HSAC Member Comments Regarding April 21-22, 2009 Consultation on Anthrax TAD
As of 4-20-09, 10am

I. Dr. John Bartlett: 4/16/09 comments

Please note that I am an infectious disease physician so my review focuses based on that background.

A) General Comments

I reviewed the document and have some comments to pass on. Please note that I am an infectious disease physician so my review focuses on my background.

An overview is that the document is good but the two major areas of concern are:

1) the assumption that this will be a mail attack and
2) no mention of engagement with the regional health system.

B) Specific Comments to the 2003/2005 draft Environmental Response Technical Assistance Document For *Bacillus anthracis* Intentional Releases (BA-TAD)

Section 4.1 Discovery

There may be too much emphasis on the letter mechanism of distribution. Please include other scenarios such as contamination of food and water (such as the chocolate contamination in South Africa) or an aerosol via a ventilation system (similar to the B. thuringiensis in Canada). I worry that we think too narrowly about letter because that is our major frame of reference. The document really needs to address multiple types of building exposures.

The recommendations are to leave the area and close the doors. Sources of aerosols should be shut down including air conditioners, heaters and other sources of ventilation.

Section 4.6 Identification of exposed personnel:

The statement is to consult a local plan and/or appropriate medical experts. This seems very open ended. Someone will need to make some rapid decisions and that really needs to be an authority on anthrax. It may be an identified local expert, but there needs to be clarity in who gets called and what. Information is essential. I suggest the local health department or the CDC for contact with an anthrax expert. If this is a credible exposure there will need to be rapid institution of antibiotics for those exposed and Abx plus PPE for those who enter for cleaning, for evidence, etc.

Chapter: Health and Safety

A few points worth emphasizing are the following:

- I urge liberal use of antibiotics if there is credible evidence of anthrax. Doxycycline and cipro used in 2001 were generally well tolerated and apparently 100% effective (since none of the 5,000 exposed persons who took it acquired anthrax). Main issues are children and pregnant women who will not be in the clean-up but may have been exposed.

- Workers and others need to know anthrax is not transmitted from person-to-person so their families and other contacts are safe (very important message).
- The PPE plan is fine – but N95 masks must be fit, tested, individualized and don't work well with face hair. This part of prevention is a potential problem.
- For hygiene – alcohol-based cleaning is poor vs. spores. Preferred – soap and water.

Section 5.4 Medical program

A major concern based on the 2001 experience is the communication with the regional health care system, especially in Washington DC. Please remember that the first case was identified by a private physician by gram stain, and the NY cutaneous case was a private MD group puzzled by the child's lesion. All care was in local hospitals. Local doctors will see most of the cases (worried or well) and take relevant phone calls. The problem was communication with that sector. Local physicians need to know who is at risk, and what to do. This applies to those responsible for clean-up as well.

- There needs to be a system to rapidly deliver antibiotics for those exposed and those who will be exposed by clean-up. The best record I know is the NYC Health Department which had an auditorium, used a simple form, had a physician available (but ran it with midlevel nurses) and gave out cipro or doxy to 1000 people with a put-through time of 10 minutes.
- The antibiotics to use are the four approved by the FDA for anthrax – cipro, levofloxcin, doxycycline and penicillin. It is said that Russia engineered resistance, but that is not verified. I think you can count on these, know well what can be used when the first strain is tested (because they will all be the same) and resistance development by B. anthracis is unlikely. Side effect to these drugs are common but serious side effects are rare.

Table 5.1 – Medical tests need to include chest x-ray and blood cultures.

Table 5.2 – Not sure about the emphasis on immune deficiency. This pathogen does not need the help.

Section 5.4 Post exposure

The option to go 100 vs. 60 days was confusing – who and why.

In 2001, the recommendation was to give the antibiotic 60 days or 100 days, and to consult your physician. There was also the vaccine option. Patients asked their physicians who didn't know anything about anthrax and had never seen a case. So they said "who and why" (for 100 days) and no one knew except for the primate data. My point is that the treating doctor does best with specific guidance when it comes to a rare disease that is lethal in 45% of the cases. I think the problem here is that we really don't have supporting data. I think I would go 100 days, especially if it was well tolerated or the exposure was high risk.

Section 5-3 Medical monitoring: Who will be doing this?

Section 6.1 Sampling plan: Might state that nasal cultures of exposed persons should or should not be done due to the confusion on this point in 2001.

Section 9.2.3 Communication: This is a critical facet of the plan based on the prior experience. It must be someone with great credibility and knowledge of the specifics of the outbreak.

Safety Data Sheet

The drug susceptibility line suggests penicillin is inappropriate for inhalation anthrax "since mortality remains high". Penicillin was not advocated due to penicillinas production by the 2001 strain, but that was extra cautious and probably not very important. The fact is the mortality is high for anthrax treated with the recommended antibiotics (45% for 2001).

With hand washing it may be important to mention friction.

Medical surveillance: What immunologic techniques?

Anthrax Guidance

Occupational Exposure: OSHA

The document is generally good based on my understanding of anthrax. A few suggestions/concerns

- There is a lot of information on mail exposures and prevention but little on these types of anthrax spores in food, water, outside air (that enters building selectively) and spores in the ventilation system. (Note that mail exposure accounts for #9-12, but other exposures are barely mentioned).
- Antibiotics (#16) need a better review. In the document they are not indicated "unless there is strong or compelling evidence . . . of exposure" and you should "discuss this with your healthcare provider". There needs to be greater clarity here since private MDs will need guidance and please note that the antibiotics are highly effective, resistance by B. anthracis is very unlikely and serious side effects are rare. (I am not advocating broad scale use – the recommendation is clarity and perspective on this issue.
- There is reference to "an employee who tests positive for anthrax exposure" (#28). Nasal cultures were done in the HART Building episode in 2001, but I thought this was discouraged. It would be good to have clarity on what microbiology should be done in the event of possible exposure.

II. Dr. Paul Lioy: 4/7/09 comments

Here is a manuscript that we published on Anthrax (see attached document: "Mechanistic Modeling of Emergency Events: Assessing the Impact of Hypothetical Releases of Anthrax", by S. S. Isukapalli; P. J. Lioy; and P. G. Georgopoulos).

It deals with a situation beyond finding a package or letter with anthrax laden dust in an office. I am puzzled that the document we received is limited to a letter or package anthrax incident, section 4.1, the copy cat rule of preparedness? There is limited or no information about "outdoor releases," and response in this document. A point that we need to discuss further

III. Dr. Mary Durfee: 4/16/09 comments

Thank you for encouraging me to submit my comments on the antrax materials for the upcoming HSAC meeting. I'm sure the discussion will be vigorous and productive; I regret that my teaching duties prevent me from attending.

The document is aim at the FOSC, who coordinates the response to an actual or suspected anthrax incident. Most of the coordination, if I understand the documents correctly, is with other government agencies, including state and local personnel. The document outlines main steps for identifying, decontaminating, checking the decontamination, and communicating results. While primarily aimed at an indoor release, the charge to the HSAC is to give guidance on outdoor releases. Also, the HSAC has been asked to comment on the communications plan.

The Chair of the committee, Dr. Fischhoff asked for comments in the following general categories:

Professionals who will be concerned with how well the charge questions are answered and how well individuals being protected by professional judgments will be served.

It is unclear if the communications are primarily with professional people or can include communications with elected officials. The communications would, presumably, take rather different turns to these two types of officials, even as all communications would be structured by the TAD and the efforts at the site.

The FOSC would be communicating in a highly centralized structure with many potential organizational contacts.

A. There is no evidence that the impact of organizational structure for the emergency has been factored into the brief comments on communications. At best it says the FOSC has a public affairs officer (PAO) who will take care of things. In a highly centralized command structure, the FOSC will give information to the PAO from above and will expect solid information from the PAO back up. Is there any evidence from any situation that procedures are clear on this?
B. Even if the structure of the response is centralized, the reality, reiterated throughout the document, will be operations in a much more fluid set of jurisdictional rules. There is clarity in the document on what to do about storing and labeling materials for transport, but very little else. Is there a quick guide on who to call at local, county, and state levels?
C. How will the FOSC be expected to guide the PAO's communications with these subnational governmental units?
D. There seems to be no real consideration, at least in this document, to how the FOSC will related each major stage of the response to different agencies and to the public's concerns. The immediate fear of workers will be supplanted by those who have been in the building. People will object to the materials being transported through their neighborhoods. While tons of hazardous wastes roll by communities every day, public awareness will be sensitized to movements of anthrax waste.

Dr. Fishhoff asked that we offer ideas for improvement.

What mental models do citizens have of anthrax? This needs to be studied in advance, so that the entire response team can develop effective communications strategies. A more advanced project would be to see if their models change when localized to real locations in which they live and work on a daily basis. Beyond that, there are powerful network analysis tools

We can see from the one public comment that elements of the public will have a very high standard for clean up, one that may just not be achievable. The FOSC should have a guide to help understand this in order to provide relevant, authoritative guidance in the centralized structure to the Public Affairs Officer.

It would be a good idea to have ways of explaining why the use of some normally dangerous chemicals are permitted in this context. I suspect (but can't cite you literature) that both public officials and the public would be accepting, at least at first. But this should be on the list of things the FOSC has a passing understanding of in order to be more effective.

I would urge much more clarity on the existing SOPs for communicating between Federal agencies and between the Federal government and subnational units. I do not believe the FOSC can execute the technical details well without at least a general understanding of these.

Dr. FIshhoff also asked if we saw any gaps. I wonder about the advice at 8.2 Notification of Waste and Recycling Service Providers. What will you say to these handlers who may already have contaminated material? How does information from the waste and recycling providers get back to the FOSC.

I look forward to learning how the meeting went.

Sincerely,
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IV. Dr. L.D. McMullen: 4/16/09 comments

Charge Question #4

For critical infrastructures or wide area locations, a "Zero-Culturable-Spore" (ZCS) decontamination goal may not be achievable.

- What are possible cleanup strategies for minimizing risk to facilitate re-occupancy in industrial, commercial and residential buildings where a "ZCS" decontamination goal was not achieved?

This question requests advice in two areas: 1) critical infrastructure and 2) wide-area locations. It seems to me that the approach taken for each may be significantly different. As such, my discussion will be to separate them.

Critical infrastructure may have many different definitions. It may include health care facilities, public safety, telecommunications, energy, water, wastewater, etc. However, for re-occupancy were a "ZCS" decontamination goal was not achieved, the list could be narrowed to only those facilities where there is minimal redundancy and have a significant impact on public health. This will vary from city to city and locations within a city. In general, most health care facilities, public safety, and energy facilities have adequate redundancy or can ration available resources until adequate decontamination can be completed. Telecommunications also fall into

this area with cellular technology being able to move portable facilities into a particular area until the fixed systems are decontaminated. Wastewater treatment usually does not have redundant facilities due to the design of gravity collection systems. If these facilities are out of service for a period of time, there is potential for environmental damage. However, the threat to public health would be minimal. The one infrastructure which is difficult to replace is drinking water. Many cities do not have full redundant treatment facilities at multiple locations. When a treatment plant is lost and a city's water supply is lost or reduced significantly. Public health is compromised not only from lack of drinking water, but as important, the movement of sanitary wastes and fire protection. Therefore, water treatment infrastructure will need to be operated before a "ZCS" decontamination.

Most water treatment plants have automatic/remote control that can be remoted to a safe location. Critical chemical delivery can also be handled in a short period of time. However, strategies for maintenance activities will have to be developed. There should be a period of time to develop this since there is normally redundancy within a water treatment plant that would allow a period of time before a required re-entry to the plant. The more interesting question is how to treat the water to make it safe. It does not seem reasonable to assume that this can be done in a short time due to the resistance of the spores to normal water treatment systems.

The second question deals with wide area locations. This is by far the more difficult question to address. It seems a "washdown" with water by rain or manual washing is the approach that can be used, but the bigger issue is what to do with all the wash water. Due to the large volumes and the natural runoff to streams or lakes, the major problem is the potential contamination of source water for water treatment plants. This is the same problem as above since normal water treatment plants do not have the equipment to treat for B anthracis.

V. Dr. Rae Zimmerman: 4/16/09 comments

This response primarily concentrates on risk communication, Charge Question #5:

The FOSC would, in a B. anthracis event, be functioning within the Incident Command System which typically includes a centralized communication structure with specific roles and responsibilities. The BA-TAD will address the key issues pertinent to the cleanup of environmental contamination with B. anthracis. What recommendations does the SAB-HSAC have for scientifically-sound communications to be included in the BA-TAD? More specifically, for the purposes of the BA-TAD, what recommendations does the SAB-HSAC have for the content of these communications?

GENERAL COMMENTS

According to the white paper, the new BA-TAD "will be a technical resource document developed specifically for use by FOSCs . . ." and "will not be intended for use by a wider audience . . . The wider audience would include . . . the public (e.g., nearby residents; stakeholders) (White Paper, April 21-22, 2009, p. 4). The earlier 2003/2005 TAD referred to communication with the public indirectly. Its purpose was to provide "technical information on a wide range of activities – initial actions when a potential release is discovered, selection of personal protective equipment, evaluation of decontamination technologies, communication with

the public, etc." (TAD, p. 2) Its intended audience was stated as "first responders ... government agencies .... and facility managers and owners..." (TAD, p. 1). Thus, although the general public is not indicated as an intended direct user of either document, communication with the public by the intended audiences is at least mentioned as a primary purpose at least indirectly.

The comments below can be used to incorporate communication into the BA-TAD for the public. This is important, since the Federal On Scene Coordinators (FOSCs) will at least indirectly have to take this into account in their function of "managing response actions associated with . . . release of B. anthracis," especially since the responsibilities now cover a wide-area release.

Communications need to be framed differently for managers, responders, various involved professionals (health, transport, police, fire, etc.) and at least at community and individual levels. In support of other HSAC member comments, the target of communications should include the extremes – those who might underestimate and overestimate their exposure and vulnerability to a particular attack – and everything in between.

TYPES AND CONTENT OF MESSAGES

Types of Messages

Facts about B. anthracis (abbreviated Anthrax)
Messages for Effective Transmission
Messages over Time and Place
Actions People Are Expected to Take in Light of Exposures
Uncertainties
Process

Message Content for each Type of Message

1. Anthrax Facts

People expect facts specific to the threat to be communicated. For Anthrax, these facts can be organized along the following lines: likelihood of attacks, identification (when an attack does occur what are the signs and how does the public know it is there), mechanisms by which anthrax acts from release to ultimate effect, intermediate effects of exposure to anthrax, mode of transmission to humans, how will people know it affects them in particular and in what way, and what are the uncertainties in identifying individual risk (see uncertainty section below).

Facts specific to Anthrax should include whether effects are dose dependant, portal of entry (inhalation, ingestion, cutaneous), infectivity, the length of time symptoms appear for different portals, availability and effectiveness of antedotes, etc. The CDC fact sheets are a useful place to start as well as review articles, for example Ingleby et al. (2002):

CDC. Fact Sheet: Anthrax Information for Health Care Providers. Page last updated March 8, 2002; Page last reviewed February 22, 2006.
http://www.bt.cdc.gov/agent/anthrax/anthrax-hcp-factsheet.asp

CDC. Division of Foodborne, Bacterial, and Mycotic Diseases (DFBMD). Anthrax. Last Page last modified March 2008.
http://www.cdc.gov/nczved/dfbmd/disease_listing/anthrax_gi.html

2. Designing Messages and Message Content for Effective Transmission. How people process communications and overcoming obstacles to message transmission is a critical aspect of communication. Below is a list of some of the obstacles to effective transmission of messages and some suggestions about ways to overcome them.

a. Message is not heard:

Failure to Hear. This could be a function of technology, or the physical or psychological state of the intended recipients.

- Draw upon more effective technology or decentralize the message transmission closer to the intended recipients.
- Where hearing impairment is suspected, special messengers would be needed.

Failure to Listen.

- Incorporate attention getting efforts. Incorporating emotion into messages has been known to draw people to information about risks and to seek out ways to reduce the risks. This was cited in connection with arsenic in drinking water (Sunstein 2003) and the understanding by laypersons of the effects of SARS (Lerner et al. 2003).
- Use messengers people will respond to. Messengers who are trusted are considered the most effective. In the context of other kinds of releases, effective messengers have been identified as doctors for health information (Blendon et al. 2003) and meteorologists for dispersion of a contaminant (Henderson 2004).

b. Message is heard, but:

It is Misheard or Misunderstood. A case example is instructive. A clerk misheard a person was going to be working at a nuclear power plant as saying that the person "came to blow up the place," but the person claims he actually said that he "hoped he wouldn't blow up the place" because of his inexperience. The mistake resulted in the evacuation of hundreds of employees in a nuclear power plant for several hours. (Associated Press, April 9, 2008).

- Provide multiple sources of information for cross-verification.

It is Not Comprehensible. This may occur because of language or education barriers.

- Tailor messages to different audiences.
- Message content should be translated into different languages based even on scant knowledge of the population in the affected area.
- Formulate messages in a more easily understood format with simple easy to understand phrases.

It is Inaudible. This could be a technology problem.

- Multiple means of transmitting messages should be tapped.

It is Ignored.

- As in the case of failure to listen above, attention getting mechanisms and effective messengers should be tapped.
- In addition, however, communicating the process by which discovery, deployment of emergency and healthcare workers, and cleanup is being undertaken is critical to getting and sustaining people's attention.

3. Messages need to be staged over time since the purpose of a message changes over time and place relative to the point of the release

Time

- Prior to any attack: no easy way to anticipate an attack, etc.
- At the time of discovery: alert people in the vicinity of the release that something has occurred
- When exposure is suspected
- When clear symptoms appear

Place

- Those closest to the release. As studies of the World Trade Center attacks in NYC revealed, those closest to a release are more likely to be more stressed (Schuster et al. 2003) and exhibit fear and risk avoidance behavior (Fischhoff et al. 2003).
- The "worried well"
- Distant onlookers
- Those concerned about people they know might be affected

4. Actions Desired

Gear messages to what you want people to do. Identify what activities have to be done before, during and after an attack, noting where people should go in the event of an anthrax attack and under what conditions. Where actions are mentioned specifically for the general public, communications should comprehensively cover these alternative actions, and each type of action might need a different type of communication. One action is evacuation. Another action is having individuals get to a health facility for treatment (triage center, hospital, etc.).

Compliance with messages that are geared toward desired actions is the subject of a relatively large literature. Compliance tends to be associated with prior experience with similar risks (Lichtenberg and Zimmerman 1999), trust in the messengers discussed earlier, etc.

5. Uncertainty

Uncertainty is perhaps the most critical factor in risk communication, and a failure to confront it openly and honestly can bring down any level of trust people might have had in managers. It will affect how people react to and their expectations about false positives and false

negatives. Some important examples of uncertainty for Anthrax organized according to the stages in the emergence of the threat are:

- Detection of the agent. Appearance of a white powder or actual symptoms has typically been the trigger in most instances. Sampling uncertainty is described in detail in the 2003/2005 TAD (p. 42) and has to be communicated in a way that gives the public an understanding of imperfect knowledge about detecting the existence of the substance.
- Prophylaxis: Supplies of antibiotics are limited, and not sufficient for civilian use; use of vaccines can have adverse side effects; amount of time needed to develop an immunity is variable (2003/2005 TAD p. 24)
- Defining the geographic extent of the problem.
- Exposure. The appearance of symptoms seems to be highly variable for the various forms of exposure, ranging generally from 1-7 days and longer.
    - Symptoms appear relatively quickly (in less than a day) for Cutaneous Anthrax.
    - For inhalation anthrax it could be as long as two months (CDC fact sheet for health care providers). Also, the threshold of exposure for inhalation anthrax is not well known: "It is not yet known how many spores cause inhalational anthrax or how many spores a responder may be exposed to during environmental sampling or decontamination activities." (2003/2005 TAD p. 24-25). "Experimental data indicate that viable spores may persist in the lungs for 100 days after exposure." [this can be a factor in the timing of antibiotic use]. The longer it takes for symptoms appear the more difficult it is to link symptoms to a source.

6. Process. Communicating the process for the chain of activities through which anthrax passes as it is collected, treated, etc., e.g., goes to wastewater treatment plants, other handling facilities needs to be communicated so people won't leave this to their imagination.

OTHER SUGGESTED ITEMS TO INCLUDE

Concepts of Risk Communication

Communication concepts for emergency responders to use would be very useful. A basic primer of risk communication should be contained in the report or at least guide the risk communication procedures the report contains, including some of the basic underlying tenets of risk communication that have been around for years. Basic risk communication principles, perceptions that influence communication effectiveness, and the framing of messages have been around and have been applied for decades. These should be summarized up front. There are many and they are interrelated. Some of the simpler ones include: trust in messengers and the institutions is a strong determinant of who and what messages will be listened to; people tend to misrepresent technical information, underestimating large risks and overestimating small ones, but this can depend on the type of risk; people will personalize risks and are most concerned with what happens to them or those close to them and less concerned about the general public; prior experiences will shape people's perceptions of new experiences; etc.

Cases

A number of cases occurred during and after the 2001 Anthrax incidents that have important lessons for risk communication, and would be useful to write up in detail.

1. Eatontown, NJ: Two postal workers at the USPS Monmouth Processing and Distribution Center (PDC) are hospitalized with "suspected" anthrax exposure (eventually disproven) potentially associated with a case in Hamilton, NJ confirmed as being infected with anthrax. This case, specifically about suspected anthrax (Bacillus anthracis), indicates the influence of prior events related to post 9/11 anthrax-related deaths on people's reactions, particularly postal workers, the need to divide audiences ("communication triage"), the critical importance of communicating uncertainties in sampling, and other aspects of communication.

Reference: Chess, C., J. Calia, and K. M. O'Neill. 2004. Communication triage: An anthrax case-study. Biosecurity and Bioterrorism 2, 106-111.

2. Reported March 2005. Washington, DC. Actions precipitated by an accidental false negative from a testing error.

This is an account about anthrax and risk (mis)communication – its costs and consequences, and acting on an accidental false negative. A sampling mixup "rattled the stock market, set the White House on alert, shut three post offices in the Washington area and led to more than 800 people being offered antibiotics"

Reference: Scott Shane, "Anthrax Scare Is Attributed to a Testing Error," The New York Times, March 16, 2005. http://www.nytimes.com/2005/03/16/politics/16anthrax.html

3.Reported March 2005. Glenshaw, PA. Actions from an intentional false negative.

State legislator falsely accuses a political adversary of putting anthrax in his mail, setting off an investigation.

Reference: The Associated Press, "Lawmaker Charged in an Anthrax Scare," The New York Times, March 31, 2005. http://www.nytimes.com/2005/03/31/national/31penn.html

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Ingleby, T. V. et al. (2002) "Anthrax as a Biological Weapon, 2002," *JAMA*, 287, pp. 236-252.

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Sunstein, C. (2003) "Terrorism and Probability Neglect" *Journal of Risk and Uncertainty*, Vol. 26, No. 2-3, pp. 121-136.

VI. Dr. Vicki Bier, 4/7/09 comments

I have some substantive comments on risk communication:

The advice given on risk communication is extremely generic, and could apply to almost any hazard. Surely, after the anthrax attacks of 2001, we know more about risk communication for anthrax IN PARTICULAR.

For example, many people clearly have an incorrect mental model that anthrax is contagious. This causes much higher levels of fear than may be justified by a particular event. After all, if a disease is highly contagious (like smallpox, for example), then even five cases might be enough to start a major epidemic. For diseases like anthrax, which are not spread primarily by infectious contact with sick people, the chance of starting an epidemic is much less; people should be worried less about current infections spreading, and more about whether additional attacks are credible. It would seem like a reasonable minimum standard to expect that guidance on risk communication for anthrax should include that information, and some field-tested communication materials on how to overcome the flawed mental models.

For a more challenging problem, consider the following. In 2001, many people around the country had what turned out in retrospect (and realistically were probably knowable even at the time) to be excessive levels of concern, as judged by the number of people around the country who called emergency-response teams for relatively innocuous packages or white powders. At the same time, the postal workers in D.C. received false reassurances that they were at low risk; two died as a result. Are there ways to avoid this imbalance of concern?

Perhaps it's too much to expect that we could SIMULTANEOUSLY reduce excessive concern among people at low risk, and ALSO increase levels of concern about people at higher risk; that would be a tough challenge. However, can't we at least provide guidance to reduce the risk of giving out false reassurances? For example, might there have been a subconscious class bias at work among the epidemiologists and risk communicators (reassuring postal workers that they were not at high risk, because they weren't prominent enough to be targets of intentional anthrax attacks)? Are there ways to at least reduce overconfidence about judgments of reassurance (e.g., telling people that "We think you are not at risk, but if you still want to take protective measures, here are some steps that can't hurt, and might be helpful")? The answers to some of these questions might not be known yet, but are they researchable at a realistic level of effort? Given that we had two deaths basically due to failures of risk communication, this would seem to be a reasonable goal.

VII. Dr. David Ensor, 4/17/09 comments

My comments are general impressions at this point.

Unfortunately, in the defense and security world we don't have the luxury to select the mode of attack.

It would be helpful to the HSAC to know if other assistance documents have been or are being developed for other biological agents. There is always the possibility that the material may be a biological agent, but not anthrax. Much of the guidance might be similar for other biological agents, in particular on how to manage the situation. However if no other guidance is available on other biological agents it might be useful for the document to offer comments to provide insights for broader application.

Section 4.1 is based solely on the assumption that agent will be delivered as a package. It is probably the most popular method and the precedent set in the cases after 911. Perhaps, the document should sensitize those responsible for security of the possibility that other delivery methods are possible and offer/reference some tips for detection. The mode of attack in an indoor space will affect the spatial distribution of agent.

Finally, a document of this size and with the possibility of use under stressful conditions should have a keyword index to allow rapid search.

VIII. Dr. Daniel C. Walsh, 4/17/09 comments

Purpose of document

Page 4 of the charge says BA-TAD will be a technical resource document. Charge question 1 says it will be a technical assistance document and not a resource document. The exact usage of the document is not clear. Review against the document purpose without a clear statement of its function is incomplete.

There are remarkable new capabilities for reference documents like the BA-TAD. Given the almost unparalleled value of this document under stressful field conditions, I exhort EPA to consider use of the most advanced and cutting edge forms of document design to enable the greatest function by the user.

What is good about document that should be carried over to next redraft:

- Interactive elements such as links to web based documents were very useful and should be expanded
- the bulleted and detailed treatment of incident response action presented in the appendix. Reads like a 1980s document but can be modified to be more interactive with more links and possibly bubble information
  inclusion of phone number for access to federal agency support (pg 13) provides for immediate use
- inclusion of local health professionals on the UC
- template for preparing anthrax HASP: great! This approach should be used more in the revised document. Templates and boilerplates provide more direct value in actual incident response.
- linkage to URLs
- the delivery of information in the appendix appears to be more usable for responders than the content of the main text. Perhaps consider use of approach in main text.

What may be valuable to include

- more interactive document design using more advanced virtual technology enabling users in field conditions to enable a 'look up' of information needed
- capability to follow information down second or third tier information paths using a virtual capability
- search capability in an interactive mode
- use of phone numbers for critical contact are valuable within text. However, all relevant phone numbers and other pertinent information should be coupled and printed together elsewhere in the report (appendix). A directory of such contact information for critical emergency response information providers would be valuable.

1. The current report only addresses conventional attack scenario: a discrete release in a controlled environment in a reasonably controlled manner. Complex conjunctive attacks need to be considered and addressed in the CA-TAD revision. Current document essentially 'looks back' at past known events but does not consider innovative forms of attack that could represent the next generation of attack. That new approaches will be used is the only clear pattern of past attacks.

2. Linkage of conventional attack, such as a blast, with anthrax release mechanisms should be considered. Response to anthrax risk conjoined with large scale debris management in an open space environment presents real response difficulty. In the early stage of WTC response, rumors of anthrax mixed in the debris pile caused a short but strong reaction. Such response work would have been extremely difficult if a conjunctive attack had been utilized.

3. Consideration of conjunctive attacks that include conventional attack modes with release of anthrax.

4. The document needs to reach beyond the limited EPA response focus. EPA may be the lead under many response scenarios but there are cases, particularly in large cities where local resources are available and political will calls for local control.

5. A more user compatible format to enable advice to be "pulled out" would be valuable.

6. The report recognizes the complexity of the confluence of environmental and public health management performed in the context of a crime scene investigation. However, the document itself does not elaborate beyond this statement. The redraft should consider the ramifications of such an endeavor. Efforts to minimize a public health threat may tamper with evidence in the crime scene and thus be halted by FBI. Such issues were encountered in the early stages of WTC response.

7. The difference in presentation of anthrax threats and response in this document compared to that for anthrax in earlier documents reviewed by the committee is substantial. The anthrax threat to water supply posed specifically challenging identification and consequence management scenarios. The revised document should address these identification, testing and response to water supply threat scenarios, or other wise refer to existing documents that provide such information.

8. Reported state level issues include environmental impacts, permits, worker safety, transportation, impacts on public health (pg 22). State level issue for state (pg 22) can be expanded to include issues like disposal

9. The list of local level responsibilities is simplistic for the most likely attack scenario. Listed local level responsibility includes traffic control, public treatment facilities, utilities, building codes and permits. Most likely attack scenarios are larger cities where the impact will be greatest. Most large cities have much greater response capability (many have built this capability since WTC) and may insist on a more advanced response role. Many cities have larger

governments and consequent resources than many states. There seems to be little appetite for response scenarios that do not include federal government as the lead agency.

10. The report seems to be limited to only the simplest attack scenario (a mail attack). The redraft should be more creative in anticipating attack scenarios.

11. The report only generally addresses the immediate response of people in the affected area and suggests that they "leave the area" (pg 24). Some past reports reviewed by the committee note that affected parties should be kept in the release location to minimize spread of anthrax. Others suggest immediate evacuation. This should be addressed directly.

12. The report indicates that local emergency responders are typically 'fire departments.' This may be the case for small cities and towns but not for large cities where attacks may be most likely. Many cities now have hazmat teams and sophisticated response capability. Consequently, the revised report should consider the value that may be brought to the work of these advanced, non-federal response teams.

13. Suggest an anthrax certification program for sampling including establishing minimum standards.

14. Document states that it "may be necessary to expand HASP to protect community." (Pg 28). There should always be a Community Air Monitoring Plan.

15. Overly simplistic in incident prediction. There seems to be a disconnect with earlier documents. More imagination needs to be applied to consider the threat scenarios that the document's user may encounter.

16. Actual consequence management and cleanup and disposal are given less treatment here, similar to other reports reviewed by the committee. Expansion of treatment for back end work is valuable to improve use of document.

17. Should there be more information for the health practitioner overseeing monitoring? I think so (pg 34)

18. Report reads at times like a general textbook with very general treatment of subject matter. The report makes statements like "consideration should be given to the cost of transporting material and the potential for spreading contamination." This is overly simplistic and has virtually no value in its present form (pg 68). This is common in the document. The redraft should consider all statements from a user perspective and envision use in an emergency response scenario, and build content accordingly.

19. Not clear if there are methods to effectively detect anthrax in a complex medium, such as those that might be posed by extensive amounts of debris in a conjunctive attack.

20. The report stays very general. For instance: "if needed a higher level of isolation can be achieved with negative air pressure" is there no criteria to aid in making this determination? Shouldn't this criteria be identified in the report so it can be used? (pg 70)

21. Use of the document is not clear; as a text it provides general advice. As an immediate use document, it seems fall short of providing high value to real time users.

22. Process diagram may be helpful to describe process (example Pg 78).

23. More virtual linkage with reference material is useful as a reference document

24. Some areas with extra detail provide very good, detailed instruction. For example, on page 79 the advice for shipping waste; useful details shown here. This should be accentuated in the revision. Other areas only have vague and general references (more common).

25. Pg 80 refers to best management practices onsite; what are they? They BMPs should be fully defined. Perhaps a listing of all BMPs may be a useful form of an appendix.

26. In Appendix A, on discovery of an anthrax incident, there is no description of what the people in the room should do? Do they leave or stay?

27. Suggest the next version of the document be a crisper use manual for first response. Good info needs better user interface.

Charge Document

28. For response action technical assistance, breakdown of the event by actual steps is recommended. The more steps that are identified the more clarity of the presentation fin the document and the easier for FOSC to search for needed information.

29. Issues of scale of response action must be addressed. This is most critical for large scale and conjunctive attacks. Scale effects can include draw of a larger catchment of response workers, including many that do not have appropriate training for job at hand, and those not accustomed to using the proper protective equipment, and not inclined to do so. These effects need to be addressed.

30. There are major difficulties associated with large scale event that occur outdoors, particularly those with infrastructure damage and large debris fields. These should be examined. These include societal factors, such as inability to control response frontier and the strong desire to get the affected area back into normal use.

IX. Dr. Lynda Knobeloch, 4/16/09 comments

Charge Question #1: Given the intent that the BA-TAD serves as a technical assistance versus technical methodology or resource document, what tools and strategies should be addressed in preparing the FOSC to successfully manage and oversee the components of a response (i.e., characterization, decontamination, disposal, and clearance) to an intentional indoor release of *B. anthracis* in industrial, commercial and residential buildings?

Reviewer comments: Although the federal coordinators will likely not have primary responsibility for conducting a criminal investigation of an intentional release of anthrax, he/she must be knowledgeable regarding this aspect of the government's response since preservation of the crime scene, timely securing of on- and off-site evidence, and interviewing of possible witnesses and suspects are all essential if the perpetrators are to be identified and prosecuted. Increased screening of people leaving the area may also be necessary. The ability to do this will require almost immediate sharing of information with the appropriate federal and local law authorities. The TAD should address these aspects of the initial response to an event.

Other elements I would anticipate seeing in the TAD include:

Strategies for securing and evacuating the building(s) involved.

Criteria for determining the need to evacuate
At what point is this done?
When is a threat of contamination deemed credible?
Who will be evacuated?
How will the building be secured during the investigation and clean-up?
Who can have access to the building during the investigation.
A log of everyone in the building at time 0 and throughout the sampling and clean-up period should be kept with contact information.

Sampling protocols should be discussed including the following topic areas:
Statistically valid sampling techniques
The most time and cost effective sampling methods and tools
If real time monitoring methods, if available.
Guidelines for the number of air, dust and/or wipe samples needed for building(s) of different sizes.
Guidelines for the establishment of contamination versus safe zones
A listing of approved laboratories with addresses and phone numbers
PPE or prophylactic medications for workers involved in sampling and clean-up

Appropriate decontamination methods should be described including:
The most effective decontamination methods for an indoor environment
The process of disposing of contaminated furnishings, floor coverings, etc.
Post-decontamination sampling protocols
Criteria for re-entry

Communication protocols should be described including how to prepare for and conduct:
- Briefings with local and federal officials
- Press interviews
- Communication with the affected community
- Appropriate use of cell phones and electronic communications
- Clearance of sensitive information that could impact criminal investigation

Charge Question #2: Given the intent that the BA-TAD serves as a technical assistance versus technical methodology or resource document, what tools and strategies should be addressed in preparing the FOSC to successfully manage and oversee the components of a response (i.e., characterization, decontamination, disposal, and clearance) to an intentional outdoor or **wide-area** release of *B. anthracis?*

Reviewer comments: See above comments some of which apply to both indoor and outdoor releases. Since containment, confirmation, and investigation of a suspected outdoor release of B. anthracis spores are inherently very difficult, and because these events pose a unique threat to the general public, it is essential that the TAD provides FOSCs with a detailed and rigorous protocol for responding to these events. The TAD should provide guidance on criteria for evacuation and rapid establishment of safe and unsafe zones. In addition, the TAD should describe statistically rigorous sampling protocols, a listing of approved laboratories, and sample shipping methods.

Elements I would anticipate seeing in the TAD include:

Threat Characterization and Analysis
- Protocol for assessing a threat or report of anthrax contamination
- How is the threat verified or discounted?

Securing and evacuating the area
- Methods used to secure the site should be defined.
- If a large area, such an open shopping area or amusement park needs to be secured, how is this accomplished? How is the perimeter defined?
- What type of evidence is needed to enforce an evacuation?
- How will an evacuation be carried out and enforced?
- Who should be evacuated?
- What agency will enforce the evacuation?
- Where should evacuees go if they cannot return to their homes?
- What are the criteria for declaring the area safe?
- Re-entry criteria should be defined in the TAD.
- Who enforces an evacuation?

Sampling
- Protocol for statistically valid sampling should be defined?
- Can real time monitoring be done?
- What sampling tools are appropriate?
- How many air, soil and wipe samples are needed?
- A listing of approved labs should be provided.

Can samples be combined to reduce cost and time?
PPE/prophylaxis for clean-up workers should be explained in the TAD.

Decontamination strategies and tools.

The TAD should provide guidance on the appropriateness of decontaminating prior to sampling or before sample analysis can be completed. If possible, the TAD should identify the most effective decontamination methods and tools for a variety of outdoor settings and media.

Prevention of offsite transport of BA spores should be discussed.

Can vehicles or personal items leave the site without being decontaminated?

Disposal methods for contaminated solid and liquid waste should be discussed, including:

Where does the waste go?
What treatment, packaging and labeling is needed prior to disposal?

Communication protocols should be described including how to prepare for briefings with local and federal officials, press interviews, business owners, and meetings with the affected community. The appropriate use of cell phones and electronic communications should be discussed as well as the process of protecting sensitive information that could compromise a criminal investigation.

Charge Question #3: Are there worker health and safety issues, particular to *B. anthracis*, this document should address?

Reviewer comments: Because of its ability to persist in the environment for long periods of time and cause serious, life-threatening infections, anthrax contamination poses a unique threat to the safety of workers. As we learned from the 2001 event, government office workers and mail carriers died as a result of our inability to identify contamination in their work places and prevent them from being exposed to bacillus spores; or to identify them as 'at risk' and provide them with PPE and/or prophylactic antibiotics or vaccines. The TAD should provide FOSCs with guidelines they can use to protect and track people who work in areas of suspected or confirmed contamination and ensure their protection. In addition to decontamination of the workplace, worker protection can be accomplished using a combination of strategies including re-assignment of non-essential workers to an alternative workplace, the use of PPE and prophylactic medications by essential workers such as those involved with the investigation and clean up, and the use of medical surveillance and screenings to ensure rapid diagnosis and treatment of infections.

Charge Question #4: For critical infrastructures or wide-area locations, a "zero-culturable-spore" decontamination goal may not be achievable. What are possible cleanup strategies for minimizing risk to facilitate re-occupancy in industrial, commercial and residential buildings where a "zero-culturable-spore" decontamination goal was not achieved?

Reviewer comments: In cases where clean-up cannot provide 'zero culturable spore' conditions, sealants and air filtration can help to prevent re-suspension of spores. Hard surface floors, for example, can be coated with urethane to encapsulate spores and foam caulking products can be used to seal cracks and crevices. HEPA vacuums can be used to clean soft surfaces. Furnishings, floor coverings, and electronic devices that cannot be decontaminated should be replaced. Repeated treatments with chlorine dioxide, radiation, or other approved disinfectants should be done to reduce the spore counts to background levels.

Charge Question #5: The FOSC would, in a *B. anthracis* event, be functioning within the Incident Command System which typically includes a centralized communication structure with specific roles and responsibilities. The BA-TAD will address the key issues pertinent to the cleanup of environmental contamination with *B. anthracis*.

- What recommendations does the SAB-HSAC have for scientifically-sound communications to be included in the BA-TAD?
- More specifically, for the purposes of the BA-TAD, what recommendations does the SAB-HSAC have for the content of these communications?

Reviewer comment: The BA-TAD should prepare FOSCs to share as much factual information as they have with the exception of sensitive information that is critical to a criminal investigation or prosecution. The public and media can be expected to ask the typical Who, What, Where, Why and When questions. In addition, they will want to know about risks to the environment, general public, and workers and about the outcome of any testing that has been completed. They may also have questions about disruptions of their daily activities. The BA-TAD should help FOSCs prepare for such questions and prevent factual errors and vague or misleading statements. In addition, the TAD should specify types of information that could compromise a criminal investigation since that information may need clearance before its release. The TAD might provide templates for fact sheets that could quickly be amended for specific situations. Separate fact sheets for medical responders and the general public may be helpful.

X. Dr. Baruch Fischhoff, 4/17/09 comments

I thought that there might be some interest in the attached plan, reflecting how another agency is addressing a related problem. It will be discussed at the meeting described in the second attachment. I have asked Ed to make it available at the website for our meeting.

See Attached FDA Strategic Plan, and FDA meeting agenda

XI. Dr. Christina Egan, 4/20/09 comments

Attached please find some comments on Charge Question 4. I will also have additional comments that I will present at the April 21st and 22nd meeting.

Charge Question #4

What are possible cleanup strategies for minimizing risk to facilitate re-occupancy in industrial, commercial and residential buildings where a zero-culturable- spore decontamination goal was not achieved?

Reviewer comment:

The clean-up strategies that are used must include a carefully design risk assessment and analysis. This is critical for re-occupancy of any area. It must include an analysis of the population that will be occupying the space. For example, if the area to be considered is a critical infrastructure site, such as a health-care setting, the clean-up strategy would have to differ significantly than a strategy used in an industrial setting or outdoor setting due to the population of immuno-comprimised individuals that could have significantly greater health risk than the average population. A detailed discussion of the components of performing this risk analysis should be included in the TAD.

In addition, clean-up strategies for the most likely scenarios as described in http://www.osha.gov/SLTC/etools/anthrax/response.html should be included in the TAD (Localized exposure to a white powder (such as a contaminated letter or package sent through the mail; Contamination of a closed air supply (such as the ventilation system of a building; Broad contamination of outdoor air (such as release of anthrax spores via a crop duster or similar aircraft; and Contamination of a commercial food or beverage source (which would cause gastrointestinal or oropharyngeal disease)). The TAD does not need to contain specific details, but a discussion of the important considerations for each type of scenario should be included as the focus of this document has broadened from just an indoor release.

Since 2001 there has been significant advances in research involving various methods of decontamination that poses less health risk and is non-destructive when certain methods. Some of the 2001 anthrax contaminated buildings and areas have been utilized in this research. One method that has been successfully used in research laboratories working with anthrax and other highly infectious pathogens has been studied for use outside the laboratory. EPA first reviewed data related to the safety and effectiveness of using paraformaldehyde for inactivation of *Bacillus anthracis* spores in relation to a request by the U.S. Department of Justice (DOJ) to decontaminate a large mail sorting and stamping device located at its mailroom in Landover, MD. Available data indicated that paraformaldehyde would reduce bacterial spore populations under specific conditions including concentration, pH, and contact time. EPA determined that the product could be used safely and effectively, and that no unreasonable adverse effects would occur from the requested uses (http://www.epa.gov/pesticides/factsheets/chemicals/paraformaldehyde_factsheet.htm.) On February 14, 2002, EPA also issued a crisis exemption to allow the U.S. Department of State (DOS) to treat up to 200,000 diplomatic mail pouches with paraformaldehyde, subject similar conditions as the DOJ crisis exemption. The use of this product as a clean-up strategy should be included in the TAD.
http://www.epa.gov/pesticides/factsheets/chemicals/paraformaldehyde_factsheet.htm

The EPA also granted to 2 crisis exemptions under FIFRA for use of vapor hydrogen peroxide in decontamination of a mail facility in VA in 2003 and a building in the Naval Yard in Washington D.C. in 2002. **EPA (Environmental Protection Agency).** Pesticides: Topical and chemical fact sheets: vaporized hydrogen peroxide. 2006 Nov 26. Hydrogen peroxide based products such as Oxonia Active (EPA Registration Number 1677-129), KX-6049 (EPA Registration Number 1677-158), Actril Cold Sterilant (EPA Registration Number 52252-7), and Spor-Klenz Ready to Use (EPA Registration Number 52252-7-1043 have been issued exemptions for use. EPA also issued a crisis exemption for the unregistered product Virex STF, which contains only hydrogen peroxide. These products have been utilized in the medical community for sterilization of surgical instruments with success and have data to show that some of these products may be beneficial in residential, commercial and industrial settings, especially in areas containing critical infrastructure.

EPA issued two crisis exemptions (February 14, 2002 and February 27, 2003) to the University of Florida and Cobra Termite Control for the limited sale, distribution, and use of methyl bromide. http://www.epa.gov/pesticides/factsheets/chemicals/methylbromide_factsheet.htm. The data for these studies helped demonstrate the efficacy of methyl bromide in inactivating surrogate bacillus anthracis spores during structural fumigation. Although further research is needed to address other issues such as how to reduce and remove methyl bromide after fumigation the use of this decontaminant should be included in the BA-TAD.

The current thoughts on a acceptable level of decontamination of *Bacillus anthracis* spores has been greatly debated, but the standard of practice that has been utilized is a zero-culturable spore or no spores present in an environment. Clean-up strategies for re-occupation of sites that are going to move away from this practice or policy of zero-culturable spore levels should be also be included for discussion. The use of a zero-spore level has lead to hugely expensive clean-up operations that are cost prohibitive. In recent cases in CT and NY in which low level contamination was observed as a result of processing animal hides for drum making, residential and industrial spaces were decontaminated as well as an automobile, in the case of the NY inhalational anthrax case. In these settings, especially sites that are not in urban setting could utilize an acceptable level of reduction in spore number in order to avoid destruction of personal items etc. The concept of using a decrease in spore number or activity rather than the zero-culturable-spore level is appropriate for certain settings and is utilized for various other EPA classified pests. When evaluating the efficacy of decontaminants for prions, a decrease in prion activity is used rather than a zero-level of activity as measured by infectivity studies.

This charge question is a difficult one. The use of appropriate clean-up strategies is dependent on individual circumstances surrounding each event and must be done in consultation with appropriate local, state, and federal agencies. It would be helpful in developing a comprehensive response to this question to review the new draft chapter that was mentioned in the white paper which is devoted to clean-up strategies. I look forward to reviewing the draft of the new document to comment on the additional chapters added for clean-up strategies.

(a) Identify the professionals who will be primarily concerned with how well that charge question is answered and the individuals whose welfare those professionals are entrusted with serving.
While the focus of this document is to serve as a resource tool for the Federal On-Scene Coordinators (FSOCs), a number of other professionals will be concerned with the resulting document. They include public health epidemiologists and laboratorians, environmental health personnel, first responders, health care personnel, all of which will be involved in developing an appropriate strategy for decontamination. In addition, the general public will also be effected by the response developed to this question.

(b) Identify any major gaps in the issues that the draft TAD addresses, in terms of providing the information and resources needed by these professionals and those whom they serve.
It is difficult to determine the major gaps that are missing without a thorough review of the most current working version TAD. Since this document has undergone a significant in focus, the target audience, each chapter must be carefully redesigned for that purpose. Is there going to be an additional document for other groups involved in a response to anthrax contamination? The white paper details several important changes or revisions that seem to be very appropriate. However, the document does not comment on how the FSOC will interact with the various agencies. For example, there is a review of potential federal agencies that will be involved in a response to an anthrax release, but does detail how the FSOC will interact will local and state partners or a discussion of pre-planning or communication with these entities pre-event.
I will also include some gaps in the TAD at the April 21-22 meeting.

Additional References:
Phillip N. Price*, Michael D. Sohn, Kristina S.H LaCommare and Jennifer A. McWilliams. Framework for Evaluating Anthrax Risk in Buildings. *Environ. Sci. Technol.*, 2009, 43 (6), pp 1783–1787

http://www.epa.gov/pesticides/factsheets/chemicals/paraformaldehyde_factsheet.htm

XI. Dr. James Rogers, 4/20/09 comments

Chapter 4.1
The early sections focus on letters/packages as the delivery vehicle, and that is understandable. However, there should be direction as to how to handle different types of delivery methods, or references to information on these (What about water, food, spills, environmental contamination), especially since other types of materials that can be intentionally contaminated or involved in an incident are referred to later in the document.
I would think that the sequestering of those exposed should occur very early in the process (not wait until 4.6). That way you control their movement, reduce possible subsequent exposure and can treat all at once. And I might have missed it, but what about a decon line for exposed personnel?

Chapter 4.2

Most facilities have an evac plan in place, so it may be best to let the building security handle this. Also, shouldn't restricting access and shutting down HVAC, etc., occur here?

Chapter 6.1

This reads as though the sampling of the "package" would always occur onsite. My experience suggests that, once an all clear on whether there were explosives have been detected, the package would be transported to some high containment facility for examination and evidence collection.

Chapter 6.2.6

Is it really possible to decon 100%? Also, there are studies regarding equivalence between commercial spore strips and B.a. regarding decontamination. May want to specify something here.

Chapter 6.4.1

I believe that there are a number of studies completed regarding the utility of smart tickets. And sample prep of environmental samples for PCR. May need to review and change this section. Same with 6.4.2.

Chapter 6.4.4

LRN labs have been supplemented with the FERN labs for food testing. Are there any for water and environmental testing? DoD/Army/Aberdeen Proving Grounds does some of this. We may want a listing of labs that can do the testing and what type, in addition to LRN. The labs would certainly appreciate an early call out to determine sample capacity so that they could prepare or redirect/defer.

ATTACHMENT TO DR. LIOY'S COMMENTS

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Mechanistic Modeling of Emergency Events: Assessing the Impact of Hypothetical Releases of Anthrax

S. S. Isukapalli,[1]* P. J. Lioy,[1] and P. G. Georgopoulos[1]

A modular system for source-to-dose-to-effect modeling analysis has been developed based on the modeling environment for total risk studies (MENTOR),[1] and applied to study the impacts of hypothetical atmospheric releases of anthrax spores. The system, MENTOR-2E (MENTOR for Emergency Events), provides mechanistically consistent analysis of inhalation exposures for various release scenarios, while allowing consideration of specific susceptible subpopulations (such as the elderly) at the resolution of individual census tracts. The MENTOR-2E application presented here includes atmospheric dispersion modeling, statistically representative samples of individuals along with corresponding activity patterns, and population-based dosimetry modeling that accounts for activity and physiological variability. Two hypothetical release scenarios were simulated: a 100 g release of weaponized *B. anthracis* over a period of (a) one hour and (b) 10 hours, and the impact of these releases on population in the State of New Jersey was studied. Results were compared with those from simplified modeling of population dynamics (location, activities, etc.), and atmospheric dispersion of anthrax spores. The comparisons showed that in the two release scenarios simulated, each major approximation resulted in an overestimation of the number of probable infections by a factor of 5 to 10; these overestimations can have significant public health implications when preparing for and responding effectively to an actual release. This is in addition to uncertainties in dose-response modeling, which result in an additional factor of 5 to 10 variation in estimated casualties. The MENTOR-2E system has been developed in a modular fashion so that improvements in individual modules can be readily made without impacting the other modules, and provides a first step toward the development of models that can be used in supporting real-time decision making.

KEY WORDS: Anthrax spores; dose; emergency events; exposure; MENTOR; modeling; risk

1. INTRODUCTION

During the *B. anthracis* attacks on the U.S. postal system in the fall of 2001, six letters, each containing 1 to 2 g of anthrax spores, caused anthrax infections in 22 individuals, and resulted in five deaths,[2] despite aggressive treatment and care.[3] In addition to the human cost, the economic costs of the *B. anthracis* attacks were significant. U.S. postal facilities contaminated by *B. anthracis* required more than two years of decontamination at a cost of more than $200 million.[4] Understandably, concerns have been expressed that small amounts of powdered *B. anthracis* inserted into the air intakes of subways, airports, shopping malls, sports arenas, and other public complexes could be devastating,[5] with long-term consequences potentially posing greater challenges than the short-term impact.[6]

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Several studies have attempted to quantify the overall impact of large-scale releases of *B. anthracis*: concluding (a) an aircraft release of 50 kg of *B. anthracis* over an urban area would result in tens to hundreds of thousands of deaths,[7] (b) an airborne release of 100 kg of *B. anthracis* upwind of Washington, DC, would result in 130,000 to 3 million deaths,[8] and (c) 1.49 million people out of 11.5 million people (13.1%) would be infected downwind from a point of release of 1 kg of *B. anthracis*.[9] The economic costs were estimated to reach over $26 billion per 100,000 people exposed,[10] not including the cost of decontamination. However, unlike nuclear weapons, the consequences of *B. anthracis* attacks can be mitigated.[5]

Though the consequences of a bioterrorism event are often enormous, it is prudent to not overestimate their impact,[11] as the scenario may appear unmanageable to responding agencies, leaving both the public and responders feeling helpless. Proper planning based on more complete interpretation and evaluation of available knowledge and experience can reduce public anxiety as well as increase confidence on behalf of the professionals responding to an adverse event.[12]

Planning and responding to a bioterrorism event, including vaccinations and postexposure prophylaxis, is a challenging task. Vaccines for anthrax exist,[13,14] but in practice several obstacles are present in the form of potential adverse effects,[15,16] lengthy dose regimen requirements,[17] and widely varying perceptions of risk.[18] Furthermore, vaccination of the majority of populations in large urban areas would be impractical due to limited availability of prophylactics, and the costs associated with procuring and handling large supplies.

1.1. Planning for Emergency Response

Several public health issues need to be addressed in planning and responding to emergency events.[19,20] While postattack response to bioterrorism is vital, preattack measures, such as detection, planning, and training, are just as important.[5] Spatial and temporal patterns of detected levels of biological agents can be combined with diagnostic modeling methods and real-time meteorological data to estimate release source strength and location and, consequently, high impact areas. This in turn will allow targeted emergency response planning, including targeted prophylaxis administration in high impact areas, because timely initiation of treatment is a critical factor.[21,22] As a first step toward rapid detection and response to bioterrorism, a national monitoring network in the United States, called BioWatch, has been set up.[23,24] It is being expanded to detect the presence of a number of airborne biological agents, including anthrax spores; however, currently the results are not available in real time. Recent modeling efforts have also focused on evaluating response based on syndromic surveillance and on prioritizing threats.[25–27]

After the anthrax attacks in the United States in 2001, several modeling studies focused on estimating effects of *B. anthracis* releases, with varying levels of model detail and scale. Reshetin and Regens[28] modeled the release of *B. anthracis* inside a 50-story building. Webb and Blaser[29] modeled the transmission of *B. anthracis* through cross-contamination of postal letters, whereas Ho and Duncan[30] modeled the aerosol hazards from a letter containing anthrax spores. Fowler *et al.*[31] performed a probabilistic comparison of vaccination and antibiotic prophylaxis based on probabilities of exposure. Wein *et al.*[9] and Craft *et al.*[32] performed detailed modeling analyses linking *B. anthracis* dispersion over large areas with infection and disease progression mechanism, hospital response logistics, and corresponding outcomes. More recent efforts include Biowar,[33,34] an agent-based model of bioattacks that links simple dispersion models with models for social networks and behavioral attributes such as health-care-seeking behaviors and pharmaceutical purchases.

One of the limitations of existing *B. anthracis* modeling studies is that they have employed substantial simplifying assumptions. For example, Craft *et al.*[32] assumed uniform population density over a large area, uniform population demographics, Gaussian dispersion with uniform wind speed and direction, constant inhalation rates for all individuals, and personal exposure concentrations being the same as outdoor concentrations. The rationale for such simplifying assumptions is that the equations become mathematically tractable and result in analytical solutions. However, such simplifications limit the model applicability to only a small set of potential scenarios and conditions and minor changes in modeling assumptions may require rewriting underlying model equations.

2. APPROACH

This study presents a prototype modeling system for performing source-to-dose-to-effect analysis

of inhalation anthrax infections from airborne weaponized anthrax spore releases. The main principle guiding the development of the present system is that prioritized exposure analysis[35,36] should be conducted in order to minimize misclassification of exposure. Consistent quantification of exposures and doses for different release scenarios, as well as for different emergency response strategies, provides a sound scientific basis for developing and then implementing plans for response strategies. The main objective of this system is to utilize available databases of distributions of demographics, human activity patterns, etc., and to provide sufficient flexibility so that this system can be useful in planning multiple emergency response scenarios for training purposes and for rapid decision making in the aftermath of emergency events.

A modular, mechanistic framework that links available models and databases for characterizing exposures and adverse impacts would improve risk assessment in terms of (a) providing consistency, (b) allowing assessments on multiple scales, and incorporating the important processes from release source to dose received by individuals, (c) optimizing the use of the most up-to-date models and databases for individual processes, and (d) allowing systematic sensitivity and uncertainty analyses to identify the important factors that affect the outcomes the most. The underlying person-oriented exposure modeling approach has been utilized and evaluated in the past for different types of contaminants.[37,38]

2.1. Important Factors Influencing the Impact of *B. anthracis* Releases

There are several factors that influence inhalation exposures and doses of *B. anthracis* to humans from airborne releases.

2.1.1. Release Source(s)

The magnitude, location of source(s), and patterns of release are the primary factors and major unknowns in performing dispersion modeling for emergency events. An attack scenario can include single or multiple sources (differing in location or time), with anthrax spores released quickly ("instantaneous") or slowly over time ("continuous"). These are required as initial inputs to the exposure and dose modeling analysis.

2.1.2. Meteorological Conditions and Topography/Terrain

The meteorological conditions and local topography (rural, urban, etc.) influence the extent of dispersion of anthrax spores and, thus, the overall impact of a release. These include variables such as wind speed, direction, temperature, atmospheric stability, boundary layer thickness, surface topography, surface roughness, land use, etc.,[39,40] which can together contribute to over a factor of 20 variation in potential casualties.[8]

2.1.3. Population Distributions

The distribution of population in the areas affected by the releases ("downwind locations") determines the intensity and spread of exposure and potential infections. This is a highly variable and often ignored factor, in the sense that the population distribution changes in time (e.g., commuting to major urban centers or large gatherings at major events). However, it is manageable to an extent, for example, through evacuation of people from downwind locations or enforcing shelter-in-place.

2.1.4. Human Activity Patterns

The location of the individual at any given time (e.g., outdoors versus indoors), and the activity performed (e.g., running versus sleeping or resting), determine the exposure concentrations, the breathing rates, the efficiency of particle uptake, and thus the number of inhaled anthrax spores. These factors are also important in characterizing the potential contact or lack of contact with a contaminant. However, they are often overlooked or poorly characterized in emergency event analyses.[9,28,29,31,32,41]

2.1.5. Physiological Characteristics of Individuals

The base inhalation rates are dependent on the age, gender, and physical characteristics such as body weight and life style patterns. Furthermore, the infection potential of *B. anthracis* is dependent on the age of the individual.[29,32]

Other factors that are important in determining exposures are socioeconomic attributes, such as housing characteristics (age, size, ventilation, etc.), which determine the fraction of outdoor *B. anthracis* that gets entrained indoors.

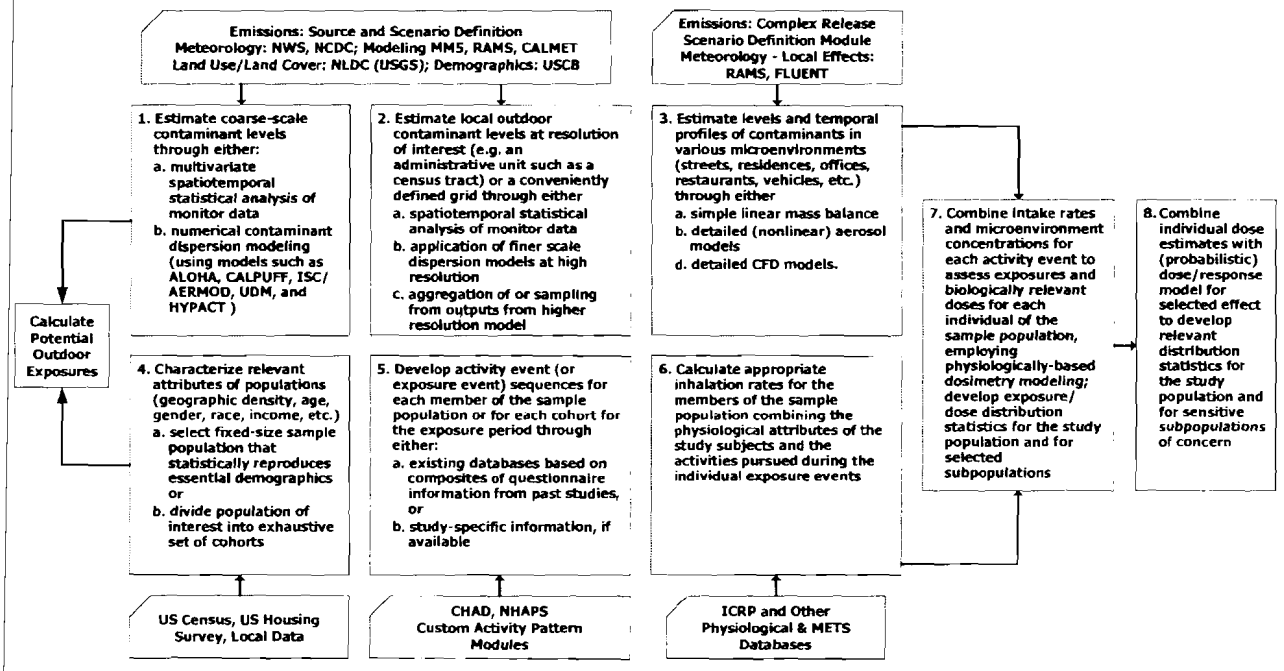

Fig. 1. A generalized eight-step flowchart describing the processes involved in assessing risk using a source-to-dose-to-effect framework, adapted from Georgopoulos *et al.*[37] this is also referred to as person-oriented population-based exposure modeling (POM/PBEM). This flowchart reflects the structure of the MENTOR approach and provides a general "template" for comparing the application of risk assessment systems. A subset of the models appearing in this flowchart has been used in this study.

2.2. Steps and Resources in the Estimation of Exposures, Doses, and Infections

Based on the approach introduced by Georgopoulos *et al.*,[37] several modeling steps (or components, as some of them do not have to be performed in sequence) are needed in assessing the impacts of airborne releases of *B. anthracis*. In general, the following eight steps are needed, as shown in Fig. 1:

1. Estimation of outdoor concentration levels of airborne anthrax spores through one of the following:
   a. Spatiotemporal analysis of available data. This can involve interpolation of detection data from monitors such as the BioWatch monitoring network[23,24] using statistical techniques such as SpatioTemporal Random Field (STRF)[42] and Bayesian Maximum Entropy (BME).[43]
   b. Numerical modeling of the atmospheric dispersion of *B. anthracis*. This involves application of atmospheric dispersion models such as California Puff Model (CALPUFF),[44] Hazard Prediction and Assessment Capability (HPAC),[45] or Hybrid Particle and Concentration Transport (HYPACT).[46] These models use dynamic meteorological profiles as inputs (either user-provided or from meteorological data sources) and provide contaminant concentration profiles at different spatial and temporal resolutions. Dispersion modeling at finer scales, for example, within a building or within the vicinity of the release location, can be accomplished through detailed subgrid modeling approaches such as Computational Fluid Dynamics (CFD) based models.[28]
2. Estimation of local *B. anthracis* levels at the scale of interest (such as a census tract) or a conveniently defined grid through one of the following:
   a. Spatiotemporal statistical interpolation of monitor data or outputs of a "coarse-scale" model, using the techniques mentioned in Step 1a.
   b. Aggregation of the outputs of a "fine-scale" model. This is important when the atmospheric dispersion model provides concentration profiles at a finer scale than the

resolution of other model components, such as population distributions, which have a typical resolution of a census tract or a census block.

3. Characterization of attributes of populations (geographic density, age, gender, race, income, etc.) through one of the following:

   a. Selection of a fixed-size sample population ("virtual individuals") that statistically reproduces essential census demographics.
   b. Division of the population of interest into an exhaustive set of cohorts based on different relevant population attributes.

   The population attributes, such as the distributions of age, gender, employment, and housing, can be developed from available census data (see, e.g., USCB[47]). Sometimes, relevant databases are available as components of other modeling systems, as in the case of the Air Pollution Exposure Model (APEX),[48] which provides databases for housing as well as for commuting profiles. Depending on the emergency response scenario, relevant adjustments to the distributions of population profiles may be necessary (e.g., changes in the population distribution during special events).

4. Development of activity event (or exposure event) sequences for each member of the sampled population or for each cohort for the exposure period through one of the following:

   a. Existing databases from composites of past studies (for baseline assessment).
   b. Hypothetical scenario-based or "simulated" activity patterns based on options such as "shelter-in-place" versus different evacuation options.

   For baseline assessments, the Consolidated Human Activity Database (CHAD)[49] can be used. It contains over 22,000 person days (diary records) of activity patterns developed from preexisting human activity studies. Each diary record provides a basis for simulating the movement of the "virtual individual" through geographic locations and microenvironments during the simulation period. Each event is defined by geographic location, start time, duration, microenvironment visited, and an activity performed. The attributes of CHAD records include age, gender, employment status, and smoking status of each individual, which can be used for matching the demographic characteristics of each sampled individual.[50] For planning and training purposes, several additional options can be considered for protective action, including evacuation, "shelter-in-place," or a combination.[51] The corresponding activity profiles can be either synthesized independently or through scenario-specific modifications to existing CHAD diaries.

5. Estimation of personal exposure levels and temporal profiles of *B. anthracis* concentrations in various microenvironments (residences, offices, restaurants, vehicles, etc.) through either one or more of the following methods:

   a. Simple linear, steady-state mass balance.
   b. Nonlinear, dynamic models.
   c. Detailed computational fluid dynamics models.

   Several modeling studies of indoor/outdoor relationships of fine particles have been presented in the literature, addressing issues such as contaminant penetration of indoor environment and corresponding particle size dependence.[52–54] The Stochastic Human Exposure and Dose Simulation (SHEDS) application[55] provides distributions of air exchange rates for different types of residential microenvironments, while other models and databases provide distributions for air exchange rates for general nonresidential microenvironments[56] and vehicle microenvironments.[57]

6. Calculation of appropriate inhalation rates for the members of the sample population by combining physiological attributes of study subjects and activities pursued during the individual exposure events. The CHAD diary records also provide information on energy expenditure, which can be used directly to estimate inhalation rates, as discussed in Step 6 of Section 4. Alternatively, probability distributions or tables describing age-specific inhalation rates of humans can also be used.[58–60] The inhalation rates, along with personal exposure levels, provide intake rates of anthrax spores.

7. Calculation of target tissue dose through physiologically-based respiratory deposition

modeling by estimating the amount of inhaled *B. anthracis* that is deposited in the lungs. The International Commission on Radiological Protection (ICRP)[61,62] provides deposition fractions of fine particles in different regions of the human lungs. These fractions are age and gender dependent, and are also dependent on the size of the particles.

8. Estimation of probability of infection for each simulated individual based on calculated dose and physiological attributes, and summation of these probabilities to estimate the total number of potential infections for each local area in the simulation domain (e.g., each census tract in the modeling domain). Sparse data are available for describing the dose-response relationships of *B. anthracis* in humans,[29] and several dose-response models have been proposed in the literature, as described in Step 8 in Section 4.

3. MENTOR-2E IMPLEMENTATION

The steps outlined above were implemented in a modular manner as part of the Modeling Environment for Total Risk studies (MENTOR).[1,37] The general approach of MENTOR is to utilize existing models when available and to provide new modules to "fill gaps" in the source-to-dose-to-effect sequence. In that sense, MENTOR is not a "new model"; it can be viewed as a computational toolbox intended to facilitate consistent multiscale risk assessment. In this particular study, several existing models and approaches relevant to exposure estimation have been used. For example, various concepts from the SHEDS approach, which has been applied for studying exposures to particulate matter[55] and pesticides,[63] have been adapted and incorporated into the formulation of different MENTOR modules.

The MENTOR-2E system has been coded in Matlab[64] (www.mathworks.com), while various relevant programs such as the CALPUFF model[44] have been linked in a pipeline manner. The model code and the underlying data files are available upon request. The computational time for the CALPUFF simulation is dependent on the extent of the modeling domain, the grid resolution, and the duration of the simulated period. For the case of 250 m resolution, and an area covering the entire State of New Jersey, the CALPUFF simulation required about 2 CPU hours on a 3 GHz Pentium Processor. The computational time for calculation of exposures, doses, and effects of *B. anthracis* release is dependent mainly on the number of virtual individuals simulated per census tract, the number of census tracts, and the time period considered in the simulation. This study used 500 virtual individuals per census tract, and the exposure and dose calculations required about 4 minutes of CPU time per census tract for population sampling, exposures, and dose calculations. However, the calculations involving activity patterns, exposures, and doses are run in a distributed manner on a computer cluster, as these calculations for each census tract are independent of those for other census tracts.

4. CASE STUDY APPLICATION

The location and timing of the hypothetical scenarios used in this study to demonstrate the MENTOR-2E system were assumed to represent potential variations of the anthrax attacks of 2001 through the postal system in the State of New Jersey. The main difference is in the amount and release characteristics. *B. anthracis* was assumed to be released in the air and the release was assumed to occur starting at 08:00 hours on September 18, 2001 in the vicinity of the Hamilton Post Office (the site and the day of the mailing of letters containing anthrax spores in 2001), as shown in Fig. 2. A hypothetical release of 100 g (1 trillion spherical spores per gram) of weaponized anthrax spores was assumed, similar to the release characteristics assumed by the modeling study of Craft *et al.*[32] Two types of releases were considered in the simulation: a "quick" release, where the spores were assumed to be released over a period of one hour (release scenario A), and a "continuous" release, where the spores were assumed to be released over a period of 10 hours (release scenario B). The study focused on the impact of these releases on the general population of the State of New Jersey, and exposures during the day of September 18, 2001 were simulated. Only the census tracts in New Jersey (totaling 1944 census tracts) were considered here, instead of the entire region of potential impact, to illustrate the application of the system to targeted administrative areas by responding agencies. The inclusion of other census tracts in other states is straightforward.

The specific MENTOR-2E application for this case study used the following eight steps (Fig. 1) for assessing exposures, dose, and potential infections.

Step 1: The ambient *B. anthracis* concentrations were calculated using the CALPUFF model,[44] which

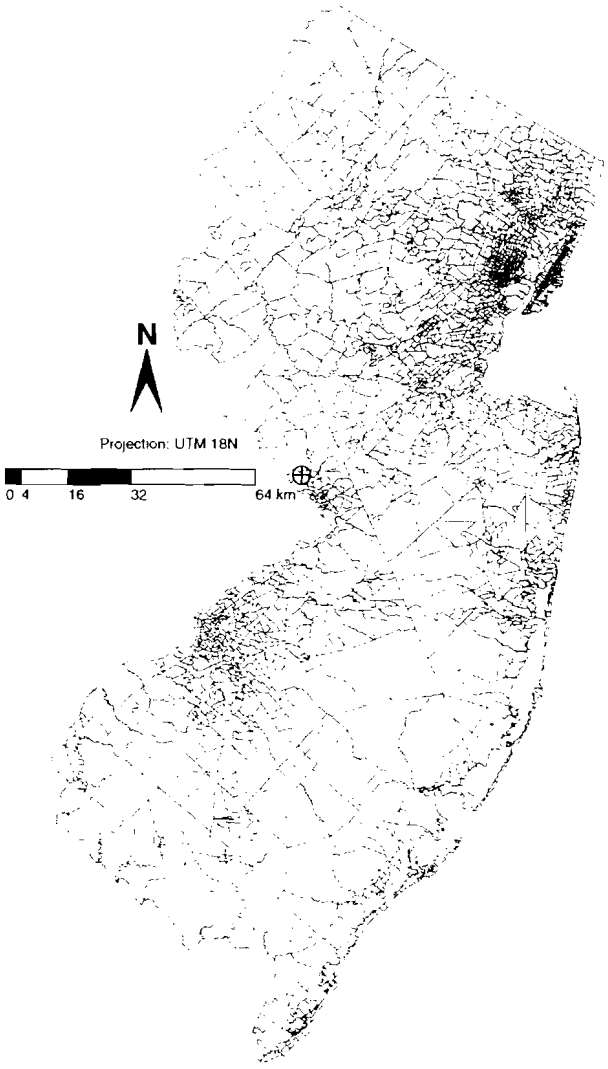

Fig. 2. The location of the hypothetical release of anthrax spores and the distribution of the census tracts within the State of New Jersey. The hypothetical release location corresponds to the Hamilton Post Office, the place from which envelopes containing *B. anthracis* were mailed on September 18, 2001.

is a generalized nonsteady-state air quality model that simulates the transport, transformation, and dispersion processes of "puffs" of material from emission sources, and provides hourly average estimates of concentrations. CALPUFF has been adopted by the USEPA in its Guideline on Air Quality Models[65] as a preferred model for assessing long-range transport of pollutants, and on a case-by-case basis for certain near-field applications involving complex meteorological conditions. Meteorological data were retrieved from the National Oceanic and Atmospheric Administration (NOAA)[66] and converted into CALPUFF input format. In this study, it was assumed that the hourly averages provided by the CALPUFF model at a resolution of 250 m are adequate for characterizing *B. anthracis* exposures and doses, based on the general guidance on CALPUFF modeling.[67] In this study, a 1,000 × 1,000 grid at 250 m resolution was used.

In general, the selection of a particular dispersion model and modeling options depends heavily on the type of release and the response options, including the scale of attack, detection time, complexity of the geography, and population densities in the downwind regions. Some emergency events need to be modeled at high temporal and spatial resolutions. Examples include large releases of chemicals such as chlorine, where high-resolution concentration profiles are important in order to capture peak concentrations. However, in the case of *B. anthracis* releases, the main metric of concern is the total uptake of anthrax spores, so hourly averages were considered adequate. In general, a tradeoff can be made by considering model resolution, model complexity, and setup and simulation time.

In order to perform comparative evaluation, a simplified dispersion equation was also used[32] to characterize ambient concentrations of anthrax spores. A constant wind speed of 1.5 m/s was assumed blowing toward the northeast, at 45 degrees, corresponding to the general direction and speed of the wind during September 18, 2001, as part of this simplified application.

Step 2: Concentration estimates from CALPUFF at regularly spaced grid points at 250 m × 250 m resolution were aggregated at the level of a census tract; the average of concentrations at all grid points within a census tract was assumed to represent the concentration at the geometrical centroid of the census tract. The spatial averaging approach can sometimes result in artificial "discontinuities" in the census tract level concentrations, as is the case of Fig. 3, where two census tracts close to the plume show a zero concentration, whereas the surrounding census tracts show nonzero concentrations; however, this approach follows mass balance. The spatial averaging approach was used here because detailed allocation of concentrations can be computationally very demanding. It should be noted that for finer-scale spatial resolution (e.g., exposures studies focusing on census block level resolution or on regularly spaced grids), the CALPUFF model outputs can be

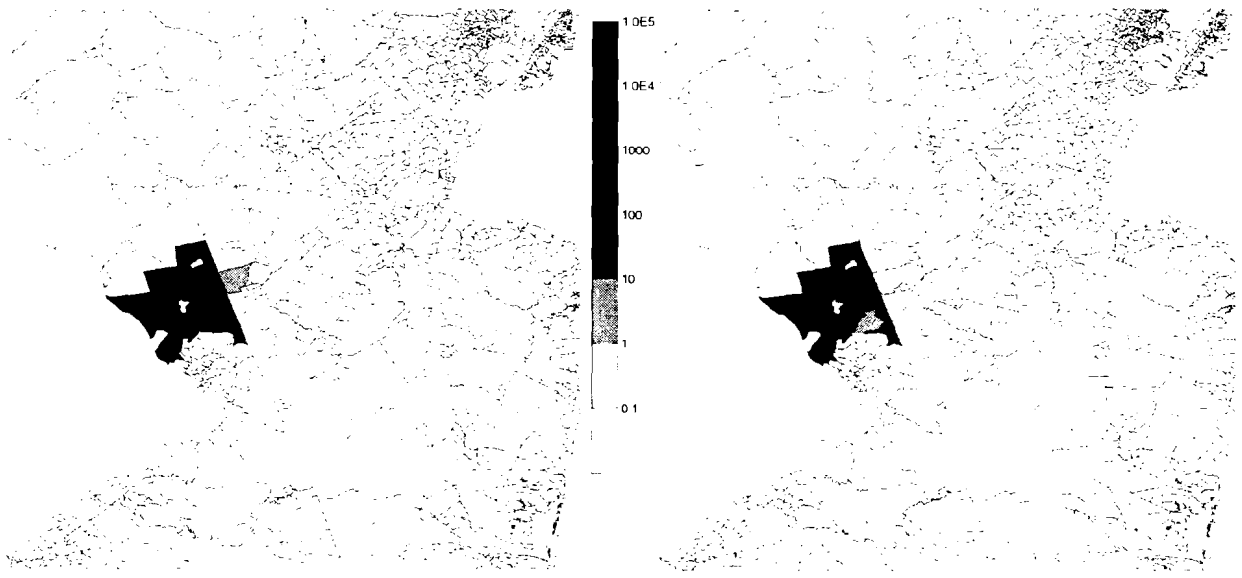

Fig. 3. Outdoor number concentrations of anthrax spores ($1/m^3$) during 08:00–09:00 calculated by CALPUFF for a release of 100 g of *B. anthracis* over a period of one hour (left) (release scenario A) and 10 hours (right) (release scenario B), for the day of September 18, 2001, with the release starting at 08:00 hours (values less than 1 indicate the probability of finding one spore per m^3).

aggregated or interpolated depending on the resolution. In case of the simplified dispersion modeling, the concentrations were estimated directly at the geometric centroid of each census tract.

Step 3: The attributes of the population under study were retrieved from the 2000 U.S. Census Survey.[47] Due to the variability of the urban population, in order to statistically reproduce essential demographic distributions of age, gender, housing type, and employment status, a rather large statistical sample of 500 "virtual individuals" was sampled for each of the 1944 census tracts under study.[37,55] In this study, the effect of commuting on population distributions was not considered, and the residential distributions were assumed to represent the population distributions throughout.

Step 4: A 24-hour activity diary for each "virtual individual" was selected from the CHAD diaries using the approach described earlier. In this study, the 113 microenvironments in the CHAD diaries were grouped into four categories: home, other indoor, outdoor, and vehicle.

Step 5: The outdoor concentration levels of *B. anthracis*, aggregated at the census-tract level, were used as inputs to the MENTOR modules for estimating microenvironmental concentrations. The estimation of *B. anthracis* levels in the various microenvironments in this study was based on the simple mass balance equation:

$$\frac{dC_{in}}{dt} = f_p \cdot A \cdot C_{out} + \frac{S}{V} - (A + F_d) \cdot C_{in}, \qquad (1)$$

where C_{in} is the indoor *B. anthracis* concentration (number/volume), f_p the penetration factor (dimensionless fraction, indicating the amount of *B. anthracis* that can penetrate indoors), A the air exchange rate between outdoor and indoor (1/time), C_{out} the outdoor *B. anthracis* concentration (number/volume), S the indoor *B. anthracis* source rate (mass/time), V the indoor volume (volume), and F_d the decay rate of *B. anthracis* indoors (via deposition, absorption to walls, etc.; 1/time). This equation was further simplified on the basis of the following assumptions: (1) steady-state approximation (which can provide a reasonable approximation for time durations of hours), (2) $S = 0$ (i.e., no indoor sources), thus resulting in $C_{in} = A\, f_p . C_{out}/(A + F_d)$ Furthermore, the anthrax spores were assumed to behave similar to fine particulate matter in the estimation of penetration and deposition. The resuspension of anthrax spores was assumed to be negligible at the modeling time scale in this study. However, it will be a critical factor in the decontamination process.

For each microenvironment corresponding to the activity event, the parameters in the mass balance equation were generated through random samples.

The residential parameters include day- and night-time air exchange rates, house volumes, and penetration and deposition factors; these were sampled once for each individual from the corresponding distributions (see Table 2 from Burke *et al.*[55]), and were held constant throughout the simulation. Parameters for other microenvironments, such as the air exchange rates in the vehicles, stores, etc., were sampled separately throughout the simulation from two distributions: one for the general nonresidential microenvironments[56] and one for vehicles References 37 and 68. In the simplified application, all virtual individuals were assumed to be outdoors, and anthrax spore concentration at the census tract centroid is assumed to be the exposure concentration.

Step 6: In this study, exposure to *B. anthracis* was assumed to occur solely through the inhalation of contaminated air. Thus, one of the main factors in *B. anthracis* exposure is a person's inhalation rate. For each activity event of a virtual individual, inhalation rates were calculated using a combination of age- and gender-dependent ideal body mass, basal metabolic rate, and activity-specific energy expenditure and METs (Metabolic Equivalent of Tasks; described in detail in References 37 and 68). In the simplified application, the breathing rates were assumed to be constant across all individuals.

Step 7: The population-based lung dosimetry model employed by Georgopoulos *et al.*,[37] based on the HUMTRN model,[69] was used to calculate the delivered doses for individuals of both genders and of different ages. The calculated inhalation rates were combined with the corresponding microenvironmental concentrations to estimate the inhaled dose delivered to the lung for each virtual individual. Lung deposition of anthrax spores was calculated for three regions of the lungs: nasal-pharyngeal (NP), tracheobronchial (TB), and pulmonary (P), using empirical values of deposition fractions from the International Commission on Radiological Protection (ICRP) databases.[61,62] Total uptake of *B. anthracis* for each virtual individual was estimated for the day of September 18, 2001, from the sum of event-based doses inhaled by the individual during the exposure event sequence. In the simplified application, all inhaled anthrax spores were assumed to be initially deposited in the lung.

Step 8: Calculation of the probability of infection for each sampled individual in a census tract through the application of a *B. anthracis* dose-response model, and scaling that to the total population of the census tract. Several empirical dose-response models have been proposed for *B. anthracis*,[9,29,32,41] and the range of potential infections spans an order of magnitude, solely based on the choice of the dose-response relationship.[41] Six different dose-response models were used in this study to estimate the probability $P(s, a)$ that an individual of age a would be infected from a dose of s spores. Here, the dose is assumed to represent the number of spores "initially deposited" into the lung, whereas the dose-response models are assumed to account for the subsequent, time-dependent cilial clearance.

1. $P(s, a) = \min(1, \frac{s}{c_1 - c_2 a_1})$,
   based on Craft *et al.*,[32] where $c_1 = 38{,}000$ and $c_2 = 450$, $a_1 = \min(a, A_{cut})$, and A_{cut} is the cut-off age of 80 years, beyond which the dose response is assumed to plateau with age.
2. $P(s, a) = \Phi(\alpha + \beta \cdot \log(s) + \gamma \cdot a + \delta \cdot a^2)$,
   an age-dependent probit model based on Wein *et al.*[9] where Φ is the *cdf* of the normal distribution, and parameters $\alpha = -9.733$; $\beta = 1.025$; $\gamma = -0.016$/year; and $\delta = 0.0006$/year.[2]
3. $P(s, a) = \Phi(\alpha + \beta \cdot \log(s))$,
   an age-independent probit model from Wilkening,[41] where $\alpha = -2.6361$, and $\beta = 0.291$, corresponding to an ID_{50} of 8,600 spores, and a probit slope of 0.67.
4. Another age-independent probit model from Wilkening,[41] of the form $P(s, a) = \Phi(\alpha + \beta \log(s))$, with $\alpha = 5.6263$, and $\beta = 0.621$, corresponding to an ID_{50} of 8,600 spores, and a probit slope of 1.43.
5. $P(s, a) = \exp(\frac{-\lambda s}{\lambda + \theta})$,
   an exponential model that accounts for probability of spore destruction and spore germination in the lungs,[41,70] where $\theta = 0.109$/day, and $\lambda = 8.8 \times 10^{-8}$.
6. $P(s, a) = \frac{\beta \cdot (\exp(s/\alpha) - 1)}{1 + \beta \cdot (\exp(s/\alpha) - 1)}$,
   an age-dependent logit model from Webb and Blaser,[29] where α and β are derived from age-dependent values for ID_{50} and ID_{10}, classified into four age groups.

In principle, the uncertainties in the dose-response relationship modeling directly translate into the corresponding uncertainties in the number of probable infections. However, the age-dependence of dose-response and activity patterns warrant explicit characterization of these uncertainties.

The total number of potential infections in each census tract was obtained by summing the

probabilities of infections across all the virtual individuals in that census tract, and scaling that value to the population of the census tract. The summation is possible because infections of different individuals represent independent events.

$$X_j = \left(\sum_{i=1}^{N_{\text{sample},j}} P(s_{ij}, a_{ij}) \right) \frac{N_j}{N_{\text{sample},j}}, \qquad (2)$$

where X_j is the number of potential infections in census tract j, $N_{\text{sample},j}$ the number of sampled virtual individuals in census tract j, s_{ij} the dose of inhaled *B. anthracis* for sampled virtual individual i in census tract j, a_{ij} the age of sampled virtual individual i in census tract j, and N_j the total population of census tract j.

The impact of *B. anthracis* releases on sensitive population subgroups, such as the elderly, can also be studied easily using MENTOR-2E. Since the virtual individuals are described via several attributes that include age, gender, body weight, employment status, etc., the potential infections within subgroups of interest can be obtained by selecting the virtual individuals that belong to that subgroup. In general, for a subgroup M, the corresponding potential infections can be calculated through

$$X_{j:M} = \left(\sum_{i \in M} P(s_{ij}, a_{ij}) \right) \frac{N_j}{N_{\text{sample},j}}. \qquad (3)$$

5. RESULTS

Fig. 3 shows the average outdoor *B. anthracis* concentrations during 08:00–09:00 hours for both release scenarios. Fig. 4 shows the average outdoor concentrations during 14:00–15:00 hours; this corresponds to six and a half hours after the start of the *B. anthracis* release, and five and half hours after the end of the one-hour release. As the maps show, the pattern of *B. anthracis* concentrations varies significantly depending on the pattern of the release. Though the initial concentrations are high in the quick-release case (scenario A), high-airborne concentrations of *B. anthracis* remain in the slow-release case (scenario B).

Median and 95th percentile values for individual biological doses per census tract for the general population are shown in Fig. 5 (for release scenario A) and in Fig. 6 (for release scenario B). The MENTOR-2E system also allows focusing on susceptible subpopulations; the 95th percentile doses for the elderly (65 years and older) are shown for both release scenarios in Fig. 7.

5.1. Effect of Simplifying Approximations Used

In order to illustrate the differences in estimates arising out of differences in model assumptions, the MENTOR-2E results were compared with those obtained using two approximations: (a) the constant inhalation rate of 5×10^{-4} m^3/s (1.944 m^3/h) used by Craft *et al.*,[32] and (b) a reference constant inhalation rate of 0.78 m^3/h from the USEPA exposure factors handbook (EFH).[71] The corresponding average breathing rate for the study population in the MENTOR-2E simulation was about 0.71 m^3/h, which is approximately equal to the inhalation rate from the EFH. In employing the Craft *et al.* and EFH approximations, the outdoor concentration values were assumed to represent the personal exposure concentrations, and the corresponding doses and probabilities of infection were estimated.

The estimated percentiles of biological doses of *B. anthracis* (i.e., number of deposited anthrax spores) for the individuals in the entire study population are shown in Fig. 8 (release scenario A) and Fig. 9 (scenario B). The corresponding percentiles of probabilities of infection shown in Fig. 10 (release scenario A)

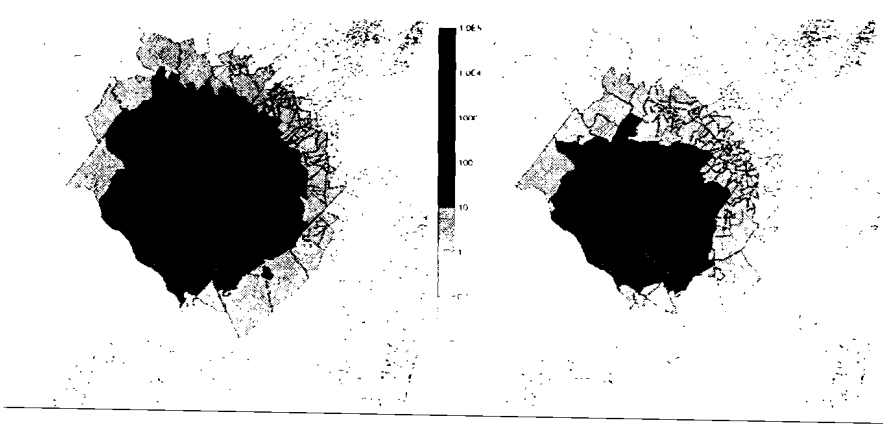

Fig. 4. Outdoor number concentrations of anthrax spores (1/m^3) during 14:00–15:00 calculated by CALPUFF for release scenario A (left) and release scenario B (right). Values less than 1 indicate the probability of finding one spore per m^3. In the case of scenario A (left), the release has already been completed and no spores were released during the previous five and a half hours.

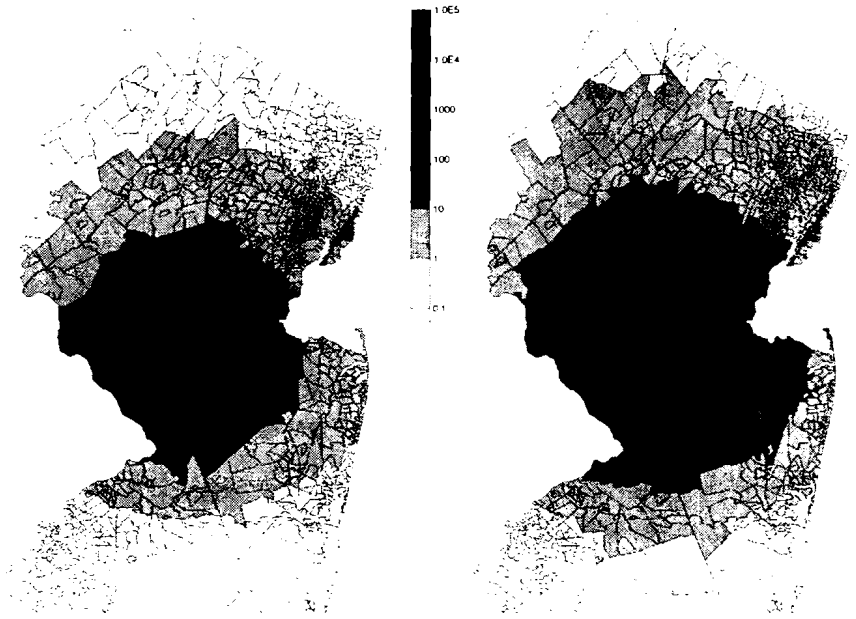

Fig. 5. Estimated individual biological doses (spores/day) of *B. anthracis* in each census tract due to a release scenario A: median (left) and 95th percentiles (right) of doses for the simulated population in each census tract. Values less than 1 indicate the probability of inhaling one spore.

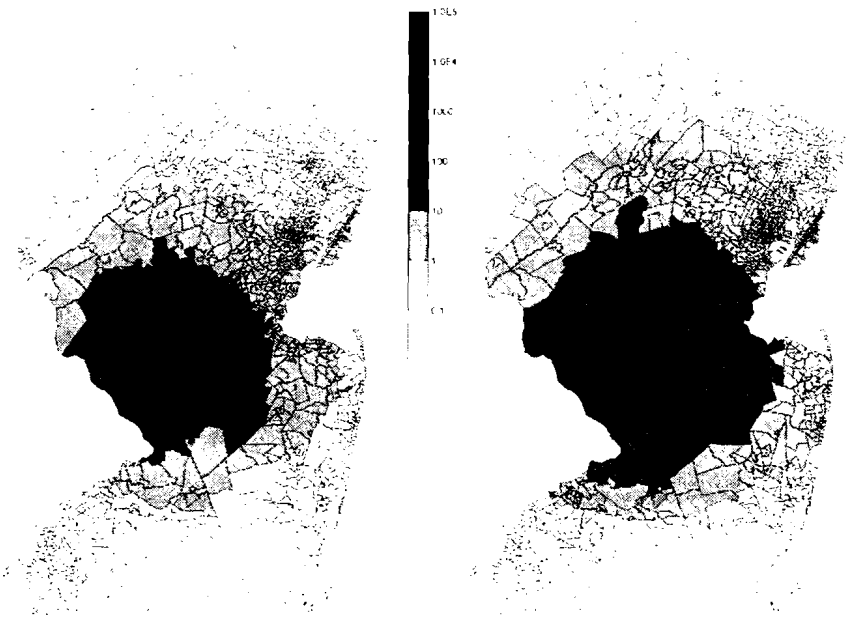

Fig. 6. Estimated individual biological doses (spores/day) of *B. anthracis* in each census tract due to a release scenario B: median (left) and 95th percentiles (right) of doses for the simulated population in each census tract.

and Fig. 11 (release scenario B). The total numbers of probable infections for the entire study region were also estimated, as shown in Table I. In both release scenarios, the infection estimates derived using the constant inhalation approaches are about five to ten times higher than those derived through MENTOR-2E. The dependence of the potential infection estimates on the choice of the dose response is also strong, as shown in Table II. The estimates span an order of magnitude, solely based on the choice of the dose-response model. This, coupled with the order of magnitude change in estimates based on inhalation rates and microenvironmental calculations, results in a range of two orders of magnitude for the estimates. Further approximations, such as constant wind speed, are likely to overestimate the impacts in some areas.

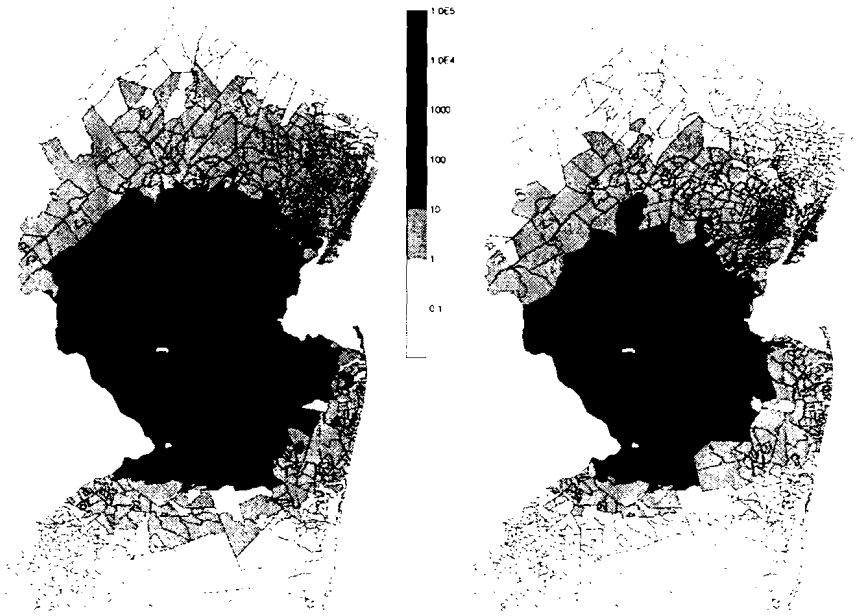

Fig. 7. Estimated 95th percentile biological doses of *B. anthracis* for elderly individuals (over 65) in each census tract due to release scenarios A (left) and B (right).

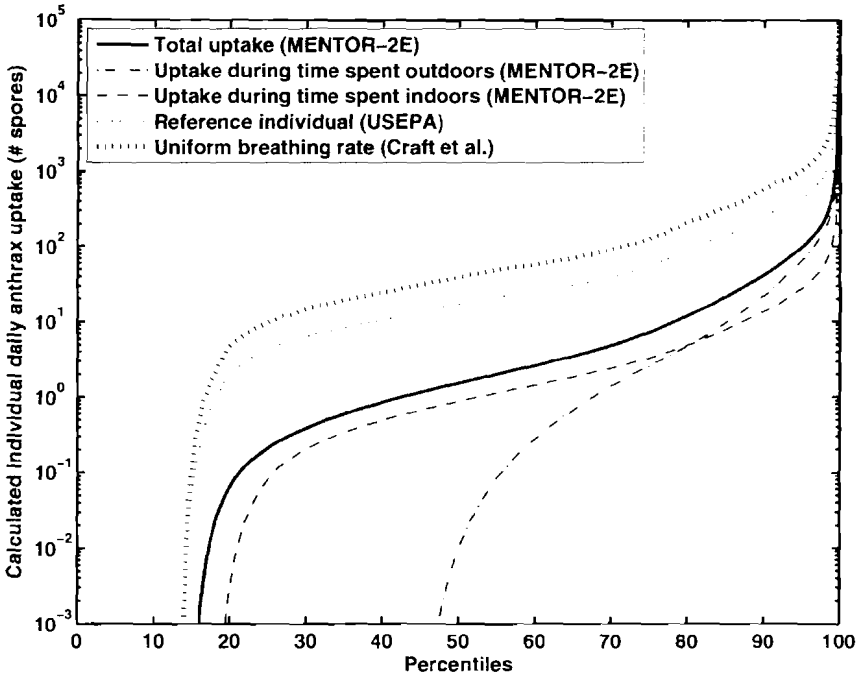

Fig. 8. Comparison of individual biological doses of *B. anthracis* estimated via different approaches. Percentiles of individual doses are shown for the entire study population for release scenario A (100 grams *B. anthracis* released over one hour).

while underestimating the impacts in others. In fact, as shown in Table II, the estimates using a constant wind speed and simplified dispersion equation employed by Craft *et al.*[32] are substantially higher. In fact, the corresponding doses are high enough that the differences due to various dose-response formulations become negligible. As noted earlier, such overestimations and underestimations can have significant adverse impact on response to emergency events.

6. DISCUSSION AND CONCLUSIONS

This study presents a demonstration application of the integrated MENTOR-2E system for assessing

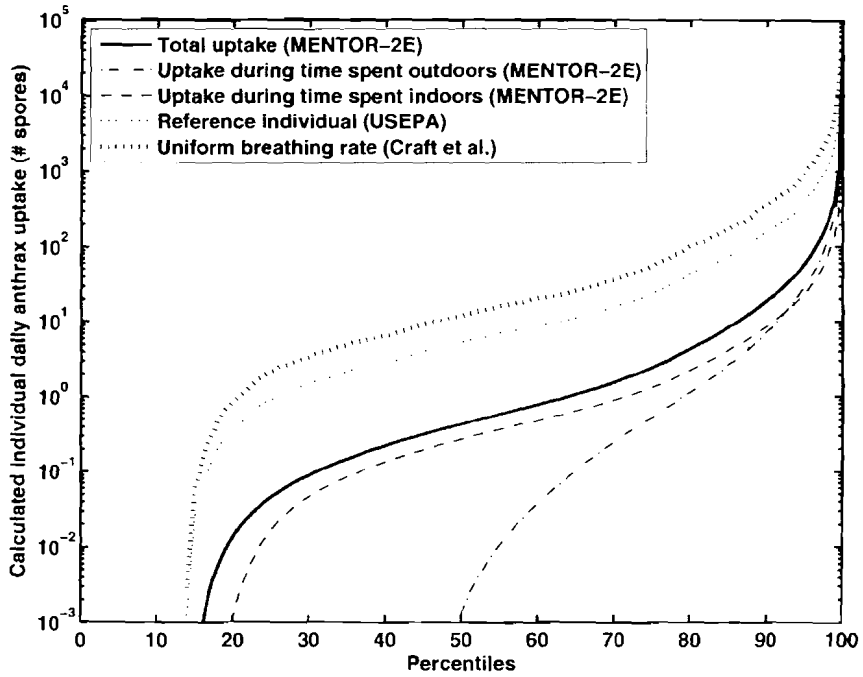

Fig. 9. Comparison of individual biological doses of *B. anthracis* estimated via different approaches. Percentiles of individual doses are shown for the entire study population for release scenario B (100 grams *B. anthracis* released over 10 hours).

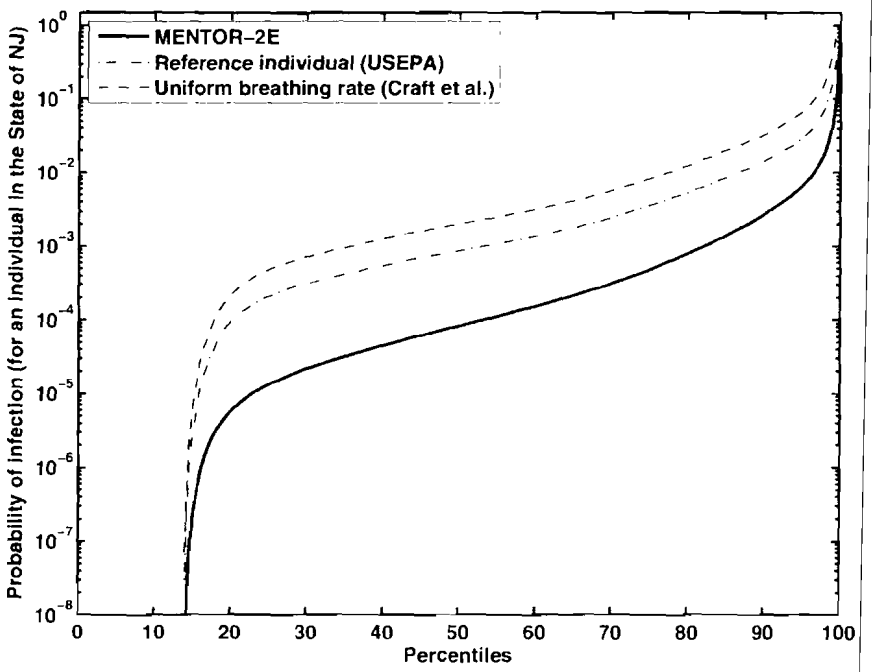

Fig. 10. Comparison of probabilities of anthrax infection estimated via different approaches. Percentiles of probabilities of infection are shown for the entire study population for release scenario A (100 grams *B. anthracis* released over one hour).

the impact of airborne *B. anthracis* releases, with a main focus on mechanistically consistent linkage of modules in the source-to-dose-to-effect sequence. Future work can focus on characterization of commuting patterns, population gathering at different events, and custom response scenarios, such as "shelter-in-place" versus evacuation.

The difference in dose estimates between the release scenarios, shown in Fig. 5 (release scenario A) and in Fig. 6 (release scenario B), is solely due to the difference in the concentrations profiles, which in this case are influenced by the *B. anthracis* release patterns. However, variations in meteorological conditions can result in significantly different concentration

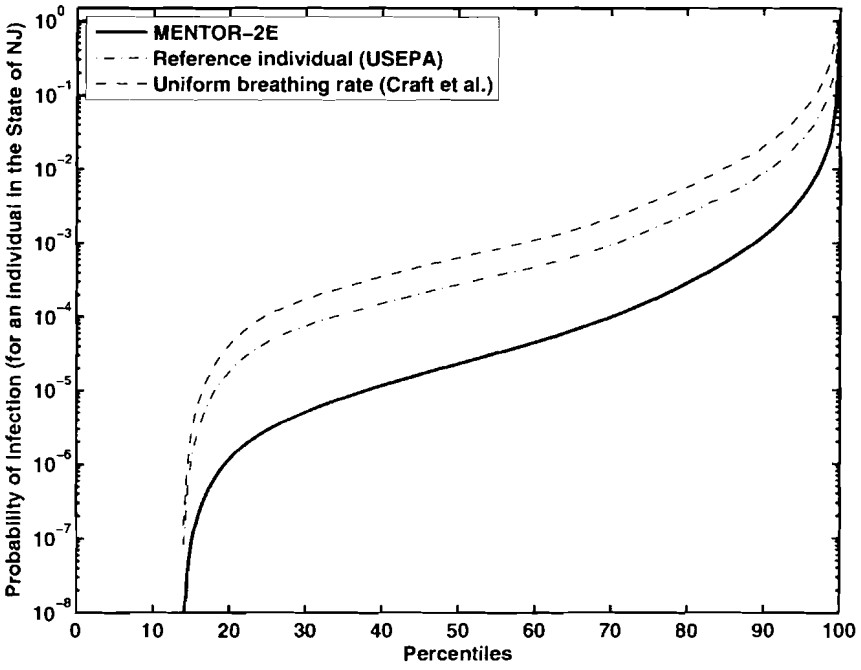

Fig. 11. Comparison of probabilities of anthrax infection estimated via different approaches. Percentiles of probabilities of infection are shown for the entire study population for release scenario B (100 grams *B. anthracis* released over 10 hours).

Parameter	Value and/or Source
Number of anthrax spores released (hypothetical releases over 1 h and 10 h)	1015 [32]
Start time for the simulation (coinciding with mailing time of anthrax letters)	9/18/2001 08:00 h [2]
Location of the release (coordinates calculated using information from Reference 2)	Lat: 40.277; Lon: −74.813 [2]
Variable wind speed (obtained for Mercer County airport for 9/18/2001); the simplified dispersion case used a constant 1.5 m/s blowing toward north-east 0–3 m/s (Reference 66)	0–3 m/s [66]
CALPUFF grid resolution (general guidance from Reference 67)	250 m × 250 m [67]
Number of census tracts modeled (for application to the State of New Jersey)	1944 [47]
Census tract level population distribution (age; gender; occupation)	[47]
Virtual individuals per census tract	500 [37]
Activity patterns/metabolic equivalents (consolidated human activity database)	[49]
Distributions of parameters for residential microenvironments (air exchange rates; housing volumes; penetration and deposition factors; a total of 10 parameters)	Table II in [55]
Distributions of air exchange rates for general nonresidential microenvironments	[56]
Distributions of air exchange rates for vehicle microenvironments	[57]
Distributions for body weights (function of age and gender)	[37]
Empirical factors for deposition of anthrax spores in the lung ("uptake")	[37,61,62,69]
Parameters for empirical dose-response models (details in Step 8 in Section 4)	[9,29,32,41]

Note: Further details on the exposure parameters are available in Reference 68.

Table I. Sources and Values of Parameters Used in the MENTOR-EE Application for Simulating Impact of Hypothetic Releases of Anthrax Spores

Table II. A Comparison of the Estimates of Probable Infections Derived Through Different Approaches for Exposure and Dose-Response Modeling

	Dose-Response Model					
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Scenario A; Craft *et al.* (simplifying assumption regarding breathing rates and location)	166,750	119,910	**719,160**	161,930	172,230	141,310
Scenario B; Craft *et al.* (simplifying assumption regarding breathing rates and location)	140,660	109,940	**525,920**	140,910	145,650	124,870
Scenario A; EPA EFH	85,669	56,020	485,770	75,747	88,549	70,466
Scenario B; EPA EFH	71,954	52,118	355,560	70,046	74,994	61,247
Scenario A; MENTOR-2E	25,013	**15,631**	187,840	21,059	25,908	20,472
Scenario B; MENTOR-2E	19,747	**12,950**	129,420	17,416	20,247	16,458
Scenario A/B; Craft *et al.* (simplifying assumptions regarding breathing rates, location, and plume dispersion)	1,180,932	1,090,121	1,076,816	1,049,390	1,144,563	**1,187,637**

Note: Total number of probable infections in study area are shown for the two release scenarios (100 g of anthrax released over (A) 1 h and (B) 10 h). The columns correspond to the different dose-response models used, and the rows correspond to different exposure modeling approaches used.

profiles. Similarly, different forms of release, for example, releases from multiple locations, either simultaneously, or in a staggered manner, influence the concentration profiles. Therefore, for emergency response modeling, improved estimates of concentration profiles are very important. It must be noted that the estimates of infections are "probalistic" expected values, and do not take into account the time for incubation between the exposure and the actual infection; therefore, the results do not reflect the estimates of possible number of potential hospital admissions within days of the *B. anthracis* release. Furthermore, the exposures modeled here included only those occurring during the day of September 18, 2001, and subsequent exposures were assumed to be negligible as the *B. anthracis* plume expands and becomes significantly diluted.

The simplifying assumptions have a strong impact on estimates of probable infections, as shown in Table II. In both release scenarios considered, the same concentration profiles were used for the three exposure and dose calculation approaches (Table II, Rows 2–7). Furthermore, even higher estimates of infections are possible if simplifying assumptions are used for calculating the concentration profiles (e.g., Table II, Row 8, which shows results for the case where simplified dispersion modeling and simplified population characteristics are assumed, both used by Craft *et al.*[32]).

Wilkening[41] discusses the uncertainty associated with the selection of the dose-response model for inhalation anthrax, and concludes that a factor of 10 uncertainty exists based on the choice of the dose-response model. However, as shown in Fig. 10 and Fig. 11, the impact of simplifying assumptions with respect to microenvironments and activity patterns spans about a factor of 7–10. Therefore, all components of the source-to-dose-to-effect modeling, including dispersion, exposures, and dose response, need to be improved in order to use such models in planning, intervention design, and training.

Integrated modeling applications such as the one presented here need to be considered in the context of multiple sources and types of uncertainties, including natural uncertainty/variability (atmospheric turbulence, population demographics and variability, etc.), model/structural uncertainties (selection of the population units, alternative dose-response models, etc.), input/parameter uncertainties (estimates of source strength, wind speed, direction, etc.), and evaluation data uncertainties (data used in parameter estimation for the underlying models). This study focused on the population variability model uncertainty in exposure calculation approaches, and model uncertainty in dose-response relationships. However, there is a need for further systematic uncertainty analyses focusing on identifying major uncertainties in emergency response planning, and characterizing the contributions of these. Such characterization will further improve the confidence in simulation models used for planning, training, and decision support.

Ongoing work focuses on improving the performance of MENTOR-2E by performing some of the modeling steps beforehand and using those outputs toward achieving a real-time impact assessment and

real-time evaluation of alternative response strategies. The approach as presented here can be easily parallelized (e.g., representative activity pattern generation, sampling of microenvironmental factors, housing characteristics, physiological parameters, etc., can be performed beforehand, and the "concentration profiles" can then be used to calculate the exposures). Furthermore, since each administrative unit is modeled independently (e.g., each census tract level), they can be run in parallel on a distributed cluster of computers.

A comprehensive planning scheme for detecting and responding to a bioterrorism event should consist of effective and efficient monitoring, ability to characterize the release sources based on detected values, and ability to accurately estimate the potential impact, not only in terms of the overall magnitude, but also in the spatial distribution. It should provide means to assess alternative response strategies, e.g., flexibility to define custom activity patterns, modification of population distributions and activity patterns (e.g., during population evacuation from affected areas), as it can be used for training of emergency responders. Furthermore, such a system should be tuned for near real-time application for maximum benefit.

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D R A F T – April 15, 2009

ATTACHMENT TO DR. FISCHHOFF'S COMMENTS

Strategic Plan for Risk Communication at the Food and Drug Administration

Draft: April 15, 2009

U.S. Department of Health and Human Services
Food and Drug Administration

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Strategic Plan for Risk Communication at the Food and Drug Administration

Purpose

The purpose of this document is to describe the U.S. Food and Drug Administration's strategy for improving how the agency communicates about regulated products. The strategy is intended to guide program development and research planning in a dynamic environment where rapidly evolving technologies enable patients and consumers to become increasingly involved in managing their health and well-being. We define three key goal areas—policy, capacity, and science—in which strategic actions can help improve how we ourselves produce communications about the risks and benefits of regulated products, as well as how we oversee those communications produced by regulated entities. Box 2 on page 3 summarizes these three key goal areas and the associated strategies on which we will focus our efforts.

Background

FDA recognizes the importance of communicating effectively about FDA-regulated products to achieve the agency's mission of protecting and promoting the public health. Effective communication supports both optimal use of medical products and safe consumption of foods to maximize health. In 1999, FDA released a report that acknowledged risk communication as a key component in the effective management of medical product risks.[1] More recently, FDA asked the Institute of Medicine (IOM) to investigate the agency's drug safety efforts and to recommend improvements to its existing systems. In response, the IOM produced the report *The Future of Drug Safety: Promoting and Protecting the Health of the Public*, which it released on September 22, 2006.[2] Although the report focused on drug safety, it highlighted communication more generally, referencing FDA's mission of "helping the public get the accurate, science-based information they need ..."[3] to use FDA-regulated products to improve health, and recommending the formation of an advisory committee on communication (IOM Recommendation 6.1).

Although the IOM's recommendation to create a communications-focused Advisory Committee was directed to Congress and focused primarily on medical products, FDA independently responded by launching its Risk Communication Advisory Committee in 2007 to give advice about FDA's risk communication approaches for all FDA-regulated products (Box 1). The Committee was established to advise the agency on how it could improve its communication policies and practices, to review and evaluate relevant research, and to

[1] Managing the Risks from Medical Product Use: Report to the FDA Commissioner from the Task Force on Risk Management, FDA, May 1999.
[2] See http://www.iom.edu/CMS/3793/26341/37329.aspx
[3] See http://www.fda.gov/opacom/morechoices/mission.html

advise on implementing communication strategies consistent with the most current knowledge.[4]

Box 1: FDA's Risk Communication Advisory Committee provides advice on how best to communicate with the public about the risks and benefits of FDA-regulated products so as to facilitate optimal use of these products.

At the August 2008 Advisory Committee's meeting, members voted unanimously to accept two resolutions:

1. FDA should consider risk communication as a strategic function, to be considered in designing FDA core processes.
2. FDA should engage in strategic planning of its risk communication activities.

To that end, FDA has developed a Strategic Plan for Risk Communication, which is described in this document. FDA has the capacity to empower the public by providing medical professionals, patients, and consumers with the useful information on FDA-regulated products they need to take action, in the form they need it, and when they need it. The plan presents FDA's strategies for risk communication and proposes ways to improve its science base, its capacity for action, and its policy processes. FDA takes the approach that risk communication:

- is integral to carrying out FDA's mission effectively
- involves two-way interaction
- must be adapted to the various needs of the parties involved
- must be evaluated to ensure optimal effectiveness

Currently, FDA uses various formats to reach multiple audiences, but the agency is exploring which of those formats are most preferred and easily understood. Evolving technologies are making it possible for the public to access a broad variety of information about FDA-regulated products. The agency must increasingly take advantage of these technologies to receive, analyze, and communicate important information, including risk and benefit information.

The following strategy document lays out FDA's role in communicating the risks of regulated product use, defining risk communication anew for a 21st century in which evolving technologies have enabled the increasing involvement of patients and consumers in the management of their health and well-being. The document defines the three key areas (policy, capacity, and science), in which strategic action can help improve the generation and regulation of risk communication about regulated products. Finally, 14 specific strategies are identified and explained in detail.[5]

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[4] The Risk Communication Advisory Committee (RCAC) met three times in 2008 and is scheduled to meet four times in 2009. For more on the RCAC, see http://www.fda.gov/oc/advisory/OCRCACACpg.html.

[5] Note that the Plan provides a conceptual framework and FDA's commitment for improving the agency's risk communication. Except for some examples of specific actions the agency has already begun, the Plan does not provide a comprehensive listing of specific actions that the agency will take to implement the identified goals and strategies. Such actions will be identified and selected as part of FDA's overall strategic planning effort by the new administration over the coming year.

Box 2: FDA Risk Communication Strategic Plan – At a Glance

Strengthen the *science* that supports effective risk communication

Science Strategy 1: Identify gaps in key areas of risk communication knowledge and implementation and create a risk communication research agenda

Science Strategy 2: Evaluate the effectiveness of FDA's risk communication and related activities and monitor those of other stakeholders

Science Strategy 3: Translate and integrate knowledge gained through research/evaluation into practice

Expand FDA's *capacity* to generate, disseminate, and oversee effective risk communication

Capacity Strategy 1: Streamline and coordinate more effectively the development of communication messages and activities

Capacity Strategy 2: Plan for crisis communications

Capacity Strategy 3: Streamline processes for conducting communication research and testing, including evaluation

Capacity Strategy 4: Clarify roles and responsibilities of staff involved in drafting, reviewing, testing, and clearing messages

Capacity Strategy 5: Increase staff with decision and behavioral science expertise and involve them in communication design and message development

Capacity Strategy 6: Improve the effectiveness of FDA's Web site as a primary mechanism for communicating with different stakeholders

Capacity Strategy 7: Improve two-way communication and dissemination by strengthening partnerships with governmental and non-governmental organizations

Optimize FDA's *policies* on communicating product risks and benefits

Policy Strategy 1: Develop principles to guide consistent and understandable FDA communications

Policy Strategy 2: Identify consistent criteria for when and how to communicate emerging risk information

Policy Strategy 3: Re-evaluate and optimize policies for using partnerships and other leveraging activities to facilitate effective communication about regulated products

Policy Strategy 4: Assess and improve FDA communication policies in areas that have a major impact on public health

The Strategic Plan

The Evolving Role of FDA Risk Communication

FDA has seen its responsibilities increase exponentially in recent years as globalization, emerging areas of science, evolving technologies, and people's growing interest in managing their health and well-being have presented the agency with unprecedented challenges and opportunities. These factors have enormous implications for the ways in which the agency communicates the risks and benefits of the products it regulates.

In the past, FDA's communication efforts were largely restricted to overseeing the key vehicle for communicating risk information to the public—the labeling of FDA-regulated products. The process of negotiating with product manufacturers about changes to labeling or decisions to recall a product was often lengthy. But as the Internet and emerging technologies have both enabled and fed the public's demand for greater transparency and communication frequency, these protracted waiting periods have given way to communication in real time. Thus, designing a contemporary risk communication strategy is key to FDA's efforts to reposition itself to realize its potential for effective protection and promotion of health, enabled by 21st century knowledge and technology.

Communicating the appropriate use of FDA-regulated products is crucial

An important facet of FDA's risk communication strategy and mission has been educating the public about the appropriate use of FDA-regulated products. Today, however, we recognize that education involves more than ensuring the accuracy of product labeling; we must communicate the context of the message so that the words make sense to the audience. For example, in reviewing certain premarket submissions, FDA determines that a product is *safe and effective*. But that decision is made within a specific legal context, which is that the product meets the legal standard of *safe* and *effective* for its labeled or intended use—to read either word as an absolute would be misleading. Whether the public—medical professionals, consumers, patients, and caregivers—fully understands the ramifications of the legal context within which approvals are made is questionable.

The public also may not understand the context within which FDA makes decisions about whether recalls of particular foods or medical products are appropriate. Consequently, helping the public better understand both the product approval and recall processes would naturally complement FDA's rigorous premarket reviews, postmarket changes to product status and labeling, and compliance actions. Product users need to understand the closely associated concepts of *risk* and *benefit*—as well as each person's role in managing the risks of using FDA-regulated products—to be able to act in an informed manner in relation to products coming on the market as well as those being removed.

Equally important to understand is the natural tension that results from communicating what we know from research about a product's risks and benefits. In research, scientists collect evidence for a population: summary risks and benefits are therefore accurate for a *population* in general, but may not be so for a specific individual, who may react differently from that expected for the "average" individual.

Emergency-related communication is particularly challenging

Communicating during emergency events, such as with food recalls, presents unique challenges. Over the course of a recall, as both FDA and the industry gather more information, advice for consumers can change significantly. That change can result in confusion. Once a recall is over, effective communication is needed to ensure that consumers can understand and be assured that it is once again possible to safely consume the previously recalled product. There may be significant nutritional consequences should consumers decide permanently to shun such products.

Defining Risk Communication for the Future

In the past decades, FDA's awareness has grown about the breadth of what constitutes risk communication. This is consistent with the general growth in acceptance of risk communication as a broader process than one-way messaging about risks from experts to non-experts.[6] Risk communication that seeks to be effective needs to consider processes and procedures in addition to content. In pursuit of a shared acknowledgment of how FDA conceptualizes risk communication, a cross-FDA group of staff involved in communications agreed on the below working definition of FDA risk communication (Box 3).

Box 3: FDA Risk Communication is

— Interactively sharing risk and benefit information to enable people to make informed judgments about use of FDA-regulated products

— Providing guidance to relevant industries about how they can most effectively communicate the risks and benefits of regulated products

Risk communication is multifaceted

In the context of FDA's responsibilities, its risk communication activities fall into two broad categories. The first relates to FDA's function as an information-generator. In this capacity, FDA produces and disseminates its own information about regulated products to the press and various stakeholders, including consumers, medical professionals (e.g., physicians, nurses, physician assistants, pharmacists, veterinarians, hospital administrators, and health plan managers), caregivers, patients, public health officials, and regulated industry. Such information includes notices of product approvals, announcements and advisories about new public health related information, notices of product recalls, and educational information about proper product use and safe food handling practices.

The second category relates to how the agency oversees what regulated industry says about its products. Manufacturer- and producer-generated product information represents most of what users hear about FDA-regulated products. This information makes up a large part of what users know about a product and is critical to ensuring that they use a product appropriately to achieve maximal benefit. By enforcing the rules and providing useful guidance to industry around product information (labels, labeling, and in select cases,

[6] National Research Council. Improving Risk Communication, National Academy Press: Washington, DC, 1989.

product advertising) FDA can have a significant effect on user knowledge and consequent behavior.

Risk communication conveys the potential for good and bad outcomes

Risk communication is about conveying the possibility of both bad *and* good outcomes. For example, with respect to medical products, without the expectation of benefit, people are unlikely to accept even a small amount of risk. With respect to foods, there are many questions concerning the net value of particular foods or nutrients for addressing health conditions. Further, in the absence of understanding that foods provide nutritional benefits, members of the public may respond to a food product recall by stopping permanently their use of that food or food type. This would be an unintended bad outcome of a recall notice. Therefore, risk communication must involve describing both *the risks* and *the benefits* of regulated products, including adequate instructions to guide appropriate use.

Risk communication is a two-way street

FDA recognizes that risk communication with the public is a two-way street. Without a dialogue, FDA cannot learn the needs of its varied audiences or attempt to meet those needs successfully. This concept of a two-way sharing of information is implicitly embedded in FDA's provision of guidance to regulated industries. The government is committed to an interactive process in policy development. Similarly, we believe the same should be true, whenever possible, of risk communication.

Underlying this definition is the recognition that even if people are getting direct FDA recommendations, it is ultimately an individual's personal choice to, for example, purchase a prescription drug and take or give it to their pet, pick the "right" food choice for their health, use a medical device appropriately for a particular patient, or avoid unnecessary exposure to radiation. It is critical that individuals receive information that is adequate to ensure that they make informed choices.

Underlying Principles

A number of underlying principles guide FDA's strategic planning and commitment to activities that will improve how the agency conveys the risks and the benefits of regulated products.

Risk communication is science-based

First, FDA has a long-standing commitment to being science-based and science-led—a commitment that also includes risk communication activities. FDA fully supports using scientific methods to design and assess communications that will ensure maximal effectiveness. The science of risk communication and previous work in this area demonstrate important ground rules.[7] For example, it is crucial that the information in a document be both cognitively accessible[8] and relevant to the target audience.

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[7] National Research Council. Improving Risk Communication. National Academy Press: Washington, DC, 1989; Morgan, M.G., B. Fischhoff, A. Bostrom, & C.J. Atman. Risk Communication: A Mental Models Approach. Cambridge

However, having general ground rules is not enough. While there are general principles for designing communications, they are not algorithms; we must still assess whether specific messages are reaching and being understood by the various target audiences. To use an analogy, consider how FDA assesses products like drugs. Previous work has established the general principle that an effective drug will show a dose-response curve. The dose for the specific drug and its use in particular populations, however, must still be assessed before FDA can decide whether the drug is effective and how it should be administered. Risk communication must be viewed similarly.

Risk-benefit information provides context and is tailored to audience needs

A second guiding principle is that for people to make informed decisions, they need to have critical risk and benefit information available to them—and tailored to their specific needs—when, where, and in the form needed to best understand and apply this information.

Audiences have different levels of understanding about the context in which they receive information. For example, information that could be interpreted as representing a change in FDA's position on a product's overall value could be misleading or confusing to patients and other members of the public. To enable informed decision making that ensures the greatest possible benefit at the lowest possible personal risk, the complete information people require may include not only objective facts about the risks and benefits of product use but, when appropriate, facts about the risks and benefits of not using a particular product.

Communications must address the possibility that people may react to facts from emerging risk information out of context, choosing actions that are not beneficial and may be harmful. FDA recognizes that patients and consumers make the choices to take particular actions. One of FDA's essential roles is to ensure that its various audiences get the information they need to make *informed* choices. But audiences must also be given and must understand *the context* of that information or it will have little meaning. Thus, communications about regulated products should include what is known and not known about the product—and perhaps even the limitations of that knowledge. Communications must also be framed so that audiences can understand the decision-making process that led to the communication and any recommendations.

Strategic Goals

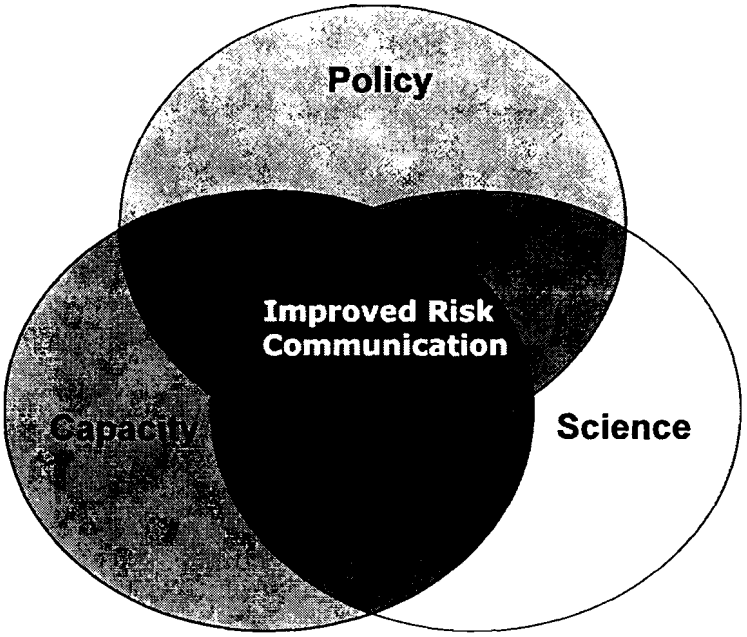
The graphic below shows the three areas of strategic focus that form the foundation for FDA's Risk Communication Strategic Plan: science, capacity, and policy. Depicting these three focus areas as intersecting circles illustrates that in practice they often overlap. Separately and together they support improved risk communication. Some of the strategies discussed later in this document contribute to two or even all three Strategic Goals.

The three overarching Strategic Goals that will help the agency develop a 21st century communications model are as follows:

University Press: Cambridge, U.K., 2002; Wogalter, M.S., D.M. DeJoy, & K.R. Laughery. Warnings and Risk Communication. Taylor & Francis. 1999.

[8] Day, R.S. Comprehension of Prescription Drug Information: Overview of a Research Program, Proceedings of the American Association for Artificial Intelligence, Argumentation for Consumer Healthcare. 2006

- Strengthen the ***science*** that supports effective risk communication
- Expand FDA's ***capacity*** to generate, disseminate, and oversee effective risk communication
- Optimize FDA's ***policies*** on communicating product risks and benefits



Strengthen the *science* that supports effective risk communication

FDA depends on the best and latest science to make regulatory decisions about product safety and effectiveness (i.e., risks and benefits for consumers or patients). FDA acknowledges that, to the extent possible, this same science-based approach should guide our communications activities. The agency recognizes that time and resources largely determine the extent to which it can apply science's lessons in the communications arena. For example, we can't do external formative and evaluative consumer research of every individual announcement before releasing it, but we can incorporate more testing than we presently conduct. Although FDA has made progress in providing the scientific support for some communications and communications-related policy decisions, more needs to be done. Toward that end, FDA has identified three basic strategies that should ensure more consistent application of the scientific perspective to communication activities.

Science Strategy 1: Identify gaps in key areas of risk communication knowledge and implementation, and work toward filling those gaps
It is apparent that many gaps remain in our knowledge about the communication needs of our various audiences. A few sample questions include the following.

- How much and what kind of information do physicians and patients need to make informed decisions on appropriate prescribing or use of a particular medical product?
- How much quantitative information on the risk of using a recalled food should FDA give the public?
- How much quantitative information should FDA provide or require manufacturers to provide about prescription drugs or medical devices?
- How much benefit information is needed about risk information to create a "balanced" perception of a medical product?
- What are the major motivators to persuade an individual to use nutrition facts labels for effective decision-making about weight management?

Furthermore, to provide audiences with the context they need to understand FDA's actions, especially the degree to which FDA can take specific actions to ensure public safety, we need to better understand the public's knowledge of the scope of FDA's authority.

With this in mind, a key action item under this strategy to strengthen FDA's risk communication science is to create a prioritized risk communication research agenda. This would have a dual purpose—to guide FDA's own decisions about the risk communication research it should conduct and to facilitate academic and private-sector research that explores risk communication issues of interest to FDA.

Science Strategy 2: Evaluate the effectiveness of FDA's risk communication and related activities and monitor those of other stakeholders

It is essential to understand our audiences' basic needs. How do we best communicate the facts we have so that audiences will understand and use them? In addition, effective health and risk communication involves conducting formative and evaluative research. Formative testing includes initial research into audience needs and decision strategies around particular issues, along with message pre-testing. Such steps are important to ensure that audience feedback is incorporated so as to maximize the efficacy of the message design process. In this way, initial areas of confusion and misinterpretation can highlight aspects of a message that require further work. Conducting evaluative research following the use of a message or tool is also necessary—especially if using a new approach—to determine if it has been effective in achieving its objectives, and to clarify whether revision is needed.

FDA uses research to test materials

FDA's Office of Women's Health (OWH) regularly uses focus groups to test the educational materials it issues. OWH also provides those materials in multiple languages.[9] OWH works with its dissemination partners to assess the materials'

[9] See http://www.fda.gov/womens/pubs.html

effectiveness on individual beliefs and behaviors. FDA's Center for Food Safety and Applied Nutrition has similarly evaluated educational campaigns about safe food handling practices to ensure that communication objectives are met. Surveys of consumer food safety knowledge, attitudes, and behavior are regularly conducted to help determine the effectiveness of food safety campaigns and the direction of future education programs. But evaluation is not a consistent practice across the agency. FDA is committed to working toward more consistency in assessing and evaluating its own communications.

FDA is also striving to ensure that it and regulated industries, as appropriate, evaluate the communications and communication-related activities conducted in response to regulatory mandates. For example, Section 901 of the Food and Drug Administration Amendments Act of 2007 requires evaluations be conducted to determine whether to modify the elements of a Risk Evaluation and Mitigation Strategy (REMS)[10] for a subset of prescription drugs with serious risks.

As a further example of ongoing efforts, in renewed dialogue between FDA's Office of Special Health Issues (OSHI), including its MedWatch staff, and multiple healthcare professional organizations, FDA asked for feedback about what their members knew about the MedWatch program's products. The agency also asked how to improve written communications so it could help these organizations inform their membership about emerging risks associated with medicines and medical devices. The information gleaned from this dialogue is providing feedback about success to date and is guiding FDA in improving future communications.

Science Strategy 3: Translate and integrate knowledge gained through research/evaluation into practice

Knowledge is gained through basic research, formative testing, and message or program evaluation. However, that knowledge has no value to any organization unless it is packaged in a form that can be circulated and used by those who need it. Having formal processes in place to disseminate research results and lessons learned within the organization will prevent the same mistakes from recurring. FDA is committed to ensuring that knowledge acquired through research and evaluation will be translated so as to be useful to communication designers, effectively disseminated, and incorporated into agency communication practices.

FDA has recently completed and is analyzing data from a survey of physicians about their use and perceptions of emerging risk information on medical products, including:

- the impact of news about emerging risks on their patients and practices
- when and how they would like to receive such information
- what sources they find most trustworthy
- the degree to which they use electronic sources
- the factors that influence whether they report medical product problems and adverse effects

[10] formerly known as Riskmaps

For this information to be useful, it must be analyzed with an eye to the needs of its audiences—in this case, FDA staff. The information must be marketed internally and presented in a way that will best meet the requirements of relevant staffers to help produce communication materials that reflect this new data on stakeholders' needs.

Expand FDA's *capacity* to generate, disseminate, and oversee effective risk communication

Along with obtaining the scientific knowledge needed to prepare effective risk communications and evaluate impact, FDA must be able to apply that knowledge. Doing this effectively and efficiently requires that the operational capacity of FDA's communications be adequate and that the processes associated with developing and coordinating risk communications be optimal. FDA has identified seven strategies it believes will expand its capacity both to generate effective risk communication and to oversee effectively the risk communication-related activities of regulated industries.

Capacity Strategy 1: Streamline and more effectively coordinate the development of communication messages and activities

Risk communication-related activities take place at many levels within FDA, including within the product-focused centers, the Office of Regulatory Affairs, and the Office of the Commissioner. To ensure that FDA speaks with one voice, efficient internal and external coordination are required. In addition to coordinating internally and with the Department of Health and Human Services (DHHS), FDA often shares responsibility for dealing with certain products or addressing food-related contaminations or outbreaks with other government agencies, including, among others, the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA). In these cases, seamless coordination among the agencies increases the timeliness and consistency of communications on identical issues.

Capacity Strategy 2: Plan for crisis communications

Many crisis communication situations—especially disease outbreaks related to food contamination—are true emergencies in which FDA and its partners (see Capacity Strategy 1) must develop and disseminate communications unexpectedly, swiftly, and often on a continual basis. In such cases, FDA is unlikely to have thoughtfully developed and tested messages available for a specific emergency. But the agency can apply lessons from similar past experiences as well as its knowledge of the products that are most vulnerable to contamination—accidental or deliberate. FDA can use these lessons learned to develop general procedures, tentative communication dissemination plans, and prototype messages for various audiences that can be adapted to specific circumstances.

For example, FDA is analyzing data from interviews with consumers focused on their preparedness for a food terrorism event. The agency will use this information to develop strategies to communicate more effectively with consumers should such an event occur. The agency is also creating an FDA call center that will improve how the agency handles phone calls about regulated products that are received outside of normal business hours. In a related move, FDA is increasing its surge capacity for managing a larger-than-normal volume of emergency-related calls during and outside of normal business hours.

Capacity Strategy 3: Streamline processes for conducting required communication research and testing, including evaluation

FDA is committed to:

- conducting and encouraging others to conduct the research and testing needed to develop and disseminate communications according to evidence of how they are likely to be encountered, attended to, understood, and acted upon by target audiences
- evaluating the degree to which a communication process was successful in achieving its objectives

In fact, past FDA research has informed various communication-related initiatives, including development of:

- the Nutrition Facts label for foods
- the Drug Facts label for nonprescription drugs
- format revisions to prescription drug prescribing information

FDA is conducting research on both the detailed information ("brief summary") required for inclusion in prescription drug advertising directed to consumers, and on how consumers interpret various statements on the front-panel display of food labels. However, this research often takes years to develop and implement. FDA is committed to streamlining the required processes for moving research projects from conception to implementation so as to make these processes as efficient as possible.

Producing effective communications requires that initial drafts be tested, preferably with target audience members. This enables drafters to determine whether the communication is meeting its objectives and whether there are likely to be unintended negative effects. However, the lengthy process needed to gain approval for conducting research and testing can make it difficult to test communications with more than nine[11] members of the public in the time needed for rapid communication, especially about emerging risks of regulated products.

[11] Requirements of the Paperwork Reduction Act of 1990 include the need to seek public comment and clearance from the Office of Management and Budget when information is collected from more than nine members of the public.

Piloting message testing using government employees as public surrogates

Streamlining processes as much as possible is one part of this solution. Another part relates to FDA's policies (see also Policy Strategy 3). While FDA moves toward these improvements, it is also piloting the feasibility of using government employees as public surrogates to informally test messages and communication formats before issuing messages, especially when it is critical to communicate quickly with the public.

FDA recognizes that, scientifically, this is not an ideal solution because these employees may not be completely representative of the agency's target audiences. However, this approach is much more readily implemented than an external study and allows testing prior to making the message public. There are many employees who could be reasonable surrogates for different members of the public on a given topic because their work lies in areas significantly different from that topic. Additionally, using employees allows testing messages that could be difficult to test with the public because the information is confidential.

Capacity Strategy 4: Clarify roles and responsibilities of staff involved in drafting, reviewing, testing, and clearing messages

Within FDA, there is a need for greater clarity about who in the communications review chain is responsible for determining that an information piece has been sufficiently refined for a particular target audience. FDA's messages about regulated products are scrupulously reviewed by staff members with different types of expertise. Depending on the product and issue, reviewers may include physicians, pharmacists, biologists, chemists, pharmacologists, nutritionists, engineers, communications professionals, attorneys, compliance officers, and policy analysts.

Although the targeted audience is often patients or caregivers, it is uncommon for anyone from that target audience to be included in the review chain. Consequently, messages initially designed to communicate a simple point can grow excessively lengthy and complex. Expert staffers want to ensure that the message is scientifically and legally precise but stakeholders have frequently told FDA that the resulting messages are too complicated and not easily understood by non-specialists.

FDA also believes that it can improve the internal review process by raising reviewers' awareness about factors that must be explicitly balanced for the best communications results. For example, reviewers could be further educated to consider the needs of certain vulnerable populations, including those with limited English proficiency, health literacy, or limited ability to understand and use numbers (numeracy).

Reviewers can also be educated to weigh the benefits of including highly detailed information that provides greater precision against the increased likelihood of information overload. A shorter, more focused message may not address an issue's every nuance, but it ensures that a less literate audience will be able to understand

critical messages and recommendations. Tiering the information—providing a shorter and simpler message first, followed by additional detailed information for those who want it—may help achieve a balance in these competing but worthy objectives.

Capacity Strategy 5: Increase staff with decision and behavioral science expertise and involve them in communication design and message development

As a result of the issues discussed in previous sections, producing effective FDA risk communications and ensuring that regulated industries produce effective risk communications have become increasingly important FDA functions. Fischhoff[12] asserts that effective risk communication requires the contribution of four types of specialists:

- domain specialists
- risk and decision analysis specialists
- behavioral science specialists
- systems specialists

Applying this framework to FDA staffing, it is clear that the agency has many domain specialists—individuals with expertise in medical and physical sciences who understand the risks and benefits data that need to be communicated to product users. But FDA is not well staffed with the risk and decision analysts needed to identify the information that is necessary to user choices. Nor is it well-staffed with the behavioral scientists it needs to design and evaluate messages. Finally, while communications systems specialists are somewhat better represented within FDA, more are needed to create and use communication channels more effectively.

Capacity Strategy 6: Improve the effectiveness of FDA's Web site as a primary mechanism for communicating with different stakeholders

FDA's Internet Web site is a primary vehicle for communicating with the public—both directly and through the press. This is especially so when FDA is conveying information about new and potentially uncertain or emerging risk information, product recalls and warnings with significant public health consequences. FDA's Web site provides a wealth of information about:

- how products are reviewed
- how product quality is monitored
- the myriad regulatory and policy actions the agency takes
- how external advice has been given to FDA
- how FDA takes advice into account when it acts

However, the volume of information provided itself has a downside. In December 2005, FDA held a public hearing about the effectiveness of the agency's risk communication strategies for human drugs. Stakeholders told FDA that its drug-related Web information is difficult to navigate and needs to be redesigned to make

[12] Presentation to Risk Communication Advisory Committee Meeting, August 14, 2008. See slide 10 at http://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4377s1-01.pdf

it "more accessible and user-friendly as well as to address specific health concerns of patients, caregivers, and healthcare professionals."[13]

FDA is preparing to launch a Web Content Management System that will improve the timeliness, ease of navigation, usefulness, and usability of its Web materials. As part of this modernization effort, FDA is also removing outdated, extraneous, and unused materials. The agency has also begun making changes to its Web site to improve its information architecture.

In addition, FDA recognizes its need to explore the variety of electronic tools that fall under the broad scope of the Internet. The agency already uses email distribution lists, RSS feeds, podcasts, widgets, and other tools when appropriate for a particular communication purpose. However, the always-expanding supply of new tools highlights the need for constant vigilance in assessing the potential value of these tools for improved communication.

Forming Web partnerships to broaden FDA information distribution

The agency has begun forming partnerships with organizations to maximize the distribution of FDA's information. It recognizes the current limitations of its Web site and that many stakeholders access other sites more frequently than FDA's. Thus, in early December 2008, FDA announced a formal partnership arrangement with WebMD, which will make consumer health information associated with FDA-regulated products more accessible by having an FDA-focused Web page on WebMD's site.[14] The agency is pursuing other partnership arrangements, including with the CDC, to examine the value of social media and networking tools to communicate time-sensitive product information expeditiously.

Capacity Strategy 7: Improve two-way communication and dissemination through enhanced partnering with government and nongovernment organizations

At the December 2005 public hearing on the effectiveness of FDA's risk communication strategies for human drugs, some participants commented that the agency should "concentrate on its traditional role of providing benefit–risk information to healthcare practitioners that would improve patient dialogue." Participants also advised FDA to target specific specialties and work closely with those groups to "optimize education in risk communication."[15]

Improving relationships with medical professionals

FDA acknowledges that ensuring continual dialogue with medical professionals is crucial. In fact, within the past few years, FDA has reestablished its efforts to develop and maintain productive relationships with medical and pharmacy

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[13] See http://www.fda.gov/cder/meeting/RiskComm2005/summary.pdf.
[14] See http://www.webmd.com/fda
[15] See http://www.fda.gov/cder/meeting/RiskComm2005/summary.pdf.

professional organizations, and is committed to continuing this approach. The Office of Special Health Issues (OSHI) and the MedWatch staff are working with several organizations to devise a mechanism for targeting MedWatch safety alerts and monthly notices of changes to the safety labeling of prescription drugs to a subscriber subset who wish to receive selected notices. Through OSHI, FDA is working with the American Medical Association to develop an "FDA Specialty Network." Among other things, this network would target particular medical specialties for two-way communication. OSHI is planning to pilot targeted messaging with the American Academy of Clinical Endocrinologists, a member of the Specialty Network.

Improving relationships with other government stakeholders

FDA also recognizes that it needs to establish and continue to improve working relationships with other government agency stakeholders like CDC, USDA, the Agency for Healthcare Research and Quality (AHRQ), the Centers for Medicare & Medicaid Services (CMS), the Department of Defense (DoD), the Department of Homeland Security (DHS), and the Veteran's Administration (VA).

Sharing early information with other stakeholders should make working relationships more effective and place greater value on collaboration. FDA has already established Memoranda of Understanding with DoD and VA to improve communication with these organizations, which have information about and responsibility for large numbers of patients. The agency's Planning Office's Risk Communication Staff has also set up regular teleconferences with regulatory and communications officials from Health Canada to improve coordination of strategic risk communication.

FDA and the foods industry, through a non-profit consortium, have collaborated successfully on joint education efforts. This collaboration represents another type of partnership that FDA aims to advance. Along with USDA and CDC, FDA is a member of the Partnership for Food Safety Education, which also includes the Food Marketing Institute, the Grocery Manufacturers Association, and other industry groups. This not-for-profit organization is the steward of the "Fight Bac" campaign that is designed to keep food safe from harmful bacteria through public education about safe food handling practices.

Optimize FDA's *policies* on communicating product risks and benefits

The third strategic goal focuses on FDA's policies on risk communication. Applying the results of the science goal strategies and implementing some of the capacity strategies requires streamlining internal and externally focused FDA policies. Three strategies under the policy goal target internal policies around FDA-generated risk communications. The fourth strategy targets policies associated with risk communications that FDA oversees.

Policy Strategy 1: Develop principles to guide consistent and easily understood FDA communications

Risk communications would be better understood and applied if internal policies were established specifying the kind of information that should be consistently included. For example, FDA's Risk Communication Advisory Committee has repeatedly recommended that FDA's risk communications include both product benefit and risk information, presented to the extent possible in quantitative formats.

Additionally, some Committee members have noted the need to ensure that the public understands fully the context of approvals and recalls. For example, risk communications about approved products may at times need to state clearly that efficacy and risk information was established only for the product's intended use(s) and might not apply if someone uses it in another way. FDA also may need to address how to improve public understanding of the limits of FDA's authority, at least to the extent it is relevant to informed decision-making about regulated products (see also the discussion in Science Strategy 1).

Based on the information from literature, testing, and basic research, other evidence-based principles for communication documents could address the following.

- When to include the risks and benefits of *not* using particular products associated with emerging risks.
- How to ensure that lower literacy audiences are given only essential information.
- How tiering or layering messages can improve communication of critical information.
- How to ensure the clarity of product use recommendations.
- How people can get additional risk communication/information.

Policy Strategy 2: Identify consistent criteria for when and how to communicate *emerging* risk information

Although FDA has moved toward communicating earlier and more transparently about emerging risks of regulated products, particularly medical products, it does not have a comprehensive, science-based set of principles about when and how to communicate this information.[16] Therefore, the criteria that FDA uses to determine when to communicate about regulated products are likely to be unclear to the public. Additionally, FDA uses different types of communications to address emerging risks for different types of regulated products. Issuing multiple documents with similar purposes can be confusing for stakeholders. To avoid this,

[16] Emerging risks of medical products refers to information about potential product risks that is still uncertain – that is, there is either not yet a full analysis or a clear confirmation that a specific identified risk is associated with the product in question.

the agency must clarify, both internally and externally, when and how it will communicate about emerging risks of FDA-regulated products, and how to standardize communication formats.

Policy Strategy 3: Re-evaluate and optimize policies for using partnerships and other leveraging activities to facilitate effective communication about regulated products

It is generally accepted that critical communications should be tested prior to use with the intended target audience. However, as discussed earlier, this process is often time-consuming and therefore may not be feasible for crisis situations. As Capacity Strategy 7 notes, FDA is committed to partnering with both governmental and nongovernmental entities to improve the value and reach of its risk communications. In addition to creating a more effective interactive risk communication environment, sharing messages before issuance with organizations representing critical stakeholders (especially when the target audience is medical professionals) could provide some timely feedback. However, FDA's policies on confidentiality, ethics, and other considerations require that acceptable parameters be established for such interactions.

Policy Strategy 4: Assess and improve FDA communication policies in areas of high public health impact

FDA recognizes the need to consider how to optimize policies on its oversight of the communications of regulated industries. This is especially critical when industry communications deal with issues that have a major public health impact. Some of the areas that FDA is currently examining are listed below.

- ***Modernize effective communication in a recall.*** FDA issues some communications on recalls. However, product manufacturers have the primary responsibility for most of the notices and for follow-up with wholesalers or retailers to decide whether recall activities are addressing the particular safety issue satisfactorily. FDA is examining the impact of a recent food recall and will investigate the degree to which, if at all, new social media tools that FDA and CDC used contributed to the recall's outcome. This investigation's results could have implications for how FDA asks regulated industry to act in future food recalls.

- ***Ensure that patients get useful written information about the prescription drugs they use***. On the basis of a congressionally mandated study, FDA recently determined that private-sector efforts have not succeeded in meeting congressionally mandated goals to ensure that patients filling new prescriptions get useful written information on the drugs they are given.[17] The failure of these efforts allows FDA to examine and potentially take regulatory action to ensure that patients get this information.

[17] See http://www.fda.gov/cder/news/CMI/default.htm

However, the combination of private sector-produced information and increasing numbers of manufacturer-drafted, FDA-approved information (Medication Guides and Patient Package Inserts) has created a potentially bewildering array of written information for patients—multiple formats, inconsistently distributed. Various stakeholders have noted that the excess of information and inconsistent content and formats could confuse patients and lead to error. Consequently, FDA is revisiting the current approach to the content and format of written prescription drug information provided to patients. It is evaluating how best to ensure that patients getting prescription drugs (including biologics) receive the information they need, in an optimal form and format, to use products with maximal benefit and minimal risk.

- ***Ensure that medical professionals get useful information about FDA-regulated products when and in the form they need it***. Historically, FDA has focused on communicating with medical professionals about medical products. As well as having primary responsibility for using significant medical devices and animal drugs, these professionals have the most influence on the decisions that patients make about product use, especially drug and certain device use, and the decisions that consumers make about human and animal nonprescription drug use. As Capacity Strategy 7 describes, FDA has recently devoted additional resources to re-establishing and maintaining relationships with medical and pharmacy professional groups. Part of that effort has involved looking at how FDA can better provide more effective two-way communication with these professionals. The agency is also seeking opportunities to work with them to make available information that professionals need at the time of clinical decision-making.

- ***Modernize the regulation of prescription drug promotion***. FDA regulates both advertisements and labeling (including approved prescribing information and promotional materials like mailed literature, brochures, scientific study reprints, videos, and press releases) for prescription drugs and biologics. The current regulations were developed when such promotional materials were only directed to medical professionals, and may create confusion when applied to consumer-directed advertising. For example, these regulations require that FDA enforce regulatory distinctions in information disclosure ***between*** the two categories of promotional materials (advertisements versus labeling), even though such distinctions are not meaningful to a targeted consumer audience.

  Other regulations require that FDA enforce identical information disclosure requirements ***within*** each promotional material category (ads and labeling), regardless of whether the target audience is medical professionals or consumers. The result is that consumer-directed advertisements generally include highly technical information that can be difficult to sort through.

  In recent years, FDA has researched and solicited public comment on consumer-directed prescription drug advertisements. It has issued guidance (some draft and some final) on how advertisements directed to consumers can provide information in language that is more easily understood by this audience and still

meet regulatory requirements. In light of direction from the Food and Drug Administration Amendments Act of 2007, research data, and public comment, FDA is proactively developing additional guidance and devising regulations that will further address these communication issues to better meet the needs of consumers and medical professionals, and provide greater clarity for industry.

Conclusion

FDA considers risk communication as a strategic activity. To this end, the agency must address its audiences' needs more effectively in planning and implementing its own risk communications for regulated products and in its oversight of regulated industry communications. The agency has identified the areas in which it needs to improve and has begun:

- enhancing the science behind FDA risk communication
- expanding the agency's capacity to generate, disseminate, and oversee risk communication about regulated products
- optimizing its policies on communicating product risks and benefits

These actions will help FDA achieve its goals of improved public health and safety through increasing the appropriate use of regulated products.

FDA Risk Communication Advisory Committee

Location: 5630 Fishers Lane, Room 1066, Rockville, MD
April 30-May 1, 2009
AGENDA (DRAFT)

April 30, 2009

8:00 Call to Order
8:05 Conflict of Interest Statement – Designated Federal Officer
8:10 Introductions of Committee Members

8:30 Introductory Remarks
Baruch Fischhoff, Ph.D – Objective of meeting

8:45 Strategic Planning at FDA
Malcolm J. Bertoni, M.S., Assistant Commissioner for Planning
Member Questions/Answers

10:00 Break

10:15 Goal: Expand FDA's Capacity to Generate and Oversee Risk Communication
Susan C. Winckler, RPh, Esq., Chief of Staff
Member Questions/Answers

Discussion of Capacity Goal and associated FDA Discussion Topics

12:00 Lunch

1:00 Open Public Hearing

2:00 Goal: Optimize FDA's Policies on Communicating Product Risks and Benefits
Jeffrey Shuren, M.D., J.D., Associate Commissioner for Policy and Planning
Member Questions/Answers

Discussion of Policy Goal and associated FDA Discussion Topics

3:15 Break

3:30 Goal: Strengthen the Science Supporting Effective Risk Communication
Nancy M. Ostrove, Ph.D., Director for Risk Communication
Member Questions/Answers

Perspective: Select Models for Conducting Research Needed by Government Agencies
Baruch Fischhoff, Ph.D., Professor, Carnegie Mellon University
Member Questions/Answers

Discussion of Science Goal and associated FDA Discussion Topics

5:00 Adjourn for the day

May 1, 2009

8:00 Call to Order
8:05 Conflict of Interest Statement – Designated Federal Officer
8:10 Introductions of Committee Members

8:20 Prioritization of Risk Communication Research
Nancy M. Ostrove, Ph.D., Director for Risk Communication

Member Questions/Answers and Discussion

10:15 Break

10:30 Open Public Hearing

11:30 Lunch

12:30 Summarize what has emerged from discussion regarding FDA discussion topics

2:30 Adjourn