PROCEEDINGS

Biological and Chemical Agents of Bioterrorism in Food

December 12–13, 2001

Washington, DC

Workshop on Biological and Chemical Agents of Bioterrorism in Food

December 12-13, 2001

Wyndham Washington, D.C.

PROCEEDINGS

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The North American Branch of the International Life Sciences Institute
Technical Committee on Food Microbiology
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and the

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Preface

Post-September 11, heightened concerns about the potential for intentional contamination of the food supply led ILSI North America (ILSI N.A.) to sponsor a ***Workshop on Biological and Chemical Agents of Terrorism in Food***, held December 12-13, 2001, in Washington, D.C. Organized by the ILSI N.A. technical committees on Food Microbiology and Food Toxicology and Safety Assessment, in partnership with the International Association for Food Protection (IAFP), and the Centers for Disease Control and Prevention (CDC), Food and Drug Administration, National Institutes of Health, and the U.S. Department of Agriculture, the workshop was attended by some 150 invited participants representing government agencies, including the Department of Defense, and the food industry.

The workshop program was developed to address the specific needs of ILSI N.A.'s members and associates, the major North American food companies and organizations, as well as government agencies. The planning committee selected four of the biological agents on CDC's Category A list (Morbidity and Mortality Weekly Report, April 21, 2002, 49(RR04): 1-14): ***Bacillus anthracis*** (anthrax), ***Yersinia pestis*** (plague), ***Clostridium botulinum*** toxin (botulism), and ***Francisella tularensis*** (tularaemia), and invited speakers to discuss what is known about the action (persistence, survival, detection, and inactivation) of these agents in foods. Other experts addressed the action of acute (fast-acting) and chronic toxins and toxicants in food, contamination of food with radionuclides, and the use of ionizing radiation to control pathogens. Potential security threats to the water supply and methods for detecting microbial and biological contaminants in water, as well as strategies for mitigating biological, chemical, radioactive, or physical threats to the food supply were also covered.

In the workshop's opening address, Surgeon General Dr. David Satcher characterized public-private partnerships as critical to future terrorist response strategies, calling for a new emphasis on such partnerships to support and bolster vital public health infrastructures. Dr. Satcher described the workshop as a model for the nation in terms of responding to future threats of bioterrorism.

After the workshop, ILSI N.A. arranged for the workshop deliberations to be taped, transcribed, and summarized in the series of extended abstracts that are contained in this publication. In addition, ILSI N.A. used the material from the workshop to develop a consensus statement on key research needed to improve our ability to respond to biological and chemical threats food security. This statement appears at the end of this publication.

ILSI N.A. is pleased to make this important information available in the hope that it will contribute to national initiatives to improve the safety of the food supply.

Acknowledgements

ILSI N.A. expresses its profound gratitude to all those who participated in the *Workshop on Biological and Chemical Agents of Terrorism in Food*, and whose involvement was critical to the successful outcome of this meeting. Special recognition is given to the workshop presenters who gave so freely of their time and expertise to help us understand and address these critical issues.

ILSI N.A. acknowledges with sincere appreciation its partners in this endeavor, the Centers for Disease Control and Prevention, Food and Drug Administration, National Institutes of Health, and U.S. Department of Agriculture. ILSI N.A. is especially appreciative of the special role played by the International Association for Food Protection, who cosponsored the workshop and coordinated registration and other important logistics.

ILSI N.A. also wishes to thank the following individuals whose assistance before and during the workshop were critical components of its success: Dr. James Behnke, President, ILSI N.A.; Dr. Richard Black, Executive Director, ILSI N.A.; Mr. David Tharp, Executive Director, IAFP; Ms. Karen Huether, Chair, ILSI N.A. Technical Committee on Food Microbiology; and Dr. Joseph Scimeca, Chair, ILSI N.A. Technical Committee on Food Toxicology and Safety Assessment.

Dr. Don Zink's important role as the workshop rapporteur, and his contribution in preparing the extended abstracts of the workshop presentations, are hereby acknowledged with deep appreciation.

This project would not have been possible without the commitment and support of the ILSI N.A. Technical Committees on Food Microbiology and Food Toxicology and Safety Assessment, whose members included Campbell Soup Company, The Coca-Cola Company (including The Minute Maid Company), E.I. du Pont de Nemours and Company (including DuPont Qualicon and DuPont Haskell Laboratory), Future Beef Operations, LLC, General Mills, Inc., Gerber Products Company, H.J. Heinz Company, Kellogg Company, Kraft Food NA, Unilever Bestfoods, M&M/Mars, Nestlé USA, Inc., The Pepsi-Cola Company, The Procter & Gamble Company, Sara Lee Corporation, and Tyson Prepared Foods Group. The following committee members and scientific advisors, who participated in the workshop planning group to develop the program and identify speakers, deserve special recognition: Dr. Stan Bailey, Mr. George Evancho, Mr. Paul Hall, Ms. Karen Huether, Dr. Marguerite Neill, Dr. Nick Nickelson, Dr. Steve Olin, Dr. Laurie Post, Dr. Joseph Scimeca, Dr. Les Smoot, Dr. Bala Swaminathan, Dr. Isabel Walls, Dr. Martin Wiedmann, and Dr. Don Zink.

ILSI N.A. gratefully acknowledges the efforts of Ms. Catherine Nnoka and Ms. Pamela Copeland who ensured that the workshop fulfilled the very highest of expectations. The assistance of Ms. Julie Cattanach and Ms. Bev Corron from IAFP, and Ms. Regina Randall and Ms. Pauline Rosen from ILSI N.A., with the workshop logistics and other details was also critical to the success of the meeting and is sincerely appreciated. Mr. Daniel Copeland's capable handling of the security aspects of the workshop deserves special recognition. Additional mention should be made of Ms. Nnoka, Ms. Rosen, and Ms. Roberta Gutman's work on preparing this proceedings publication. Many others, who worked behind the scenes to help make this meeting successful, including Mr. Daniel Copeland who so capably handled the security aspects of the workshop, also merit our gratitude.

BIOLOGICAL AND CHEMICAL AGENTS OF BIOTERRORISM IN FOOD

Opening Address

David Satcher, M.D., Ph.D., Surgeon General, U.S. Department of Health and Human Services, and Senior Visiting Fellow, Kaiser Family Foundation

I was introduced to ILSI several years ago when I became director of the Centers for Disease Control and Prevention and Alex Malaspina came to talk to me about ILSI and how critical it was that we work together. I believe that in the area of food safety, we have had more cooperation among different agencies over the last several years than for any other issue. By the same token, we probably have the greatest public-private partnership, and I think that public-private partnerships are going to be critical in the future in responding to the threats of bioterrorism.

For years, we have discussed bioterrorism—we've made preparations, we've developed strategies, we've had tabletop exercises—but before last October, we never actually experienced bioterrorism. For the most part, this attack with anthrax has been an attack through the mail, and I can tell you that we had not anticipated a bioterrorist attack through the mail. In terms of considering modes of attack, food was much higher on our agenda. As you know, approximately 22 people have been infected with anthrax, including 11 cases of inhalation anthrax, five of whom died. We've had seven confirmed cases of cutaneous anthrax and four or five cases that the CDC is still calling "suspect." So we are talking about 22 to 23 people who have actually been infected with anthrax over the past 2 months. But the impact is much greater: almost 35,000 people have been put on prophylactic antibiotics, and at least 5,000 of them have been continued on antibiotic therapy for at least 60 days. There have been a lot of questions about how the American people respond to prophylactic treatment and their level of awareness about antibiotics and vaccines. We have lost five people too many, but we have saved hundreds of lives because of our ability to move rapidly and implement prophylactic therapy.

What have we learned from recent experience? The first lesson is a very painful one: that despite all of the articles that have been written, there are no experts when it comes to bioterrorism. There are so many things that we don't know about the nature of anthrax and how it operates. For example, we still don't understand how the last two people became infected, especially if you believe, as has been written, that it takes eight to 10,000 spores of anthrax to cause inhalation anthrax. That is almost certainly not true.

The second lesson that we have learned is that there is no substitute for a strong public health infrastructure. We need a public health infrastructure that can do at least four things well: the first is to prevent bioterrorist attacks, and right now that is the weakest. CDC was given authority a few years ago by Congress to monitor the movement of agents of bioterrorism, but there is no registry of agents of bioterrorism. The second is that the public health infrastructure must be able to detect an attack as early as possible. We must have the ability to detect bioterrorist attacks and to diagnose not only at the laboratory level, but also at the clinical level. The third is that the public health infrastructure must be able to respond rapidly. We have given a lot of thought and attention to this. We have developed a national stockpile of agents that can be used to respond to bioterrorist attacks and chemical attacks. We have developed antibiotics and vaccines and antitoxins, and we've developed supplies that can be moved rapidly. In fact, the stockpile is so mobile that we can make these supplies available anywhere in the country within 12 hours. Fourth, the public health infrastructure must have strong research and training programs. This research must continually upgrade and enhance detection and response potential and look for new prevention strategies.

I have argued that there are three layers to the public health infrastructure. One layer is what we call the public health service: the Food and Drug Administration, U.S. Department of Agriculture, Centers for Disease Control and Prevention, and National Institutes of Health. Broadly speaking, the public health service is federal, state, and local. Therefore, we support not only a strong CDC, a strong FDA, a strong NIH, and a strong USDA, but also strong state and local public health departments. The first layer of the pub-

lic health infrastructure is this public health service at the federal, state, and local levels. Can the public health infrastructure be effective in the absence of public-private partnerships? With respect to anthrax and the mail, we've learned how little we knew about how mail is sorted and about what can happen to envelopes moving to the post office. Our epidemiologists had to become knowledgeable in what happened to mail. Effective public-private partnerships to support the public health infrastructure are critical.

The second layer of the public health infrastructure is the network of health care providers: physicians, dentists, nurses, pharmacists, and others on the front line providing health care. It is at the front line where unusual disorders and experiences are first detected. We've had an active surveillance system for the past few years. It consists of a number of primary care providers, emergency rooms, hospitals, and other health care organizations, which have been reporting on a regular basis on several infectious diseases. This allows us to gain much more information, especially on foodborne diseases, where we have invested more than in any other area. This layer is critical to the extent that physicians take their public health role seriously. Clearly, we cannot have a public health infrastructure without a well-informed and highly motivated private health care sector.

The third layer is the general public. If we have learned anything during the anthrax attack, it is how important the general public is to the success of the public health infrastructure—for example, how important it is that the general public is informed so that people do not panic and demand antibiotics when they don't need them. We've been trying to get people to cooperate in public health practices, and now we are trying to get them to understand the appropriate role of antibiotics and vaccines. In the future, beginning in grade school, we've got to spend more time preparing people for good public health practice—in their individual lives, in their family lives, and in their community roles. This is one of the real challenges that we face.

Regarding our major strengths, whether we are talking about the FDA, CDC, or NIH, we have the best laboratories in the world. We have the best-trained epidemiologists in the world. We have been training people not only to work in laboratories, but to go out into the field to trace diseases, and these epidemiologists have been sent all over the world. They were sent to India when the plague broke out. They were sent to the Sahara when the Ebola outbreak took place—and 30% of the deaths were among physicians and nurses. These epidemiologists were sent out there to fight epidemics. We now have at least 17 or 18 field epidemiology training programs in other countries. We can deliver these epidemiologists quickly to where they are needed to deal with an outbreak. We also have a system through the FDA for food safety that's probably unmatched. We also have a drug safety program to ensure the safety and efficacy of drugs. The FDA has protected the people of the United States from tragedies that other countries have experienced.

We also have some weaknesses. We have not adequately invested in the upkeep of the public health infrastructure. For example, some of our federal laboratories have outdated equipment that compromises the quality of their work. At the state and local level, it's even worse. Only in the last few years have we been able to secure funding from Congress to strengthen state laboratory systems. At the local level, the quality of public health laboratories is very mixed, ranging from the outstanding public health departments in New York City, Los Angeles, and Chicago to municipalities that do not even have a local board of health! Some states don't have a single trained epidemiologist! We have never said, in this country, that there has to be a basic unit of public health below which we will refuse to fall. That weakness is going to be one of the major threats as we move forward. We've got to make the commitment, and again, it has to be a public-private commitment.

Our technology is wonderful, but it can also pose an innate threat to the safety of our food supply. In the past, an outbreak of foodborne illness may have been a problem in one small community, but now an outbreak of ***E. coli*** O157:H7, ***Salmonella***, or some other infectious agent can hit 20 to 30 states at one time because of the way we process and distribute food. We must be aware of the dual potential of technology.

I will close by discussing some major concerns. Our global food supply can pose a tremendous challenge to our safety, and we must make the investment needed to monitor the safety of that food supply. An increasing number of biologi-

cal and chemical agents can impact food in so many different ways. We've been dealing with anthrax, and we know that anthrax can be delivered through food. Botulinum toxin is another pathogen we are concerned about. We have to be aware of these and other pathogens, for which there are several different potential points of attack. Because of the inadequate number of epidemiologists and inspectors to monitor food and respond to foodborne disease outbreaks, we need a more informed front line of health care providers. The new emphasis on public-private partnerships discussed at this meeting could strengthen our future by providing a model for preventing and responding to bioterrorism. As tragic as our experience has been since September 11, there is a lot of hope, such as that represented here today, in moving this nation forward to deal with bioterrorism.

Food and Drug Administration Counterterrorism Programs: Food Safety and Security

Andrea Meyerhoff, M.D., Office of Antiterrorism Programs, Food and Drug Administration

The Food and Drug Administration's mandate in the area of antiterrorism involves two main categories of involvement. The first is as a law enforcement agency responsible for investigating tampering with food, blood, radiation health devices, and any other FDA-regulated product, such as drugs, vaccines, and other medical devices. The second is as a public health agency responsible for the availability of safe and effective drugs, vaccines, and medical devices for individuals exposed to any agent of a terrorist threat, whether biological, chemical, or nuclear.

Beginning 2 or 3 years ago, components of the agency have been involved in antiterrorism activities. In September 2000, it was determined that these activities needed to be coordinated. It was recommended that there be a director of the antiterrorism programs based in the office of the commissioner and that this coordinated effort could administer and organize the agency's antiterrorist programs and activities. This position was filled by temporary people while a search was conducted for a permanent person. I assumed that job in July of this year. My office is the point of contact for both intra- and extra-agency antiterrorism activities. We are responsible for the agency's overall strategic planning in this area. We are organized internally around an antiterrorism steering committee made up of representatives of a number of different areas of the agency. Among these are our emergency operations, including a 24-hour emergency line for the notification and investigation of any product tampering (including food products). We have representation from FDA's five product base centers.

Externally, we collaborate with a number of other federal agencies. These include the Department of Health and Human Services, Centers for Disease Control and Prevention, U.S. Department of Agriculture, Environmental Protection Agency, U.S. Customs Service, and the Federal Bureau of Investigation. On the military side, we collaborate with various Department of Defense agencies, such as the U.S. Army Medical Research Institute of Infectious Diseases. Our relationships with industry are an important and active area of antiterrorism activity. Also, we work with members of academia and foreign governments, with which we have collaborative relationships and cooperative arrangements.

The FDA's food strategy is divided into four basic areas: threat assessment, surveillance, deterrence and prevention, and (should an event occur) containment through rapid response. A key principle to keep in mind as we look at antiterrorism approaches to food safety and security is the gains that we have made in food safety and the attempts to protect the food supply from accidental contamination. Also, surveillance programs such as FoodNet and PulseNet will help as we look to identify possible intentional events of food tampering or contamination.

When we move from accidental to intentional food contamination, we need to recognize that added vigilance is needed. The FDA is trying to answer very difficult questions about what a terrorist might want to do. Certainly, there are almost infinite possibilities. We need to think very broadly and at the same time maintain our focus. There are two incidents from the past that help illustrate the nature of the threat. In 1984 there was an outbreak of ***Salmonella*** Typhimurium traced to a salad bar in Oregon in which more than 700 people got sick. It wasn't until a substantial period of time had passed that this was recognized as an intentional act. A second event, in 1996, occurred in Texas when a woman baked muffins and intentionally introduced ***Shigella dysenteriae*** into the food she served to a number of colleagues at work.

Both of these events tell us a couple of things we want to keep in mind when we think about food terrorism. The first is that while some of the most glaring and recent terrorist events represent an international effort, the 1984 and 1996 efforts were domestic. The second is that the agents used in these incidents were ones that we see accidentally contaminating foods. This reminds us that we need to think very broadly when we think about what an individual might attempt to introduce into a food. These two events also raise the question of what a terrorist might try to

do. We need to consider that there could be a number of objectives to a terrorist act. The intentional acts in 1984 and 1996 resulted in a lot of sick people, but not much death. But they were disabling, and disablement is a potential terrorist goal.

The FDA is addressing food security through a multifaceted approach that covers a number of areas. These include bolstering current prevention operations; increasing the agency's presence, particularly at the borders where imported foods come into this country; identifying control measures and working with industry; building capacity and providing training; building our scientific expertise and testing capability; strengthening surveillance and intelligence gathering; improving industry and consumer education and communication; and increasing emergency preparedness and response.

The agency's antiterrorism activities can be categorized into four general groups: (1) budget and legislative initiatives to increase our border coverage and our domestic coverage and to increase our authority to prevent food security problems and improve our ability to trace foods once an outbreak has been identified; (2) improved interagency coordination and communication through consultations on what security measures may work, by providing consistent guidelines, through consistent consumer messages, by sharing information, and through collaboration and cooperation; (3) increased domestic and international outreach through consultation with state and local governments, and consultations with some of our international partners; and (4) working with industry associations through consultations and collaborations to identify control measures, share information, and establish contact and communication protocols.

In summary, our efforts to meet our responsibilities in food safety are a three-part effort in preparation, partnership, and communication.

Safety of the Water Supply

Ron Hoffer, Office of Ground Water and Drinking Water, U.S. Environmental Protection Agency

I will review four issues relating to water supply safety: the universe of drinking water systems, potential threats, key roles and responsibilities, and activities now under way to bolster security.

What is the universe of drinking water systems? There are many public water systems—those that serve 25 people or more or that have 15 or more connections—whether they are run by a private company or by a municipal authority. The ones I will focus on are those that serve people year around. There are 54,000 community systems that serve the bulk of the U.S. population. We should also remember that one of the things that make the job more tractable is that 82% of the population receives drinking water from the largest systems, with fewer than 400 in this category. In a simplified way there is a two-tier approach: one for the largest systems (those that serve 10,000 or more and especially those that serve 100,000 or more), and those that serve fewer. There is a big difference in the capabilities of larger and smaller systems to implement protection measures. The large systems have on-staff security officers and more elaborate means of securing access. The smaller systems may not have a full-time operator, and the smallest may not even have a fax machine. I can assure you that security is not a new issue to the large systems. Large systems have been worried about security and maintenance issues for a long time. They've already been thinking about natural disasters and things like breaks in the power supply. But the one thing that is new is how to protect water systems from terrorism.

With respect to waste water, most people are served by what are called publicly owned treatment works or POTWs. We also have septic tanks in smaller communities. There are more than 600,000 miles of municipal sewer service, and we know that many of these POTWs have emergency operation plans in effect. There are a lot of waste water systems and a lot of drinking water systems. But each of them is run by an entity that we can work with, which is good.

Regarding potential threats, what do we need to worry about? We are most worried about not the exotica, but the physical destruction of the drinking water infrastructure. Taking out a storage reservoir, blowing up a dam, interrupting a supply canal, destroying part or all of a treatment plant, or taking out part of the distribution system would do some serious harm. There are also electricity and transportation interdependencies. Many drinking water systems have back-up power, but some smaller systems do not. For transportation, if we are relying on a disinfection chemical to deal with agents introduced into the water, we need to be able to get that chemical to the treatment plant.

Waste water systems are vulnerable as well. The physical destruction of part of a waste water system by explosives or hazardous chemicals would certainly cause some lack of confidence by the public. With regard to cyber attacks, computer systems are very common in drinking water plants. Thankfully, in this particular area there was a lot of strengthening in the drinking water systems in preparation for Y2K. Also, many if not most of U.S. drinking water systems can still be operated without computers.

Many people are worried about the release of biological, chemical, or radiological contaminants in source waters, storage reservoirs, and treatment and distribution systems. The positive side is that many of these agents are really difficult to obtain and, in the case of drinking water, to deliver in sufficient quantities to affect a reservoir or large storage system. This would be a real challenge. Putting an agent in water hoping that it will get to consumers is a much less direct route than some other means of delivery. Common disinfection practices at most treatment plants can handle many but not all of the biological agents. Flocculation, coagulation, and filtration can also help greatly in reducing contaminants that get to the consumer. We are also worried about smaller quantities that can contaminate the distribution system. The pressure that lets you open the tap and have the water come in is the same thing that's protecting you, and this is not invulnerable to attack. In other parts of the world, that's not the case. Those of you who work outside the

United States know that breaks in the distribution system that cause pressure drops are very common. In those situations the possibility of attack is greater.

Another thing that we worry about are lethal chemicals that are stored near treatment plants. If a criminal could destroy or disrupt a chemical plant, this could cause some problems in the water system. With regard to potential biological and chemical contaminants, we are working on this with many of the agencies and individuals at this workshop. We are looking at more than 40 potential biological agents and more than 200 chemical agents. We are trying to ascertain what is known about the stability of these agents in water. Can they be treated and by what means? There are a number of studies and research projects that have been undertaken, and a lot of them are reinterpreting data already out there. But we need to look at data and work with our colleagues in other agencies and do some additional studies.

With respect to roles and responsibilities, much was done long before the events of 9/11. In 1998, Presidential Decision Directive 63 gave the Environmental Protection Agency the lead to work with the drinking water industry to identify and correct infrastructure vulnerabilities to terrorist and criminal attacks. For a long time we've had in place a fundamental statute for drinking water, the Safe Drinking Water Act. It requires the states to deal with emergency response planning for both natural disasters and human-induced events. There is a provision in the act for penalties for those who tamper with or threaten public water systems. Like many agencies, EPA has a criminal investigation division, and it has been very involved in decontaminating some of the buildings in Washington. We are concerned not only about terrorist groups, but also about hoaxes and individuals who might try something crazy. Our own statutes have language to deal with those who tamper with water utilities.

In terms of whom we work with, there is a critical infrastructure protection advisory group under the Association of Metropolitan Water Agencies (AMWA) that also includes the American Water Works Association (AWWA). Industry groups such as AMWA and AWWA are critical in communicating to the water utilities. If a crime is suspected, the utilities normally would contact the local police, the FBI, and then state emergency and drinking water officials. They are the first line of defense. Emergency response plans are also in place, including those for outbreaks or public health emergencies, because unless it is obvious that water is the source, the alert would probably come through the public health infrastructure.

As an example of federal roles in counterterrorism, we are working with the Federal Bureau of Investigation and the national infrastructure protection advisory group to ensure that they have access to the best expertise. This includes expertise on which labs to go to for detecting biological or chemical agents and on maintaining evidence. We have been working with the military, which has expertise in biological and chemical contaminants. We also have been working with the Centers for Disease Control and Prevention for the last couple of years. I can second Dr. Satcher's respect for the epidemiologists and the laboratory folks at CDC. On another front, EPA has on-scene coordinators directly involved in oil spills, chemical spills, and other accidents. We also have been working with a number of other agencies, including the Army Corps of Engineers, which is used to dealing with major infrastructure issues and has cadres of consultants and technical staff who can do amazing things in a crisis. As you know, for most emergencies, the Federal Emergency Management Agency plays a key role.

Waste water preparedness is still being defined. There is no requirement under the Clean Water Act for specific emergency response, but most of the larger POTWs have emergency response plans in place.

For what we are doing now—before the events of 9/11 and after the 1998 presidential directive—we have five sets of tools. The first tool is helping the utilities safeguard water, to understand the threats, and to respond to them. A series of notices directed to water utilities address such things as monitoring, emergency response, and dealing with local law enforcement. We're also working with them on vulnerability assessment methodologies, for example, where you look in a water utility for weaknesses. Second, much of what we do now is training. We are looking at training for three groups: operating officials of the water utility, security officers at the utilities, and the actual operators. There is a parallel effort in

the small-system arena as well. Third, we are trying to develop a secure information sharing and analysis capability. If there is a credible or actual threat, we want to get information out to the utilities in a secure manner. This is in the process of being set up with the AMWA, and we are also working with the National Infrastructure Protection Center and the FBI. Fourth, we need to increase our knowledge of these activities, these agents, and these modes of delivery and response. We have expanded and will continue to do so. We are looking at contaminants, detection systems, and treatments. We're working with the CDC, Department of Defense, Department of Energy, and U.S. Geological Survey on modeling the fate and transport of contaminants in source water. This helps us know when to shut off water intakes and when to turn them back on.

People can go to a number of places for information, which is getting better and more accessible by the week. The easiest thing to do is go to http://www.epa.gov/safewater.

Bacillus anthracis (anthrax)

David L. Huxsoll, D.V.M., Ph.D., Plum Island Animal Disease Center, U.S. Department of Agriculture

Anthrax was the first disease convincingly shown to be caused by a microorganism, in work done by Pasteur and Koch. During World War II the causative organism, Bacillus anthracis, was developed as a biological warfare agent. Much of the information used today to deal with issues arising from the recent terrorist dissemination of the organism through the postal system comes from the disestablished offensive biological warfare program.

The organism is a Gram-positive, spore-forming, nonmotile, capsulated rod. In the infected host where it is actively multiplying, it exists as a vegetative bacillus. In the environment, it exists as a spore that is highly resistant to environmental stresses. It causes an acute disease in virtually all warm-blooded animals, including man. However, there is a difference in species susceptibility. Cattle, sheep, goats, horses, pigs, camels, and man are species where disease is often seen. Disease in dogs and cats is rare. Also, mice and guinea pigs are highly susceptible, but interestingly enough, rats are very resistant.

In man the disease has been described in farmers, ranchers, and others who handle carcasses of diseased animals. In the past the disease was most frequently identified in people working in industries that process hides, hair, wool, and other animal by-products. Three forms of anthrax have been described in humans. The cutaneous form of anthrax makes up about 95% of reported cases. Of these, about 90% spontaneously recover. If untreated, 10% will progress to the regional lymph nodes and then to a fatal septicemia. While many of the people who worked in woolen mills contracted cutaneous anthrax, others associated with the mills developed inhalation anthrax.

Inhalation or pulmonary anthrax, the second form of the disease, has been referred to as "wool sorters disease." It was long thought that 8,000 to 10,000 spores were needed to induce disease. This figure is the LD_{50}, and the question has come up of what is the LD_5 or the LD_1. The number of spores required to produce a 5% or 1% infection rate may be much less. One must also consider the impact of infection in people who are immunocompromised.

The third form of the disease is gastrointestinal anthrax. Most gastrointestinal outbreaks involve the consumption of contaminated meat, and most occur in primitive societies. It is interesting to note that cattle are highly susceptible by the oral route but are relatively resistant by the cutaneous route. The vegetative cell may be important in establishing infection, particularly by way of the intestinal tract. In cattle, lesions appear in the very upper portion of the small intestine and eventually lead to systemic infection. In man, the incubation period is 3-5 days.

Anthrax spores are resistant to environmental stress. Spores contained in a soil sample remained viable for 60 years. The organism was reported to have been cultured from bones recovered at archeological diggings in northern regions of Kruger National Park in Africa. The bones were radiocarbon dated at 200 ± 50 years old.

The spores are also resistant to heat. For spores autoclaved at 120ºC , the death time was 10 minutes. The spores are even more resistant to dry heat. Dry heat inactivation took 3 hours at 140ºC and 60 minutes at 150ºC when they were placed on glass and exposed to dry heat. A study using spores from 17 strains suspended in saline and heated in an oil bath showed that at 100 and 105ºC, the death time ranged from less than 5 minutes to 10 minutes. At 90ºC, there was a variance among strains of from 15 to 45 minutes.

When a mixture of spores and vegetative cells was inoculated onto nutrient agar and then exposed to sunlight, the vegetative cells survived 11 hours and the spores survived for more than 2 days. Another study reported that nutrient agar cultures stored at room temperature remained viable for 47 to 50 years. The organism remained viable in sewage stored at room temperature for 35 days. In another study, spores remained viable for 71 years dried on silk threads and stored in the dark at room temperature. The spores survived for 22 days in naturally infected meat that had been cured with a solution of salt, sugar, and saltpeter. In nutrient broth, the organism is able

to grow in a 7.7% salt concentration but not at 10%. In one study, spores from eight strains were irradiated by a cobalt-60 source. One strain survived 1.4 Mrad but not 1.5 Mrad.

The vegetative cells are also durable. In a study using an asporogenous strain in blood, the cells survived 50 days at room temperature and less than an hour at 5ºC. It is interesting that the organism survived 10 years in milk taken from the udder of a cow that had died of anthrax. It has been reported that the organism will multiply and sporulate in milk under suitable conditions, so there is concern about milk residues in milking machines and factory equipment that may become contaminated.

Francisella tularensis (tularemia)

Robert L. Buchanan, Ph.D., Center for Food Safety and Applied Nutrition, Food and Drug Administration.

Tularemia is also known as rabbit fever, deerfly fever, hare fever, and trapper's fever. As the names imply, the disease is associated with rabbits and other wild animals. It has been isolated from over 100 different species of mammals. Tularemia was first described in the medical literature in 1907 and got its name from the fact that it was isolated originally in Tulare County, California.

Francisella tularensis can be transmitted by a number of different means, but probably the most studied has been through blood-sucking arthropods and insects. However, people have been infected simply by working in a contaminated environment. It can be contracted by handling infected wildlife, consuming contaminated wildlife, from contaminated water supplies, and by working with the organism in a laboratory. Since the 1930s, when we started keeping records on this organism, to the current time, there has been a dramatic decrease in the incidence of tularemia. The number of cases of endemic tularemia per year has dropped from thousands to around 200. Much of this decline is due to the chlorination of municipal water supplies. Currently, one of the environments most often associated with tularemia is diagnostic labs: ***F. tularensis*** is considered to be one of the most dangerous organisms to work with in a laboratory, and there is a considerable case history of laboratory-acquired infections.

Interestingly, there is seasonality with the different etiologies of the disease. Typically, we see the arthropod-borne disease in spring and summer. Rabbit-borne disease tends to be in fall and winter, and the waterborne form tends to be almost always in the winter. Different forms of the disease are defined by the route of entry into the body. Ulceroglandular tularemia is a cutaneous-initiated form of the disease and of closely related infections of the eye and mouth. Glandular tularemia is a general systemic form of the disease where there are no external signs except a painful swelling of the lymph nodes, whereas typhoidal tularemia is a systemic infection without obvious swelling of the lymph nodes or any involvement of the skin. We just see a general systemic infection. Other forms of the disease include inhalation tularemia and gastrointestinal tularemia. While the specific symptoms may vary with the different forms of the disease, all can lead to a life-threatening general systemic infection.

I will focus on the cutaneous, inhalation, and gastrointestinal forms of the disease. Once the organism has reached the systemic stage—that is, a whole-body infection—mortality can be as high as 30–60% if left untreated. In such instances, the infection is referred to as a fulminating infection; that is, the infection progresses so rapidly that the patient dies before the diagnosis can be completed. The rapidity of the fulminating infection appears to be dose related. In the case of a large dose, death can occur within 48 hours of onset of initial symptoms. The infection can be treated with antibiotics, but it does not respond to all antibiotics. For example, the organism is resistant to penicillin.

The cutaneous infections represent about 80% of the reported cases. The typical incubation, from exposure to onset of symptoms, can range from 2 to 10 days, but the average is 3 to 4 days. The early symptoms are similar to many of the diseases discussed at this workshop. It begins with general flu-like symptoms, but in cases of cutaneous infection, there is a very distinctive red punched-out necrotic ulcer. The ulcer is not very big but has a characteristic shape and appearance. If the ulcer is on the hands, face, or shoulders, it's typically due to an environmental exposure or to handling an animal. If it is on the lower extremities, particularly the legs, it's typically associated with an insect or arthropod bite. The organism then spreads to the nearest lymph node from the initial site of contamination at the ulcer. The lymph node becomes very enlarged and inflamed and is sometimes misdiagnosed as plague. From the lymph node, the disease can progress to septicemia and then finally to endotoxemia. Endotoxemia is a generalized toxic reaction to large numbers of an organism. If untreated, approximately 5% of the cutaneous infections will

become septicemic and ultimately the patient will die.

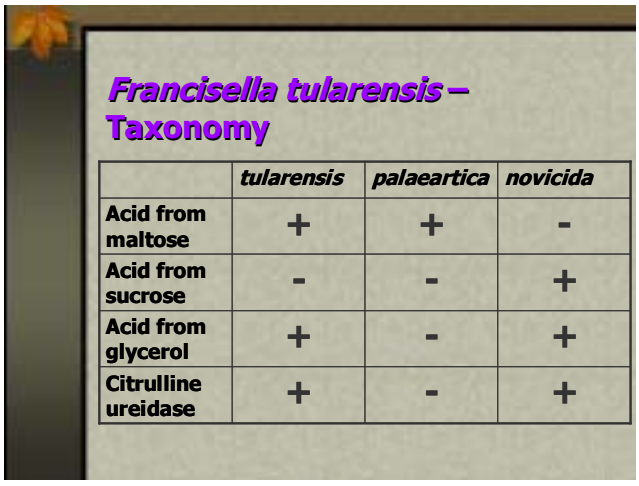
Pulmonary infection occurs by true inhalation of the organism, but in some cases, even though the lung is the site of the primary infection, it is actually the beginning of a whole-body infection. These types of infections tend to progress rapidly to septicemia or fulminating disease. Older individuals seem to be the most at risk in terms of the inhalation route of entry.

The gastrointestinal illness is associated with the consumption of contaminated water or food. The first symptom is persistent diarrhea with characteristic abdominal pain and lower-back pain. The course of the infection can range from self-limiting cases with chronic mild diarrhea to cases that become septicemic. People who have died of tularemia from the gastrointestinal route of entry characteristically have massive ulceration of the intestinal tract.

We are able to make good estimates for both cutaneous and inhalation infectious doses. As little as 10 cfu by subcutaneous injection (which is used as a model for arthropod bites) is enough to produce infection. Inhalation infection can be produced by extremely low doses, 10 to 50 cfu. With respect to gastrointestinal infection, the only data available come from outbreaks where they examined foods containing possibly as much as 10^8 cfu Very high levels of people are infected at doses this large, but I do not believe that the required dose is this large. My guess is that with lower doses, smaller percentages of the population will be affected.

Francisella was named for Edward Francis, who in the early 1970s was honored for his lifelong study of this organism. It is a very small coccobacillus, only 0.2 × 0.2 µm, which is small enough to get through some of the microbiological filters that we use. It has a characteristic thin, rather unique capsule that is mostly lipid with a very distinctive and unique fatty acid profile. The organism requires a variety of different nutrients and is a true microaerophile. So far, no one has shown that it is stimulated by CO_2. It is a nonspore-forming organism. There are three biovars of the organism. Biovar ***tularensis***, or ***F. tularensis*** subsp. ***tularensis***, is isolated only from North America and is considered the most virulent of the biovars. Another one is ***palaeartica***, which has worldwide distribution, and the third is novicida. A couple of other biovars are being looked at, so the taxonomy of this organism is in flux. We can separate the biovars biochemically or use gene probes to distinguish them. Figure 1 shows a biochemical profile for differentiating the biovars. An important point is that biovar ***tularensis*** is substantially more virulent than the other two biovars. Also, within biovar ***tularensis***, there seems to be a relationship between the levels of catalase associated with the strain and its virulence. The more catalase activity it has, the greater its virulence. Virulence is also very strongly associated with the lipid capsule: if you eliminate the lipid capsule, you eliminate the virulence as well as its acid resistance.

Traditional methods of culturing the organism are poor at best, and it is very difficult to isolate, particularly if present at low levels. If there is a competing microflora, it is very hard to recover the organism from a food sample. In food outbreaks associated with wild rabbits, less than 10% of the cases have ever had the organism isolated from any source other than the patient. Very few studies specifically look at isolation methods from foods. Enrichment techniques are generally required. Enrichment media included thioglycolate broth with additives, BHI broth with added cysteine, and modified Müeller-Hinton broth. One of the best ways to recover the organism from a highly contaminated sample is to inject a sample into a mouse and later try to isolate the organism from the mouse spleen and liver. For direct plating, several different agars are used. The most widely used is cysteine heart agar with chocolatized blood and antibiotics. Plain chocolatized blood agar can also be used. The low



catalase activity of the organism makes isolation difficult if it has been injured. If the organism is stressed, direct plating it onto a selective medium or putting it into a highly nutrient-rich medium would probably kill it.

A variety of rapid methods have been developed to detect the organism. These include several different primers for use with polymerase chain reaction, or rDNA separations can be done, and there are probes for both the species and the entire genus. There is a direct fluorescent antibody method available and slide and tube agglutination methods for confirming identity. However, the available commercial antisera don't always work. Further work also needs to be done on the fatty acid profile, which could be useful for confirmation because of the unique composition of the capsule. Most of the detection methods for this organism have been developed either for clinical samples or for environmental samples but not for foods.

Regarding characteristics of the organism in relation to food processing, I was unable to find reports of studies specifically looking at the growth, survival, and inactivation of ***Francisella*** in food. However, I extracted some characteristics from the clinical, basic-research environmental literature that I think are relevant for food. What follows are my own inferences about its possible behavior in foods. It can survive for extended periods in mud, water, and decaying matter, particularly in cool weather; it's not uncommon to find it surviving in the environment over the winter. There is at least one report where it survived in cold mud for up to 16 years. Therefore, it would not be surprising to see it survive very well in foods with high moisture content at low temperatures. Elimination of its capsule reduces both its virulence and its acid tolerance. Thus, food processes that would strip off that capsule would have an impact both on the ability of the organism to survive and on its virulence. The organism may be vulnerable to detergents that could remove this capsule.

is a non-spore-former. It is inactivated by temperatures of 55ºC for 10 minutes. We would expect the organism to be inactivated by mild heat treatments and thorough cooking. It is also likely to be sensitive to a number of other technologies known to inactivate vegetative cells. For example, I would expect that a 5 kGy irradiation treatment would inactivate this organism. The organism can be stored for years by lyophilization in a carrier such as skim milk if it if is maintained in the temperature range –70 to 5ºC. Thus, it seems that ***Francisella*** is likely to be resistant to drying, particularly if done at low temperature and maintained in subsequent storage at low temperature. It seems to be less resistant if dried and then stored at a higher temperature. Clinical specimens can be held for reexamination for extended periods by maintaining them between –70 and –30ºC. Thus, the organism is likely to be highly resistant to freezing for extended periods. Since the chlorination of municipal drinking water has largely eliminated waterborne tularemia outbreaks in the United States, we can infer that chlorination is likely to be an effective means of killing in the food-processing environment.

The natural habitats of the most virulent of the biovars of ***F. tularensis***, ***tularensis***, is limited to North America, so one would not expect to see this biovar in foods or food ingredients coming from other parts of the world. The identification of this biovar in an imported food would need to be interpreted appropriately. Because ***F. tularensis*** is one of the leading causes of serious laboratory-acquired infections—in fact, most of our knowledge of its clinical attributes comes from people infected in the lab—it is an agent that should not be worked on without proper training and facilities. I would particularly caution against working with this organism in a laboratory connected to a food-processing plant, to ensure that nothing goes back from the lab to the plant. This is a highly infectious agent at very low doses.

Dr. Andrea Meyerhoff talked about the fact that Food and Drug Administration is looking for partnerships. FDA's Center for Food Safety and Applied Nutrition has had a long, ongoing partnership with people in the area of food safety, particularly in the area of food safety microbiology, and we need your continued help on potential bioterrorist threats to the food supply. We are starting from a situation where we really don't have much information on these agents in foods. Although a number of highly effective, rapid methods have been developed for detecting ***F. tularensis*** in clinical and environmental samples, they need to be validated in food systems. We know what a barrier this can be in terms of their applicability to foods. The FDA is looking for help in validating

existing methods in a wide variety of foods. I extrapolated the behavior of this organism in foods from observations in clinical and environmental settings, but this is my interpretation of other data. We need some hard information on the behavior of ***F. tularensis*** in a variety of foods: its growth, its survival, and the factors that inactivate it. ILSI, the food industry, and the FDA can work together to provide the kind of information that can be used to prevent bioterrorist activity with this agent.

Yersinia pestis (plague)

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In the days before modern sanitation, rodent control, and antimicrobial agents, plague occurred in great urban epidemics and killed many of its victims. The first well-described outbreak of plague occurred in the sixth century A.D. It started in Egypt around 540 and swept through the Byzantine Empire, killing approximately 100 million people during the next 50 years. The organism continued to cause illness in small outbreaks until the next pandemic, which is the well-known black death of the 14th century when it killed about 50 million people. In 1894, the third pandemic erupted from an ongoing epidemic in China. Technological changes in mode of travel from sailing ships to steam ships resulted in plague's rapid spread throughout the world. It reached 77 ports on five continents by 1903, including ports in the United States in 1900. Rat-associated urban plague epidemics continued to occur in the United States until 1925. In North America, a low level of endemic plague activity continues in wilderness areas from the Pacific coast to the Great Plains and from southwestern Canada down into Mexico.

Yersinia is in the family Enterobacteriaceae, and the three species of public health interest are ***pestis***, ***enterocolitica***, and ***pseudotuberculosis***. ***Yersinia*** spp., including ***pestis***, grow under aerobic and anaerobic conditions from 0 to 45ºC. Their optimal growth temperature is 25–28ºC. ***Yersinia pestis***, ***pseudotuberculosis***, and the pathogenic bioserotypes of ***enterocolitica*** all show a tissue predilection for lymphoid tissue and spread by the bloodstream. Although the three pathogenic species of the genus cause different diseases, they share a number of pathogenic mechanisms. They all use the type III contact-dependent secretion apparatus, and they share a 70–75 kb plasmid that contains genes for adherence, invasion, and secreted antiphagocytic proteins called ***Yersinia*** outer-membrane proteins (YOP) E, H, and T. YOP M binds thrombin and inhibits platelet aggregation, and ***Y. pestis*** also has other plasmid-mediated and chromosomal pathogenic attributes.

Yersinia pestis circulates around the globe in tropical, subtropical, and warmer temperate climates between about 55º latitude north to 40º latitude south, except for Australia. Within this broad range, it picks landscapes that support stable high populations of rodents and rodent fleas. Today, the distribution of plague coincides with these natural foci and is no longer focused in urban rats around seaports. The true number of plague infections that occur worldwide is unknown owing to poor diagnosis and reporting, but the World Health Organization receives reports of 1,000 or 2,000 cases each year. The United States averages about 13 cases a year, mainly in Western states during the summer. Of U.S. cases, 85-90% are bubonic, and most of the rest are septicemic. Primary pneumonic plague is rarely reported in the United States. About 10% of septicemic and bubonic cases develop secondary plague pneumonia, creating a risk of outbreaks of primary pneumonic plague from person-to-person spread.

Human exposure to plague usually occurs from infected domestic rodent populations or from pets bringing rodents or their fleas home, and from incursions into wilderness areas where plague exists. Indirect transmission to humans occurs from flea bites. Direct transmission also can occur from handling infected animals, skinning them, or cutting up the meat. Usually, ***Y. pestis*** enters humans through breaks in the skin or mucous membranes, but it can also be transmitted directly through person-to-person contact.

Although we really don't know the human infectious dose of ***Y. pestis***, it is likely to be low. By the oral, intradermal, subcutaneous, and intravenous routes, as few as 1–10 cells of ***Y. pestis*** are sufficient to cause infection in rodents and nonhuman primates. Estimates of infectivity by the respiratory route in nonhuman primates are between 100 and 20,000 organisms. Differences in host susceptibility and strain virulence create a fairly wide range of exposure doses that are likely to cause disease. During the incubation period of 2 to 8 days, the bacilli grow at the point of introduction and then commonly spread to a regional lymph node. If untreated, the disease can progress to septicemia and cause death.

Human infections with ***Y. pestis*** result in one of three clinical forms: bubonic plague, which typi-

cally follows an infection from a flea bite; primary septicemic plague, which causes whole-body infection; or primary pneumonic plague, which follows inhalation of the aerosolized microorganism [1]. Our experience with naturally occurring plague doesn't tell us much about foodborne plague, because it appears to be an uncommon means of infection, although gastrointestinal signs may be prominent in other forms of the disease.

In cases of bubonic plague, the patient suddenly develops fever, shaking chills, headache, and discomfort in the region of the lymph node. In approximately 6 hours, this discomfort turns into excruciating pain, local erythema develops, and then the bubo erupts and becomes obvious. With antibiotic treatment, fever and general constitutional signs slowly subside over 3–5 days. Primary septicemic plague is a progressive, overwhelming bloodstream infection in the absence of an apparent bubo. Although it occurs in all age groups, people older than 40 are more likely to develop primary septicemia, and septicemic patients less than 30 years of age appear to be at elevated risk of dying from their infections. Plague septicemia leads to disseminated intravascular coagulopathy and spreads to many organ systems. Plague pneumonia, either primary or secondary, is characterized by the abrupt onset of fever, coughing, and difficulty breathing. Death usually ensues in a few days if antibiotics are not begun early in the course. Oral exposure to ***Y. pestis*** results in plague pharyngitis, generally followed by septicemia and/or pneumonia.

Diagnosis of plague is confirmed by isolation of ***Y. pestis*** from blood, buboes, or other tissues or body fluids [2]. Direct fluorescent antibody tests, immunohistochemistry, and polymerase chain reaction can be used to identify the organism in tissue samples. Serologic assays can be used to diagnosis cases retrospectively. Food laboratories are not accustomed to working with ***Y. pestis***, but they work with a number of related organisms, and should not find ***Y. pestis*** difficult. It is a BSL-2-level organism, like many other human pathogens that are more commonly encountered in food samples. Confirmation requires special reagents, however, and identification of presumptive positives in food samples should result in rapid notification of proper authorities and transfer of work to an appropriate public health laboratory. Food samples suspected of being contaminated at high levels can be inoculated into broth, streaked onto CIN or MacConkey's, and incubated at 26–28ºC. If contamination levels are likely to be low, samples can be cold enriched at room temperature or cooler in a broth, or laboratory animals can be inoculated. Biochemical differentiation is presumptive only. The Centers for Disease Control and Prevention uses a specific phage lysis to confirm ***Y. pestis.***

There are two major areas of deficiency in our understanding of the risk posed by agents of mass destruction, including ***Y. pestis***, intentionally introduced into food. First, these agents are not normally foodborne hazards, so we have little natural experience to draw upon when they are used for a bioterrorist assault on the food supply. Second, our recent experience with anthrax indicates that what we have learned from studying naturally occurring disease doesn't always apply when we are in a situation of intentional contamination. We thus have to be cautious about the assumptions on which we base the information we do have.

The first uses of plague as a bioweapon probably occurred in 1346 and 1347, and involved intentional exposures to plague victims during the siege of Caffa. During and after World War II, additional research and development programs for weaponizing ***Y. pestis*** were carried out. If plague is used as a contemporary bioterrorist agent, we could expect a sudden outbreak in people who had no obvious risk factors and were not experiencing plague in the area. Because most attention has focused on the mass-casualty potential of infectious aerosols, it is likely that pneumonic plague would be overrepresented among the cases.

We have only limited experience with the natural transmission of plague to humans by the foodborne route to guide our preparation for bioterrorist attacks through intentional contamination of food. In 1894, Yersin showed that rats fed liver and spleen of dead animals contracted plague, and foodborne transmission clearly occurs in natural infections in rodents and carnivores. Therefore, it was clear early on that foodborne exposure posed a credible threat to humans. However, in contrast to ***Y. enterocolitica***, which causes an enteric infection, oral exposure to ***Y. pestis*** causes systemic infection without gastrointestinal colonization. Published reports on foodborne

plague are hard to interpret, and it is sometimes difficult to separate the effects of handling contaminated meat from the effects of consumption in these accounts [3]. Therefore, it is difficult to predict the range of incubation periods and clinical presentations that are likely from foodborne exposures. Based on available experimental data and clinical experience, we would expect foodborne plague to present with oropharyngeal symptoms similar to other bacterial and viral causes of sore throat, with rapid progression to severe systemic disease. It is likely that infection and disease would occur with low oral exposure doses, but dose-response relationships are unclear.

Likewise, it is difficult to predict the behavior of ***Y. pestis*** in food based on available data. ***Y. pestis*** is readily inactivated by environmental factors, including sunlight, high temperatures, and desiccation. Therefore, aerosol contamination of field crops is unlikely to create a persistent foodborne risk. Ordinary disinfectants, such as Lysol and chlorine bleach, also kill ***Y. pestis*** readily. None of the pathogenic ***Yersinia*** spp. is thermotolerant, and 71.8ºC for 18 seconds and 62.8ºC for 30 minutes inactivate them. However, ***Y. pestis*** survives freezing well, even repeated refreezing. It can be recovered from the spleen of dead rodents for a couple of weeks if they've been at room temperature or slightly cooler. In the 1920s in Russia and Siberia, it was discovered that exhumed corpses buried during the winter were culture positive for 6 months but that those buried in unfrozen ground during the summer were culture positive for 30 days or less. More recent experience suggests minimal survival of ***Y. pestis*** in corpses for more than a month or two. These data and the referenced outbreaks suggest that ***Y. pestis*** intentionally introduced into raw meat may survive refrigeration for many days and freezing for many weeks. However, determining the true persistence of risk in various raw meat products under likely conditions of storage will require carefully designed studies.

Limited experimental data on the survival of ***Y. pestis*** are available for other food products. These studies demonstrate variable survival at room temperature in moist produce (apples, bananas, tomatoes) for 2–4 days. It survived in refrigerated cooked pork for 3 days and for a couple of weeks in pickled meat and in butter. ***Y. pestis*** survived in sterilized milk held at room temperature for 90 days and did not ferment the milk. We need to do a great deal more work on the survival of this organism in foods and through food processes to clarify major points of risk.

The threat of intentional contamination of food with exotic agents of mass destruction such as ***Y. pestis*** and with more common agents of foodborne disease is real. The food industry and government agencies must assess threats, identify vulnerabilities, and develop the capacity to prevent and respond to bioterrorism directed against the food supply.

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Rapid Detection Methods for Microbial and Chemical Agents

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abstract not available for publication

Acute Toxins

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I will focus on biological toxins as intentional contaminants of food. I am going to emphasize bacterial toxins, marine toxins such as saxitoxin, and mycotoxins. I will briefly touch on plant toxins. Also, there are various animal toxins where food could serve as a vehicle.

I would like first to mention two deliberate contamination incidents that have not been covered by other speakers. In 1961, there was an infectious hepatitis outbreak at a naval air station with 23 cases. The outbreak was caused by an individual urinating on the salad dressing. In another incident, four university students became ill from food maliciously infected with pig roundworm ova. Other speakers have discussed the Oregon incident with the 751 cases including several dozen people hospitalized and the Texas pastry incident. To date, there has not been a documented large-scale outbreak from the intentional contamination of food with biological toxins. But as this talk will conclude, the possibility does indeed exist.

Biological toxins are poisons produced by living organisms. They are not infectious agents, so they do not replicate in the human body. Many are very toxic and can be lethal or incapacitating. There are hundreds of biological toxins found in nature, but I will emphasize only the more toxic ones, because only a few are potent enough to be effective as intentional biological contaminants. Generally, these toxins, especially if they can be weaponized, are more toxic by inhalation than by ingestion. One of the exceptions is botulinum toxin, the most poisonous substance known, which can be highly lethal by the ingestion route. One of the take-home lessons from this presentation should be that there is limited information regarding the stability of toxins in foods. Of course, there has been considerable work done in foods where certain toxins are naturally found. However, there is not a great deal of understanding about the stability of toxins in other foods that could serve as potential vehicles.

There are criteria for a biological toxin to be used as an effective intentional food contaminant. The source bacterium or agent must be easy to obtain, and in many cases this is true. Also, the toxins must be relatively easily produced or extracted, and I'll give some specific examples of this. Their potency should be rather high, and they should be quite stable to thermal processing or to other food-processing conditions. Finally, they must be able to cause incapacitating illness or death when delivered. For example, ricin can be fairly easily extracted from castor beans. In some varieties of castor beans, ricin comprises about 2.5% by dry weight of the castor bean. Other sources of toxins are ubiquitous in nature. Spores of ***Clostridium botulinum***, ***Bacillus anthracis***, ***C. tetani***, and ***C. perfringens*** are present in many soil samples throughout the world. Even our own bodies can be a source: ***Staphylococcus aureus*** can be obtained from a pimple. Also, theft from research labs or hospital labs continues to be a concern as potential sources.

Here are some examples that you probably are aware of. During the Gulf war, Iraq was known to have large stockpiles of botulinum toxin, ricin, aflatoxin, and several other mycotoxins. They produced 19,000 liters of botulinum toxin, which was reportedly weaponized (put in warheads) but not deployed. This quantity of toxin is reportedly enough to kill the world population three times over. As for the former Soviet Union, we've learned much about their toxin warfare program and much has been published. There are reports that some of the Soviet toxin inventory is unaccounted for.

Most of the enteric toxins are not lethal by the oral route. However, anthrax toxin and botulinum toxin could be lethal on oral ingestion. It is possible that if they were stabilized for ingestion, they could be administered by the oral route, with even more severe consequences. We have little evidence or research in this area.

I will focus first on botulinum neurotoxins. These are large-protein toxins of approximately 150 kDa that are produced by ***C. botulinum.*** It is presumed that the toxins are horizontally transferred to nonpathogenic organisms because the genes have been found in ***C. baratii*** and ***C. butyricum***. These clostridia are common contami-

nants of foods. Botulinum toxin is the most potent substance known. There are seven antigenic serotypes, with the primary serotypes causing disease in birds and humans. It is known from primate studies that the other serotypes, except perhaps D and G, can cause botulism in primates as well. Mike Foster and Ed Schantz from our institute found that botulinum toxin could indeed be a major biological threat through the gastrointestinal route. Other investigators have shown that botulinum neurotoxin can be lethal by aerosolization and inhalation. As we know, botulism is an extraordinary disease compared with many other foodborne diseases. The toxin binds extremely tightly to peripheral motor neurons: the binding is about 10^{-13} K_M, and it is one of the tightest tissue-binding compounds known. Because it is active at a concentration of about 10^{-13} mol/L, extraordinarily low concentrations of toxin can cause paralysis, which typically lasts 2–3 months, depending on the serotype of toxin. It prevents the release of acetylcholine, leading to a flaccid paralysis. The onset of botulinum toxin, depending on the dose, occurs within 2 hours to several weeks. Early symptoms are difficulty seeing, speaking, and swallowing. At first it affects the cranial nerves—first the eyes—and then it descends and can paralyze every muscle in the body. There is no preventive measure that can be administered after the toxin binds to nerves, so the brief window of treatment opportunity is only a few hours. We need a treatment that can reverse the binding to the nerves. Currently, we must rely on supportive care. You can administer antitoxins if you can catch the unbound toxin within the narrow window of opportunity. Recovery from botulism often takes months. Some patients I have dealt with say it takes years. With good supportive care, the mortality has decreased to a very low percentage.

One of the most tragic forms of botulism is infant botulism. The baby is very sensitive to organisms in the intestine, and I would assume also to toxin administered orally. The toxin does not physically enter into the central nervous system, which is good, because recovery is generally complete with the regeneration of muscular activity. Botulism can be extremely debilitating in adults because they are aware that they are sick and may not recover for 6–8 months, which can lead to some severe psychological ramifications. Some animals, cattle and horses particularly, are extraordinarily sensitive to botulinum toxin. You may be aware that in California and in New York in the last 2–3 years, two herds with 300–400 cows have come down with botulism. In one case, it was due to preparation of the feed. Apparently, the person preparing the feed saw that there was a dead cat in the alfalfa. For whatever reason, he ground it up anyway, and then fed it to these animals, and 300–400 came down with botulism. It is still being debated whether the toxin can be shed into milk. The milk was made into butter, but so far nobody has come down with botulism.

The lethal dose in man by the oral route is estimated to be about one-tenth of a microgram to a microgram. The crude toxin, from a specific toxicity standpoint, would be less lethal; however, you have to realize that this is the most stable form of the toxin and that this is the type that would be made by terrorists. It is relatively easy to make. You can acid-precipitate 20 L of a culture of toxin made with a good potent strain and end up with 200 mg of toxin. That's a lot of lethal doses from a small fermentation. We have had calls about the stability of the toxin in tap water, in lake water, etc. It's rather unstable and is inactivated by chlorination, by ozone, and by reverse osmosis, so water is probably not a good route of intoxication. It's very stable in an acid environment and to freezing, and it's moderately stable in a number of foods during storage. In some foods, we have been able to detect toxin after 2–3 years of storage. The good news is that it's quite heat labile and is destroyed by boiling food. However, it is debatable whether protective components in food would prevent the destruction of toxin during heat inactivation. More work should be done on the heat inactivation of the toxin.

Tetanus toxin is not lethal by the oral route, but it is similar to botulinum toxin. Its potency is second to botulinum toxin. However, it is not produced in a complex where proteins protect the toxin through the digestive tract. Also, most people in the United States are immunized against tetanus toxin, so it would not be a good terrorist agent.

Staphylococcus toxins are interesting, and Merlin Bergdoll at our institute worked on these for decades. They are very heat stable and are produced by a number of staphylococci, especially ***S. aureus***. They can survive commercial steriliza-

tion processes in various foods. Thermal inactivation occurs more rapidly at boiling rather than at higher or lower temperatures. Their thermostability is affected by the nature of the food, the pH, and the serotype of the toxin. They are stable in most foods and survive long after the organisms that produce them have died. Unlike botulinum toxin, they are susceptible to low pH, but are fairly stable, as botulinum toxin is, to irradiation of foods. There are several antigenic types that have long been known to cause food poisoning. They are quite potent—in the microgram range—and can cause incapacity and gastroenteritis. Several of the staphylococcal enterotoxins are superantigens that can cause shock and immunological cascades, and can be involved in incapacitation or even death by their antigenic activity. Intoxication by the traditional foodborne route leads to gastrointestinal symptoms, sweating, and chills within 30 minutes to 8 hours. These toxins are rarely lethal, but they are highly incapacitating. There are several immunological assays, but these take many hours to days to get conclusive results.

Bacillus cereus is an emetic toxin. It is a small molecule composed of some amino acids and possibly fatty acid components. It is remarkably heat stable and survives autoclaving. It has typically been associated with cooked rice and pasta. It is incapacitating and moderately potent and, depending on the dose used, could be potentially incapacitating.

C. perfringens makes a number of toxins, and I will briefly discuss the enterotoxins, although other toxins produced by ***C. perfringens***, such as iota toxin, are potentially incapacitating by the oral route. The enterotoxin itself probably does not withstand passage through the gut. The organism has to get into the bowel, where it produces its toxin during sporulation. However, it is possible that the toxin can be stabilized. The enterotoxin is heat labile, and causes a relatively mild illness characterized by diarrhea and vomiting.

Ricin is one of the more likely toxins to be used as a terrorism agent or weapon. It is relatively easily obtained by extraction from castor beans. It is a protein toxin with two disulfide-linked chains, so it is inactivated fairly readily. It is horribly cytotoxic and causes hemorrhaging and necrosis in various organs. The minimal lethal dose is estimated to be 1(g/kg, maybe less. A number of other plant toxins, such as abrin and suporin, are potential agents, but ricin has a history of use. It was used in the assassination of a Bulgarian political opposition figure. Also, an individual tried to transport 130 g of ricin into the United States from Canada. It was known to have been stockpiled by Iraq during the Gulf war. It has been used in cancer chemotherapy, but its use has been limited because of its cytotoxicity. Although it is readily inactivated, ricin has not been commonly thought of as a foodborne agent, so we really do not have data on its survivability or stability in milk or other food systems. It could potentially be administered in foods as a vehicle, and it is generally stable under ambient conditions. Detection methods are rudimentary and have not been tested in food systems.

Regarding marine toxins, saxitoxin has been extracted from clams in Alaska after red tides. It would be difficult for individuals to make saxitoxin, although there are reports in the literature that certain bacteria can make saxitoxin. If these reports are true, a fermentation process could potentially be developed. It is an extraordinarily rapidly acting toxin. If you inject a high dose in mice to assay for toxin, the mouse dies in your hand. Tetrodotoxin is very closely related to saxitoxin. Both toxins are heat stable. There are other toxins such as anatoxin, the snail toxin, but again, our knowledge about the potential use of these is rudimentary at best.

Many mycotoxins have the potential to cause chronic toxicity, and many of them, such as aflatoxins, are potent carcinogens. They also have acute toxicity, but it is much lower than that of bacterial protein toxins. Other speakers at this workshop will discuss mycotoxins.

There are quite a number of animal toxins, but I doubt that many venoms are readily able to be introduced into foods.

In summary, I think that the three toxins most likely to be used as terrorist agents are botulinum neurotoxins, staphylococcal enterotoxins, and ricin. For the first two, we have quite a bit of data on their biochemistry and even occurrence in various foods. For ricin, we have virtually no data on its behavior in foods. These toxins can be produced fairly easily, and many different organizations have sufficient microbiological and chemical skills to produce botulinum toxin. You can wonder whether, if botulinum toxin were intro-

duced into a food and thousands of people became ill, we would have the local hospital facilities to keep these people alive. Probably not. I should also mention that, unlike many chemical toxins, biological toxins are odorless and tasteless at toxic doses. Staphylococcal enterotoxin is potent, is quite stable during food processing, and can incapacitate people and also cause shock. Ricin, extracted from the castor bean, is produced relatively easily, has moderate potency, and is very toxic.

A deliberate act of food contamination would be difficult to detect quickly. In some cases symptoms might not develop until 5–7 days after consumption. Also, the symptoms are common to more than one type of toxin, which makes diagnosis difficult. There are limits to our ability to screen foods for toxins, and for some the tests are costly and time consuming. There is an urgent need for rapid testing methods.

In conclusion, although there are numerous biological toxins, only a limited number fit the criteria for bioterrorist agents in foods, but much research is needed on their stability and other properties in foods.

Acute Chemical Toxicants

P. Michael Bolger, Ph.D., D.A.B.T., Center for Food Safety and Applied Nutrition,
Food and Drug Administration

I will briefly review how the Center for Food Safety and Applied Nutrition approaches acute threat assessments in terms of food safety. By acute toxins, I mean not just those derived from human activities. I am mostly including natural toxicants, which together literally comprise thousands of compounds. The consideration of the universe of potential acute toxic threats is a very daunting effort, so we started by thinking about what the major threat factors are that should be considered when assessing this type of foodborne threat.

The first factor that we took into account was historical use. This was important because when you think of terrorism, there has to be name recognition. The threat has to be perceived by the public and the media. Although there are many potential threats out there, not many have the name recognition that grabs attention and gets the deep emotional reaction terrorists are after. The next factor was ease of use. This became an issue with nerve agents. While nerve agents are quite potent, we felt that the nerve agents are difficult to work with. Accessibility is another factor. This became an issue with the seafood toxins. Although these toxins are potent neurological agents, they are not easy to obtain. We did not consider accessibility solely in terms of this country, but thought about it in a global sense.

Another factor is detectability, especially organoleptic detectability. This became an issue with, for example, cyanide. If a consumer can readily detect the presence of a toxin (e.g., almond flavor), this it tends to minimize the chances of ingestion and, therefore, adverse outcomes.

Stability, ease of handling, and transport were other factors that were evaluated. Potential foodborne threats have to be fairly stable in terms of handling and transport, as well as in the food itself.

The clinical spectrum of signs and symptoms of adverse outcomes in humans was also considered to be an important threat factor. For example, vomiting, transient diarrhea, dizziness, and headache are common to these agents, since many of them are central nervous system-acting agents. Many of them show the same spectrum of adverse outcomes, which can be a cause of concern. If someone shows up in an emergency room, how is the primary care physician going to be able to distinguish exposure to a particular toxicant from a microbiological or viral infection?

Another important issue is whether the effects are reversible at low doses and whether there is the potential for a lethal outcome. You do not necessarily have to have lethality as an outcome, but in terms of threat recognition and how the public would react, death does tend to get everybody's attention, whereas an incapacitating agent tends not to.

A chemical agent of terrorism has to be readily available. If it's difficult to produce or obtain, or requires advanced technological resources, this limits the potential threat in that insufficient quantities are available. It has to be easy to conceal and easily stored for long periods. One of the major factors we considered was stability in food. What is the half-life in foods? Are we talking, for example, about less than 1 day, about 3 days, or more than 3 days?

In considering these factors, we set up a threat matrix that incorporated these factors with a list of the major classes of potential acute threats. We applied a numerical value for each factor to derive an overall numerical value for each agent so that we could start to rank order potential threats. We clearly have to focus our resources on the threats most likely to occur.

I will review some of the categories of potential threats that we considered. This is not the final list, nor is it intended to be comprehensive, but it represents our initial attempt to try to describe the universe of potential acute threat agents. Bear in mind that this is a work in progress within the Center for Food Safety and Applied Nutrition. I do not want to leave you with the impression that if a class of compounds is not on the list, we have eliminated it from the list of potential threats. We have not. This is merely a first attempt to describe what the potential acute dietary threats might be.

- Acetylcholine esterase inhibitors, such as

organophosphate pesticides like parathion and paraoxon, are well-known toxins that should be considered potential threats.

- Plant toxins are exquisitely potent and are very easy to work with in terms of stability and transport. Ricin and abrin are notable examples, as are nicotine and solanine from potatoes.
- Drugs are another class of compounds that we considered, because some of them are exquisitely toxic. Although drug availability may not be an issue in the United States, it may be elsewhere.
- Mushroom toxins—several classes come to mind—demonstrate extreme toxicity.
- Mycotoxins are classic compounds, but they are more than acute. They can show acute outcomes, but the doses required to elicit acute effects are not of the same order of magnitude of other classes of compounds. Some, like aflatoxin, have the name recognition, but from an acute standpoint, we concluded that it did not have as high a priority as some other classes of compounds.
- Marine toxin accessibility is limited. Unless you have a fairly sophisticated laboratory, you may not have access to them. The one exception could be tetrodotoxin, which can be purchased from Internet websites. It is controlled in this country, but overseas this is not the case
- Elements were another group of compounds, and those that come to mind immediately are lead, arsenic, and chromium. We concluded that from an acute standpoint, they are not of the magnitude of some of these other classes.
- Pesticides beyond the organophosphates that were also considerd are strychnine and sodium monofluoroacetate, which is very potent.

Eventually, we will share this information and additional analysis with people outside the Center for Food Safety and Applied Nutrition.

The Use of Chronic Toxicants by Terrorists to Disrupt the Food Supply

Ronald T. Riley, Ph.D., Agricultural Research Service, U.S. Department of Agriculture

The purpose of this presentation is to address the question "Could chronic toxicants be used to create a terrorism incident?" If so, what might happen and what could be done to minimize the impact? Chronic toxicants are chemicals that are known or suspected to cause disease through mechanisms that require low-level, long-term exposure. This is in contrast to acute toxicants, which are usually used at high dosages or are extremely poisonous, and the toxic effects are seen very quickly. For chronic toxicants, the food safety impact is presumably an increased risk of chronic disease. There are political impacts as well.

Why would someone choose to use a chronic toxicant in food as an agent of terror? For a chronic disease to develop, there must be long-term and persistent exposure. However, everyone is exposed to low levels of many toxic chemicals over their lifetime, but this does not mean that this exposure will lead to disease. One of the fundamental principles of toxicology is that the dose makes the poison. For this reason, it is extremely unlikely that intentional adulteration could persist long enough to significantly increase the likelihood of chronic disease in a country like the United States with a highly diverse food supply. This applies equally to most developed countries where the food supply is diverse, where people eat lots of different foods, and where there are many different food suppliers. The sophistication required to plan and execute a prolonged program involving chronic toxicants is unlikely because the terrorists we have seen in the news lately appear incapable of the highly coordinated, widespread, and prolonged attack against our food supply that would be necessary to cause increased chronic disease in humans. The exception would be the use of single-dose carcinogens or single-dose developmental toxins. But the fact is, these would still be dose- and time-dependent processes. For example, in young trout, a single short-term exposure to aflatoxin B1 can cause increased liver cancer incidence in adults; however, the process is still time- and dose-dependent. For this reason, the effective use of a chronic toxicant to cause an increase in human disease is a low-probability impact even if chronic toxins were used to contaminate the food supply.

The loss of consumer confidence in the safety of the food supply is a high-probability impact. The consumer threshold for risk increases with familiarity. High-risk activities are acceptable if they are familiar and controllable; for example, driving a car is a high-risk activity for which most people also have a very high-risk threshold. Conversely, intentional contamination with chronic toxicants will be perceived as unfamiliar and uncontrollable, and therefore consumers will set their risk threshold very low. This concept is most clearly shown in Faustman and Omenn [1] and is summarized in Figure 1. Figure 1 has risk axes. On the horizontal axis to the far right are uncontrollable risks and to the far left are controllable risks. The vertical axis ranges from observable at the bottom to not observable at the top. The upper- right quadrant is considered the quadrant of "dreadfulness." It includes PCBs, pesticides, DES (which is an animal growth drug), mercury, heavy metals, and DNA technology. DNA technology is a very unfamiliar and uncontrollable risk, but as far as we know right now, it's unlikely to cause much chronic disease, yet is highly feared by the public. Somewhere in this upper quadrant would be chemical terrorists' activity.

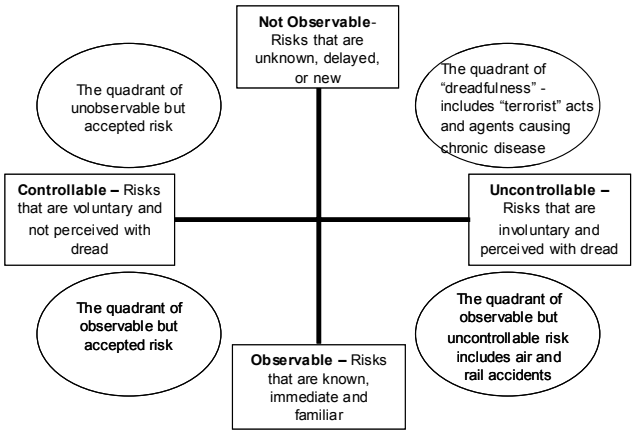

Figure 1. The risk space, modified from Faustman and Omenn [1].

For a chronic toxicant to inspire the public with terror, it or its effects must have "name recognition," for example, carcinogens such as TCDD, aflatoxin B1, heavy metals, PCBs, pesticides, street drugs, anabolic steroids, animal drugs like somatotropin, and foreign DNA. Foreign DNA is included not because it is a chronic toxicant that causes disease but because it is perceived as causing disease or having the potential to cause disease and is uncontrollable and unobservable. When an intentional contamination event is revealed, it will result in product removal from the marketplace and increased government activity. The public's low threshold for the unfamiliar and uncontrollable will override the fact that chronic health effects are an unlikely outcome. Products intentionally contaminated are avoided by consumers, and responsibility for restoring consumer confidence will fall to industry and government.

Is it possible that our own regulations could make us vulnerable to a terrorist attack using chronic toxicants as the weapon? Regulatory limits, tolerances, and guidelines are set to protect consumers. An important component of any regulatory action is public perception. If the public reaction to a perceived risk is large, then regulatory action will proceed more quickly. If it is known that a terrorist has added something to food, even if the dose and duration of exposure pose minimal health risk, the public reaction will be great, which will pressure the regulatory agencies to act. In the case of contaminants, the law is written so as to distinguish between unavoidable and avoidable contamination. If a terrorist contaminates a food with an "unavoidable" contaminant such as a mycotoxin, even at a very low level, the regulatory position shifts from unavoidable to avoidable and the regulatory agencies must take action. This will happen regardless of whether or not there is an appreciable human health risk. One solution would be to establish more flexibility under special circumstances where contamination was intentional but did not cause appreciable risk.

Given the public sensitivity to uncontrollable and unobservable risks, the official standards that establish risk are likely to be the targets that a "food terrorist" will aim at to create "an incident," since the amount of material that would have to be added to exceed these limits will be the easiest to attain. Consumers rightfully believe that regulatory agencies have set tolerances or limits for the purpose of protecting the public health. However, many people will not accept that the health standards are "situational," that is, that brief exposure to chronic toxicants at levels that exceed regulatory limits, action limits, or guidelines will have negligible health risk and therefore under certain circumstance are acceptable.

The following are some specific examples of how established regulatory limits could be used to drive down the amount of material that is necessary to create an incident harmful to the food industry but that poses little or no risk to the public. Each example has particular chemical properties that make its use in certain products or processes more logistically feasible. The first example is fumonisin B1, a carcinogenic mycotoxin that is water soluble, a property that would allow it to be introduced into certain processes very easily. The name recognition is not good, but industry knows about it, especially the corn industry. Crude culture material containing 100 g of fumonisin would be enough to contaminate 40 metric tons of high-fructose syrup with 10 ppm of fumonisin. If this corn syrup were used to make a cola beverage, it would result in at least 1 ppm in the cola, which would exceed the Joint FAO/WHO Expert Committee on Food Additives provisional maximum tolerable daily intake of 0.2µg/kg body weight per day.

Aflatoxin is another carcinogenic mycotoxin that has good name recognition and could be easily made as a crude preparation. It is oil soluble, and 1 g of aflatoxin could contaminate 20 metric tons of vegetable oil at 200 ppb well above the action limit of 20 ppb set by the Food and Drug Administration.

TCDD (a dioxin contaminant of PCBs) has good name recognition and has contaminated farm products, causing considerable economic and political turmoil. In previous cases of TCDD contamination, the source of TCDD was contaminated oil/fat used in the making of animal feeds. In poultry, 1 ppt in edible meat is all that is necessary to exceed regulatory limits. Production of PCBs stopped in 1978, but it would not be difficult to find a transformer filled with dioxin-contaminated PCBs, especially in salvage yards in many developing countries. The material in the transformers is ready to use, and no preparation is required. It is possible that 1 kg of this oily, colorless, odor-

less liquid could contaminate 1 metric ton of poultry feed at 10 ppt TCDD, and this could in turn potentially contaminate many tons of poultry meat.

Lead is a compound that is not really that toxic, but over a long-term exposure it is, and its name recognition is very good. Availability is very good; for example, it can be bought over the Internet. No expertise is required, and it is very water soluble. The target product could be bottled water. The limit for bottled water is 5 ppb, and bottled water is probably one of the things in which lead acetate will work, because there is nothing that is going to chelate or precipitate it. It is possible that a concentrated 1 mL aqueous solution (clear and odorless) could be used to contaminate 27,000 L of bottled water to a level of 5 ppb, which is the point at which it must be pulled off the shelf.

There are many other examples of ways that our regulations, intended to keep our food supply safe, could also serve to make the food supply vulnerable to intentional contamination by terrorists. For example, terrorists could take advantage of labeling requirements by simply adding sulfites (or other allergens) where they are not supposed to be and then letting it be known that the product contains an undisclosed allergen. This could also be done with foreign DNA; for example, the Cry9 protein could be added to corn products. In all of these cases, the health risk would be minimal, if any.

In conclusion, the probability that a terrorist could cause increased risk of chronic disease through intentional contamination of foods with toxic chemicals known to cause chronic diseases is very low. However, intentional contamination, even with nontoxic doses and short-term exposure, could be very disruptive to the food supply. The amount of material that would be required to create an incident could be very small because of the public's low tolerance for uncontrollable and unobservable risks. The choice of which product to contaminate would depend on the chemical, physical, and organoleptic properties of the food and the toxicant.

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Use of Ionizing Radiation for Pathogen Destruction

James S. Dickson, Ph.D., Iowa State University

Irradiation is a commercially viable industrial process. Irradiation is not a new technology per se; it has been used in industry for more than 40 years. All irradiation facilities have a source, a biological shield, some kind of a transport system, and various support systems to keep the operation going, typically air-handling systems, control systems, things of that nature. The major differences in irradiation processing are in the source. There are two common types of sources: isotope sources and machine sources. The most common isotope source is cobalt-60, and cobalt-60 produces photons of energy, which have no mass. There is also cesium-137, which only rarely is allowed for use. From a practical standpoint, there is no difference between irradiating with cobalt or cesium. The issue with cesium is that it is slightly soluble in water, and many isotope irradiation facilities use water as a biological shield.

The other sources are machine sources. Unlike isotope sources, these machines generate electrons. They are turned on or off. There is no residual radioactivity in the unit when it's turned off. The electrons are simply accelerated using electricity. The maximum allowable energy for the electron machine is 10 MeV, 10 mega electron volts. When we discuss irradiation of mail, this is what people are primarily interested in. Compared with an isotope source, an electron source has a very high output, and it also has the advantage of not requiring the same levels of shielding as an isotope source. In contrast to isotope sources, electrons have mass. This means that they have a limited ability to penetrate materials, based on the acceleration energy. The lower penetration reduces the amount of shielding. It also reduces the thickness of the product that can be irradiated. Thus, the advantage of an isotope source is that it can penetrate a considerable thickness of product, and the disadvantage is that it requires substantial biological shielding. In contrast, a machine source requires relatively little shielding but is limited in the thickness of the product that can be irradiated. High-energy x-rays have the advantage of combining the best of both: x-rays are generated by the same machines that generate electrons, the electrons are simply directed into a steel or metal target, and the electrons are converted to x-rays. The x-rays have a penetration comparable to gamma rays, which increases the thickness of the product that can be irradiated. The disadvantage is that more biological shielding is needed around the unit. There are advantages and disadvantages to both facilities, but from an irradiation processing standpoint, there is no practical difference in the type of source. The differences between the source types are engineering questions, not questions regarding the end result of the process.

For irradiation processing, the key parameters are the intensity of the source and the exposure time. The more intense the source (the higher output of the source), the shorter the required exposure time. This is relevant in comparing an electron machine with isotope sources and in determining how much isotope source is needed. The more isotope you have, the more intense your source is and the shorter the processing time.

There are two main effects that we see with ionizing irradiation: the direct effect and the indirect effect. The direct effect involves a direct hit of a photon of energy or an electron (depending on your source) with the nucleic acids within the cell. We are causing energy, whether a photon or an electron, to collide with and break the DNA of the cell. If the DNA is broken enough times, the cell cannot reproduce, and it is dead. We do have a concern about the single-stranded versus double-stranded breaks. Single-stranded breaks are repairable and in some cases can cause mutations. In general, double-stranded breaks are lethal. The direct effect also affects proteins and other substances within the cell. However, the main direct effect we see is the breakage of genetic material within the cell, which is what kills the cell. The indirect effect involves the interaction of radiation with other cell molecules. If we are talking about a vegetative cell, which is about 80% water, the photon or electron interacts with the water molecule to produce a hydroxyl radical. This hydroxyl radical interacts with either the

genetic material or other components of the cell, and breaks those components down and causes death of the cell. An issue with the indirect effect is that if you have low moisture, such as in a bacterial spore, you have essentially no indirect effect. The same effect is seen with refrigerated food and frozen food. By freezing the food, you reduce the amount of free radicals that are produced, and this causes a perceived increase in the resistance of bacteria and spores to radiation. For a typical spore with a moisture content of 5–15%, compared with the 80% moisture in a vegetative cell, we see a dramatic difference in irradiation resistance.

The older units of measurement for radiation are krad and Mrad. The new SI units are gray (Gy) and kGy, with 1 Mrad equivalent to 10 kGy. The transition from using krad and Mrad to using kGy as the unit of measure occurred approximately at the same time that the U.S. Army program at Natick was transferred to the U.S. Department of Agriculture, in the late 1970s. The army data from Natick from the 1950s through the 1970s are presented as krad or Mrad.

I want to explain bacterial reduction or D_{10} values. The D_{10} value is the decimal reduction value: the reduction or dose required to reduce the population by 90%, or a one-log reduction. In the radiation literature, there are many references to D_{50} reductions, which is the dose required to reduce the population by 50%. D_{50} values and D_{10} values are not interchangeable. A D_{50} value would be going from a million cells to 500,000 cells, whereas a D_{10} value would be going from a million cells to 100,000 cells.

For ***E. coli*** O157:H7, the D_{10} values are somewhere between 0.25 and 0.3 kGy. A one-log reduction in ***Salmonella*** spp. on average is somewhere between 0.45 and 0.5 kGy, which is typical of some of the other Gram-negative enteric pathogens. Although I reviewed the literature, I could not find a report of anybody irradiating ***Yersinia pestis***. But if the data from ***Y. enterocolitica*** are any indication, the D_{10} value for ***Y. pestis*** should be somewhere below 0.2 kGy. If it is a Gram-negative vegetative cell, it is very straightforward to kill it with irradiation. By contrast, for ***Clostridium botulinum*** spores, which are not vegetative cells, we have reported D_{10} values as high as 3.5 kGy. Spores are much more resistant to irradiation than vegetative cells. The 3.5 kGy figure is the high end of the data for ***C. botulinum*** spores; you can find reports of D_{10} values for ***C. botulinum*** spores from about 1.5 and higher.

Similarly, if you were to extrapolate from ***Bacillus cereus***, which is genetically similar to ***B. anthracis, B. cereus*** has reported D_{10} values of 1.5–3.0 kGy. Recently, we began to investigate the radiation resistance of ***B. anthracis*** spores. We used the relatively avirulent vaccine strain and grew it under standard conditions to produce spores. We used a cold preparation (ethanol) to prepare the spores. The spores were inoculated into nonfat dried milk and placed in number-10 business envelopes. The envelopes were irradiated at Iowa State at the linear accelerator with a machine source. We performed a series of irradiation doses to approximately 24–25 kGy. Our average D_{10} value was approximately 3.4 kGy, which was higher than we would have predicted based on the data available for B. cereus, which was somewhere between 1.5 and 3.0 kGy. A 1996 study of 38 strains of ***B. anthracis*** reported results as D_{50} values. I extrapolated the data to D_{10} values, using a poor-quality fax copy of the article. The average value for all 38 strains was almost 8 kGy. That seems unusually high, given what we know of ***C. botulinum, B. cereus***, and the data that we derived with ***B. anthracis***, but that is in the literature. The authors reported that when 10 mL suspensions of spores with a population of up to 10 log /mL were exposed to 44 kGy, seven of the 38 samples failed sterility tests. We had a few instances where bacteria survived beyond the 25 KGy dose, but when we evaluated those surviving organisms, we found that they were not ***B. anthracis.***

With respect to toxin inactivation, proteins are very resistant to irradiation. Irradiation would have very limited effectiveness against preexisting toxins. For example, in a report of enzyme activities with different classes of enzymes in fresh sheep liver, irradiation of the liver to 400 kGy failed to eliminate detectable enzyme activity. Thus, irradiation would have a very limited effectiveness against any type of preexisting toxin in a food.

Viruses are more resistant to irradiation than vegetative bacteria. Viruses have very low moisture and a very small particle size. Typically we see radiation inactivation doses for viruses comparable to those for spores. There are some pub-

lished data on foot-and-mouth disease virus, which is a single-stranded RNA virus with a particle size of 230 nm. The nucleic acid is fairly small, about 7.2–8.4 kb. If you are trying to inactivate foot-and-mouth disease virus in an aqueous form versus a dried from, there is an increase of almost 50% in perceived radiation resistance: in aqueous solution a D_{10} value of about 4.8 kGy, and in a dried powder about 6.3 kGy. There is a report on hepatitis A virus in an aqueous solution similar to that on foot-and-mouth disease, where the D_{10} value was 2.0 kGy. The experiment with hepatitis virus was not designed to produce a D_{10} value, so this 2.0 kGy value may be somewhat lower than we would normally expect.

Ebola virus is a single-stranded RNA virus with a particle size slightly larger than that of foot-and-mouth disease or hepatitis A. The nucleic acid size is also slightly larger than foot-and-mouth disease virus. There is no published work on the irradiation inactivation of Ebola virus. However, given these characteristics of the virus, we would expect to see D10 values comparable to what we see for foot-and-mouth disease and hepatitis, that is, about 4-6 kGy.

African swine fever is a double-stranded DNA virus with a particle size and nucleic acid size larger than foot-and-mouth disease virus or hepatitis A virus. These studies were done with viruses in naturally infected tissues. I mention African swine fever virus because it is very similar in size to smallpox. Based on the data we have on African swine fever, we would need a minimum of 20 kGy to ensure that infective virus does not survive. Double-stranded DNA viruses are more susceptible to irradiation damage and have a larger particle size, so we are probably not talking about as much irradiation to inactivate them as is needed for foot-and-mouth disease virus, but still we are talking about an infectious agent with radiation resistance comparable to that of bacterial spores.

In conclusion, radiation is an effective intervention technique in some situations. It is a well-documented industrial process widely used to sterilize medical devices, pharmaceuticals, and cosmetics. It is easily used to inactivate vegetative cells. Spores and viruses become much more problematic to eliminate. Irradiation is not applicable to the inactivation of toxins.

Radionuclides

Steven L. Simon, Ph.D., National Cancer Institute, National Institutes of Health

I have several goals for this presentation, but in particular, I want to promote understanding of some basic concepts about radiation and radionuclides. Radionuclides are already present in our food to a small degree, and that's important for you to know. I will describe some possible scenarios that could lead to contamination of foods with radionuclides and some countermeasures and remediation strategies. I'll briefly mention the international guidance on the contamination limits for foods that are bound for commerce. I'll give you some quantitative values of the risks involved from ingesting foods contaminated with radionuclides and some requirements for detecting radionuclides, some examples of accidents that led to food contamination, and contact information in case of a radiological emergency.

I'll begin with some definitions. ***Radiation*** is energy released from the decay of atoms that are naturally unstable. Ionizing radiation is radiation that is energetic enough to remove electrons from the material that is irradiated. Radiation can be in the form of x-rays or gamma rays, beta particles, or alpha particles. Alpha particles have the least amount of penetrating ability; they cannot even go through the epidermis of your skin. Beta particles, x-rays, and gamma rays are increasingly more penetrating. Each radionuclide has a characteristic fingerprint of the type of radiation that they emit, thus enabling their identification with proper instruments. The penetrating ability of the radiation that each radionuclide emits also determines how we protect ourselves against exposure from it. Obviously, alpha particles, if they are emitted inside a package, could not reach your body, yet gamma rays could. I will give more examples later. ***Radioactivity*** is the spontaneous emission of radiation. Radiation is the energy, and radioactivity is the spontaneous emission of that energy. A ***radionuclide*** is a radioactive species of an element. There are many radionuclides, several thousand in fact. Fortunately, we don't have to worry about most of them, because many are very exotic and difficult for anyone to obtain in any appreciable quantity. ***Radioactive materials*** include radionuclides but also any material that emits radiation, including pure radionuclides, metals, soil, and anything that might be contaminated with radioactive atoms. For example, you may have read recently of the idea of a "dirty bomb." A dirty bomb could be made from conventional explosives attached to nuclear fuel. Nuclear fuel is uranium or plutonium and is used for reactors or nuclear weapons. Nuclear fuel can be either enriched or depleted, which simply describes how much of the material is of fissionable quality. After fuel has been used in a reactor, it has undergone fission, and that fission process creates an immense array of radioactive by-products, and this is what we call "spent" nuclear fuel. It's extremely dangerous and initially highly radioactive.

In contrast to the use of "dose" in the world of pharmaceuticals, we have a very particular definition of "dose" in the radiation physics field. Radiation dose is a quantitative measure of the energy that is absorbed per mass of the radiated material. As that alpha particle or gamma ray goes through material, it deposits a certain amount of energy. Physicists can calculate this deposited energy very precisely under the right conditions. Even in the most uncertain cases, radiation doses can usually be crudely estimated.

Some radionuclides are found in the environment, and some of them are normally found in common foods at very low levels. There is a group of radionuclides that we call natural that are part of the crustal material of the earth and the aquatic environment. These include ^{3}H (called "tritium"); ^{14}C, which is a product of the interaction of carbon dioxide in the atmosphere with high-energy particles from space; ^{22}Na; ^{32}P; and ^{40}K. Three chains of radionuclides are also present in the earth's crustal material: two begin with different forms of uranium and one with thorium. These chains are long, with twenty or so radionuclides in each. Table 1 lists many of these as well as their half-lives. The half-life is the length of time for a quantity of radioactive material to reduce by natural processes to half its activity.

You can see here that half-lives for these selected radionuclides range from 14 days to 14

Table 1. Radionuclides Commonly Found in the Environment and in Some Foods

Natural	*Half-life (yr)*	*Man-made*	*Half-life (yr)*
^{3}H	12.3	^{60}Co	5.3
^{14}C	5730	^{90}Sr	28.8
^{22}Na	2.6	^{99}Tc	0.2 million
^{32}P	0.04	^{137}Cs	30
^{40}K	1.3 billion	^{239}Pu	24,000
^{238}U + series	4.5 billion (the longest of the series)		
^{232}Th + series	14 billion	"	
^{235}U + series	0.7 billion	"	

billion years. Some are man-made radionuclides that are the result of atmospheric nuclear testing that took place primarily in the 1950s and 1960s. One radionuclide, ^{60}Co, was discussed by another workshop participant. We have a little bit of ^{60}Co in the environment, primarily only near former nuclear testing sites. In addition, there is ^{90}Sr, ^{99}Tc, ^{137}Cs, and also some plutonium distributed globally from nuclear testing

I tried to imagine some terrorist-related activities that would result in contaminating food with radionuclides, and some possibilities are shown in Table 2. I cannot say with certainty what specific things people might try to do-they have amazing imagination when it comes to trying to hurt one another-but radionuclides theoretically could be in liquids, particulates, or solids-in a whole array of different forms because there are many different elements. However, I think that many of the likely actions by terrorists would have only a very localized influence, simply because it would be too difficult to carry out complex dispersion activities on a large scale. Even if one considers the release of radioactive air particulates, the likely degree of dispersion is low to moderate at best, simply because of the difficulties involved in carrying out a release.

All conventional explosions that are obviously terrorist acts should be monitored for radioactivity, because it would be relatively easy to release radioactivity by an explosion with the intent to contaminate the local environment. This is essentially what a "dirty bomb" is. However, the degree of dispersion for most incidents is likely to be low, as I have suggested. Even considering nuclear explosions, a terrorist action could likely produce only a very small nuclear explosion, so the probable degree of dispersion of radioactive contaminants is probably low (<< a few km). In my opinion, the destruction of a commercial

Table 2. Possible Terrorist-related Activities That Would Result in Contaminating Food with Radionuclides

Activity Type	*Likely Degree Of Dispersal*
Overt	
Release of contaminated liquids	Low
Release of contaminated air particulates	Low
Conventional explosions (including "dirty bombs")	Low to moderate
Nuclear explosions	Low to moderate
Destruction of commercial power reactor	Moderate to very great
Covert	
Production of contaminated foods for importation	High

power reactor is much more frightening, and the adverse impact on society would be much worse.

What are some countermeasures to prevent radiological contamination of food? The answer depends on the stage of food preparation when the contamination might take place. During plant growth, it might be very difficult to prevent contamination, since plants can take up radionuclides via their roots just as they take up nutrients from the soil. However, there may be many other preparation steps before that plant product reaches the consumer. If the contamination is strictly external, say from contaminated dust or from particulate debris, you can peel or remove the exterior of the plant food. Very little radioactivity might move inside a plant food from the exterior, because many radionuclides are not particularly soluble. Thus, some countermeasures to prevent contamination of prepared foods with radionuclides are the same measures that you might take to prevent microbial transfer from the plant exterior to the edible interior portions. Note that it is not necessary to prevent the unintentional irradiation of foods; in fact, if terrorists were to do that, they might be doing you a favor, since radiation is an effective way to sterilize microbes. Unintentional irradiation is not one of our large worries.

Is there a hazard to handlers of foods that might be contaminated with radionuclides? I believe that it is probably not a significant problem. If the contaminant is a gamma emitter, it could expose the handler, but the concentration of the radioactive element that could be in or on food would never result in a large or significant external radiation hazard.

Are there options for cleaning or reclaiming radiologically contaminated food? Some options are available, but I can't say whether they are practical, economical, or socially acceptable. Some foods, such as milk, could be cleaned of certain radioactive contaminants by running the milk through ion exchange columns to remove radioactive ions. I doubt that it would be economically feasible or reasonable, considering the large milk supply we have in this country. For contamination by radionuclides with short half-lives, simply holding the food until the radioactivity decays is a possible option. This was done in the former Soviet Union following an incident of contamination of milk with ^{131}I (one variety of radioactive iodine). Because its half-life is 8 days, you wait 80 days. You keep the milk refrigerated or make it into cheese or powdered milk; through natural processes, the radioactive material decays. Whether this would be publicly acceptable is a different issue.

The disposal of radiologically contaminated foods is mainly a problem of expense and finding good options. Most likely, the food industry would have to dispose of contaminated food within the guidelines of the national and state regulations for low-level radioactive waste. Because of disposal cost considerations, volume minimization would be necessary. Disposing of radioactive material in this country is difficult and expensive, and drying and compaction would be one of the first steps to get rid of contaminated material. Radiologically contaminated foods would likely be classified as low-level radioactive waste. Technically, low-level radioactive waste is contaminated material that does not fall under other categories. It is not high-level waste in that it is not spent nuclear fuel. It is not uranium milling residues, and it is probably not waste with greater-than-specified quantities of elements heavier than uranium. Therefore, it is probably going to be low-level radioactive waste, with few facilities available and very strict guidelines on allowable concentrations, and other constraints. Disposal could become a problem of expense and logistics if large volumes of contaminated foods needed to be disposed of.

There are some guidelines that govern how much radioactivity is allowed in foods bound for international commerce. The values in Table 3 are from the guidance of the World Health Organization/Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. These values, which have been reviewed by international groups and are accepted worldwide, are concentrations in kBq/kg (i.e., 1,000 becquerel per kilogram of food), where 1 Bq is equivalent to one disintegration per second. As an example, the international limit on cesium in food bound for commerce is 1 kBq/kg food. These limits also vary according to the likely consumer, i.e., whether the foods are for general consumption or for children. They also vary according to the radionuclide, because different radionuclides have different energies and different decay patterns.

Why do we worry about radionuclides in food? Ingesting radionuclides in foods can lead to a radiation dose that will lead to an increase in

Table 3. International Guidelines for Limiting Radionuclide Contamination of Foods Bound for International Commerce

Radionuclides	*Foods Destined for General Consumption (kBq/kg)*	*Milk, Infant Foods, Drinking Water (kBq/kg)*
^{134}Cs, ^{137}Cs, ^{103}Ru, ^{106}Ru, ^{89}Sr	1	1
^{131}I	1	0.1
^{90}Sr	0.1	0.1
^{241}Am, ^{238}Pu, ^{239}Pu	0.01	0.001

the lifetime risk of cancer. The health risk following ingestion or inhalation varies according to the chemical and physical properties of the radionuclide; thus, it is difficult to generalize which pathway of exposure gives greater risk. In general, we assume that risk increases linearly with increases in the radiation dose received. Table 4 gives some very approximate quantities of radionuclides (in MBq, i.e., 1 million bequerels) that, if ingested or inhaled by a population of mixed ages, would increase the background cancer mortality rate by about 10%. You can estimate other values of added risk by scaling the radionuclide concentrations in the table. The data here were derived from Federal Guidance Report 13, an important 1998 publication from the Environmental Protection Agency. These amounts are many times (generally many thousands of times) the guideline contamination limits. Also, the health risks from exposure to radiologically contaminated foods are different from the health risks following exposure to biological contaminants. Exposure to biological contaminants in food could lead to a high probability of illness and death. Exposure to radiological contaminants in food is very unlikely to lead to sickness or death in the short term, and that is a message I would like you to remember: radiological hazards primarily lead to an increase in the long-term risk of cancer. Exposure to radiologically contaminated foods does not mean that you will develop cancer; rather, it leads to an increased probability that you will develop cancer, with the magnitude of the risk dependent on the magnitude of the radiation dose received.

Contamination of food would also lead to another major problem: loss of the public's trust in the quality of the food supply. I think that this probably is a more significant national problem than the long-term cancer risk, which would likely affect only a relatively small number of people. In the case of real or alleged radiological contamination, it may be exceedingly difficult to assure the U.S. public of the safety of the food supply.

The detection and measurement of radioactivity and radiation is a well-developed field and could be used to the food industry's advantage, if necessary. The different degrees of penetration of different kinds of radiation determine the kind of instrumentation necessary to detect the contaminating radionuclide. A variety of instruments may be needed to detect various radionuclides in the many ways that food might be packaged during or after production. Also, the screening of foods for radioactivity would be much easier than making precise quantitative measurements of concentrations of nuclides. Screening can be done on a conveyor belt or even on a whole truck. Screening measurements by the food industry are probably feasible, but quantitative measurements would require a degree of capacity building. Simple but continuous monitoring of the food preparation environment could possibly offset the need to monitor all prepared foods.

Table 4. Approximate Amounts of Radioactivity That Must Be Ingested or Inhaled to Increase Background Cancer Mortality Rate By ~10%.

Radionuclide	*MBq (inhalation)*	*MBq (ingestion)*
^{60}Co	20	60
^{90}Sr	5	15
^{131}I	225	125
^{137}Cs	50	40
^{210}Po	0.1	0.5
^{226}Ra	0.1	5
^{238}U	0.1	15
^{239}Pu	0.03	5

A few accidents have led to the contamination of food. For example, in Goiana, Brazil, in 1987, a cesium medical therapy source was discarded and found its way to a junkyard, where people recovering discarded metal broke it open. Something glowed in the dark: a 5×10^{13} Bq (1,400 curie [Ci]) source of cesium, which exposed a number people quite badly. Only four people died of exposure, but about 1,000 were irradiated, with most of the exposure from external contamination of their bodies. The reason I bring up this example is that some of these people were also exposed internally from contamination of food by normal food preparation activities. Another, probably more familiar example is the Chernobyl reactor accident in 1986, in which a nuclear reactor in Ukraine exploded and caught on fire. There was not a containment building around that reactor, whereas reactors in this country have very strong containment domes over them. The explosion and fire released about 9×10^{16} Bq (2.4 million Ci) of cesium and about 1.5×10^{18} Bq (40 million Ci) of ^{131}I. There were 28 immediate deaths from radiation exposure. This does not include the long-term cancer risk. There are other serious, immediate sequelae from radiation exposure if the exposure is high enough. Contamination of foods would certainly not cause these kinds of problems. The Chernobyl accident is believed to have caused, over the decade or so following the accident, about 1,000 excess thyroid cancers cases in Eastern Europe. The impact on the food supply was as follows: temporarily restrictions were put on milk as the result of ^{131}I contamination. Fortunately, ^{131}I has a short half-life of 8 days, but the contamination moved across Europe and, because of its high solubility, came down in large quantities in rain. Some other restrictions resulted from contamination with ^{137}Cs, which has a 30-year half-life. About 15,000 cows in Ukraine and about 2.4 million sheep in northern England were slaughtered and disposed of. Restrictions were also placed on consuming fish from some English lakes and in Sweden.

Table 5 gives sources of information or assistance should it be required. In the case of emergencies related to radiation contamination or exposure, there are state radiation protection offices that are generally part of the state health department. State and private universities also have departments experienced in making radioactivity measurements. In addition, there are commercial laboratories and national research laboratories under U.S. Department of Energy sponsorship. I suggest that partnerships be built with these kinds of institutions before emergencies occur. These laboratories are probably not set up to analyze large numbers of samples, but they know how to conduct analyses and could be set up for that scenario if strategic partnerships are established early enough. Also, the food industry might consider determining the background of radioactivity in foods, which could be used as a baseline for future comparisons. This should probably not be on the top of your list of initiatives, but it is something that might be considered. Places to contact when radiological contamination is suspected include the state radiation control office, state department of health, and the U.S. Nuclear Regulatory Commission, which has regional and national offices, as does the EPA. One department or institution cannot respond to all kinds of radiological emergencies, but these are the kinds of places you would want to notify under emergency conditions.

Table 5. Emergency Contacts When Radiological Contamination Is Suspected

- State radiation control office (state health department)
- U.S. Nuclear Regulatory Commission regional or national offices
- U.S. EPA regional or national offices
- Radiation Emergency Assistance Center (REAC/TS) , Oak Ridge, TN
- U.S. Federal Emergency Management Agency

In conclusion, radiological contamination of food will not likely occur on a large-scale geographic basis as a consequence of terrorist actions, notwithstanding a major nuclear reactor accident. Furthermore, radiological contamination of food will generally not pose a life-threatening risk in the short term. The long-term health risk to the population would be an increase in cancer rates, although that would require significant contamination to reach a substantial number of consumers. Public fear of radiological contamination, however, could substantially erode trust in the safety of the American food supply and lead to immense economic damage on a national scale.

Prevention and Control Strategies: Identifying and Mitigating Vulnerabilities to Biological, Chemical, Radioactive, and Physical Hazards

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Threat can be defined as a function of three major input variables: the capability of the perpetrators, their intentions or motivations, and our own vulnerabilities. Generally, we know very little about a perpetrator's capability and we know even less about their intentions. Thus, many threat assessments are concerned about the threat as a function of vulnerability. When you read threat assessments, see which of these variables are addressed and which are not. A true threat assessment will address all three to some degree.

I will address strategies for mitigating a threat in terms of these variables. Strategy 1 could be to reduce the inherent capability of the attacker. On a national scale, this is largely the responsibility of law enforcement and the defense and intelligence communities. They try to find out who is doing what and who is capable of doing what and, most important, they try to stop them from doing that. Strategy 2 is to anticipate the intentions or motivations that would result in someone trying to attack your product or your organization. This is something we can discuss in more detail. Much of the literature differentiates ***biological warfare*** from ***biological terrorism*** from ***biocrime***. These distinctions are based largely on the motivation or intentions of those committing the act. Biological warfare tends to be nation versus nation. Biological crimes tend to be individual based or small-group based, done by people with a grievance or for revenge. Biological terrorism is a political statement and often has a domestic origin. Terrorists seek to generate panic through injury, incapacitation, or mass murder. From the standpoint of creating panic, it almost doesn't matter whether it is biological warfare, terrorism, or crime. However, from a preventive standpoint, the distinction can make a big difference.

Take the case of the ***Salmonella*** outbreak in Oregon [1]. It was difficult to tell whether this was an intentional act or an accidental outbreak. This point leads me to the conclusion that there are only three ways to tell whether you've been intentionally attacked using biological agents: if you catch somebody in the act, if they admit it, or if you have amassed such a body of epidemiological evidence that there is no way that it can be anything else. Perpetrators are hard to catch and may not admit their crime, so usually you are left with trying to prove a single source of contamination. Epidemiological evidence is almost never strong enough to constitute legal evidence. A year after the Oregon outbreak, the nurse of this commune admitted to intentionally contaminating food-and that is the take-home message from this outbreak. Another case involved a medical center in Houston, Texas [2], and the attacker was a hospital laboratory technician. What is common to the two people who initiated these attacks? Capability! This leads to my personal belief that the most dangerous individual in the world is the disgruntled employee. Looking within is sometimes more important than looking outside.

Single-issue terrorism also deserves attention. This form of terrorism is commonly defined as extreme militancy associated with a perceived grievance and is usually targeted at a large institution or government. The three domestic kinds of classic single-issue terrorist motivators are animal rights, environmentalism, and anti-abortionism [3]. For example, some animal rights organizations, such as the Animal Liberation Front and People for the Ethical Treatment of Animals (PETA), target research facilities and, more recently, food processors and retailers.

Two concepts from military doctrine are useful as we try to identify potential targets of terrorism: "asymmetric warfare" and "center of gravity." The concept of asymmetric warfare is defined by the unlikelihood of an attack on the United States using conventional forces and weapons. Because of our military strength, not many groups or nations will attempt this. Asymmetric warfare means they will attack us where we are weak. Flying planes into buildings was not something that we anticipated, and the defense of that was not one of our strengths. A center of gravity can be defined as that essence of your enemy which,

if successfully attacked, will bring the war to a quick end. Examples of this are seen in the history of the Civil War. For the South, its center of gravity was its Army of Northern Virginia. For the North, its center of gravity was the city of Washington. The Civil War is an example of a conflict where the opposing forces had two totally different centers of gravity. This begs the question of what the center or centers of gravity are in the United States today. Your opinion is at least as good as mine, but I believe that the safety of the U.S. food supply is one of our centers of gravity. Our agricultural strength is an indicator of this. We feed not only ourselves, but many others as well. Of possibly more significance than the food supply is our more fundamental confidence in our government's ability to protect us, which is a major center of gravity. Americans have an inherent belief that somebody is watching over them, which provides some people with the potential motivation to attack us. Knowing the motivation of our potential attackers may serve us in our defensive efforts.

Strategy 3 is to address your vulnerability. We are better at this because it is more obvious than the previous strategies. We can use the principles of operational risk management to prevent a breakdown in the farm-to-fork continuum. The first principle is to define your production process in terms of the inputs and outputs at nodes of vulnerability. Obviously, the first task is to prevent the easy things, the risks you can easily correct or control. As for the hard things, the risks you don't think you can do much about, you at least try to minimize their effects. From a terrorist's standpoint, foods that are eaten uncooked or that can be contaminated after cooking are the ones to go after. The large scale of the U.S. food industry means that a single terrorist attack could threaten many people. We've seen cases where imported foods were either naturally or intentionally contaminated prior to arriving in the United States. Foods intended for a target group can be adulterated prior to delivery.

From an attacker's standpoint, the choice of methods and weapons is determined by the target and the delivery medium. It is very rare that someone wants to cause harm without it mattering to whom or to how many. There is usually a target, which is defined by the motive. So the target population, or whom they represent, may then define the vulnerabilities. When assessing your food/water vulnerability, focus on the potential hazards, critical control points, and the storage and distribution steps in that continuum that often get underemphasized. We do a good job of looking at production, and we look mainly at inputs to production, but when a product leaves the plant, we no longer focus on risks and we may even lose control over it. How long does it take a delivery truck to get from point A to point B? Does anybody check to see if there were major discrepancies in that time? Who had control over the truck then? Who did that transportation for you? Was it your own employees, was it a contractor, or do you even know? Have in place a rational employee hiring procedure, and monitor the systems rather than the end product. Testing your system or monitoring the system is usually more rational than just doing endpoint testing. Know the value and limitations of laboratory data: what does a positive test result mean, and how is it going to be used to go back and assess the system? Rapid reporting is obviously important. However, what if something bad happens? Do you have a process in place to test that system? Do you run exercises? Give consideration to physical security. Do you have procedures for investigating unusual activity? What about hazardous chemical storage? Often things that you can be attacked with are chemicals you store right there anyway. Do you keep daily rosters of who showed up for work or, more importantly, who didn't show up for work? Knowing who's there can potentially help you out. For restricted-access areas, use door locks or key cards where it's documented that the individual who had that card was in there and for what periods of time. Water is something we tend to take for granted because we have that luxury, but we may not always be able to take that for granted. Who controls the supply and storage? We tend to believe those are safe, even from a military standpoint, but I am not sure that we can always rely on that to remain true. Regarding computer access, who can get in through your computer system? Who has access to your computer system? The computer system, for many of us, largely controls our production process. In terms of information security, if I can get out on the Internet, somebody else can theoretically get in. Run an evaluation exercise.

Finally, risk communication and public relations are of the utmost importance, and we definitely tend to underemphasize them. Your willingness and ability to communicate with your beneficiaries in an honest and credible fashion may be the sole determinant of the longevity of your company or industry.

One of the thoughts along this line is one I learned from a former air force surgeon general: every major decision that we make in our lives, whether personal or corporate, has three major input variables: science, emotion, and politics. Almost nothing is pure science, pure emotion, or pure politics. As medical people, as food safety professionals, we tend to answer questions for the public and for the press thinking that science is going to impress them or mollify their fears. I would counsel you to take into account the source and attitude of the question. If you answer emotion with science, you will be wrong no matter what you say. So take into account where the question is coming from and couch your answer in the correct science, but realize that emotion and politics are almost always lurking in the background. I think it is incredibly important to be able to say, "I don't know; however, I'm in this just like you, and together we are going to figure this out, we are going to address this."

I'll leave you with an interesting anecdote I heard the other day about the counterproliferation of war and terrorism in general. Throughout recent history, there has apparently not been a major conflict fought by two countries in which both had McDonald's franchises. Therefore, perhaps our counterproliferation efforts ought to be focused on proliferating McDonald's rather than on the much more problematic objective of limiting the weapons and motivations for war!

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Operational Risk Management Applied to Food Security

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abstract not available for publication

Lessons Learned/Knowledge Gaps/Research Needs

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I would like to remind everyone of ILSI's role. ILSI is a research foundation. It is not a lobbying group; it is not a trade association. ILSI deals with science. It stays out of politics and it tries very hard to stay out of emotion. But the whole purpose of ILSI is science, both in organizing workshops like this where we discuss science and in funding research—a key part of how science gets done. For federal agencies interested in getting unbiased information, you cannot find a better organization than ILSI. ILSI has all of the mechanisms in place to screen out individual company bias and come to a perspective that represents what the processed-food industry sees as important. The overarching theme that I have heard in this conference is public-private partnerships. When I refer to partnerships, I am talking about ILSI partnerships. It's a personal view, but I feel very strongly that if you really want to find out what's going on, you need to get involved with ILSI. Of course, research and training was another strong theme that Dr. Satcher addressed, and this is also part of ILSI's base.

What is the economic impact of food and agriculture in the United States? Over $1 trillion in economic activity! That is the base of the U.S. economy in 1999. That is what agriculture gives to the U.S. economy. In terms of farm income, you are talking about $59 billion. In terms of a positive balance of trade, food and agriculture is one area that truly contributes to a positive balance, with $12 billion. Food and agriculture employed 2,800,000 U.S. workers in 1994. I don't have figures for 2001, but it's still a very significant part of the economy.

Risk versus consequence is a very important theme that we need to discuss on several levels. Let's begin by comparing water and food. I was very heartened to hear the talk about water because I was not sure whether the water supply was vulnerable. We heard that the bioterrorism threat is "quite limited"—difficult to achieve and generally limited to a threat of physical destruction. While this news does not make me feel good, I am at least relieved that the threat of bioterrorism with regard to the water supply is not a major problem. Presumably, we will have enough security to protect dams and treatment plants from those kinds of threats, and this makes me feel pretty good about the water situation. We did learn that if you really want to introduce a threat into the water distribution system, you'll have to do it under pressure. That's a little piece of information that some plumber may know, but I'll bet many of you did not. It makes me feel better to know that it is not easy to do. I already knew that a lot of toxins were unstable in water, but the fact that they are hard to get into the water is rather reassuring.

On the other hand, we have talked about food, where bioterrorism clearly is an issue. But I'd like to say that in addition to bioterrorism, there is also a risk of major damage to the food industry. Let me show you what I mean in terms of just livestock. There are large poultry flocks of 75,000 birds, and 8.6 billion chickens, 290 million turkeys, and 84 trillion eggs are produced each year. There are as many as 125,000 beef cattle per feedlot, and there are swine farms that have nearly 5,000 sows. These are major assets. A disruption in animal production could profoundly affect the food supply.

So what kinds of biological threats are people worried about? Figure 1 lists some of the agents we are concerned about. We talked about foot-and-mouth disease virus. Various viruses, including avian influenza, can infect people. Some of them are strictly animal disease, but some are not. Figure 2 shows some of the plant pathogens, such as rice blast and wheat smut, that could be used to disrupt farm production. Now it would be easy at this point simply to throw up your hands and say, "There are so many things to worry about; how I can even start to prioritize?" It is important to realize that we share this challenge with many others such as farmers and agricultural officials, regulatory and practicing veterinarians, public health officials, and so on. These are the people who must prioritize and address these risks. Most attendees at this workshop, except for some who are associated directly with the commodity groups, are not going to be concerned

Agent	Animals	Zoonotic?	Contagious?
Foot and mouth disease virus		Very minimal	Extremely
Rinderpest virus		No	Yes
African swine fever virus		No	Yes
Classical swine fever virus (hog cholera)		No	Yes
Mycoplasma mycoides mycoides (CBPP)		No	Yes
Newcastle disease virus		Very minimal	Extremely
Highly pathogenic avian influenza		Possible	Extremely
Burkholderia mallei (glanders)		Yes	Yes
Bacillus anthracis (anthrax)		Yes	Minimally

Figure 1.

about this. I think that ILSI really needs to be concerned about risks and consequences within the context of processed foods and food-processing facilities. That would be our center of gravity, as one speaker put it. This is just my view, but I think it ought to be discussed within ILSI to see if that judgment is on target.

Figure 3 briefly summarizes microbial pathogens. I have put anthrax at the top of the list because anthrax has received an enormous amount of publicity. We don't know a lot about its stability in food other than that it is almost certainly very stable. I think this is one area that needs to be researched more thoroughly. The spores are difficult to kill, and there is at least one terrorist out there with a supply of this stuff. If one person has it, perhaps others do also. I don't think you can be too quick in doing as much as you can about this risk with regard to your industry. If anthrax spores were introduced into a food plant, it would probably result in it being closed for a long time, even if the spores didn't get into the food. The fact that those spores are there in some kind of aerosolized form would be a disaster, and certainly the emotional aspect would keep the issue alive.

Figure 2. Potential Agents

- Anthrax
- Glanders
- Screw worm
- Cowpox, sheep pox viruses
- Blue Tongue virus
- Rice Blast
- Wheat Smut
- Rye Stem Rust

Figure 3. Microbial Pathogens

1 Anthrax
2 Other "exotic" pathogens
3 Typical food-borne pathogens
4 Importance of public-private partnership

There are other, more "exotic" pathogens. By "exotic" I simply mean pathogens that you don't normally find in food. They could be some of the things discussed here: tularemia or plague, for example. These are things that you need to think about and talk about, but to me they are not likely to garner the kind of attention that anthrax does. Although they might be introduced into a single product or single plant, I'm not sure that these agents are as great a threat to the industry as is anthrax.

We deal with the typical foodborne pathogens, ***Salmonella*** spp., ***E. coli***, and ***Listeria*** spp., all the time. The industry has systems in place to check for these, and I think that's a very important consideration. I consider these to be very real threats. These pathogens have been intentionally introduced in the past, so we know it can happen again. We have controls and response plans in place, so when Dr. Meyerhoff of the Food and Drug Administration said that we could build on our food safety base, I think that's where you are going.

I want to emphasize again the importance of the public-private partnership. Dr. Meyerhoff indicated that the FDA is developing a strategy based on what a terrorist may conceivably do. I think it's absolutely imperative that ILSI—and this is my personal view—be involved in that, and the sooner the better, because you cannot get the information you need without dealing with the food industry, and ILSI is a way of dealing with the industry as a whole. I really think that FDA needs to sit down as quickly as possible and begin developing that strategy with ILSI. We have got to get past the security issues and work together to protect the food supply. To me this is absolutely essential, and I feel that this message came through from everything we heard at this workshop.

Toxins are more problematic in one sense: they are arguably easier to obtain and use than the exotic pathogens. Toxins are easier to use because you can't get infected from them, but the fact that they are not infectious also means that they are hard to disseminate broadly. You can use them locally and sporadically, but again, it would be very hard to attack the whole country with a toxin. Some of the toxins that we need to be concerned with are ***Clostridium botulinum*** neurotoxins, ricin, staphylococcal enterotoxins, saxitoxin, and mycotoxins. These are the top five toxins discussed at this workshop. We already know a lot about ***C. botulinum*** neurotoxins-the whole canning industry has built its control system around this organism and its toxins-but we still don't know how to detect them very fast and efficiently. Also, we need to have better ways to treat people affected by these toxins. Ricin is very easy to get, and we heard about an attempt to move ricin across the border from Canada into the United States. Anybody can grow the plant and extract ricin. We need better and more rapid methods for detecting ricin, and we need better ways to treat persons affected by it. Staphylococcal enterotoxins have been around a long time, and we deal with them all the time. But they are heat stable and potentially a problem. Saxitoxin is a very fast-acting toxin that depolarizes the nerves and relaxes the muscles so that you just collapse and die. Professor Johnson did an excellent job of putting it into perspective: he didn't say it was impossible, but it's still something that we need to keep in mind. Finally, we have mycotoxins, which are inevitably present and which you can produce in your basement real fast, and the acute toxicants that Dr. Bolger discussed. If you want a list of all plant toxins, go to the 1990 International Food Biotechnology Council report 225. It lists plant and nonplant naturally occurring toxins, but mostly plant toxins.

Figure 4 shows some other toxins that are feasible. This list presents a real challenge for even a committee to go through and figure out how to prioritize. This is not a totally hypothetical exercise. Iraq's biowarfare program is headed by a United Kingdom–trained Ph.D. microbiologist. She is apparently a very bright person who can do exactly what we just did here: she can sit down and bring in people and talk to them and learn everything we've learned and then some. What do we know that the Iraqis have? Anthrax, smallpox, aflatoxin, ricin—and some of these things you can even buy over the Internet.

We talked about radiological contamination, which apparently presents a much bigger emotional risk than a real risk. I am under the impression that it would be fairly easy to detect this, and maybe you need to monitor your raw material supply with a radiation counter, especially raw materials that may come from a questionable foreign source.

Finally, a theme that came through over and over was perception versus risk—the science, the emotion, and politics. ILSI deals with the science, but we can't forget about the perception. One of the speakers mentioned LD_{50}. Perhaps we ought to be thinking about an LD_{1} or $LD_{0.1}$, or $LD_{0.001}$ and what the infectious doses are. Without a

Figure 4. Potential Chemical Threats in Food

- ACh inhibitors
- nerve agents, Ops (e.g., parathion and paraoxon)
- Plant toxins
- ricin, abrin, aconitine, nicotine, solanine
- Drugs
- digoxin, lysergic acid, colchicine
- Mushroom toxins
- ***Amanita phalloides, Galerina, Gyromitra,*** Muscarine species (Amanita, Inocybe, Clitocybe), Coprine species
- Mycotoxins
- Aflatoxin, ergotamine, vomitoxin, T2
- Animal/marine toxins
- Tetrodotoxin, saxitoxin, conotoxin, ciguatera
- Elements
- arsenic trioxide, potassium silver cyanide, selenious acid, hexavalent chromium
- TSCA industrial compounds
- sodium cyanide and sodium arsenite
- Pesticides
- Strychnine, sodium monofluoroacetate, paraquat,
- Allergens/hypersenitivity
- Peanuts, sulfites

doubt, this is an area where ILSI needs to get involved. If we do not have good science here, you could end up with a Delaney clause for toxins or pathogens. Nobody wants that, but we do need to know what a realistic assessment is of the infectious dose for pathogens and toxins, and that is a scientific issue that ILSI can get involved in.

I will finish with Figure 5, which came from Dr. Riley's presentation. You have four quadrants dealing with whether a risk is observable or not observable and whether it is controllable or not controllable. The things that are not observable and not controllable are the ones that people worry about the most. Even though, as scientists, we may make a different kind of a list, this is what the public is looking at and this is what drives politics. Just talk to the people in Europe who are putting all the restrictions on food biotechnology to see how that goes. I think that we ought to ask ourselves what we would put in this upper-right quadrant as the issues that we consider most important with regard to being not observable and not controllable. These risks could very well be the ones that are keeping us awake at night worrying about what's affecting our industry. This may be the sort of thing that ILSI can get involved in by helping to bring in the science so that we can get them out of the not-controllable and not-observable category.

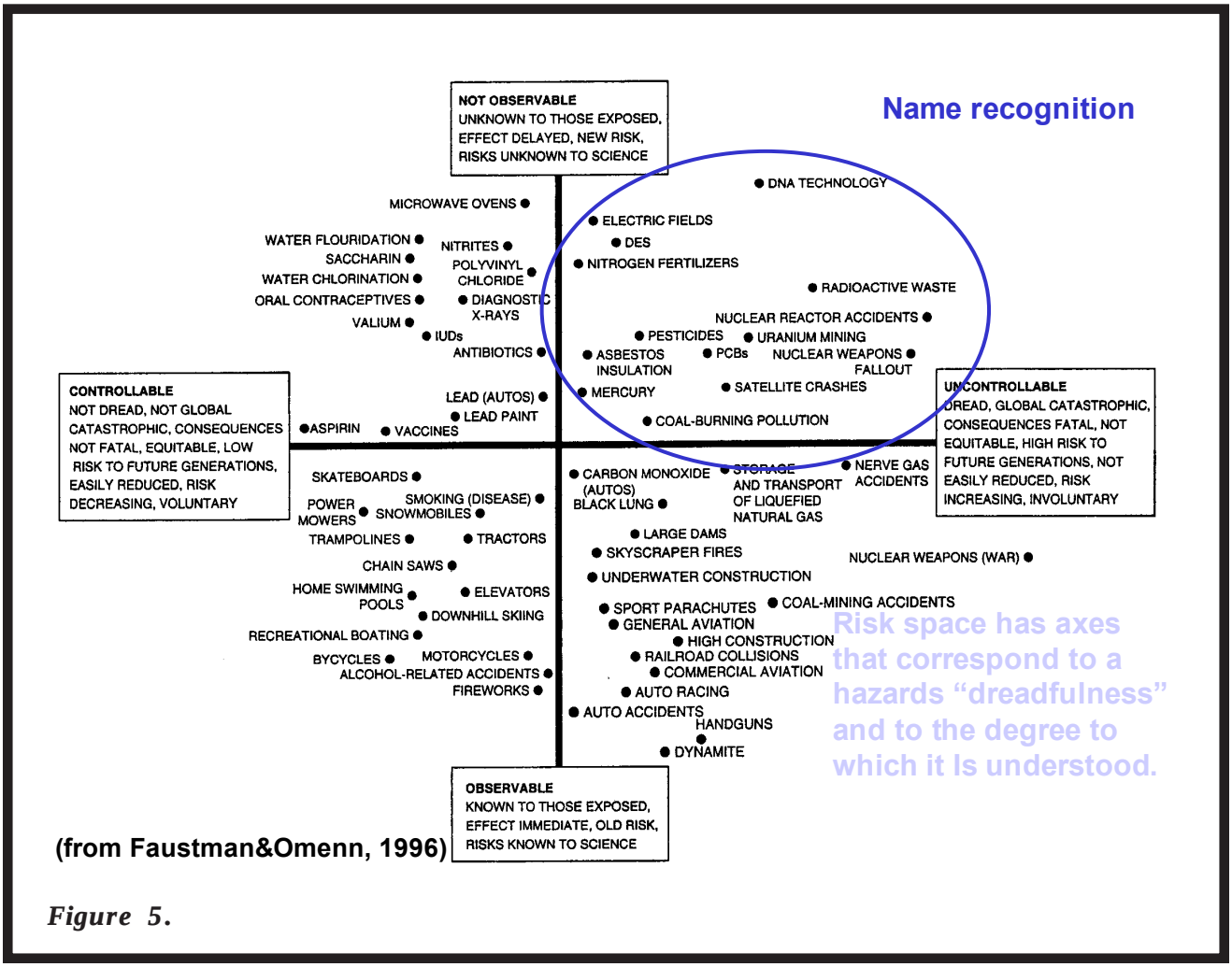

Figure 5.

Workshop on Biological and Chemical Agents of Terrorism in Food, December 2001, Washington, D.C.

CONSENSUS STATEMENT RESEARCH PRIORITIES

The topics below were extracted and adapted from the extended abstracts of the workshop presentations and developed by the ILSI North America (ILSI N.A.) technical committees on Food Microbiology and on Food Toxicology and Safety Assessment to form a consensus statement on key research areas to fill gaps in our current knowledge about potential biological and chemical threats to the safety of the food supply. The order in which the topics are presented reflects the committees' efforts to synthesize the material presented at the workshop rather than an order of importance.

General Topics

- What is the effect of common raw ingredient and food manufacturing processes on a variety of potential bioterrorism or biowarfare agents? For example, what concentrations and contact times of chemical sanitizers (hypochlorite, quaternary ammonium compounds, phenolics, oxidizers, etc.) are needed to kill, inactivate, or destroy these agents?
- What is the effect of manufacturing and processing treatments such as wet and dry heating, bleaching, freezing, irradiation, dehydration, and fermentation on these agents?
- What is the stability of various agents of bioterrorism or biowarfare in a variety of foods and in water?
- What is the effect of ionizing radiation on the inactivation of potential bioterrorism or biowarfare agents (both bacteria and viruses)?
- How can we develop simple and rapid methods for sample preparation for analysis of agents of bioterrorism or biowarfare? A number of technologies show promise for the rapid detection of these agents, but sample preparation (including steps to concentrate the agent, remove interfering substances, or simply convert the sample to a form that can be tested with an instrument) may be a barrier to the efficient use of these rapid methods.

Microbiological Agents

- What is the stability of more "conventional" microbial pathogens (i.e., ***Salmonella*** spp., ***Shigella*** spp., ***Listeria monocytogenes***, and ***Escherichia coli*** O157:H7) in foods where we might not ordinarily expect these agents to be found?
- How can we increase our knowledge base on pathogens that are not of conventional concern in food-processing facilities but that could be used intentionally as agents of bioterrorism or biowarfare in food production, storage, and transport systems; in water storage, purification, and distribution systems; and in the wider environment? The following pathogens were discussed, and research needs were identified to improve scientific understanding of the pathogenicity and control of these agents and to improve the means of diagnosing and treating resulting disease in humans.

Bacillus anthracis

- the dose needed to infect, say, 1% or 5% of the human population
- effective means of destroying ***B. anthracis*** spores in the environment, such as in buildings, in ventilation systems, and on machinery; the safe disposal of materials from remediation efforts
- improved diagnostic techniques to identify the infection in humans in its very early stages

- better understanding of variations in human susceptibility to inhalation anthrax. E.g., some individuals can be exposed to fairly high numbers of spores and develop only cutaneous anthrax, whereas others in the same exposure group but exposed to very few spores develop inhalation anthrax.
- better understanding of interspecies variation in susceptibility to anthrax. E.g., mice and guinea pigs are highly susceptible, rats are very resistant, and humans are somewhere in the middle.
- exploration of possible infection routes other than a break in the skin to contract the cutaneous form of anthrax
- examination of the vegetative cell versus spores to determine which is the more virulent means of causing infection via the oral route
- better understanding of the ecology of B. anthracis. E.g., does the infection occur more frequently in wildlife than we are currently aware of? Can the organism be isolated from the feces of scavengers?
- development of a good nonprimate animal model to study the disease in humans

Clostridium botulinum and its toxins

- improved understanding of the stability of botulinum toxin in a variety of foods (particularly those where ***C. botulinum*** cannot ordinarily grow and produce toxin) that might be used as vehicles of bioterrorism
- development of more rapid and more sensitive methods to detect botulinum toxin in foods
- better treatment regimens for people affected by botulinum toxin (e.g., the development of drugs that act rapidly to remove bound toxin from nerve receptors)
- examination of the potential for intoxicated dairy cows to secrete toxin into their milk and whether it will survive dairy processes such as pasteurization and cheese or butter manufacturing
- exploration of the potential for certain food components to protect botulinum toxin from heat inactivation

Yersinia pestis

- expanded database on the stability of ***Y. pestis*** in a variety of foods
- rapid and more sensitive methods to detect ***Y. pestis*** in foods and in water
- data on the effects of various food manufacturing processes on the inactivation of ***Y. pestis***

Francisella tularensis

- expanded database on the growth and stability of ***F. tularensis*** in a variety of foods
- more rapid and more sensitive methods to detect ***F. tularensis*** in foods
- exploration of the ability to rapidly classify isolates into one of the known biovars, which could prove useful in distinguishing a naturally occurring infection from a bioterrorism incident
- expanded database on the effects of various food manufacturing processes on the inactivation of ***F. tularensis***. E.g., can we exploit the vulnerability of the lipid capsule to reduce virulence or eliminate acid resistance?

Chemical and Biological Toxins

- More rapid and more sensitive assays should be developed for phyco- and mycotoxins such as ricin, abrin, suporin, aconitine, and amanitine in food matrices.
- Greater understanding is needed of the stability of phycotoxins such as ricin, abrin, and suporin in a variety of foods and of the effect of common food manufacturing techniques on the stability of these agents in foods.
- Improved assessments of the organoleptic changes (visual, odor, taste) that occur in various food matrices after contamination by various chemical agents need to be conducted.
- Better and more rapid methods are needed to detect staphylococcal enterotoxins in foods.
- Better and more rapid assays are needed for marine toxins such as saxitoxin, tetrodotoxin and anatoxin in food matrices.
- Better methods for treating patients affected by chemical agents such as plant and marine toxins must be developed.
- Realistic risk assessments of the infectious or hazardous dose for a variety of microbial pathogens and chemical toxins are needed should we be faced with having to assess the public health impact of a contamination incident for which current regulatory standards

are inappropriate (e.g., one-time exposure versus longer-term chronic exposure).
- Rapid methods are needed for the detection of certain pharmaceutical drugs such as digoxin and colchicin in food matrices.

RECOMMENDATION

The research priorities identified above reflect significant gaps in our current knowledge and understanding that should be addressed through collaborative and concerted efforts on the part of the private and the public sectors. ILSI N.A. believes that its members can and should offer valuable perspectives on the scientific issues surrounding food security and potential terrorist threats. The members of the technical committees on Food Microbiology and on Food Toxicology and Safety Assessment are committed to maintaining an active role in ensuring the security of our nation's food supply. ILSI N.A. proposes to host a series of face-to-face meetings with the relevant government agencies to elaborate a role for these technical committees that would contribute to and build on other initiatives in these areas.

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