research.
- More research is needed on means of artificially recharging aquifers.
- Water delivery is a fundamental problem in many places; consideration should be given to the economics of building pipelines to connect water-wealthy with water-depleted areas.
- Unequal water usage is having increasingly far-reaching effects and research is needed so that water draw upstream is not excessive and takes account of downstream needs.
- Research is needed to develop new cropping systems to maximize ecosystem services, particularly water usage.
- Food waste has been calculated at 1,400 calories per person per day, with concomitant misuse of water and energy. By appropriate conservation, preservation and handling, 30% of these losses could be eliminated.
- Continued research is needed to produce cultivars that use water more efficiently. There remains huge untapped genetic resources within currently grown crops—and plants that may be grown as crops—to produce sources of food that are adapted to higher temperatures, higher rainfall or less rainfall, and can withstand extremes of weather.
- Nutrition, health security, food security and water security are intimately interrelated.

Regulatory/Policy Aspects

- Providing testimony to Congress and/or to regulatory agencies can have greater impact than talking to the media. However, both are important.
- As stated above, how the general public reacts to measures taken to improve food security and safety is influenced by whether they perceive direct benefit.
- Increasing food production is most pressingly important for Africa yet only a handful of African countries have biosafety laws. Assistance should be given to those countries to develop infrastructure and expertise to achieve appropriate regulatory oversight.
- On the other hand, we could run into a Goldilocks conundrum of how much regulation is appropriate. Over-regulation—as judged by some to apply in the

EU—can be fatal and preclude reaping the food benefits that may come from biotechnology, for example.

- Should legislators encourage farmers to produce and sell more-nutritious food locally? How much regulation would be appropriate? What would be the impact of the Tester Amendment[5]?
- Means should be considered whereby farmers can be penalized for poor soil-management practices, to mitigate against the philosophy that it's "their" land.
- Discussions of agricultural policy need to be broad to include climate change, agricultural adaptation, and resilient crop genotypes that will thrive in stressed environments.
- Low-cost food policies are in effect in several countries. Does this policy encourage increased food production?
- In the United States and Canada, the cost of food is <10% family income. Accordingly, citizens show little interest in food policy. How are they to be engaged in this issue for the global common good?
- Policy tends to be barrier-based. Research is needed on design and implementation of outcome-based policy.
- Research is needed on design and implementation of state and federal policies to address the challenges of water sharing and shortage.
- Water budgets should be determined for every state.

Communication/Education

- As scientists, when we talk of the benefits of genetic engineering and other new technologies, the concepts can be difficult for the lay person to understand. Overuse of technical jargon often evokes an adverse cultural response. We need to learn to lay out benefits in understandable terms to help consumers make informed judgments.

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[5]Senator Jon Tester (D-MT) has sponsored an amendment to the food safety bill (S. 510) to further protect small, local food processors and producers. In the 2002 Bioterrorism Act, Congress required that all facilities that manufacture, process, pack, or hold food must register with FDA, but it exempted from that requirement "retail food establishments." FDA defined the term at 21 CFR 1.227(b)(11). For purposes of the definition, the Tester amendment would require FDA to clarify that "direct sales" of food to consumers includes sales that occur other than where the food was manufactured, such as at a roadside stand or farmers' market. Food facilities would qualify for an exemption from the preventive control/HACCP (see footnote, page 211) provisions in section 103 of S. 510 under certain conditions: (1) they are either a "very small business" as defined by FDA in rulemaking; or (2) the average annual monetary value of all food sold by the facility during the previous 3 year period was less than $500,000, but only so long as the majority of the food sold by that facility was sold directly to consumers, restaurants, or grocery stores (as opposed to 3rd party food brokers) and were in the same state where the facility sold the food or within 275 miles of the facility.

- Food security is a multidisciplinary entity. The disciplines involved need to be defined to understand the social factors involved in decision-making. Accordingly national and international initiatives will require taking local priorities into account. Each country has unique strengths and weaknesses, therefore, optimization of national strengths will be needed to feed 9.5 billion people by 2050. Education and training clearly are important and improving scientific literacy of the population as a whole will be necessary to ensure accurate risk assessment of genetically engineered crops and animals, food irradiation, *etc*.
- As climate change occurs, education can help farmers make good decisions with regard to planting patterns (what to plant, how much to plant, when, *etc*.).

Risk

- How is risk assessment to be taught, particularly environmental risk assessment? Multidisciplinary input will be needed including a strong social-science component. Inevitably, risk assessments will be underpinned by cultural values yet must be based on scientific data.
- Formal protocols are needed for analysis of risk from new technologies, which includes input from diverse experts. We usually cope well with engineered systems, but less so with ecosystems, and with terrorism we are just inching our way in. Some say risk analysis will not help to prevent terrorism; on the other hand, we need to take what we know as far as possible. The weakest link issue is still a concern.
- Risk-analysis protocols must be expanded to encompass terrorism, including behavioral analyses of adaptable adversaries.
- What is an acceptable level of risk where food is concerned? The FDA allows risk/benefit assessments for drugs. However, with food there is no accepted standard for risk/benefit assessment. From a cultural aspect, the risk is expected to be zero. For genetically engineered crops, for example, we must attempt to balance benefit with acceptable risk. Often the risk component is emphasized whereas potential benefits are missed or ignored.
- Again, improving scientific literacy in the population as a whole will be necessary to ensure scientifically based risk assessment.
- What model should be adopted by countries devising litigation for risk assessment of genetically engineered crops? The US model isn't seen favorably by many.

Biofuel and Energy

- Research is needed to provide better understanding of the role of biofuels in recent increases in food prices globally.
- Although second-generation biofuels hold much promise, environmental implications of exploitation of marginal lands—from large-scale planting of switchgrass

for example—needs thorough examination. The consequences of stover removal and energy-crop production—for soil fertility, water budgets, soil-nutrient content, and herbicide and insecticide needs—are largely unknown; research is needed for construction of sound economic models and to inform policy.

- Using algae as biomass for biofuel production requires more research.
- Perennial crops will help prevent soil erosion, and conserve energy. However, grain crops have evolved to use limited resources for maximum production. Research is needed to understand the ecological effects of changing life cycles.

PART III—PLENARY SESSIONS

SUSTAINABILITY AND NEEDS OF 2050 AGRICULTURE

The Importance of Convergence of Sustainability, Food Safety and Defense for Food Security

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The problems of food security, sustainability, and food safety and defense are not new, nor is the idea of convergence new. With more than 900 million people chronically undernourished, we are not on the verge of food crisis, we have been in one for a number of years. This is true for the number as well as percentage of the global population who do not consume sufficient calories.

Food safety is an historic problem with 5,000 people estimated to die of foodborne illnesses each year in the United States and 7,000 in the European Union. In 2010, the Pew Charitable Trusts estimated the annual health-related costs from foodborne illness in the United States at $152 billion. Food defense and the intentional destruction of crops, livestock and water supplies go back to ancient times.

What is new is the recognition that these problems are global and inevitably cut across national boundaries. The value of agricultural trade is ten times larger than it was in the 1960s, and the global population is much larger and more mobile. Natural-resource degradation and climate change are raising concerns that we are nearing a tipping point where disaster may be imminent if we continue on the same unsustainable path. In the *Wall Street Journal* in May, 2011, Peggy Noonan called unsustainability "the first buzz word of the 21st century." This recognition may have come about in any case due to concerns about population growth and climate change, but what really served as the wake-up call for food security was the political instability that grew out of the 2007/08 food-price crisis. This got everyone's attention and, on top of avian influenza and the financial crisis, raised awareness beyond anything that advocacy had acccomplished that neglecting problems and doing the wrong things will eventually cost us, and that global disaster is a possibility. It is clear that decades of progress may be wiped out very quickly. The issues are now elevated, and rightly so, to be seen as threats to national security.

Global Food System

Why did this not happen earlier? It is noteworthy that the global food system has worked well for the majority of the world's population. For a long time, food production had a low priority; prices were declining, and agriculture looked like a sector that developing country governments and donors wanted to move out of, not invest in. This led to lack of attention, poor policy choices, and low investment in global agriculture. As a result, we have a longstanding problem, even without any new crisis of one billion chronically undernourished, plus perhaps a billion more with micronutrient deficiencies. About three-quarters of the chronically hungry are rural who produce food, either as smallholder farmers or landless laborers. Their crop productivity is low and they do not produce sufficient amounts or earn enough or enjoy access to a social safety net to get enough to eat. We should have tackled this much earlier and we didn't.

What comes next, however, makes the goal of global food security a lot more challenging, and *new* threats instill urgency into the importance of convergence. Solutions to food security have always required integration, which partly explains why progress has been slow. Now there is recognition that there is no alternative—addressing these global problems in isolation will not work. Solutions will come only through convergence of approaches, disciplines, and cooperation among people with diverse perspectives.

Interconnected Threats

The major threats are interconneted and they start with food production and the challenges of feeding a lot more people over the next 40 years (against a backdrop, remember, of 925 million people who are chronically undernourished). The rate of total population growth is steadily declining and we will reach, in the not-too-distant future, a point at which population will no longer grow. This will be a very important development, but, before we get there, the world will add another three billion people, requiring a doubling of food production. FAO's estimate is 70% more globally and 100% more in developing countries; other estimates, using somewhat different assumptions, come up with higher or lower figures, but all show a very serious production-increase challenge.

This will be the last time we need to double production, but how to achieve it? Global annual growth in wheat and rice yields have stagnated at 0.6% to 0.7%, whereas we need double that rate. Almost all of the increase in production will have to come from increased productivity, without adding more land. In addition, all of the population growth will be in developing countries, coupled with much greater urbanization. Incomes for most people will continue to rise and diets will change, with people eating a lot more meat, which will affect what is produced, how it is produced, and where.

We have had good experience with raising productivity levels in the past, but rates of increase are slowing. Recent estimates of the impact of climate change for the period from

1980 to 2008 indicate that global wheat output is lower by 5.5% than it would have been otherwise, and corn 3.8% lower. These may seem like relatively small amounts, but as current supply and demand are very tight for both crops, these losses of production are probably responsible for the current price spike.

Food production is consuming the world's resources at an unsustainable rate. It accounts for 70% of water use and 34% of land use. These investments of resources cannot continue at this pace while production is doubled. We are already using more than can be sustained, even without the additional requirements. Something has to change. In fact, a lot has to change. We need more production to resolve food security, particularly by poor families who raise food, but this has to be accomplished on a more sustainable environmental footing. The political reality is that without food security we won't make progress on sustainability. Resolving hunger is a requirement for environmental health, and sustainability is a requirement for achieving food security for the current population and for the larger population in the immediate future.

Food production is, of course, only one part of the food-security equation, but the challenges of production and the problems of the environment are very closely linked, as they are to income growth. Crop and livestock production, natural-resource degradation, food safety, climate change and political instability have mutual effects and none can be resolved in isolation.

Most emerging infectious human diseases are of animal origin and most of the microorganisms that cause foodborne illness come from animals. Changes in population density, changes in livestock production, and changes in land use have direct impacts on food safety. The inability of societies to ensure access to affordable food by all of its people leads to political unrest and social strife, which, in turn, can lead to severe disruption of agricultural production—as in Kenya in 2008—and to additional land degradation.

On top of that, agriculture contributes somewhere between 17 and 30% of greenhouse-gas (GHG) emissions, depending on what data are included in the calculation. Much of this comes from land-use change and from livestock. Climate change will reduce the rate of growth of agricultural productivity and, depending on the region, it may reduce productivity to levels below those of today. Climate change also is likely to affect the spread of disease, and to cause additional food-safety problems.

Future security threats will come less from foreign armies than from the unintended consequences of social, political, economic and environmental changes. Threats may also result by doing the wrong thing in one area, propagating risk in another domain or exacerbating the original problem:

- After forests are cut to make way for new crop production, new diseases may emerge from animals that spread within the human population;
- Climate change may cause greater variability in rainfall with more-frequent crop failures and more marginal land brought into production, releasing more GHGs;
- Biofuel production, designed to reduce oil imports may take land out of food-crop production, contributing to food-commodity price volatility, leading to political unrest that increases the price of oil;

- Some research results indicate that feeding the corn-ethanol byproduct, distillers dry grains, to cattle increases the presence of *E. coli* 0157 in the rumen, with food-safety implications.

Global Food Supply

The food-supply chain is truly global. Animal diseases cross national boundaries with ease, facilitated by trade, the movement of wildlife and personal travel. The connection between animal health, human health and environmental health is the central feature of emerging infectious diseases. The only way to prevent and control food-safety issues is to address the underlying causes and interactions. Land degradation and lack of development lead to migration, legal or otherwise, with its own problems and impacts. All of these issues cut across borders. They are global challenges that transcend social and political boundaries. None can be solved without the application of multiple disciplines.

The challenges can appear overwhelming. A 2011 report by the UK government, *The Future of Food and Agriculture*, states:

> *To address the unprecedented challenges that lie ahead the food system needs to change more radically in the coming decades than ever before, including during the Industrial and Green Revolutions.*

What happens now will have a huge impact on the future. We are at a turning point; can we transition into greater sustainability and security? The answer of course is "yes," but it will require doing things differently and recognizing the importance of convergence between these principle challenges to food security:

- sustainability as a basis for expanding production and reducing risks from climate change;
- managing food-safety risks; and
- defending the food supply.

Integrated Approaches

This, then, is the focus of the conference. We recognize that we cannot deal with the problems in isolation, and that integrated solutions need to be built around systems that include both science and society. Progress is, of course, very challenging, especially policy change that cuts across boundaries and involves stakeholders and policymakers with diverse values, perspectives and priorities. How might we address these challenges, frame the search for solutions and learn from experience? Everyone attending this conference has good ideas and insight from their own professional experience, and the speakers will, no doubt, address the challenges. We are not alone in placing emphasis on the converging themes of sustainabilty, development and security. Before offering some food for thought on organizing the convergence challenges, here are two examples from very different sources.

The first is from the European Union and its 2010 report *Europe 2020: A European Strategy for Smart, Sustainable and Inclusive Growth*, which recognizes the need for significant changes.

The crisis is a wake-up call, the moment where we recognise that "business as usual" would consign us to a gradual decline…This is Europe's moment of truth. It is the time to be bold and ambitious…Our short-term priority is a successful exit from the crisis…To achieve a sustainable future, we must already look beyond the short term. Europe needs to get back on track [through] three mutually reinforcing priorities:

- *Smart growth—developing an economy based on knowledge and innovation.*
- *Sustainable growth—promoting a more resource-efficient, greener and more competitive economy.*
- *Inclusive growth—fostering a high-employment economy delivering social and territorial cohesion.*

In brief: The need is for economic growth from knowledge-driven innovation, within a greener, sustainable environment that is inclusive and achieves social cohesion.

The second example is from PepsiCo and its 2009 Corporate Citizenship Report, *Performance with Purpose: Investing in Sustainable Growth.* It takes a roughly similar approach highlighting three inter-related themes:

- Human sustainability, focusing on healthy products;
- Environmental sustainability, focusing on water and greener production processes; and
- Talent sustainability, focusing on staff training and skill development within a diverse and inclusive culture.

In other words: Healthy products, from sustainable processes made by skilled and empowered people.

These are interesting formulations that, in many ways, embody what member states want FAO to achieve. Both represent similar themes on the value of what is produced, they acknowledge the centrality of environmental sustainability as a concurrent objective, and they include social concerns of inclusion, capacity and cohesion. How do they—and the forthcoming presentations at this conference—converge in meeting the component, inter-related parts of the food-security challenge? I would suggest three overarching principles.

Win-Win Solutions

First, we need to combine two or more simultaneous objectives. Forget trade-offs; we are looking for win-win or triple-win solutions that link drought relief, for example, to longer-term development, dealing with short-term disasters in ways that enhance long-term potential and reduce recurrent vulnerabilities. We need to increase production and productivity while increasing sustainability. This is very clear in the work on agriculture and climate change; we need solutions that increase production, reduce vulnerability to extreme weather events and mitigate the impact of climate change. This is the concept underpinning "climate smart" agriculture that has the objective of looking for solutions that simultaneously increase productivity, reduce vulnerability and increase resilience to change, reduce or remove GHG emissions, and contribute to food security and national-development goals.

A related concept is "sustainable intensification," which is now the stated objective of FAO's work on agricultural production. Conservation agriculture is an excellent example that is, likewise, a central thrust of FAO's work. The main tenets are continuous minimum mechanical disturbance of the soil, permanent organic soil cover, and diversification of crop species grown in sequence or in association. Productivity should go up as moisture retention is improved, soil erosion diminishes, and the land (and its production) becomes less vulnerable to the impacts of rising temperatures and extreme weather events. Ideally, there is no trade-off; rather there are simultaneous benefits on several fronts: production, income, carbon sequestration, soil improvement, water management, decreased vulnerability. Similarly, integrated pest management seeks simultaneously to increase production while decreasing input costs and use of pesticides.

New approaches to food safety offer other examples. We need ways to intensify livestock production (particularly in developing countries) that reduce their environmental impact and also diminish entry of animal-origin pathogens to the food supply. The world is consuming increasing quantities of meat, which needs to be produced in ways that are sustainable, that diminish rather than increase GHG emissions, and that do not pollute water supplies or otherwise increase food-safety risks.

Convergence of Disciplines

The second area is the convergence of disciplines, integrated within systems-based approaches. Solutions that meet the simultaneous objectives mentioned above often derive from an ecosystems approach. Similarly, analyses at the landscape level expand our ability to see beyond the field level and integrate data to understand complex systems. The "One Health" paradigm is another excellent example, as it recognizes that emerging infectious diseases and many other threats can be dealt with only by integrating animal, human and environmental health. Food safety experts have taken a systems approach for a long time and HACCP[1] analysis is, at heart, a systems approach to hazard analysis. The evolution toward a more thorough risk-management approach from farm to table takes it further.

Convergence of Science and Society

The third theme is convergence of science and society. Addressing very challenging, complex problems requires empowering people and communities to understand the issues—and the science—to make informed and creative decisions: "Talent sustainability," if you will, on a large scale. No matter how converged the objectives, or cross-disciplinary the systems-approach, no one person can successfully implement solutions to complex problems if the definition of the problem varies among stakeholders. No single leader or institution is in charge of any one issue and the outcome will depend on a host of behavioral changes and cumulative decisions. There are, however, good examples of how science and society can converge for better outcomes, and we need many more.

[1]Hazard analysis and critical control points, see footnote, page 211.

My favorite example is the reduction of groundwater use for irrigation by farmers in India, through the Andhra Pradesh Farmer-Managed Groundwater Systems (APFAMGS) project. Groundwater, in small, hard-rock aquifers is being depleted at an unsustainable rate, as in many other parts of the world. The hydrology is well known, as are the problems associated with common-property resource management. The solution, implemented by a consortium of ten local NGOs—with support from FAO—covers about a million farmers in six districts, organized in village-based groundwater-management committees. The focus of the work is on participatory monitoring of hydrological data and crop-water budgeting, without any outside-imposed water-use targets or coercion, or, indeed, recommendation by outsiders that reduction of groundwater use is a goal.

The core concept of APFAMGS is that sustainable management of groundwater is feasible only if users understand its occurrence, cycle, and limited availability. To achieve this, the project adopted an approach aimed at demystifying the science by translating the concepts of hydrogeology and groundwater management to make them accessible to farmers, many of limited literacy. Based on this knowledge, the outcome has been crop diversification and changes in practice with increased income and reductions in groundwater withdrawal leading to improved (but often still elusive) sustainability of water supply. This process of adult learning for better farm management may sound obvious, but this may be the only example globally where it has led to reduced water use. Often, when water is used more efficiently, total usage goes up. This case is also a good example of converging objectives (less water use and more farmer income) and converging disciplines (hydrology, agronomy, economics, community organization). Its success, however, clearly comes from the convergence of science and society, equipping and empowering farmers and their communities to make better decisions.

Other examples come from ways that some countries have dealt successfully with HIV/AIDS, approaching it not as a complicated problem of limited resources for distribution of anti-retrovirals and healthcare, but as a complex problem where people and institutions can be empowered to come up with creative solutions to seemingly intractable problems. Brazil is a good example, highlighted in a Canadian study of how to improve its own health system. Brazilians could have framed the spread of HIV as a complicated problem with more or less foregone and dire conclusions (*e.g.* the drugs were too expensive to be given to all, so limiting choices had to be made; illiterate people cannot be expected to comply with a complicated regime of therapy; resources are very limited so the main focus should be on prevention rather than treatment). These, in fact, were the conclusions of a World Bank study. Rather than this approach, however, the country found ways to reduce the cost of drugs (breaking international patents); found creative ways to induce illiterate people to follow their treatment regimens; used informal networks to supply food and train people to care for themselves; and combined prevention as part of treatment and used treatment to encourage prevention strategies.

Food safety and defense, along with other security threats, require a greater appreciation by society of the science and, in turn, people's understanding of science-based risks. Risk communication is a big part of this, as are educational and training programs. This is a major challenge, especially where there is conflict over desired outcomes, where values, perspectives and priorities differ among participants, all of whom need to be involved to achieve meaningful solutions.

Obstacles to Convergence

This leads us, in conclusion, to two significant obstacles to convergence. The first is the difficulty in designing meaningful indicators. Cross-disciplinary work and programs that are designed to achieve multiple objectives naturally increase the desire to have common indicators. This makes sense, but it has its own problems, both practical and conceptual. Are we measuring the right things? The head of the UK's Department for International Development defended its new emphasis on demanding impact measurement by opening with a question: Does emphasis on measuring impact . . .

> *. . . encourage us to indulge in a host of evils—to focus narrowly on the easy wins, to adopt 'one-size-fits-all' methodology, to take simplistic views of complex societies, and to mortgage long-term change for short-term gain?*

The second obstacle is the inherent difficulty in creating a shared understanding of the problems and shared commitment to solutions. The theme of the 1933 Chicago World's Fair was "A Century of Progress," with the motto: *Science Finds—Industry Applies—Man Conforms*. This was probably never true, but clearly is not operative today. It is very difficult to integrate science and society where values are in conflict, where experts from science or industry expect to dictate policy objectives or command conformity. There is, for better or worse, reduced faith in the ability of science to manage risks, coupled with increasing communication within communities of like-minded individuals who share strong beliefs and opinions regardless of the evidence. We do not have consensus on issues like GMOs, climate change, animal welfare, international trade and many others.

Nevertheless, convergence of sustainability, food safety and defense is essential. I hope that the concept of the importance of simultaneous win-win objectives, the integration of disciplines in a systems-approach, and the convergence of science and society will help us think through the issues that the NABC-23 conference speakers will present.

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Prior to joining FAO, Dr. Gustafson was the program director for Agriculture and Natural Resources at the University of Maryland's International Development Management Center, and from 1977 to 1988 he worked in Brazil for the Inter-American Institute for Cooperation on Agriculture (IICA).

Simultaneously Addressing Food Security and Global Sustainability Challenges: A Summary[1] *of Jonathan Foley's Verbal Presentation*

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Feeding the World

- The question of how we will feed 9 billion people by 2050 is daunting. In 2011 the global population increased to over 7 billion. Two billion additional people will constitute a 28% increase. More people will be economically prosperous and will want to eat meat and other nutritious foods, and there will be increasing demands for biofuels; these factors, with population increase, will require a doubling of global agricultural output.
- While meeting the challenges of doubling output, agriculture will have to be reinvented so that it doesn't contribute to environmental damage in the long term. Doubling output while reinventing agriculture will make what is already a huge problem instantly larger, because we need to think in terms of agriculture's already vast environmental footprint.
- The acreage that is used to grow food is by far the largest use of land in the world. Arable farming occupies about sixty times more land than all of the cities and suburbs in the world combined—about 18 million square kilometers, equivalent to the size of South America. Pastures constitute the largest ecosystem, larger than any biome by far at about 34 million square kilometers, equivalent to the size of Africa. Together, agriculture already uses about 40% of the earth's land surface to grow food, leaving rainforest, Siberia, Antarctic and the Sahara and other deserts.

[1]From a transcript of *Solutions for a Cultivated Planet: Simultaneously Addressing Food Security and Global Sustainability Challenges*, a verbal presentation made at NABC 23 by Jonathan Foley, University of Minnesota, St. Paul, Minnesota, jfoley@umn.edu.

Water

- Withdrawals from the Colorado River—primarily for irrigation—are such that it no longer flows into the ocean from Mexico. The Aral Sea, between Kazakhstan and Uzbekistan, provides another example. One of the four largest lakes in the world with an area of 68,000 square kilometers, in the 1960s its tributaries were diverted by the Soviet Union for irrigation, mainly of cotton. By 2007 it had declined to 10% of its original area.
- Agriculture is the biggest user of water globally. About 70% of water withdrawals are for agriculture. It is 80% to 90% in terms of consumptive use, *i.e.* taken out of a watershed, used in some process, and then not returned to the water shed. Industry uses water, as do we in our homes, but most of that returns to the water shed in one form or another. Water that is transpired to the atmosphere is consumed by plants rather than used and returned to the water shed.
- Agricultural practices, because they are so vast, are the single largest cause of pollution of water.
- Through agricultural applications, the amount of available nitrogen in the environment—especially in water—has quintupled in the past 60 years, and phosphorus has doubled.

Crop Productivity

- Crop productivity is plateauing and even declining in many places; rice, over the past 20 years, provides a good example. On the other hand, maize has shown significant gains in productivity in the richest areas of the world, where incomes and infrastructure foster it—Iowa, Minnesota, Europe, parts of South America—but with declines in most of Africa except South Africa.
- On the other hand, total crop production has increased because the area of land that is harvested has increased. Fewer crop failures occur and more of the world is becoming double and triple cropped; land is being used more efficiently.
- Two strategies are available for the production of more food: expanding agriculture into new areas, and intensification of agriculture. The former has far-reaching implications for carbon emissions/climate change and biodiversity decline. Intensification usually requires increased inputs of water, fertilizers and energy, with increased environmental pollution.
- The total amount of farmland in the world has increased by only 2.5% over the last 20 years. However, this statistic conceals a more subtle picture. Agriculture has expanded considerably in the tropics whereas agricultural lands have been lost in the mid-latitudes due to urban expansion and agricultural abandonment—mostly in China, some in Europe and less in the United States.
- An international team just finished a 2-year study, evaluating core strategies to double food production with acceptable trade-offs in environmental impacts.

- It was strongly recommended that agricultural expansion be slowed. Theoretically agriculture could be expanded in Africa, Latin America and Indonesia, but only at the expense of biodiversity and reserves of carbon in savannahs and rain forests. The damage to the environment would not justify relatively minor increases in food production; the ratio of carbon loss to food gained would be unfavorable.
- Also recommended was closure of yield gaps. Huge variations in crop yields exist around the world, by a factor of about 100 between the least productive and most productive corn farmers, for example. This variation is partly due to climate, soils and crop genetics, but it is mostly due to management, including providing enough water and fertilizers for the genotype in question. Yield attainment—how well a farmer is doing compared with other farmers with the same soil and climate—was found to vary from 0% to 100%. Farmers in the United States and Western Europe, as well as parts of China and Brazil are doing well, achieving 90% to 100% of current maximum yields. In some places, farmers are doing poorly: parts of sub-Saharan Africa and even Mexico. In the latter, some farmers, using modern hybrids and farming practices, are achieving 100% of their yield potential, whereas farmers close by, using open-pollinated varieties with no fertilizers or irrigation, on collectively owned land, are getting 10% of their maximum yields. Probably the best place in which to add more calories to the world is Eastern Europe. Although, at one time that region was the breadbasket of Eurasia, farming under the Soviet regime was inefficient, and deteriorated further after the collapse of the USSR. Yield attainments stand at about 20%, and much farmland is underutilized and even abandoned. Huge opportunities for increased crop production exist in parts of Africa, Latin America and Eastern Europe.
- For a modest boost in yield of 20%, most of the world doesn't need more genetics; genetic engineering won't help. Areas of the world that are limited by genetic potential are the Midwest and parts of Europe and China. Yields in the rest of the world are limited by resources—fertilizers and/or water—not genotype improvement. On the other hand, for 50% yield improvements, genetics become more important, and to double yields genetic improvements are essential. A phased-in approach is needed in some of the poorly performing regions, with nutrients and water limitations addressed first and genetic improvements made later.
- If the productivity of the worst-performing farmers is improved to that of the best-performers for all of the major crops, 50% to 60% more food could be added to the world. Improvements via molecular genetics and traditional breeding would significantly increase food production further. Clearly, opportunities exist, but it is vitally important that this intensification of agriculture is achieved sustainably.

Efficient Use of Resources

- We need to increase crop productivity with less nitrogen, less phosphorus and less irrigation water. On average it takes about 1 liter of water to make 1 calorie; however, the worst farmers and the best farmers are 100-fold different from each other in this regard. In parts of northwestern India, for example, 30 liters of water are used per calorie, whereas in Israel and in places in the United States farmers use 0.1 liters per calorie of extra yield. So, the marginal benefits from irrigation vary hugely around the world, suggesting that adoption of improved practices may be broadened. Also, irrigation may be curtailed, especially where it is most damaging and/or least sustainable.
- The same thing pertains with nutrients. The amount of fertilizer applied per unit of extra yield gained is relatively low for the United States, and much higher for India and China where perverse policies encourage much more fertilizer use than is recommended or even logical, causing tremendous environmental damage. These problems present significant opportunities for improvement.

Diet and Bioenergy

- Overall, some 60% of global crop production is used directly as human food, 35% as animal feed, and roughly 5% is converted to biofuels. In India, Africa and China, 90% to 100% of crop production—grains, cereals, pulses, fruits, vegetables, *etc*.—is directly consumed by humans. In the United States only 10% to 15% of crop production is eaten directly by humans; the rest is mainly animal feed, which eventually becomes human food after loss of about 95% of its energy, or it goes into biofuels. We need to think hard about how we use the crops we grow, both in terms of diet and bioenergy.
- As a thought experiment, if everyone were vegetarian, how many calories would be delivered to the world? We could have grazing animals, but delete grain-fed animals and grain- and sugar-cane-derived ethanol from consideration. What if our crops constituted 100% of food instead of 60% of food? In fact, we could add 50% more calories to the world.
- Certainly, something we can all agree upon, regardless of what one thinks of diet and bioenergy manipulation—is the need to save the roughly a third of the food in the world that is wasted one way or the other. In rich countries, wastage occurs often at the consumer end, in refrigerators, restaurants and cafeterias, whereas in poor countries wastage occurs more often at the production end, from crop failure, poor distribution and post-harvest losses to pests. However, losses occur all along the supply chain—different in different regions—presenting many possibilities of increasing calories available for human consumption.
- By adding up these solutions, global food availability could be doubled while simultaneously cutting in half greenhouse-gas emissions from agriculture, water

losses, water-quality problems, *etc.* No one solution is good enough, but altogether we could get where we need to go, albeit with very little margin for error.

Greenhouse Gasses

- When we discuss climate change, it is often in terms of greenhouse gasses from power production and transportation, and it is true that fossil-fuel combustion is the single largest contributor to atmospheric CO_2. However, if considered in terms of economic sectors, agriculture, including land use, is responsible for 30% to 35% of greenhouse-gas emissions, more than all of the world's transportation. Transportation is responsible for about 18% of global emissions, and industry about 15%. Electricity production is responsible for about 19%.
- Contrary to popular belief, food transportation uses only about 1% of global petroleum. Similarly, production of fertilizers and pesticides uses relatively little energy.
- Most of the greenhouse-gas emissions from agriculture come from deforestation by burning and conversion of the land for agricultural use, mainly in Brazil, Indonesia and parts of Africa. Then comes methane production from paddy rice and cattle, and nitrous oxide from overuse of N-fertilizers with flooding.

Climate Change

- Food productivity will be affected by climate change. For some crops in some locations, yield losses of 20% to 40% are predicted. On the other hand, for some crops in some locations yield gains of up to 200% are predicted. Furthermore, the overall picture may be even more positive if we simultaneously boost yields while climate change is occurring.
- If we allow adaptive capacity to work, *i.e.* let farmers be flexible and smart, develop new crops, and use appropriate technologies, we may be able to adapt to the issues concomitant with climate change, but it will be hard work.
- We need to get to work on adaptation to climate change as well as mitigation. There are ways to adapt—especially regarding water use—but they will not be easy.

In Conclusion

- The "Michael Pollen vs. Monsanto" debates are not helpful. Let's bring all stakeholders to the table for fact-based conversations.
- Agricultural production has doubled six times in history. Doubling it again is equal to all the previous effort combined, and it must be achieved in only 40 years. It's a huge challenge. Fortunately there are levers in the system: slowing the rate of expansion into sensitive ecosystems; closing yield gaps; raising crop-yield ceilings; improving the efficiency of environmental resource use; diet modification, at least a little; bioenergy strategy modification; and waste reduction.

- Foley is working with Google to put relevant global environment and agriculture data online free to everyone around the world to foster fact-based conversations about how we will meet the simultaneous food security/environmental sustainability challenge. Whether located in North America, South America, Europe, Africa or Australasia, everyone will have access to the same information and the level playing field will foster fact-based honest-brokered conversations.
- The task is to feed the world while sustaining the planet. Failure is not an option. Civilization depends on solving this problem literally. We have to get it right and we get only one try at it. We'd better get to work.

The Minnesota Water-Sustainability Framework: A Plan for Clean, Abundant Water for Today and Generations to Come

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Minnesota, the land of nearly 12,000 lakes and 63,000 miles of rivers and streams, has more freshwater than any of the country's other contiguous forty-eight states. Water is part of Minnesota's identity and a defining force in our state's history, heritage, environment, and quality of life. At the headwaters of three of the largest river basins in North America, Minnesota receives 99% of its water from rain and snow—consequently, most of our water quality problems originate right here in our own state. While this means we are not forced to clean up water problems originating elsewhere, it also means we have a responsibility to take care of our waters for our sake and for all those downstream.

Minnesota has had a tendency to take this abundance of clean freshwater for granted. But this complacency could lead to our undoing. Over time, as Minnesota was settled, cleared, developed, and farmed, and our population grew, our lakes, rivers, groundwater and their related ecosystems have taken an unintended toll from the cumulative impacts of human-induced changes on the land. Minnesota's population will grow—an estimated 22 percent larger by 2035—and that increased population will result in ever-greater demands on our finite water supply and its quality, unless we make intentional and strategic changes now

It was in part due to Minnesota's love of water and concern for the environment that, in 2008, its citizens passed the historic Clean Water, Land and Legacy Amendment to the state constitution, dedicating a portion of a small increase in the state's sales tax for the next 25 years to create the Clean Water Fund to protect and enhance our water resources. This rare and unique opportunity allows Minnesota to do what no other state has done: to truly take action *now* for a sustainable water future.

The legislature directed the University of Minnesota Water Resources Center to construct a framework describing what needs to be accomplished and how to get it done. The legislature defined sustainable water use as that which *does not harm ecosystems, degrade water quality, or compromise the ability of future generations to meet their own needs* (Minnesota Laws 2009, Chapter 172). Aspects of water sustainability to be addressed included drinking water, stormwater, agricultural and industrial use, surface and groundwater interactions, and infrastructure needs, and within the context of predicted changes in climate, demographics and land use. The result is the Minnesota Water Sustainability Framework. The 140-page report presents the ten most pressing issues of the day that must be addressed to achieve sustainable water use, presents strategies for what should be done, and provides recommendations for how to meet these challenges (Swackhamer, 2011).

It is important to acknowledge and celebrate the successes Minnesota has had with its water policies, while identifying and working on deficiencies. We have made strides in reducing and controlling point-source water pollution, and we have an active citizenry and buy-in from many levels of government. We have a strong program of farmers adapting best management practices. Unfortunately, these achievements have not been sufficient to protect our waters. Forty percent of the state's surface waters are estimated to be in violation of clean water standards; water extraction has lowered groundwater as much as 40 feet in parts of the state; and nitrate concentrations are increasing in surface and groundwater in much of the state, rather than decreasing.

A core team led by the University of Minnesota Water Resources Center collected, compiled, considered, and synthesized the knowledge, insights, and perspectives of hundreds of the best scientists and water-management professionals in the state and region, as well as the input of a wide range of citizens and interest groups. Initially, Technical Work Teams were formed to compile what is known and not known about water use for agriculture, industry and energy, domestic purposes, recreation and culture, and ecosystem services, and what problems would need to be addressed to make water use sustainable. In addition, teams assessed water-related education, state water policy, and economic issues. Each team produced a white paper that summarized their findings. The Water Resources Center produced three white papers that documented the current understanding of water use, water supply, and water quality in Minnesota. These white papers are available to the public (WRC, 2011).

The Framework process was also advised by two important groups—an external advisory committee called the Headwaters Council, and the Citizen and Stakeholder Advisory Committee. The Headwaters Council was made up of thirty thought-leaders from around the state and region who had lifelong careers related to water, from professors to farmers to CEOs. They did not act as stakeholders, but as water professionals with a wide range of perspectives, and their charge was to keep us thinking bold and on track. The Citizen and Stakeholder Advisory Committee was also made up of about thirty professionals who specifically represented non-governmental organizations, citizen groups, and others with vested interests to ensure that we heard from citizens of the state and also had a mechanism to reach out to them.

Finally, the Synthesis Team integrated the findings of the white papers and other information to help form the Framework. They consisted of a highly diverse team of water professionals known for their broad thinking and ability to integrate complex information.

The resulting Framework offers a step-by-step roadmap toward water sustainability, identifying problems in a holistic way and offering concrete solutions and action steps based on current science and best practices. It is the only water plan of its kind that addresses water quality and quantity, surface water and groundwater, and human and ecosystem use of water in an integrated way.

Several cross-cutting themes emerged during the development of the Framework, and they are reflected throughout the plan. These include:

- systems thinking—groundwater and surface water are one system and should be managed that way;
- science-based decision-making—knowledge of this system should provide the underpinning of decisions;
- decision-making in the face of uncertainty—one must make decisions on a weight-of-evidence approach;
- adaptive management—decision-making should be flexible enough to allow new knowledge to improve policy over time;
- watershed-based approach—water should not be managed based on political boundaries;
- outcome-based approach—all actions taken should have clearly articulated outcomes;
- accountability—state government, business, local units of government, and citizens need to be responsible and accountable for their actions;
- compliance with existing regulations—local capacity should be supported to ensure compliance with existing law and rules;
- transboundary stewardship—Minnesota must work with its state and international neighbors on boundary waters and share responsibility to effect change, and also provide leadership on protecting the headwaters of the Mississippi River, the Great Lakes system, and the Red River of the North.

The Framework provides a long-range plan that frames major water sustainability issues and provides strategies and recommendations for addressing those issues. It is *not* a specific spending plan for the Minnesota Clean Water Fund, nor should it be limited by the availability of Clean Water Funds; rather, it includes recommendations for investments that may come from sources beyond the Clean Water Fund (other state funds, private funds, *etc.*), as well as recommendations that require little or no investment by the state.

The Most Pressing Issues

The Framework identifies ten major issues that present the challenges and solutions to those challenges that must be addressed if water sustainability is to be achieved in Minnesota. These issues are not independent at all, but are highly interdependent. These issues (labeled A–J) fall within the three areas that define sustainability: environmental, economic, and social (UN, 2005).

The Strategies ("what should be done") to address the Issues are described in Tables 1A and 1B, along with declarations in terms of the corresponding Desired Minnesota Future:

TABLE 1A. ISSUES, STRATEGIES AND DESIRED OUTCOMES IDENTIFIED IN THE FRAMEWORK.

Desired Minnesota Future	Issue	Strategy
A water supply that is protected for all future generations, that is of high quality, and that is sustainable for all uses of water.	A. The need for a sustainable and clean water supply	A.1: Determine the state's water balance and improve water appropriations permitting. A.2: Improve privately supplied drinking-water quality. A.3: Plan for water re-use.
The "Land of Unimpaired Waters," where we have met all of our water standards for nutrients and solids, we are not contributing to eutrophication problems beyond our borders, we can safely eat local fish.	B. Excess nutrients and other conventional pollutants	B.1: Reduce excess nutrient and conventional pollutant loads by strengthening policies to meet clean-water standards and require implementation of pollutant load reductions by all sources. B.2: Establish a farmer-led, performance-based approach to meeting clean-water standards. B.3: Address "legacy" contaminants.
A society that has embraced green manufacturing and chemistry so as to eliminate new toxic contaminants, and where drinking water, recreation water, and food are free from harm from microbial contaminants.	C. Contaminants of emerging concern	C.1: Enact Green Chemistry Act. C.2: Develop a framework for managing contaminants of emerging concern. C.3: Address beach pathogens to improve recreation.
A society where all of our land-use decisions and plans are inextricably linked with sustainable water use and planning.	D. Land, air, and water connection	D.1: Require integrated land and water planning; integrate water sustainability in permitting.
A society where healthy ecosystems are considered the foundation on which human well-being is based, and that all damaged ecosystems have been remedied and all ecosystems are protected while maintaining a healthy economy. Changes to the hydrological system are minimized and historic changes have been addressed to achieve water quality and aquifer recharge needs.	E. Ecological and hydrological integrity	E.1: Enact Ecosystems Services Act. E.2: Prevent and control aquatic invasive species. E.3: Improve management of hydrologic systems. E.4: Preserve and encourage land set-aside programs.

Table 1B. More issues, strategies and desired outcomes identified in the Framework.

Desired Minnesota Future	Issue	Strategy
A society in which energy policy and water policy are aligned.	F. Water/energy nexus	F.1: Understand and manage water and energy relationships.
A society in which water is considered a public service and is priced appropriately to cover the costs of its production, protection, improvement, and treatment, and the economic value of its ecological benefits.	G. Water pricing	G.1: Include the value of ecological benefits in the pending water-pricing schemes. G.2: Provide for shared resources between large- and small-community water supplies.
A society that maintains and protects its infrastructure for drinking water, wastewater, stormwater, and flood protection in a manner that sustains our communities and our water resources and maintains and enhances ecosystems; and reuses water where appropriate to conserve our sustainable supply.	H. Infrastructure needs	H.1: Determine a long-term strategy for fund ing new, expanded, and updated infrastructure and its maintenance. H.2: Incorporate new technologies and adaptive management into public-water infrastructure decisions.
A resilient society that values, understands, and treasures our water resources, and acts in ways to achieve and maintain sustainable and healthy water resources.	I. Citizen engagement and education	I.1: Ensure long-term citizen engagement. I.2: Ensure youth and adult water literacy and education.
Governments, institutions, and communities working together in implementing an overarching water-sustainability policy that is aligned with all other systems policies (land use, energy, economic development, transportation, food and fiber production) through laws, ordinances, and actions that promote resilience and sustainability.	J. Governance and institutions	J.1: Provide a governance structure to ensure water sustainability. J.2: Ensure that the Water Sustainability Framework is reviewed and updated regularly and informed by current, accessible data and information.

The Framework in Summary—A Ten- and Twenty-Five-Year Plan

The following "dashboard" presents the complete list of Recommendations in the Framework that are needed to implement the Strategies listed above for addressing the ten important Issues. It provides the following information:

- *Individual recommendations* (the "how")—recommendations are grouped by the issue they address (identified by A–J), and in relationship to a specific strategy (identified by number). For example, A1a indicates Recommendation "a" for Strategy 1 under Issue A. The most critical recommendations are shown in italics.
- *Who should implement*—if funding is appropriated by the legislature, this indicates whether a given recommendation would be implemented by the legislature, the executive branch, or others.
- *Research task*—this column contains an R if the recommendation is a research task rather than an implementation or management task.
- *Implementation phase*—the phases refer to the general timeline for initiation of a given recommendation's implementation. Phase 1 corresponds to the first two years (2011–2012), Phase 2 corresponds to the next three years (2013–2015), Phase 3 corresponds to years 6–10 (2016–2020), and Phase 4 corresponds to years 11–15 (2021–2025). The Ten-Year Plan contains recommendations in Phases 1–3, while the Twenty Five-Year Plan contains all recommendations from all Phases. The timeline for implementation does not always correspond to how critical the action is relative to others; rather, it reflects Minnesota's readiness to implement the action (*i.e.*, "low hanging fruit"), the urgency of starting the action, and/or the fact that outcomes from the action will take significant time (a decade or more).
- *Level of benefit to water resources*—this gives an indication of each recommendation's potential impact on improving or protecting water quality and quantity for future generations. The scale is given as one to three drops, with three drops indicating maximal benefit and one drop indicating modest benefit.
- *Multiple benefits*—this indicates whether the recommendation as implemented would benefit other state-defined natural and human resources, including wildlife, fisheries, forest resources, air, recreational resources, or human health.

As shown in the "dashboard," it is evident that most (about two-thirds) of the Framework recommendations should begin in the first five years (Phases 1 or 2). Phase-1 recommendations relate to issues A, B, D, and J (need for a sustainable and clean water supply; excess nutrients and conventional pollutants; land, air, and water connection; and governance and institutions). With few exceptions, these will provide high levels of benefit to water resources, and most provide multiple benefits to natural and human resources. Phase 2 recommendations relate to strategies within all of the issues except Issue F (water/energy nexus). These recommendations will provide good-to-excellent benefits to water resources, and again, most would provide multiple benefits to natural and human resources. Phase 3 recommendations are less urgent and, though important, do not need

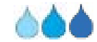
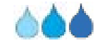
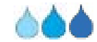
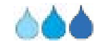
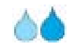
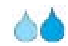
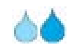
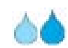
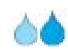
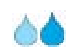
Recommendation	If funded, who should implement	Research task	Implementation phase	Level of benefit to water resources	Multiple benefits
A1a i, ii, iii: accelerate water-balance mapping needs and implement hydrologic-monitoring network	Executive		Phase 1		
A1a iv: design and complete the water-balance hydrologic models	Executive	R	Phase 1		
A1b i, ii: develop a web-based screening permit system	Executive		Phase 1		
A1b iii: restrict water exports from state	Legislative		Phase 3		
A1b iv: develop eco-based thresholds for minimum flows	Executive	R	Phase 1		
A2a: improve quality of private drinking water	Other		Phase 2		
A3a: plan for water reuse	Executive		Phase 4		
A3b: develop reuse standards	Executive		Phase 4		
B1a: require compliance of pollutant load reductions by all sectors	Legislative		Phase 1		
B1b: strengthen approaches to stormwater pollution	Executive		Phase 3		
B1c: strengthen shoreland rules	Executive		Phase 3		
B1d: increase capacity for local land-use compliance	Lebislative		Phase 2		
B1e: strengthen rules managing septic-treatment systems	Executive		Phase 3		

Table 2. The "dashboard" of recommendations in the Framework.

Recommendation	If funded, who should implement	Research task	Implementation phase	Level of benefit to water resources	Multiple benefits
B1f: research cyanotoxin sources	Other	R	Phase 2		
B2a: establish farmer-led performance-based approach to meeting standards	Legislative		Phase 1		
B2b: establish agricultural sustainable water certification	Executive		Phase 3		
B3a: address contaminated sediments	Executive		Phase 2		
B3b: evaluate coal-tar sealant alternatives	Executive		Phase 1		
B3c: further eliminate mercury sources	Executive		Phase 1		
C1a: enact Green Chemistry Act	Legislative		Phase 1		
C2a: develop framework for managing contaminants of emerging concern	Executive		Phase 1		
C2b: expand MDH Contaminants of Emerging Concern program	Executive		Phase 3		
C2c: prioritize facilities' needs for advanced treatment technologies	Executive		Phase 3		
C2d: develop comprehensive policy for pharmaceutical disposal	Legislative		Phase 2		
C3a: establish state policy for pathogens and beaches	Legislative		Phase 3		
C3b, c: research pathogen indicators and sources	Other	R	Phase 2		
D1a: require comprehensive land and water planning	Legislative		Phase 1		

Recommendation	If funded, who should implement	Research task	Implementation phase	Level of benefit to water resources	Multiple benefits
D1b: integrate sustainability in land use permitting	Legislative		Phase 1	💧💧💧	◯
D1c: increase local enforcement and compliance capacity	Legislative		Phase 2	💧💧	◯
D1d: monitor effectiveness	Executive	R	Phase 1	💧💧	◯
E1a i: enact Ecosystems Services Act	Legislative		Phase 3	💧💧💧	◯
E1a ii: determine ecosystem services and their economic value	Other	R	Phase 1	💧💧💧	◯
E2a: develop statewide policy for aquatic invasive species	Legislative		Phase 1	💧💧	◯
E2b: research control measures for aquatic invasive species	Other	R	Phase 1	💧💧	◯
E3a: accelerate watershed hydrological characteristics and response landscape model application	Executive		Phase 1	💧💧💧	◯
E3b: model drainage from field scale to watershed scale	Other	R	Phase 3	💧💧💧	◯
E3c: require multi-benefit drainage-management practices with new or replaced tile drainage	Legislative		Phase 1	💧💧💧	◯
E3d: expand cost-share program for retrofitting existing tile drainage	Executive		Phase 1	💧💧💧	◯
E4a: preserve and encourage conservation land set-asides	Executive		Phase 1	💧💧💧	◯
E4b: work to ensure next Farm Bill has strong conservation elements	Executive		Phase 1	💧💧	◯
F1a: understand and quantify the water/energy nexus	Other	R	Phase 3	💧💧	

Recommendation	If funded, who should implement	Research task	Implementation phase	Level of benefit to water resources	Multiple benefits
F1b: review energy policy for water sustainability	Legislative		Phase 3	💧💧	
F1c: encourage renewable energy that minimizes water impacts	Executive		Phase 3	💧	✓
G1a: include ecological benefits in water pricing	Legislative		Phase 2	💧💧💧	
G1b: include other economic incentives in water pricing	Legislative		Phase 2	💧💧💧	
G1c: transition business to more equitable pricing	Executive		Phase 2	💧💧💧	
G1d: research and model value of water ecological benefits	Other	R	Phase 1	💧💧💧	✓
G2a: provide for shared resources between small and large community water supplies	Executive		Phase 3	💧💧	✓
H1a: create a standing advisory committee on new technologies	Executive		Phase 2	💧💧💧	✓
H1b: address water reuse	Legislative		Phase 4	💧	
H1c: adopt Effective Utility Management program	Other		Phase 1	💧💧	✓
H2a i: determine long-term funding strategy for public water infrastructure	Executive	R	Phase 1	💧💧💧	
H2a ii: implement long-term funding strategy for public water infrastructure	Executive		Phase 3	💧💧💧	
I1a: ensure long term public engagement support	Executive		Phase 2	💧💧💧	✓
I2a: ensure child water literacy	Other		Phase 2	💧💧💧	✓

Recommendation	If funded, who should implement	Research task	Implementation phase	Level of benefit to water resources	Multiple benefits
I2b: ensure adult water literacy	Other		Phase 2	💧💧💧	◎
J1a: review statutes and laws for water sustainability	Legislative		Phase 1	💧💧💧	◎
J1b: enact Water Sustainability Act	Legislative		Phase 1	💧💧	◎
J1c: re-establish the Legislative Water Commission	Legislative		Phase 1	💧💧💧	◎
J1d: create Water Sustainability Board	Legislative		Phase 2	💧💧	◎
J1e: form Watershed and Soil Conservation Authorities	Legislative		Phase 3	💧💧	◎
J2a: create interagency data and information portal	Executive		Phase 1	💧💧💧	
J2b: maintain Framework as “living” document	Legislative		Phase 3	💧💧💧	◎

to be initiated in the first five years. Phase 4 recommendations, most related to water re-use, are not urgent. Non-urgency should not be interpreted to mean a recommendation is non-essential. In some cases, the Phase 3 or 4 recommendations cannot be initiated until the recommendations in the earlier phases have been instituted, yet are essential to sustainable water resources in Minnesota. The most important actions are shown in italics (see below for explanation).

The dashboard also demonstrates that three-fourths of the recommendations have multiple benefits to other natural resources and public health. Many of the remaining one-quarter are positively linked to economic benefits.

The Essential Top Five Actions

The Framework is comprehensive in its recommendations and at first glance may seem like a daunting challenge on many levels, including financial. The quality and diversity of knowledge and perspectives that contributed to the final form of these recommendations cannot be overemphasized, and implementation in their entirety provides the best assurance of water sustainability. However, in the expert view of the Framework's authors, five overall actions—encompassing eight recommendations—are most critical. In fact they are considered essential to achieving water sustainability and their implementation will take us closer to water sustainability than any other limited combination of actions. These five actions can be grouped into two parts: (i) Protect and restore water quantity and quality and (ii) Address the interconnected nature of water. They are all Phase 1 actions, of high impact to water quality and have multiple benefits. They are shown in the "dashboard" in italics.

- Protect and restore water quantity and quality through comprehensive, integrated, and informed management and policy.
  - —Revise water appropriations permitting (Recommendation A1b), and model the state's water balance (A1a).
  - —Comply with water-quality standards through implementation plans for reducing pollutants (B1a) and bring farmers to the table to be part of this solution (B2a).
  - —Address future contaminants (C1a, C2a).
- Address the interconnected nature of water by integrating and aligning planning and policies.
  - —Integrate water- and land-use planning (D1a).
  - —Align water, energy, land, transportation policies for sustainability (J1a).

A Model for the Nation

The Framework addresses the most important issues that have been identified for Minnesota. However, several national studies have been conducted (*e.g.* NAS, 2001, 2004; USGS, 2007) in the past decade that have articulated the most important water challenges facing our nation as a whole, and these issues mirror those faced by Minnesota.

In other words, Minnesota is representative of water issues and problems across the nation. Therefore, the Framework can serve as a model for what the entire nation needs to consider. The United States does not have a federal water policy *per se*, but delegates implementation responsibilities of the federal Clean Water Act and Safe Drinking Water Act to the states, and allows each state to manage its own water rights and water withdrawals. This recognizes the diverse needs and cultures of the states, but leads to a patchwork approach to water management and does not address the multijurisdictional nature of water. It does not serve the nation's best interests in terms of water quality and quantity. Should the nation decide to provide an overarching, holistic framework to guide state water policy, the Minnesota Water Sustainability Framework could serve as the model for a national framework.

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Sustainability and the Needs of 2050 Agriculture: Developed and Developing World Perspectives

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I will discuss the topic described on the conference agenda: *Sustainability and the Needs of 2050 Agriculture*, but I will turn it around. Rather than talk about the needs of agriculture in 2050 from developed- and developing-world perspectives, I will talk about what the developed and developing worlds will need from agriculture by mid-century, and how sustainability is inextricably linked to meeting those needs.

Needs by 2050

In short, by 2050 the world will need food security, meaning that all people, at all times, have access to sufficient, safe, nutritious food to maintain healthy and active lives. Agriculture already plays an essential role in the supply of this food.

However, the reality is that, even today, we do not have food security. An estimated one billion people go to bed hungry every night. Childhood hunger remains particularly acute. Approximately 200 million children suffer the irreversible effects of chronic under-nutrition, including heightened vulnerability to illness and diminished cognitive development.

Food security is not only a matter of supply. Even where there is an adequate food supply, there is not always adequate food access because of income limitations. Also, poor dietary use can cause nutritional imbalance. It is estimated that poor nutrition is the underlying cause of the deaths of 3.5 million mothers and children under age five each year (Thousand Days, 2011).

These under-nutrition woes are not limited to the developing world, though. In developed countries, half of those over age 75 and in hospitals are thought to be nutrient deficient, as are, ironically, many obese people (Anonymous, 2011).

On the access-to-food issue, consider that, already in 2011, the UN Food Price Index has eclipsed its previous all-time global high (FAO, 2011). We last saw comparable escalation in food prices in 2007 and 2008. That spike was mitigated by favorable weather that helped farmers deliver record grain harvests, and by a severe recession that helped temper demand.

But the forces elevating demand and constraining supply have only grown stronger in the intervening years. Demand increase is coming not just from population growth, but from a growing global middle class that is moving up the food chain, consuming more grain-intensive products such as meat, milk and eggs. At the same time, the United States in particular is converting more grain into fuel. As a result, the price of grain is now linked to the price of oil as it becomes more profitable to convert carbohydrates into hydrocarbons (Henshaw, 2011).

Access and affordability issues are in play even here in the United States, where approximately 49 million people—including 17 million children—live in households struggling to put enough food on the table. In fiscal year 2010, our government spent an estimated $80 billion to subsidize meals and food purchases for more than one in four Americans. Minnesota is not immune from the problem. According to Hunger-Free Minnesota (2011), a statewide coalition, hunger in Minnesota has doubled in five years. The coalition notes that one in ten Minnesotans run out of resources before the end of every month, missing an average of ten meals every 30 days. That's 100 million meals missed every year, with devastating effects.

Despite steady improvements in agricultural productivity, enabling food security on a global basis will be more challenging in the next 40 years. By 2050, there will be an estimated 2 billion more people to feed as the global population grows from the 7 billion it is expected to reach this October to more than 9 billion. And while 9 billion was previously expected to be a population plateau, in May of this year the United Nations revised upward its estimates for global population growth for the balance of the century. The new UN data estimate a global population of 10.1 billion by 2100 (UN, 2011). Much of the growth will be concentrated in Africa, where the population could more than triple, reaching 3.6 billion by the end of the century.

Sobering Reality

To ensure food security for the global population at mid-century will require producing twice as much food as we do today. By the century's end, according to Jason Clay (2011), a senior leader at the World Wildlife Fund, feeding the planet will require producing an amount of food that is 2.5 times the amount that all human societies have produced in the last 8,000 years. If not daunting enough, that increased output will have to come from less land and less water. As often-cited World Wildlife Fund research points out, continuing with business-as-usual in food production will require the resources of three planet Earths to support human activities (WWF, 2011).

Less Land

Agriculture already uses an estimated 40% of the globe's arable land, with some 3.75 billion acres in production. So, among the questions confronting us are how we double agricultural production without further deforestation and its attendant problems of soil erosion and of pollution of streams and waterways.

Again, this is not a problem unique to the developing world. In May, 2011, in a letter to the House and Senate agriculture committees, groups representing grain and feed traders, livestock producers, fertilizer manufacturers, meatpackers and others urged Congress to put back into production millions of acres of farmland that are now enrolled in the Conservation Reserve Program (Brasher, 2011). The land in the program serves to prevent soil erosion and the degradation of streams and rivers, sequesters carbon and also serves as valuable habitat for wildlife. It is expected that any effort to put these acres back into production will face ferocious opposition from environmental and wildlife-advocacy groups.

Less Water

Water availability is equally constraining to output growth. Of the fresh water utilized by man, which is a fraction of what is available on earth, 70% is used by agriculture. However, this varies widely by region of the world and by crop. For example, in the United States only 15% of corn is irrigated; the rest is largely rain-fed.

But crop losses due to water scarcity are becoming endemic throughout the world, as exemplified by the crop-destroying drought and fires in Russia in 2010, and severe droughts in Texas and the Southwest United States in 2011.

In India and China, groundwater withdrawals are increasing at an unsustainable pace. Here in the United States, we are also on an unsustainable water-use curve. The Ogallala Aquifer, which supplies 70% to 90% of the irrigation water for three of the top grain-producing states, is fast becoming depleted. Groundwater levels have declined by more than 100 feet in some areas according to US Geological Survey data (USGS, 2011). Without water for irrigation from this aquifer, this region—the breadbasket of the world—would be dramatically less productive.

Role of Sustainability

In this rather bleak picture, what is the role of sustainability? In a word: essential. It is inextricably linked to solving the global food-security challenge.

"Sustainability" is used in many contexts today. Sometimes the term is applied to organically produced crops or commodities, to locally grown produce and to small-scale farming operations. There are merits and elements of sustainability in all of them.

It is incorrect, though, to juxtapose intensive farming against organic, small scale or locally grown options in ways that suggest intensive operations are not also sustainable. Therefore, "agricultural sustainability" is used here in the context of efficient employment of finite, scarce resources in a manner that results in beneficial outcomes for the environment. That means thinking about sustainability in the context of growing more from less through the smart use of proven practices and a suite of agricultural technologies. Agricultural sustainability refers to a system that can meet global requirements for food, feed, fiber and fuel indefinitely, with beneficial economic and environmental effects in areas such as water and fossil-fuel usage, biodiversity preservation, land stewardship, carbon sequestration and more.

Defined in that fashion, sustainability is, clearly, fundamental to food security. Simply put, intensive farming, done sustainably, improves efficiency of use of resources. Consider, for example, the impact of crop losses. On a global basis, cereal-crop losses—to weeds, pests and disease—are estimated to average about 40% of the attainable yield (Oerke and Dehne, 1997). Given the food-production challenges we face to achieve global food security, how can that be tolerated? Said another way, natural resources—the soil and water utilized by the unattained yield—would be more efficiently used if the crop losses are mitigated by smart use of chemical and biological inputs, improved tillage practices and other crop-protection technologies and techniques associated with intensive farming.

The resource conservation that results from intensive farming—done sustainably—is not theoretical. A Stanford University study concluded that a land mass larger than Russia has been saved from cultivation because farmers have used modern technology to grow more on their farms in the last 50 years (Burney *et al.*, 2010). Russia covers more than 17 million square kilometers. That means an area more than twice the size of the continental United States has not been put into cultivation to support global food, feed, fiber and fuel needs even as the population has grown.

In Brazil, the rate of deforestation plunged to a historic low in 2009 even as agricultural productivity increased there at a rate faster than that of any other country in the world (Anonymous, 2010). By contrast, European restrictions on the use of certain inputs—genetically engineered crops, among others—mean that feeding Europe consumes the agricultural production of a non-European land mass the size of Germany (von Witzke and Noleppa, 2011).

Brazil's example underscores a profoundly important point: the absolute necessity of growth in agricultural productivity and the absolute necessity of conservation of scarce resources and the preservation of our environment are not in conflict. In fact, they can and should be in harmony.

Benchmarks Beyond Bushels

What can the developed world do to debunk the perceived conflict between productivity and sustainability? What can the developed world do to propagate a sustainable form of intensive agriculture that will help remedy our global food-security challenge, create economic opportunity and improve social stability? Of myriad opportunities, I will discuss three contributions the developed world can make to putting us on a sustainable path to global food security. Those contributions are in three categories:

- Incorporation of outcomes-based sustainability measures into our mindset;
- Investment in the development and dissemination of technologies that enable improvements in these sustainability outcomes, including productivity; and

- Use of market power of buyers of major commodities to propagate adoption of sustainability principles and practices among producers while respecting producers' legitimate interests.

Sustainability Measures

With respect to measuring sustainability outcomes, a new perspective must take hold in agriculture in the developed world. This new perspective will be enormously helpful to propagating the sustainability outcomes that will close the gap on food security and determine the practices in production agriculture that truly result in improvements. It can best be summed up as a "benchmarks beyond bushels" approach to measuring sustainability in agriculture. As a practical matter, this will mean measuring productivity not only on the basis of yield in terms of bushels per acre, but also on the basis of resource utilization per bushel produced. If we measure output in this more holistic fashion, productivity becomes integral to how sustainability is defined and measured, and maintains focus on the environmental, economic and social outcomes to be achieved.

Intensive farming can stand this scrutiny. Consider the facts on corn production. In the United States, although corn yields have steadily increased, the environmental footprint is smaller in every category. Data from the Keystone Center show that in the two decades ending in 2007, land use per bushel of corn produced, soil loss per bushel, irrigation-water use per bushel, energy use per bushel and greenhouse-gas emissions per bushel all declined (Anonymous, 2009).

Field to Market: The Keystone Alliance for Sustainable Agriculture is an initiative of the Keystone Center comprising forty-six diverse stakeholders that include Cargill, Conservation International, Monsanto, Environmental Defense Fund, National Corn Growers Association, General Mills, The Fertilizer Institute, Syngenta, and the Nature Conservancy. The outcomes-based focus represented by Field to Market's measurements is critical. Many parties are at work on defining a standard way to measure agricultural sustainability. Some of those definitions characterize sustainability by specifying inputs, such as prohibition of genetically engineered crops. Others advocate definitions based on outcomes, such as improving water-use efficiency by some targeted percentage. The accepted approach will likely affect sustainability ratings and consumer-product labeling. A concern, however, is that an inputs-based approach could restrict farmers' freedom to operate and to make the best choices for improving productivity and efficiency on their land. That is why Syngenta supports and participates in Field to Market's model for measuring agricultural sustainability.

Field to Market's initial suite of metrics includes indicators encompassing soil loss, irrigation-water consumption, land and energy use and climate impact. We believe this outcomes-driven approach is more likely to motivate the kinds of innovation and improvement needed to meet sustainability and food-security challenges. Prescriptive practices, on the other hand, tend to motivate compliance rather than invention.

Investment in Technology

Improved performance on outcomes-based measures of sustainability can be enabled by further investment in the development and deployment of productivity-enhancing technologies. The range of opportunity is broad, encompassing everything from technologies to increase yields, to improve plant performance and to enhance nutritional content. For example, precision breeding—what we at Syngenta call Gene Blueprinting—and genetic modification technologies are enabling new crop capabilities that typically serve sustainability, including productivity. Among them are improved disease resistance, drought tolerance and nitrogen-use efficiency, to name a few. For example, Syngenta introduced for planting in 2011 hybrids containing Agrisure Artesian™ technology, which preserves yield under drought stress. In field trials, this unique trait, developed through work solely within the corn genome, has shown the ability to preserve up to 15% of the yield that might be lost to moisture stress without inflicting a yield penalty under adequate moisture.

We are also becoming proficient at developing nutrient-enriched crops. Examples include vitamin-enhanced rice, canola with enhanced omega-3 oil content, and tomatoes with higher concentrations of the antioxidant lycopene. These innovations overcome the nutrient deficiencies mentioned above as an element of food insecurity globally. But they can only do that if their adoption is not constrained for non-scientific reasons, as has been the case with vitamin-enriched rice in parts of Asia.

Meanwhile, new output traits are helping enhance the use of crops in downstream processes. For example, Syngenta's Enogen™ corn amylase is the first corn optimized for ethanol production. It produces within the kernel an enzyme that helps convert starch to sugar. Sustainability benefits accrue from the reduced use of water, electricity and natural gas required in the Enogen-enabled production process. For example, in a 100-million-gallon ethanol plant, Enogen corn amylase can save 450,000 gallons of water, 1.3 million kilowatt hours of electricity and 244 billion BTUs of natural gas. Those energy savings translate into a 106-million-pound reduction in greenhouse-gas emissions, the equivalent of taking more than 4,600 passenger cars off the road (Urbanchuk *et al.*, 2009).

Enogen corn is approved for food and feed purposes, the same as conventional corn. But because its value is in the ethanol-production process, it will be cultivated in a closed system. Ethanol-production plants will contract directly with growers in their immediate areas for their supply. Growers, in turn, will need to abide by strict stewardship requirements, and agree to provide their Enogen corn only to the contracting plant.

It's important to understand that what I'm calling "crop capabilities" encompass multiple technologies that deliver compound benefits when used together and systematically. For instance, no- or low-till farming improves soil's ability to absorb water, reduces moisture loss, erosion and run-off into lakes and streams and enhances carbon sequestration. Herbicides that control weeds lower the need for tillage, making no-till or low-till farming more feasible, hence enabling no-/low-till farming and all its environmental benefits.

Another example are seed treatments that protect plants during early growth to help more seeds germinate with less crop loss right from the start. In addition, certain seed treatments also help emerging plants develop robust roots. Superior root structures help plants better use available soil moisture or irrigation water, as well as soil nutrients. That can mean less water and nitrogen applied to fields, reducing the potential for both run-off and nitrification, which results in the release of nitrous oxide, which is 300 times more potent as a greenhouse gas than carbon dioxide.

In another example, a plant growth regulator, like Syngenta UK MODDUS™ for application to wheat and barley, can be used to reduce crop height. This is desirable for lodging control and yield protection. Root lodging will occur where the plant is insufficiently anchored, however, even in the absence of lodging, the regulator's effects on root structure benefit water and nutrient use, enabling the related environmental benefits.

The "big bang" benefits for agricultural productivity and sustainability come when all these technologies and more are integrated. In Brazil, for instance, Syngenta is pioneering an entirely new way to plant, grow and harvest sugar cane, which meets 70% of global sugar needs and is the most cost-effective feedstock for plant-derived ethanol. Traditionally, however, this crop attracted little technology investment and yields were far below potential. Even so, production is under pressure as demand outstrips the capacity of what has been a largely manual planting and cultivation process. Syngenta has developed a solution that simplifies operations, improves output and ensures sustainability. Our PLENE™ technology integrates multiple technologies including:

- A treatment for sugar-cane cuttings that protects against insects and disease;
- Shorter cuttings—4 cm compared with the conventional 40 cm—that enable mechanized planting with lighter equipment for less soil compaction and less fuel consumption;
- Insecticides that control sucking and chewing pests and deliver an additional vigor effect that results in a 10% yield advantage;
- Our MODDUS plant-growth regulator in Brazil allows growers to schedule harvesting to achieve maximum sugar yield;
- A solution for termite control that does not persist in the environment or harm beneficial insects that help break down cane residues after harvest; and
- A fungicide to prevent orange rust in sugar cane.

Clearly, technology and innovation are firmly on the side of enabling further improvements in sustainability through agricultural productivity and environmental quality. Our PLENE system for sugar cane means greatly enhanced yield, lower water usage and better carbon sequestration—in short, a more productive and sustainable crop enabled by sustainable intensification.

Market Power

A third way the developed world can help propagate sustainable practices is by harnessing market power to create appropriate incentives all along the farm-to-fork supply chain. One of the organizations leading the way in this regard is the Consumer Goods Forum (CGF), a global industry network that brings together the CEOs and senior management of more than 650 retailers, manufacturers, service providers and other stakeholders across seventy countries. It was created in June 2009 by the merger of the Food Business Forum, the Global Commerce Initiative and the Global CEO Forum.

Last November, the Forum announced two climate-change initiatives, one aimed at ending deforestation, and the other focused on phasing out the use of refrigerant gases with high global-warming potential. The Forum pledged to mobilize its collective resources to help achieve, by 2020, zero net deforestation, which currently accounts for 17% of greenhouse-gas production. In announcing the zero net deforestation initiative, Forum leaders said:

> *We believe that our industry has a responsibility to purchase commodities in a way which encourages producers not to expand into forested areas. Our task is to develop specific action plans for the different challenges of sourcing commodities like soya, palm oil, beef, paper and board sustainably.*

This kind of commitment is spreading. In an essay for the *New York Times*, the World Wildlife Fund's Jason Clay (2011) pointed out that major food brands are demanding greater sustainability from their supply-chain partners through increased productivity, efficiency and the elimination of waste. In a TED Conference[1] presentation, Jason Clay (2010) had kind words for work that Cargill, Coke and Mars are already doing in this regard. He pointed out the huge opportunity that still exists, noting that a hundred companies control about 25% of the trade in all fifteen of the most significant agricultural commodities. He made a compelling case for the sustainability gains that could be wrung from the purposeful application of that market power, contending that mega-buyers of agricultural commodities can push producers toward sustainable practices faster than consumers can. Clay's point is straightforward: If mega buyers decide they want to source a commodity produced in a certain way, then producers will get in line to fulfill that demand, as long as doing so makes economic sense. When buyers are incented by self-interest to source agricultural commodities sustainably, then producers' self-interests should be well served by fulfilling that demand for sustainably produced commodities. In short, get the market forces and incentives aligned and the seeds for a self-reinforcing virtuous cycle are planted.

Developing World

Three ground rules govern the discussion of the developing-world perspective on agricultural productivity, sustainability and food security. The first is to accept the premise that long-term food security in the developing world cannot be accomplished solely via philanthropy or technology.

I am not dismissing the important work being done by numerous foundations and NGOs in this regard, but food aid and hunger relief, as valuable as they are, cannot be the enduring fix for the problem. An Oxfam study cited in the *New York Times* in May, 2011, stated the case clearly (Rosenberg, 2011). It costs much less to prevent a famine than to save lives after one has struck. Oxfam estimates that it costs seven times more to provide emergency food relief than it does to prevent a food-security disaster. Similarly, simply providing new technologies to the developing world will not solve the food-security challenge.

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[1]TED Conference, "Ideas Worth Spreading": http://www.ted.com/.

Hence, the second ground rule is to accept that there will be no global food security without productivity increases among smallholders. By United Nations' and other estimates, there are some 450 million farms of less than 5 acres in non-OECD[2] countries. The owners of these very small farms are providing—or trying to provide—sustenance for two billion people. Improved productivity on these small farms will be essential to sustainable food security.

The third ground rule is basically a corollary to the second: closing the yield gap between what is possible in the developed world and what is realized in the developing world without encouraging resource waste is the imperative.

The path to the levels of productivity required will involve sustainable intensification. In the developing world, this means creating the means for smallholders to progressively evolve from subsistence farming, to semi-commercial farming to commercial operators to advanced farmers.

If this sounds more aspirational than realistic, it is important to realize that it's been done before. From the 1960s to the 1980s, productivity improvement in Asia and Latin America resulted in a doubling of food production, which saved millions of lives and laid foundations for economic growth in countries like India and China.

More to the point, it is being done now. Private foundations, public entities, private-public partnerships and NGOs are all helping create the capacity required to enable smallholder farmers to pursue sustainable intensification. What's required is access to improved genetics, crop protection, fertilizer, soil and water management, agronomic and extension services, financial services, markets, infrastructure, *etc*. Furthermore, the provision of these resources needs to be combined with the provision of education and training that enables smallholders to use them wisely and effectively. That's one reason why Syngenta trains millions of farmers annually—4.3 million last year and more than 10 million over the last three years.

As an example of the essential linkage of provision of improved resources with provision of required education, consider what can happen when smallholder farmers are provided with elite corn hybrids. The temptation in subsistence and pre-commercial operations will be to save seed from those hybrids for the next season's planting. Of course doing so ultimately defeats the purpose of providing the improved technology. Instead, smallholder growers need the education and support to understand that the increased yield from the elite hybrids is worth more than the saved seed. And they, of course, need supporting technology and services to realize that increased yield.

As that example illustrates, there is a "high touch" component to creating the capacity that will enable sustainable intensification in the developing world. It will be a long and steep climb, but I believe the commitment is there. It's evident in projects being advanced by organizations such as the Bill and Melinda Gates Foundation, the Consumer Goods Forum, numerous NGOs and by companies like Cargill, General Mills, Coca-Cola and Syngenta.

[2]Organization for Economic Co-operation an Development

Syngenta Foundation for Sustainable Agriculture

At Syngenta, this capacity-building work is being advanced by both the company and by the Syngenta Foundation for Sustainable Agriculture. An example of a corporate initiative is our partnership with the International Maize and Wheat Improvement Center (CIMMYT) in Mexico, announced in April, 2010. As the director of the Center's wheat program pointed out when this partnership was announced, global wheat production is increasing at less than 1% annually whereas demand is increasing at 1.5% or more, creating conditions that foreshadow persistent shortages. The agreement enables Syngenta's genetic-marker technology, advanced traits platform and wheat breeding for the developed world to be combined with the Center's access to diverse wheat genetics, global partners and wheat-breeding programs targeted at the developing world to improve yields.

India

Another corporate-sponsored venture is a "crop health center" in India called Krishi Shakti. The center provides agronomy advice and resources to farmers from surrounding villages. In parallel, Syngenta started operating Krishi Shakti vans to support farmers on their farms. These programs provide crop diagnostics, soil testing, library facilities, training and education, demonstration plots and interactions with scientists to improve crop yields and quality.

Africa

Syngenta, in collaboration with the Syngenta Foundation for Sustainable Agriculture, is also building capacity and capability for sustainable intensive farming among smallholders. In East Africa, for instance, our Scaling up Laikipia Project, begun in June, 2009, aims to reach as many as 30,000 smallholder farmers in an extension-services model with assets and information to help them raise vegetables as cash crops, improve water management, gain access to markets and take advantage of new technologies.

One of the farmer beneficiaries saw her potato crop increase from two bags a year to six, which tripled her income from $61 to $186. That $125 improvement is the difference between living on the edge of starvation, vulnerable to disease, and opening a bank account and buying more land.

Elsewhere in Africa, the Syngenta Foundation runs a program that provides fast-growing, drought-resistant maize to smallholders while offering them a first-of-its-kind crop insurance program that enables growers to enroll via mobile phone and provides payouts when automated weather stations report severe drought rather than requiring the farmer to prove economic loss. This innovative program makes it feasible and affordable for smallholders to take on the risk of planting higher quality seed—a risk too great otherwise.

Noble Work

These examples underscore the point that what may look like unrealistic ambition—improving smallholder productivity through propagation of intensive, but sustainable, practices—is, in fact, achievable. That is why meeting the global food-security challenge, while certainly daunting, is also achievable.

Improved agricultural productivity, in both the developed and developing worlds, is essential to meeting the challenge. In the developed world, it will require sustaining gains in agricultural productivity through continued investment and implementation of advanced technologies, measuring agricultural productivity holistically and harnessing the market power of major players to create farm-to-fork incentives for sustainability.

The most problematic barriers in the developed world will likely continue to be overzealous, under-informed and unsynchronized regulatory strictures.

In the developing world, we should be mindful of a Marshall McCluhan quote, uttered decades ago, but more apt than ever now:

> *We have moved into an age in which everybody's activities affect everybody else.*

Many of the catalysts that can help accelerate the evolution of smallholder, subsistence farmers into viable commercial farmers are likely to come in the form of new hybrids, new traits, new seed treatments and new crop-protection chemistries. The adoption of these new technologies can move ahead rapidly if it is not unnecessarily constrained by unscientific policy or regulation. Consider Brazil, which doubled its soybean production within a decade thanks in part to rapid adoption of new technologies.

The need to solve our global food-security challenges through improvements in sustainable agricultural productivity is certainly among the most urgent and important challenges we'll face in the next few decades. The concerted effort of the public and private sectors, academia, foundations and NGOs will be essential.

This is noble work and it is both gratifying—and humbling—to be engaged in it.

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Terry Stone is Syngenta's NAFTA Sustainability Value Chain manager. He is responsible for working with Syngenta's customers to develop initiatives that utilize the company's agronomic expertise and crop protection, seed and trait products to enhance the sustainable production of food, feed, fiber and biofuels. Mr. Stone has more than 25 years of experience in the research and development of agricultural products, specifically biotechnology-derived plants. He holds master's degrees in entomology and international business.

Sustainability and Needs of 2050 Agriculture

Q&A

Moderator: Francisco Diez-Gonzalez
University of Minnesota
Minneapolis, Minnesota

Francisco Diez-Gonzalez: The speakers will join me on the podium and we'll take questions from the audience.

Sonny Ramaswamy (Oregon State University): Dr. Swackhamer, what do farmers say about the Water-Sustainability Framework? They are a significant part of this. Are they buying into it?

Deborah Swackhamer: The agricultural community was well represented in the 250 or more people who put the Framework together. A lot of folks with an agricultural perspective participated. If you are familiar at all with the restoration of the Everglades—the Consent Decree—the sugar farmers in Florida were confronted with a judge deciding what they needed to do, and the farmers themselves said they would prefer to decide how to meet the load reductions required by the Consent Decree. We thought that was a great idea. So, we are using the concept developed by farmers for the specific situation in the Everglades. In addition, I had many discussions with people in the agricultural community. It's clear that one size doesn't fit all. That even one farm next to another farm might need a different solution. And I think that the majority of the agricultural community would admit that it is only fair that everyone be part of the solution. I think we are all searching for how to have that solution be a productive one and not bifurcated and full of tension. But the short answer is that although they aren't jumping up and down and saying, "Oh, let's grab that solution," they have not rejected it out of hand.

Richard Isaacson (University of Minnesota): It seems as though there are challenges ahead, and that's the politically correct term: challenges. There's also the movement from the other direction, which is dealing with threats due to contamination to trying to grow and consume foods locally. It seems as though they are on a collision course at least listening to what I heard today. How compatible are local foods with the concept of sustainability?

Jonathan Foley: That's something I have thought and written a lot about recently. The local food movement has been a cultural movement, rather than a significant food-security movement. If you look at local and organic food on the planet right now—what's labeled anyway as "local" and "organic"—it's about 0.6% of the world's calories. It's not even a round-off error. It's very small, relevant only to upper- and middle-income people in Europe and North America. It's not a solution to world-food security, although some great lessons may be learned from it. The local- and organic-food movements are cultural and aesthetic movements, and if the barrier between that world and the conventional agricultural world could be reduced—if the best ideas of the Michael Pollans and local food-movement folks could be adopted then scaled to the real economy with conventional agriculture and large agrobusiness being at the table too—that would be tremendously beneficial. But, right now, there's a schism between those two worlds which is unfortunate because there are good ideas on both sides and they are creating a tension that doesn't need to be there. Local food has some environmental benefits, but not many. It is based a lot on the false assumption that energy used in transporting food is a significant contributor to climate change. It's not. Actually, for the typical Walmart tomato, let's say, less carbon is used to ship it to you than, lets say, a local CSA tomato. Even though Walmart may ship it a lot farther, they are dealing in so much more volume. I don't like that fact because I like the local farmers' market. But neither of them is really large. It turns out that the big emissions of greenhouse gases come from deforestation, cows, rice and nitrous oxide, so forget about food miles *vis-à-vis* climate change. It's not that important. On the other hand, local food opens up people's eyes to how the food system works. It encourages more education and participation in the food system. Is it safer to have local food than distant food? I don't know. Intuitively you'd think it might have a role to play. There are lessons to be learned here, but there's a lot of mythology out there too, on all sides of the table, and I think we should look for the best from all these different food worlds and bring them together.

Koel Ghosh (University of Minnesota): People welcome changes related to improving sustainability if no additional costs are incurred. Changes that are adopted quickly are those that actually save costs for companies. But making the changes that matter often means that additional costs are incurred. In cases where there is an additional cost burden, who will pay?

Terry Stone: This is one of the biggest issues we are dealing with right now. I have heard it stated an awful lot in groups like the Sustainability Consortium, which was originally founded by Walmart and a number of other big retailers and food companies, and I can tell you that things are very different today in comparison to when they started. The awareness of the cost and the resource requirements—and, frankly, the risk—that a lot of growers feel in documenting their performance, making that information available, is much greater than was perceived before and the costs need to be borne throughout the supply chain. There's also a perception that the only way to incentivize a grower is by paying a premium for a product. In reality, over time, premiums haven't really held up because they eventually become the standard and everything that's not gets docked. So, creative ways should be explored to understand how best to incentivize their participation, their documentation, their desire to establish a baseline for their water, energy, and carbon use on the farm and being able to continue to document and implement practices for improvement. What we will find, and it's beginning to happen, is that there will be a shared cost throughout the supply chain.

Foley: There's a public roll here too, of course. Agricultural subsidies amount to $350 billion in OECD[1] countries. A billion dollars a day just in western countries. That's a lot of money even for these countries and that doesn't include money for things like food aid and food stamps. So, that's part of this economy as well—a small part, but a part of it that has a lot of influence. We should be using that more effectively, perhaps.

Stone: Dr. Swackhamer mentioned the importance of the upcoming Farm Bill. When you look at the conservation programs and other subsidies that are being paid to growers, we need to make sure that conservation programs aren't thrown out because they are increasing the budget, that they are recognized for the broader benefits that they provide.

Audience Member: Dr. Stone. You briefly talked about Golden Rice. What are the main barriers to its usage?

Stone: A lot of them are regulatory-related. Issues have been brought up regarding food safety that have not been borne out. There have been issues on intellectual property that have been dealt with, and I believe should not be a barrier at this point. But, in the end, it's really regulatory, and influences by non-governmental organizations who are concerned about its proliferation.

Esther McGinnis (University of Minnesota): Dr. Stone, is there any strategy for overcoming some of the obstacles? I think there is an obstacle to using a sustainable outcomes-based approach and that is because GM crops must be deregulated by APHIS[2] and they have to comply with the National Environmental Policy Act. The National Environmental Policy Act doesn't look at the totality of outcomes. It focuses on environmental impact, sometimes in isolation. For example, if even just one or two organic farmers have the

[1]Organisation for Economic Co-operation and Development.
[2]Animal and Plant Health Inspection Service of the USDA.

possibility of cross-pollination that is enough to, in fact, be an ecoviolation, and there have been cases within the last five years—alfalfa, and sugar beet—and sugar beet really involved one farmer in the Willamette Valley who was growing a compatible organic crop. So how do you deal with the National Environmental Policy Act to move forward with GM crops?

Stone: That's a complicated question because part of the responsibility of the USDA is to perform an environmental assessment to determine whether there is significant impact or not. On the basis of that, they have the responsibility to determine whether they need to perform a natural and environmental impact statement, an NEIS. In the beginning, for APHIS, there was certainly a desire to be able to come to a finding of no significant impact with all of the crops that were seeking deregulation, and they found they were able to do so because they were also regulating under the Plant Pest Act, which is their principle authority to be able to review and deregulate these products. Over time, and this is very similar to many other environmental issues that have occurred and goes back actually to the establishment of the National Environmental Policy Act, which was written very broadly and without a great deal of necessary detail on how an environmental impact or environmental assessment should actually be performed. This is why there have been so many lawsuits under the National Environmental Policy Act and many have gone to the Supreme Court to find resolution. What we are seeing today at USDA is that same kind of process. In the beginning it was new, and a lot of issues had to be dealt with and there were differences of opinion—as far as whether it's safe or not—but at the same time they were able to go forward until it reached a point where there were products that perhaps were deregulated because of their open pollination or other reasons that led to greater scrutiny and, frankly, groups finally decided to use the courts as a way to assess whether these things should continue to move forward. So, it's a process and the USDA is getting better at doing environmental assessments and considering when they need to do environmental impact statements. So that's one part of it from a regulatory piece, and I won't get into the merits of Roundup Ready alfalfa or Roundup Ready sugar beet. From a sustainability perspective, however, when you consider that a lot of technologies take many years to get to the market—it's all part of the developing process—and years that it takes including regulatory oversight and the like are borne by the companies that are developing them and then, of course, after they are commercialized, their desire is to be able to recoup that investment so that they can continue more innovation, develop other products and keep the circle going. So, from a sustainability perspective, I don't see there being any distinction between whether it's a genetically modified crop or whether it's developed by traditional plant breeding. It's part of the process. What is important are the outcomes that we are trying to achieve in developing these products, like reducing water usage, reducing energy usage or improve nitrogen-use efficiency. The means to get there—if we are able to achieve these outcomes given that we are not causing other problems as an offset—are, I think, the more important points. So, I am hopeful that there will be more innovation and that products that require new technologies will find a way to the marketplace more quickly than they have in the past.

Tony Shelton (Cornell University): Dr. Foley, one of your conclusions was to halt agriculture expansion, especially in sensitive areas, and then in those areas where things can be improved, to adopt technology to try to improve the yield per unit of land. Is that correct?

Foley: More or less.

Shelton: Terry Stone, you mentioned that, in Brazil for example, agricultural production had doubled in a specific period of time, and so I am wondering if you and Dr. Foley might have a conversation about that example, and also maybe question whether technology makes it easier to adopt a crop in a particularly sensitive area?

Foley: I was thinking the same thing when I heard that comment. The productivity of soybeans did not come about through GMOs. It was conventional plant breeding in Brazil to overcome day-length requirements. It's a temperate crop that needs daylight triggers to produce seed and that was overcome just as the demand was exploding in Europe and Asia for vegetable protein. So it's a tremendous economic success story. The land that soybeans are moving into in Bolivia and Brazil primarily was formerly mostly pastureland, not newly cleared rain forest, but almost every soybean field in Brazil today was probably in rainforest within a decade ago. The usual approach is to clear rainforest for a pasture because you just simply can't plow the land due to stumps and hummocks. You leave it as pasture for a while and then the soybean folks move in, who often claim, "Oh, we didn't cause deforestation, it was those pasture guys." So there's a lot of back and forth about that and it's interesting looking at land-tenure patterns. You have to admit the land was cleared recently and whether that led to further deforestation or not is another question. Now there's a question about whether sugar-cane expansion in Brazil for biofuel production will accelerate that further.

Stone: Well, technology is a very broad term. Biotechnology is one form of technology, but there are a many other pieces of the puzzle. I think it's a combination or things. There is no doubt that breeding in Brazil was a major influence on the changes as were IPM practices. Markets began to explode in other parts of the world, and, frankly, Roundup Ready soybean had a tremendous impact on adoption as well. There were many factors. On your point of whether technology enables the production of crops in sensitive areas, I think this is a matter of policy. Technology is an enabler. It's a tool. It's not the reason to grow crops in a particular area. It may enable that to happen. But there also needs to be government policy and corporate policy that dictates also whether that is permitted or not. As mentioned—I thought this was interesting—they require buffers between fields in Brazil. We don't have that same requirement here in the United States. That kind of policy enables technologies to be employed with less risk to the environment.

Foley: There are some success stories from Brazil although in the last year deforestation rates spiked again due to land speculation, but overall it's been declining recently, thanks in part to companies like Cargill who work with NGOs. There's a road in Brazil that is very controversial called BR 163 from the Mato Grosso, the heart of the soybean part of Brazil, up north, not south to Rio and Sao Paulo, where most of the soybeans were going, but north to the deep-water port of Santarém on the Amazon River and which could ship soybeans much more quickly to Europe or the Panama Canal. The problem is, if you pave and widen that road, then it would just spur more deforestation and more clearing. So Cargill and NGOs and the governor and others proposed to pave and widen the road, but then create huge parks on either side of the road that cannot be deforested and give them to indigenous peoples and environmental groups and so on, to find a way to have a win-win.

Abel Ponce de León (University of Minnesota): Jon, similar to what Tony Shelton spoke about, you indicated that increased productivity will require increased inputs of fertilizer *et cetera*. Another necessity is to reduce water pollution. These seem to be mutually exclusive.

Foley: I suspect we are in agreement. Regarding fertilizers, it's the goldilocks problem again. Half the world has too few fertilizers and very low crop production and the fertilizers they are using aren't really getting the job done, and the other half of the world has too much, including the United States, but especially China and India. We are actually using too much. Often, only about a third of applied fertilizer creates plant nutrition, maybe a half if we are lucky. Then the other half or two-thirds is an environmental pollutant whether it is nitrate, nitrous oxide, excess phosphorus, *et cetera*, all potentially affecting water quality. What we don't have anywhere in the world is somebody who is doing it just right. If you look at the distribution of fertilizers and their benefits for food production, it is bimodal—too little or way too much. We all know what the optimum is, but incentives are perverse on one side and on the other side poverty and lack of infrastructure prevail. A lot of Africa would benefit from a lot of fertilizers and a lot of Minnesota would benefit from using less. There's a middle ground that nobody has gotten to yet. I would love to hear what Deb thinks.

Swackhamer: Everything that Jon just said I would agree with, but I would emphasize that we do know the answers. We know how much nitrogen to apply to get optimum yield. It requires conservation-based agriculture. It requires modern agriculture and that costs money. It needs incentives. It needs support from the government. This is a great segue—I'm going to change the conversation. We could do a far better job on the nitrogen and phosphorus thing. We just don't do it because it costs money. In the United States we could do a much better job. We are a wealthy country and we could actually invest—part of the Farm Bill, perhaps—to protect our natural resources. But much of the conversation today—in fact the three gentleman here spoke on a global scale whereas I spoke at a national scale and the problems globally are far worse than what we face here in this country in terms of producing food and feeding our hungry, *et cetera*. And yet I just heard for the first time just now the word policy. This is all predicated on policy. It's not predicated on whether we have the technologies or whether we know how much nitrogen to apply. We know all that and we have really the technologies and I would submit to the three of you—and would love to hear your answers—and to the audience, that the biggest barrier here is governmental. It's not the technology. It's not having enough seed. It's not having enough land. It's politics and policies.

Ponce de León: So, let me add one more question, and this if for Dan now.

Swackhamer: You're not going to answer my question, Abel?

Daniel Gustafson: I'll incorporate the answer into my response to this question.

Ponce de León: What is the role of FAO and other global institutions in this regard?

Gustafson: Let me see if I can combine those two. A lot of what we work on, of course, is policy, but I think—following up on Jon's comment too—that, almost invariably, where there is too much fertilizer use it's a policy issue. The incentives are just all wrong either in formulation or in subsidies or manufacturers or other things. Now—the other side of the equation—where you have too little fertilizer use, I don't think that policy *per se* is the issue in quite the same way. It could be to the extent that it is a policy of lack of investment, but often it is just too expensive to transport fertilizer very far. So the cost of fertilizer in Rwanda, for example, is five times more expensive than it is in Kenya because it has to be transported from Mombasa. It's the same stuff, so the use of technology by really poor farmers is largely one of economics rather than a policy. Why that is the case relates back to policy choices and what was invested in; whether agriculture is seen as a declining sector, with people moving out of it, is certainly related to policy. Or similarly with donors not investing in agriculture for a long time, but instead investing more in social services, health in particular, that have much easier connection between investment and observable outcomes, and so on. Okay, with regard to FAO, policy is a difficult issue. We do a lot of work on policy and we do a lot of work on supporting groups that are working with stakeholders in order to change policies, because governments are not amenable to pressure in that sense outside of longer-term education and awareness and pressure within the society. However, when you look at the renewed interest in agriculture and in investment and policies that would promote agricultural growth and food-security improvement and so on, when you get right down to it, it is really all about the food prices of 2007 and 2008. I don't really see that any of the work on advocacy and policy addressing this issue in a big way made any headway relative to the crisis. And it may be that way here too. If we had a water crisis in Minnesota, I think that a 25-year plan would be developed faster. How to deal with these long-term issues outside of a crisis is a huge challenge.

Diez-Gonzalez: One last question.

Ralph Hardy (National Agricultural Biotechnology Council): Let me make one comment and ask one question. Michael Pollan was invited last year to be a plenary speaker when the topic was *Promoting Health by Linking Agriculture Food and Nutrition*, right down Michael Pollan's line. He declined to attend the meeting. He basically said that he will not speak with agricultural groups. It's difficult to deal with Michael Pollan who uses the *New York Times* and other sources to distribute his mix of facts and non-facts. Part of it is his lack of familiarity with the reality of agriculture. You can't get him into an open forum such as this meeting which welcomes comments from all sorts of people. End of my comment. Question—agriculture has not many log-step improvements. It's been quite a while since agriculture made a log-step improvement. We've made little steps. Herbicide tolerance was obvious and it was easy and a good way to enter the biotech market. Drought tolerance is going to be a little bit more challenging, but I think that we are saying that we need revolutionary new ways of doing things. We've been talking about the fertilizer area. Nitrogen fertilizer has its problems in the environmental cost, the energy cost, carbon dioxide emissions, all those sorts of things. We need to be putting some effort in terms of high-risk research with huge high-return possibilities. Self-nitrogen-fertilizing crops I think is an area to revisit at this particular time. We've been able to make a synthetic genome. All we need to do for self-nitrogen-fertilizing crops is to put in the genes that enable nodules on the stems of corn, *et cetera*, and replace the energy-wasteful nodules that are on the roots of soybeans. We know that there are rhizobia out there that can directly receive solar energy and can use that energy to fix the nitrogen. A big problem with biological nitrogen fixation in root nodules is the huge energy cost to the plant. So this is the sort of thing I would urge us to start thinking about and I'd welcome your comments. What areas of new technology should academe, should industry, should government be putting a percentage of their bets on—because those are the things that are really going to change the game down the road. Thank you.

Swackhamer: As the non-agricultural person up here, I will start. Thank you for your comments. Terry talked about where do you want to get to, what do you want the outcome to be, and then back out, what are the solutions to those problems? What are the technologies that would be needed? So if you want to reduce nitrogen, figure out how you are going to do that and implement those strategies. I hear you. We need transformational strategies. These little tinkerings around the edges—as much as I really like buffer strips, I think if we put 50-foot buffer strips across every stream in the United States, it still wouldn't work. We need transformational changes, but we have to decide what the outcome is going to be and then back calculate what needs to happen. That's my two cents.

Foley: I would echo the same comment in a lot of ways and I like Terry's comment too—outcome-based performance rather than prescriptive. We need to deliver more food with more nutrition with less environmental harm, bottom line—however you can do that, that's great. The way you are talking about it is really fascinating. Wherever he is, Michael Pollan's ears are burning right now. He's a good guy actually, I wish he would come to meetings like this. But, what we call GMOs today are going to be obsolete pretty soon as a result of synthetic biology and computational capabilities. We will compute the genome and then go make it. Some incredible tools are coming on line. There's a legitimate concern that people in this room need to think about: most of this technology is being developed in the private sector. The private sector has a huge roll to play in innovation, as it did in the IT revolution, but the calculus of where to invest and where to deploy is a business model that has to provide return to the shareholder, as it should. There ought to be some places where the public good is put first too. And that is where public investment in universities, nonprofits, foundations and so on comes in; that needs to be there and be a partner to the private sector. Let them be partners together to make sure those kinds of technologies are deployed. I hear all this talk about, "Oh, we're going to create crops that are drought-resistant and perennial and nitrogen-producing," yet that would be a terrible business model for Syngenta or Monsanto. They would be out of business if they were successful. Why would they do that? So, I'm a little skeptical. I think that these things should be done, but who is going to really do them?

Hardy: The IP from self-nitrogen-fertilizing crops would be substantive.

Foley: But should that be in the public domain? People like me would say that that should be given to the world. That's a lousy business model.

Hardy: I think it should be government doing that because it's high risk. And maybe too high risk for a university and probably it's too high risk for industry.

Stone: Think about all the budget issues that are going through Congress right now. People are fighting over pennies. We deal with similar things in our business too. Every decision we make essentially should take into consideration return on investment. So, does that mean that we don't fund or don't do high-risk research? No, but we tend to place our bets in areas where the risk is acceptable. For areas where it's not, we fund a tremendous amount of research in academia and in small start-up companies and the like. We have to determine where our best bets are, frankly, and maximize our core competency. I would like to come back to something that both Deb and Jon said that's relevant. Where do you begin? I like Deb's analogy of a bank account. Most growers are really not good record keepers from the perspective of understanding what they've used or what they've applied versus what they've received in terms of whether its yield or return on their investment. Growers need to be able to develop their own bank accounts—call it a sustainability account, in terms of things like energy per bushel, water use per bushel—so they know where they can improve. Companies are getting into lifecycle assessment, and when they do the work to understand their carbon footprint or energy footprint, they realize something incredible: they save money. Walmart is a great example. They are saving millions of dollars a year because they turned off the light bulbs in their Coke machines overnight. There are so many examples of that. Farmers need to get to the same point. It's one of the biggest challenges we have. In my mind, if there's a place to start it's educating growers on the importance of being able to document what their practices are, what their inputs are and the impacts those things have on their outcomes, not just in bushels but in resource efficiencies. By doing that, it's a tremendous starting point. Growers won't cut down on the amount of fertilizer they are going to use because it's an insurance policy. They can't predict the weather, so they can't take a risk of not applying more. So there has to be some way to be able to inform that decision that, right now, is not readily accepted by growers. So, document, benchmark, establish a baseline, identify improvements, continue to document and adapt to be able to continue to improve, and focusing on the outcomes that allow that to happen. And then the technologies come along.

SYSTEMS-BASED APPROACHES TO FOOD PROTECTION AND SECURITY

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(No manuscript.)

[*Editors' note:* Dr. Medford described how techniques in synthetic biology—with funding from the Defense Advanced Research Projects Agency and the Department of Defense—are being developed to modify plants to detect with high sensitivity the presence of chemicals (*e.g.* pollutants, explosives) or pathogens and reveal their presence by rapid de-greening of chlorophyll, for use in agriculture and at high-population terrorist targets such as airports.]

Some of the information presented by Dr. Medford at NABC 23 has been published:

Antunes MS *et al.* (2006) A synthetic de-greening gene circuit provides a reporting system that is remotely detectable and has a re-set capacity. Plant Biotechnology Journal 4 605–622. doi: 10.1111/j.1467-7652.2006.00205.x

Summary: Plants have evolved elegant mechanisms to continuously sense and respond to their environment, suggesting that these properties can be adapted to make inexpensive and widely used biological monitors, or sentinels, for human threats. For a plant to be a sentinel, a reporting system is needed for large areas and widespread monitoring. The reporter or readout mechanism must be easily detectable, allow remote monitoring and provide a re-set capacity; all current gene reporting technologies fall short of these requirements. Chlorophyll is one of the best-recognized plant pigments with an already well-developed remote imaging technology. However, chlorophyll is very abundant, with levels regulated by both genetic and environmental factors. We designed a synthetic de-greening circuit that produced rapid chlorophyll loss on perception of a specific input. With induction of the de-greening circuit, changes were remotely detected within 2 h.

Analyses of multiple de-greening circuits suggested that the de-greening circuit functioned, in part, via light-dependent damage to photosystem cores and the production of reactive oxygen species. Within 24–48 h of induction, an easily recognized white phenotype resulted. Microarray analysis showed that the synthetic de-greening initiated a process largely distinct from normal chlorophyll loss in senescence. Remarkably, synthetically de-greened white plants re-greened after removal of the inducer, providing the first easily re-settable reporter system for plants and the capacity to make re-settable biosensors. Our results showed that the de-greening circuit allowed chlorophyll to be employed as a simple but powerful reporter system useful for widespread areas.

Antunes MS *et al.* (2009) Engineering key components in a synthetic eukaryotic signal transduction pathway. Molecular Systems Biology 5; Article number 270; doi:10.1038/msb.2009.28.

Abstract: Signal transduction underlies how living organisms detect and respond to stimuli. A goal of synthetic biology is to rewire natural signal transduction systems. Bacteria, yeast, and plants sense environmental aspects through conserved histidine kinase (HK) signal transduction systems. HK protein components are typically comprised of multiple, relatively modular, and conserved domains. Phosphate transfer between these components may exhibit considerable cross talk between the otherwise apparently linear pathways, thereby establishing networks that integrate multiple signals. We show that sequence conservation and cross talk can extend across kingdoms and can be exploited to produce a synthetic plant signal transduction system. In response to HK cross talk, heterologously expressed bacterial response regulators, PhoB and OmpR, translocate to the nucleus on HK activation. Using this discovery, combined with modification of PhoB (PhoBVP64), we produced a key component of a eukaryotic synthetic signal transduction pathway. In response to exogenous cytokinin, PhoB-VP64 translocates to the nucleus, binds a synthetic PlantPho promoter, and activates gene expression. These results show that conserved-signaling components can be used across kingdoms and adapted to produce synthetic eukaryotic signal transduction pathways.

Antunes MS *et al.* (2011) Programmable ligand detection system in plants through a synthetic signal transduction pathway. PLoS ONE 6(1): e16292. doi:10.1371/journal.pone.0016292.

Background: There is an unmet need to monitor human and natural environments for substances that are intentionally or unintentionally introduced. A long-sought goal is to adapt plants to sense and respond to specific substances for use as environmental monitors. Computationally re-designed periplasmic binding proteins (PBPs) provide a means to design highly sensitive and specific ligand sensing capabilities in receptors. Input from these proteins can be linked to gene expression through histidine kinase (HK) mediated signaling. Components of HK signaling systems are evolutionarily conserved between bacteria and plants. We previously reported that in response to cytokinin-mediated HK activation in plants, the bacterial response regulator PhoB translocates to the nucleus and activates transcription. Also, we previously described a plant visual response system, the de-greening circuit, a threshold sensitive reporter system that produces a visual response which is remotely detectable and quantifiable.

Methodology/Principal Findings: We describe assembly and function of a complete synthetic signal transduction pathway in plants that links input from computationally re-designed PBPs to a visual response. To sense extracellular ligands, we targeted the computational re-designed PBPs to the apoplast. PBPs bind the ligand and develop affinity for the extracellular domain of a chemotactic protein, Trg. We experimentally developed Trg fusions proteins, which bind the ligand-PBP complex, and activate intracellular PhoR, the HK cognate of PhoB. We then adapted Trg-PhoR fusions for function in plants showing that in the presence of an external ligand PhoB translocates to the nucleus and activates transcription. We linked this input to the de-greening circuit creating a detector plant.

Conclusions/Significance: Our system is modular and PBPs can theoretically be designed to bind most small molecules. Hence our system, with improvements, may allow plants to serve as a simple and inexpensive means to monitor human surroundings for substances such as pollutants, explosives, or chemical agents.

June Medford, a professor of biology at Colorado State University, is a leader in the field of plant synthetic biology. She received her BS in botany from the University of Maryland and a PhD in biology from Yale, followed by postdoctoral training with the Plant Molecular Biology group at Monsanto.

Dr. Medford's research focus is on plant synthetic biology, the forward engineering of plants for specific purposes, both basic and applied. She has developed a synthetic signal-transduction system based on conserved histidine kinase components and a field-level synthetic readout system. By linking these synthetic systems together with computationally re-designed receptors, the Medford lab has produced the first sentinels to allow plants to serve as inexpensive and highly specific detectors of substances such as explosives, environmental pollutants and chemical agents. Detection levels are approximately 10- to 100-fold better than the detection abilities of dogs. Work is in progress to add ultra-sensitivity and memory for specific application (*e.g.* transportation hubs) and expand the detection platform to biological agents. Furthermore, the synthetic system is a biological input-output system and, hence, is being used to control biofuel and agronomic traits.

Vulnerability and Environmental Risk Assessment

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Over the past half century, environmental risk assessment (ERA) has become increasingly important in political decisions. It forms an important basis within the World Trade Organization's Sanitary and Phytosanitary Agreement (SPS) and is an important touch point within the Convention on Biological Diversity. The scope of ERA is expanding rapidly both in the issues that it covers and in its role in policy formation. Classic environmental risk issues—starting in the 1960s—include air and water pollution and pesticide usage. However, new ecological challenges include hormones in the environment, invasive species and the GM issue. Also, new technologies are becoming the focus of ERA. Importantly, the way that ERA is used in policymaking is changing as well. Historically, ERA was used primarily as a decision-support tool. In other words, risk-assessors provided information that decision-makers took into account to guide policy. However, in the last few decades, ERA has been increasingly used to legitimize environmental policy; when the public knows that a risk assessment was done, it is likely to legitimize the eventual decision. Thus, the process now is important in terms of acceptability of the decision, which can create tension if the risk-assessment data are lacking in some regard. In addition, risk assessment has been expanded in ways to set environmental policy. In the developing area of comparative risk assessment, certain policy options are favored, rather than certain policy decisions, which has raised additional challenges for risk assessment. The expansion of the scope of these issues has increased vulnerability because, as we address new problems, we have to keep revising our *modus operandi* merely to keep up.

Genetically Modified Crops

It is clear that, overall, some GM crops are better for the environment than non-GM crops; one clear example is *Bt* cotton in Arizona where reduction in pesticide use has been substantial. On the other hand GM crops do require local risk assessment. Three dimensions vary around the world in terms of governmental frameworks that consider risks associated with GM crops and these are whether or not the following are examined:

- only direct or both direct and indirect effects of the crop
- only non-agricultural or both agricultural and non-agricultural effects
- effects mediated by both humans and non-humans or non-humans only.

In Australia, agriculture is dealt with through a separate ERA process, so GM-ERA only addresses non-agricultural effects. In contrast, most of the European frameworks consider agriculture as part of the environment and, therefore, farming issues are a part of the overall assessment of risk. In the United States, only some aspects of agriculture are considered part of the environment. So there is variation on that point around the world. As far as direct and indirect issues are concerned, genetically engineered herbicide tolerance provides a good example. Herbicides are applied to many crops to control weeds. With herbicide-tolerant crops, we examine the direct effects of the transgene on the environment; every regulatory system around the world considers this. However, those regulatory systems vary in terms of indirect effects on the environment. Of the many possible indirect effects, one is the accompanying switch in herbicide product. USDA/APHIS defines the transgenic plant as the transgene itself and any change in the herbicide is not required when using the GM plant, and, as a result, it and its consequences are not regulated. In contrast, the European system considers the change in the herbicide as part of the regulatory process. In the United States, because herbicides are already regulated, it is believed that there is no reason to regulate them again. On the other hand, we do know that when we switch herbicides we alter selection pressures on weeds, potentially causing development of evolutionary resistance, which has occurred in the southeast of the United States, leading to new patterns of weed development. In the United States we have not regulated the evolution of weed resistance, in Europe some of these issues are considered. Thus, the many indirect effects may or may not be considered under different regulatory processes. Factors considered important or unimportant in the United States may or may not be considered similarly in other countries.

With regard to possible environmental effects of GM crops, three categories garner attention:

- transgene flow and subsequent effects including increased weediness in the recipient
- resistance evolution
- unintended effects on organisms and ecosystems.

The high-dose refuge approach towards *Bt* resistance has been a great success. We have never had an insect pest-control method used as widely that has not resulted in resistance evolution. Of course, we will continue to monitor this approach for many years. Low-dose situations are not quite as successful; all of the examples of resistance evolution occurring in *Bt* crops around the world are associated with low-dose crops. However in this talk, I will focus instead on unintended effects on organisms.

The Value of Culture

Bt maize produces a protein that is toxic to many Lepidoptera. Pollen containing the toxin, dispersed in the wind, falls onto the leaves of plants that other insects—including monarch-butterfly larvae—eat and then may die, possibly threatening the insect population. Although that's the risk story involving monarch butterflies, several published studies have shown that *Bt* corn does not constitute a serious risk for monarch butterflies. Fortunately, the varieties of *Bt* maize that were commercially successful have very low toxicity in the pollen, whereas some of the varieties that were less successful actually have higher toxicity, otherwise the outcome of the story may have been different. Monarch butterflies are exposed to many risks, but only minor ones related to GM maize.

Why was there so much uproar about *Bt* maize and monarchs in the United States? It's just a butterfly, of which many types exist. Monarchs aren't endangered, nor is their conservation value considered very high. Part of it is that monarchs are amazing in that they migrate from Canada and the United States to Mexico for the winter, as well to parts of California and Florida. They aggregate in huge numbers in certain locations in Mexico. Programs such as Monarchs in the Classroom elicit great interest among school children: their larvae are grown and allowed to pupate and emerge and then are set free, which has a considerable emotional impact on youngsters. Monarchs are even on US postage stamps, reflecting their cultural significance.

In fact, issues of cultural significance are actually quite important *vis-à-vis* environmental risk. We need to expand our approaches to ERA to include cultural dimensions. The bald eagle is also important in the United States, and I have talked to people around the world and found that other species have special cultural significance in other countries, creating heterogeneity in what are seen as important parts of the environment.

So, my first conclusion is that cultural significance needs to be incorporated into ERA.

Assessing Sustainability

Sustainability has been a buzz word for some time and has permeated universities and industry, and in some ways it's a "mom and apple pie" type of thing. Those of us who work in the area know that it's actually quite complicated to accomplish. I'm not going to go into this in its tremendous complexity, but rather focus on one element: risk-assessment associated with chemical toxins, which goes back to the beginning of ERA in the 1960s. This approach to ERA has been promoted by several stakeholders for application to GM crops. I will argue that this approach doesn't really get at the problem of sustainability.

The general model is that, to make an ecological risk assessment, you conduct toxicology tests in the laboratory—which are easier and less expensive than field tests—using exposure rates that are much higher than normally applied. If an effect is observed, then the logical step is to continue testing. If there is no effect, the basic logic is that because the toxin levels are higher than would be seen in the environment, then you can stop. However, one has to ask how good are the tests. In particular, one doesn't want a "no effect" conclusion when there actually were effects that were undetected.

Biological Control of Pests

Biological methods of controlling insect pests employ insects or other organisms that feed on pests and thus control them. Figure 1 shows a few examples that, in addition to pathogenic micro-organisms, are biological control agents.

Figure 1. Examples of natural and biological control of insect pests.

Meta-Analysis

I should note that there is ongoing scientific dispute on what I will present here. One of the areas under debate is meta-analysis, which provides a means of combining information from multiple studies to show overall trends. It is regarded as less subjective than summarizing summaries because it uses data that are statistically significant as well as data that are non-statistically significant. So, for example, suppose I studied the effect of Cry1Ac, one of the *Bt* toxins, on a species of ladybird beetle, *Cycloneda munda*, and suppose I come up with two non-significant effects on development and growth, both with p values of 0.09. If I did this study, I would conclude that I wouldn't see any effect of Cry1Ac on *Cycloneda munda*. Now, supposing ten studies showed similar results. Now the null-hypothesis of no effect across the ten studies would be rejected at a very low p value of 0.0029, meaning that even though none of the studies showed a significant effect, there really were significant responses. It would be wrong to conclude that lots of non-significant effects implies that the effect is non-significant, which is counter-intuitive. Meta-analysis shows that lots of non-significant effects may imply that there are significant effects.

Considering how we do meta-analysis, there are two kinds of null hypothesis. There is a null hypothesis that is common within medical meta-analysis literature and then there is a null hypothesis that hasn't really been well recognized in the ecological literature. The main difference is whether or not you assume that the data you are looking at are underlain by one basic response or multiple responses. In medical literature you basically study the effect of some chemical on humans and it's the same chemical and basically the same protocols, therefore you expect that all of the studies are measuring the same things. Everybody is trying to measure one response, which is either positive or negative, and as a consequence—which is a key assumption within meta-analysis—we say that if study one shows evidence for a significant positive effect and study two shows evidence suggestive of a significant negative effect then, combined, the two studies show that there was no significant effect because it can't be both positive and negative at the same time. Technically, the null hypothesis is that if there is one real response then the data and evidence are distributed in a standard normal distribution around the real response value, whatever that real response value is. If there are many responses, the problem is different. The real responses can be positive and negative, and with ecological data often this is the case because in ecology we rarely replicate the exact same experiment. Even if we are looking at the same natural enemy with the same toxin, people do the experiment in different ways, with different toxin concentrations, for example. They'll look at different responses and will measure responses differently, so you can't assume that they are measuring one thing. You are actually measuring many different things. But we still combine all the data. Where study one finds a significant positive effect and study two finds a significant negative effect then the final conclusion from this approach is that there is a mixture of significant effects—a very different conclusion to come to. If there are multiple real response values and all of them are zero, in other words all of them are no effects, then all of evidence will be distributed as standard normal around zero. It provides a nice prediction. Significantly, we cannot conclude that if it's not standard around zero then there are multiple real responses because that is part of the assumption; we have to conclude that there are some non-zero effects. This is a way of determining whether effects are hidden within data.

*GM-*Bt *Crops*

We pulled together laboratory data on the effects of *Bt* toxins on natural enemies of insect pests. We looked both at direct and indirect effects; we found fifty-five studies with 273 responses measured. Figure 2 shows the fraction of observations plotted against the degree of effect on predators and parasites, with a standard normal distribution showing the zero-effects prediction. There was a slight skewing towards a negative effect, but it turned out to be non-significant; we can't say that *Bt* crops had significantly more negative effects than positive effects, but we can say that the *Bt* crops had both negative and positive effects. We don't know what those positive and negative effects were, nor do we know how big they were, but, again, the main conclusion was the presence of non-zero effects. We broke the data down for the following finer analyses:

- Separate common species
- Separate toxin types
- Separate direct and indirect effects
- Separate response types (survival, development, growh, reproduction, behavior, enzyme activity)
- Controls for non-independence among response types.

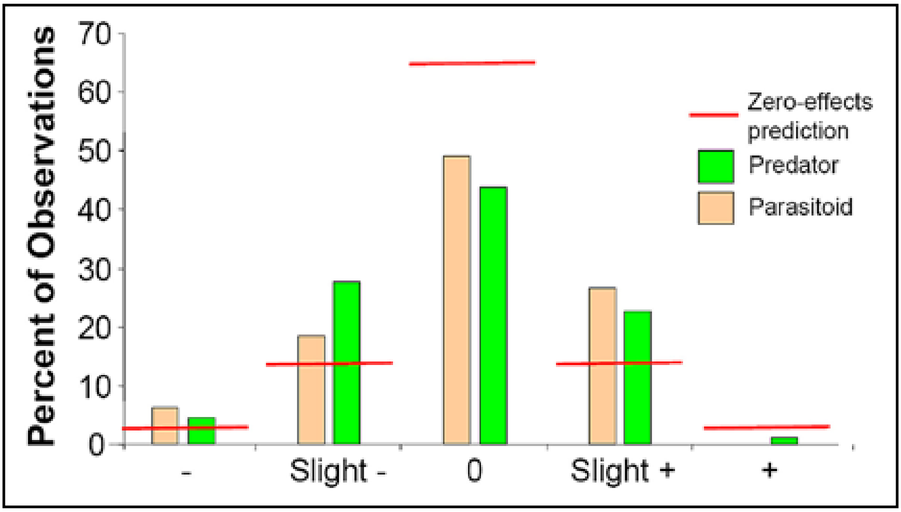

Figure 2. *Bt* toxins: non-zero direct effects (Lövei *et al.*, 2009)

Figure 3 shows that 70% of sixty-six comparisons had *p* values of <0.05, whereas twenty comparisons, with relatively low sample sizes, showed non-significant differences. In all of the original papers the authors reported no direct effects, and in all of the review papers the authors reported no direct effects. Yet meta-analysis suggests that there were many undetected effects. We suggest the need to improve this ERA methodology so as to reduce the number of false negatives and to assess sustainability more accurately.

This is just one case. The general issue of how we assess sustainability within a risk-assessment context is a challenge that we have not yet grappled with in its full complexity.

The Last Organism Will Be an Insect

Mirid Bugs in China

Last year, Lu *et al.* (2010) reported positive effects of *Bt* cotton on populations of mirid bugs (Heteroptera: Miridae) in China. Figure 4 shows that numbers of these insects have increased since 2002 on *Bt* and non-*Bt* cotton alike. In other words where *Bt* cotton is planted in large areas, mirid bugs have become a pest. As it's a secondary pest, nobody intended to control mirid bugs with *Bt* cotton, so the technology cannot be faulted. However, in an ecological context, a new plant pest has emerged with attendant crop losses and increased applications of insecticides. Consequently, the financial and environmental benefits from *Bt* cotton have been degraded.

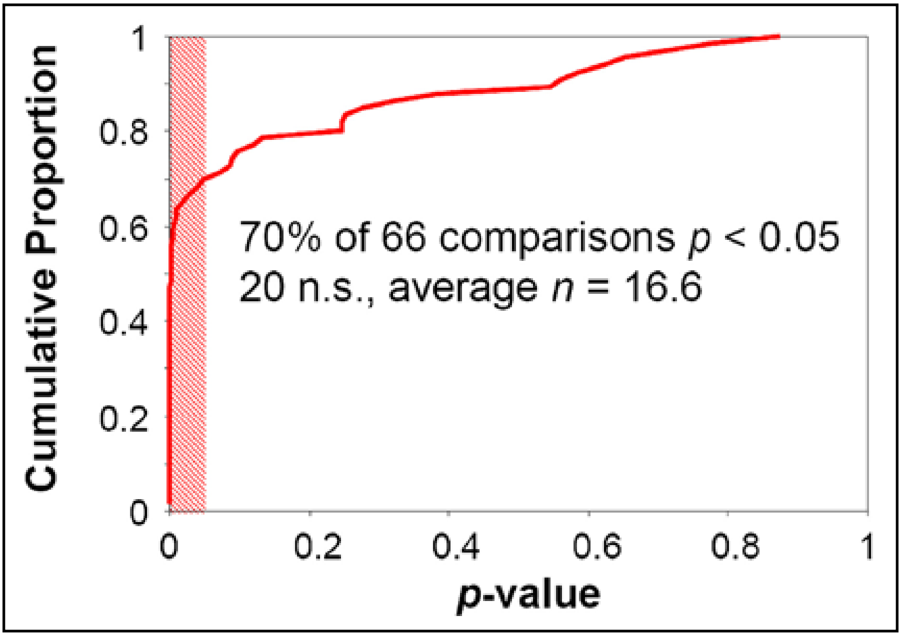

Figure 3. Test for non-random responses.

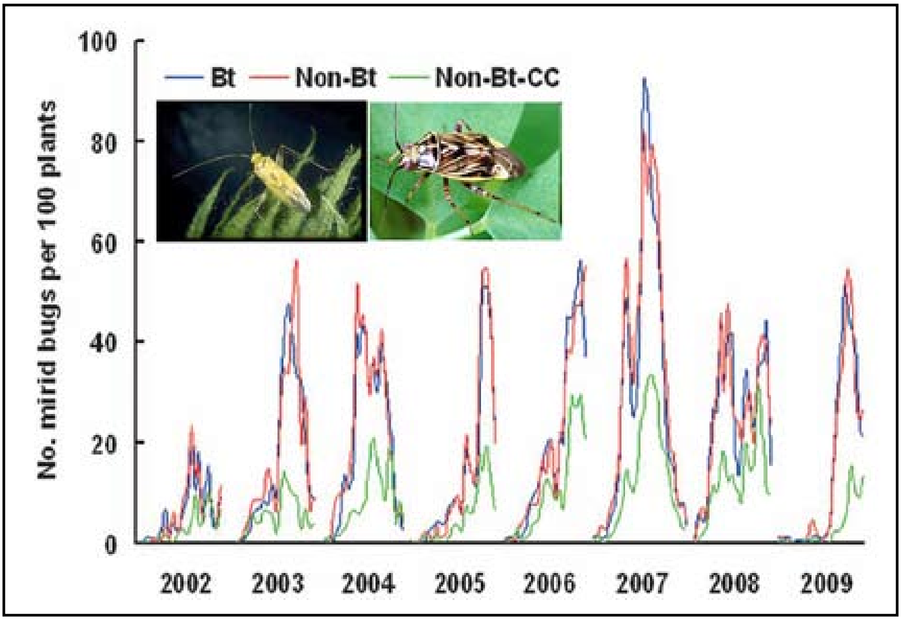

Figure 4. Mirid bug populations on cotton in China (Lu *et al.*, 2010).

We have a similar situation in the southeast of the United States that's less well known (Zeilinger *et al.*, 2011). Planting of *Bt* cotton has resulted in increased incidence of stink bugs such that they are now the most important pest of cotton in the southeast and most of the insecticide applied to cotton in that region is for control of stink bug. Attendant crop losses have not been huge. There has been an increase in insecticide application, but not to the level applied to non-*Bt* cotton; in other words there are still some net benefits from *Bt* cotton, which I consider to be a consequence of our excellent extension system which monitors these things and figures out solutions to problems so that we can actually respond and the financial benefits can be retained by farmers. Thus, sustained benefits from GM-*Bt* crops may depend on a vigorous public-extension service, and should not be attributed solely to the seeds.

Secondary Infestations

Another question we addressed was, "What are the causes of these secondary infestations?" One of the major explanations is that reduced insecticide application is a contributing factor. However, a contributing factor is not the whole story. We have mirid bugs in southeastern United States, but they have not become a problem.

Currently, we have several research projects to try to determine underlying factors. Three other possible explanations are as follows:

- Enhanced colonization and/or reproduction on *Bt* cotton
- A more likely factor is competitive release, *i.e.* killing the Lepidoptera that attack the bolls releases stink bugs from competition
- Also likely, on the basis of two years of data, is a build-up in the landscape within and/or between years.

Figure 5 shows data generated with two species of stink bug (*Nezara viridula* and *Euschistus servus*) when challenged by caterpillars of cotton bollworm (*Helicoverpa zea*) or tobacco budworm (*Heliothus viriscens*) on cotton bolls. Unchallenged stink-bug controls are on the far left. The data reveal an interaction; in some cases, the stink bugs grew significantly more slowly when challenged with the higher numbers of caterpillars.

A stronger effect has been demonstrated in terms of where stink bugs lay their eggs. We did a simple study where we damaged the lower leaves of cotton plants with caterpillars and gave stink bugs the choice of undamaged leaves on damaged plants and undamaged leaves on undamaged plants (Figure 6). We found that, by a large margin, the stink bugs preferred to lay their eggs on the leaves of undamaged plants. We know that caterpillar damage causes both aerial signaling and induced signaling within the plant, but we don't know which applied here. However, this may play a role in the competitive release of stink bugs as discussed above.

Conclusion

Why are opinions on GM crops so polarized? As scientists, we know that most technologies have attendant risk and we tend to frame problems in terms of balancing benefits and risks in a way that is positive for society. I think that this is too narrow a framing of the problem. The core problem really is that some people see mostly benefits and some

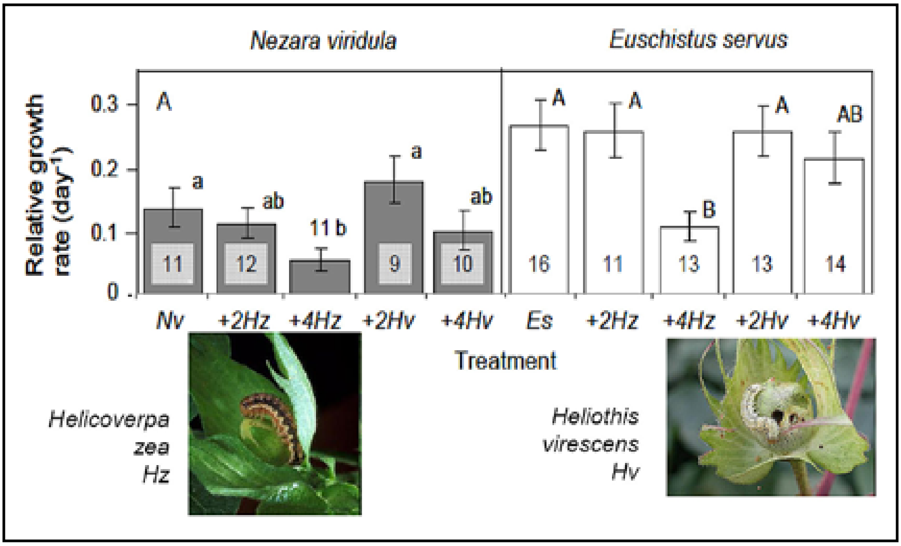

Figure 5. Resource competition when combined on the same boll
(from Zeilinger *et al.*, 2011).

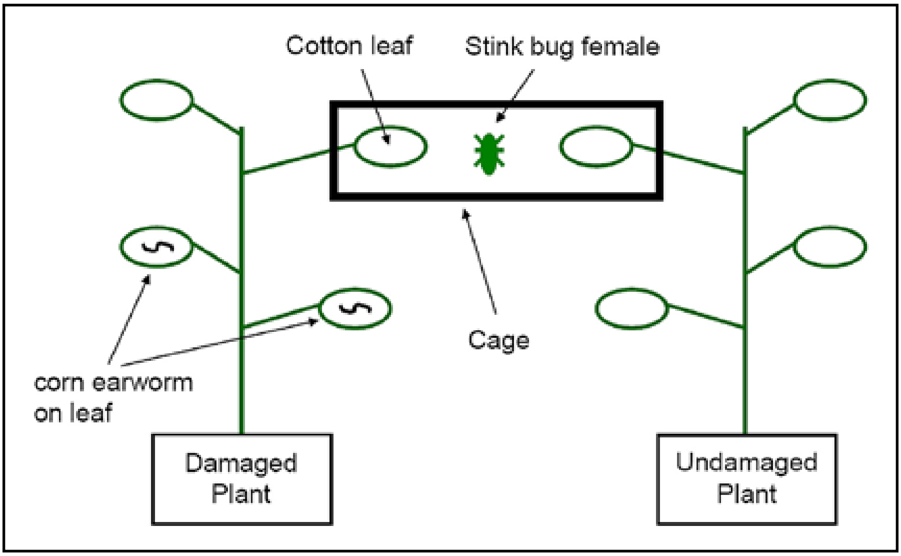

Figure 6. Stink-bug oviposition choice: experimental set-up

people see mostly risks and everyone balances the risks and benefits differently, including scientists. It's a social phenomenon with no agreement about how we weight the factors involved and, therefore, it is impossible to reach a consensus. Vulnerability arises from these socio-cultural factors and biological factors that need to be evaluated.

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David Andow has been the distinguished McKnight university professor in insect ecology at the University of Minnesota since 2005. He has a BS from Brown (1977) and PhD from Cornell (1982) in ecology.

Dr. Andow's awards include fellowships from Japanese Society for the Promotion of Science (1991, 2004), consultancies to EMBRAPA, Brazil (2004, 2009, 2010), and appointment as the international delegate to the Brazilian Entomological Society (2008). He teaches courses in insect ecology, population dynamics, and ecological risk assessment.

Detection of Foodborne Pathogens

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Canada's food-safety system is controlled by provincial/territorial and municipal governments, food-producing companies, the agricultural sector, consumer organizations and four federal departments that share responsibility for food safety, *i.e.* Health Canada (HC), the Public Health Agency of Canada (PHAC), the Canadian Food Inspection Agency (CFIA), and Agriculture and Agri-Food Canada (AAFC) (Figure 1).

Part of the responsibility of the AAFC is to develop food-safety programs that are applicable to on-farm production. PHAC maintains surveillance systems that track foodborne illnesses, diet-related chronic diseases and works in the coordinated management of food-related emergencies. The CFIA is responsible for the design and delivery of federal food-inspection programs while monitoring industry's legal compliance. The CFIA enforces policies, regulations and standards set by HC. If a food-safety emergency occurs, CFIA, in partnership with HC, Provincial Agencies and the food industry, operates an emergency response system. And HC establishes food-safety policy and develops methods and standards for the food industry. HC also conducts health-risk assessment, sometimes at the behest of CFIA, and provides information to the public on potential health hazards.

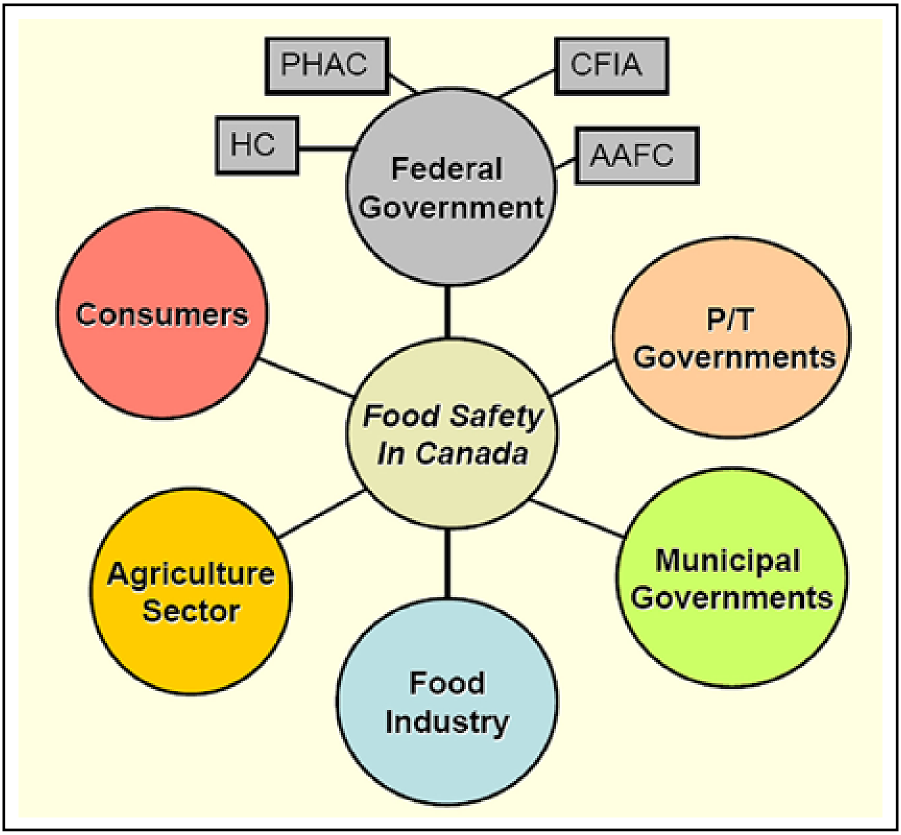

Figure 1. Canada's food-safety system.

Foodborne-Pathogen Detection

Detection of a foodborne pathogen—and validation of a suspected health risk—comprises several steps:

- Sampling
- Sample preparation
- Enrichment
- Pathogen detection
- Pathogen isolation
- Pathogen identification
- Pathogen typing

To protect today's complex food system against intentional or unintentional contamination requires addressing various needs relative to detection.

What?

First of all, what is to be detected? Pathogens and toxins are of many types, and the correct target must be selected for assay development. Also, the target may change during the investigation as the microorganism evolves, and the matrix in/on which the microorganism exists may be air, liquid or solid, or a surface. The end product or the food-processing environment may provide the best source location, or, alternatively, it may be the environment in general.

Where?

In this complex system, a risk-based approach is required to keep the samples to a reasonable number; it is impossible to test everything in a food chain. A trend is emerging of lab-testing being superseded by field-testing as new time-saving methods are developed.

When?

Timing of sampling can be critical to the detection of a pathogen.

Why?

Detection may result from routine surveillance and monitoring, checking for foodborne source attribution, or during regulatory-compliance activities. Alternatively, detection may result from investigation of an outbreak of foodborne disease.

How?

A wide range of technologies are available for investigating the possible presence of pathogens and/or toxins in food. An important factor is the choice of technology appropriate for detection of the micro-organism and/or toxic compound in question.

Ideal Method

The ultimate method for detecting microbial pathogens in food will be/have:

- Rapid in real-time
- Sensitive
- Specific, with no false positives or false negatives
- Reliable
- Portable and field deployable
- Robust
- Inexpensive in production and operation
- Easy to use
- High throughput
- Customizable (for use with a range of pathogens)
- Usable in multiple food matrices.

However, significant challenges remain in the development of a broadly applicable detection system. A key issue is sample preparation, the importance of which has been underestimated in the past. It has to be unaffected by food type, with no interference from the matrix or background flora. Low numbers of cells of the pathogen in a food are likely to mean non-uniform dispersal and the need for a lengthy enrichment period. There has to be an acceptable balance between the sensitivity of the assay and its specificity. And polymerase chain reaction (PCR)-based detection methods can give false positives resulting from the presence of dead cells. A wide variety of agents—viruses, spores, bacteria, parasites, *etc.*—can cause foodborne diseases, therefore, simultaneous detection of multiple pathogens would be greatly advantageous. Again, because of the range of possible pathogenic agents, coupled with the many food types that may be affected, emerging threats may result from unanticipated food-agent combinations as well as from "traditional" foodborne pathogens. Furthermore, some pathogens require only low numbers of cells to be infectious. Another key issue is cost associated with detection—in time, training, equipment, requirement of consumables, *etc*.—since the numbers of samples tested can be large.

Conventional Culturing

Conventional culture techniques remain the "gold standard" for the isolation, detection and identification of target pathogens, despite the disadvantages that they are applicable only when the microorganism of interest can be enriched and that the enrichment process may be lengthy. Newly developed assays are always compared with the "gold standard" for validation.

Affinity-Based Assays

The specificity of antibodies, including recombinant antibodies, or fragments of antibodies, is being exploited to detect pathogens, *e.g.* via enzyme-linked immonosorbent assays. Phage-display libraries are now being similarly utilized. Disadvantages of methods that use antibodies include their potential lack of stability, specificity and sensitivity. Nucleic acid aptamers that have stable secondary structures that function as ligands are increasingly used, particularly for the detection of non-immunogenic molecules.

Sequence-Based Assays

PCR, real-time PCR, nucleic acid sequence-based amplification, fluorescence *in situ* hybridization, microarrays and nanoarrays are all being used as methods to detect and identify DNA in samples, with the advantage that they are generally more sensitive than affinity-based assays and are highly specific. However, appropriate target selection is critical, and the presence of compounds in foods that inhibit nucleic acid amplification may be problematic. A disadvantage of PCR-based commercial kits is that some enrichment is necessary, requiring up to 18 hours. Where nucleic-acid enrichment is done on a bacterial colony, the PCR portion may be rapid but it can take three days to grow the colony, which, again, is a sample-preparation challenge.

Next-Generation Tools

There is a trend to miniaturize sensors. For example, microbiologists are working with physicists and engineers to develop biosensors, microfluidic systems and magnetic nanoparticles that capture bacteria.

Typing of Bacteria

After a bacterium has been detected and identified, often typing beyond the species or subspecies level is essential in food-safety investigations. Analyses by more than one typing method may be required with some pathogens:

- Serotype
- Phage type
- Antimicrobial resistance profile
- DNA "fingerprinting" by pulsed-field gel electrophoresis (PFGE)
- Multiple-loci variable number tandem repeat analysis (MLVA)
- Whole-genome sequence
  - Pan-genome analysis of core genes or accessory genes.

Opportunities for designing next-generation genotyping targets are constantly being sought.

Currently, PFGE is considered the "gold standard" for most foodborne bacterial pathogens, and is used by PulseNet[1] scientists. However, MLVA is being employed increasingly to type bacteria, as is whole-genome sequencing, as DNA-sequence analysis becomes less expensive, permitting pan-genome analysis of core and accessory genes for strain comparison.

Bureau of Microbial Hazards

At Health Canada's Bureau of Microbial Hazards (BMH), stakeholder needs are addressed by scientists who contribute to policy development, formulation of guidelines and industry standards, provision of advice to consumers and industry, and the maintenance of the *Compendium of Analytical Methods* which provides validated methods, standards and guidelines relative to microbiology and extraneous material for the food industry.

The BMH is organized into two divisions: the Microbiology Research Division and the Microbiology Evaluation Division. In the Research Division, scientists are conducting research and method development for high-risk foodborne pathogens. The Division also houses reference services that investigate botulism and listeriosis in Canada. Scientists in the Evaluation Division are responsible for policy development and conducting health-risk assessments.

Listeriosis Outbreak

In 2008, an outbreak of listeriosis in Canada—the largest on record—resulted in fifty-seven

[1]http://www.cdc.gov/pulsenet/. Page 174.

confirmed cases in seven provinces, with twenty-two deaths. Subsequently the federal government commissioned an enquiry by independent investigator Sheila Weatherill, to elucidate the causes of the outbreak and propose preventative measures. The report provided fifty-seven recommendations to improve the food-safety system and enhance the responsiveness of laboratories to national foodborne emergencies.

Reference Center

In response to Weatherill's report, a Reference Center for Rapid Diagnostics, Regulatory Science and Food Safety was established as a joint initiative of HC/BMH and the Industrial Material Institute of the National Research Council of Canada (NRC), co-chaired and led by Nathalie Corneau (HC) and Teodor Veres (NRC). The objective of the Reference Center personnel is to design, fabricate and implement next-generation technologies for rapid diagnostic tests for foodborne pathogens and to facilitate deployment of these technologies throughout the food chain. The NRC's Industrial Material Institute (IMI) has a unique infrastructure in Canada, suited to polymer-based micro- and nano-fabrication, which is less expensive than silicon- or glass-based approaches. The objective is to develop portable lab-on-a-chip platforms capable of simultaneously detecting and isolating bacteria—even viable but non-culturable bacteria—viruses and parasites from various food matrices. A sample-preparation method has been designed to accommodate a wide variety of foods and environments, with detection possible without enrichment resulting from high sensitivity and specificity. The portable technology—not yet finalized—is designed so that it can be multiplexed to detect multiple pathogens. The integration of sample preparation, detection and typing will be achieved using microfluidic and microarray systems (Figure 2).

The system is modular and uses various chips for flexibility. Food samples of 25 g—ground beef, brie cheese and deli meat (*i.e.* of varied fat content) have been tested—are

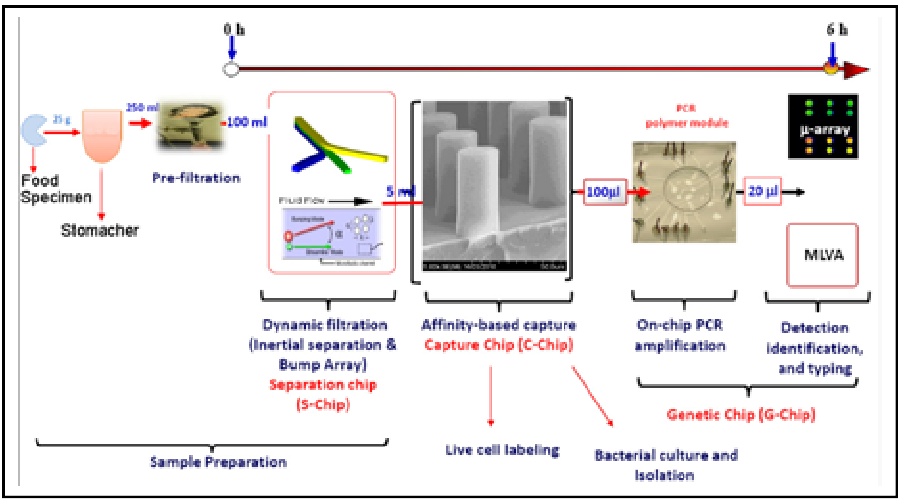

Figure 2. HC-NRC microfluidic detection approach

homogenized with a stomacher, and a pre-filtration step removes large food debris (>100 μm) without significant loss of bacteria. Pathogens are separated from food particles (>8 μm) by inertial focusing, then "bump" arrays are employed as a means of fine filtration and to concentrate the target cells (≤3 μm). Inertial focusing involves microfluidic continuous filtration in which randomly distributed particles are focused near the channel walls, resulting from an inertial lift effect. In rectangular channels, particles are focused at about 20% of the channel height from each wall surface. As the aspect ratio of the channel increases, the majority of the particles are focused near the larger walls, and the central part of the channel containing the smaller particles, *i.e.* the purified sample, can be collected. Bump arrays continue particle separation and can be used also to concentrate particles. Post-separation distance is critical. For example, an inter-post distance of 5 μm will "bump," or tend to exclude, particles larger than 2 μm, and thus separate them from the main stream. At the next stage, the capture chip again has a "forest" of posts (640,000, 25 μm in diameter), and antibodies or surface chemistry can be used to capture cells of interest. Partners at the NRC (John Pezacki and David Kennedy) are working on a click chemistry technique to improve capture of specific live cells and facilitate their release for the last stage, the genetic chip. This on-chip detection and identification approach involves cell lysis, DNA/RNA extraction, multiplex PCR amplification and microarray identification.

Next Steps

We will continue to optimize each microfluidic module, investigating new capture molecules in various food matrices, with particular emphasis on development of more-rapid detection methods and further miniaturization.

Martin Duplessis is the manager of the Food Emergency Preparedness and Response Unit (FEPRU) for the Food Directorate in the Health Products and Food Branch of Health Canada. He is responsible for policy areas on a wide range of issues related to food safety, food defense, and chemical, biological, radiological and nuclear (CBRN) emergency preparedness and response. Additionally, he is a scientific advisor on several research projects involving CBRN-agent detection.

Prior to assuming his current position, he was a scientific advisor responsible for research-development strategies and intellectual property management in universities for the government of Quebec.

He holds a PhD in food microbiology from the University of Laval, Quebec City.

Systems and Risk Analysis for Food Protection and Security

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As I put this presentation together, I reflected on the two streams of research that I have pursued for the past decade. One is systems analysis which is my current job and the other is risk analysis. I serve as director for CREATE, the National Center for Risk and Economic Analysis of Terrorism Events at the University of Southern California, the first center of excellence funded by the Department of Homeland Security. Of course, Minnesota is home to the second center of excellence, the National Center for Food Protection and Defense, which is represented here by Director Emeritus Frank Busta. At CREATE, our primary focus is on risk analysis applied to terrorism and most of my examples are from that area. Since 2009, I have been the director also of the International Institute for Applied Systems Analysis (IIASA) in Laxenburg, Austria. There, our tools are forms of modeling applied to global problems, including the major theme of water security. Other themes are energy, climate change and policy. I will outline systems analysis and risk analysis, and provide three examples, and prioritize some terrorism issues.

Systems Analysis

Why systems analysis? Here are quotes by Larry Summers[1] from 2009 after reading *Decision Analysis* by Howard Raiffa, IIASA's first director:

> *Many children were taught to believe in God, I came to believe in the power of systems analysis.*

[1]The 71st United States secretary of the treasury from 1999 to 2001 under President Clinton, and director of the National Economic Council for President Obama until November 2010.

and from the *IIASA Strategic Plan 2011–2020*:

> *Today, policymakers around the globe ask for problem-focused, solution-oriented, interdisciplinary research to help them with their complex decisions. They may not know it, but they are really asking for systems analysis.*

Systems analysis is a group of model-simulation analysis tools—applied mathematics if you will—specifically applicable to very complex systems that undergo dynamic changes and are fraught with uncertainty. A classic example of a problem that lends itself to systems analysis is the collapse in the financial system, which indicated many of those features and which we are not very good at modeling. Ecosystems are another area where we are applying it, energy systems, food production, and so on. All of this is applied mathematics, but, more importantly, it is guided by some major overriding factors: the analysis should be problem-focused and solution-oriented. You start with the problem. You don't start with a mathematical model and look for a problem, and you look for solutions, not necessary optimal solutions but acceptable solutions, and eliminate poor solutions. The model is usually developed by a multidisciplinary team taking a holistic view of the problem.

Risk Analysis

Why risk analysis? Michael Chertoff[2] has stated the following in several versions:

> *We have to identify and prioritize risks—understanding the threat, the vulnerability and the consequence. And then we have to apply our resources in a cost-effective manner.*

Frequently, I use that quote to motivate risk analysis. It's what risk analysis is supposed to do, *i.e.* help decision-makers. It is a combination of risk assessment and management that involves identifying the risks, quantifying them—*i.e.* quantifying the possibilities of events that could occur as well as quantifying their consequences—and then looking at decision-opportunities, intervention and risk reduction, and evaluating them. The tools that we use in risk analysis are on one level just formal expert elicitation of probabilities. Often event trees and fault trees, Bayesian networks and influence diagrams are used. The combination of systems analysis and risk analysis can move us forward in a qualitative step when we need them for problems like systemic risk in the financial sector, ecosystem risk, food risk, and so on.

Challenges of Terrorism

Terrorism imposes particular challenges. Terrorists tend to search for high vulnerabilities and consequences, unlike technological or natural disasters that occur randomly. They observe our defenses and try to attack the weakest remaining links, then change their modes and targets of attack. They also try to create events that produce ripple effects through instilling fear and eliciting behavior change that can be more damaging than the direct results of the event. For example, the direct cost of 9/11 was $20 million to $30

[2]Second United States secretary of homeland security under Presidents G.W. Bush and Obama.

billion, including insurance for lives lost, whereas the indirect costs were more like $200 billion, due to reduction of air-travel, *etc*.

Several attempts have been made to apply risk analysis to terrorism—probabilistic risk analysis, event trees and elicitation of expert probabilities. More recently, decision-tree analysis has been employed and game theory—attacker-defender games and experimental games—as well as vulnerability and risk-scoring systems.

Lugar Report

Three years ago, Senator Lugar conducted a survey of eighty people, for their opinions of the probabilities of a major attack, *i.e.* nuclear, biological, chemical or radiological, somewhere in the world (Figure 1).

Event	Median Probability (5 Years)	Median Probability (10 Years)	Appr. Sample Size
Nuclear Attack	10%	20%	80
Biological Attack	10%	20%	80
Chemical Attack	15%	15%	80
Radiological Attack	25%	40%	80

Figure 1. Lugar report informal expert elicitation.
Survey of probabilities of major attacks.

The median probability of a nuclear or biological attack was judged to be 10% in the next 5 years and 20% in the next 10 years, and more so for chemical and radiological attacks. I think that these numbers are too high and we can do better. Those surveyed were prominent people from Harvard, the CIA, the Senate, the military, *etc*., but I would argue that they weren't the right people to answer that question. We should be using the right experts, asking the right questions and using the right procedures (Figure 2).

Bioterrorism Risk Assessment

In an exercise in the context of bioterrorism risk assessment for the Department of Homeland Security (DHS), we tried to do things better. This was in the context of the DHS biannual report to the president, particularly to prioritize biological events and guide investments for risk management. CREATE provided help with expert elicitation for threat assessment. We began by creating a list of twenty-eight biological agents that were prioritized by intelligence analysts and social scientists to provide probability assessments of threats and risks, and also of consequences. We helped the development of elicitation protocols and gave them tools, and while we didn't do the actual elicitation—which was highly classified—mostly we tried to find elicitators, the people who did the work, and we provided software support. We also made sure that they were able to quantify uncertainties in their assessments. Most of the intelligence analysts that I have worked with in the past say, "It's probably between 5% and 20%"; so, we helped them to be more specific in terms of setting their probability distributions.

Figure 2. Possible improvements over the Lugar survey.

Figure 3 provides a hypothetical, but relatively realistic, example of a result. Certain infectious agents are generally found at the top of such probability assessments. For example, this particular operation estimated roughly a 25% chance of an event involving *Bacillus anthracis* (anthrax) in the next 10 years and a 13% chance of an event involving *Yersinia pestis* (bubonic plague), botulinum toxin or ricin occurring in the next 10 years. These are cases where there is some bias towards events that have already happened. An important aspect is that only four to seven biological agents are deemed most dangerous, and many are assigned low probabilities although not necessarily for good reasons. Figure 4 is an example from the report, unlabelled because the information is classified, showing agents of high, medium and low risk. This was used in the first report to the president in 2006 and in the second in 2008, and I assume it was in the 2010 report, but I was already at IIASA then. This provides a reasonable first baseline on risk assessment, but it needs to have a closer tie to risk management. We need to figure out how these numbers change with interventions and that was not done in the parts that I was involved in, but I understand that there is some effort in that direction now. Also, we need to go beyond event trees to model complex systems, and we need to consider terrorists' shifting tactics.

Hi Lethal - Comm	RP
Yersinia pestis *	13%
Variola Major Virus	1%
Ebola	6%
Lassa	6%
Marburg	6%
Hi Lethal- Non Comm	
Bacillus anthracis *	25%
Clostridium botulinum *	13%
Ricinus communis (castor bean)	13%
Burkholderia mallei	1%
Nipah virus	1%
Bovine Spongiform Encephalopathy *	1%
Vibrio cholerae **	3%
Other Agents	**9%**

Figure 3[3]. Relative probabilities (RP) of selected agents (given a bioterrorism attack—hypothetical expert).

Systems with Interdependencies

Los Angeles airport and Long Beach harbor are complex systems that involve people movement and supply chains, and fully protecting them is tricky because necessary resources are lacking. So, decisions were needed as to where to place defensive resources. One of our ideas that worked well was to use smart randomization. Everything can be protected by employing a randomization scheme to protect valuable targets randomly and thus confuse terrorists. Accordingly, patrols, inspections and surveillance are randomized. A student of ours came up with a wonderful idea to use a Stackelberg game—a business game—also called a leader-follower game. He developed a game that involves a defender and an attacker and two assets, asset A and asset B where asset A is more valuable than asset B. If only asset A is protected then the attacker will attack asset B because he will know that you protect asset A and then you lose and the attacker gains. If the attacker is stupid and attacks A while you are protecting A then you win and the attacker loses. In contrast, if you protect B the attacker will attack A and not B. To solve this zero-sum game, you can randomize between A and B and thereby find a way to get the attacker to achieve the minimum expected value. In our analysis, we extended this to non-zero-sum games, multiple targets, multiple attackers, with certain real-world constraints—patrol personnel have to eat sometime, somewhere—with fast algorithms and real-world implementation.

[3]Comm = communicable; Non Comm = noncommunicable.

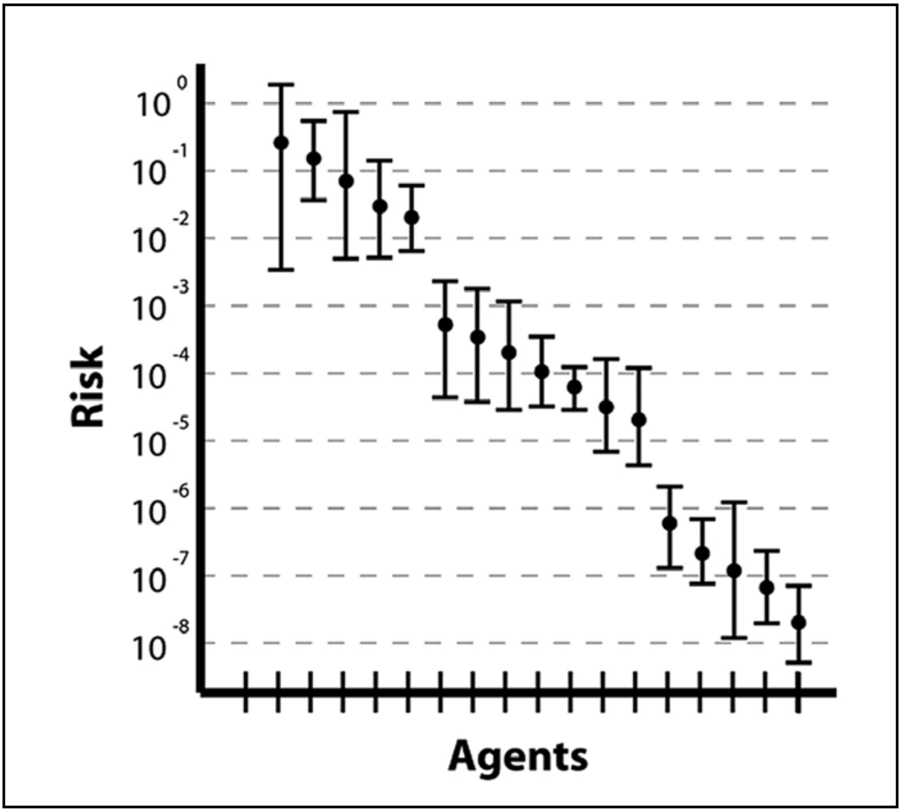


Figure 4. Biological agents (classified) of high, medium and low risk on a relative scale.

The assistant for randomized monitoring over routes (ARMOR) project was implemented in cooperation with the Los Angeles Police Department which provided inputs into ARMOR which were randomized by the game-theory algorithm and the randomized schedule was then given back to the police. There was some override capability because flexibility is essential, but they never did change it during the first two years of operation. ARMOR is still being used at the airport and there is statistical evidence that the intervention rates a LAX improved substantially after the system was implemented. It is now used also by the TSA to randomize the assignment of federal marshals on airplanes, and other projects.

Combining Systems for Food Protection

My last example illustrates combining systems and risk analyses for food protection. The initial idea was to formulate a model of the food-supply chain and then to superimpose a risk model. Although this is an elegant approach, it is also cumbersome. But, once you have a model of the food-supply chain, the threats, vulnerabilities and consequences can be assessed as can baseline risks. Then protective measures can be identified, including optimal sampling procedures, inspections and randomized patrols. Figure 5 shows a relatively simple supply chain, *i.e.* for milk in Minnesota, starting with the cow and ending in the grocery store, and passing through many stages. (On the other hand, the supply chain for a hamburger is much more complicated.) There are many storage and testing locations and transportation stages, *etc*., and when they are mapped out a mathematical model of the flow may be constructed, and points of vulnerability may be identified (Figure 5).

A terrorist attack would most likely occur close to the end of the supply chain, depending on the volume of material; the larger the volume the less likely the intervention will be detected. With a deterministic model—looking at attack modes, for example introducing pathogens, radionuclides or chemicals into the process—come indicators of deaths, both acute and delayed, illnesses, and direct and indirect economic costs. This is less of a risk analysis, and essentially a systems-analysis model, and an advantage of turning it into a computer model is that we can allow the user to adjust the input parameters through sliders and scrollbars in Excel.

The next steps with risk analysis are to identify the highest risks and risk-management options, assess uncertainty over systems-model parameters—like uncertainty over LD_{50}, or uncertainty over mode of attack—then assess probabilities of attacks with and without risk management and conduct cost-benefit analysis of risk-management options.

Risk Transfer

The discussion above applies to just one supply chain, raising the issue of the enormity of the task of doing this for all supply chains, comprising many kinds of complicated food products. Another complication is the problem of risk transfer, because terrorists can observe our defenses. On the other hand, if they don't observe our defenses it may be that they should be told, so that they won't want to go there. But, once they know, they will adapt and change modes and attack other targets, so risks will be shifted to less-defended parts of the system and the overall risk level may change little. Nuclear detection and nuclear defense provide a good example. You can put radionuclide-detection portals around the United States at main entry points, but terrorists will find holes in the system as do smugglers entering the United States from Mexico and Canada. That is a significant problem.

Further to risk transfer: within a given system—*e.g.* a supply chain for a food item—risk transfer can by analyzed. Once you have plugged one vulnerability, you can then see how the risk shifts to another vulnerability. In theory, you can plug many of them and stop at a point where it is no longer cost-effective. Across systems, where there are multiple supply chains for a food item, it is harder. And for multiple food items and multiple supply chains, the task becomes daunting. We need a bottom-up approach, which is the one that I just described, in connection with a top-down approach to provide a holistic view of the food type and the pathogen or chemical that a terrorist might use. However, working both from the bottom and from the top and hopefully finding appropriate linkages will be time consuming and involve much effort.

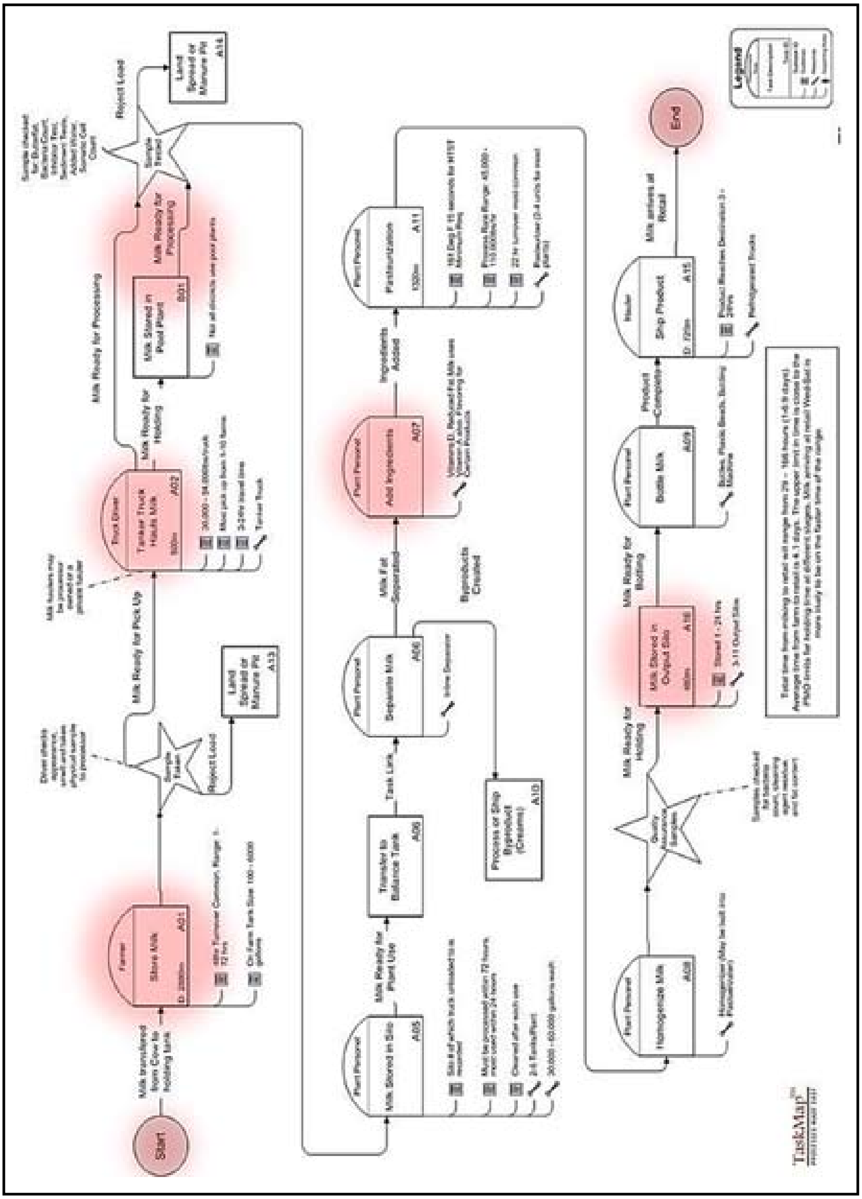


Figure 5. Minnesota fluid-milk flow diagram showing potential threat points—easy access at points of vulnerability presents possibilities of attack without detection and causing the most harm.

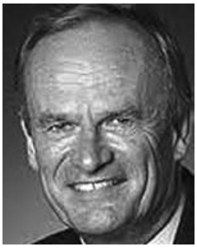
General Insights

The Department of Homeland Security has focused too broadly on too many risks, and I similarly fault our own center of excellence. We look at everything, whereas I think it would be wise to focus defenses on high-threat, -vulnerability and -consequence scenarios, radiological, nuclear and some chemical and biological. For other scenarios, it is useful to employ intelligence analysis and police work to intervene early or upstream rather than to defend. One of the undersecretaries of homeland security once said:

You are to find the bomber not the bomb.

With food, the objective should be to find risk-management options with large co-benefits that pay for themselves. For food defense, you might think in terms of strategies to prevent a terrorist tainting something that may be beneficial for other food-safety reasons. Equally, solutions that address regular safety issues by introducing new testing and inspection procedures may help prevent terrorism. Systems analysis and risk analysis have helped in the past, mostly to prevent the government from making stupid decisions, which is a worthy achievement. In one case, for example, we helped to avoid the implementation of laser-based counter-measures to be put on all commercial airplanes to prevent surface-to-air missile attacks, which would have cost $30 billion dollars. We were partly responsible for that outcome.

The main challenge is how secure is secure enough? Clearly, we will never be completely safe from terrorism. Nor will we ever have a completely safe food supply. Because security measures increase dramatically when we get closer to zero risk, the cost goes up tremendously. Perhaps most importantly, increasing security creates other risks and inconveniences, and restricts civil liberties. We should always be aware of the need for a well balanced system, and avoid over-reacting in terms of security, thus compromising other values important to our society.



Detlof von Winterfeldt is the director of the International Institute for Applied Systems Analysis in Laxenburg, Austria. He is on leave from the University of Southern California (USC), where he is a professor of industrial and systems engineering and a professor of public policy and management. Concurrently he is also visiting the London School of Economics and Political Science as a centennial professor in the Operational Research Group of the School of Management.

In 2003, Dr. Winterfeldt co-founded the National Center for Risk and Economic Analysis of Terrorism Events (CREATE) at USC, the first university-based center of excellence funded by the US Department of Homeland Security; he served as CREATE's director until 2008.

For the past thirty years, he has been active in teaching, research, university administration, and consulting. He has taught courses in statistics, decision analysis, risk analysis, systems analysis, research design, and behavioral decision research. His research interests are in the foundation and practice of decision and risk analysis as applied to the areas of technology development, environmental risks, natural hazards and terrorism. He is the co-author of two books, two edited volumes, and (co)author of over a hundred journal articles and book chapters on these topics.

Systems-Based Approaches to Food Protection and Security

Q&A

MODERATOR: CAROL ISHIMARU
University of Minnesota
Minneapolis, Minnesota

Carol Ishimaru: The speakers will now join us for the panel discussion and questions from the audience.

Michelle Martin (University of Arkansas): Dr. Medford, have you found a chemical or pathogen that gives a false positive?

June Medford: Not yet, but we are testing for that rigorously. We are working with colleagues at Colorado State University to obtain microorganisms for application to plants for tests with drought and insects. The computational design in bacteria is specific. For instance, it picks up TNT—2,4,6-trinitrotoluene—it does not pick up 2,4- or 2,6-dinitrotoluene. As for pathogen specificity, Lindsay Triplett is just back from the Philippines and is looking at that. Basically, it's garbage in garbage out. Our components are signaling fairly well and we are testing them right now. I suspect that the computational design will be very specific, and what I can do with the pathogen ones with my toggle switch is add a threshold so that I can design around the low level of noise, just as a cell phone does that.

Sonny Ramaswamy (Oregon State University): Along those same lines, are you going to be looking for a generalist receptor or a specialist receptor, considering the multiplicity of ligands out there in the environment?

Medford: For things like explosives or nerve gas I want to be as specific as possible. If we are going to evacuate Mall of America then we want to know that the threat is real. For agricultural applications, I'm dependent on people in the community in terms of should I be more specific for an application or should I be general? I don't have all the answers.

Ramaswamy: If that's the case, you'd have a whole bunch of receptors on the plant that respond to, potentially, tens of thousands of chemicals and pathogens. How do you do that?

Medford: How many receptors can we put on there? We can now put in multiple computational designs as receptors. I'm not sure where we should go in terms of pathogen receptors—should we do one, two or more? A simple way would be to put out multiple sentinel plants.

Robert Buchanan (University of Maryland): A follow up—you have highly specific receptors and you could run into two situations. One: pathogens have a natural mutation rate and they have all kinds of exclusive mechanisms for beating receptor sites. So, what do you think the half-life of your receptor will be in effectiveness? Two: using these in fairly open locations, I could drive you crazy by setting them off, and after two or three times you would lose all faith in the receptor because of the consequences of false positives. How will you handle that?

Medford: Again, the computationally designed receptors are quite specific. We are looking for very specific ligands. Histidine kinase is involved in inter-bacterial quorum sensing and we are trying to target those that are specific to cells. These are signal molecules that bacteria typically use to say, "Okay we have a quorum." One of the challenges we have is to find the specificity. We can redesign receptors for small molecules. As for pathogens, we are working on that right now. The jury is still out. We do not want false positives, absolutely not.

Ramaswamy (Oregon State University): Dr. Winterfeldt, application of the game theory is fascinating, but much of what we have done in the United States has been reactive, almost like a chess game, trying to figure out what the terrorists are doing. Have you also considered actually getting to the core of the problem—not the bomb and bomber analogy, but actually going through the reasons why we have this situation today. Does your center look at that part of it, as well as what sort of risks and benefits one may get from actually addressing the core problem of where those terrorisms come from?

Detlof von Winterfeldt: We have looked at the problem, but we have not done a cost-benefit analysis on fixing it at the root cause. Another center, START[1], is a support organization that deals with causes of terrorism and motivations of terrorists. At CREATE, we have an exercise to understand the objectives of terrorists, which turns out to be interesting

[1]National Consortium for the Study of Terrorism and Responses to Terrorism.

because—in common parlance and in the media—it is always about killing Americans. Well, it's more than that. It's a lot more than that. It includes things like establishing fundamentalist regimes based in the Middle East and redeveloping respect. A complex web of values is involved, and it's hard from that angle to change things. One thing we know is that one big concern of fundamentalist terrorists has to do with the presence of the American military in the Middle East. A major objective is to get the Americans out of the Middle East. Now, I'm saying this rhetorically—I know how to fix that, right? But certainly it's not something I would throw on the policy table.

Frank Busta (National Center for Food Protection and Defense): Frequently in food safety we talk about minimal acceptable risk when trying to determine just how safe we need to be. Can you see how the work that you are doing will help politicians and public-health agencies come up with the ability to say that we will accept, let's say, one *E. coli* case per 100,000 people or a million people. And how do we sell that to the public?

von Winterfeldt: Well, this is a common problem. The Environmental Protection Agency has that problem and they are trying to prioritize risks based on what they know about consequences and threats. I don't think there is a magical number, when you say one in a million or that one outbreak in a year is okay. I think the real answer has to come from the cost effectiveness of the remaining risk-reduction options. At some point it gets too expensive; you are spending more money than you are reducing the risk, and you have to find that point. Ironically, it's different for different risks. For example, in highway safety you can save a life for about $50,000 dollars, roughly. In nuclear power to save a life you have to invest something like $10 million. At some point you cross a boundary of whether it's worth investing more money for risk reduction. But, I don't think there's an acceptable risk in absolute terms. What remains after you make all the prudent decisions is an acceptable risk.

Ishimaru: David, in terms of ecological assessment what are acceptable limits to risk?

David Andow: Dr. von Winterfeldt gave a more sophisticated answer than I will give. It's difficult to get anybody to talk about what they consider to be acceptable, and getting agreement on what is acceptable by approaching the subject directly is probably unrealistic. That's certainly true in terms of human lives, but also for the environment because not everybody is clear exactly how they think about these things, and so when you ask those kinds of questions you are asking for people to give you information on things they haven't thought through. So, you get gut feelings. The idea that the previous speaker suggested—to think about how much it costs to do certain things and to try to figure out ways of doing these things more cheaply, looking at the political consequences of those kinds of actions or proposals—gives you a better sense of what people are really willing to do. Also, in the environmental area, the issues are quite dynamic. They change in decadal timeframes; things that were acceptable 20 years ago are not necessarily considered acceptable currently.

Robert Buchanan (University of Maryland): Following up on Frank Busta's question and comment—the description you gave was basically the traditional approach where you would establish the stringency of your control systems, typically by establishing some kind of standard or frequency of inspection or some other activity where you were basically hiding your risk-management decisions from expert consideration. However, with the emergence of more sophisticated types of analysis, now it doesn't take people like me or others to just go back and say, "Okay this is what you did. This is the calculation that says this is what you are actually willing to tolerate." It's becoming a problem for policymakers and professional risk managers because they are not hiding out anymore. They have to deal with these things and I think we are on the cusp of a very important debate in terms of policy, particularly in the food area, because we can now calculate the number of potential cases, the number of deaths that occur, *etc*. I would love to hear your thoughts on that—where this debate and where the modern techniques of risk assessment are actually going to take the policymakers.

von Winterfeldt: There was a case, many years ago, concerning the Ford Pinto. The Ford Company had done a cost-benefit analysis of the risk of explosion due to a defective fuel system and found that they could avoid the risk for the trivial cost of about $50 per car. After several of these explosions, they were taken to court and this analysis came up, leading the judge to level huge punitive damages because the argument was like what you said: "We made this conscious decision not to make that $50 change because it wasn't cost effective." I recognize the problem, but I'm not sure what to do about it. Although in many ways it makes it more transparent if the decision is based on risk assessment, cost effectiveness, analysis and so on, I don't see what the alternative is. Keeping it nontransparent doesn't seem the right thing to do either. We have to deal with it and I think you will find much more willingness by at least the US-government agencies to be open and expressive about it—and that's encouraging—and then defend it. You don't have to go as far as putting a value on a life. You can do sophisticated analysis, break-even analysis, that says, "This saves so many lives and that's definitely worth spending $10 million." You don't have to go through the really crude calculations.

Ishimaru: June, in terms of your research, your technological approach to looking at surveillance and detection, what part of this conversation informs you in terms of molecules or agents that you are targeting. How do you reach conclusions? What kinds of assessment do you use to make decisions?

Medford: In terms of what we build detectors to—it's what the Department of Defense and people in the community say will work. So, Dr. Buchanan, you asked about specificity. I'm dependant on those who came before me who say, "I know this is the one that's specific." For the computational design, we have a limit in the size of the molecule. Ours is an emerging technology that provides tools for risk analysis and for people to make decisions. It does bring up an interesting thing: if we can detect a variety of compounds, where would we draw the line?

Ishimaru: But are there costs associated with the development of these technologies?

Medford: Our technology will be very inexpensive. I actually tried to fill out a Defense Department form, and I came down to pennies and it didn't fit onto the form. They were asking cost per unit.

von Winterfeldt: And you had these wonderful co-benefits.

Medford: But it does bring up the huge complexity of where do you guys draw the line of what is risk? If we can detect compounds everywhere inexpensively, where do you draw the line? How much contamination can we tolerate? That's not for me to do. I'm the scientist. You guys are the publicists.

Ishimaru: Along that line, though, some of the mandates that have come to DHS have affected scientists in terms of their ability to do research. In particular, the select-agent list has affected us quite a bit. Dr. von Winterfeldt, I noted from your comments about when you did a risk analysis of different agents—which are reported to have a higher risk associated with them—is that kind of information then going to inform decisions about things like select agents?

von Winterfeldt: I would think so. Certainly in my discussions at the time with the Department of Homeland Security officials—at a pretty high level—they were interested in having more work done on the high-threat, high-consequence spectrum. And so, in that sense, yes, I think it was leading to decisions in that area. And certainly in the nuclear area, we are investing a huge amount of money compared to biological or chemical. The nuclear defense system has a budget of $300 million a year just on that one issue. Again, risk analysis isn't easy with this business, so they actually established a fairly sizable group within the Department because so much of this is secret work that deals exclusively with risk analysis and risk management, and that group's intention is to inform the decision-makers inside the DHS to make better risk-informed decisions.

Francisco Diez-Gonzalez (University of Minnesota): A question for David. You talked about our need to incorporate cultural factors in risk-assessment, and I'm wondering whether—in the case of genetically modified wheat—have cultural factors over-ridden everything else? Varieties of GM wheat have been developed, but nobody is growing it as far as I know.

Andow: With GM wheat, there are economic issues as well as cultural issues. Perceptions of risks and benefits vary around the world. High-quality durum wheat is produced here, and sold where the best price is obtained. Those buyers may see few benefits and significant problems from, say, herbicide-tolerant wheat. So, their economic calculus will influence what they buy which will then have effects throughout the supply chain.

Ishimaru: In particular with wheat, an important global crop, that's a decision that is based on the particular nation's ability to feed itself, it's food security. Risks associated with GM wheat will probably outweigh other considerations simply because the crop is needed for basic food.

Andow: In some cases that will apply. Focusing on GM varieties in the Red River Valley, which produces high-quality durum wheats, may be inappropriate because of marketing issues.

Koel Ghosh (National Center for Food Protection and Defense): I want to visit the question of expert edification in risk assessment. Because answers given by experts often inform risk assessment, how do you go about managing—or what would be the best practices for—expert solicitation? And I have a secondary question for the whole panel. When you do risk assessment within an area—say ecological or terrorism—different attributes will define benefits and costs. When you combine these systems and are examining risk assessment as a whole—especially when you are considering sustainability within risk assessment—what would be the common denominator for leveling out the differences between the systems?

von Winterfeldt: There are standards for getting probability decisions from experts—protocols, tools—that have slight variations, but they pretty much are all similar in the sense that they consist of a conscious selection of the experts, not just willy-nilly people off the street, usually by set criteria of both expertise and diversity of opinion; it's important to have diversity in the pool of experts. That's one. The second one is that training is required because substantive experts typically are used to expressing their opinions in probabilities. So that takes some work. The third one is that it shouldn't just be "ask a question, get an answer." It should be a dialogue where the answer is documented with references to source information to support the argument. When I build a probability distribution, I typically have at least three points with well documented reasons. And then the third aspect is how you deal with multiple experts, and that is where you have some diversity of approaches. You can either do a consensus approach or you do a Delphi or whatever to bring them together, but, in the end, you have to combine them. What we have learned in those processes is that the disagreement among the experts is often huge and the arguments often come from basic assumptions that they make. It's not about small variations in probabilities. It's important to document that as well. On common metrics—yes there are always many attributes that you have to consider. Cost is one, health is another one, cultural impact values is another, and ecosystem impact is another. I, actually, prefer not to roll them into one, but to keep them apart and do the analysis. So, for example, in our very simple example of milk we had morbidity, mortality, indirect and direct economics, and, of course, cost of intervention. We kept them apart; we didn't roll them up. It's useful to keep them apart for as long as you can.

Andow: In the environmental area, we like to think that we can get to a single metric at some point, but actually we don't achieve that often. A lot of the risk-assessment methodologies are aimed at coming to a determination of no significant risk. So, there are lots of findings of no significant impact, rather than trying to get some value associated with it. And then when there are risks, such as with pesticide use; the idea is to modify the management system to reduce those risks. A lot of approaches on the environmental side aren't oriented to trying to get into a metric. When we do go that way we tend to not have enough data to really fill that out, so the expert solicitation process tends to produce more crude ranking methods, in which case the confidence you might have in that in terms of "this means this much value" is undermined somewhat. So, then we tend to maintain these multiple criteria and start asking if we understand the tradeoffs between them as we go into decision-making. On the other side, we sometimes take specific criteria that aren't related to monetary value specifically, and key in a decision off of that. For example, in resistance evolution one of the key variables is how long it will be before resistance failures occur, so then you orient a lot of the information around that and, of course, the longer you push that the more expensive it may be. There's a number of variables and covariables and that is the framework that the decision-maker ends up using.

Ishimaru: Martin, in terms of detection and prevention, you focused a lot on technology and improving sensitivity and specificity, but in terms of the chain of events that produce a hamburger and milk, are you looking at specific components within that in terms of risk of where there might be certain places that you would want to target that detection?

Duplessis: In the food industry right now, programs are in place that already identified potential risks along food-supply chains (*e.g.* HACCP[2], the CARVER+Shock Vulnerability Assessment tool). In our project, we designed our detection system to make sure that it can be used anywhere during food-processing/production steps, from farm to fork. Our system is flexible and can be customized to detect pathogens in food samples, but also in environmental samples for monitoring and surveillance purposes. We have not targeted specific risks where we wanted to target detection.

Ishimaru: Also, we understand more about the ecology of the microorganisms in our food and that they often come from plants or soil. But we haven't done a good job of connecting that chain of events from plants growing in the field to their purchase in the supermarket, and identifying points of vulnerability. One more question.

Jozef Kokini (University of Illinois): This is for the whole panel. How close are we in terms of developing truly impactful and practical tools? For example, in terms of the competition that we have for risk assessment, are we at the point where the Department of Defense is able to use these tools and, therefore, come up with better defense strategies? One speaker talked about tools focused on nanotechnology. Of these, which are closer to delivering tools that can actually be used to reduce risk? Another speaker talked about taking us through a small garden of plants. How close are we to having this at the airport instead of going through x-ray machines?

[2]Hazard analysis and critical control points, see footnote, page 211.

Duplessis: In terms of microfluidics, nanoparticles and so on, we are still quite far from field use. There are examples, such as biosensors, that may be useful in the short term, but the major challenge will be the cost of those new technologies. And we need to validate those assays, sometimes requiring people with technical expertise to use them. Technologies are moving faster and faster, and we are making progress, but funding for multidisciplinary teams is needed to solve complex issues. It will be a while before a microfluidic device will be available for use in the food industry.

Ishimaru: June, do you want to follow up on the question of using plants instead of x-ray machines?

Medford: Yes, walking through a greenhouse rather than through the typical TSA thing—as soon as possible. People in the Department of Defense have told me that if we had our plants working in the field today, they would use them today. So, we are addressing a real, critical need. I had hoped to have a field test done this summer. We are a bit behind. I'm thinking if the DOD gives me the money, I would love to do it this winter in Hawaii, but they may not go for that. They want me to go to Mississippi and test it. Mississippi versus Hawaii? Okay. We hope to get some prototypes out in a year or two. So, hopefully in the near future—our work is growing.

PREPARING FOR EMERGING AND UNKNOWN THREATS

Preparing for Emerging and Unknown Threats: Public Health

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In this presentation, I will discuss:

- Factors affecting emergence or re-emergence of threats
- A framework for considering research needs, and
- The potential role of biotechnology innovation.

I will focus on food safety with concentration on infectious diseases. What I will talk about *vis-à-vis* food safety will be equally conceptually important in terms of animal and plant diseases. All three are important to food security both in terms of availability of foods and the ability of developing countries, in particular, to trade food in the global marketplace as a source of hard currency; it's important that they have access to North America and Europe.

Much of what I will say in terms of research needs and potential tools will be equally applicable to food defense, although I will not emphasize that subject. Anything that I say about the emergence of a new foodborne disease is equally important in terms of the re-emergence of a foodborne disease. I define re-emergence as a known agent that "pops up" in new forms or locations, and the example I like to use is *Clostridium botulinum* because about every 10 years it goes through a rediscovery period. It originally started in Germany as an issue in fermented meats. Then as canning became more important it showed up in canned products. In the early 1960s, it appeared as infant botulism, an infectious rather than a toxigenic agent. It has shown up in the past 10 to 12 years in adulterated cosmetics and it is now a food-defense concern. Also, we are seeing increasing numbers of cases of adult "infant botulism," *i.e.* colonization of the intestinal tracts of adults where it produces toxin.

Emergence/Re-Emergence

Regarding emergence of a new food-safety concern, two important factors involve genetics. One is the pure chance of a change in a microorganism as a result of normal low-probability evolutionary events. And the second is that drivers can "push" microorganisms to change rapidly in potentially predictable ways. My working hypothesis is:

> *The emergence or re-emergence of a new food-safety concern is primarily the result of societal, technological or environmental changes that are primarily the result of human activities.*

Although we cannot predict far into the future, like weather forecasting (versus climate change):

- We can look at current trends to anticipate events in the near term (5 to 10 years), and
- We can establish a network for data-gathering to enable such forecasts.

Food-borne disease is dependent on the "balance" between the biological agent, the consuming population, and the food. Based on my working hypothesis above, as long as that is stable and the dynamic balance is maintained, there should be a minimum emergence of disease. The problem is that there is nothing about foods, there is nothing about the food industry, there is nothing about consumers and there is nothing about microorganisms that stays the same. They are in a continuing state of dynamic flux. That flux is increasing, which means that the rate of emergence is increasing.

Drivers

Global Demographics

One of the drivers causing disease emergence is global demographics. The burgeoning population is facilitating the secondary spread of agents by increasing interpersonal contact. Also, with the exception of sub-Saharan Africa, average age in all parts of the world is increasing, and, as populations age, susceptibility to infectious diseases increases. Furthermore, in many countries, rates of obesity are escalating along with related chronic diseases that increase susceptibility to infectious agents. Furthermore, birth rates are falling in much of the world, largely because parents have increased expectations of their children reaching adulthood. This affects the political landscape in terms of acceptable risk, particularly *vis-à-vis* infants and young children. And there are child substitutes: the sensitive issue of pets has important political overtones.

Global Food Industry

The food we consume comes from all over the world. Food-borne diseases that were previously limited geographically can now be disseminated widely. We have moved from what used to be microbiologically stable commodities to fresh products shipped via increasingly complex supply chains. It is possible to get to almost anywhere in the world within 48 hours. Accordingly a new biological agent could be disseminated worldwide via people or products within that time.

Processing

There has been a continuing trend toward milder processing of food, which may result in selection of mocroorganisms with increased resistance. "What doesn't kill you makes you stronger" is true for infectious agents. Also there is a perception that organically produced foods are safer, which may be true if the concern is over pesticide residue, but is not true microbiologically. And then there is a reemergence of the consumption of uncooked foods. This reflects the fact that we have been encouraged to eat more fresh produce and increasing demands mean that it is brought in from all over the world. It is transported in two-week segments from the tip of South America all the way to Alaska to ensure that fresh produce is available to us every day of the week. It used to be that cantaloupes were available in New Jersey for just two weeks in the year. Now they are available year-round. And there's a reemergence of consumption of raw milk and similar products. People have forgotten that unpasteurized milk used to be a source of tuberculosis. And since raw tuna, in sushi in particular, is popular and more nutritious than the cooked alternative, raw beef, raw liver and raw chicken are also being eaten as sushi, particularly in Japan, with several attendant outbreaks of foodborne disease. Japanese public-health officials are trying to convince the public to quit eating raw chicken.

Bacterial Gene Transfer

The importance of horizontal gene transfer between bacteria cannot be overstated. *E. coli* provides a good example. In the 1890s, it was thought to be non-pathogenic, whereas new strains continue to emerge through gene transfer causing various kinds of foodborne disease (Figure 1.).

- **1890's: First used as a non-pathogenic indicator of fecal contamination**
- **1940's: Implicated as a cause of infantile diarrhea**
- **1970's: Role of enterotoxigenic strains as foodborne pathogens**
- **1980's: Role of O157:H7 and other EHEC as a cause of hemorrhagic colitis and hemolytic uremic syndrome**
- **1990's: Identification of other classes of pathogenic *E. coli*, some of which may be foodborne**

Figure 1. Importance of horizontal gene transfer—*Escherichia coli*.
(EHEC = enterohemorrhagic *E. coli*)

Research Needs

Breaking the Disease Cycle

What knowledge and tools do we need to do the following three things?

- Anticipate and prevent the emergence of diseases from new, infectious agents. Although this is potentially the most cost-efficient approach, it is conceptually the hardest and it is difficult to obtain funding to look at something that hasn't happened yet. On the other hand, it is encouraging to see an RFA for this kind of work within the USDA Agriculture and Food Research Initiative (AFRI).
- Eliminate or contain the emergence of diseases before they become established. This can be achieved only within a short time window because many agents are hard to get rid of once they are established.
- Eradicate emerging pathogens that have become fully established in a new niche. This is particularly difficult with organisms that have multiple reservoirs and vehicles.

Anticipating/Preventing Emergence

In anticipating and preventing, a basis is needed for selecting the microorganisms that are most likely to be involved, to avoid investment of funds in an organism or group of organisms that is of low risk or has little impact. There is need to know what portion of the population and what foods or food technologies are likely to be involved. And, with this approach, it is necessary to have the technologies and strategies available to intervene in the riskiest situations.

As an example, during the past ten years, *Cronobacter sakazakii* has emerged as a food-borne pathogen in neonates. Although there are multiple sources for this organism, a furor arose because it was associated with powdered infant formula. We now know that a variety of other Enterobacteriaceae are occasionally associated with this type of infection, causing bacteremia, meningitis and necrotizing colitis, again in neonates. We also know that neonates aren't the only ones consuming powdered formulas. The biggest growth market in powdered formulas is actually at the other end of the age scale; they are being recommended increasingly as nutritional supplements for seniors and geriatric patients. It's noteworthy that seniors constitute the most rapidly growing segment of the population in the United States with susceptibilities similar to those of neonates. Their immune systems are starting to decrease, and, through achlorhydria, they produce less gastric acid, begging the question, "Should we be monitoring assisted-living centers for incidences of infections from Enterobacteriaceae?"

Eliminating/Containing Emergence

To eliminate or contain emergence of a disease before it becomes established, rapid identification of the new agent and cases is needed, as is identification of vectors, vehicles and reservoirs to determine its origin and how it is infecting humans. Also needed is an effective means of quarantining the emerging pathogen. However, "quarantine" raises hackles because of the days when immigrants were sent to Roosevelt Island for six months to two years if they had symptoms of tuberculosis. And an effective means of eliminating the pathogen from localized agricultural and environmental sources is necessary. Finally, an effective means for removing conditions that are fostering emergence must be developed.

Probably the best example is severe acute respiratory syndrome (SARS) caused recently by a coronavirus. It is noteworthy that SARS is now identified as a foodborne pathogen that is transmitted person-to-person. This respiratory agent is closely related to a virus found in civet cats and other animals in Chinese live markets. It appears that bats were the original source of the virus, particularly the Chinese horseshoe bat that then infected civet cats that also inhabit tree canopies. In the civet, an intermediate host for the virus, a mutation occurred that extended host range to humans who readily transfer it by respiratory means. Massive international efforts by a number of governments and intergovernmental agencies resulted in total control. It involved a massive quarantine whereby people with symptoms were barred from international travel. Live-animal markets in China were closed. Parts of hospitals in Canada were quarantined, preventing people from entering or leaving. Sources and intermediate hosts were rapidly identified and intermediate hosts were removed to break the infection chain; civets are no longer available for purchase in China. Evidence indicates that the problem resulted from a loss of habitat for bats outside of China, forcing their migration into China and infection of local bats, which, in turn, infected the civet cats.

Eradicating an Established Pathogen

To eradicate a fully emerged pathogen and its ability to cause disease, understanding of the following factors is needed:

- The etiology of the disease
- The ecology of the organism
- Mode of dissemination of virulence factors
- How to decrease human susceptibility
- Whether alternative food production, processing, marketing and consumption tools are available
- Means of effective communication to convince people of the need to change their ways, and
- Mobilization of political will and funding.

Such projects typically cost hundreds of millions of dollars. How much money was spent to eradicate small pox?

To date, no established foodborne disease has been completely eradicated. The closest is the poliovirus, which has not been fully eradicated. Others are in a state of control, but can reemerge if controls are ignored or are circumvented. Two that immediately come to mind are brucellosis and tuberculosis. The latter is particularly troubling because of the emergence of antibiotic-resistant strains. It is extremely difficult—and may be impossible—to eradicate pathogens that are free-living or have multiple hosts.

Research Needs

Basically there are two types of research needs. Short-term acute needs and longer-term needs.

Acute

With a new emergence, the need is to assemble an international research team immediately. Application of significant resources is needed; international establishment has to be prevented in less than a month.

Longer Term

Longer term needs include informatics to rapidly identify emergence events, rapid means for detecting and characterizing new pathogens, proactive approaches to predict where and when emergences are likely, and technologies for preventing them. Although difficult, unintended-consequence analyses should be done—by broad groups of knowledgeable people—to think through and quantify likely outcomes from changes in technology, marketing, *etc*.

Biotechnology's Role

Any discussion of emerging pathogens must include enterohemorrhagic *E. coli* strain O104:H4, the cause of the outbreak of foodborne disease in German in May 2011, which demonstrated the potential contributions of rapid, advanced biotechnology. The fact that the genome was sequenced within a week was amazing. On the other hand, having that information and making sense of it are not the same thing. I still haven't figured out how an organism that has no known attachment factor actually caused disease. None of the press releases that I saw provided insight into why it became a pathogen. Even the most advanced tools will be ineffective if the basic incident-command system is flawed.

Stopping Promiscuity

Infections by *E. coli* O157 in the United States and around the world have decreased dramatically in recent years. The problem is, infections by other enterohemorrhagic strains of *E. coli* (*e.g.* O104:H4) are likely to continue as long as *E. coli* exists and is capable of horizontal transfer of genes. O104 is not a new emergence; it's an extension of O157 because of the gene-transfer process. Whether gene-transfer can be stopped is hard to say. Certainly total elimination of *E. coli* from the food supply is virtually impossible. Taking a serotype approach has been successful here in the United States in the short run. However, it's becoming clear that it will not be successful in the long run, and so a new approach is needed.

What conditions foster promiscuity in food production and processing, and in specific animals, *etc*.? Are technologies or conditions available, or can evolutionary pressures be brought to bear, to suppress horizontal gene transfer? Is it possible to predict which strains are most likely to become the next source of foodborne enterohemorrhagic infection? *E. coli* O104 was not seen as a threat until it emerged; public policies were focused on six other serotypes.

Overcoming Diversity

Some pathogens, like *Salmonella enterica*—the leading cause of foodborne disease in the

United States—thrive because there are so many serotypes. With over 2,400 serotypes, no effective vaccines exist. Effective immunity would require both humoral and mucosal responses, but no common antigen is currently available. Compounding this, a high percentage of carriers are asymptomatic. About one in ten Americans carrying salmonella show no signs of it.

What factor do all salmonellae have in common that we can take advantage of in formulating new biotechnologies to prevent foodborne outbreaks? The rate of infection by salmonella has been constant for 20 years, although the primary vehicle has changed, from *S. enteritidis* to *S. enterica*. Furthermore, outbreaks of disease associated with fresh produce are significantly more common.

Predicting Emergence

If the number of hurricanes that will hit the United States each year can be predicted, why can't foodborne-disease emergence—and what new organisms will appear—be predicted? Forecasting weather is based on models, a lot of data-gathering and hard-core computational activities. We could develop models that are based on understanding factors that influence genetic stability and on understanding the impact of environmental, economic and demographic factors. It will require a team effort because the simulation modelers don't understand infectious diseases and infectious-disease people don't understand modeling.

Sentinel Populations

This was mentioned *vis-à-vis* elderly people. It provides the strongest opportunity of predicting where new emergences will occur. We need to start monitoring populations, locales and foods that carry inherently more risk in terms of food-born disease, for example:

- The very young, the elderly and the debilitated
- Foods that are consumed without cooking (fresh produce), and
- Areas of high population density and poor sanitary infrastructure.

Biotechnology may provide new tools to assist in this endeavor.

Long Standing Unfulfilled Needs

I have been asking for these research items for 15 years. I have put out RFAs, underpinned by significant funding, to try and get people to do this work and have been unsuccessful.

Sample Size

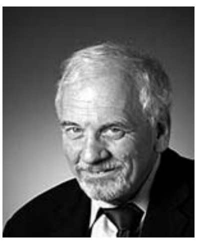
Dealing with food, sample size determines method sensitivity; as the sample becomes smaller, assay sensitivity is lost. With a sample weight of 2 μg, minimum sensitivity is somewhere between 3,000 and 5,000 organisms, providing only a 50% chance of detecting the organism. Molecular biologists need training in sampling statistics. In the papers I review, it is common to find, in discussions of new detection systems, poor understanding of how to calculate lower limits of sensitivity.

Assessing Immune Status

During an outbreak of foodborne disease, assessment of immune status of potentially exposed individuals is problematic. A non-invasive, rapid, field-deployable, inexpensive tool is needed—similar to a breathalyzer, for example—to provide a fairly accurate estimate of a person's current immune status. It would help in risk assessment to determine what factors need emphasis.

Concluding Remarks

We need to foster "just in time" research, particularly when responding to an emerging situation. We need to assemble research teams quickly, properly resourced, who understand how they fit into the overall structure. The longer the time between emergence and control the more it will cost both in public health and in dollars. There is need to think in terms of "right sized" technologies. Most of our food is produced by a few companies and many other companies produce a small percentage of our food. In order to solve emerging foodborne disease problems we need to think both high tech and low tech. And we need to look at the world like the microorganisms we are trying to control look at it, to find out what makes them tick. Their basic goal is to reproduce, but I encourage thinking of how a microorganism—as it is getting ready to merge—actually thinks and that will help us figure out where it is going to pop up.



Robert Buchanan, director of the University of Maryland's Center for Food Safety and Security Systems, received his BS, MS, MPhil, and PhD degrees in food science from Rutgers University, and postdoctoral training in mycotoxicology at the University of Georgia. Since then he has 30 years experience teaching, conducting research in food safety, and working at the interface between science and public-health policy, first in academia, then in government service at both the USDA and FDA, and most recently at the University of Maryland.

Dr. Buchanan's scientific interests are diverse, and include extensive predictive microbiology, quantitative microbial risk assessment, microbial physiology, mycotoxicology, and HACCP systems. He has published widely on a broad range of subjects related to food safety, and is one of the co-developers of the widely used USDA Pathogen Modeling Program. Buchanan has served on numerous national and international advisory bodies. He is a permanent member of the International Commission on Microbiological Specification for Foods, and has been the US delegate to the Codex Alimentarius Committee on Food Hygiene for 10 years.

Recent Animal Disease Outbreaks and their Impact on Human Populations[1]

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Animals occupy a special place in human societies. They are utilized for food (*e.g.*, milk and meat), transportation, raw materials (*e.g.*, wool and hides), energy (*e.g.*, manure), recreation, and money (*e.g.*, bartering). Furthermore, animals such as dogs, cats, and horses in some societies often are viewed as "companions." Their value in long-term care facilities and for the emotional well-being of AIDS patients has been documented (Siegel *et al.*, 1999). In addition to these valuable contributions, there is growing concern about diseases that humans can acquire from animals (*e.g.*, zoonoses). Zoonoses are overrepresented among human diseases that are defined as emerging (Table 1). Taylor *et al.* (2001) documented that 61% of all human pathogens are zoonotic. And of the 175 newly emerging pathogens in humans, 75% are listed as zoonotic (Cleaveland *et al.*, 2001). From 1996 to 2006, eleven of the twelve global emerging diseases originated from animals (Gerberding, 2004).

However, it is also important to remember that some diseases affect animals only, often with economic, environmental and/or societal implications. Recent examples include chronic wasting disease in elk and deer, foot-and-mouth disease, toxoplasmosis in sea otters, and salmonella in song birds. In 1994, canine distemper jumped the "species-barrier" and infected African lions of the Serengeti (Roelke-Parker *et al.*, 1996), killing over a third of the population within 6 months.

[1]Adapted from Bender JB *et al.* (2006) Recent animal disease outbreaks and their impact on human populations. Journal of Agromedicine 11(1) 5–15.

Table 1. Recent zoonotic agents identified.

Agent	Identified	Common illness in humans	Common illness in animals
Cryptosporidium parvum	1976	Profuse and watery diarrhea	Diarrhea in calves
Ebola virus	1977	Hemorrhagic fever and death (high case-fatality rate)	Hemorrhagic fever and death in primates
Hanta virus	1977	Fever and hypotension	None
Campylobacter spp.	1977	Diarrhea, abdominal pain, and fever	None
Escherichia coli O157	1982	Hemorrhagic enterocolitis	None
Borrelia burgdorferi	1982	Arthritis and skin rash	Arthritis in companion animals
Ehrlichia chaffeensis	1987	Fever, headache and malaise	None
Anaplasma phagocytophilum	1990	Fever, headache and malaise	Fever, lethargy in dogs and horses
Bartonella henselae	1992	Lymphadenitis and fever	Rare illness in cats, fever
Sin nombre virus (Hanta virus)	1993	Pulmonary syndrome, fever, myalgias	None
Hendra virus	1994	Pneumonia/encephalitis	Respiratory disease and death in horses
West nile virus	1999	Fever, encephalitis	Fever, muscle tremors, encephalitis
Nipah virus	1999	Encephalitis	None
SARS-coV	2003	Pneumonia	None

New diseases emerge for a number of reasons: world trade, animal translocation, ecological disruption, climate change, pathogen adaptation, and agricultural husbandry changes (Smolinski *et al.*, 2003). These factors represent the dynamic relationships among the pathogenic agent, host, and environment (Figure 1). This epidemiologic triangle includes the *intrinsic* characteristics of an individual's susceptibility to disease, including immune status, general health, genetic makeup, lifestyle, age, sex, and socioeconomic status, and *extrinsic* factors, which include the host's biological, social, and physical environment. Coincidentally, the triangle describing this relationship is the same as delta, the symbol for change; change is the one constant in the on-going tension between humans and microbes.

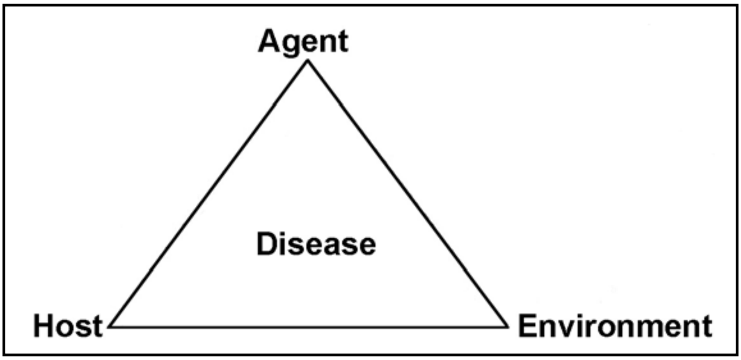

Figure 1. The epidemiologic triangle.

This article will discuss some recent outbreaks of disease, lessons learned, and challenges for the future. We will describe:

- the strong connection between animals and humans,
- the challenge of effective risk communication where there is limited knowledge of the risks,
- the dwindling and fragile animal-health and public-health systems,
- the lack of oversight and regulations to prevent disease transmission,
- changes in agricultural practices that result in new or re-emerging diseases, and
- the relationship between culture and disease.

We will discuss the specific examples of foot-and-mouth disease (FMD), chronic wasting disease (CWD), monkeypox, severe acute respiratory syndrome (SARS), and avian influenza.

The Strong Connection Between Animals and Humans

Foot-and-Mouth Disease

Some diseases may not have a direct impact on human health but, nonetheless, exert significant societal pressure by disrupting local economies as well as world trade. This is exemplified by the 2001 outbreak of FMD in the United Kingdom, which spread to other countries in Europe (Figure 2).

Figure 2. The impact of culling sheep during the outbreak of foot and mouth disease in France, 2001.

Foot-and-mouth disease is primarily a disease of cloven-footed domestic and wild animals. It is endemic in Asia, Africa, and parts of South America. However, some areas of the world are free of FMD, including North and Central America, Australia, New Zealand, Japan and most European countries. The causal agent is considered one of the most highly contagious viruses, and its contagiousness has huge implications on trade of livestock and livestock products. The disease may spread by direct or indirect contact with infected animals, aerosol from infected animals or milk trucks, and fomites, as well as through artificial insemination. People who come into contact with infected animals can serve as mechanical vectors, as sufficient FMD virus survives in their upper airways for 24 hours to potentially serve as an ongoing source of infection to livestock (Sellers *et al.*, 1971).

During the FMD outbreak in the United Kingdom in 2001, an estimated 2,000 confirmed cases and an additional 6 million animals were slaughtered to achieve containment (DEFRA, 2005a). The cost of controlling the outbreak and losses due to decreased tourism were estimated at £6.2 billion (DEFRA, 2005a). The postulated source was illegally imported food that eventually ended up as scraps in garbage fed to pigs (DEFRA, 2005b). The psychological and economic impact on the British population—farmers and non-farmers alike—was huge. Increases in suicides among farmers were reported and substantial economic losses were incurred from a trade embargo, travel restrictions, and reduced tourist income (DEFRA, 2005a). This does not take into account the loss of genetic stock and the cost of controlling the outbreak. A psychological assessment of the impact of FMD noted that farmers in the impacted area had significantly higher psychological morbidity scores compared to farmers in non-impacted areas (Peck *et al.*, 2002).

Cryptosporidiosis

Although FMD rarely is detected in humans, human health did not go entirely unaffected by the outbreak. The presence of FMD, an exotic animal disease, correlated with a decreased incidence of an endemic zoonotic disease, cryptosporidiosis, caused by *Cryptosporidium parvum*. Cryptosporidiosis is the most common parasitic infection among people in the United Kingdom, where an estimated two-thirds of cases are due to *C. parvum*. Two separate reports described a significant drop in *Cryptosporidium* cases during the FMD outbreak. Hunter *et al.* (2003) reported a 69% decline in cases in the northwest of England (Figure 3). Strachan *et al.* (2003) reported a 34% decline in Scotland, with a noticeable difference between FMD-infected areas and FMD-free areas. Reasons for these reductions were restrictions of farm-animal movement, possibly the presence of fewer young animals (the major source of exposure), and fewer animal-to-human interactions that allow transmission.

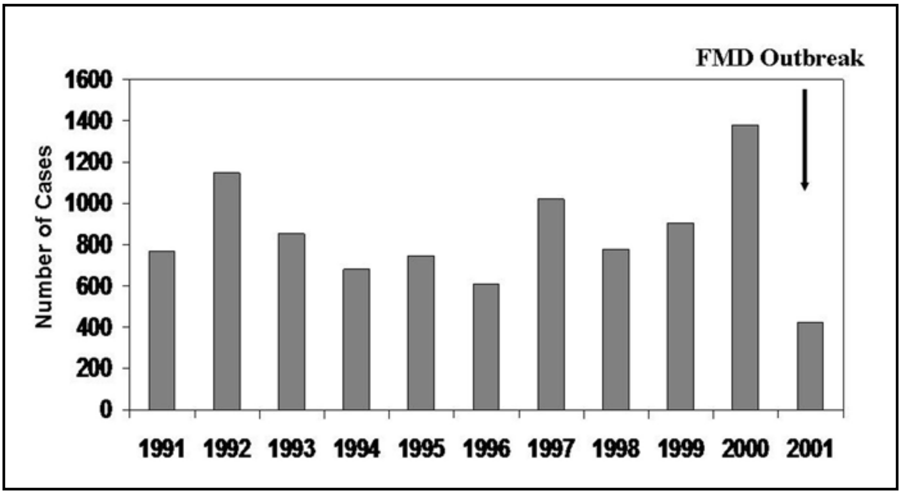

Figure 3. Reported cases of cryptosporidiosis in northwest England, 1991–2001 (Hunter *et al.*, 2003).

This outbreak of FMD highlights the strong and varied interrelationships between animals and humans. Although it is a disease primarily of animals with limited direct transmission to humans, it can have a significant public-health impact in terms of psychological effects, and its presence can send shockwaves through local economies. In addition, FMD is one of the primary agents of concern for agroterrorism, not only because of the economic and trade ramifications it can inflict on the livestock industry, but also because of the severe societal impact it may have. We must never underestimate the societal impact of diseases even when they directly impact the health only of animals.

A Challenge in Effective Risk Communication

A second animal disease capturing the headlines is CWD, a disease of the nervous system found in Cervidae: white-tailed deer, mule deer, black-tailed deer, and elk. CWD belongs to the family of diseases known as transmissible spongiform encephalopathies or prion diseases, and is a slowly progressive, invariably fatal neurologic disease in cervids. First recognized as a new disease among captive mule deer in a Colorado wildlife unit, it was later found to be endemic in both mule deer and elk in Colorado and Wyoming (Williams and Miller, 2003). The origin of the disease is unknown, but some have speculated that CWD 1 (Williams and Miller, 2003):

- is an adapted strain of the scrapie agent found in sheep,
- arose as a spontaneous evolutionary event, or
- originated from a yet unidentified prion reservoir.

CWD has been found in various areas throughout North America, both in captive and in free-ranging cervids (Figure 4). The perceived spread from the initial endemic areas is likely attributable to the movement of deer and elk in commerce, local expansions of farmed herds, and increased surveillance efforts (Williams and Miller, 2003).

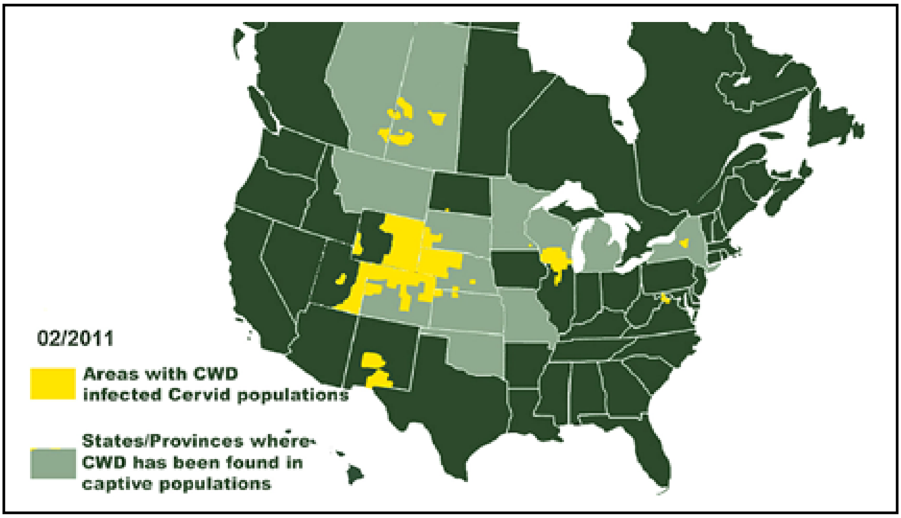

Figure 4. Chronic wasting disease in captive and free-ranging cervids (courtesy of the Chronic Wasting Disease Alliance, http://www.cwd-info.org/index.php/fuseaction/about.map).

Since cervids were found to have CWD, hunters, farmers and venison consumers have become concerned about the risk of zoonotic transmission, largely because of the connection between bovine spongiform encephalopathy (BSE) and variant Cruetzfeldt-Jakob disease (vCJD). Creutzfeldt-Jakob disease occurs around the world at a rate of 1–2 per million humans. The majority of cases has occurred among British citizens and persons who have resided in the United Kingdom. All vCJD cases to date have lived in countries with BSE.

If CWD is a zoonotic disease, what would it look like in humans? Would people living in endemic areas be at greater risk? To date, investigators have not seen higher numbers of human spongiform encephalopathies in CWD-endemic areas. However, prion diseases are rare, have long incubation periods, and can be difficult to detect. Because of recent concerns about prion diseases, epidemiologists are investigating neurologic diseases focusing on young people with unusual clinical presentations or neuropathology. Several documented clusters of cases have been investigated, often in response to concern from family members believing that deer-meat consumption was linked to illness (Belay *et al.*, 2004). These cluster investigations are a challenging exercise in risk communication about human and animal health. One investigation involved three elderly men, all of whom had a history of eating venison, who died of degenerative neurologic illnesses (CDC, 2003a). However, further diagnostic work-up revealed that only one actually had evidence of a prion disease. Currently, it is the consensus of the World Health Organization and the Centers for Disease Control and Prevention that there is no scientific evidence that CWD causes human illness (Belay *et al.*, 2004; WHO, 2005).

As with FMD, CWD has a psychological impact on humans although it does not directly harm human health. No definite link has been found between CWD and human brain disease, yet the detection of CWD in free-ranging deer in Wisconsin and Illinois in 2002 had a substantial impact on the human psyche. Nine months after CWD was discovered in Wisconsin, there was an 11% drop in deer-license sales (Heberlein, 2004). Also, similar to FMD, the discovery of CWD hurt local economies. Businesses that served Wisconsin hunters saw sharp declines in sales, as did feed dealers and local butcher shops. The decrease in license sales resulted in reduced revenues for the State of Wisconsin, and state expenditures increased $14.7 million to control CWD; overall, the estimated economic impact in 2002 was between $53 and $79 million (Bishop, 2004). This situation illustrates the emotional and economic impacts of infectious diseases and the challenge of effectively communicating evolving risk with reference to emerging animal diseases.

Dwindling and Fragile Animal- and Public-Health Infrastructure

National economies are vulnerable to outbreaks of animal disease, both intentionally malicious and accidental. Recent terrorist attacks have exposed the vulnerability of our transportation, food, and medical infrastructure. Several episodes have been documented in which food was intentionally contaminated for terrorist purposes (Manning *et al.*, 2005). However, in recent years, the most dramatic impact on national economies has not come from terrorism, but from the accidental introduction of foreign animal diseases. The threat is very real when we consider the volume of travelers and traffic that enter the United States each year, both legally and illegally. There is no feasible way for each vehicle and piece of luggage to be thoroughly checked for microscopic travelers. In addition, millions of animals and animal products are imported. They can serve as silent disease carriers or can harbor insects and ticks that serve as disease vectors. Clearly, we need to give greater attention to training of, and cooperation among, veterinarians, livestock producers, extension personnel, and healthcare professionals. Specifically, since some of these diseases can be zoonotic, veterinarians and people who work to protect human health need to combine forces to quickly diagnose and control their spread, especially in rural communities.

The West Nile virus is another dramatic example of the animal- and public-health challenges of understanding an emerging disease with only limited personnel dedicated to understanding insect vectors and viral spread through wild-bird hosts. Originally a disease of Africa and Europe, it was first observed in New York in 1999 (Lanciotti *et al.*, 1999). Initially misdiagnosed as St. Louis encephalitis, this disease, new to the Western hemisphere, was astutely diagnosed with the combined efforts of a veterinary pathologist, a physician, and epidemiologists. The virus now has been documented in all states of the continental United States. Migratory birds and competent mosquito vectors were instrumental in the rapid westward spread. The ensuing epizootic has had a dramatic effect on horse, bird, and human populations. In 2002, over 15,000 horses were reported ill, and 30% died as a result of the infection (CDC, 2002a). The impact on raptors and corvids (blue jays and American crows) has also been well documented (Wunschmann *et al.*, 2004). However, the broader impact within ecosystems, especially on wildlife, is unknown. From 1999 through 2004, over 16,700 human cases and 666 deaths were reported in the United States (Hayes and Gubler, 2005). This disease highlights some of the new challenges for human clinicians of unusual disease presentations (*e.g.*, acute flaccid paralysis syndrome) and new routes of transmission (*e.g.*, blood transfusion and organ transplantation). The appearance of West Nile virus required the training and funding of public-health officials in mosquito trapping, vector control, and close collaboration with academic institutions for disease surveillance and public education.

Lack of Oversight and Regulations

Monkeypox was first documented in 1958 in a colony of primates (hence the term). The first human cases were identified in 1970 in Zaire by local health officials on the lookout for the re-emergence of the smallpox virus. This rare disease was documented among people who lived where hunting was an integral aspect of their lifestyle. The natural disease hosts are likely several species of squirrel.

In 2003, an outbreak in the United States associated with legally imported African "pocket pets" led to seventy-two suspected human cases in six states (CDC, 2003b). Eighteen persons were hospitalized, some because of the potential for human-to-human spread. Interestingly, a number of the cases were veterinarians and veterinary technicians exposed while treating ill pets, highlighting potential occupational risk. The majority of patients had direct or close contact with prairie dogs that were infected by close contact with imported animals from Ghana, shipped to a distributor in Texas. The shipment included six genera of African rodents, including rope squirrels (*Funiscuirus* sp.), tree squirrels (*Heliosciurus* sp.), Gambian giant rats (*Cricetomys* sp.), brushtail porcupines (*Atherurus* sp.), dormice (*Graphiurus* sp.), and striped mice (*Hybomys* sp.). There was a real concern of spillover of the virus from these imported animals to susceptible wildlife populations in the United States.

Even though this outbreak was not directly related to agriculture, it exemplifies the problem of both legal and illegal animal movements. The US Fish and Wildlife Service estimates that the global trade in endangered wildlife is $4.2 billion annually, second only to illegal drugs. Other examples of emerging diseases linked to live-animal trade, include the spread of rabies from trapping raccoons in Florida for game farms in West Virginia (CDC, 1981), the collection of prairie dogs for pet markets that were subsequently diagnosed with tularemia (CDC, 2002b), and the shipping of elk infected with CWD to Korea (Sohn *et al.*, 2002). All of these examples clearly demonstrate potential consequences when humans move animals from one area to another and the need for regulations and federal policies that control the transfer/exchange of exotic animals. Currently, there are regulations for rodents from Africa and poultry from Southeast Asia, but numerous animals still pass through US ports unregulated (DHHS, 2003). Currently, no regulations control the interstate movement of exotic animals or wildlife within the United States.

Changes in Agricultural Practices and Food Processing

The emergence of BSE demonstrated the role of animal-feed commodities such as meat and bone meal (MBM) in the spread of disease. Meat and bone meal is an important recycled byproduct used as an inexpensive protein source. Since the 1950s, this protein source has increasingly been added to the diets of high-producing or rapidly growing animals, for example, beef and dairy cattle. While the BSE outbreak has largely been confined to Great Britain, the movement of affected animals and/or contaminated MBM spread the disease throughout Europe and beyond including sporadic cases in Japan and North America. As a result, "firewalls" were devised to decrease the amplification and spread of the disease when a clear understanding of the risks was identified.

In addition to changes in feed ingredients such as those that led to the spread of BSE, other agricultural and food-production factors that might appear to be innocuous can also provide a mechanism for disease transmission. For example some have speculated that the move from pasture feeding in the mid-20th century to intensive grain feeding has altered the gastrointestinal tracts of cattle in a way that favors the growth of *Escherichia coli* O157:H7 (Russell *et al.*, 2000) A second example is *Listeria monocytogenes*, a bacterium recognized as an animal pathogen more than 100 years ago, but seen as a significant cause of human illness only since the 1980s. The emergence of *L. monocytogenes* as a foodborne pathogen is due to pathogen survival at refrigeration temperatures, the increasing number of immunocompromised individuals in the population, the centralization and consolidation of food production, and changes in consumer food habits (*e.g.* consumption of ready-to-eat foods) (Swaminathan, 2001). This disease reflects the impact of changing food-processing techniques, with which post-contamination of cooked foods can be a source of infection. These factors demonstrate the complex and evolving nature of pathogens and the need for animal- and public-health surveillance systems to quickly identify and characterize new and emerging pathogens.

Cultural Practices and Disease Emergence

In many communities, there exist cultural or societal practices that can inadvertently encourage disease transmission by artificially causing animals to congregate. Recently, *Mycobaterium bovis* was identified among deer in northern Michigan, and its presence was attributed to the congregation of the deer due to "baiting" or feeding by deerhunters (Miller *et al.*, 2003). As a result, Michigan passed legislation prohibiting the feeding of deer in an attempt to limit the transmission of *M. bovis*. A similar phenomenon is occurring with birds: when songbirds congregate at feeders, their increased proximity can lead to the spread of salmonellosis and their subsequent illness and death.

Examples of global problems of disease transmission abound. In November 2002, the detection of an atypical pneumonia quickly challenged the world public-health system. SARS caused illness in over 8,000 persons around the world with 774 documented deaths. The identification of this rapidly spreading disease had a dramatic impact on healthcare workers and patients' willingness to utilize medical services (Emanuel, 2003; Chang *et al.*, 2004; Maunder, 2004). Half of the first sixty cases identified were healthcare workers, but, despite the risk, they continued to care for patients. The impact was felt globally with cancelled air flights and record low hotel occupancy rates; for example, in Hong Kong hotels, they dropped to 17% compared to 83% a year earlier (Emanuel, 2003). The economic cost to Toronto, Canada, was estimated at nearly $1 billion in 2003 (Blendon *et al.*, 2004).

SARS is a corona virus that likely emerged from a wild-animal source (Lau *et al.* 2005). This is supported by the detection of initial cases among restaurant workers handling exotic animals in Guangdong Province (Zhong *et al.*, 2003). SARS-CoV has also been isolated from masked palm civets and other wild animals in a live-animal market (Guan *et al.*, 2003; Lau *et al.*, 2005). Seroepidemiology of animal traders and handlers further supports this; 13% of animal traders had IgG antibody to SARS-CoV, as compared to 1 to 3% from community control groups (CDC, 2003c).

Researchers speculate that SARS-CoV likely originated from animals with which humans have infrequent contact, such as exotic species. The zoonotic link has been attributed to the phylogenetic relationship between corona viruses and those isolated from wild animals such as the palm civet and the raccoon dog. Contact likely occurred among southern Chinese who periodically consume wild-game meat for medicinal purposes. Zhong *et al.* (2003) have suggested that viruses that are transmitted between species tend to undergo more rapid genetic change as they adapt to new hosts. It is likely that novel viruses such as Ebola, HIV, and SARS-CoV will continue to appear with increased human interaction with wild animals. The lucrative wild-animal markets in Southeast Asia, a smorgasbord of wild and domestic animals, are often unregulated (Karesh *et al.*, 2005).

Avian influenza is another example that illustrates the relationship of cultural and social practices and the appearance of animal disease. Southeast Asia is considered the epicenter of recent influenza outbreaks. This is linked to agricultural practices in a highly populated area. Rice fields often have standing water that attracts waterfowl. These waterfowl are natural reservoirs, potentially spreading the disease to other domestic animals (*e.g.* chickens, ducks, and pigs) raised outdoors. In 2005 it was estimated that there were 1.3 billion humans, 508 million pigs and 13 billion chickens in China (Osterholm, 2005). The identification of novel avian influenza strains over the past 15 years documents the continual re-assortment of influenza viruses among birds, pigs and humans. Fortunately, sustained human-to-human transmission has not been documented (Ungchusak *et al.*, 2005). But with aquatic wild birds as the natural reservoir, it will be nearly impossible to eradicate this disease. The H5N1 strain responsible for the 1997 Hong Kong outbreak of influenza in domestic poultry resulted in the culling of 1.5 million birds and the identification of eighteen human cases with six deaths (Bridges *et al.*, 2002). Similarly in the Netherlands, 28 million birds were culled with eighty-nine reported human cases and one death (Fouchier *et al.*, 2004). The 2003–2005 H5N1 outbreaks in Asia affected eleven countries, with 109 reported human cases and fifty-five deaths (CIDRAP, 2005). Like SARS, the economic impact in Southeast Asia was substantial. The South Korean Ministry of Health and Welfare estimated that the cost of avian influenza to Asian countries at about $130 billion. Unlike SARS, influenza is a potentially greater problem with a common wildlife reservoir (*e.g.* aquatic birds). This is complicated by minimal public-health and medical infrastructure and large numbers of other potential reservoirs, such as pigs and domestic poultry commingling with humans in village settings. Avian influenza demonstrates the immediate need for international cooperation and interdisciplinary interventions for disease detection, control, and prevention. It also illustrates the need to engage local farmers in the development of sustainable strategies to identify suspect cases and prevent the commingling of domestic and wild-bird populations.

Summary

We face some critical needs as we combat emerging diseases. We must understand the global consequences of moving animals and animal products around the world and assess the impact of an increasing human population on the environment. This combination sets the stage for potential mixing of microorganisms around the globe in contact with susceptible populations. The influenza epidemic of 1918–1919 killed 50 to 100 million people worldwide, but since the 1960s, many of us have had the luxury of forgetting about the enormous death toll brought by outbreaks of infectious diseases (Osterholm, 2005). Even today, however, we cannot disregard the possible catastrophic effects of currently emerging diseases.

To control emerging diseases requires early detection and intervention. The phenomenal speed in the diagnosis and identification of the SARS-CoV demonstrates how technologies have improved our response and mitigation efforts. These rapid diagnostic tests need to be incorporated in the field to shorten detection and response times. This is especially true for exotic animal diseases that can harm our domestic livestock. These tests could also be used to quickly identify exposed individuals for early treatment or isolation. Another important learning point from both SARS and avian influenza is that agricultural workers may often be the first to acquire these new or re-emerging diseases. Therefore, it is imperative to have adequate healthcare for workers. With healthcare, timely information needs to be collected by public-health personnel to also assess the population health of agricultural workers.

Our public-health and veterinary infrastructure needs to be improved. We must build the expertise, resources, and tools necessary for developing the capacity to respond to threats posed by vector-borne and zoonotic diseases (Smolinski *et al.*, 2003). Our universities need to train more medical entomologists, vector ecologists, mammologists and ornithologists who have a thorough understanding of the interactions among human, animal, and ecosystem health. There is a need to develop interdisciplinary infectious-disease centers for training, research, diagnostic systems and data sharing. Furthermore, public-health authorities should look beyond traditional disciplines and training when hiring new epidemiologists and microbiologists. These and other recommendations have been clearly outlined (Smolinski *et al.*, 2003; NRC, 2005).

In the 19th century, Rudolf Virchow stated that animal and human health are inextricably intertwined. Our common environment is where this weaving of lives takes place, hence, we must guard the health of our ecosystems. Recent examples include decreasing wetlands and the subsequent congregation of waterfowl in smaller areas, resulting in outbreaks such as avian influenza and Newcastle disease. Deforestation and the greater interaction of wildlife with domestic animals and humans are likely factors for the emergence of novel viruses such as hendra, lyssavirus, and Nipah (Parashar *et al.*, 2000). Conversely, reforestation and suburbanization are likely contributing factors for the emergence of Lyme disease in the northeastern portion of the United States (LoGiudice *et al.*, 2003). Dramatic weather events have also been linked to disease emergence. This was documented with the outbreaks of Rift Valley fever among ruminants and people in East Africa and the Arabian peninsula (CDC 1998, 2000), following periods of above-normal precipitation and subsequent increases in mosquitoes. We can be sure that diseases will continue to emerge, and the complex relationship between animals, plants, and humans will require the interaction and cooperation of a broader range of scientists and medical professionals. The time to train them is now.

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Preparing for Emerging and Unknown Threats in Crops

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Diseases of plants have had significant impact on the course of human history. Almost every schoolchild learns of the devastating famine that occurred in Ireland in the mid-1800s, when unusually cold, damp conditions caused an oomycete pathogen, *Phytophthora infestans,* to wreak far more damage than usual on the potato crop on which millions of subsistence farmers and their families relied. The stories of a million starving Irish who perished as a result, and of the 1.5 million who emigrated—many to the United States—are familiar to us (Large, 1940). But countless other stories of plant diseases have helped to shape social, political, military, and financial decisions and actions around the globe. Why do the British drink tea? It wasn't always that way. At about the same time that the Irish potato famine was causing such misery in the British Isles, the rust fungus *Hemileia vastatrix* was devastating what was then the greatest coffee-growing region of the world, the island of Ceylon (now Sri Lanka), then a British colony. Despite extensive efforts to manage the disease, the coffee industry was unable to survive the severe economic losses, and British farmers on Ceylon began to transform their acreages into tea plantations. Soon, British consumers were drinking tea, and the habit stuck. On a more serious note, severe food shortages during the most critical period of World War I resulted after cool and humid conditions on both sides of the Atlantic Ocean favored pathogens of potatoes and wheat, forcing military leaders of both sides to alter their troops' movements and strategies.

Plant diseases still affect human health and society (Stack and Fletcher, 2007). Although they are unlikely to cause significant food shortages or malnutrition in the United States and other developed nations (in the event that a particular crop—even a major staple—were to be eliminated by disease we, in the United States, would just eat something else), it is a different story in developing nations. Imagine, for example, the loss of the rice crop in southeast Asia, or of cassava in eastern and central Africa. Such events are not merely speculation; the International Institute for Tropical Agriculture in Nigeria reports that cassava brown streak virus has been spreading in central and eastern Africa, seriously threatening food security in already-unstable regions such as Rwanda and Tanzania (Ferguson *et al.,* 2010).

That a clear relationship exists between food security and the stability of social and political systems has been demonstrated repeatedly (Chakraborty and Newton, 2011), and a number of recent and even current examples are available. Low-income economies are more sensitive to food inflation as the poor spend a higher percentage of their incomes on food. In the aftermath of the 2010 earthquake in Haiti, slow distribution of aid and supplies to hard-hit areas and refuges established for newly homeless citizens led to squalid conditions of hunger and disease. Sporadic violence, rioting and looting resulted as food prices skyrocketed; the price of rice more than doubled in the post-quake period. Limited resources and desperation triggered by deplorable conditions pushed tempers and patience past the breaking point and vigilante groups took matters into their own hands. Soaring food prices of staple commodities such as sugar, rice and milk have forced people in many Arab states to allocate larger portions of their income to the basic necessities of life, pushing them deeper into poverty and sparking a revolutionary wave of demonstrations and protests known as Arab Spring (Javid, 2011). A similar food-price crisis in 2008 led to protests and riots in more than thirty countries.

Crop Vulnerability to Disease

The United States' agricultural enterprise includes myriad crop species grown in many systems from extensive field acreages (corn, wheat, barley, *etc*.) to small plots of exotic, organic and specialty crops (artichokes, microgreens, jicama, herbs, *etc*.). Every plant species is vulnerable to a variety of diseases caused by microbial agents, including fungi, bacteria, viruses and viroids, nematodes, protozoa, and even parasitic plants. Increasing the complexity of the plant-pathogen relationships, many plant pathogens are transmitted by plant-feeding insects such as leafhoppers and sharpshooters, aphids, whiteflies, and beetles.

The vulnerability of US agriculture to emerging pathogens and pests derives from a number of factors (NRC, 2002a; Whitby, 2002; Gullino *et al.* 2008; Fletcher *et al.*, 2010). First is the monetary value of these crops, considering that they generate a sixth of our gross domestic product and represent between 15% and 20% of our employment. Features of our agricultural practices also contribute to vulnerability. Most of our crops are planted as monocultures, the genetic identity of which ensures that a pathogen sickening one plant has the potential to sicken them all. Vast acreages planted to field crops go unmonitored for extended periods, usually from planting until harvest. Naturally occurring plant resources, such as forests and rangelands, are similarly un-watched. These factors can result in very long lag periods between the introduction of a pathogen and its detection and identification, and the initiation of a response. Vulnerability results also from the ease and frequency with which exotic new pathogens traverse our borders, whether on the winds of hurricanes, in the bilge water of ships, on the shoes of tourists who visited farms outside the United States, on the imported fresh fruits and vegetables that we now expect as year-round supplements to our menus, or by a thousand other pathways that occur daily, naturally, and predictably.

Additional vulnerability comes from the cost of plant diseases and crop losses (NRC, 2002a; Whitby, 2002; Madden, 2003; Gullino *et al.*, 2008; Fletcher *et al.*, 2010). These include reductions in yield and quality of the commodities (blemished fruit, toxins in grain), as well as the costs of growing less-desirable crops. These factors often lead to higher food prices and to shortages of certain types of foods. Costs of disease prevention and management also add up, including the cost of short-term control strategies such as pesticide application, biocontrol adoption, or crop replacement, as well as long-term strategies such as the incorporation of disease-resistance genes into high-value crops. Even more critical, however, are the national and international trade disruptions brought about by quarantines and embargoes against the presence of specific pathogens or toxins in particular crops or commodities. Subsequent downstream impacts are often felt in rural communities where the economy is often tied to the success of their agricultural ventures.

Challenges for Assuring Food Stability Nationally and Globally

Vulnerabilities from New Crops and Pathogens

New crops and new pathogens bring new vulnerabilities. The USDA Animal and Plant Health Inspection Service (APHIS) maintains, and regularly updates, a list of plant pathogens of unusually threatening nature, called select agents (USDA APHIS, undated). This list helps in the prioritization of resource allocations and defines the boundaries of the stringent regulatory policy deemed essential for US crop security. All of the plant pathogen select infectious agents are exotic to the United States. Since the creation of the list, two plant pathogen select agents have arrived and become established within US borders (*Phakopsora pachyrhizi,* causal agent of soybean rust, in 2004 and *Liberibacter asiaticus*, causal agent of citrus greening, in 2006). Once clearly established, the causal pathogens were removed from the select agent list to facilitate research to manage these diseases. However, plant pathogens other than those on the select agent list also pose significant threats to US agriculture. Most notably, a relatively new race of the wheat stem rust pathogen, *Puccinia graminis* f. sp. *tritici* race TTKS ("Ug99")—which emerged in Uganda in 1998 and has since spread well beyond the area initially affected—is of significant concern because of the lack of resistance in most of the wheat varieties currently grown in the world, including in the United States (Njau *et al.*, 2010). The FAO (2010) has described the potential impact on the human condition in certain wheat-dependent regions as "disastrous." A high priority for US wheat breeders is to identify and incorporate resistance to this fungal race into key US wheat varieties.

Climate Change

The predicted transitions of global climate zones will affect the optimal distributions and possible ranges of plants, insects and pathogens (Coakley *et al.*, 1999; Eastburn *et al.*, 2011; Garrett *et al.*, 2011; Shaw and Osborne, 2011) It is likely that members of all of these groups will become prevalent in areas not now occupied, and will cease to thrive in others. In some cases, the outlines of new geographical ranges for a plant species may not precisely coincide with those of certain pathogens or insect vectors, creating the possibility for new host-pathogen-vector associations. The range changes constitute a new vulnerability for food security as well as for emerging pathogens and pests.

Nefarious Use of Plant Pathogens

Plant pathogens offer attractive features to those with harmful intent, whether their motives are terrorism, economic gain, revenge, or social/political expression (NRC, 2002a; Fletcher and Stack, 2007; Fletcher *et al.*, 2010). They are easily available at little or no cost and offer little or no threat to the health of the handlers. Although a plant disease may not be perceived as catastrophic, its impacts on food insecurity and social instability may be quite serious, as noted above. Plant pathogens were included as components of consideration in the biowarfare programs of a number of nations prior to the Biological Weapons Convention in 1975, which commits the 163 state signers to prohibit the development, production, and stockpiling of biological agents and toxins.

Human Pathogens on Plants

Foodborne illnesses are on the rise worldwide, and, although they once were considered to be associated primarily with meat contamination, an ever-increasing percentage of outbreaks is associated with fresh produce such as tomatoes, spinach and sprouts (Brandl, 2006; Teplitski *et al.*, 2009). Although most disease outbreaks result from accidental contamination, some have been linked to cases of criminal negligence (in which distributors failed to maintain sanitary conditions, or knowingly released contaminated products). However, remarkably, to our knowledge, only one significant case of intentional contamination, resulting in hundreds of illnesses, has emerged. This incident was the 1984 deliberate contamination by a religious cult of restaurant salad bars in Oregon, as part of a plan to sway a local election. However, the recent outbreak of a particularly aggressive and virulent strain of *Escherichia coli* in Germany, in which forty-six died and nearly 4,000 were taken ill (Kupferschmidt, 2011), demonstrates our lack of preparedness to prevent, quickly detect and diagnose, and minimize damage from such events—whether naturally occurring or intentionally caused.

Elements of a Strong National Security Plan

A report produced by the National Research Council (2002b) suggested that a strong national biosecurity plan should consist of:

- early detection and diagnostic systems;
- epidemiological models for predicting pathogen spread;

- reasonable but effective strategies and policies for crop biosecurity;
- distributed physical and administrative infrastructure;
- a national response-coordination plan and infrastructure, and
- strategies for forensic investigation and attribution in cases of intentional or criminal activity.

Homeland Security Presidential Directive 9, issued by President Bush in 2004, mandated a National Plant Disease Recovery System (NPDRS). The task was assigned to the Secretary of Agriculture, then Anne Veneman, who made it the responsibility of the USDA Office of Pest Management Policy. The initiative consists of the preparation of response plans for each of the APHIS plant pathogen select agents as well as a number of other threatening plant pathogens; completed plans can be viewed at http://www.ars.usda.gov/Research/docs.htm?docid=14271. The NPDRS's purpose is to ensure that the tools, infrastructure, communication networks, and capacity required to mitigate the impacts of high-consequence plant-disease outbreaks are such that a reasonable level of crop production is maintained in the United States. The recovery plans represent a cooperative effort of university, industry, and government scientists managed by the American Phytopathological Society (APS) in partnership with the USDA.

A second initiative emerging after the 2001 attacks was the establishment of the National Plant Diagnostic Network (NPDN) (Stack *et al.*, 2006). This nationwide system of plant diagnostic laboratories—an initiative led by the USDA's CSREES[1] (now NIFA[2])—was a achieved through strong cooperation among USDA agencies, land-grant universities, state Departments of Agriculture (SDAs), and private laboratories. Prior to this time, plant diagnostic laboratories, of which there was generally one per state, were in some cases associated with a land-grant university and in other cases part of the SDAs. They often were under-funded and their diagnosticians operated in isolation and without coordination. The NPDN structure and funding brought, for the first time, all of the laboratories into a single framework. Organized into five regional units, but coordinated as a whole, the network assured a minimum level of capability through training and equipment resources. By adopting common assay protocols, positive and negative controls, and reagents, data and records could be shared and compared among the labs. Expertise from each lab was available to the other state laboratories. Plant disease diagnosticians, now recognized for their important contributions to the US agricultural enterprise, took new pride in their accomplishments. The NPDN is a true success story in which preparation for potential threats against our agricultural systems generated substantial benefit for managing everyday agricultural problems. As this paper is being written, the future of the NPDN is threatened by severe federal budget cuts. Its loss due to lack of funding would erase a decade of progress, value and capability, and turn the business of plant-disease diagnosis back to an inefficient and minimally supported enterprise lacking optimal capability to anticipate, detect, respond to and mitigate the effects of the ever-increasing emerging pathogens and pests that continue to threaten our crops.

[1]Cooperative State Research, Education, and Extension Service.
[2]National Institute for Food and Agriculture.

In addition to the NPDRS and the NPDN, many other initiatives that emerged following September 11, 2001, addressed agricultural vulnerability and preparedness. The USDA established an Office of Homeland Security within the office of the secretary, APHIS developed new response and regulatory policies (including the select agent list), the USDA Agricultural Research Service (ARS) initiated research programs related to pathogens of concern, and CSREES developed and supported new initiatives in education, outreach and research (now under the auspices of NIFA). The newly formed Department of Homeland Security (DHS) established the National Biodefense Analysis and Countermeasures Center (NBACC[3]), within which the National Bioforensic Analysis Center (NBFAC) was charged with developing and providing forensic capabilities for attribution and prosecution of those involved in criminal actions related to homeland security (both NBACC and NBFAC are now managed by a non-governmental organization).

The Need for New Capability in Microbial Forensics

A study commissioned by the US defense community in 2002, following the mailing of letters containing anthrax spores to a number of targets, called for the development of greater capability in microbial forensics (Budowle *et al.*, 2005a, 2005b). Although most of the effort that followed was focused, logically, on solving the anthrax case, the report included specific language indicating the need for plant-pathogen forensics. A panel of plant pathologists was charged to review existing capabilities that could be brought to bear in the investigation of a criminal case involving plant pathogens, as well as to identify needs and gaps and recommend priorities for near-term funding, research and applications. In their report (Fletcher *et al.*, 2006), the authors noted a difference between plant-disease diagnostic activities carried out following "normal" disease outbreaks, when the goal is to identify the pathogen to species or strain as needed to formulate effective management strategies, and those needed for a crime-scene investigation, which must be conducted at a high level of stringency with validated tests having high confidence levels so as to stand up to aggressive counter-arguments in court. Furthermore, challenges particular to the development and application of microbial forensic science to plant pathology were explored. For example, forensic scientists dealing with human victims need concern themselves with only one host species and the pathogens and toxins to which that host is susceptible, whereas plant pathologists deal with hundreds of host-plant species, each having a different set of pathogens. Because so many plant species are important to us, the basic biology of both host and pathogen is well understood for only a fraction of them. For many lesser-known plant pathogens, diagnostic technologies often are still rudimentary, and, even when molecular approaches are developed for them, the databases (public genome libraries, databases of substrate utilization and fatty acid profiles) lack information for these plant pathogens and their relatives. And, despite a growing recognition on the part of federal policymakers of the importance of our nation's agricultural enterprise, funding for work on plants remains comparatively very low and even some post-2011 funds targeted to this area have since been eliminated.

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[3]http://www.bnbi.org/.

The National Institute for Microbial Forensics & Food and Agricultural Biosecurity

While the work of the NPDN, the NPDRS, APHIS, and ARS and others is relevant to plant-pathogen forensics, the mission and focus of each of these entities are directed to different goals. At Oklahoma State University the concept of a new program to focus specifically on plant-pathogen forensics and its role in agricultural biosecurity grew as the needs and gaps in this emerging discipline were clarified in the assessment study. OSU administrative leaders at all levels were supportive and provided encouragement and preliminary resources for the program's initiation. In 2007, the National Institute for Microbial Forensics & Food and Agricultural Biosecurity was established as a cross-disciplinary and cross-departmental unit at OSU. Its goal is to identify, assess, prioritize, facilitate and conduct research, education and outreach (the three activities fundamental to any land-grant university) related to national needs in microbial forensic science with respect to pathogens of crops, forests, rangelands and other plant resources, with an additional component related to human pathogens on fresh produce. Its mission statement is:

> *NIMFFAB will build on, connect and enhance existing programs that support and address issues of crop and food security.*

The Institute's core staff of five faculty members, enhanced by a growing group of partners and collaborators, has strong expertise in plant pathology, forensic sciences, microbiology, vector-plant pathogen interactions, diagnostics and detection design and development, microbial population biology, molecular biology, metagenomics and next-generation sequencing, bioinformatics, produce safety, and human pathogens on plants.

The NIMFFAB uses targeted strategies and approaches to accomplish its mission. A key role is to serve as a link between the plant-pathology community and law enforcement and security communities, policymakers, and funding agencies. Critical to its effectiveness is maintaining strong and open ties with end-users and other stakeholders within the Department of Homeland Security's affiliated National Bioforensic Analysis Center (of which NIMFFAB is a Spoke Laboratory), the Federal Bureau of Investigation (FBI), the USDA's Office of Homeland Security, APHIS, ARS, NIFA, NPDRS, and NPDN, the Defense Threat Reduction Agency, the Food and Drug Administration (FDA), and other government agencies, industry, and scientific societies.

Education

NIMFFAB directs and mentors graduate students in novel MS and PhD programs that blend multidisciplinary programs in new ways. For example, funding from an innovative USDA program designed to address emerging national needs has allowed NIMFFAB graduate students to be the first in the United States to take coursework and perform research that incorporates both plant pathology and forensic sciences. An invaluable opportunity afforded our graduate students is the summer internship that they complete at a homeland security-related federal agency or industry. For example, two PhD students spent 3 months doing research at the FBI laboratory in Quantico, VA. Because young scientists rarely have a realistic understanding of careers in law enforcement or homeland security, these internships provide a unique opportunity to experience these environments.

Research

Almost all plant-pathology research is relevant in some way to agricultural applications of microbial forensics and homeland security. However, NIMFFAB faculty and their postdocs and students focus their research on initiatives targeted to support the forensic investigator's capabilities in evaluating a criminal case involving plant pathogens or human pathogens on fresh produce. Most projects involve collaboration and partnerships with the agencies concerned. Examples of research areas include adaptation of current or novel plant-disease diagnostic methods for forensic investigation, adapting existing human forensic technologies to plant pathogens, and developing new investigative tools that facilitate the work of forensic investigators at the scene of a crop-focused crime. Plant pathologists have a unique advantage as developers of field-targeted tools and technologies, in that model systems involving locally common plant pathogens can be readily field-tested. Furthermore, data from naturally occurring plant-disease outbreaks can be compared directly to those from outbreaks of the same disease generated in field plots (following all regulatory requirements) by the investigators.

Outreach

Outstanding training courses and exercises related to crops and plant pathogens are offered frequently by the NPDN and APHIS. Such activities are generally targeted toward NPDN plant-disease diagnosticians, APHIS personnel, and local and regional responder communities. The training niche that NIMFFAB addresses is designed specifically to bring federal forensic and security investigators into the picture, to provide information and practice for law enforcement in agricultural crime-scene settings, and to create opportunities for security and law-enforcement personnel to interact with the agricultural community, including Cooperative Extension educators, crop advisors and farmers. Furthermore, NIMFFAB facilitates interaction between the plant-pathology and law-enforcement/security agencies by organizing members of the APS—the primary professional association for plant pathologists—interested in these disciplines into interactive groups. The APS Microbial Forensics Interest Group and the APS Food Safety Interest Group meet yearly during the APS annual meeting, as a forum for prioritizing needs, providing community input, and developing collaborative initiatives in forensic plant pathology and fresh-produce safety.

Final Thoughts

US preparedness for maintaining the most secure and abundant food supply in the world has been improving, but gaps remain. Justifiable concerns about new and emerging pathogens and pests that threaten agricultural resources demonstrate the need for greater exploration of new and more effective ways of addressing these issues. Greater blending of disciplines will facilitate the creation of new knowledge, support the development of new technologies and capabilities, and allow the broad, cross-disciplinary training that young scientists will need to address these global challenges.

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Jacqueline Fletcher has a BS in biology from Emory University, Atlanta, an MS in botany from the University of Montana, and a PhD in plant pathology from Texas A&M. She joined Oklahoma State University in 1984, where she was appointed Sarkeys Distinguished Professor in 2001 and Regents Professor of Plant Pathology in 2008. She was named a Fellow of the American Phytopathological Society (APS) in 2005 and a Fellow of AAAS in 2007.

Dr. Fletcher is Director of the National Institute for Microbial Forensics and Food and Agricultural Biosecurity (NIMFFAB), a multidisciplinary OSU initiative that addresses high-priority national issues in research, teaching/education and outreach, with emphases in microbial forensics applications in plant pathology and produce safety. The NIMFFAB serves as a spoke laboratory for the DHS-affiliated National Bioforensic Analysis Center in the area of plant pathogen forensics.

She served on the APS Council for ten years, including the four-year presidential sequence. In the months following September 11, 2001, she led APS responses and input to new national biosecurity initiatives. Her research focuses on mechanisms of virulence and insect transmission of plant-pathogenic bacteria, the relationships between human pathogens and plants, and on the emerging disciplines of microbial forensics and agricultural biosecurity.

Preparing for Emerging and Unknown Threats

Q&A

Moderator: Richard Isaacson
University of Minnesota
St. Paul, Minnesota

Francisco Diez-Gonzalez (University of Minnesota): About reducing promiscuity—that seems really challenging.

Robert Buchanan: If it were easy I would have done it already. Let's at least find out what's fostering promiscuity. I think we are doing a number of things during normal processing of food that actually stimulates it. In the case of *E. coli*, certain antibiotics activate its SOS repair system, and then you scramble everything.

Richard Isaacson: Shaun Kennedy[1], director of the National Center for Food Protection and Defense here at the University of Minnesota, will now take Bob Buchanan's place as a panel member.

Steven Slack (Ohio State University): Jackie, you have been a thought-leader on food production and protection. How should we raise these issues in a way that will awaken consciousness so that the public relates to them in the same way as they relate to public-health issues?

Jacqueline Fletcher: It's difficult to raise awareness because we have such plentiful food that is healthy and safe in this country. It takes a little bit of shaking for people to wake up to what the potential is, and the 2011 outbreak in Germany may be one of the things that can do that. I don't mean to make light of that terrible event, but if we use incidents like that to illustrate what the impacts can be and the fact that it can happen here, then those kinds of things can help. But, we can't sit back and wait for disasters. We also have to approach the public in other ways, and we don't generally do that that well. I'm referring to elementary-school level as well as all the way up, with educational programs. Certainly in

[1]Pages 191–207.

our universities we can increase awareness by creating possibilities for students to interact across disciplines. It's a challenge, and I don't think we can ever let up.

Isaacson: Are there any lessons from the animal side that speak to this? Jeff?

Jeffrey Bender: Back in 2001 when I was dealing with anthrax and animal-related agro-terrorism issues, one of the things that I quickly had to learn about—and was not well versed in—was the plant world. As Jackie mentioned, we've had some significant events in the plant world and I don't know if we have highlighted them well. A lot of us have taken for granted the cassava issue, for example. We need to get on the bully pulpit and talk about these and economic impacts associated with them, as well as related direct impacts on people. Sprouts are one issue, but clearly we have significant issues regarding leafy greens. In the past ten years we've had a lot of issues regarding fruits in general. With those stimuli, we've come a long way, but we can do a better job.

Isaacson: When *E. coli* first hit the fan, it was clearly a beef problem and particularly a ground-beef problem. I think the statistics now show that there is at least an equal number of plant contaminations as there are beef contaminations.

Dan Gustafson (Food and Agriculture Organization): A question for Shaun. Bob Buchanan mentioned technology as part of a prevention strategy—technology to suppress horizontal transfer of genes in *E. coli*. What kinds of technologies?

Shaun Kennedy (University of Minnesota): What Bob was referring to is that we don't understand the horizontal transfer of bacterial genes to the point where we can stop it. Gaining a better understanding of that process is the first step.

Bender: I don't know that you can stop *E. coli* from transmitting genes, but, on the flip side of that, what wasn't mentioned was the concept of co-selection. We don't know what the co-selection factors are, so, for example, if one looks at antibiotic-resistance determinants in *E. coli*, salmonella and other enteric organisms, you see things that cluster together, that are co-transferred. They are not necessarily related to specific resistances such as to heavy metals or quaternary ammonia compounds used as disinfectants. We don't know what virulence factors might be co-selected for simultaneously. But, if we could start understanding co-selection factors—I don't know that we could intervene—there's a possibility of figuring out ways of reducing virulence with new strategies.

Allan Eaglesham (National Agricultural Biotechnology Council): Jeff, with the lack of a link between CWD[2] and CJD[3] in the three gentlemen who died after eating venison, how surprising is it that one of those men died of a prion disease, and what did the other two die of?

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[2]Chronic wasting disease.
[3]Creutzfeldt-Jakob disease.

Bender: The CDC[4] sent out investigators who were aware of these individuals who had neurologic degenerative disease and, basically, tried to characterize them. Fewer than 7% of individuals who die are autopsied, so, going back to the records, they tried to identify the actual diseases. Even physicians make mistakes in their diagnoses. In going back to these and pulling the case reports and any pathology, they found that one of them did, indeed, have Creutzfeldt-Jakob disease. One of the others had Ménières disease and I can't recall the third, but they were unrelated diseases. So, initial suspicion, because these three individuals had actually hunted at the same camp—although they didn't know each other—raised a lot of public concern. There have been investigations of other hunters showing some CJD, but no substantial link has emerged. Now, there's interesting science behind prion diseases: can you induce the prion to infect human tissue? If you force the prion to adapt, you can actually do that. So, it cannot be said that this can absolutely never cause disease, but, at the current stage of our understanding of CWD, we have no evidence that it does cause this disease. Those three cases were unrelated. Only one was a prion disease.

Karin Wittenberg (University of Manitoba): One of the problems that we encounter in our communication with the public is the fact that messages from the producers, processors, distributors and retailers aren't always consistent, and then, on top of that, you have the various government layers. Traceability hasn't been mentioned at all at this conference. What is your sense of the value of that tool and whether it may present better messaging to the public.

Kennedy: Traceability technologies have improved. However, it's a challenge in that the interoperability of traceability systems is very limited. If one company has one food supplier and another has another, by sharing information they may be able to rapidly move upward and backward. In the peanut outbreak that has been mentioned a couple of times, several of the affected companies do have traceability systems, yet it took them as much as four months to figure out where some of their products were being contaminated. The systems in place have gotten better, but until we have a common platform for information sharing it's not really a full solution. To your point though, that's how to restore consumer confidence. As soon as you tell consumers exactly what is and what is not contaminated, you gain their trust again.

Bender: Gene Hugoson[5] touched on this. There is a desperate need for clarity in how we do this better. How do we evaluate that system? The jalapeño pepper case provided a clear example of the complexity involved. Historically, here in Minnesota, we have utilized this technology and it has been very helpful. I look back at the Schwan's ice cream salmonella case. That was a good example of determining where the product was; that outbreak looked like it was regional. It looked like the focus was a restaurant versus a national outbreak. Looking at traceability gave us the strength to crack the case. We had epidemiological

[4]Centers for Disease Control and Prevention.
[5]Pages 227–232.

evidence and no microbiologic evidence at that time, but we felt comfortable using those data to craft the appropriate risk communication.

Francisco Diez-Gonzalez (University of Minnesota): A question for Jeff, about the spread of influenza. We are fortunate that the 2009 pandemic wasn't as infectious as in 1918. What did we learn to help prepare us for the big one in relationship to what Bob said about anticipating threats. A major pandemic will impact every aspect of human activity.

Bender: That's a big question with a few possible answers. What did we learn from the H1N1 pandemic? One is that we were right in saying that this could happen—that reassortment is possible, that new strains can form with potential for pandemics. We expect it every 30 to 50 years. We have the technology to watch the emergence of new strains and we are starting to understand what we don't know. The second issue is preparedness. If you remember, there was a lot of panic and there were missteps in communication. A clear example is the issue of vaccines. We didn't have enough time to prepare the vaccine and, when it was produced, availability was delayed. There was public concern about the vaccine's effectiveness and confusion as to whether it induced the disease, and whether it contained thermisol and was associated with autism. So, improved diagnostics are needed as is transparent risk communication especially regarding vaccination. Also needed is more-rapid vaccine production, part of which is appropriate monitoring of how strains vary over time. H1N1 comprises a number of clades with divergences within those clades. Within H1N1 there's resistance to some of the antivirals. And further to what Jackie was saying, we can't forget about this. We've already seen cuts in funding for influenza research because the thinking is that we've just had a pandemic and won't have another for a while.

Bill McCutchen (Texas A&M University): What are the prospects for increasing outbreaks of foodborne illness, including regulatory implications for the use of radiation especially for leafy greens, fruits and vegetables, as well as meat products?

Kennedy: The first step in successfully getting irradiation adopted by the public is to change the Delaney clause so that irradiation is no longer defined as an ingredient and doesn't have to be mentioned on the front label and can be treated as electronic pasteurization. Having to put the radura saying "irradiation" on the front is the reason consumers are not adopting it. If consumers knew that many of their spices have been irradiated—because they are exempted from the Delaney clause—you would have the same problem. Without radiation or gas treatments you would end up with all sorts of "extra value" in your spice. With that change in labeling, I don't think it would be hard to move forward because of benefits in protecting public health.

Bender: It's a tool that we need to continue to pursue, but, unfortunately, I don't think we'll see that change in our lifetime. We need to focus on the fact that we do need terminal pasteurization-type procedures and, clearly, irradiation is one. We have a technology that works and we have a public-perception problem precluding acceptance. Also, we need to continue to push for other technologies. We have high-pressure technologies for controlling microorganisms on products. Instead of focusing on one bug we have technologies, like cooking, that kill many. We need to continue to try to educate and also look for alternatives, including policy approaches to working with the public.

Kennedy: The marketing campaign should be relatively easy: eat the same foods the astronauts eat.

McCutchen: You're exactly right. Texas A&M has been preparing the food for NASA for a long time. That is what they eat. We eat it as well.

Isaacson: What challenges are there with fresh fruits and vegetables that are different from meat?

Kennedy: Well, irradiation has been tested on a number of fresh fruits and vegetables like strawberries, to extend the shelf-life. Really the only problem with it is on foods that have a high fat content—you end up with rancidity.

Fletcher: It would probably help with post-harvest plant diseases as well.

Michael Kahn (Washington State University): Yesterday, the focus was on food availability and food security and today it's been much more on food safety as a component of food security. One of the things that we've been seeing is how much investment there has been in the food-safety area—anti-terrorism and contamination of food—and yet the number of people who died of *E. coli* in Germany, for example, was relatively small. The magnitude of the food-availability question is huge and I'm wondering if there are opportunities for investment in food safety to have more impact on, and inform the question of, food availability?

Fletcher: That they are linked to me is obvious. A previous speaker mentioned One Health, which is focused primarily on human pathogens and animal pathogens. I'm a member of One Health as are other plant pathologists, and that is an area where those elements come together. Did I understand your question correctly—are we missing the boat by spending so much on food safety when food security may be the larger issue?

Kahn: That's a component, but at this point my question is: are things being developed? It's a microeconomic-macroeconomic kind of difference. Food safety is a collection of anecdotes about particular diseases at the present time in relatively small numbers of people and yet we were informed yesterday that we are looking at another two and a half billion people by 2050. That's a lot of people, and if we don't meet crop-production targets, many will be starving, which is a public-health problem, not a disease problem directly. It will lead to enormous disease problems. But, by investing in rapid scanning for diseases, food-preservation technologies and so forth, are we investing in these anti-terrorism things in a way that allows us to make the transition—to blend the technologies—to a macro situation that can lead to significant increases in food production, enhanced food distribution and food preservation? This conference to me is in two parts. We talked about huge problems yesterday. But the problems discussed today, albeit serious, affect relatively small numbers of people. I don't quite see where the two discussions for long-term food security are coming together. I think this is something that really needs to be thought about because people aren't getting excited about the prospect of two and a half billion more people—and we don't have food to feed them—in the next 35 to 40 years.

Fletcher: The two are definitely connected and we are doing things now about terrorism and food safety that can translate. Where that is possible we should make sure that the opportunity isn't lost. It can happen through One Health, programs that the State Department has and even AAAS, but your larger question is a philosophical one that is difficult to answer.

Kennedy: One way to look at it is—whether or not it is right—food safety hits rich countries directly. Food security does not hit rich countries directly yet. So, until there is some actual pain for rich countries it takes altruism and politicians are not necessarily known for altruism. And the second thing is that the foodborne illness problem in the United States, you could say, is relatively small. It's estimated at 3,000 deaths. Internationally, especially in the developing world, it is fairly significant: 2 billion cases of foodborne illness a year with 1 million deaths. So we still have a problem with food safety and unsafe food may be worse than no food at all depending on what it's contaminated with. There are some cases where, in animal health, there's been a direct link to food security. Investments have been made by DARPA[6] in Central Asia to build animal diagnostic labs to help prevent highly pathogenic avian influenza outbreaks. That has a direct benefit on food security in Central Asia, but the motivation for DARPA is that those countries have nuclear weapons and if they lose a protein source there is the potential for public unrest leading to government overthrow, and someone else gets control of the nukes.

Tony Shelton (Cornell University): This is a question for Dr. Fletcher. I am interested in the historical perspective of NIMMFAB[7]. It seemed to develop because of a particular coming together of various forces—9/11, maybe the foresight of American Pathological Society—but as you talked about it and the need for it, and thinking about getting future funding, has the university or the federal government made any longer-term commitments to making sure it will continue? And then are there other scientific societies who could also learn about the model based on your experience in developing it?

Fletcher: I don't have any funding beyond contracts and grants. The only secure funding really is the faculty positions. All of my faculty, except me, are assistant professors and

[6]Defense Advanced Research Projects Agency.
[7]National Institute for Microbial Forensics & Food and Agricultural Biosecurity.

don't have tenure yet, so that's not even totally secure—but they are good so they will get it. There is definitely interest on the part of various agencies in what we are doing, but they have not offered avenues for a permanent situation.

Shelton: What about the private sector—food companies, Grocery Manufacturers Association—have you approached them for funding?

Fletcher: No. Maybe we should. I have been trying to get high visibility at a number of different types of venues speaking at various programs, moving into new areas. I'd love to talk to you about how one might go about that because we have to be creative. Some of our initial sources of funding, as I pointed out, have fallen by the wayside because of the economy. I've seen institutes at universities come and go. There are surges of needs, and to keep NIMMFAB operational and make it viable for the long term, we must be flexible. Each of the scientists in my group at NIMMFAB has a home department and several of them are in my department, Entomology and Plant Pathology. Each has a scientific area that should survive on its own if NIMMFAB should cease to exist. I am hopeful that NIMMFAB's contributions will continue to be important and needed.

Carol Ishimaru (University of Minnesota): Thinking about sustainability and food security, one of the things that comes to mind for me is the vast quantity of food that is imported every day through our ports and the relatively miniscule amount of food that is inspected. How can we improve our ability to detect pests and pathogens? Are there technologies or regulations that could be used to decrease risk?

Fletcher: Those containers are the size of large trucks and they just open the doors and look in. Do they see insects crawling around? New methods of sampling the interiors are being developed—assaying for volatiles, for example—and basic research along those lines is necessary. We simply can't afford to hire the number of people required for full inspection without delaying the transit of fresh produce.

Kennedy: At road ports of entry, from Mexico for example, if they identify a truck for inspection, they have between five and ten minutes to conduct that inspection before they have to release the truck. We don't have the technology to effectively sample a truck full of watermelons in five or ten minutes and find out if anything has been sprayed on them. However, there are some basic technologies. You can look at what is being done to detect bombs and nuclear weapons at ports of entry to see what is needed. Every container that comes into a US seaport now goes through a specialized radiation detector. It's just run through so it doesn't interrupt commerce. I don't know how we would get to the point where we could do that for biological materials and chemical contaminants, but that's how we may end up, not interrupting trade.

Bender: One important aspect is working with exporting countries and actually engaging producers to understand risks. Another thing is risk assessment of particular pathogens of concern, particular products of concern, particular countries of concern and characterizing them and picking out which parts you want to look at. These are all things that are actually included in the Food Modernization Safety Act. Also important is the issue of "shopping": if I am rejected at one port can I gain entry at another? We need the infrastructure to be able to say, "You were rejected at Port A, therefore we are not going to let you enter Port B." We need to support the Food Modernization Act because that will actually help do that. Credit is due the Department of Homeland Security for identifying the products of concern, the countries of concern, and the pathogens of concern and prioritizing them in terms of risk assessment.

Liangliang Gao (University of Minnesota): What can be done to encourage funding from the private sector? And what will be the job prospects over the next five to ten years in food security and public health?

Fletcher: I talked about education and training and the fact that our graduate students who had interned at the FBI both ended up going to the FBI or to the defense community in some aspect. There definitely are these types of jobs, but the challenge is that students have to work at finding them. That's one of the goals of my program. For example, the ARS lab at Fort Detrick is looking to hire people from our program because it's unusual to have the combination that we offer. It's knowing where things are needed and then preparing students to move into those areas.

Kennedy: To your first question, it's important for us to look for a diversified portfolio of funding support. The private sector is an important part of that, which is actually something we are doing because we can't count on a single source for steady funding, such as the government. Regarding where the jobs are, one of my friends calls the Food Safety Modernization Act, the "Food System Employment Act," because a number of inspectors and third-party auditors will be required for full implementation. In year one, an additional 4,000 FDA food inspectors will be needed. So, if you are in food that might be a place to look.

Bender: I liked Dr. Fletcher's slide showing the cross-training at the FBI. I wouldn't have thought that plant pathology would be of interest to the FBI, but that's a phenomenal networking and cross-training opportunity and it's the kind of thinking you need as a graduate student. You never know where you will end up and I encourage you to think along those lines.

Stephen McCurry (Grains for Health Foundation): A follow-up comment to Shaun's response to the question about food supply versus food safety. I don't dispute your answer at all that wealthier countries are more concerned about safety. However if, say, China were to request repayment of the money lent to the United States in bushels of wheat rather than in dollars, that might suddenly get our attention.

Kennedy: Those kinds of things actually do come up as far as the role of China is concerned. China is the reason the corn market is tight. And China has made an intentional effort to become a dominant player in the global dairy industry. So they are going to impact us even more.

Isaacson: I didn't know how much question and answer we would have. I had prepared a list of my own questions, which we didn't get to. It's really been wonderful—a thoughtful set of questions, very stimulating and engaging. I want to thank the audience. I also want the audience to thank the panel for their excellent presentations.

EMERGING BIOTECHNOLOGIES TO PROMOTE SAFETY, ENABLE DEFENSE, AND DISCOURAGE FRAUD

Emerging Biotechnologies to Promote Food Safety

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We have seen a massive explosion in technologies, especially in molecular biology, that started affecting public health in the 1990s and continues to accelerate. It's a good time to discuss the impact that biotechnology will have on food safety, especially in my specialty of foodborne-disease surveillance. Many technologies—MALDI-time[1] of flight mass spectroscopy, microarrays, sequencing, microfluidics, *etc.*,—are changing our concepts of microbial life, which is affecting how we detect and how we control microorganisms in their natural environments.

Each year, one out of every six Americans—48 million people—are thought to become sick with a foodborne illness, and 3,000 die. I'll provide background on foodborne-disease surveillance, and what it does for us, and on some of the limitations of surveillance and the impacts of technology.

The main points I will make are:

- Foodborne-disease surveillance is an important, but often overlooked, component of our food-safety system.
- How well it functions—or doesn't function—is vitally important to industry and to the public.
- The current system operates at only a fraction of its potential.
- New technology can exponentially magnify its effectiveness.

Recent Outbreaks

2010 started out with *Salmonella* Typhimurium infections reported from forty-one states, caused by human contact with African dwarf water frogs. In the same year, widespread salmonella infections were associated with shell eggs, frozen meals, alfalfa sprouts, Romaine lettuce, and salami made with contaminated pepper, and *E. coli* O157 outbreaks were traced to beef and cookie dough. 2011 is shaping up to be another banner year for foodborne disease.

[1]Matrix-assisted laser-desorption ionization.

Prevention

Much can and should be done to prevent foodborne illness, from farm to fork: good agricultural practices, good manufacturing practices and inspections, designing processes for safety, microbial monitoring, restaurant and food-store inspections, and consumer education. However, in spite of everything we do, foodborne illness will occur because we are imperfect beings. Some 356 billion pounds of food are consumed annually in the United States and it's impossible to monitor it all. Contamination, which can occur anywhere along the food chain, can't be seen and is unevenly dispersed within the affected product. Accordingly, detecting pathogens in food is an insensitive process. On the other hand, essentially all of the food consumed in the United States is, in a way, being tested because it is being eaten, and disease surveillance provides information on what can be done to reduce the burden of illness. Furthermore, surveillance can help limit ongoing illness by recalls, public notices, and publishing of guidelines.

PulseNet

Figure 1 lists US recalls—some of which have been massive—in which PulseNet played a role in detecting outbreaks and averting disease. The much more profound impact of disease surveillance is that it allows identification of underlying problems and their solution, providing feedback to industry, to regulators and to consumers about problems that would otherwise be unrecognized.

Year	Pathogen	Food	Amount recalled
2010	*Salmonella* Enteritidis	Shell eggs	>500,000,000 eggs
2010	*Salmonella* Montevideo	Ready-to-eat Italian sausage products/pepper	>1,263,754 lbs
2009	*E. coli* O157:H7	Non-intact steak and ground beef outbreaks	1,115,049 lbs
2009	*E. coli* O157:H7	Cookie dough	300,000 cases of product
2009	*Salmonella* Typhimurium	Peanut butter/peanut products	>3000 types of products
2008	*E. coli* O157:H7	Ground beef	5,300,000 lbs
2007	*E. coli* O157:H7	Frozen pizza	5,000,000 pizzas
2007	*E. coli* O157:H7	Ground beef (3 outbreaks)	35,400,000 lbs
2006	*Salmonella* Tennessee	Peanut butter	326,000,000 lbs
2004	*Salmonella* Enteritidis	Raw almonds	13,000,000 lbs
2003	*E. coli* O157:H7	Blade Tenderized Frozen Steak	750,000 lbs
2002	*Listeria monocytogenes*	Ready-to-eat poultry products	27,400,000 lbs
2002	*E. coli* O157:H7	Ground beef	18,600,000 lbs
2000	*Listeria monocytogenes*	Ready-to-eat poultry products	16,900,000 lbs
2000	*E. coli* O157:H7	Ground beef	1,100,000 lbs
1998	*Listeria monocytogenes*	Hot dogs, deli meats	35,000,000 lbs
1998 & 2008	*Salmonella* Agona	Toasted oats cereal	>3,000,000 lbs
1997	*E. coli* O157:H7	Frozen ground beef	25,000,000 lbs

Figure 1. Largest US food recalls in which PulseNet played a prominent role.

Figure 2 shows a few of the industrial processes that, over the years, have been changed in order to reduce the burden of illness. And Figure 3 shows the result of a study done by Rob Tauxe at the CDC on recent outbreaks, showing vehicles that were not formerly realized to be risky and weren't high on the "radar screens" at the FDA or USDA. Who would have thought that peanut butter would be a significant vehicle for salmonellosis, for instance, or that raw cookie dough could cause illnesses? These were picked up through our disease-surveillance system, allowing regulators and industry to direct their scarce resources towards where problems were actually occurring.

Figure 2. Addressing underlying problems.

Figure 4 shows some ingredient-driven outbreaks, which, formerly, would have been difficult to identify. To a certain extent, the recent situation in Germany was ingredient-driven; alfalfa sprouts are seldom eaten alone.

Figure 5 provides an illustration of the surveillance system. People become ill and visit their doctors who request stool samples and microbial cultures are sent to a laboratory. If a reportable pathogen is found, an isolate is sent to the Health Department for sub-typing. Representatives of the Health Department interview cases to find out what they ate and what they were exposed to. When the information is uploaded to PulseNet, it is reported to the CDC. FDA and USDA and other organizations are involved in tracking the cases of disease, using the information to try to minimize the impact. Other modes of finding information are used also. There is a system whereby state health departments are called up with clusters that are recognized by physicians or the public, but Figure 5 illustrates one of the more powerful methods that we have for discovering unrecognized problems in the food supply.

Figure 6 shows what PulseNet does. Every state has a laboratory in a large city where these pathogens are sub-typed. Each lane has a pulse-field gel electrophoresis (PFGE) pattern that is investigated in local databases, then clusters of cases with matching patterns are uploaded and we look at them on a national scale at the CDC database. The regulatory

2006	*E. coli* O157 and bagged spinach	2008	*E. coli* O157 and ground beef
2006	*E. coli* O157 and shredded lettuce (x2)	2008	*Salmonella* and fresh produce items
2006	Botulism and commercial pasteurized carrot juice	2009	*Salmonella* and peanut butter containing foods
2006	*Salmonella* and fresh tomatoes	2009	*Salmonella* and imported white and black pepper
2007	*E. coli* O157 and frozen pizza	2009	*Salmonella* and alfalfa sprouts
2007	*Salmonella* and peanut butter	2009	*E. coli* O157 and prepackaged cookie dough
2007	*Salmonella* and a vegetarian snack food	2009	Multidrug resistant *Salmonella* and ground beef (x2)
2007	*Salmonella* and dry dog food	2009	*E. coli* O157 and blade tenderized steaks
2007	*Salmonella* and microwaveable pot pies	2009	*Salmonella* and salami made with contaminated pepper
2007	*Salmonella* and dry puffed breakfast cereal	2010	*E. coli* O145 and romaine lettuce
2007	*E. coli* O157 and ground beef	2010	*Salmonella* and alfalfa sprouts
2007	Botulism and canned chili sauce	2010	*Salmonella* and frozen meals
2008	*Salmonella* and cantaloupe	2010	*Salmonella* and shell eggs

Figure 3. Selected recent multi-state outbreaks of foodborne infections (2006–2010): new food vehicles (underlined).

agencies also contribute from their food-monitoring programs. Data from FDA are directly uploaded and those from USDA come indirectly through a network called VetNet. A new network is being formed in industry called Voluntary Net; companies are keeping their own inventories of PFGE patterns for rapid early detection of potential problems.

PulseNet USA comprises all fifty states, and several large counties and cities have laboratories that are connected electronically (Figure 7). It started in 1996 in Minnesota, and was officially opened in 1998 by then Vice-President Gore. By 2001, it was present in all fifty states. Each year some 1,500 clusters are investigated at state and local health departments. About 250 multi-state clusters are examined by the CDC, of which ten to fifteen large, dispersed multi-state outbreaks are further scrutinized. At weekly meetings, we triage about fifty clusters and direct our resources accordingly.

PulseNet increases the sensitivity of cluster detection, strengthens the association between illness and exposure, and increases the speed of detection of outbreaks. It does this by amplifying the signal indicating ill cases. The number of patterns uploaded to PulseNet has stabilized at around 50,000 per year (Figure 8). The decrease in 2009 resulted from the emergence of novel H1N1; some states had insufficient resources to investigate both flu and foodborne disease.

2006	*E. coli* O157 and bagged spinach	2008	*E. coli* O157 and ground beef
2006	*E. coli* O157 and shredded lettuce (x2)	2008	*Salmonella* and fresh produce items
2006	Botulism and commercial pasteurized carrot juice	2009	*Salmonella* and peanut butter containing foods
2006	*Salmonella* and fresh tomatoes	2009	*Salmonella* and imported white and black pepper
2007	*E. coli* O157 and frozen pizza	2009	*Salmonella* and alfalfa sprouts
2007	*Salmonella* and peanut butter	2009	*E. coli* O157 and prepackaged cookie dough
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2007	*Salmonella* and dry puffed breakfast cereal	2010	*E. coli* O145 and romaine lettuce
2007	*E. coli* O157 and ground beef	2010	*Salmonella* and alfalfa sprouts
2007	Botulism and canned chili sauce	2010	*Salmonella* and frozen meals
2008	*Salmonella* and cantaloupe	2010	*Salmonella* and shell eggs

Figure 4. Selected recent multi-state outbreaks of foodborne infections (2006–2010): ingredient-driven (underlined).

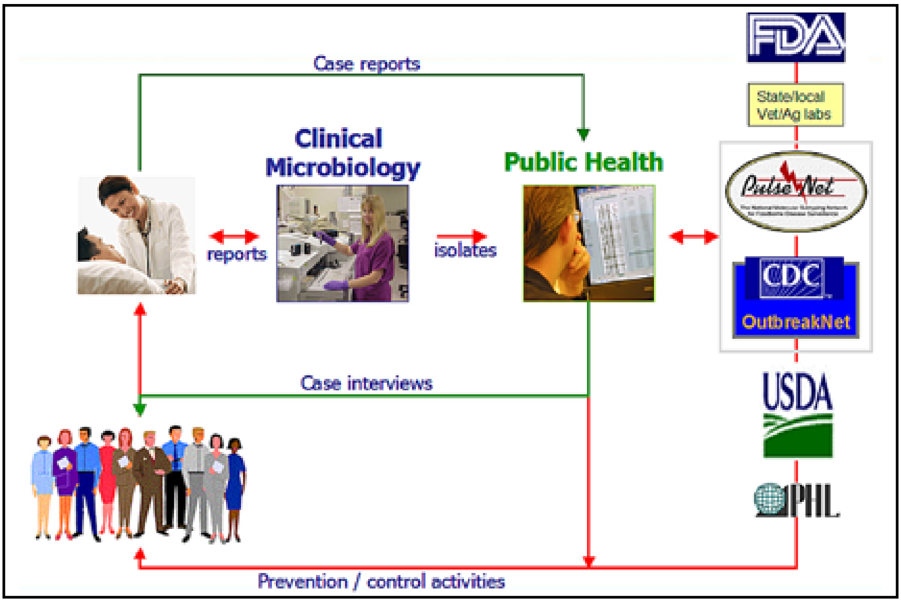

Figure 5. Pathogen-specific surveillance.

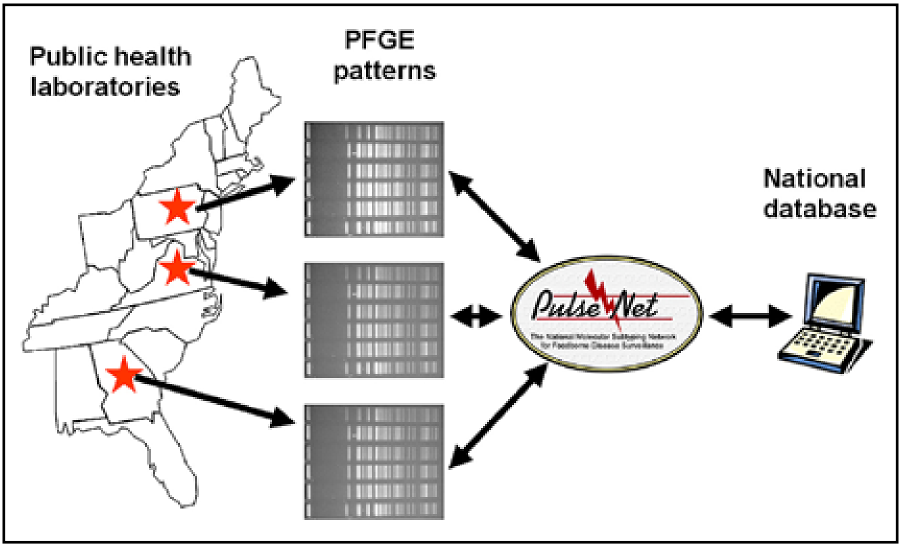

Figure 6. PulseNet electronic communication.

Figure 7. PulseNet USA.

Figure 9 provides an example of how it works. These are cases of *E. coli* O157H7 in Oregon in 2006. Interviews of all of these cases showed a variety of exposures, whereas a subset, sharing a common PFGE pattern, revealed that these individuals had consumed fresh, bagged spinach. It is safe to say that, in the absence of this system, this outbreak—199 cases in twenty-six states, three deaths, and thirty-one cases of hemolytic uremic

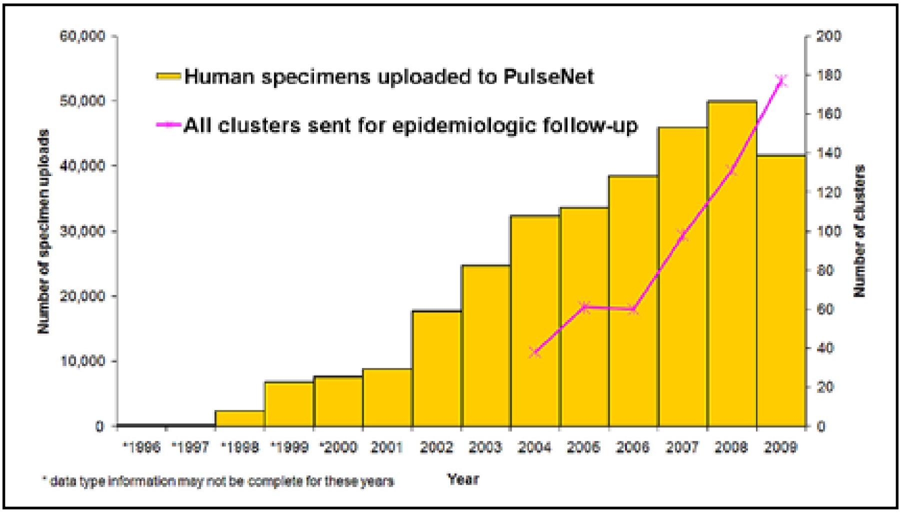

Figure 8. Human specimen isolates uploaded to PulseNet USA and identified clusters, 1996–2009.

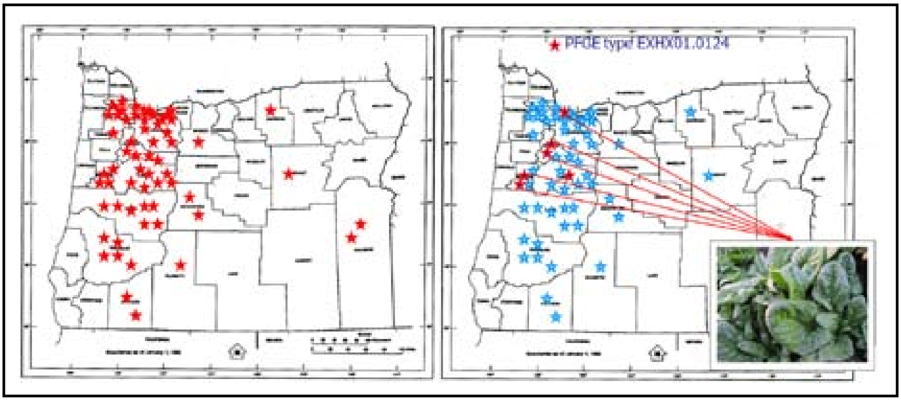

Figure 9. *E. coli* O157:H7, Oregon 6/1/2006–10/9/2006.

syndrome—would not have been detected. Each case of hemolytic uremic syndrome costs about a half-million dollars in medical expenses. A death has been costed at about $6 million. By comparison, the 2011 sprout-associated outbreak in Germany resulted in 3,304 cases, thirty-eight deaths and 786 cases of hemolytic uremic syndrome. Adding the international cases associated with travel to Germany increases the cases of hemolytic uremic syndrome to 828, which is unprecedented.

Figure 10 provides another example of the signals received, this time for *Salmonella* Typhimurium over a 3-month period. Buried in these data were cases from around the United States that shared a PFGE pattern (Figure 11). They were traced to peanut products that led to 3,000 different items being recalled.

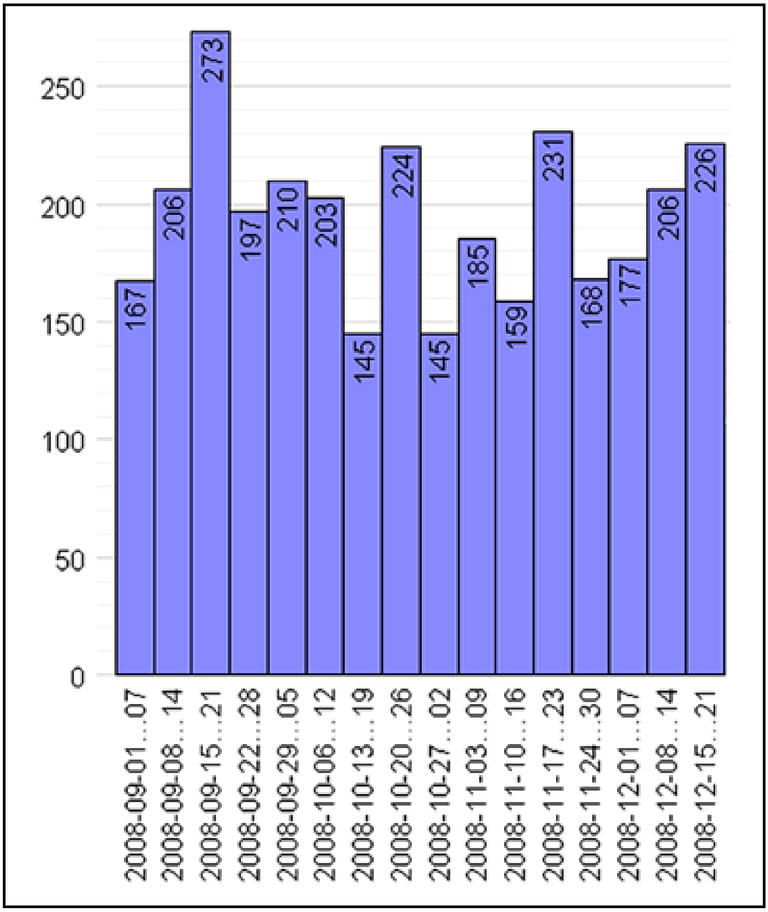

Figure 10. All *Salmonella* Typhimurium, 9/1/2008–12/15/2008, weekly.

"Before" and "after" pictures are shown in Figure 12. The upper "before" picture is the epidemiologic curve from the Jack In The Box outbreak of *E. coli* O157 in 1993, which took a long time to detect and resulted in many cases and four deaths. After seven weeks, 150,000 hamburger patties were withdrawn. The lower "after" pattern, of a 2002 outbreak of *E. coli* O157:H7 in Colorado, starts out looking similar whereas rapid detection led to early recall of hamburger meat and curtailment of the outbreak. This is an example of how PulseNet works and a hundred similar examples exist.

The theory underpinning PulseNet is that by detecting more outbreaks and curtailing them, future disease incidence will be reduced. We have seen this occur with listeria (Figure 13). Subsequent to the initiation of PulseNet for listeria in the 1990s, we detected more outbreaks, and, recognizing the roots of the problems, disease incidence fell. We have a long way to go with shiga-toxin-producing *E. coli* and salmonella, but every case of those diseases is potentially preventable; we need to work harder to reduce the burden of disease.

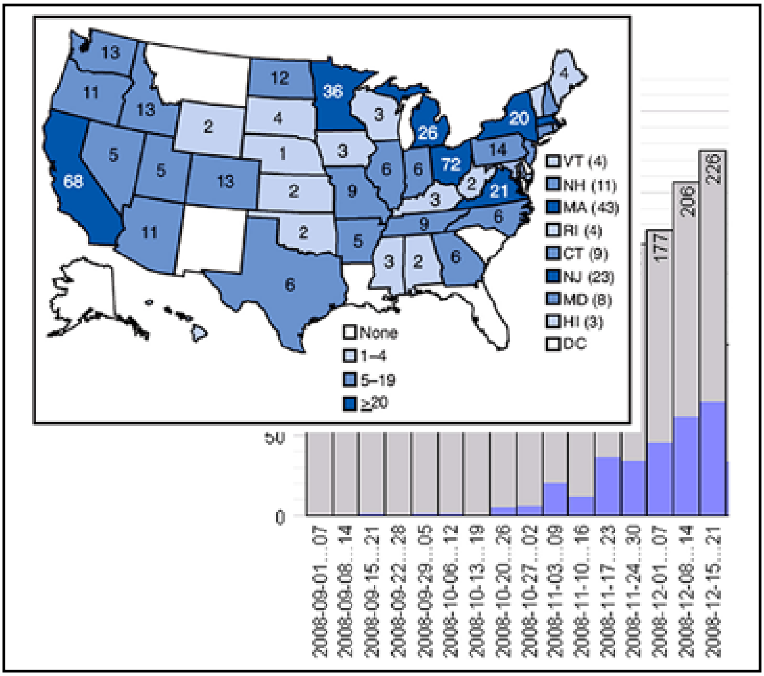

Figure 11. All *Salmonella* Typhimurium 9/1/2008–12/15/2008, weekly; JPXX01.1818, JPXX01.1825 and JPXX01.0459 highlighted.

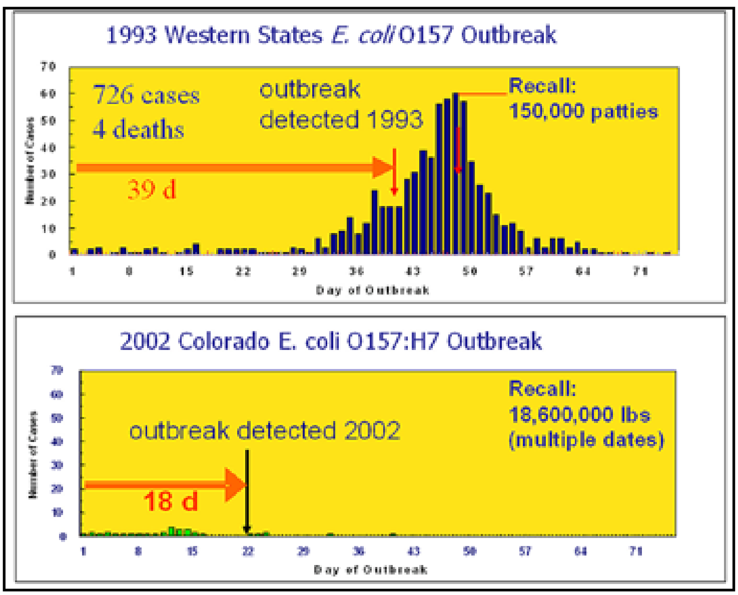

Figure 12. Foodborne outbreaks of disease caused by *E. coli*, before and after PulseNet.

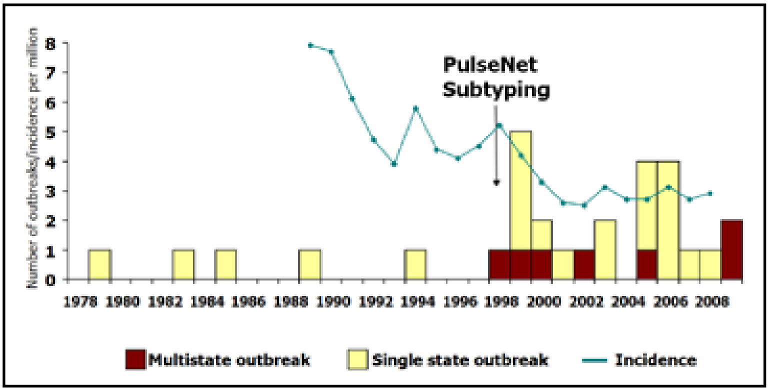

Figure 13. Listeriosis in the United States, 1978–2008.

Bioterrorism

The only major act of foodborne terrorism in the United States occurred in 1985, when—to influence an election—members of the Rajneeshi sect in Oregon contaminated the salad bars of ten local restaurants with salmonella, infecting 751 people, of whom forty-five received hospital treatment; all survived. The source of the infection took months to identify, whereas if it occurred today it would likely be detected and resolved quickly.

Global Surveillance

Our system is the most sensitive method for detecting unrecognized problems in our food supply—including from terrorism—with organisms that are under surveillance. PulseNet has been so successful in the United States that it has been adopted in many other countries. PulseNet International comprises eighty-four countries. The system in Canada is fully integrated with that in the United States. The Chinese have recognized the negative impacts that foodborne disease can have on trade and they are putting a lot of resources into PulseNet China. PulseNet Latin America and Caribbean is operational. However PulseNet Europe isn't fully integrated because some of the countries there prefer to operate autonomously, and many of the counties in Germany act like independent states. A benefit from the recent *E. coli* outbreak in Germany may be a refocusing of effort in Europe on disease surveillance.

Food is a global issue. Meat, and ingredients in processed meat products, consumed in the United States come from all over the world. The importation of fruits, vegetables, meats and grains has been increasing with our free trade agreements. Even the components of bread come from abroad. Clearly, foodborne disease is a problem of global scope and has to be solved in a global manner.

Current Limitations

A number of limitations exist:

- We have minimal ability to control strain evolution.

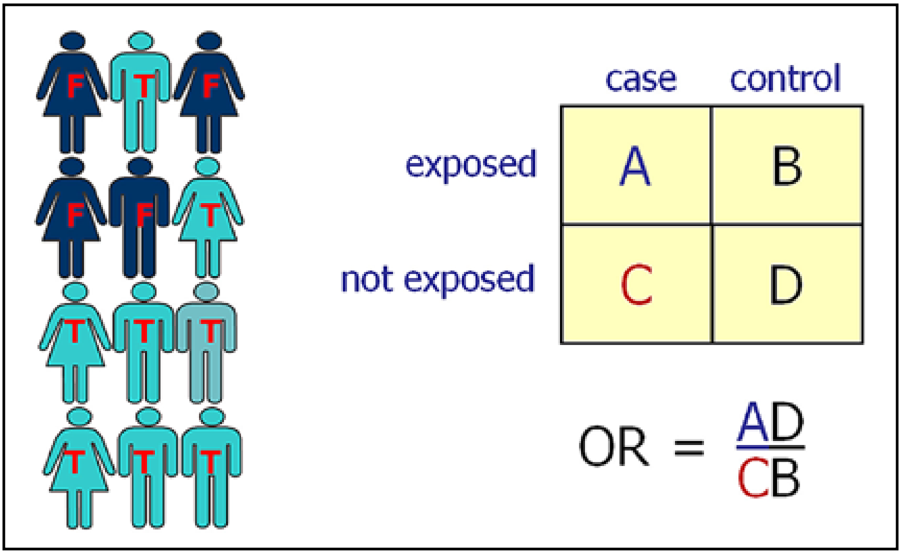

Figure 14. Case definitions for cluster detection and hypothesis generation/testing—1.

- The system is inherently slow and at every outbreak the media question why it takes so long to get information.
- Exposure information is difficult to obtain.
- Effective surveillance is limited to pathogens we know and can detect.

Strain Resolution

Figure 14 shows a group of cases with a particular disease, some of whom are truly associated ("T") or falsely associated ("F") with a particular product in an outbreak setting. Of course, when cases are reported to the public-health authorities, it is never known what they have been associated with. And on the right of the figure is a measure of association that is used in case-control studies when looking at what exposures ill people ("case") had vs. people who are not ill ("control"). This produces a statistical measure, the odds ratio (OR), which I will use to illustrate how sub-typing and case classification help strengthen the association between illness and exposure. If we limit our study to individuals who are more likely to have a common association—in other words if they share a fingerprint pattern in their pathogen—we eliminate cases that are more likely to be falsely associated than truly associated (Figure 15). This improves the proportions in our statistical analysis, and increases the strength of association between illness and exposure. For a more-stringent case definition, we could use two PFGE enzymes instead of one (Figure 16A) and knock out some of the additional falsely included cases; however, we start knocking out truly associated cases as well. If we keep doing that and use, say, ten enzymes (Figure 16B), then fewer cases are left and eventually confidence in the results becomes smaller with smaller sample size. Eventually, with whole-genome sequencing every case would be

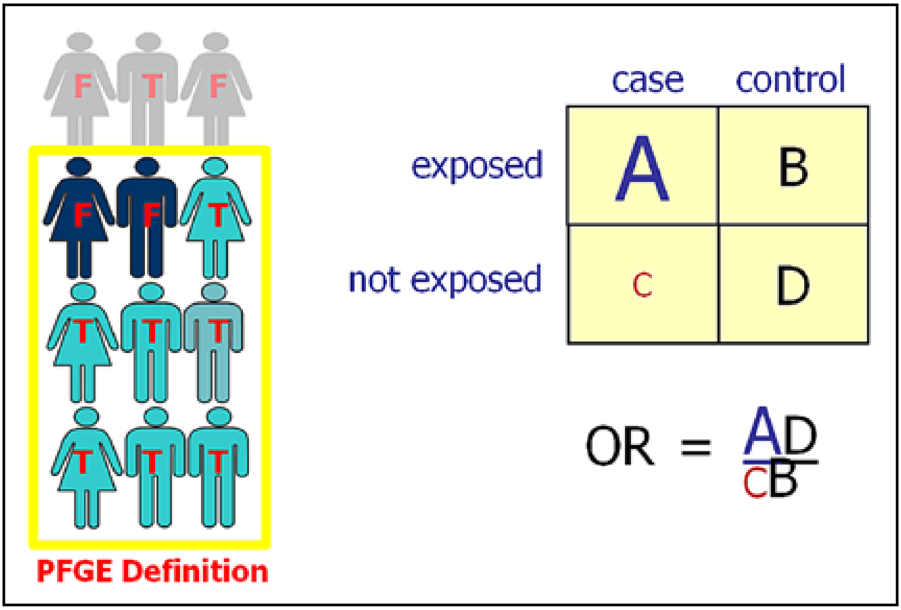

Figure 15. Case definitions for cluster detection and hypothesis generation/testing—2.

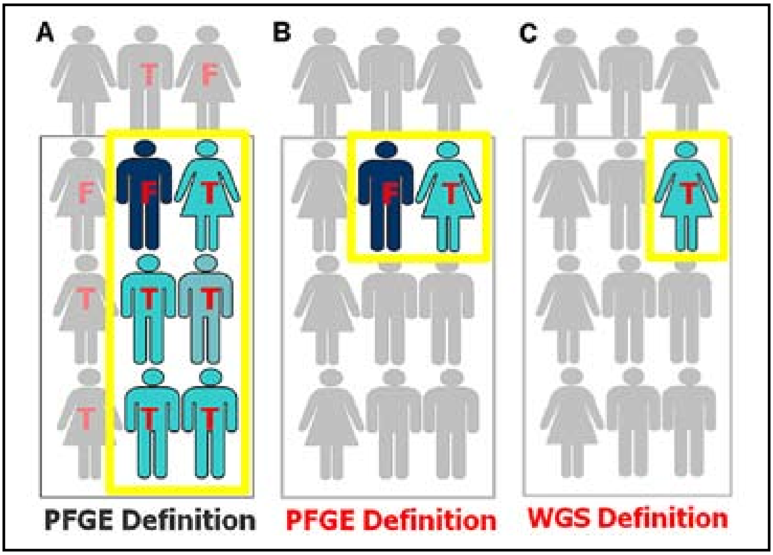

Figure 16. Case definitions for cluster detection and hypothesis generation/testing. A–two-enzyme PFGE case definition, B–ten-enzyme PFGE case definition, C–whole genome sequence case definition.

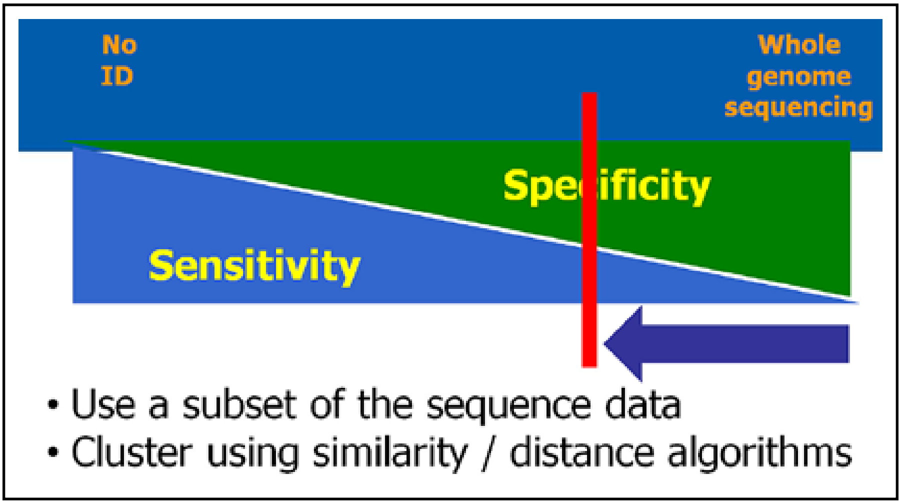

Figure 17. Relationship between sensitivity and specificity.

different from every other case and we would have 100% specificity and 0% sensitivity (Figure 16C), which would be as specific as you could have a case definition.

This relationship between sensitivity and specificity exists in all laboratory tests. At one end of the scale there is full specificity and zero sensitivity, whereas at the other end of the scale there is sensitivity with no specificity. Grouping together people who are sick, without knowing if they have salmonella or *E. coli*, would be a very inclusive case definition without specificity; it would be difficult to show an association between illness and exposure. We need to "move the bar" (Figure 17) to get a strong signal that's neither too specific nor too sensitive. It has to be somewhere in the middle, which is achievable by using a subset of our data or clustering algorithms, like tuning a radio by maximizing the signal and minimizing the noise. One of the impacts of new technology is fine tuning our signals. When we layer upon that different time intervals and geography, we can look at demographics. These can be done simultaneously in an automated fashion to have multi-dimensional continuous analyses of surveillance data. This would not have been possible a few years ago because of the massive amounts of computing necessary. Soon we will be able to look at surveillance data exposure by exposure and ask the question, "Are any of these exposures potentially different from what we would expect?"

Slow System

Sick patients have to seek medical help and provide stool samples (Figure 18). The pathogens have to be cultured and identified. The cultures have to be shipped to the public-health laboratory. Each case has to get interviewed, and each culture has to be serotyped and sub-typed. This process can take anywhere from a few days to a few weeks. The most important part of the procedure is that interviewed cases must recall what was eaten approximately three weeks prior. It's amazing that the system works as well as it

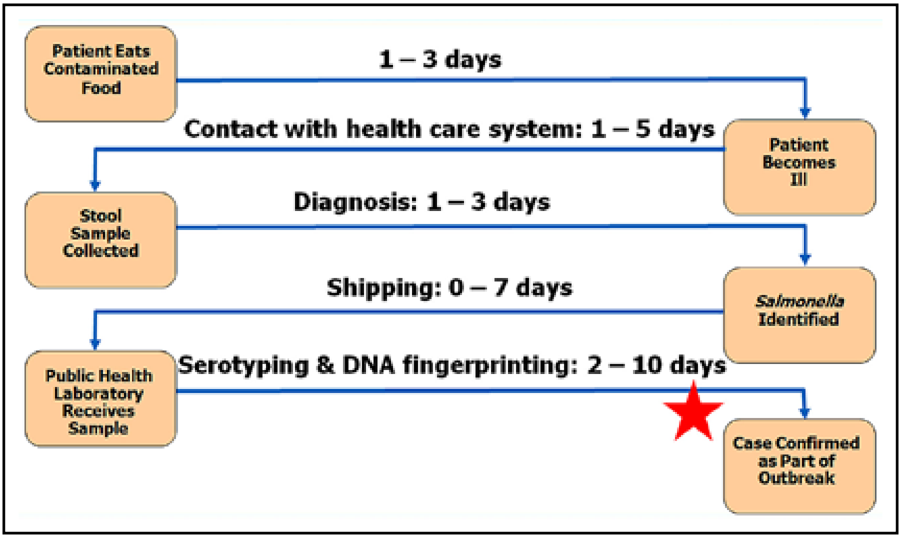

Figure 18. The surveillance process: laboratory reporting takes time

does. But recall drops off asymptotically with time. Ability to remember what was eaten three weeks ago is low, but it's orders of magnitude lower after four weeks, five weeks and six weeks, and at some point reaches zero.

There is potential to shave off a substantial amount of time by developing laboratory tests that can be done directly when the isolate is identified. Sub-typing could be done in doctors' offices and the results electronically communicated to PulseNet.

We are developing a rapid plate test for shiga-toxin-producing *E. coli* to simultaneously look at sero-type and virulence factors—whether it has shiga toxin, what type of shiga toxin, and whether other toxins are produced. And new tests are coming into clinical laboratories—where one would go to have an illness diagnosed—that are rapid and don't necessarily need stool samples. Accordingly, we need a crash research program to change from PFGE to something else. Although PFGE works well, we need alternative, more-rapid options. Certain micro-arrays can generate data directly from the stool, and we are looking at the possibility of single-cell sequencing of DNA. Experts from around the world will confer with us in Atlanta in November, 2011, to discuss technologies that will help us get at this problem.

Exposure Information

To identify an outbreak, we have two sources of information. The germs that made people sick and the interviews about what the people ate and what they did. We have discussed the technology that helps us get at the issue of the causal bacterium. Referring back to Figure 14, determining who is a "case" and who is a "control" is helped by the microbiological methods and PulseNet, but determining who was exposed and who was not exposed comes from the interview. Mathematically, from the 2×2 table (Figure 14), they are equally important and we are starting to focus on refining this issue. We've developed what we call OutbreakNet sentinel sites, of which there are, currently, five in the United States, with the goal of development of multiple models to serve the many systems used by states for:

- rapid collection of standardized exposure data,
- rapid laboratory testing (including PFGE),
- rapid cluster investigation, and
- rapid product tracebacks and environmental assessments.

Some of this is technology-related and some not. A chief requirement is a commitment from government to follow up, as Minnesota does, on all of the cases to extract good information. The states have different political systems, with different issues to be addressed. Therefore, we are trying to develop different models that will work in different locations around the country. Ultimately, we want all of the states to function at a high level, whereas currently they are operating, on average, at about 5% of potential. It's amazing what we have achieved at 5%, but what we could do if all states were operating optimally is astounding.

The FDA recognizes this and they are now emphasizing informational trace-backs (Figure 19). When clusters emerge, they can start triangulating back on products through each case. Industry also needs to work actively at making their products traceable. In the produce industry, in particular, problems can result from commingling of products. The 2006 *E. coli* outbreak, linked to spinach, resulted in the whole industry going down for a long period of time. With a rapid trace back, the intervention could have been confined to a single farm in California. Industry is starting to recognize that it's to everybody's advantage to make products traceable and new technologies are being developed accordingly.

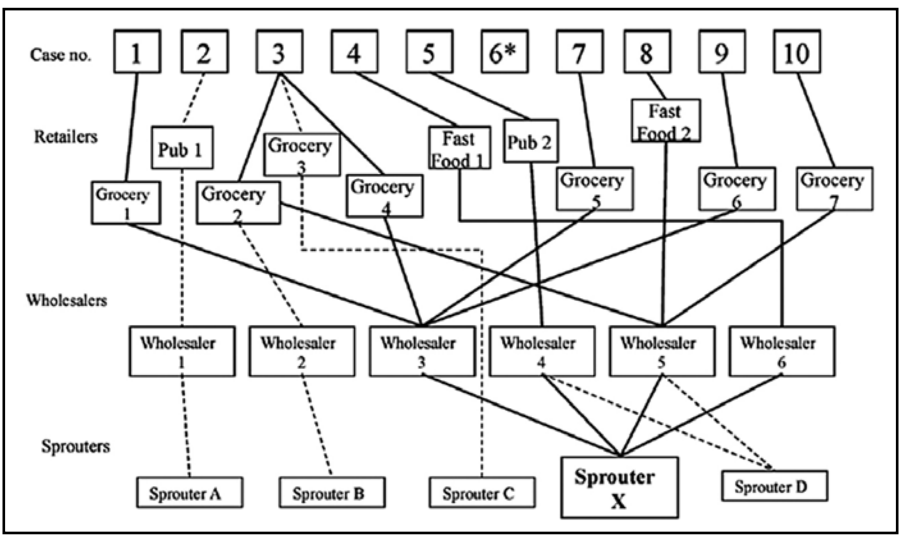

Figure 19. Epidemiology trace-backs.

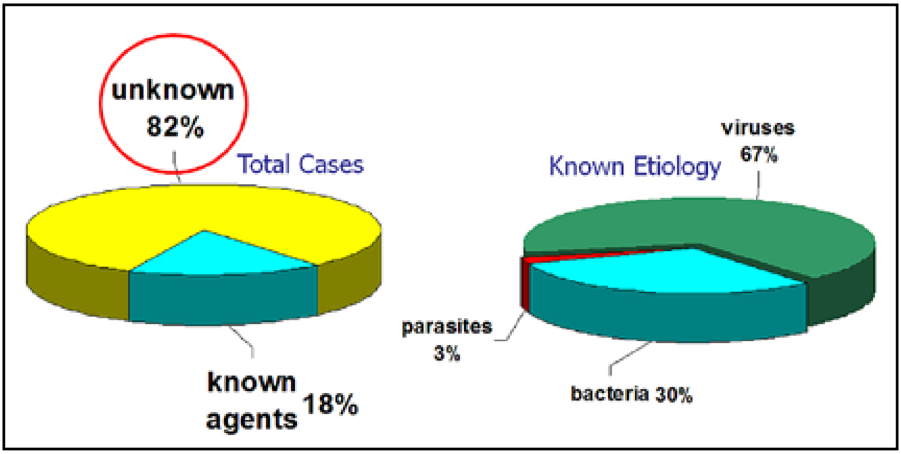

Figure 20. Etiology of acute gastroenteritis in the United States.

Pathogen Limitation

Surveillance is limited to pathogens that we know about. Data suggest that most foodborne pathogens fall into the "unknown" category (Figure 20). The bacteria that we track constitute only 30% of those that cause gastroenteritis. PulseNet and OutbreakNet activities cover only about 3.5% of all the cases of foodborne disease.

What interventions would be possible if we knew what pathogens cause the other 96.5% of cases? It's hard to get at, but outbreaks of undetermined etiology present the possibility of finding out what's actually making people sick. There are so many germs in the human gut, it would be very difficult to say which are causing disease. However, outbreaks provide a means for detecting pathogens and for triangulating them to the cause of the illness. When I worked in Minnesota, we did a national study of outbreaks of undetermined etiology and quickly found a number of new pathogens; this is worth pursuing nationally.

By employing metagenomic analyses, it is now possible to examine every single germ in the human gut of every single case. It's not easy or cheap, but it's possible and it will become less expensive. We then look at each germ as a risk factor for disease through our statistical analysis. As mentioned, these new methods are changing the way we view germs. Each time we sequence the genome of a germ, we find additional genes, with only about 3,000 genes stably present. It appears that, in nature, germs maintain only part of their genetic potential in their cells. The other genes are in the community and the cell can access different qualities as they need them. It's an efficient way of evolving. This is exactly what we saw in the recent sprout-associated outbreak in Germany. The pathogen picked up new factors to help it adapt to a new niche. Not only will we be able to detect new pathogens, we will be able to detect the potential for outbreaks of disease like that in Germany by understanding not just the individual germ, but the whole system and its potential to cause harm to humans.

Scientists in approximately a hundred groups around the world are sequencing all of the strains from Germany and comparing those that cause hemolytic uremic syndrome to those that don't, with virulence studies in animals. It will be one of the most studied germs in history, thanks to new technology. There are now elegant new ways of looking for new types of germs. Using metagenomic techniques, Ian Lipkin found a putative cause for colony collapse disorder that affects honey bees. Handheld metagenomic devices now are coming onto the market that will allow us to identify new pathogens more quickly.

John Besser has served as the deputy chief of the Enteric Diseases Laboratory Branch at the Centers for Disease Control and Prevention since July 2009, where he is involved in national and global programs, to detect, characterize, and track enteric infectious diseases.

For two decades before joining the CDC, Dr. Besser managed the clinical laboratory at the Minnesota Department of Health where he was involved in the development of PulseNet and other innovative disease-surveillance programs. He received his BS, MS, and PhD degrees from the University of Minnesota.

Emerging Food System Defense Risks and Technology Needs

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Figure 1 shows how we tend to define the differences between security, safety, defense and protection. In engineering terms, security is a sufficiency definition: you have a sufficient supply. Safety is a reliability definition: the system reliably prevents unintended failures. Defense is a resiliency concept: how resilient the system is to intentional or catastrophic perturbations. Then protection is the continuum of safety and defense. Almost everything that impacts food safety also impacts food defense, and the reverse is also true.

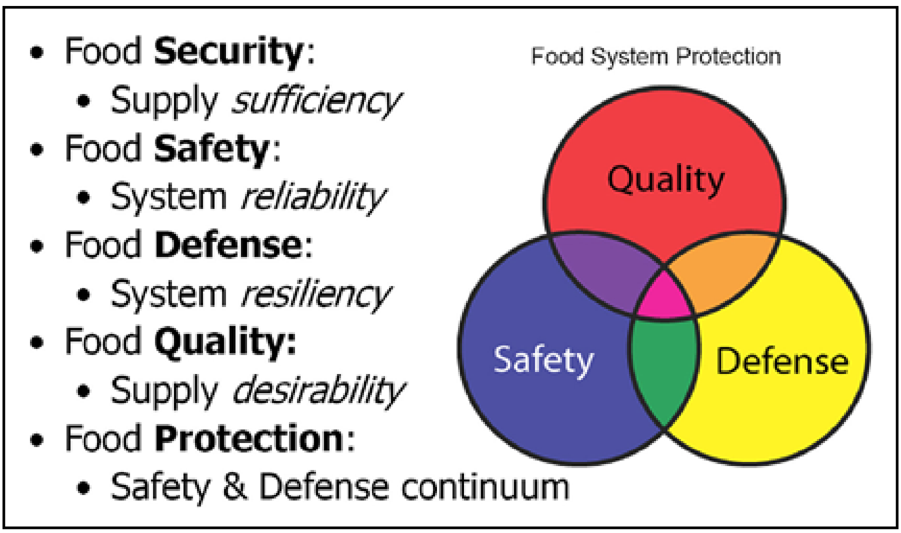

Figure 1. Food continuum paradigm.

I will discuss emerging intentional threats and examine technology needs in two areas: the food-system drivers that generate concerns for intentional contamination; and the intentional contamination drivers. We will deal with each of the items in Figure 2, because aspects inherent in our food system make intentional contamination a concern and there are behaviors of individuals and groups that also make intentional contamination a concern.

John Besser[1] talked about delay in identifying foodborne illness outbreaks and Figure 3 provides a simple way of illustrating part of that problem. First, the food has to be consumed, and then onset of illness presentation is delayed, during which there is no opportunity for public-health recognition. Therefore, foodborne-illness outbreaks usually occur after the peak of consumption, which is a problem for investigating the source. And while that is bad for normal foodborne illness, for intentional contamination with highly pathogenic agents, it can be catastrophic.

- Food system drivers
  - Public health surveillance system
  - System complexity & Globalization
  - Developing world value added agriculture
- Intentional contamination drivers
  - Economically motivated adulteration
  - Disgruntled employees
  - Criminals and deviants
  - Terrorists

Figure 2. Emerging intentional threats.

Epidemiology of an Outbreak

Figure 4 illustrates that delay with the epidemiological curve of the 2006 disease outbreak in the United States caused by *E. coli* O157:H7, associated with spinach. The initial contamination occurred on August 16, and the first case was reported on August 20. On September 8 the first clusters were detected through PulseNet in Oregon and western Wisconsin. And then, on September 14, the FDA made what was considered a rapid announcement of a recall of a product based solely on public-health information. The problem is that the circle (Figure 4) indicates when the product's shelf life had expired. Therefore, the product had expired 10 days before the announcement was made; the

[1]Pages 173–189.

product was gone by the time the recall was announced, and for episodic contamination events, this tends to be the case. Recalls are announced when there is actually very little left to be recalled. In systemic contamination events, like that of the Peanut Corporation of America (PCA), we have a greater opportunity to do a recall for effectiveness because

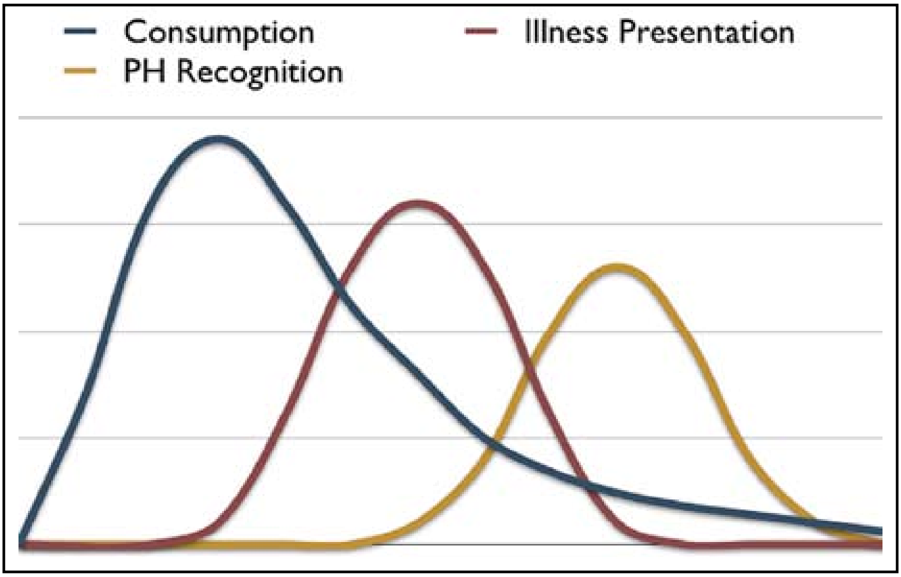

Figure 3. Food-event identification timing considerations.

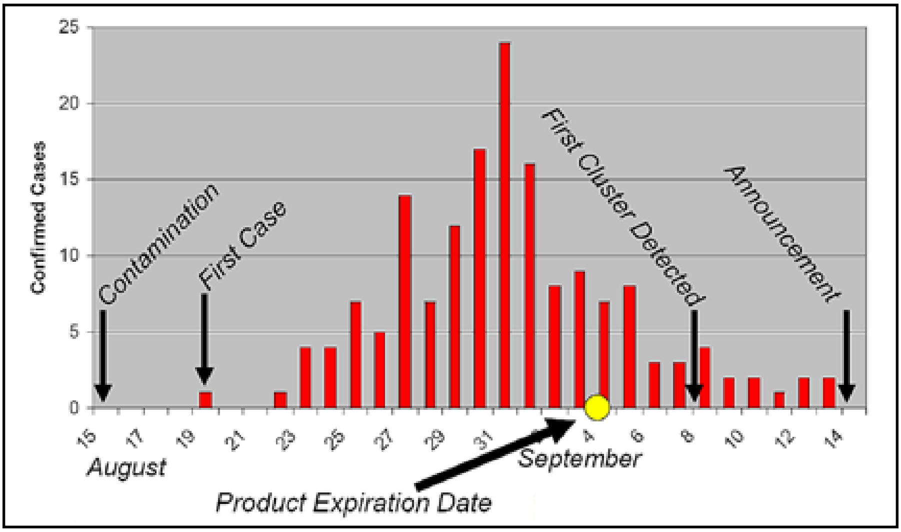

Figure 4. Spinach *E. coli* O157:H7 contamination challenges of rapid event detection.

low-level contamination is on-going. Unfortunately for food defense, foodborne illness is more likely to be episodic and developing methods for earlier detection is important. That is, as was pointed out[2], a function of the variability and effectiveness of the public-health system by state.

The Center for Science in the Public Interest went through data from the Centers for Disease Control and Prevention (CDC) from 1998 to 2007 and categorized the numbers of foodborne-illness outbreaks reported by state per million in population (Figure 5). This study revealed wide variation in the effectiveness of state public-health systems. From an intentional contamination standpoint, these data raise a concern; a terrorist is more likely to strike in the southern states. Trying to improve our public-health capabilities at the state level, including addressing the inherent technology bias, is an important part of our food-defense preparedness.

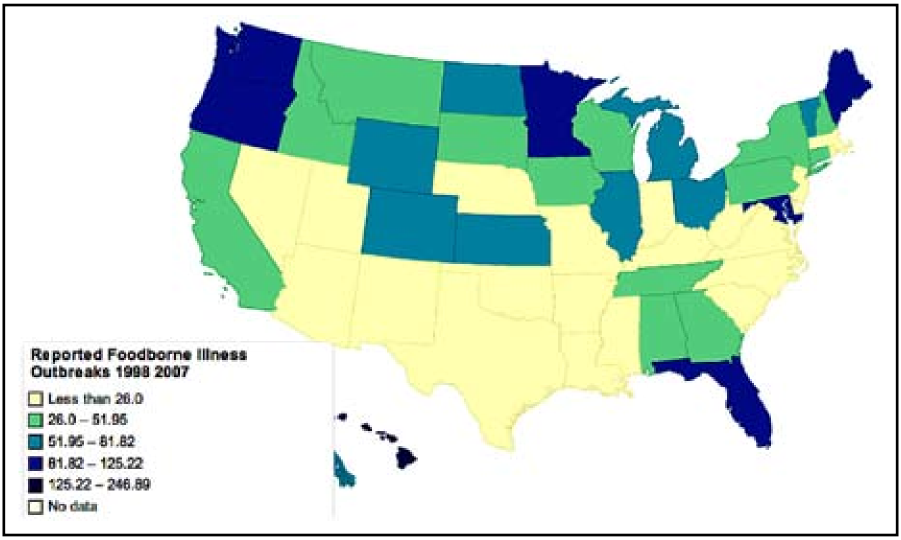

Figure 5. Wide variation in state outbreak performance:
Foodborne illness outbreaks per 1,000,000 population 1998–2007.
(source: Center for Science in the Public Interest)

Traceability

Traceability is affected by the complexity of our food system. Figure 6 provides a simplified characterization of the supply chain for a cheeseburger and, at the bottom of the figure, the major points of distribution from primary production through processing to consumers. If a terrorist announced that he had contaminated the supply chain at three points and nothing else, roughly 48,000 permutations and combinations of threat scenarios would have to be worked through to determine the contamination profile. A daunting task. Figure 7 shows the ingredients of a Big Mac, taken from the McDonald's nutrition

[2]By John Besser, page 187.

website. Now, if a terrorist announced the same thing—supply-chain contamination at three points—the potential contamination scenarios would be increased from 48,000 to 2.5 million. Furthermore, each ingredient has its own supply chain, therefore achieving traceability for all ingredients in all products is still not achievable, although it's something the industry is working toward.

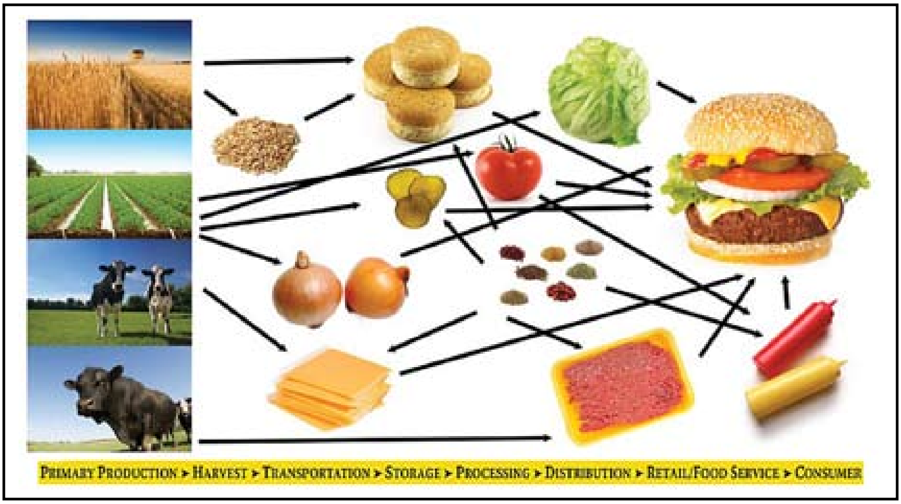

Figure 6. Global supply-chain complexity, cheeseburger–1.

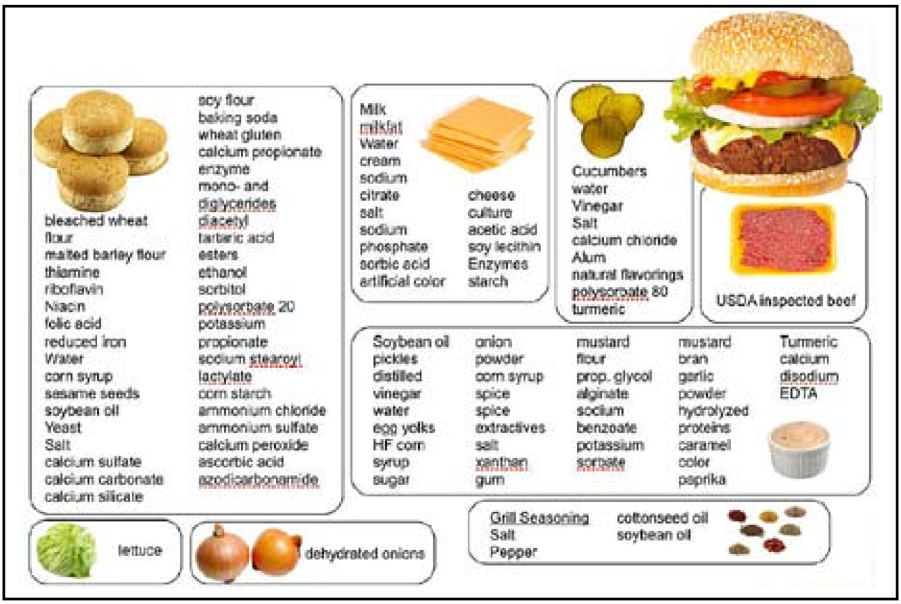

Figure 7. Global supply-chain complexity, cheeseburger–2.

Sometimes these supply chains fall back upon themselves, which was a complicating factor in the 2009 PCA case. Figure 8, from FDA, is a simplified characterization of the traceback of the PCA peanut paste, illustrating that some of the paste went from manufacturer to distributor back to manufacturer to distributor back to manufacturer to distributor before it finally entered retail trade. These multiple processing steps made it difficult for companies to deduce if they actually had the peanut paste in their products. The supplier of peanut paste to an ice-cream manufacturer may have no idea where the paste comes from. As an illustration of the complexity of this particular recall, from its announcement until the final product was recalled was 16 months; it took that long for the last company to figure out that it had shipped a product that contained the peanut paste. The needs for improved traceability to help us improve food safety and food defense are clear.

Global Economy

In Figure 9, countries in color are those to which the United States exported food products in 2010. We provide foodstuffs to almost every country. Figure 10 shows countries from which the United States imported food. Several of these source countries don't like us very much, like Iran, or don't have strong food-safety systems, like most of central Asia.

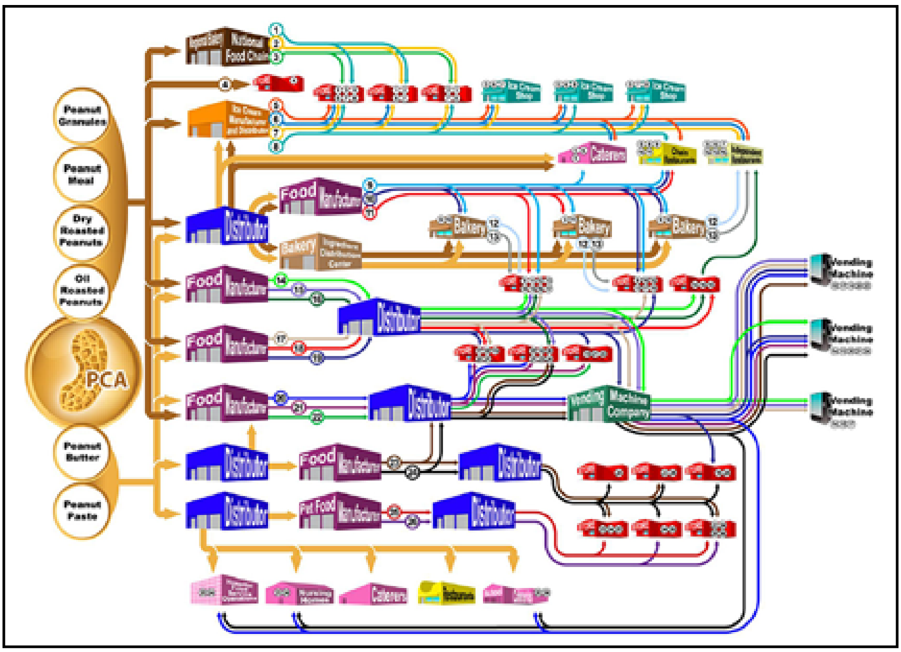

Figure 8. Peanut-paste supply chain.
The circled numbers represent products that were made using at least one ingredient originating from PCA's peanut-processing facility in Blakely, Georgia.
(source: FDA)

Some aren't logical sources of food products such as sugar from Zimbabwe, which has a dysfunctional food-system infrastructure; that we import any food from there is surprising, and whether it is safe is highly doubtful.

Figure 9. 2010 US food-export destinations. (source: USDA-ERS)

Figure 10. 2010 US food-import sources. (source: USDA-ERS)

Clearly, the food system is globally interconnected, and, to illustrate further its complexity, the numbers in Figure 11—from the FDA's bioterrorism registration database—show suppliers of food to the United States that are either in the United States or at foreign locations. More foreign processing sites are registered overseas to provide food to the United States than are registered in the United States. More foreign packers and repackers are registered to provide food to the United States than are registered in the United States. We are heavily dependent on the global system. Internationally, we have no idea how many farms supply the United States. On a recent visit to China, I asked representatives of several agencies how many farms are in the country and the estimates ranged from 20 million to 200 million. With an error bar so large, it is impossible to estimate the risk profile, and characterizing and understanding our supply chains is an important aspect both in food safety and food defense. We refer to this as "supply chain visibility."

Returning to the cheeseburger, Figure 12 shows source countries for some ingredients—vinegar, garlic powder, tomatoes, beef and wheat gluten—some of which, again, don't make sense. On the other hand, the fact that we import beef from Australia is a good thing as their food-safety system is probably better than ours. The fact that we import wheat gluten from Kazakhstan may be not such a good thing. Understanding where ingredients come from and what risk they pose is a challenge for industry and for the government.

As a developing country progresses from commodity production to value-added production, it becomes a different type of contributor to our supply chain, which may introduce new risks. The United States funds such development because it helps promote local economies. For example, the United States has helped develop the pomegranate business

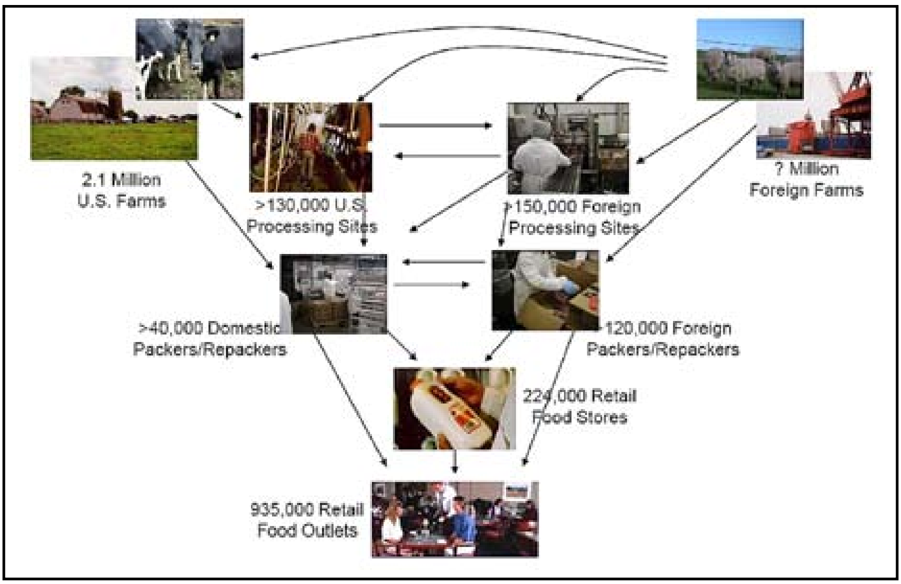

Figure 11. The US food system is increasingly global.

in Afghanistan, partly because Afghanistan produces perhaps the tastiest pomegranates in the world. However, "product of Afghanistan" on the label probably is not a selling point for many US consumers.

It is important to understand that the tariff system can blind us as to where imported foods and ingredients actually come from. Figure 13 shows the relative sizes of imports to the United States of cocoa and cocoa preparations, revealing that Canada is our single largest source of cocoa and cocoa products. Under the sugar tariff, it costs less to import sweetened cocoa liquor than to bring in cocoa powder and sugar separately. Realizing this, industry has set up supply chains that utilize Canada as a blending site. Clearly, using import data as a basis for raising concerns for food safety or food defense is entirely insufficient.

Economically Motivated Adulteration

Other trade data are surprising. We import wheat gluten from Singapore and shrimp from a landlocked country in central Asia that doesn't like us. From the challenges of understanding developing agriculture and how we must ensure that those countries develop their food-safety and food-defense infrastructures as they expand their agriculture, we must be concerned also regarding economic crises and greed leading to economically motivated adulteration (EMA)—intentional contamination of food products to make money. The most recent familiar example is the contamination of proteins in dairy products in China with melamine—for financial gain—that resulted in 290,000 children being made ill. EMA is viewed as a food-defense issue not because it is an intentional threat to public health, but because it illustrates the ability to evade the quality-assurance systems that are in place, simply to make a profit. If someone with a profit motive can get around the quality-assurance systems he could get around them to cause harm. One of our concerns is that some EMA events are test runs before serious contaminants are applied.

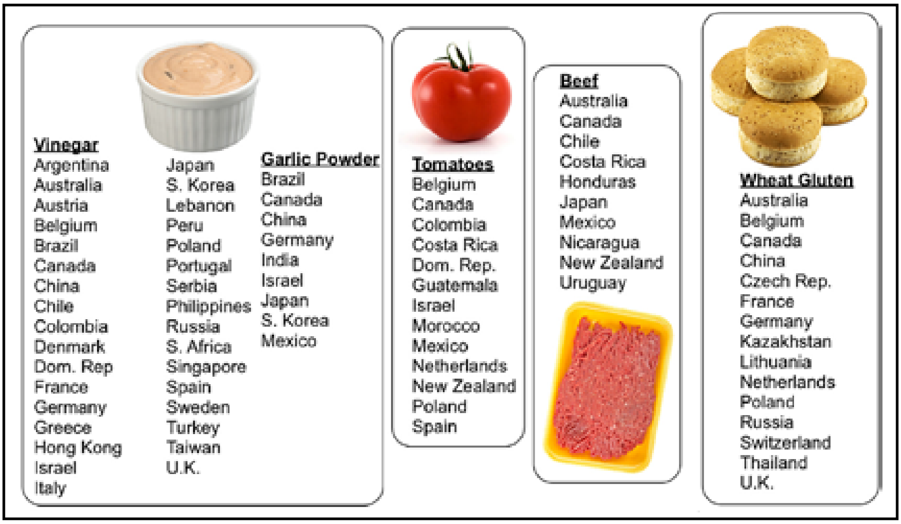

Figure 12. Globalizing the cheeseburger.

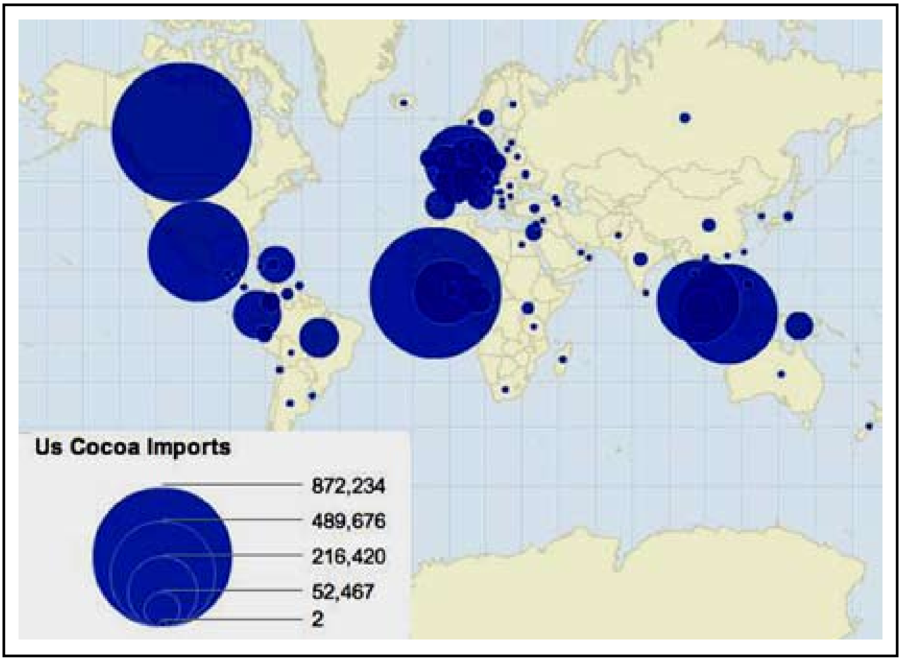

Figure 13. 2010 Cocoa and cocoa-preparation imports to the United States.
(source: USDA-ERS)

It is surprising how commonly EMA occurs and in how many ways. The data in Figure 14 are from FreightWatch, a trade group that appraises problems in the freight industry. In 2009, electronics and food/drink, at 23% and 20%, respectively, were the largest causes of theft from over-the-road trucks. Several semi trailers disappear each week and the goods sold. How can one be sure that the robbers don't contaminate the product before selling? Three years ago, a truck of contaminated ground-beef patties was stolen from a detainment lot before they could be disposed of. The patties were sold door to door in Texas and to restaurants.

Figure 15 shows products that, in recent years, have been the focus of EMA activity. When a company is hit by an EMA event that goes public, it results, according to the Grocery Manufacturers Association (GMA), in significant loss of revenue, between 2% and 15% for that year. The total annual impact is estimated at $10 billion to $15 billion and, based on a GMA survey, up to 10% of products in retail may contain an adulterant.

Intentional Adulteration for Other Reasons

Another longstanding problem, as far as food defense is concerned, is the disgruntled employee, who, in frustration, does something to a product, usually to cause a loss of income to the company. For example, a former supermarket employee in Michigan added insecticide to ground beef, and, in Kansas, a woman contaminated salsa with another insecticide. In both cases the perpetrators—subsequently jailed—had issues with their

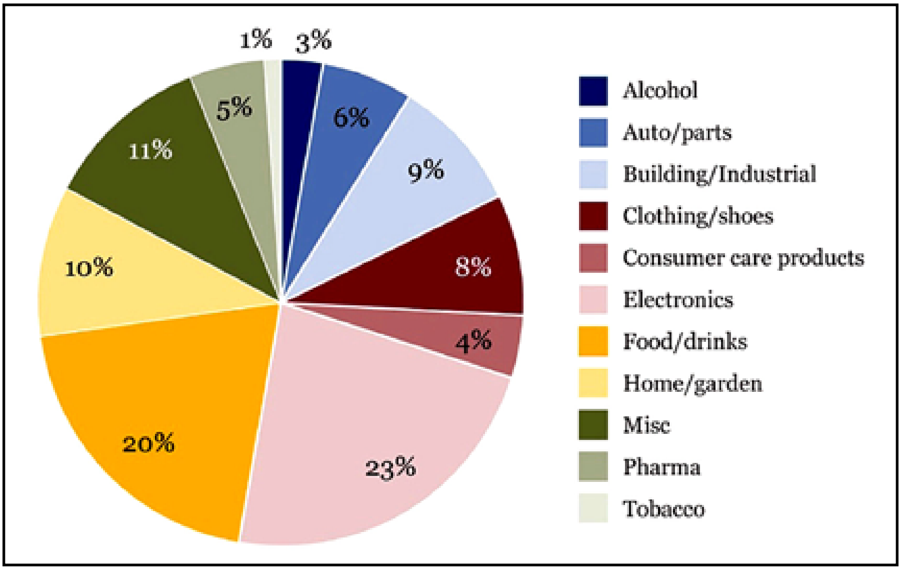

Figure 14. 2009 thefts by commodity: thefts of food and drinks are a significant problem. (source: FreightWatch)

employers and contaminated the food as a means of getting back at them. Forty and seventy people, respectively, were sickened, but if these crimes had been committed in large production facilities, the results would have been much worse.

Then there are challenges from criminals and deviants. For example, in the United Kingdom a man claimed to have contaminated baby food—with ricin—at nine branches of Morrisons Supermarkets. Because of the difficulty of proving a negative, the company had to remove all baby food from its stores in order to demonstrate safety. A hoax alone can cause significant problems for a food company. In Italy in 2008, someone injected a soapy solution into plastic bottles of water, the discovery of which caused mass economic harm to the bottled-water industry. Of greater concern was that the Italian police believe that it was a practice run to determine how many bottles could be contaminated before discovery, to see if it would be worthwhile as a terrorist target.

Intentional contamination by disgruntled employees and the like is not uncommon. From a study by Greg Dalziel, Figure 16 shows agents that have been used to contaminate food and the countries in which those contaminations occurred. These were contamination events designed to cause mass casualties, meaning three or more people. The list becomes lengthy with inclusion of the most common form of intentional contamination of food: spouse on spouse.

Then we get to extremist special-interest groups and threats they posed—such as the Rainforest Agribusiness Campaign, the Animal Liberation Front and the Earth Liberation Front that have issues with agribusiness in general and animal agriculture in particular. For example, the mission of the Animal Liberation Front mission is "to inflict economic damage on those who profit from the misery and exploitation of animals." Cases have been documented in which they have considered causing human-health harm as a way of eliminating agribusiness.

- Pet Food
- Vegetable Proteins
- Cooking Oils
- Mushrooms
- Apple juice
- Orange juice
- Grape juice
- Grapefruit juice
- Maple syrup
- Honey
- Infant formula
- Alcohol
- Bottled water
- Wheat flour
- Cough syrup

- Milk
- Dairy Proteins
- Liquid Eggs
- Gums
- Honey
- Vanilla Extract
- Olive oil
- Sunflower oil
- Seafood
- Horseradish
- Tofu
- Maple syrup
- Infant formula
- Toothpaste

- Shell Eggs
- Rice
- Cheese
- Tomato Sauce
- Fiber Supplements
- Luncheon Meats
- Pomegranate Juice
- Ground Beef - Water
- Ground Meat - Species
- Reduced Butter Fat Cream
- Basil
- Oregano
- Shrimp
- Dog Treats

Figure 15. Recently documented economic adulteration events.

Agents

- Arsenic
- Cyanide
- Feces
- Herbicide
- Household cleaner
- Insecticide
- Nicotine sulfate
- Pesticide
- Rat poison
- Tetramine
- Thallium

Countries

- Australia
- Canada
- China
- Hong Kong
- Iraq
- Italy
- Japan
- Korea
- Philippines
- Taiwan
- Thailand
- U.S.A.

Figure 16. Contamination events since 1998.

Terrorism

Perhaps our greatest concern is the possibility of catastrophic events caused by terrorists. As an example that this is something that people are considering, in 2006 there was an intentional contamination in Iraq of food served in a mess hall, run by Australia, that supplied the police force. The motivation was Shiite/Sunni sectarianism and resulted in at least 350 policeman suffering severe food poisoning, with many air-lifted out. In this low-tech event, the perpetrators simply let a couple of chickens ferment for a few days at ambient temperature before introducing them into the lunch-preparation process.

Such intentional contamination is not new. The first documented case occurred in 590 BC, when the Athenians poisoned the water and food supplies for Kirrha so that they could overrun that city. And during World War II, the Japanese experimented with a number of food vehicles as means of delivering pathogens in China and Manchuria, presumably as test runs for similar attacks on the United States. This included airdropping candies containing *Yersinia pestis* over a village to determine if infecting children would be more effective than infecting adults. In 1996, a laboratory technician at a hospital in Dallas, Texas, contaminated pastries in the break-room with *Shigella dysentariae*, poisoning twelve coworkers. As early as 2002, the Central Intelligence Agency identified contamination of food and water supplies with chemicals and the like as being of significant interest to terrorist groups. After the invasion of Afghanistan, documents found at Tarnak Farms training grounds showed how to prepare botulinum neurotoxin, how much would have to be introduced into the food supply to cause harm and the relative infective rates of other pathogens by oral ingestion. Al-Qaeda had been working on intentional contamination of food systems well before September 11, 2001.

Although there hasn't been a large-scale attack in the United States, effort in food-system defense is justified partly because of public opinion. Figure 17 shows that consumers would invest more in protecting the food system from intentional contamination than from any other type of homeland-security threat. The fact that consumers are most interested in protecting the food system makes sense because they can't take themselves out of the

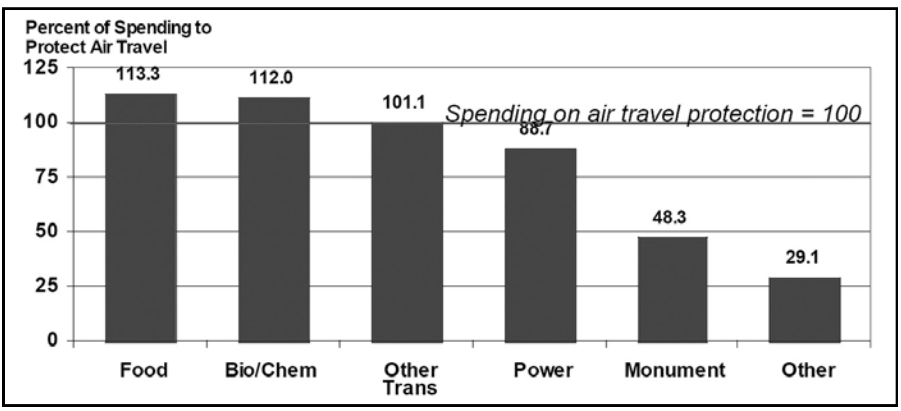

Figure 17. Public would spend more for food defense than for other threats. (source: Jean Kinsey)

target population. In their lives, they don't have to go to major-metro areas, they don't have to get on airplanes, they don't have to use trains, but they have to eat. Therefore, they want to be sure that the food system is protected. For the same reason, food-safety events have a high profile in the United States and other developing countries. People want to feel safe.

Risk Analysis

There are important conceptual differences between food safety and food security especially in terms of evaluating potential risks and vulnerabilities. Food-safety risks, as defined by the Food Safety Modernization Act, are reasonably foreseeable—events that are likely to occur and, therefore, have a probability function. Accordingly, it is possible to build economic models for investment of funds to address it. In contrast, food-defense risk is a deterministic problem that requires an intelligent adversary and not probable system failure; probability is driven by threat, which requires intelligence information. And given that we generally have little intelligence information on what adversaries are doing until they've already done it, determining probability for food defense is challenging. From an industry standpoint, companies that we have been working with approach this problem by looking at the difference in what the consequences are. They look at things as whether they are an operational risk vs. an enterprise risk:

- If it will be a write-off if it occurs, they will accept that risk and won't mitigate.
- If it will result in the potential for the firm ceasing to exist, they will invest to mitigate that risk.

The Society for Risk Analysis defines risk assessment as an analytical process to provide information regarding undesirable events. It's the process of quantification of the probabilities and expected consequences for identified risk; it's the probability of something occurring. Vulnerability assessment attempts to understand the effectiveness of the defense system. Therefore, the concept for food safety is risk assessment. For food defense it is generally vulnerability assessment. Now the Department of Homeland Security makes it a little more complicated for us because they define risk as including vulnerability; this is from Secretary Michael Chertoff[1]:

> *Our risk analysis is based on these three variables: threat, vulnerability, and consequences. These variables are not equal. For example, some infrastructure is quite vulnerable, but the consequences of an attack are relatively small; other infrastructure may be much less vulnerable, but the consequences of a successful attack are very high, even catastrophic.*

The important point here is understanding vulnerability. Chertoff pointed out that although some things are very vulnerable, the consequences of an attack would not be significant. There are other things that are relatively invulnerable, but the consequences of an attack would be high or catastrophic. With respect to intentional contamination, the government is more concerned over events that would be catastrophic rather than situations that are most vulnerable. Consideration of the aggressor is necessary because, without understanding the aggressor, the potential consequences cannot be understood.

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[1]See page 106.

Figure 18 provides a limited list of aggressor types, from the disgruntled insider to the compromised insider to the inserted insider, covert intrusion or perhaps one's own supplier. When food-defense work started in 2001, in most cases the focus was on covert intrusion; a lot of money was spent on guns, gates and guards. We were more worried about the compromised insider or the inserted insider—because they would have legitimate access to the facility and would know where to act—or the supplier because unless supply-chain verification is possible you don't know whether your supplier is a potential source of risk. Important also are potential aggressor objectives, ranging from system disruption to wholesale public confidence crisis that would result in a change in government:

- System disruption
- Brand damage
- Category damage
- Trade disruption
- Foreign affairs crisis
- Mass morbidity
- Mass mortality
- Wholesale public confidence crisis

Changes in government have occurred because of food-system failures. Look at the United Kingdom, the Netherlands and Taiwan. If we had a catastrophic food attack in the United States, we would likely have a change in government.

Detection

One of the technology needs for food defense and food safety is detection. But in detection we need to think about the approach. Are you detecting to prevent in order to control things at a site level so it never gets beyond the point where it is contaminated? Are you detecting to protect?; you may not detect it before it leaves the facility but you will detect

Disgruntled Insider	More likely to want to cause disruption/economic loss
Compromised Insider	Could be twisted to cause more significant harm
Inserted Insider	Will be able to find the most significant attack point
Covert Intrusion	Vulnerability varies significantly by system
Supplier	Importance of supply chain verification

Figure 18. Consider the aggressor.

it before it reaches the consumer. Or are you detecting to recover, also known as detect to regret; it's already out there and you are trying to find out how much is still out there. Detection raises challenges of what to test for and how. With respect to food defense, it becomes more challenging because, unlike the six most common organisms that are the focus of PulseNet, we have microorganisms that are normally associated with food and also those that are not normally associated with food as well as literally thousands of chemicals and toxins that are not associated with food at all, but are potential threats for intentional inclusion. And, unfortunately, for many of those micro-organisms, we don't understand their viability, toxicity or infectivity within the food system.

Reconsidering our public-health system and its capabilities, we have the challenge of an intentional food-system event being responded to even more slowly. Figure 19 shows data generated four years ago, when Sara Cox gave internal medicine program directors presentations for certain illnesses and asked them to make diagnoses. So, 70% of the time they got anthrax right on the first occasion. But they got plague right initially only 16% of the time. This goes back to the public-health problem of being trained to look for horses, not zebras; you are looking to diagnose something you are used to seeing, not something you are not used to seeing. If it is something you are not used to seeing, you are not likely to get it right the first time. We have a challenge on how rapidly we can identify these organisms with respect to how very rapidly our supply chains function (Figure 20). For example, bottled water, which has a potential shelf-life of several years, is likely to have an actual shelf life of only about 10 days. That's how fast it moves through the supply chain. If we don't improve our ability to detect contamination, any attack is likely to be of significant consequence.

Primary suppliers to quick-serve restaurants produce between 500,000 and a million pounds of hamburger patties a day. Once they clear quality assurance, they are shipped within 12 hours and after they get to the restaurant they are generally consumed within 48 hours. That's the speed at which the cold supply chain functions because of the cost of refrigeration. Carbon dioxide is a processing aid that speeds grinding and keeps the ground beef at about 1–2°C during grinding for good mouth-feel. An average of 66,000 pounds of CO_2 are used per 900,000 pounds of daily production. The CO_2 could be effectively used as a carrier to get a large quantity of contaminants into the ground beef. Depending on assumptions, perhaps 3.6 million people could be affected in less than 7 days by contamination of one CO_2 shipment.

In Summary

We need better capability for systems-based risk and vulnerability assessment. We need better tools for supply-chain visibility and traceability. We need improved ability to check threat agents, the ability to identify events as they occur and the ability to inactivate the agents and safely dispose of the product after the event.

At the National Center for Food Protection and Defense, our vision is defending the safety of the food system through research and education. Our mission is to reduce the likelihood of an attack, to improve the nation's ability to respond effectively and to reduce the consequences of an attack. Our goal, in brief, is to render targets unattractive.

- Based on case history presentations, correct diagnosis 30 internal medicine programs:
  - Anthrax: 70%
  - Smallpox: 51%
  - Botulism: 50%
  - Plague: 16%
- After a select agent training module, diagnoses improved to >70%

Figure 19. Physicians' ability to diagnose select agents.

- Leading yogurt manufacturer goes from plant to retail in all 48 states in <48 hours
- Quick serve restaurants can go from supplier to consumption in 24-96 hours for primary products (burgers, chicken, salad)
- Bottled water has an effective shelf life of ~10 days for 80% of production
- Only seasonally harvested and canned/frozen or specialty products have effective shelf lives of significance

Figure 20. Product speed to consumer: risks of supply-chain efficiency.

Shaun Kennedy is director of the National Center for Food Protection and Defense, a department of Homeland Security Center of Excellence. He is also the director of Partnerships and External Relations of the University of Minnesota's College of Veterinary Medicine and an assistant professor in the Department of Veterinary Population Medicine. In recognition of his leadership in research and graduate-education programs on animal health, food safety, and food-system defense, Mr. Kennedy received the Commissioner of the Food and Drug Administration Citation for advancing food defense. He provided the inaugural lecture in the FDA's Chief Scientist Lecture series and has served on several European Commission projects on food-system protection, among others.

Prior to joining the University of Minnesota, Kennedy held executive positions in Procter & Gamble and Ecolab. At Ecolab, he was vice president of global food and beverage research and development, leading his organization in developing a wide range of animal-health and food-safety technologies. These included novel sanitizers, FDA-approved process additives, new sanitation technologies, and animal-health products. Prior to this, he was director of strategic and emerging technologies at Ecolab, guiding internal and outsourced technology programs. At Procter & Gamble his positions included assignments in Japan and China, leading research and development teams and global programs.

Food Fraud: Public Health Threats and the Need for New Analytical Detection Approaches

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The US Pharmacopeia (USP) is an independent, not-for-profit, non-governmental, science-based public-health organization with a rich history of setting public standards since 1820, thus predating the Food and Drug Administration. Of course, most of that history is in pharmaceuticals, medicines and dietary supplements, and we started working on food-testing standards in the *Food Chemicals Codex*[1] (FCC) in 2006. USP is a volunteer-based organization. The information that goes into establishing our standards primarily comes from volunteers in industry and academia, and regulatory agencies, who bring those data to us, and then we have volunteer-cited experts who help to establish and determine whether our methods are suitable for their intended use.

I will discuss economically motivated adulteration (EMA), how it relates to food fraud and the public-health threat. I will talk about gaps in analytical technologies and I'll conclude by describing some of the things that USP is doing to modernize testing methods to deter EMA and fraud.

Economically Motivated Adulteration

I consider EMA to be a subset of food fraud. An expert panel at USP has defined EMA as:

> *The fraudulent addition of non-authentic substances or removal or replacement of authentic substances without the purchaser's knowledge for economic gain of the seller.*

The phrase, "without the purchaser's knowledge," which isn't included in other definitions of EMA, is important. With its removal, some people may think that this is what product developers do for a living—finding ways to reduce the costs of food formulations by find-

[1]http://www.usp.org/fcc/.

ing replacements for cream, for example, or for meat with soy-protein extender—which is not fraudulent when the product is labeled accurately. Alternative terms are "food fraud" (which we see as a larger term), "food counterfeiting" and "intentional adulteration." Examples of EMA include:

- Milk diluted with water
- Milk extended with melamine
- Wheat extended with urea
- Turmeric extended with lead chromate, and
- Olive oil diluted with hazelnut oil.

Dilution with water goes back many years to when milk was purchased on the basis of weight; it was easy to add the cheapest possible liquid, water, to artificially increase the value of that material. Of course, standards were developed many years ago to deal with that. Milk extended with melamine is a more modern example, resulting from the use of nonspecific technologies—Kjeldahl and other methods—that assay total nitrogen as an indicator of protein content instead of more specific methods. Wheat extended with urea hits close to home. It happened in the 1980s in Minnesota (FDA Consumer, 1990), and again resulted from using nitrogen as a surrogate for protein content. Several cases of lead-chromate extension of turmeric have been reported in India, where a lot of turmeric comes from. Recently, turmeric was recalled from US stores because of lead contamination (Terry, 2011), the possible culprit being lead chromate which has a yellow color similar to that of turmeric. This example provides a global perspective; what happens halfway around the world can impact us here. The olive-oil industry has had authenticity problems due to dilution with other vegetable oils. Hazelnut oil—commonly used because its fatty acid composition is similar—contains allergens and thus raises potentially serious public-health concerns.

Fraud Opportunity

Factors underpinning EMA include rising prices of agricultural raw materials, complex supply chains, and complex and variable compositions. Many of the new ingredients that we try to define and characterize are not simple food additives, but rather are complex, botanically derived ingredients that are difficult to characterize chemically and can vary season to season and with geographic origin.

Sophisticated fraudsters play into this. Some of them attend conferences on EMA, staying abreast of new technologies and one step ahead of quality-assurance (QA) systems. At USP, we feel that tools are lacking to prevent this sort of activity and, accordingly, it is a focus of our effort. Sociocultural aspects, as they affect ethics and what constitutes fraud, are important. Adherence to driving-speed limits provides a useful parallel. Do you drive right at the speed limit, five miles an hour over, or 10 miles an hour over? Sociocultural norms influence what is viewed as acceptable, irrespective of public-health considerations.

These factors together create an environment conducive to food fraud. No one knows its economic impact, but EMA most definitely is a multibillion-dollar industry.

Public-Health Consequences

As already indicated, fraudsters understand QA systems and constantly are designing adulterants and new food products to circumvent those systems. The QA system then evolves with development of new detection methods, and the end result is the creation of an endless list of new adulterants.

A good example is provided by cassia oil, an essential oil extracted from the bark of *Cinnamomum cassia* used in foods and other consumer products. For hundreds of years, rosin has been used as an adulterant, but specific gravity and optical rotation provided easy ways to quickly pick this up. Those methods were countered by fraudsters mixing kerosene and rosin together, which turned into a test for rosin specifically and is still described in testing-standard monographs today. As we moved into the twentieth century and the chemical compositions of essential oils became understood, it was discovered that cinnamaldehyde is a dominant constituent, which led to the addition of synthetic cinnamaldehyde to cassia oil to extend it. In due course, radiocarbon analysis was used to reveal the presence of synthetic cinnemaldehyde versus the biobased counterpart. In turn, fraudsters went back to the drawing board and came up with ^{14}C-enriched synthetic cinnamaldehyde, which can be analyzed only with site-specific natural isotope fractionation-nuclear magnetic resonance (SNIF-NMR), not an inexpensive tool for this purpose.

Food safety presumes knowledge of composition and, when the next adulterant is unknown, from our perspective, food safety collapses to a singularity, and that is the fraudster. The ethics and the knowledge of the fraudster define the safety of a food product throughout the whole supply chain. Melamine provides a good example. With an LD_{50} of 3.16 g/kg body weight (rat), it isn't particularly toxic. On the other hand, it caused the deaths of infants and pets. In the case of the pet-food scandal, some fraudsters used inexpensive, scrap-grade melamine that was contaminated with cyanuric acid, which hydrogen-bonds with melamine and creates a toxic co-crystalline complex that precipitates in renal tubules (Dobson *et al.*, 2008). In the case of infant formula, a similar situation prevailed. The melamine complexed with uric acid to form, again, a toxic co-crystalline complex, causing renal failure in infants.

The melamine example demonstrates that the fraudsters' ethics and, in this case, lack of knowledge—they didn't understand the toxicity of melamine and related compounds—defined food safety throughout the supply chain.

Reducing the Risk

A multi-pronged approach is needed to reduce the risk of EMA. Industry resources are being invested to manage their supply chains, know their suppliers and do trace-back, to implement good QA systems and management practices, to introduce HACCP[2] systems in their suppliers, audits, *etc*. Testing is an important component. It "anchors" the food-

[2]Hazard analysis and critical control points is a management system in which food safety is addressed through the analysis and control of biological, chemical, and physical hazards from raw-material production, procurement and handling, to manufacturing, distribution and consumption of the finished product.

safety system in reality by guaranteeing ingredient authenticity. All QA systems are built on the assumption that ingredients brought into the plant are genuine. For example: it's milk, not milk contaminated with melamine.

In terms of analytical approaches to help verify ingredient integrity, testing for a known adulterant is the easiest thing to do. Liquid chromatography triple quadrupole tandem mass spectrometry (LC-MS/MS) and gas chromatography/mass spectrometry (GC-MS)—relatively simple methods—have been developed to test for presence of melamine. The downside of this approach is that just because an adulterant is known does not guarantee that it will be detected. Melamine is good example. Pet-food adulteration occurred in 2007 and again in 2008, but people were obviously not testing for melamine when the milk-contamination scandal occurred in 2008. The other factor to consider here is that it isn't economical or even feasible to ensure safety by testing for all known adulterants, the list of which keeps growing. And, lastly, unknown adulterants cannot be tested for. It's impossible to anticipate what the fraudster will come up with next, to take preventative action.

The analytical method predominantly used at USP to develop standards is the compendial approach, *i.e.* using identity and purity tests to verify the integrity, the authenticity of an ingredient. The concept is to detect EMA by looking for a decrease in the purity of an ingredient and by examining a fingerprint for an ingredient to check that it matches the known fingerprint. The advantage of this approach is that it can detect both known and unknown adulterants. For example, if melamine is present at a significant level, the specific assay for protein will reveal a decrease in purity, and the melamine will be detected in an ID test. It's a powerful approach, although its development is challenging.

USP's FCC is a compendium of testing standards. The FAO/WHO's Joint Expert Committee on Food Additives has produced a similar book, known as the "JECFA standards." Figure 1 shows the monograph developed at USP for rebaudioside A, a new stevia-based ingredient.

Compendial Testing Standards

It is important to note that compendial methods powerful enough to detect and deter EMA of many widely used food ingredients—*e.g.* wheat gluten, whey—are virtually nonexistent. Identification tests that work in compendial and rapid industrial settings remain to be developed. Many tests that do exist even for simple, single-constituent food additives, are outdated. They are nonspecific, often based on wet chemistry methods like solubility and flame tests. For example, gums, galactomannans, are discriminated by solubility tests that only poorly detect and deter EMA. Easy ways are available to the fraudster to circumvent these.

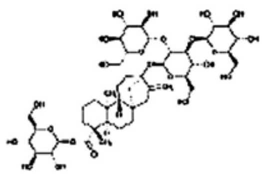
Regarding purity tests—"assay tests" in FCC—many nonspecific, outdated, again wet-chemistry tests go into these compendial standards that are not sufficient to detect and deter EMA. For example, the use of the Kjeldahl method as a way to measure protein. Many standards use titrimetric methods. Calcium-salt additives are determined by titration against EDTA, which fails to take account of anions that often are the more important constituent.

First Supplement, FCC 7 — *Monographs* / Rebaudioside A / 1

Rebaudioside A

First Published: Second Supplement, FCC 6

Reb A
Rebiana
Kaur-16-en-18-oic acid, 13-[(O-β-D-glucopyranosyl-(1→2)-O-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl)oxy]-, β-D-glucopyranosyl ester, (4α)
13-[(2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy] kaur-16-en-18-oic acid β-D-glucopyranosyl ester



$C_{44}H_{70}O_{23}$ Formula wt 967.01
CAS: [58543-16-1]

DESCRIPTION

Rebaudioside A is a white to off-white, hygroscopic fine crystal, granule, or powder having a sweet taste. It is freely soluble in ethanol:water 50/50 (v/v), sparingly soluble in water and sparingly soluble in ethanol. It is obtained from the leaves of the *Stevia rebaudiana* (Bertoni) plant in a multi-step separation and purification process. Principle steps include extraction of steviol glycosides from the leaves using an aqueous or aqueous alcoholic (ethanol or methanol) solvent, and purification of rebaudioside A from the resulting mixture of steviol glycosides by resin absorption followed by recrystallization from an aqueous or aqueous alcoholic (ethanol or methanol) solvent. It is composed predominantly of rebaudioside A, a glycoside of the *ent*-kaurenoid diterpenoid aglycone known as steviol.

Function: Nonnutritive sweetener; sugar substitute

Change to read:

Packaging and Storage: Keep dry, and store in tight containers at ambient temperature.■1S (FCC7)

IDENTIFICATION

- **A. Infrared Absorption,** *Spectrophotometric Identification Tests,* Appendix IIIC
  - **Reference standard:** USP Rebaudioside A RS
  - **Sample and standard preparation:** A
  - **Acceptance criteria:** The spectrum of the sample exhibits maxima at the same wavelengths as those in the spectrum of the *Reference standard.*
- **B. Procedure**
  - **Acceptance criteria:** The retention time of the major peak (excluding the solvent peak) in the chromatogram of the *Sample solution* is the same as that of the 4750 mg/L *Rebaudioside A standard solution* in the *Assay.*

ASSAY

Change to read:

- **Procedure**

■[Note—Rebaudioside A is hygroscopic, and accurate quantitative analysis requires moisture equilibration before analysis. Equilibrate sample and rebaudioside A standard specimens in the lab NLT 24 h before weighing. Intermittent stirring will ensure uniform moisture absorption. The *Water* content used in the calculation should be determined at the time of weighing and after equilibration.]■1S (FCC7)

Acetate buffer: Dissolve 0.125 g of ammonium acetate in 900 mL of water, adjust to a pH of 4.3 with glacial acetic acid solution, and dilute to 1 L. [Note—It may be necessary to adjust the ratio of ammonium acetate to acetic acid. Changing the pH adjusts the retention time of rebaudioside A and related glycosides. Decreasing the pH of the buffer will decrease the retention time of rebaudioside A.]

Mobile phase: ■13%■1S (FCC7) (v/v) *Acetate buffer* in acetonitrile ■1S (FCC7)

Diluent: 25% (v/v) *Acetate buffer* in acetonitrile. [Note—Allow *Diluent* to come to room temperature before use.]

Rebaudioside A standard solutions: ■250, 1000, 2500, and 5000■1S (FCC7) mg/L of USP Rebaudioside A RS in *Diluent*

Stevioside standard stock solution: 250 mg/L of USP Stevioside RS in *Diluent*

Stevioside standard solutions: ■0.5, 5.0, 25, and 250■1S (FCC7) mg/L of USP Stevioside RS in *Diluent;* from *Stevioside standard stock solution*

Sample solution: 5000 mg/L in *Diluent*

Chromatographic system, Appendix IIA

Mode: High-performance liquid chromatography

Detector: UV 210 nm

Column: 15-cm × 4.6-mm, packed with a propyl-amino silane phase bonded to silica gel (5-μm particle diameter)[1]

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection size: ■15■1S (FCC7) μL

System suitability

Samples: ■5000■1S (FCC7) mg/L *Rebaudioside A standard solution* and ■0.5■1S (FCC7) mg/L *Stevioside standard solution*■1S (FCC7)

Suitability requirements

Detector response: Peak-to-noise ratio (peak height/baseline noise) is NLT 3 for the stevioside peak from the ■0.5■1S (FCC7) mg/L *Stevioside standard solution,* where peak height is expressed in mAU, and baseline noise is the maximum deflection of the baseline (mAU) in a blank at the retention time of stevioside over the same baseline peak width in min.

[1] ■Cosmosil Sugar-D (Nacalai Tesque)■1S (FCC7), or equivalent.

Figure 1. USP-developed example of a food-ingredient compendial standard: rebaudioside A.

We are looking for ways to bring compendial testing technology into the twenty-first century. Although the technologies exist for many compounds, adapting them for real-time, accurate, and precise use as valuable compendial tools by industry will require tremendous R&D effort.

Figure 2 shows the types of identification tests we are looking at, including non-targeted approaches for making identifications, using rapid spectral techniques combined with chemometrics or multivariate data-analysis tools. With semi-targeted approaches, such as chemical fingerprinting methods, the amino-acid profile of a protein, for example, indicates if it came from soybean or from milk or another source. Isotope-ratio fingerprinting has been used with honey, for example, to pick up the addition of high-fructose corn syrup; the carbon-isotope ratio is affected by whether the source is a C4 or C3 plant; although it's a technology of great utility, no compendial standards take advantage of it.

Other technologies of potential use include PCR, differential scanning calorimetry, rheological methods and microscopy. Although microscopy has been around for a long time, there has been little use of it for botanical identification. For assay or purity tests, simple adaptation of HPLC and GC methods has significant potential and they are the predominant technologies we use for new standards at USP. Similarly, older standards—going back decades—could benefit from the addition of LC and other separation methods.

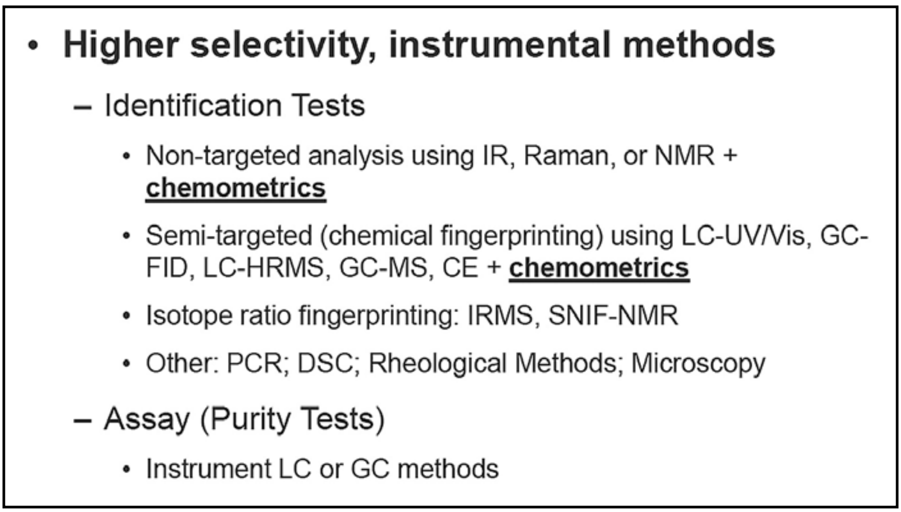


Figure 2. Opportunities to advance compendia testing standards.

Moving Forward

USP has formed an expert panel on EMA who have prioritized "at risk" food ingredients. Significant effort is being expended in assessing the vulnerability of existing FCC standards from an analytical perspective. We are also trying to generate a repository of historic incidents of EMA in food fraud, to create a baseline of what's happened in the past to provide insight into how fraudsters have evaded QA systems, and thus reveal vulnerabilities. This will also helps risk assessors to identify ingredients that pose the greatest threat.

The expert panel has formed collaborations with people who are working on predictive models for EMA, including Shaun Kennedy[3] and Frank Busta[4]. Also, it has recommended R&D projects to develop new and revised compendium standards on what are viewed as high-risk ingredients, including skim-milk powder, natural colors and cocoa powder.

Problematic Ingredients: USP Database

We have scoured scholarly literature as well as media articles and collected a substantial database on food fraud for the period 1980–2010, which will be published in 2012. Figure 3, from the database, shows the fifteen most problematic ingredients *vis-à-vi*s EMA. Olive oil is no surprise; it garners media attention regularly. Milk was a little surprising for some people. Honey also is the subject of many media reports. Some were surprising to me, such as star anise, which we actually picked up on a couple of years ago and are working

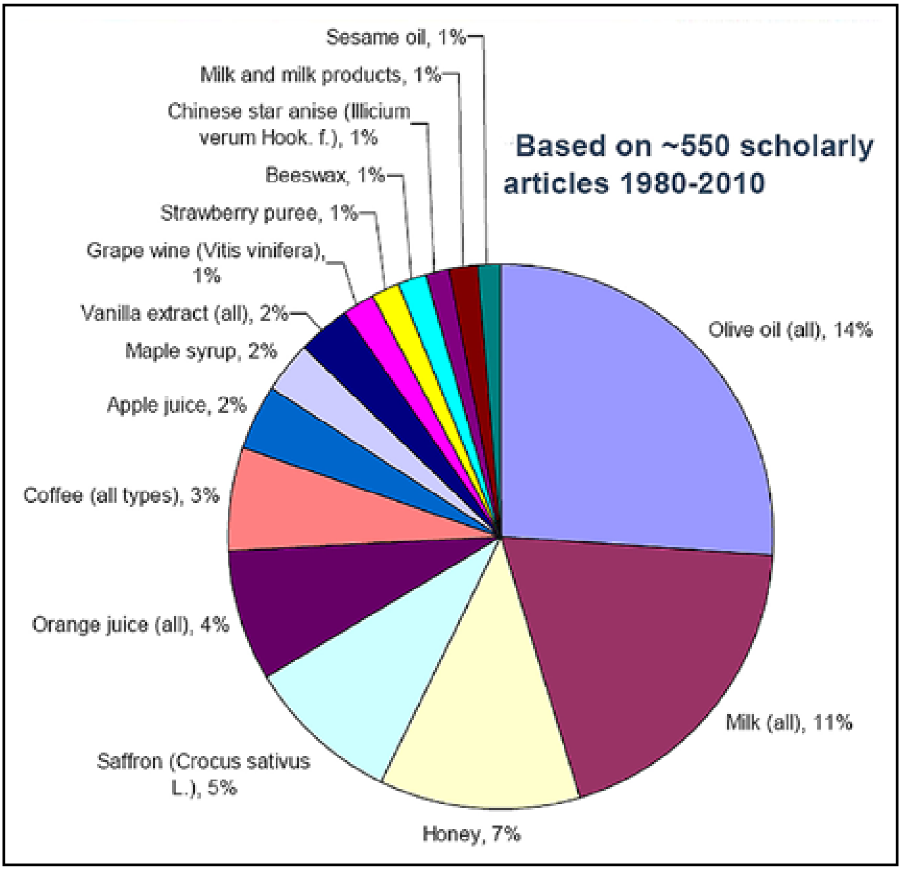


Figure 3. The fifteen most problematic ingredients for EMA.

[3]Pages 191–207.

[4]Pages 15–23, 221–224.

on better standards for Chinese star anise. I didn't expect the inclusion of beeswax, but reports stemming from China indicate that its adulteration is a significant problem.

Skim milk is a vulnerable, high-volume ingredient. In 2008, 8 billion pounds went into food products that impact infants, children and adults. Its nutritional value is based on protein content, with attendant problems mentioned above. No test is available to identify skim-milk powder, and EMA of milk ingredients includes urea in fake milk in India, melamine in China and hydrolyzed leather meal in China. The objective of our project is to develop and validate new compendial testing standards for skim-milk powder that will exclude known and unknown EMA materials. Ten organizations are involved in this collaborative effort comprising more than thirty scientists. We determined early on that there is no magic bullet—no one test solves all of our problems. Each company has unique risk-management approaches and analytical capabilities, indicating that a toolbox of standards is needed.

Rapid Screening

Rapid screening methods are particularly important to industry, where an answer is needed within 20 seconds on whether something looks normal. Also required are rapid confirmatory methods; verification of abnormality is crucial, before removal of an ingredient from the supply chain. Methods for checking purity—*e.g.* for protein as mentioned above—are essential. And, of course, supporting reference materials and spectral libraries are indispensible. Therefore, our skim-milk-powder project has two analytical strategies. One is to create methods that are capable of detecting abnormalities or aberrations in what may be thought of as the fingerprint for a food ingredient caused by a significant level of a known or unknown adulterant. We have some interesting data already for skim-milk powder. Figure 4 shows data from Fourier transform near-infrared (FT-NIR) spectral analysis, a rapid technique that picks up almost every organic compound and

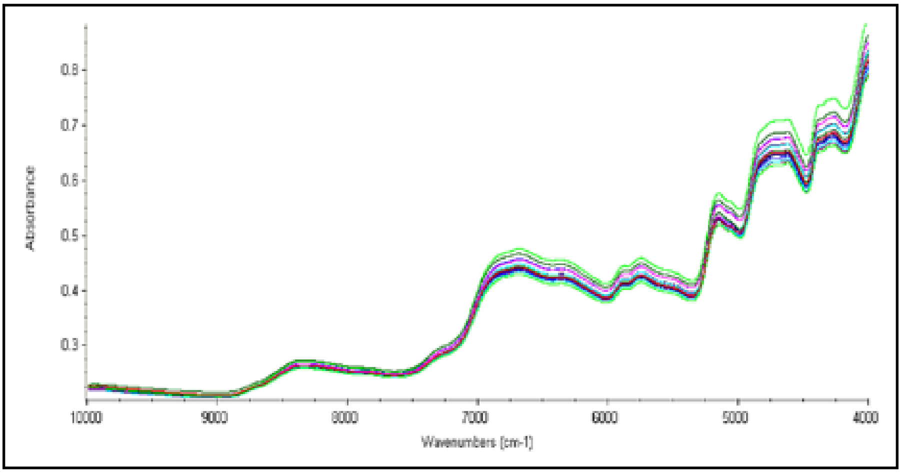


Figure 4. FT-NIR of skim-milk powder, pure and adulterated with 500 ppp to 1% melamine, cyanuric acid, and/or urea.

some inorganic compounds. These are data from a number of authentic skim-milk-powder samples as well as samples that have been spiked with adulterants, melamine, cyanuric acid, urea, or combinations, between 500 ppm and 1%. A spectrometrist may be disappointed that stronger differences are not seen in these data. However, chemometrics teases out subtle differences in the spectral fingerprints; Figure 5 shows these data analyzed by principle component analysis (PCA), successfully differentiating authentic from adulterated materials down, again, to 500 ppm, much lower than we thought would be possible using this approach.

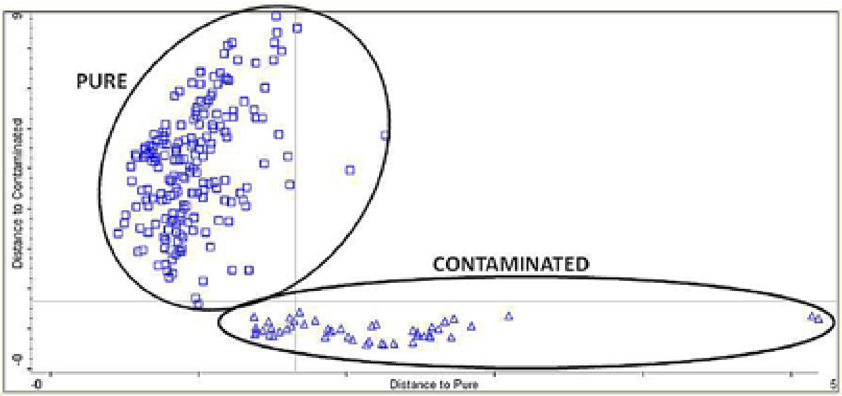


Figure 5. Principle component analysis of the data in Figure 4.

We are looking at other non-targeted analytical methods (Figure 6), including Raman spectroscopy, matrix-assisted laser desorption/ionization mass spectrometry, NMR and LC-high-resolution mass spectrometry. Also semi-targeted approaches are being appraised, including amino acid fingerprinting, intact protein analysis using ultra-performance liquid chromatography and capillary electrophoresis. We envision perhaps a hand-held instrument to scan incoming ingredients with automatic comparisons with a library of authentic data linked with chemometric analysis, providing, say, a green or red light to indicate a normal milk powder or to flag something that looks abnormal for immediate removal from the supply chain for investigation. The interface could look something like Figure 7. The protocol for skim-milk powder might provides a measurement of 85%, below a preset threshold and judged as a failure. With enough data, not only for authentic but adulterated materials, the problem may be rapidly determined and, in this case, a non-authentic protein indicated as being present.

The fusion of more than one orthogonal measurement—termed "data fusion"—provides another opportunity for improved authentication. Biometrics offers a relevant example: combination of fingerprinting with retinal scans and facial recognition provides an infinitely more powerful tool to authenticate a human than fingerprinting alone. Similarly, to authenticate a food ingredient, bringing several technologies to bear simultaneously would create an extremely powerful tool.

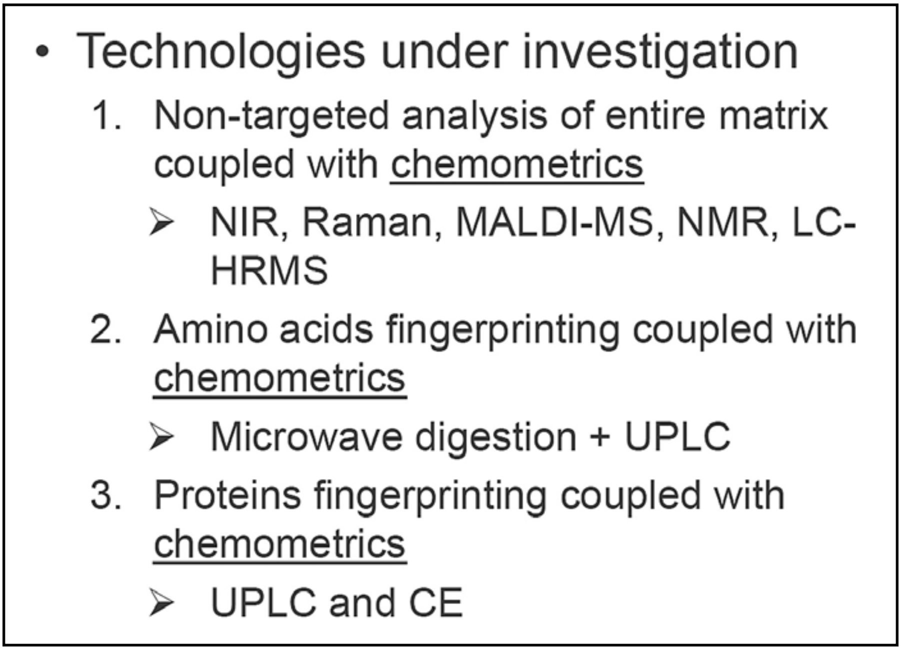


Figure 6. Skim-milk-powder project: authentication.

Figure 7. A possible interface for real-time authentication.

As mentioned, we are re-examining total-protein methods. One of the more promising approaches—albeit not a novel idea—is to define total protein on the basis of amino acid content. We are addressing many challenges, including the use of rapid microwave hydrolysis to decrease the traditional 24-hour hydrolysis to less than 20 minutes in preparation for identifying individual amino acids

Milk powder provides an example of the need for multidisciplinary approaches to make progress. Milk is complex and variable, requiring food and dairy-scientist expertise, as well as chemists to develop analytical tools. We also need chemometric and food-informatic experts to deal with the overwhelming amount of data that will result from many of these approaches. Of course, skim-milk powder is just one ingredient, many others are also at risk. Scientists from many disciplines must combine forces to meaningfully address the problem of EMA.

In Conclusion

The unknown nature of EMA and the paucity of analytical detection methods means that the safety of counterfeit foods is in the hands of fraudsters—a frightening scenario. A significant gap needs to be filled to develop analytical technologies to detect and deter EMA. Since food and agricultural scientists know the ingredients, they should lead these efforts in collaboration with scientists in other relevant disciplines.

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Jeffrey C. Moore is a scientific liaison for the *Foods Chemicals Codex* at US Pharmacopeia (USP), a not-for-profit public standards-setting authority for medicines, dietary supplements, and food ingredients. He joined USP in 2007. He is the lead scientific liaison to USP's Expert Panel on Food Ingredient Adulterants and is USP's scientific representative to the Codex Committee on Food Additives.

Dr. Moore has more than eight years experience in food science with an emphasis in functional food chemistry, analytical methods development and validation, and frozen-food research and development. He has authored more than fifteen manuscripts in peer-reviewed food-science journals. Prior to USP, Moore worked for Nestlé. He holds a PhD in food science from the University of Maryland.

Emerging Biotechnologies to Promote Safety, Enable Defense and Discourage Fraud

Q&A

Moderator: Frank Busta
University of Minnesota
Minneapolis, Minnesota

Frank Busta: Our three panelists are here and it's time for your questions.

Kim Nill (US Soybean Export Council): Dr. Moore, certain countries and certain buyers of organic commodities might consider so-called GMOs as adulterants of non-GMO commodities. Considering the detection methods, it seems to me to be hopeless because virtually all of the relevant genes in biotech products come from soil-dwelling bacteria, *Bt*[1] for instance. These commodities are allowed as much as 2% of what is called foreign material. That 2% could be entirely top soil, so you would have false positives triggered by bacteria that just happened to be present. Getting anything approaching a scientific determination of what is present strikes me as hopeless. Am I missing something, or is there a way around this?

Jeffrey Moore: Your question speaks to a real challenge in that the more specific and the more selective the method, the greater is the chance of false classification, because you simply have more and more information making it more difficult to determine whether or not something is authentic. ELISA[2]s, which are used widely do have this very real issue of false positives and false classifications. On your question about GMOs, I don't take a stance on that. At USP[3], standards are not being developed to differentiate GMOs from non-GMOs. I don't see us doing that any time in the near future, if that's what you were getting at.

Tracy Sides (University of Minnesota): Yesterday, we heard that, at the beginning of their *E. coli* outbreak, Germany turned to a lab in China rather than to a lab here in the United States, which was described as a negative reflection on public funding support. I'm curious, Dr. Besser, regarding your perspective on that occurrence.

[1] *Bacillus thuringiensis.*
[2] Enzyme-linked immunosorbent assay.
[3] US Pharmacopeia.

John Besser: I was a little mystified as to why China was the first laboratory to sequence that organism. I really don't know the story. Yes, it's true that our infrastructure is under-funded to keep up with these technologies. When the cholera outbreak occurred in Haiti some months ago, we actually did have that whole thing sequenced within a few days. We threw resources that we didn't have at it, so it's possible to do. To answer your question: yes, there is an issue but I don't know why that occurred.

Joseph Msanne (University of Nebraska): Dr. Moore, are food preservatives considered adulterants?

Moore: There are many cases where they can be, especially where they are not allowed for use in food products. Shelf-life extension adds value to it, so it may be considered EMA[4] or food fraud.

Shaun Kennedy: There are examples of that being done in which the contaminant poses public-health problems. There was a case in China where a company added formaldehyde in order to extend the shelf life of tofu.

Hongshun Yang (University of Minnesota): A question for Dr. Besser…[inaudible]

Besser: The power of PulseNet is that everybody uses the same protocol and there is a certification process for laboratories to become part of PulseNet, to use the brand name. So, yes, the results are mostly comparable throughout the world. Unfortunately in the 2011 German outbreak, although we had added a new non-O1576 protocol—details of which you really don't need to know—the Germans hadn't yet adopted it. So, we actually couldn't directly compare the patterns that they were getting with ours. Every attempt is made to have uniformity throughout the world so that we can compare—eventually instantaneously—one country to another country. The problem with PulseNet International mostly is that the surveillance systems in different countries vary tremendously, and, in many countries, surveillance as we know it barely exists. So while countries may develop this very robust infrastructure at the national level, they may have very little to work with; doctors aren't ordering tests, laboratories aren't identifying bacteria, samples aren't being sent to health departments. In order to make this work in much of the world, we have to address the underlying public-health infrastructure, which of course is a much bigger task. But we actually are doing that through a program called the Global Foodborne Infections Network, or GFN, where we are holding epidemiology and laboratory-training classes throughout the world. Interestingly, the microbiologists argue a lot about methods, but it actually doesn't matter. You hit upon the really important point that everybody should do the same thing, whatever it is. I wish I could clobber the Europeans over their heads so that they get that one point. It's important that we all do the same thing, that we speak a common language.

[4] Economically motivated adulteration.

Jacqueline Fletcher (Oklahoma State University): I have a question about the response of systems that are the same or different when an intentional contamination might be involved. Does it change who responds, who takes control and how initial decisions are made? And maybe you could put it in the context of the German outbreak. I know that people have considered the possibility that that was intentional—there are odd things about it—but, as far as I know, there's no evidence for that.

Besser: When clusters of disease occur, we don't know whether they are foodborne if we don't know why they are occurring. We don't know whether they are intentional or natural occurring. In fact, we don't know anything other than that a cluster of disease is occurring. So the initial process is an epidemiological one, attempting to answer some of those basic questions. If there's any hint of intent, then Homeland Security and other organizations would quickly come into it and we'd have phone conferences with the Departments of Defense and Homeland Security very early on because of the unique nature of this, and they would ask us directly what evidence we have that it wasn't intentional and what level of concern should they have. And we would share with them all of the available epidemiologic data to try to assess, to triage the level of concern that we have an intentional event. And, in this circumstance, while it couldn't be ruled out, there was no specific intelligence or any specific microbiological data to point towards intentional contamination. But this has to be asked every time. We are the gatekeepers because we are investigating the clusters and the threshold is pretty low. If there is any concern we get the intelligence agencies involved very quickly.

Kennedy: In the United States specifically, when it becomes a probable intentional event then the FBI becomes the lead agency and Homeland Security becomes the coordinating agency. Three years ago, we had an exercise on food defense that involved the G8 countries and, although most of them don't have an equivalent to Homeland Security, the same basic approach applied; as soon as it becomes potentially intentional the federal law-enforcement agency takes the lead, which introduces challenges in terms of potential differences in investigative protocols between public health and law enforcement. You may end up compromising the public-health investigation because you are trying to make sure you have an appropriate law-enforcement investigation.

Busta: And, at that G8 event, the German representatives said they had it all down cold.

Jacqueline Fletcher (Oklahoma State University): 99.99% of outbreaks are unintentional. What is the status of research in preparation for types of work that had to go on, say, after the anthrax attack to pin down the source—in other words, very detailed, strain-discriminatory testing, markers and so on?

Besser: The microbiological aspects are relatively easy to control. We can do whole-genome sequencing for about $100 now. Unfortunately, unlike in human DNA sequencing for forensic purposes, as used with OJ Simpson and the bloody glove, the system that we are operating in is a lot more complicated. It is sufficiently complex that microbiological data alone often don't tell the story. The natural variation in the bacteria complicates this whole concept of microbial forensics. Even with anthrax. Anthrax was a perfect case because it's something that's at an extremely low prevalence in the population and its presence in a human case is indicative of an extraordinary event. When you are talking about things that are common, like chicken pox or *E. coli,* it gets much more complicated. The germs are constantly changing on their own, and we actually pick markers that are variable. We pick them because they are variable. In the Haiti outbreak, for instance, we sequenced sixteen strains; differences occur as it's passed from person to person so they are constantly changing. While it's an emerging science and we can tell a lot from the germs, it has to be a multi-systems approach to get at these issues. The science has progressed, but we are running up against a wall; microbiology can't tell us everything.

Busta: How would you go about trying to detect whether it was a laboratory-directed change in the organism compared to one that's natural?

Besser: We haven't encountered that yet, fortunately, but we can look at the sequence level and there are certain natural insertion sites for genes that are well known in the molecular biology world. So one can look for insertions of chunks of DNA that might not be appropriate. This actually did occur with smallpox, when interleukin-2 was introduced in Britain, I believe, in the 1990s. This was not a bioterrorism event, it was just an experiment. I am not a molecular biologist, but I know that there are ways of looking for these large insertions and deletions of genes.

Francisco Diez-Gonzalez (University of Minnesota): It's been over seven years since then-US Secretary of Health Tommy Thompson said, "For the life of me, I can't understand why terrorists haven't attacked our food supply." What are we doing right, that this hasn't happened?

Busta: Alright, Shaun?

Kennedy: Part of it is, they actually have been plotting to try and do something intentionally to the food system and have been caught before they did it. Law enforcement has actually gotten lucky a few times. And part of it was touched on yesterday, about the psychology and sociology of terrorists—what their motivation is—and right now they are satisfying their membership motivation by blowing themselves up in the Middle East. Until we are out of Iraq and Afghanistan they are going to be focused there more than they will be focused here because their primary goal is to get us out. And attacking us here, as they learned from 9/11, doesn't get us out. It brings us in.

PART IV—LUNCHEON AND BANQUET PRESENTATIONS

Food Safety: The Minnesota Model

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When we talk about the Minnesota model, several things have been referenced in that regard. Our ethanol program, viewed nationally, is often referenced as the Minnesota model. Energy is also referenced as the Minnesota model because of how well we have grown it in this state. Some people might look at the election process in Minnesota and refer to that as a model, not one to be replicated, but certainly a model that gained national and even international attention.

I am referring to foodborne illness and how we respond to it in the state of Minnesota. Although it is often referred to as the Minnesota model—even recently in national legislation—in reality it's a process that evolved over a number of years. I will describe how that came into play, why it came into play and why it's important that it be considered by other states and nationally.

One Health Initiative

Daniel Gustafson[1] is intimately involved with what's referred to oftentimes as the One Health Initiative. When I discovered what that term means, I realized that I had been talking about it and doing it for a long time. The One Health concept begins on the farm and applies through the food chain—production, processing, transportation, consumer consumption—which, certainly, we need to pay attention to. When I joined the Minnesota Department of Agriculture, my main point of view was that of a farmer because I've had a corn and soybean farm in south central Minnesota for a number of years. I worked for three governors, two of whom said that the agriculture commissioner should be a farmer, so I had no choice but to keep farming in order to keep my day job. But it actually worked out well, because I took vacation and spent long weekends on the farm during the spring-planting and the harvest seasons. It was a nice way to unwind. Some of

[1]Pages 27–34.

my farmer friends thought I was crazy when I said farming was relaxing, but it was true in comparison with some of the things that went on in the capital city.

After a few years, someone asked me what was the biggest surprise that I had encountered as commissioner of agriculture. After a brief moment's thought, I said, "The amount of focus and time spent on the issue of food security. Not that we don't have a safe food supply in this country, it's just that the food-distribution system has changed over the last few years." In the fairly recent past, we had a system in which crops were raised, processed and consumed within a relatively small geographical area. Through consolidation, the integration of the food-processing systems, farms getting larger and changing distribution methods, now we have a system whereby food may be grown in one area, transported somewhere else for processing, and then within a day or two distributed all over the country or, in some cases, internationally—all from one location. This means that although efficiencies of scale may accrue, when things go wrong they can go really wrong, and certainly we have seen that occur.

The other thing that has happened is that science has gotten much better. In times past when people became ill, they seldom knew the cause. They went to the family picnic and had Aunt Emma's potato salad, and afterwards a dozen relatives became sick and concluded, "Something must have been going around." Well, it was Aunt Emma's potato salad. With modern scientific techniques, *E. coli*, salmonella and other microorganisms—which, before, the general public had never heard of—may now be identified. Paraphrasing a comment by Senator Amy Klobuchar a couple of years ago when she introduced legislation to address food-safety issues at the Food and Drug Administration:

> *It's a shame that the nation should have to wait until somebody in Minnesota gets sick or dies before there is the opportunity to address a national food-safety issue.*

For those from Minnesota, please understand that we are not saying this with great pride, but we have done some things that are worth sharing. With reference to food security, our first premise is to keep everything safe. We have regulations in place to ensure that products are moved from the farm to the consumer as safely as possible. The Minnesota Department of Agriculture is a regulatory agency and a promotional agency. While we spend part of our time promoting agriculture, we are also in the business of regulating, which includes food safety. We look at environmental issues, including pesticides and herbicides.

Team D

You have to be prepared for when something goes wrong, because, for sure, it will. In the Minnesota model, when something goes wrong *vis-à-vis* food safety, we have a central reporting system. If a general practitioner or doctor at a hospital sees people with similar symptoms they report it to the Minnesota Department of Health. Records are made and if a pattern appears, they engage what is sometimes referred to as Team Diarrhea. "Team D" is a group of graduate students working at the university in public health, who take the information and make phone calls to attempt to determine:

- what the affected people ate recently,
- where they ate,
- whether other people were at the restaurant or event,
- whether other people bought food from the same source,
- *etc.*

If commonality emerges, they look for opportunities to collect samples for laboratory testing. Partners at the Department of Agriculture then go out and investigate the possible origin of the product of interest.

Two nationally prominent cases serve as good examples. The first is the so-called jalapeño pepper/tomato issue of 2008. People in Texas first became sick and, as the symptoms spread across the country, raw tomatoes were thought to be responsible. Quickly, tomato sales decreased, even though the source of the infection could not be identified. People showing symptoms in Minnesota were found to be carrying the same strain of salmonella, having eaten at a particular restaurant. Investigating Health Department officials discovered that fresh jalapeño peppers had been on the meals consumed by the affected individuals. Invoice checking revealed that the peppers had been grown on a farm in Mexico across the border from Texas. A surprising aspect is that a relatively short period of time elapsed from the infection appearing in Minnesota to the identification of the cause, yet the problem had persisted for months nationally.

A year or so after the jalapeño problem, there was similar outbreak of illness. In fact, in Minnesota three people died at that particular time. To begin with, it appeared to be confined to long-term healthcare facilities that had purchased food supplies from a distributor in Fargo, North Dakota. Then it was discovered that long-term care facilities in the Twin Cities that purchased supplies from the Fargo source did not have the problem, so there was something unusual about purchases made by the facilities in northern Minnesota. It soon became evident that the culprit was peanut butter. Again by checking invoices for food sources, the problem was quickly traced to a facility in Georgia producing large tubs of contaminated peanut butter for industrial sale, some of which was converted into peanut-butter cookies and other products.

In such cases, publicity has to be handled carefully as false accusations can create huge economic losses. In the jalapeño case, hundreds of tomato farmers in the United States were falsely accused. A local hydroponic grower saw his sales plummet even though there was no indication of a problem with tomatoes grown in Minnesota. Such situations can become difficult for regulators—state or federal—to handle. How should the public be alerted of potential problems without creating paranoia and pandemonium, or economic disaster for those growing healthy products? In the peanut-butter case the problem was traced back to one company and upon further investigation significant problems with the cleanliness of that plant came to light. In the case of the jalapeño peppers, unsanitary water was temporarily used for irrigation on a couple of farms then the problem went away. The source of the problem was traced and corrected with repetition unlikely.

Minnesota's Heritage

As to why some of these things have worked in Minnesota and less so elsewhere—I think that there's a cultural heritage in this state of people wanting to do things right and do them well. Not that we haven't made mistakes, but generally the public mood is, "If something is wrong let's correct it, let's do it right, do it well and make life better for everybody." Another aspect is the role of agriculture. People don't always fully appreciate or understand that agriculture is a huge industry in Minnesota. We don't have a huge number of farmers—only about 5% of the state's population are farmers—but 20% to 25% of the workforce has some connection with agriculture.

Many agriculturally related activities exist beyond the farm. Because of geography, Minnesota became a central point for food processing. We are at the top of the Mississippi River and accessible to boat traffic to and from the south, and the east-west railroad system funneled through Minneapolis and St. Paul. Many large agricultural processing and supply companies developed here—public, private and cooperatives—all of which had a huge influence not only in Minnesota but across the United States and throughout the world. Cargill and General Mills are a couple of examples, as is Pillsbury (which merged with General Mills in 2001). Land O'Lakes and CHS are examples of cooperatives. A number of other companies, such as Ecolab, are involved in various agricultural activities. The jealously guarded reputations of these companies depend on their contributions to a safe food supply. Of the companies that make the Fortune 500 list, Minnesota has the highest number per capita. Half of those companies are agriculturally related and a large number of the others have medical connections. They constitute a large part of Minnesota's business and share an impetus to do things right.

With reference to the central reporting system, not all states have it. Regarding the jalapeño pepper issue, for example, it was over two months before authorities in Texas realized that there was a problem because there it was impossible to bring the facts and figures together in such a way as to detect the trend. At the local level, people didn't see the connection until the problem had persisted for some time.

Facility Sharing

Also important are the working relationships among entities involved with food safety. The Departments of Agriculture and Health and the University of Minnesota all play key roles. Historically, they have not always cooperated well. A number of years ago, during the Ventura administration, we needed new facilities at the Department of Agriculture. Our building was rented and our laboratory was substandard. The Department of Health also had some problems, with a lab in one area and workers in another. Jan Malcolm, the commissioner of health, and I met numerous times to discuss putting the Department of Health and the Department of Ag in the same building, if funding could be found. The events of September 11, 2001, induced the legislature to think about food security and needs to ensure it. In the subsequent legislative session, a bonding bill was passed to build a new laboratory and arrangements were made for construction of a new building so that lab workers in both Departments could be co-located with staff members to improve communication and sharing of ideas.

When asked "Who does what in the area of food safety?", I say that the Department of Ag is responsible for everything that goes into the body, whereas the Department of Health is responsible for everything after that. A close synergy is needed between these agencies. And the University comes into play in terms of training; the expertise that exists in the faculty is very important. To make a long story short, two new buildings, across the street from each other, are connected with a skyway. There are three floors of laboratories, with Health in one half, and Ag in the other, separated by a hallway. Scientists go back and forth across the hall to discuss issues of mutual interest. In the administrative building, Health and Ag staff members are interspersed in such a way that people can readily work together, face to face. About a year after occupation, a member of my senior staff, who had been there for several years, told me that he had talked to some of the Health people for years over the telephone but had never met them personally.

The teamwork that has emerged is important and, typically, press conferences involve members of the Department of Ag, the Department of Health and the University. Not long ago, at a press conference on H1N1, representatives of all three entities fielded questions outside the building because Minnesota was first in the United States to identify H1N1. Breaking that news was not something we looked forward to, but, interestingly, because of that collaboration, what was a major story on Friday afternoon by Monday morning was no longer newsworthy because the demonstrated synergy between the three entities lent confidence that the situation was being handled correctly.

Individual Commitment

Another thing that comes into play is what I refer to as individual commitment. Something that amazed me after being at the Department of Ag for many years was the realization that people I knew by their first names had PhDs or multiple degrees, but did not make a fuss about it and were dedicated to their jobs because they cared and were committed. That commitment is important in terms of seeing the job through. It's one thing to react to a crisis, but it's another thing to work on related issues in between times such that, when another crisis develops, rapid response is possible. That is unlikely to happen without committed people who want to see things done and done correctly. In Europe, in the spring of 2011, a salmonella outbreak had devastating consequences. It quickly faded from media coverage and the problems that resulted from it were forgotten: out of sight, out of mind. In contrast, with agency and university people devoted to learning from past instances, the next crisis may be addressed differently and more effectively. A young man at the Department of Agriculture may be referred to as the Sherlock Holmes of paperwork. He's the one who traced invoices all the way back to McAllen, Texas, to determine the origin of the contaminated jalapeño peppers. He similarly traced the origin of the contaminated peanut butter. Those individuals, even having made important contributions, often go unmentioned.

Challenges

Are there challenges? Yes there are, and one that comes into play is as follows. There has been a lot of attention in terms of legislation to correct problems at the federal level. However, in reality, legislation alone won't do the job. Individuals are needed who are committed to seeing something done and to making things happen. Unfortunately, be it in business, government or academia, silos develop and people who should communicate don't talk to each other. This can be self-perpetuating for various reasons, such as competition for funding or competition for recognition. When we looked at co-locating the Departments of Health and Ag a number of people within the agency—who no longer are there—said to me, "Don't do this. Don't co-locate with Health." "Why not?" "They'll take us over." It was true that there were twice as many people in the Department of Health as in the Department of Ag, but the reality is you have to be willing to risk a little in terms of who does what and share responsibilities so that the job gets done.

I am a firm believer that there is no perfect organizational structure for anything. I spent some time in the legislature where some legislators were constantly tinkering with how to restructure something to make it more efficient. Reality is, you need communication and if that communication doesn't take place in an agency of 5,000 people it won't take place between two agencies of 100 people who won't talk to each other. Silos are a natural tendency, and anything that can be done to eliminate them certainly is important. It takes leadership, but it also takes people who are willing to take some risks because they are committed to doing the job. Again, one of the things that impressed me about working in a state agency was the personal commitment of people who wanted to make a difference. Many could have made more money elsewhere in normal economic times, whereas their goal was to see things improve in their state. A lot of things go into making a system work and certainly it's important to have those in place, but, in the final analysis, it still comes down to the people involved and willingness to work with others in such a way that it will make a difference on a long-term basis. And it's something to keep working at as personnel changes occur.

Gene Hugoson recently joined the Global Initiative for Food Systems Leadership as a senior fellow. Previously he served as commissioner of agriculture for Minnesota for over 15 years under three governors; his focus was on food security and value-added production as well as marketing of agricultural products domestically and internationally.

Mr. Hugoson was elected five times to the state legislature. He is actively involved in his corn and soybean farm in south-central Minnesota.

Agricultural Science, the First Best Hope for the Future

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I am pleased to be able to weigh in on the theme of NABC 23: global food security. There's no question that we are living in extraordinary times and facing enormous challenges both at home and around the globe. But, to me, the most urgent problem facing us—surpassing even terrorism or nuclear proliferation—is making sure we can provide the safe, nutritious food and clean water needed to support an ever-growing population, and to do that in a sustainable manner.

As a scientist, I know that the research we need to address global food security can't wait. Research takes time, it takes long-term funding, and it takes a work force educated enough to do it. I see a large part of my mission at USDA[1] as moving the ball forward on all of those areas so that our nation can keep its place as a science leader and help the world address the challenges that lie ahead.

The United Nations projections for global population were recently revised upwards—to a global population of 10 billion people by 2100, 3 billion more than today, and they will all need to be fed. Robert Thompson uses a very startling image to illustrate that growth rate:

> *By 2050, the world population will have grown by the equivalent of two Chinas—one by 2020 and the other between 2025 and 2050.*

The challenge of such a population increase is compounded by a larger demand for protein foods in their diets. More meat requires greater inputs to produce. Given all these predictions, food production may need to double by later in this century—and agricultural research is the only way to accomplish that. Science is also essential to making those productivity gains in a sustainable manner—in a way that stewards soil, water, biodiversity, community vitality, and other natural and human resources.

[1]Dr. Woteki is under secretary for Research, Education, and Economics, and USDA's chief scientist.

The other aspect of this challenge is what I call the "preservation gap." Fully 40% of the food that's produced is lost after harvest to insects, rodents and rot. Solving the preservation dilemma will go a long way toward solving our global food-security problem.

Investment in Agricultural Science

In my role at USDA, I am keenly aware of how important the work university and USDA scientists pursue is to addressing these needs. We have focused our work on five priority areas—Food Security, Food Safety, Bioenergy, Climate Change and Nutrition—all of which tie back to making the supply of food more secure here in the United States and around the globe. To meet these priorities, however, will require funding, and that is an over-arching difficulty facing our government today.

A look at our history and at countries around the world shows that increasing our investments in agricultural science, education, and technology is the foundation needed for a strong future. Many economic studies have shown that investments made in publicly-funded research have earned substantial returns to the US economy, with total economic benefits exceeding costs by at least twenty to one. Much of the economic benefit from this research goes to consumers, who gain from more-abundant, lower-cost, better-quality and safer food. In the United States, we've seen the benefits of public research in breakthroughs that improve the productivity of our agricultural producers, giving them the tools they need to produce our food more efficiently and cost-effectively.

Today, the United States enjoys one of the safest, most abundant, high-quality, and diverse food and agricultural systems in the world. We didn't get here by accident. We got here by investing in agricultural science and education and by transferring scientific knowledge and technologies to America's hardworking farmers and businessmen.

Unparalleled Challenges

One of the best things that public investment in science and education has done over the last 149 years is building an agricultural research, education, and extension system that is unequaled and which has contributed greatly to our nation's success.

It's the system that transformed the nation by making higher education not only practical, but accessible to all. It's also the system that faces unparalleled challenges in a time of tight budgets. Budget cuts from the 2011 continuing resolution are already affecting the state experiment stations and Cooperative Extension as well as research that USDA scientists engage in to assure domestic food security and help feed the world. In addition, budget cuts are affecting our standing in the global scientific community. Our 2012 budget is currently being debated in Congress, but the outlook for USDA science is not promising. Unfortunately, USDA science has not been treated in the same manner as that of the other research agencies and has lost substantial ground, whereas others have received only modest reductions in their support.

What's worrisome here at home is also occurring globally. Growth in public research investment has significantly slowed over the course of the last three decades as the world's governments have underinvested in agricultural R&D.

In many developed countries, including the United States, public investment in agricultural science has remained flat or shifted resources away from farm-productivity research and toward other societal concerns like the environment and human-disease treatment. During the 1950s and 1960s, US public sector agricultural R&D spending grew at over 3.6% per year but growth has slowed to less than 1% per year since 1990. Private investment in agricultural research has grown somewhat faster than public R&D, and now accounts for more than half the spending in agricultural R&D in the United States. But the private sector focuses on areas where intellectual property allows it to earn a return on its research investment. It can't do the kinds of fundamental research and scientific training that have traditionally been strengths of government and academic research. And if the fundamental discoveries run out, so will the private avenues for development of new products and processes.

Scientific Successes

USDA science has had some great successes in recent years. Genetic discoveries leading to applications that help farmers, ranchers and agricultural producers, such as the FasTrack Breeding system that accelerates the growth of fruit trees, are excellent success stories. It typically takes at least four generations to develop a new fruit-tree variety. But FasTrack Breeding shortens the breeding time from 16 years to 5 via four steps:

- The continuous flowering gene from poplar (*FT1*) is introduced through genetic engineering into a parent fruit tree.
- The engineered parent tree is then crossed with normal, non-engineered parents. Because the resulting seedlings express *FT1*, advanced selections can be made in less than 1 year. These advanced selections are then used as parents.
- In the last generation, there are four types of trees to choose from: desirable types containing *FT1,* undesirable types containing *FT1,* desirable types NOT containing *FT1,* and undesirable types NOT containing *FT1.*
- The desirable non-*FT1* types are selected for potential release. In this way, genetic engineering is used only to speed up the breeding process in creating non-genetic engineered cultivars.

In another case, USDA research has worked for over 100 years to help dairy farmers breed more productive cows. Since 1940, that research has resulted in a 4-fold increase in milk yield per cow. Today in the United States, 9.1 million dairy cows each average over 21,000 pounds of milk per year. In addition, USDA and collaborators have recently made improvements to the genetic selection program by partnering with the NIH to sequence the cattle genome, and have gone on to develop DNA "chips" for genotyping bulls and cows, with associated computer software for selecting superior parents for breeding. This new technology is dramatically enhancing the dairy industry's genetic selection program for improving milk production.

While these public investments were being made, the private sector was investing in dairy-cow nutrition. Much of the feed analysis and formulation today is still done by private industry, enhancing the production of high-value feedstuffs and supplements that support efficient milk production. It's a case where private investment followed public investment, and the world has reaped the benefits.

It's important to understand that these kinds of breakthroughs require years of public investment in fundamental research before the scientific understanding is advanced enough to move toward practical technologies. Oftentimes, the technological development can be undertaken by the private sector, although even then, some kinds of technologies can't be easily commercialized and may require direct public support. A good example of complementary roles of public and private sectors working together can be seen in crop improvement. Although most new crop varieties sold to farmers today are developed in private seed companies, the steady improvements in crop yields wouldn't be possible without access to better and more diverse sources of plant genetic resources. USDA's investments in plant germplasm conservation, characterization and enhancement underpin the private seed industry. But with some crops—wheat and barley are good examples—the returns private breeders can earn are not sufficient to attract much private R&D. In these cases, the public sector has a role to play in "downstream" technology development.

It's this kind of work that points to the continued and essential need for publicly funded research, because the private sector will always need to answer to shareholders. Scientists funded by USDA—in university labs and intramural labs—aren't constrained by the limits of current commercial demand. They follow the science, and people around the globe end up benefiting. The long-term return on investment—rather than quarterly returns—pays off for everyone.

Developing-World Needs

Public-sector investments are especially critical to the developing world. Private R&D is still very weak in many of these countries and accounts for only 6% of total agricultural research in this part of the world. There is also tremendous potential for many of these countries to raise agricultural productivity by borrowing and adapting technologies developed elsewhere. For example, the research centers that are members to the Consultative Group on International Agricultural Research (CGIAR) have helped developing countries improve their varieties of staple food crops like wheat, rice, sorghum, and cassava, as well as minor but nutritionally important crops like pulses. Almost all of this work has been done by the public sector, and much of it, collaboratively, between international and national agricultural research programs. While many developing nations are stepping up their support of agricultural research, developed countries are stepping back.

The United States, Japan, Australia, Canada, and European countries have cut back on their support of international agricultural research in recent years, and some economists have attributed the decline in the rate of yield growth in major crops like rice and wheat to that underinvestment.

In contrast, a number of developing nations—most notably Brazil and China—have been expanding their agricultural research and development capacities during the last couple of decades. China now has the largest number of agricultural scientists, more than 50,000. Brazil has raised its public R&D investment to over $1 billion per year. China and

Brazil are now achieving some of the highest agricultural productivity growth rates in the world. This productivity growth has enabled China to remain largely self-sufficient in food, despite limited land and rapidly improving diets of its people, while Brazil has transformed itself from a food importer to the second largest food exporter (after the United States). Such successes are not limited to China and Brazil, however. Studies have found a clear link between countries that have invested in agricultural science and technology capacity and the ones that have been most successful at raising their productivity. The poorest and most food-insecure countries of the world today, such as those in sub-Saharan Africa, are also the ones with the least developed scientific capacities in agriculture.

In light of these studies, it's clear that we can't let agricultural research flag here at home, and need to encourage developing countries to put science on their agendas for growth. I applaud the focus and determination of countries such as Brazil and China to invest in developing a well-educated scientific workforce. The investment is paying off for them, and it is important that the United States shouldn't ignore what the competition is doing, but instead, we should pay attention.

Disturbing Trends

One particularly disturbing example, to me, of the effects of our disinvestment in research was in the recent case of the *E. coli* outbreak in Europe. When Germany needed expertise to track down the source of the virus, it turned to Chinese researchers at the Beijing Genomics Institute, not to American scientists. The Chinese researchers then sequenced the DNA of the virus and determined its origin. In the past, this outreach would have been to the United States. This is the kind of development we need to sit up and take notice of—and face the facts about what drying up the well of funding for public research will cost our country and the world.

Since then, USDA science *has* been asked by FDA, the Massachusetts Department of Health and the CDC to analyze the sequence, genes, and antibiotic resistance patterns of the *E. coli* O104:H4 isolate from the outbreak strain in Germany. This is an excellent model of government entities working together for the common good, as they unlock the mysteries of this deadly bacterium and study it to keep our food supply safe.

Other countries are also increasingly more attractive to international students who used to come here to study science, but now can stay in their home countries, or go to Korea, China or Brazil instead. Many of those international students stayed to build extremely successful science-based and technology-based businesses.

There was an opinion piece in the *Washington Post* recently called, "Go to China, Young Scientist," by Matthew Stremlau, a post-doc with Harvard and MIT. He talked about the advice he gives to students and colleagues who ask where they should look to build their careers after graduation:

> *Go to China, I tell them. Or Singapore or Brazil or the Middle East. If the United States can't fund its scientific talent, find a country that will.*

I sincerely hope that young scientists haven't read that article. I do hope that the Congressional appropriations committees did read it.

But it does seem that the United States is already falling behind in the numbers of students graduating with degrees in agriculture. The statistics reveal a "no-growth" trend in graduate enrollment or degrees awarded in the core agricultural disciplines from 2005 to 2009. What little growth there is in graduate enrollment and degrees in colleges of agriculture is coming from related disciplines: family and consumer sciences/human sciences, forestry, and natural resources.

The Educational Landscape

So, our agricultural research system is doubly challenged by underinvestment and by the failure to keep the pipeline filled with the next generation of scientists to keep the research going. And in the near future, we'll have concrete data to help us chart exactly what the status is of that pipeline.

I attended a meeting with the Association of Public and Land-Grant Universities (APLU) in June 2011, and they agreed to work with us on an analysis of the landscape of students and their scientific education. They'll be assessing the flow of students through the "pipeline" of science, K–12, and through undergraduate and graduate education. They will be a valuable partner in determining how prepared we are for the scientific workforce we will need in the future. Their findings will let us know exactly what the situation is, so we can design strategies to shore up the supply of students educated in science and ensure they get the advanced degrees they need. We're working at the president's direction to increase attention and participation in science, technology, engineering and mathematics (STEM) education, which is the foundation needed to go forward into science-related careers.

That meeting with APLU was centered on the Action Plan that I've been working on since I got to USDA 9 months ago, as part of a series of consultations with stakeholders and the National Agricultural Research, Extension, Education, and Economics (NAREEE) Advisory Board. Our Action Plan takes concrete steps to address the strategies laid out in "A New Biology for the 21st Century." We want to strengthen our research by creating both literal and virtual collaborations across agencies, and bring together stakeholders who can add to that equation. We're working through the process of planning a long-term, coordinated strategy that addresses the very real problems that challenge the world right now and in the future. We've built a plan that really is based on action and results—and, as with the New Biology—will need to find ways to determine what those measurable milestones are, so that we know we are moving forward. That's a key part of the heavy lifting we're facing now, and we will continue to use the New Biology framework as a guide.

This vision of working strategically and in coordination is a theme I see across much of the scientific community these days. And it is happening on a global scale to solve global problems.

Malthus Deferred?

I appreciate the interest that this audience has in making sure that agricultural biotechnology advances, and continues to help feed the world. I began by quoting Dr. Thompson and I'd like to end with his encouragement to support agriculture research and the technologies it can offer the world. He was talking about the prediction by British scholar Thomas Malthus, who said that the world would eventually outgrow its capacity to feed itself, saying that Malthus was wrong for more than 200 years because he underestimated the power of agricultural research and technology to increase productivity faster than demand. Dr. Thompson said:

> *There is no more reason for Malthus to be right in the 21st century than he was in the 19th or 20th—but only if we work to support, not impede, continued agricultural research and adoption of new technologies around the world.*

That's a prediction I agree with. By keeping our eye on the goal of feeding the world, doing it in ways that are sustainable, and using our country's scientific abilities in the best of collaboration and coordination, we can ensure that 21st century America is well nourished, that our farmers are prosperous, and that world hunger will one day be an issue we can see in the rear view mirror and say we've beaten. I believe, if we continue supporting agricultural science and educating the next generation of American researchers, we will get there.

Cathie Woteki is under secretary for USDA's Research, Education, and Economics (REE) mission and the Department's chief scientist. Before joining USDA, Dr. Woteki served as global director of scientific affairs for Mars, Inc., where she managed the company's scientific policy and research on matters of health, nutrition, and food safety. From 2002 to 2005, she was dean of agriculture and professor of human nutrition at Iowa State University. Dr. Woteki served as the first under secretary for food safety at the USDA from 1997 to 2001, where she oversaw food-safety policy development and USDA's continuity of operations planning. She also served as the deputy under secretary for REE at USDA in 1996.

Prior to going to USDA, Dr. Woteki served in the White House Office of Science and Technology Policy as deputy associate director for science from 1994 to1996. She has also held positions in the National Center for Health Statistics of the US Department of Health and Human Services (1983–1990) and the Human Nutrition Information Service at USDA (1981–1983), and was director of the Food and Nutrition Board of the Institute of Medicine at the National Academy of Sciences (1990–1993).

PART V—STUDENT VOICE AT NABC 23

Student Voice Report[1]

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We thank NABC for sponsoring the Student Voice program, allowing us to come here and share in this lively discussion. We leave with many issues in mind and are excited to continue the discussions. Also we thank our member institutions for participating in the program and, for some of us, for providing matching funds.

A lot of perspectives are necessary to address the issues underpinning food security. We represent a wide variety of disciplines including plant pathology, food science and soil science with projects ranging from hormonal signaling in rice to food microbiology and all places in between and beyond. As such we especially appreciated the broad spectrum of topics and the interdisciplinary nature of the presentations including experts from the fields that we are in and also from public health, entomology, water-resource science, engineering, public policy, industry leaders from both private and public sectors.

[1]To encourage graduate-student participation at NABC conferences, the Student Voice at NABC program was launched ahead of NABC 19. Feedback from those involved was positive, therefore the program was continued for NABC 20–23. Grants of up to $750 are offered to graduate students at NABC-member institutions (one per non-host institution) to assist with travel and lodging expenses. Registration fees are waived for the SV participants. NABC-member institutions are listed on page v. Student Voice delegates attend the plenary sessions and breakout workshops then meet as a group to identify current and emerging issues relevant to the conference subject matter. Information on the Student Voice at NABC 24 will be available in due course at http://nabc.cals.cornell.edu/studentvoice/.

[2]Verbal reporter at the conference and co-author with contributions from the other students.

We offer the following comments and suggestions:

- The breakout sessions promoted interaction in a more intimate setting and enabled us to hear views of attendees while also sharing our views. Many conferences lack this special feature, and even more breakout sessions or workshops would be beneficial for future conferences.
- Including farmers in the breakout sessions facilitated our understanding of some of the issues addressed in the presentations. For this reason, inviting farmers and/or extension agents as speakers would increase the interdisciplinary nature of the conference.
- We would like to see more publicity of the event in advance to the public and throughout the various universities involved (press releases; updated, detailed webpage).
- Poster sessions at future events should be considered.
- It would be helpful to have presentation materials available at or shortly following the conference.
- There was good insight on the issues of food safety and security, but there could have been more information on the issues of food sustainability and self-sufficiency (*e.g.* water/nutrient use efficiency, crop-yield increases).
- Increasing involvement of students after the conference (*e.g.* Student Voice ambassadors, a mailing list of previous participants) would facilitate discussion beyond the conference.
- As for future conferences, we feel that the following points need emphasis.
  - Water availability is becoming critical in certain areas of the world. In order to meet the future demands for water, technologies that facilitate sustainable water use should be discussed.
  - The solutions presented should take account of local, socio-economic and cultural characteristics of every agricultural region. Something that proves to be effective in one place, might not work in another.
  - More research is needed into alternative sources of raw materials for biofuel production that can substitute for food and feed material. For example, oil-rich microalgae could be an alternative model because of its ability to grow on non-arable land and use non-potable water.
  - Food security is a multidisciplinary problem. We need to address it at multiple levels by including all stakeholders, including policymakers, scientists and farmers.
  - Prevention is key. We need to be proactive rather than reactive when it comes to food security and sustainability.

- Education is fundamental to raise public awareness of problems such as food availability, food safety, population growth, water scarcity and pollution. The general public can motivate the policymakers to make changes. Targeting young generations is essential to ensure the long-term effectiveness of implemented solutions.

Ralph Hardy (National Agricultural Biotechnology Council): Thank you Caroline. Thank you Michelle. Any audience questions or comments for our future professionals in this area? And other Student Voice members—if there are other points that you would like to make, certainly that's fine.

Michael Kahn (Washington State University): Do you leave the conference more optimistic than when you came, or less optimistic?

Caroline Anderson: I am leaving more optimistic. In the beginning it was a little overwhelming to hear some of these talks with so much new information—especially since I wasn't exposed to it prior to coming here. But I'm leaving optimistic because I feel that, obviously, a lot of people are aware of these problems in different disciplines—in science as well as not necessarily in science such as policymakers—and I feel like they are starting to come together to come up with solutions.

Michelle Martin: I am leaving less with a framework of optimism or pessimism, but with more questions—not so much glass half-full or glass half-empty, but what is in the glass? Right now at a conference like this, we are realizing more and more that technology is advancing, so potential solutions are available. Now we are dealing with questions of how we can bridge this to application, and social, economic, political and environmental considerations are needed.

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