

# GRADIENT TRENDS

Risk Science & Application

## Letter to our Readers

May 2004

Dear Colleague,

## The Regulatory Framework of Acute Risks

*Acute risk provisions of a variety of regulatory programs are gaining prominence in light of recent world events.*

Human health risk assessments typically address chronic health risks associated with long-term chemical exposures. While acute health hazards are often the primary focus of industrial hygiene evaluations of workplace exposures, acute risk scenarios are not common components of traditional risk assessments for general population

*Acute health risks are the focus of several regulatory programs dealing with chemical accidental prevention, emergency planning and response, and pesticide registration.*

exposures. Beginning with the Bhopal incident in 1984, where the accidental release of methyl isocyanate resulted in the death or injury of over 2,000 people, there has been a growing interest in potential toxic releases from chemical facilities. This interest has recently been rekindled with the terrorist actions of Septem-

ber 2001, and the associated awareness of chemical facilities as potential targets of terrorist action.

Acute health risks are the focus of several regulatory programs dealing with chemical accidental prevention, emergency planning and response, and pesticide registration. The table summarizes key elements of three regulatory programs that address acute health risks associated with different industrial sectors.

The first of these, the Emergency Planning & Community Right to Know Act (EPCRA), also known as Title III of the Superfund Amendments and Reauthorization Act (SARA), was enacted in 1986 as the national legislation on community safety. Major EPCRA provisions include Emergency Response Plans (Sections 301-303), Emergency Notification Requirements (Section 304), and Community Right-to-Know Requirements (Sections 311-312). Each of these provisions addresses acute

We typically think about human health risk in terms of chronic exposures, but there exists an entire additional regulatory framework that is focused on acute risks. Although acute risks may result from exposure to a variety of environmental contaminants and media, air inhalation is generally considered the exposure route of greatest concern. This issue of *Trends* considers how some regulatory programs handle acute risks, and describes fundamentals of exposure assessment when concentration, rather than exposure time, is the key determinant to understanding risk.

Contributors to this issue include Dr. Chris Long, a Gradient environmental scientist and air exposure expert, Ms. Carrie Fields and Dr. Tom Lewandowski, both toxicologists, and Drs. Lorenz Rhomberg and Teresa Bowers, Gradient Principals with expertise in assessing unusual exposure scenarios. Joining them in our guest column is Mr. James Conrad, with the American Chemistry Council, who gives us his perspective on the challenges of information management in this age of concern over sensitive information.

We hope this issue of *Trends* will provide you with new insights on the current status of assessment for acute risks.

Yours truly,



Neil Shifrin, Ph.D.  
President

*continued on pg. 2*

	I	N	S	I	D	E
<i>The Regulatory Framework of Acute Risks</i> .....			1			
<i>Assessing Acute Risks</i> .....			3			
<i>Health Risks and the U.S. Armed Forces</i> .....			4			
<i>By The Way</i> .....						4
<i>What's New at Gradient</i> .....						5
<i>Guest Editorial: Protecting and Sharing Security Sensitive Information - Can We Do Both?</i> .....						6

# The Regulatory Framework of Acute Risks

*continued from pg. 1*

health hazards posed by the storage, use, and environmental release of hazardous chemicals. For example, in the event of an emergency involving any of 100-plus hazardous substances covered under the Emergency Notification Requirements, notification must be provided that includes identification of any known or anticipated acute or chronic health risks associated with the release, as well as advice regarding medical attention for exposed individuals.

To assist with EPCRA provisions and the need for exposure guidelines for emergency planning, prevention, and response programs, the EPA formed the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) in 1995. The NAC/AEGL Committee was specifically tasked with the development of exposure limits for the general population that address short-term inhalation exposures to airborne concentrations of acutely toxic, high-priority chemicals. The committee has developed over 100 AEGLs to date, with plans to address 400-500 high-priority chemicals over the next decade. Regulations stating how AEGLs are to be used in the emergency planning process have not yet been developed by the EPA, but it is anticipated that AEGLs will serve as important tools for assessing acute inhalation risks, and will be adopted for use in federal, state, and local regulations dealing with the storage and use of hazardous chemicals.

Acute health risks associated with accidental chemical releases are also a focus of the Risk Management Program Rule (RMP Rule) that was promulgated in 1996 under the 1990 Clean Air Act Amendments. The purpose of the RMP Rule is to reduce

chemical risk at the local level through improved accident prevention and emergency response practices. One of its principal provisions requires regulated facilities to conduct hazard assessments that include an evaluation of worst-case and alternative accidental releases. By including information on potential release quantities and potential exposures and adverse health effects to affected populations, hazard assessments are intended to help communities prepare contingency plans and to reduce potential risk in the event of an actual chemical accident.

While inhalation of outdoor air is the primary exposure pathway covered under both EPCRA and the RMP Rule, the 1996 Food Quality Protection Act (FQPA) requires that acute dietary risk assessments be performed for tolerance assessments of food-use pesticides if there is toxicological evidence that an effect of concern may occur following a one day or single exposure. The FQPA was passed by Congress in 1996 to amend both FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) and FFDCA (Federal Food, Drug, and Cosmetic Act), and one of its key provisions requires consideration of acute health effects (immediate illness) when determining health risks. FQPA requires that acute dietary risk assessments be conducted for all potentially exposed population subgroups, with intakes *via* both food and drinking water.

As the regulatory environment for considering acute risks continues to expand, acute risk scenarios are likely to become more common components of human health risk assessments. Continuing development of methods and tools for assessing acute risks (see related article) will help to inform risk management decisions to address potential acute health risks.

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## EXAMPLES OF REGULATORY PROGRAMS WITH ACUTE RISK PROVISIONS

Regulatory Program	Types of Facilities Covered	Regulated Chemical Classes	Exposure Media of Interest	Human Receptors Addressed
EPCRA	Differs depending on the provision, but triggered by threshold quantities of a large number of chemicals	Extremely hazardous substances (EHSs) and CERCLA hazardous substances	Primarily air	General population
RMP Rule	Facilities exceeding threshold quantities for listed substances	77 toxic substances and 63 flammable substances	Primarily air	General population
FQPA	Pesticide manufacturers, food processors, farm organizations	Pesticides	Diet (food, water)	General population, including sensitive subpopulations ( <i>e.g.</i> , nursing infants)

# Assessing Acute Risks

*The fundamental approach to evaluating acute risks differs from approaches for assessing chronic risks.*

Sodium chloride (table salt): chemical manufacturing agent, savior of dismal leftover dinners, ice melting tool, deadly poison? In the world of toxicology, even something as seemingly innocuous as salt can be a poisonous agent. It's all a matter of dose. This is particularly the case for acute exposures, *i.e.*, high exposures that occur over a short period of time. Most risk assessments focus primarily on the risks from chronic exposures, but in some cases, acute exposure risks need to be assessed as well.

Acute exposures of toxicological concern can occur in workplaces, with hazardous material spills, and in intentional or unintentional poisonings. Acute toxicological effects result when sufficiently high doses of chemical agents overwhelm the body's defense mechanisms, such as acid-base buffering capacity, barriers to absorption, or ability to regenerate neurotransmitters. High-dose, short-duration exposure scenarios often result in different toxicological effects than low-dose, chronic exposure scenarios.

When assessing noncancer health effects, chronic exposures are evaluated using the average daily dose (ADD). In computing the ADD, doses are averaged over the anticipated exposure period (*e.g.*, 30 year residence time, average job tenure) including periods when there is no exposure. Similarly, evaluation of

carcinogenic effects involves averaging exposures over a lifetime. By contrast, acute exposures are evaluated using the total or cumulative dose during a short timeframe of actual exposure. Thus, exposures are not averaged over some longer timeframe.

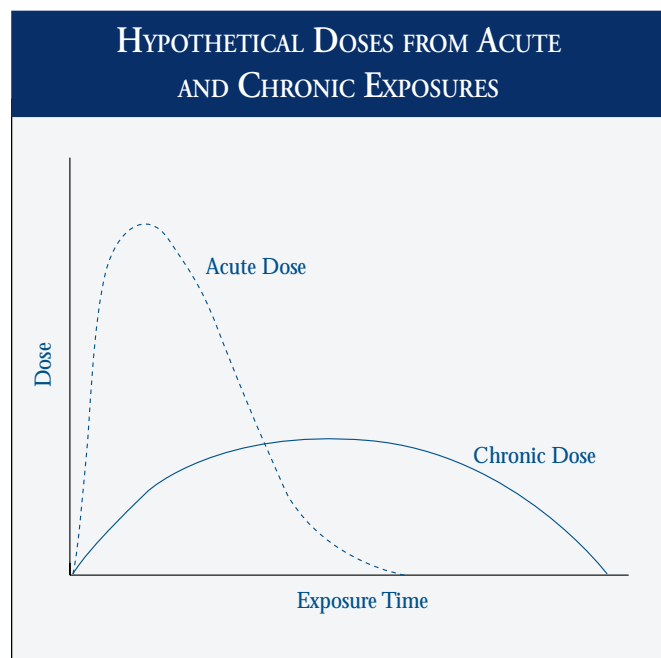
The types of chemicals that may be of concern for acute exposures may also be different from those of concern for chronic exposures. Chemicals associated with long-term health effects (*e.g.*, PCBs, asbestos) may be less of a concern for acute effects, except at extreme doses. On the other hand, chemicals not typically considered in chronic exposure assessments (caustics, carbon monoxide, hydrogen sulfide, cyanide) can have significant acute health effects at high doses. There are also chemicals for which acute and chronic effects are distinctly different. Several chlorinated solvents, for example, have been associated with cancer after chronic exposure but have central nervous system depression as the primary acute exposure concern.

***High-dose, short-duration exposure scenarios often result in different toxicological effects than low-dose, chronic exposure scenarios.***

All of the primary exposure routes can be applicable in acute exposure cases. Inhalation is generally the most important in the case of accidental releases to the air, dermal exposures may be important when considering applicators' exposure to pesticides, and ingestion exposures are the most common form of accidental poisoning in children. Exposure to contaminants *via* water or soil ingestion, which are common pathways of concern for chronic exposure, are typically less significant in an acute setting because, except for the most potent agents, concentrations are rarely high enough in soils or water to trigger acute toxicity.

As described in the preceding article, the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) has been developing guidelines for once-in-a-lifetime, short-term exposures to acutely toxic airborne chemicals. There are three tiers of AEGLs: AEGL-1 is the level above which the general population would be expected to have notable discomfort, irritation, or asymptomatic nonsensory effects. At this level of exposure, the effects are reversible. AEGL-2 is a level above which the general population could suffer from irreversible, long-term health effects such as shortness of breath, pulmonary function changes, asthma provocation, respiratory tract pathology, mild narcosis, and methemoglobin formation. AEGL-3 is the level at which the general population could suffer life-threatening health effects or even death. The AEGLs are developed for each chemical of concern for 10 minute, 30 minute, 1-hour, 4-hour

*continued on pg. 5*



***The two exposures have similar cumulative doses but different peak concentrations, which may lead to different endpoints and effects.***

# Health Risks and the U.S. Armed Forces

*Because of the unique exposure settings encountered in the military, different assumptions to quantify exposure are used.*

U.S. military personnel can have unique short-duration exposures to a variety of toxic chemicals as a result of deployment to locations outside the U.S. that are characterized by airborne contaminants, non-potable water supplies, and/or severely contaminated soils. Combat brings an additional set of potential exposures, such as depleted uranium or cordite smoke. National attention has focused on the possibility that military personnel had environmental exposures during the first Gulf War that led to currently observed illnesses.

*...unusually high exposures combined with other chemical and environmental stressors may have the potential to increase an individual's vulnerability to some toxic effects.*

As a result, the U.S. military and the Department of Defense have begun to develop frameworks for assessing risks to deployed forces associated with potential chemical exposures, and to develop "Technical Guides" for both short- and long-term exposures

to assist in making military risk management decisions.

The Technical Guide "Short-Term Chemical Exposure Guidelines for Deployed Military Personnel" (1999) lists short-term Military Air Guidelines (MAGs) appropriate for exposures of one hour and one to 14 days, and Military Water Guidelines (MWGs) appropriate for five and 14 days. The one hour MAGs are developed for minimal, significant, and severe effects levels. The effects caused by some chemicals are concentration- rather than time-dependent (see related article), and these chemicals are assigned "ceiling values," concentrations that should not be exceeded for any time duration.

The MWGs are based on drinking water ingestion rates of 5 L/day in temperate climates, and 15 L/day in arid and arctic regions. These guidelines are not standards used to approve or disapprove drinking water supplies; rather, they are tools for interpreting water quality data and aiding in risk management decision-making during deployments in potentially contaminated settings. Where possible, the Technical Guide lists lethal doses as well, developed from cases of deliberate or accidental poisoning.

The military considers acute exposure to contaminated soil to be unlikely as sufficiently large quantities of soil are rarely, if ever, ingested by adults. Chronic exposures are considered in the companion document "Long-Term Chemical Exposure Guidelines for Deployed Military Personnel."

Several factors set the evaluation of risks to deployed military personnel apart from standard risk assessment approaches. Some differences simply concern the input assumptions in the risk equations, *e.g.*, the high drinking water ingestion rates cited above. Other differences are harder to quantify. Military forces represent a healthy segment of the U.S. population and are assumed to have less overall population variability, although equal genetic variability. At the same time, unusually high exposures combined with other chemical and environmental stressors may have the potential to increase an individual's vulnerability to some toxic effects. Guidelines developed to date have been unable to account for this possibility. Moreover, in addition to the need for these protective standards, a different set of standards may be needed to estimate casualties when exposures cannot be avoided for overriding military reasons.

Some of the considerations discussed here may have applicability beyond military personnel. For example, astronauts are confined for days to weeks in small quarters with recycled air and water, and ocean scientists spend from hours to days in submersibles with recycled air. In these instances, it should be easier to anticipate which toxic chemicals may be present. Nevertheless, tools and techniques developed to improve risk assessment for the military may have application in these other arenas as well.

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## BY THE WAY...

The number of poisoning deaths in 2001 in the U.S. was 22,242, a number which has been increasing since 1990. Narcotics and psychodysleptics (*i.e.*, illicit drugs) were the largest category of poisoning agents.

Source: *Morbidity and Mortality Weekly Report* 26, 2004, 53 (11) 233-238.

## What's New at Gradient

### Gradient Welcomes Dr. David Langseth

Dr. David E. Langseth has joined Gradient as a Principal in our Cambridge office. He is an environmental engineer with expertise in contaminant fate and transport as well as development of site remediation strategies for a variety of facilities, including mercury and other metals processing, chemical/petrochemical, manufactured gas, and waste disposal facilities. Dr. Langseth earned his Sc.D. in civil engineering from MIT and his B.A. in mathematics from the University of Minnesota.

### Gradient Appointments

Dr. Teresa S. Bowers has recently been appointed to the National Research Council Committee on Superfund Site Assessment and Remediation in the Coeur d'Alene River Basin, sponsored by the National Academy of Science.

Dr. Tom Lewandowski has recently been appointed Affiliate Assistant Professor in the Department of Environmental and Occupational Health Sciences at the University of Washington.

Dr. A. Dallas Wait has been appointed to the Editorial Board of *Quality Assurance: Good Practice, Regulation, and Law*.

### Gradient Wins Award

Gradient was recently awarded a Blue Ribbon of recognition for an abstract in risk assessment at this year's Society of Toxicology meeting. The winner was "Development of a risk assessment to evaluate human health risks from exposure to tebuconazole as a wood preservative" by Bryan Shipp, Eric M. Dubé, Barbara D. Beck, Mara Seeley, Kathleen R. Radloff, Sunessa Schettler, and Cathy Petito Boyce.

### Gradient Returns to Harvard Square

Effective early June, Gradient will be located at 20 University Road, Cambridge, MA 02138. Phone numbers will remain the same. Please visit our newly updated website at [www.gradientcorp.com](http://www.gradientcorp.com).

### Upcoming Presentations

Amherst, Massachusetts. June 8-10, 2004. Barbara D. Beck will chair the Regulatory Risk session being held June 10, 2004 at the 3<sup>rd</sup> Annual International Conference on Non-Linear Dose-Response Relationships in Biology, Toxicology, and Medicine.

Boston, Massachusetts. June 21, 2004. Peter A. Valberg, "Inhalation, Deposition, and Clearance of Airborne Particles." Presentation at the Harvard School of Public Health Continuing Education Course on Fundamentals of Industrial Hygiene.

### Recent Articles

Valberg, P.A. 2003. Possible non-causal bases for correlations between low concentrations of ambient particulate matter and daily mortality. *Non-Linearity in Biology, Toxicology, and Medicine* 1:521-530.

Rhomberg, L.R. 2004. Separating Pharmacokinetic and Pharmacodynamic Components in Empirical Adjustment Factor Distributions. *Human and Ecological Risk Assessment* 10(1):79-90.

To request copies of articles or presentations, or to receive *Trends* by email, please contact us at [trends@gradientcorp.com](mailto:trends@gradientcorp.com) or telephone Melissa Marieb at (617) 395-5000.

## Assessing Acute Risks

*continued from pg. 3*

and 8-hour exposure times. Development of AEGLs includes: a comprehensive review of information on the chemical of concern, drafting proposed guidelines, public comment and review, and development of the final guidelines for use.

While AEGLs and other regulatory guidelines exist for many chemicals, there are many others for which no guidelines exist. In these cases, estimates of exposure level and duration are

combined with chemical-specific data to evaluate the risk from short-term chemical exposure.

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See <http://www.epa.gov/oppt/aegl/humanhealth.htm>.

# Guest Editorial: Protecting and Sharing Security Sensitive Information – Can We Do Both?

*Can sensitive information be shared with thousands of private sector personnel without turning up on CNN?*

For decades, federal laws had marched, seemingly inexorably, toward greater government disclosure. In 1966, the Freedom of Information Act (FOIA) declared all government information to be public unless it fell within one of a few exceptions. Congress gave this trend

***Non-governmental organizations pooh-pooed terrorism concerns as a “smokescreen,” but 9/11 ended any substantial debate over the issue.***

a sticky label with the Emergency Preparedness and Community Right-to-Know Act (EPCRA) in 1986, and expanded that right when it added the Risk Management Program (RMP) to the Clean Air Act in 1990.

The latter two laws don't just make information public, but use it to help state and local governments minimize and prepare for large-scale, acute hazard events like Bhopal. Their basic approach – with narrow exceptions – is binary. Either any member of the public can see something, or no one can.

However, the trend toward openness was not inexorable. Law enforcement and security agencies objected to putting RMP “worst case scenario” information on the Internet, arguing that it would literally provide terrorists with a roadmap to the most attractive targets. In 1999, Congress told the government to balance the risks and benefits of publicly disclosing this information, and a year later the government concluded that the consequences of “a single successful attack on a chemical facility could be considerable, and would likely cause more damage than would many accidental chemical releases.” The government then crafted a complicated mechanism to limit public access to RMP data.

Non-governmental organizations pooh-pooed terrorism concerns as a “smokescreen,” but 9/11 ended any substantial debate over the issue. Since then, Congress has passed several statutes to protect vulnerability assessments and similar terrorism-sensitive information from unfettered public release. Most notable is the Critical Infrastructure Information Act, which not only creates a FOIA exemption, but also preempts state “open records” laws, restricts open meeting rules, and limits use of information in civil litigation.

Another example is the Homeland Security Information Sharing Act (HSISA), which encourages the federal government to give state and local authorities – and vulnerable businesses – information on terrorist risks or response that is classified or “sensitive but unclassified.”

As before, these laws are intended to prevent large-scale acute hazard events. However, the new laws drop the older binary approach by allowing some – but not all – members of the public to obtain or share government information. With most critical infrastructure in private hands, Congress recognizes that effectively securing it requires giving its representatives access to information affecting their security, but keeping that information from being released to the general public.

It is too early to say how broadly these initiatives will be implemented or how well – if at all – they will work. Something like them is necessary, though, if we are going to secure private infrastructure from being used by terrorists to create large-scale acute hazards.

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## In the next issue:

*Background Risks*

*Role of Background in Risk Characterization*

*Cultural Considerations in Exposure Assessment*

*Guest Editorial: Current Initiatives to Measure Background*

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