AIRBORNE RELEASES: SHORT-TERM ADVISORIES AND CUMULATIVE EFFECTS

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ABSTRACT

Health concerns related to contaminant releases at facilities have heightened because of recent terrorist incidents, and homeland security considerations have become part of emergency preparedness and response planning. To guide incident responses associated with industrial releases, whether from stationary facilities or transport vehicles, several agencies and organizations have developed emergency guideline levels for a variety of common-use chemicals to cover the period of up to a day; for example, acute guidelines cover exposures ranging from 10 minutes to 8 and 24 hours. Other standards and guidelines exist for chronic, routine workplace exposures. However, the intentional release of contaminants by terrorists involves issues not covered by available limits. Many threat contaminants have not been well studied, so no relevant advisories exist to serve as a starting point. Furthermore, for these "intentional impact" situations, consequence management can involve large-scale rescue and recovery operations that extend well beyond a day to a month, with some lasting much longer. The interval of 1 to 30 days can also be crucial for restoring critical functions and for forensics, and it can be a make-or-break period for at least localized economic survival for small businesses. Where health-based guidelines do exist, few apply to this time period when reentry or reuse decisions must be made. This gap is being addressed by the U.S. Environmental Protection Agency under a homeland security program. The initial emphasis is on developing a process to identify operational exposure advisories for air in buildings, which involves (1) reviewing existing standards and guidelines for air to determine if they should be adopted or adapted, depending on the relevance of their bases; (2) assessing toxicity data, including for sensitive subgroups, and considering extrapolation approaches as indicated; and (3) considering cumulative exposures and effects where possible, as well as incorporating organizational factors and insights gained in assessing other exposure guidelines, such as for drinking water. During the development of this general process for defining appropriate exposure advisories, several basic findings were identified that can be used to guide the determination of contaminant-specific levels during the next phase of this ongoing homeland security effort. These finding include: no single standard or extrapolation approach can be generically applied, advisories should address specific durations and effect tiers, adjustments for sensitive subgroups should be identified, and the cancer endpoint can play a role.

BACKGROUND ON ADVISORY LEVELS STUDY

For many years, the U.S. Environmental Protection Agency (EPA) has developed health-protective levels and related toxicity values to address chronic exposures for programs such as safe drinking water, solid waste and emergency response, and ambient air, and that effort continues. The Agency has also been participating in the development of emergency guidelines for air for the general public. Because of recent homeland security events, additional contaminants that terrorists could release to buildings or drinking water supplies must now be considered, as must other time periods beyond those typically evaluated for other programs. The aim is to proactively assess toxicity information and develop working draft advisories so these can be available to help guide health-based response measures if certain contaminants are released in the future. (Many chemicals could also be released during industrial accidents, so the advisories being developed could also be used to help guide responses under other circumstances.)

For various reasons, people might want to reenter affected buildings within a day to a month following the contaminant release (consider the experience in New York City after 9/11). These reasons can include conducting rescue or recovery operations, maintaining or restoring critical functions (such as electricity, communication, or medical care), collecting evidence (forensics), and conducting essential business activities to maintain economic viability. Given various pressures for reentry, people need information about possible health effects to determine whether and when reoccupation would be reasonable. (Similar issues affect the reuse of drinking water supplies; recognizing that restoring water use is one element of returning a community to more normal conditions, complementary advisory levels for acute and short-term ingestion are also being developed under a companion effort.) Four main exposure periods can be identified that correspond to different phases of response and reuse, as shown in Table I. The first emphasis is on the near term, represented by acute and short-term exposures. The evaluation also considers the potential for cumulative exposures (to more than one contaminant, and by more than one route of exposure) and joint toxicity (e.g., synergistic and antagonistic effects).

Table I. Exposure Periods of Interest

Exposure	*Duration*	*Purpose*
Acute	Up to 1 day	Emergency response
Short term	From 1 to 30 days	Initial cleanup/reuse
Intermediate to subchronic	From 1-24 months (with subcategories) to 2 to 7 years	Further cleanup and return to normalcy
Chronic	From 7 years to lifetime	Final residual levels

A key question is what level could be considered acceptably safe for humans. The first set of advisory levels is designed to reflect a level of exposure at which some people might experience mild, temporary, reversible effects that would stop when the exposure stops and would not result in any long-term harm, while others would experience no effects. These levels could be used to guide initial rescue and recovery operations and further consequence management. Subsequent advisories will focus on concentrations at which no effects would be expected across a range of individuals, e.g., to help guide final cleanup. To frame these evaluations, existing standards and guidelines relevant to the near-term period were reviewed.

Selected Standards and Guidelines for Air

Various federal agencies and scientific organizations have developed exposure standards and guidelines for air. Those designed to protect people in the workplace, commonly addressing exposures for 8-hour days and 40-hour weeks over a working lifetime, include:

- U.S. Occupational Safety and Health Administration *permissible exposure limits* (PELs) and *short-term exposure limits* (STELs) – which are national standards.
- National Institute for Occupational Safety and Health *recommended exposure limits* (RELs) and STELs – which are recommended guidelines rather than enforceable standards.
- American Conference of Governmental Industrial Hygienists *threshold limit values* (TLVs) and STELs – which are recommended guidelines rather than enforceable standards.
- U.S. Department of Defense, U.S. Army Center for Health Promotion and Preventive Medicine *airborne exposure limits (*AELs) – which represent allowable concentrations for Army occupational and general population exposures rather than enforceable national standards.

Guidelines designed to protect communities and military personnel in emergencies, addressing acute exposures typically from 10 minutes to 8 hours, include:

- National Research Council, National Advisory Committee *acute exposure guideline levels* (AEGLs) – which are benchmark or threshold levels for the general public, including susceptible subpopulations, for exposures ranging from 10 minutes to 8 hours.

- American Industrial Hygiene Association *emergency response planning guidelines* (ERPGs) and U.S. Department of Energy *temporary emergency exposure limits* (TEELs) – which are planning guides for the general public (not all hypersensitive individuals), for 1-hour exposures.

- U.S. Department of Defense, Army Center for Health Promotion and Preventive Medicine *military exposure guidelines* (MEGs) – which are air concentrations defined for 1- to 24-hour exposures of deployed military personnel, with some guidelines extending to 14 days.

- Agency for Toxic Substances and Disease Registry *minimal risk level*s (MRLs) – acute MRLs are typically conservative screening levels for the general public, including sensitive individuals, for exposures of less than 1 to 14 days. (An intermediate MRL for 14 days to 1 year also exists.)

Basic information about these standards and guidelines is presented in Table II; air concentration guides developed by selected states, including California, were also reviewed, as were guidelines for water [1-10]. From this review, it was found that health-based standards and guidelines are not available for a number of threat agents, many of which are not commonly found or used and have not been well studied. Although certain guidelines exist for a number of industrial chemicals, most address chronic exposures extending over many years to a lifetime; relatively few address the critical time periods associated with incident response and consequence management. Beyond the emergency period, repeat exposures could occur from days to months after an event, and these conditions have not yet been well assessed.

General Approach for Addressing New Advisory Needs

The operational advisories for homeland security are being developed under a phased approach. Pilot studies are being used to identify technical issues and methodology options associated with deriving working draft values for threat contaminants over different time intervals relevant to homeland security. The development of these values builds on relevant standards and guidelines where they exist, combined with a targeted evaluation of toxicity and exposure data relevant to the durations and routes of interest. It is important to emphasize that these values address unique needs that differ from those covered by many existing exposure advisories. For example, for contaminated facilities being addressed under the Superfund process [11], cleanups have traditionally targeted residual concentrations that represent a high confidence of no adverse health effects over a long exposure period. These are typically based on projected scenarios with hypothetical receptors and would use EPA's reference concentrations to account for lifetime inhalation exposures. In contrast, the short-term homeland security situation involves specific people who would want to access affected areas and who need specific health context, e.g., to determine whether they would accept minor, transient effects as a tradeoff to be able to respond to urgent needs.

For this study, the more detailed evaluation of underlying toxicity data (most of which are currently based on chronic studies) considers the route, duration, and frequency of the exposure; the characteristics of the group for whom the levels were developed (e.g., from deployed troops to sensitive groups like asthmatics); and the thresholds for different effect tiers, from no effects and minor, reversible effects to more serious effects and death. Time-specific extrapolation approaches are also evaluated, including Haber's rule to adjust for duration, as are uncertainty or modifying factors (e.g., to account for variability within and across species) and numerical techniques.

Table II. Selected Standards and Guidelines for Worker and Community Exposures to Air Contaminants

Limit and Organization	*Summary Description*
Workplace (addressing exposures for conventional workdays and workweeks that extend over many years)	
AEL: Airborne Exposure Limit *CHPPM: Center for Health Promotion and Preventive Medicine, U.S. Army, Department of Defense*	The AEL is a time-weighted average (TWA) concentration based on 8-hour workdays and 40-hour workweeks over the long term. The Army has defined AELs as allowable concentrations for both occupational and general population exposures. The AEL is a guideline rather than a generally enforceable standard.
PEL: Permissible Exposure Limit *OSHA: Occupational Safety and Health Administration*	The PEL is a TWA concentration not to be exceeded during any 8-hour workshift of a 40-hour workweek. PEL ceiling levels (concentrations not to be exceeded) and STELs (see below) also exist. Values are periodically updated (developed over many decades, not all values reflect current scientific knowledge). The PEL is an enforceable legal standard.
REL: Recommended Exposure Limit *NIOSH: National Institute for Occupational Safety and Health*	The REL is a TWA concentration for up to a 10-hour workday during a 40-hour workweek. As for PELs, the RELs also have associated STELs and ceiling values. The REL is a guideline rather than an enforceable standard.
STEL: Short-Term Exposure Limit *OSHA and NIOSH (as above), and ACGIH: American Conference of Governmental Industrial Hygienists*	The STEL is a 15-minute TWA concentration, and OSHA, NIOSH, and ACGIH have defined these short-term limits to supplement their respective workday TWA levels (i.e., PELs, RELs, and TLVs). In contrast to those for enforceable PELs, the STELs for the RELs and TLVs are guidelines rather than enforceable standards.
TLV: Threshold Limit Value *ACGIH (as above)*	The TLV is a health-based TWA concentration for an 8-hour day and 40-hour workweek for a working lifetime. As for PELs and RELs, ceiling values exist for TLVs. The TLV is a guideline, not a standard.
General Public and Military Personnel (addressing releases, primarily for acute exposures of less than a day)	
AEGL: Acute Exposure Guideline Level *NAC: National Advisory Committee of the National Research Council*	The AEGL is for acute exposures from 10 minutes to 8 hours. It is a health-based benchmark for the public, including susceptible subgroups such as children and the elderly. The AEGL-1 is the concentration above which nondisabling, transient, reversible effects could occur. The AEGL-2 is the concentration above which irreversible or other serious, long-lasting health effects or an impaired ability to escape could occur.
ERPG: Emergency Response Planning Guideline *AIHA: American Industrial Hygiene Association*	The ERPG is for acute 1-hour exposures and corresponds to three effect levels used to guide community emergency planning for release situations. Health-based, the ERPG is a tolerable-effect level considered protective of the general public, including sensitive subpopulations but not necessarily hypersensitive individuals.
MEG: Military Exposure Guideline *CHPPM (as above)*	Short-term MEGs for deployed personnel address acute exposures of 1, 8, and 24 hours; 14-day MEGs address longer continuous exposures; most are for minimal or no effects.
MRL: Acute Minimal Risk Level *ATSDR: Agency for Toxic Substances and Disease Registry*	The acute MRL covers exposures of less than 1 day to up to 14 days. It typically represents a conservative screening level derived from the no-observed-adverse-effect level and is designed to be protective of the general public, including sensitive individuals.
TEEL: Temporary Emergency Exposure Limit *DOE: U.S. Department of Energy*	The TEEL is for acute 1-hour exposures and is designed for situations involving chemicals for which an ERPG or AEGL is not available. Based on a numerical estimate rather than a toxicological evaluation, it would not be expected to protect all members of the public.

Terrorists might use a variety of contaminants, ranging from industrial chemicals, poisons, and chemical warfare agents to biological agents/biotoxins and radionuclides. Five criteria were identified to select an initial set of contaminants for study. These are (1) threat (accessibility and inherent hazard, coupled with community threat perceptions), (2) existence of a guideline (that might be adopted or adapted; this criterion helped simplify the first effort), (3) persistence following release, (4) detectability, and (5) potential for interactions. The last criterion was included to help ensure that the working draft advisory levels would consider the potential for cumulative effects of mixtures, e.g., to account for joint toxicity where releases involve a combination of contaminants [12].

As part of this study, current guidelines were converted to common units (e.g., translating ppm to mg/m^3, and for the radionuclides, pCi to mg) to facilitate direct comparisons and offer context for the relative detection accuracy needed when the operational advisories are defined. The analyses will also consider how the form or species of individual contaminants could change during the time period studied, including because of nonstandard conditions (e.g., if temperatures in an affected building were higher than those on which current guidelines were based). As an additional complication, dispersion and deposition of released contaminants would be affected by air movement, so concentrations could vary across individual locations. Thus, it would be important to account for this effect when comparing measured concentrations to the operational advisory level(s) if a terrorist release were to occur.

Findings and Recommendations

The development of an assessment process to define operational exposure advisories for homeland security purposes is ongoing. Although contaminant-specific results are not yet available, several findings related to the development process have been identified. With an initial focus on short-term inhalation exposures, these findings reflect unique homeland security needs, differences in attributes inherent to the wide range of contaminants that could be released, and limitations in relevant toxicity data and exposure guidelines. Key findings and associated recommendations are highlighted below.

1. Homeland security advisories *can differ from existing standards and guidelines* developed for other purposes, including to address additional *durations* of interest.

   Operational exposure advisories to address homeland security needs will differ from traditional guidelines because terrorist situations are unique and necessitate real-time, practical decisions regarding actual exposures that would be incurred. Many current guidelines developed for other programs focus on either chronic exposures or the acute, emergency period of minutes to 24 hours following an incident. Additional time periods are of interest for homeland security situations. With releases potentially affecting a large area, the short-term interval from 1 to 30 days could be important for rescue and recovery operations, and in some cases those operations could extend much longer. It is expected that a variety of other activities will also be considered crucial following a terrorist release, including restoring and maintaining critical functions. Thus, exposure levels corresponding to different durations of interest can help guide integrated incident/consequence management and longer-term community recovery. Directly related to this point, levels corresponding to other than the typical "no-effect" target would also be useful, as described in the companion findings below.

2. *Effect tiers* should be considered in developing these advisories for broad application.

   Many existing guidelines are designed to represent a high likelihood that no adverse effects of any kind will be experienced by anyone, often represented by hypothetical receptors. In the event of a terrorist release, specific people will need to address various priority needs. Some of these people might choose to accept exposures that could result in minor, transient effects (e.g., in order to sustain business functions), while others might choose to accept serious effects as a tradeoff in order to participate in rescue and recovery activities. Furthermore, it is important to know what concentrations could be lethal, e.g., to guide decisions about rescue attempts. Thus, exposure advisories corresponding to different effect tiers would help address pressures for reentry or reuse following a terrorist release. The initial phase of this study emphasizes "no effects" and "minimal, reversible effects" (the latter represents the concentration at which some people might experience mild effects that disappear after the exposure stops, with no significant or long-term harm, while others would incur no effects).

3. *Existing standards and guidelines* can serve as a good initial foundation for developing homeland security advisories.

   Where related guidelines exist, some might be amenable to direct adoption as an exposure advisory for homeland security, if the underlying toxicity data and exposure conditions are appropriate to the effect level and duration of interest. Given that the availability of a relevant standard or guideline was one of the criteria for determining an initial set of study chemicals to frame the development process for homeland security advisories, this finding is not surprising. Developing advisories for chemicals for which no relevant standard or guideline exists will be more difficult. Additional context regarding the application of existing exposure limits is provided in the following finding.

4. *No single standard or guideline* will apply across all threat contaminants and exposure durations.

   From the review of existing guidelines and standards for air in this initial study, no single basis was found to be best for short-term inhalation advisories across the small set of example chemicals evaluated. In fact, several different guidelines or standards were found to be appropriate across these chemicals for the effect tiers corresponding to no or minimal/minor, transient effects. This simply reflects the differences underlying available exposure guidelines and emphasizes the importance of conducting chemical-specific assessments rather than applying a generic hierarchy to determine health-based targets for short-term exposures.

   Nevertheless, a tentative default hierarchy was developed simply to guide the review of existing advisories. The 8-hour AEGLs (which reflect extensive peer review) were consulted first, and in fact these were found to be suitable for nearly half the example chemicals. Even in those cases, other guidelines and available workplace standards were assessed to provide a weight-of-evidence context, to help determine whether a short-term advisory that represented an existing acute AEGL might warrant any adjustment. The additional standards and guidelines that were identified as useful foundations for the example short-term advisories in this initial study included (extant) OSHA PELs, ACGIH TLVs, and an Army MEG and AEL.

   Although AEGLs are considered important starting points, it is useful to explain that these have only been developed for a small number of chemicals, roughly a dozen. For some chemicals, applying 8-hour AEGL-1 values (which correspond to transient, reversible effects) for short-term exposures of 1 day to 1 month might be judged to be less protective than other guidelines might be. Thus, further evaluations of the underlying toxicity data and toxicologic judgment are required. To illustrate for the example chemical chlorine, the 8-hour AEGL-1 value was found to be a sound basis for the corresponding short-term (1- to 30-day) value. This no-effect level does not vary with regard to toxic response over the period of 1 day, i.e., no extrapolation for time was deemed necessary in the development of that chlorine AEGL-1 value. From the review of supporting toxicity information for this study, it was determined that, similarly, no duration adjustment was warranted to address exposures from 1 to 30 days because for the no-effect level, the toxic endpoint (nasal congestion and slight irritation) only depended on concentration, not duration [13]. See the next finding for a further discussion of extrapolation across duration for the more serious effect tier.

5. *No single extrapolation approach* will apply across all contaminants, durations, and *effect tiers.*

   Some methods exist that could be applied to extrapolate from one duration to another, but their applicability depends on the nature of the individual contaminant and the duration and effect of interest. Haber's rule is an extrapolation approach that reflects accumulated dose and represents toxicity as a function of concentration and exposure duration; the modified form of this rule uses an empirically determined exponent with the concentration term. This first study showed that neither Haber's rule nor the modified form was needed to extrapolate over the short-term period for any of the example chemicals evaluated, considering repeated daily exposures extending from 1 to 30 days.

   However, this approach might be useful in certain cases. In reviewing toxicity data for this study, it was found relevant for one chemical but only within the acute time period, on the order of minutes to a few hours, as further discussed in Finding 6. Extrapolating beyond 1 day resulted in concentrations that did not correlate well with indicated toxicity data or relevant guidelines. Furthermore, as a general note, this approach would not directly account for new chemicals that could form within the 30-day period (e.g., from degradation processes), which could be important for certain threat contaminants.

   The role of the effect tier in evaluating extrapolation is illustrated by considering the AEGL-2 value for chlorine, again within the acute time period. The AEGL-2 value corresponds to serious, adverse effects that are generally long-lasting and irreversible. For chlorine exposures of less than 8 hours, this value was found to depend on duration. That is, two human studies showed that when the concentration at which no effects were observed was doubled, potentially serious effects were seen in asthmatic individuals (bronchial constriction and irritation), while nonasthmatic individuals continued to show no effects [13]. This finding emphasizes the importance of conducting chemical-specific evaluations targeted to the specific duration and effect tier being addressed.

6. *Sensitive subgroups and different effect levels* should be considered in developing these advisories for broad application.

   Some existing guidelines consider specific sensitive subgroups of the general population, while others account for inter-individual variability by applying a general "uncertainty" factor. For example, the AEGL-1 value developed for chlorine (which is considered a good basis for the short-term inhalation advisory) considers asthmatics and atopics (people with allergies), whereas the young, elderly, immunocompromised, and pregnant people are less specifically accounted for by applying an uncertainty factor of ten to address human variability. This variability in response across individuals is important to consider when developing practical exposure guides for different groups, to guide targeted exposure decisions that can range from healthy adults conducting forensics or rescue and recovery operations to children returning to schools.

7. Not all advisories will be driven by *noncancer effects*.

   Acute exposure guideline levels have historically focused on noncancer effects. Although this initial study focuses on short-term inhalation of selected chemicals with an emphasis on no or minimal, transient effects, a companion evaluation of drinking covered several radionuclides and considered additional effect tiers. These tiers included the level at which serious, irreversible effects could occur, as well as potential lethality. One key insight gained from those evaluations is that in some cases the "serious, irreversible effect" tier could be based on cancer risk rather than a noncancer endpoint. For an example radionuclide, a fraction of the estimated lifetime risk from natural background radiation (which is on the order of 10^{-2}) could be considered the basis for the serious, irreversible effect level because a higher concentration would be needed to incur serious noncancer effects from ingestion exposures of 1 to 30 days.

8. *Cumulative exposures and effects* could be a modifying factor for homeland security advisories.

   Most environmental contaminant levels are low enough that detailed analyses of potential toxicological interactions from aggregate or cumulative exposures are not warranted. The default approach of additivity across multiple chemicals and routes, with segregation for common noncancer endpoints as indicated, has been considered a reasonable approach. However, releases by terrorists could involve relatively high concentrations of combined contaminants to which people could be exposed by multiple routes, such that the default assumptions of dose or response addition might not hold. Thus, it is useful to consider potential cumulative exposures and effects within and across threat contaminant categories when developing homeland security advisories, to determine whether (and how) values developed for single chemicals should be modified.

9. Development of exposure advisories for homeland security is an *iterative process.*

   Exposure advisories for homeland security should represent the best current information if they are to be implemented appropriately when a terrorist release occurs. Thus, by necessity their development and refinement will be iterative so that further relevant toxicity data and guidelines can be incorporated as they become available.

   For example, consider that in early 2004, no AEGLs existed for two common air pollutants, nitrogen oxides and sulfur dioxide. In that case, occupational standards such as PELs were evaluated to assess exposure levels designed to address repeated exposures, with further evaluation to determine whether the longer-term context of those values warranted adjustment to address the short-term duration of interest for this study. Now a year later, AEGLs have been proposed for both pollutants; thus these new values for acute exposures (a day or less) and the underlying scientific bases are being reviewed to assess how they should be reflected in short-term inhalation advisories for homeland security.

10. The process of developing these advisories identifies *knowledge gaps that can guide new research.*

    This study identified data and methodology gaps that can be used to focus follow-on research efforts, including to increase basic toxicological knowledge of threat agents so that the health implications of human exposures can be better understood, to strengthen monitoring and detection programs, and to support emergency preparedness and consequence management planning and implementation. For example, it is useful to assess whether common methods are available to detect threat chemicals at levels near or below their indicated homeland security advisory levels, also considering how long (e.g., hours to days) the analysis process could take, in order to prioritize detector research initiatives.

Related to this last finding, recommended next steps to build on this initial process evaluation to develop exposure advisories for homeland security include the following:

(1) Outline general approaches that serve as starting points to develop advisories for priority contaminants for which relevant standards and guidelines and appropriate toxicity data are not available, and support/reflect the AEGL development process as part of the inhalation evaluation effort.

(2) Develop appropriate assumptions to support the development of advisory levels for sensitive subpopulations, such as for potentially health-compromised adults in the workforce (e.g., for exposures inside buildings) and for children (e.g., for drinking water exposures).

(3) Assess changes in physical form, concentration, and toxicological properties under projected setting conditions (such as for a gas released into buildings or for highly reactive or volatile organic compounds released to water) to determine whether the suggested advisory levels are relevant (e.g., for air or water), or warrant adjustment or a complementary value (e.g., to address forms condensed on surfaces or volatilized to air).

(4) Develop approaches for accounting for cumulative effects, including to reflect combined exposures and toxic interactions across multiple threat contaminants.

The first recommendation acknowledges that the chemicals in the initial study were selected in part based on the existence of relevant standards and guidelines that serve as starting points for short-term advisories with an emphasis on one exposure route, inhalation. The approach developed for that small set of relatively well-studied chemicals will not be as straightforward for others for which guidelines do not exist, also extending to other exposure routes. Thus, flexible methodologies need to be developed and tested, including statistical methods that can be applied to assess existing toxicity information that will likely be limited in terms of data applicable to the specific durations and conditions of interest for homeland security.

The second recommendation reflects the fact that even where standards or guidelines exist, many do not consider specific sensitive subgroups such as asthmatics and atopics. Thus, further methodology development is warranted to support advisory levels that can account for varied responses and effect thresholds, to better inform broad reuse decisions (such as phased reoccupation of buildings or water use by different groups, e.g., from a healthy workforce to the general public).

The third recommendation recognizes that the conditions of the setting into which a contaminant is released, combined with the inherent properties of the contaminant, could result in the form and toxicological properties of certain chemicals and the media changing within the short-term interval of 1 to 30 days. Thus, further evaluations to characterize and account for projected changes from the original introduced contaminant(s) would support the modification of single-chemical advisories or the development of complementary ones.

The fourth recommendation addresses potentially high exposure levels that might be associated with combined contaminants that could be released by terrorists. It also considers combined exposure routes (e.g., ingestion and inhalation of volatile compounds introduced to a drinking water supply, or inhalation and incidental ingestion of contaminants released to air and subsequently deposited on interior building surfaces; dermal absorption can also play a role in both cases). Developing approaches to flexibly account for cumulative exposures and effects depending on the specific contaminant(s) involved would allow advisories based on single agents to be adjusted to account for situation-specific combinations.

ACKNOWLEDGMENTS

The authors acknowledge the extensive, invaluable contributions of Dr. Richard Hertzberg, U.S. EPA Office of Research and Development, throughout this collaborative study. The work was supported by the U.S. Environmental Protection Agency under an interagency agreement, through the U.S. Department of Energy, Assistant Secretary for Environmental Management, under contract W31-109-Eng-38.

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