A Primer on Risk Calculations

Assessing the chronic toxic effects of a chemical can be difficult and expensive. But here is a simple model for assessing cancer risks due to exposure to an environmental pollutant.

by Gerald Rich, PE, REP

In recent years, federal statutes such as the Toxic Substances Control Act, the Resource Conservation and Recovery Act, the Clean Air Act, and the Clean Water Act have given the U.S. Environmental Protection Agency (USEPA) the responsibility for regulating the release of toxic chemicals into the environment.

In order to fulfill this function effectively, the EPA must first determine which of the thousands of chemicals currently in use or proposed for use are toxic.

Detecting a chemical's ability to cause immediate or acute toxic effects is a relatively straightforward task. Assessing the long-term or chronic toxic effects is much more difficult. Chronic effects such as cancer, birth defects and genetic disease characteristically appear several years or decades after the initial chemical exposure has occurred, and long-term studies using live animals must be conducted in order to detect these latent effects.

Such studies are expensive and time-consuming, requiring the use of highly specialized facilities and personnel. A single test for a chemical's carcinogenicity may take as long as three years and cost $250,000 or more.

The number of compounds whose chronic toxicity has not been determined is overwhelming. Over 50,000 chemicals are currently in commercial production, and most of them have never been examined for chronic effects. The world laboratory capacity for long-term studies has been estimated at only 500 compounds per year, not enough to keep up with the 700 to 1000 new chemicals introduced each year.

Short-term tests have been developed to serve as rapid and relatively inexpensive predictors of a chemical's potential to cause chronic effects. These tests employ bacteria, yeast, plants, insects, isolated mammalian cells, whole animals and computer modeling.

Short-term tests can detect a chemical's genotoxicity, or its ability to alter a cell's genetic material — the DNA. An increasing amount of evidence indicates that latent diseases such as cancer, birth defects and genetic disease may be initiated by alterations in the DNA.

Short-term tests enable a large number of chemicals to be screened for their genotoxic potential at a fraction of the time and cost required for long-term tests. Results from short-term tests can be used to make more informed decisions as to which chemicals should be examined in the limited number of long-term testing facilities available.

Other uses for short-term tests include determining which of several alternative chemicals under development will be the least hazardous to human health; identifying the toxic components of complex environmental pollutants; and providing interim guidance for using a chemical when no other data is available.

A distinction is made between carcinogenic and non-carcinogenic effects. Two general criteria are used to describe risk: Excess lifetime cancer risk for constituents which are thought to be potential human carcinogens, and the hazard index (HI) for all constituents. All chemicals have non-carcinogenic effects, but only a few are known to cause cancer.

For potential carcinogens, the current regulatory approach uses an extremely conservative approach in which it is assumed that even a trace level of exposure to a carcinogen can cause cancer. This is contrary to the traditional approach to toxic chemicals, in which finite thresholds are said to exist, below which the toxic effect will not occur. This traditional approach is still applied to non-carcinogenic chemicals.

Because of these differing approaches to calculating potential risks, the risks associated with carcinogenic effects are generally much higher than those associated with non-carcinogenic effects.

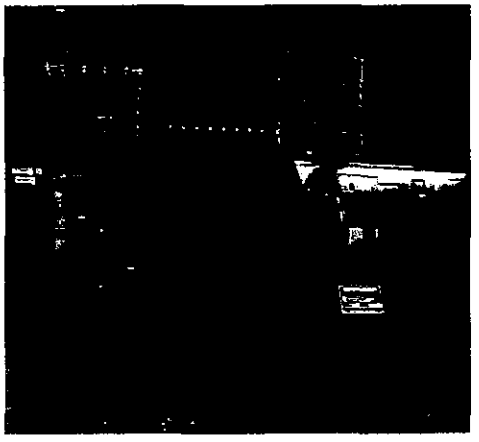
Cancer is the end result of a multistage process in which a large number of biological and environmental factors interact, simultaneously or in sequence, to disrupt normal cell growth and divi-

TURNING WASTE INTO ENERGY? TURN TO THE FAN EXPERTS:

ROBINSON.

We'll meet your needs for high-efficiency/low-cost operation based on nearly a century of fan engineering, application and fabrication experience.

Robinson fans perform dependably in applications such as in fluidized bed systems, boilers, heat recovery operations, incineration and pollution control. Robinson air-moving equipment actually saves money over the years thanks to our design experience and a quality assurance program that meets or exceeds stringent industry requirements.



Let us improve the performance of your existing fans.

Robinson can redesign and upgrade, rebuild or repair your existing equipment whether we built it in the first place or not. And Robinson repairs last because we begin by identifying and correcting the **causes** of the problem!

Send for FREE literature.

For more information on air-moving equipment for any waste-to-energy application, send for Bulletin 505. For repair and rebuild information, send for Bulletin 551.

Hotlines are answered 24 hours a day at both locations.

ROBINSON
INDUSTRIES, INC.
P.O. Box 100 • Zelienople, PA 16063
Phone: 1-412-452-6121
Telex: 866-311 • Fax: 1-412-452-0388

ROBINSON FANS FLORIDA, INC.
P.O. Box 6260 • Lakeland, FL 33807-6260
Phone: 1-813-646-5270
Telex: 866-311 • Fax: 1-813-646-1712

520-130

sion. The first stage, called initiation, involves the creation of errors in genetic coding. Because the effects of initiation are thought to occur at the molecular level, current regulatory policy assumes there is no finite dose below which the initiation effect cannot occur. In other words, there may be no absolutely safe dose, because at any dose there is some finite probability associated with the occurrence of the initiation event.

Once a cell is initiated, many other processes are involved in either promoting or blocking the development of cancer. Therefore, the frequency of cancer occurrence is very low in comparison to the hypothetical frequency of initiation events, especially at the low chemical concentrations which occur in the environment.

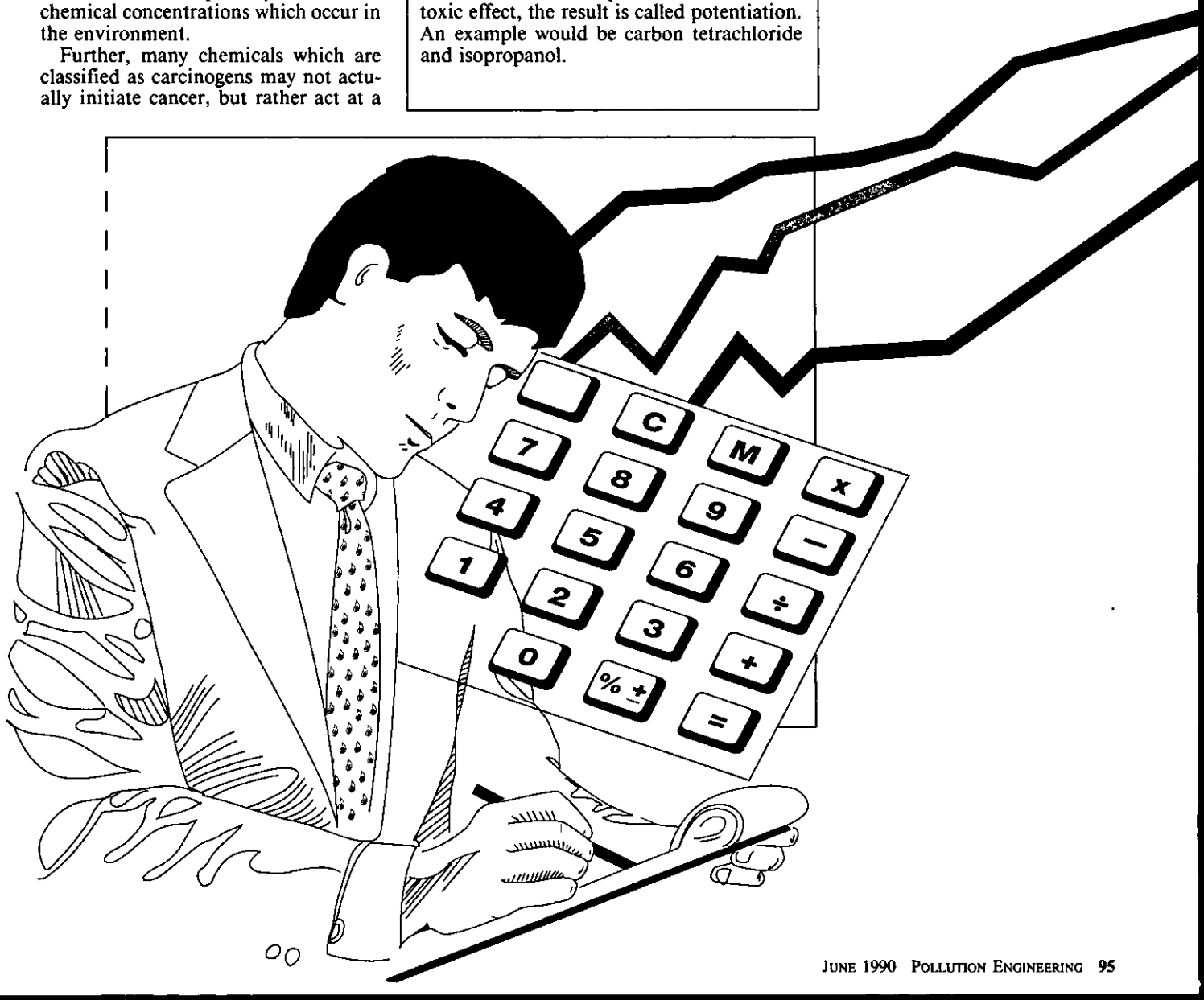
Further, many chemicals which are classified as carcinogens may not actually initiate cancer, but rather act at a

RISK ASSESSMENT TERMS

Synergism — On a scale of toxicity of 0 to 25 with 25 being the most toxic, synergism is the term used to describe the effect when the outcome of combining two chemicals is greater than the sum of the inputs.
An example would be carbon tetrachloride and ethanol.

Antagonism — Similarly, antagonism is the term used to describe the effect when the outcome is less than the sum of the two inputs. An example would be chelators and metals.

Potentiation — When one chemical has no toxic effect but combined with another chemical that is toxic produces a much more toxic effect, the result is called potentiation. An example would be carbon tetrachloride and isopropanol.



The carcinogen potency factor is used to calculate the probability of cancer

later stage on cells which were already initiated. Although these chemicals are treated as if one molecule could cause significant damage, this has not been proven.

As an example, in the case of chromium, only the hexavalent form has been proven to be carcinogenic, although it is a potent carcinogen. There is now insufficient evidence to determine that the trivalent form also is carcinogenic. A NESHAP analysis, however, assumes that total chromium releases are carcinogenic and that trivalent chromium is as potent as hexavalent chromium.

There is no information now available on the ratio of trivalent to hexavalent for emissions or ambient concentrations, but some occupational exposure studies suggest the trivalent form may dominate in some source categories. On the other hand, several source categories are known to emit at least some hexavalent chromium, and there is some evidence that changes in the valence state can occur in the atmosphere.

Thus, in the case of chromium, the problem of speciation adds one more layer of uncertainty to the risk estimate.

Identification of constituents which are included in the carcinogen category is based on a USEPA classification scheme in which chemicals are systematically evaluated for their ability to cause cancer in mammalian species and conclusions are reached about the potential to cause cancer in humans.

The USEPA classification scheme contains six categories:

- A — Human carcinogen;
- B1 — probable human carcinogen, limited evidence in humans;
- B2 — probable human carcinogen, inadequate evidence in humans;
- C — possible human carcinogen;
- D — inadequate evidence to classify;
- E — no evidence of carcinogenicity.

Categories A, B1, B2 and C are included in assessments as potential human carcinogens. Much of these evaluations are based on laboratory animal studies. In order to limit the number of animals required for testing, very high doses of chemicals are used in laboratory studies.

For chemicals which seem to cause or increase cancer, the results of these high-dose animal studies are extrapolated to the low-dose human exposure situation using mathematical models which do not depict biological reality.

A variety of mathematical models are available for extrapolating from high to low doses. The USEPA currently favors a linearized multistage model which provides a 95 percent upper-bound estimate of cancer incidence at a given dose. The slope of the extrapolated curve, called the carcinogen potency factor, is used to calculate the probability of cancer associated with the exposure dose.

The excess lifetime cancer risk is an estimate of the increased risk of cancer which results from exposure to constituents at a given concentration.

One in four Americans will have cancer.

The probability of developing cancer as a result of exposure to constituents associated with the facility is called the excess lifetime cancer risk.

The excess lifetime cancer risk is an estimate of the increased risk of cancer which results from exposure to constituents at a given concentration. Approximately one out of four Americans will have cancer during their lifetimes, and about half of those will die from the cancer.

The risk values provided in a risk assessment are an indication of the increased risk, above that applying to the general population, which results from the exposure scenarios described in an exposure characterization. The actual cancer risk is unknown and could be anywhere between zero — no risk of cancer —and the value provided, but is not likely to exceed the estimate derived in the risk assessment. The excess lifetime cancer risk is the product of exposure dose and the cancer potency factor for each constituent. Excess lifetime cancer risks can be summed across routes of exposure and constituents.

An excess lifetime cancer risk of less than 10^{-7} is generally considered acceptable. An excess lifetime cancer risk of greater than 10^{-7} is generally considered unacceptable. Excess lifetime cancer risks in the range of 10^{-4} to 10^{-7} are potentially acceptable. A range of 10^{-4} to 10^{-7} is the common target for remediation activities.

A finite dose or threshold, below which adverse effects will not occur, is believed to exist for non-cancer effects. Non-cancer effects include birth defects, organ damage, death and many others. A single compound might elicit several adverse effects depending on the dose, the route and the duration of exposure.

For a given chemical, the dose which elicits no effect when evaluating the most sensitive response (the adverse effect which occurs at the lowest dose) in the most sensitive species is used to establish an acceptable dose for non-carcinogenic effects. Acceptable doses which are sanctioned by the USEPA are called reference doses (RfDs).

The hazard index is a representation which addresses non-cancer health effects of compounds. The hazard index is the ratio of the exposure dose to the acceptable dose or RfD. A hazard index greater than one is an indication that exposure is too high; it means that, for a given constituent, exposure exceeds acceptable levels for protection against non-cancer effects. Hazard indexes can be summed across exposure routes and constituents. A hazard index of less than one suggests non-cancer health effects would not occur; less than one is a common USEPA remediation goal. However, many state agencies prefer the hazard index be in the range of 0.2. This preference is based on the realization that people may be exposed to these same constituents from sources unrelated to a specific site.

In general, cancer potency factors, carcinogen classifications and RfDs (separated by exposure route) are taken from either USEPA's Superfund Public Health Evaluation Manual (1986) or IRIS (Integrated Risk Information

System)—an EPA-approved computer data base.

Three routes of exposure are considered: Dermal (skin), inhalation, and ingestion. Whenever possible, route-specific values are used. Because acceptable levels for dermal exposure are virtually never available, oral values are used in their place. When inhalation values are not available, oral values are substituted in their place unless compound-specific information clearly indicates this would be inappropriate. In some cases, route of exposure determines the type of toxicity that will be expected.

Considerable uncertainty is inherent in the overall risk assessment process. The basic building blocks for risk assessment include source assessment, monitoring/sampling and analysis, exposure assessment, health effects measurement and risk management, all of which are combined into the regulatory decision-making process. Each of these contributes uncertainties in its own fashion. Refer to Dr. Stephen Hall's December, 1988, article in POLLUTION ENGINEERING, "Health Risk Assessment of Chemical Exposure" for the health risk assessment aspects.

Risk assessment is based, at least partially, on the assumption that the monitoring data adequately describes the situation. Environmental sampling itself introduces uncertainty because of the potential for uneven distribution of constituents in the environmental media.

Two sampling methods, grab and composite, are typically used. Grab samples determine the distribution of constituents and the variation in concentrations.

Composite samples indicate average constituent concentrations but can obscure information about hot spots. Composites of adjacent samples minimize this problem.

Uncertainty associated with sample analysis can be minimized by using appropriate analytical methods and equipment, documenting the chain of custody of samples, and implementing strict laboratory data validation and quality assurance procedures. It is also critical that sample detection limits be lower than both the applicable standards or criteria and the concentration which may present a health risk.

Exposure scenarios and constituent transport models also contribute uncertainty to the risk assessment. Transport models typically over-simplify reality, contributing uncertainty. Exposure routes include:

- Inhalation,
- ingestion,
- dermal absorption,
- intravenous,
- subcutaneous (injected below the skin),
- intraperitoneal (subject to metabolism in the liver)

The toxicity values and other toxicologic (health effects) information are associated with significant uncertainty. Most health effects information has been developed using laboratory animals exposed to high doses. Although species differences in absorption, distribution, metabolism, excretion and target organ sensitivity are well documented, available data are not sufficient to allow compensation for these differences.

Most laboratory studies strictly control as many factors as possible, yet the human population is genetically diverse and affected by a variation in diets, occupations, genetics, pharmaceuticals, pre-existing illnesses and other factors.

There also is considerable uncertainty associated with the toxicity of mixtures. For the most part, data about the toxicity of chemical mixtures are unavailable even though the effect of combining two chemicals may be known to be synergistic, antagonistic, or under potentiation. Rather, toxicity studies are generally performed using a single chemical.

Chemicals present in a mixture can interact chemically to yield a new

TABLE 1
AGGREGATE RISK CALCULATIONS

City	Ambient Concentration ($\mu g/m^3$)	Number of People Exposed	Aggregate Risk
A	6	5000	
	3	20,000	5.75
	0.5	50,000	
B	3	10,000	
	1	50,000	5
	0.1	200,000	
C	7	1000	
	5	5000	2.1
	1	10,000	

Toxicity data on chemical mixtures is for the most part, unavailable

chemical or one can interfere with the absorption, distribution, metabolism, or excretion of another. Chemicals may also act by the same mechanism at the same target organ or can act completely independently. In general, risk assessments assume toxicity is additive.

Unit risk

Assessing the cancer risks of exposure to an environmental pollutant requires three pieces of information: An estimate of the carcinogenic potency, or the unit risk factor, of the pollutant being considered; an estimate of the ambient concentration that an individual or group of people may breathe; and an estimate of the number of people exposed to those concentrations.

Unit risk is a quantitative estimate of the carcinogenic potency, or the unit risk value or factor, and often is expressed as the chance of contracting cancer (though not necessarily life-threatening) from a 70-year lifetime continuous exposure to a concentration of one microgram per cubic meter in air (1 $\mu g/m^3$) of a given substance.

The unit risk can be expressed in terms of parts per million (ppm) in diet, milligrams per kilogram of body weight per day (mg/kg/day) or, most frequently for air pollutant risk assessment, $\mu g/m^3$ in the air.

Unit risk is usually expressed as a two-digit number times a power of 10 per microgram per cubic meter, such as 5.5×10^{-6} $(\mu g/m^3)$-1. A unit risk value of 5.5×10^{-6} $(\mu g/m^3)$-1 would indicate an estimated 5.5 cancer cases per 1,000,000 people exposed to an average of 1 $\mu g/m^3$ of a specific carcinogen for 70 years.

For chemicals with good quantitative human data available, maximum likelihood or best estimate procedures are used to estimate unit risk factors.

In contrast to the 95 percent upper confidence limit procedures used for animal data, maximum likelihood procedures will generally overestimate risk 50 percent of the time and will underestimate risk 50 percent of the time. This less conservative approach is generally justified by citing lack of species to species extrapolation and less extensive low-dose extrapolation.

The unit risk estimates for a number of air pollutants have been derived from human data using maximum likelihood or best estimate procedures, as for asbestos, arsenic, cadmium, chromium and nickel.

For animal or human data with significant quantitative uncertainty, EPA most frequently uses a linearized multistage procedure to estimate unit risk.

This procedure leads to an upper bound estimate of the risk — the 95 percent confidence limit — that fits the data and also may lead to a most likely estimate (MLE) of risk. The unit risk factor is a plausible upper bound estimate of the risk associated with a pollutant. With such an estimate, the true risk is not likely to be higher than the estimate, but could be lower.

Individual lifetime risk vs. aggregate risk

Cancer risks may be reported in terms of risk estimates for an individual (lifetime individual risk) or risk estimates for an exposed population (aggregate risk).

Lifetime individual risk is a measure of the probability of an individual's developing cancer as a result of exposure to an ambient concentration of an air pollutant over a 70-year period. It is calculated by multiplying the unit risk factor by a long term average exposure estimate ($\mu g/m^3$). The maximum lifetime individual risk, which usually applies to people living in the area of highest average ambient air concentrations, usually nearest a source, is determined by multiplying the unit risk factor for the specific chemical of concern by the highest average exposure estimate in the area under examination. If the unit risk factor for a chemical is 4.0×10^{-5} $(\mu g/m^3)$-1 and the highest predicted lifetime exposure concentration is 3 $\mu g/m^3$, then the maximum individual lifetime risk estimate would be 4.0×10^{-5} $(\mu g/m^3)$-1) x $(3\mu$ $g/m^3)$ = 1.2×10^{-4}.

TABLE 2
CALCULATING INDIVIDUAL RISK*

Pollutant	Factor
Acetaldehyde	3.96×10^{-6}
Acrylonitrile	1.48×10^{-4}
Arsenic	5.27×10^{-2}
Benzene	2.65×10^{-5}
BaP	1.75×10^{-2}
Beryllium	8.85×10^{-4}
1,3-butadiene	6.19×10^{-4}
Cadmium	8.28×10^{-3}
Carbon tetrachloride	9.44×10^{-5}
Chloroform	1.12×10^{-4}
Chromium VI	2.55×10^{-2}
1,2-dichloroethane	1.05×10^{-4}
1,1-dichloroethylene	1.98×10^{-4}
Epichlorohydrin	4.54×10^{-6}
Ethylene dibromide	1.69×10^{-3}
Ethylene oxide	1.80×10^{-4}
Formaldehyde	1.60×10^{-5}
Gasoline (marketing)	1.69×10^{-6}
Hexachlorobenzene	5.71×10^{-3}
Methylene chloride	1.63×10^{-6}
Nickel-refinery dust	2.36×10^{-3}
Nickel-subsulfide	1.18×10^{-3}
Propylene oxide	8.79×10^{-5}
Styrene	2.43×10^{-6}
2,3,7,8 - tetrachloridibenzo-p-dioxin	4.35×10^{-4}
Tetrachloroethylene	3.93×10^{-6}
Trichloroethylene	9.28×10^{-5}
Vinyl chloride	1.05×10^{-5}

Factor = (unit risk factor) x (molecular weight)/(24.45 liters/mole @ 25°C)

*These are factors in common use by EPA. They are subject to and frequently do change as additional information is evaluated. For further up-to-date information, contact Pollutant Assessment Branch (MD-12), Research Triangle Park, NC 27711.

This means there is one chance in 10,000 that a person residing in the area will contract cancer as a result of the exposure to the pollutant.

Aggregate risk applies to all people within the given area of analysis. Aggregate risk is the summation of the number of people multiplied by the estimated concentration to which they are exposed multiplied by the unit risk factor of the pollutant or pollutants of concern.

The resulting aggregate risk estimate is expressed as the expected incidence or rate of occurrence of cancer among all people in the analysis after 70 years of exposure. The incidence is often divided by 70 to obtain an estimated annual incidence.

Two examples follow. The first example illustrates the calculation of aggregate risk in a single geographical area. The second example illustrates how aggregate risk can vary among geographical areas.

Calculating aggregate risk

Example 1 — Within a geographical area, three levels of ambient concentrations of chemical X have been identified: 2 $\mu g/m^3$, 1 $\mu g/m^3$, and 0.5 $\mu g/m^3$. Exposed populations to these three ambient concentrations are 1000, 10,000 and 100,000 people, respectively. The unit risk factor for chemical X is 4.0×10^{-5} $(\mu g/m^3)^{-1}$.

Aggregate risk is then calculated as follows:
(2 [1mg]g/m^3 x 1000 people x 4.0×10^{-5}) + (1 $\mu g/m^3$ x 10,000 people x 4.0×10^{-5}) + (0.5 $\mu g/m^3$ x 100,000 people x 4.0×10^{-5}) = 2.48.

In Example 1, the aggregate risk is estimated to be 2.48 lifetime cancer cases in the exposed population. Annual incidence, which expresses the number of cancer cases per year, would be equal to 0.004 (or 2.48/70).

Example 2 — Three cities have measured ambient concentrations for chemical Y. The different ambient concentrations and the number of people exposed to each are summarized below. The unit risk factor of chemical Y is 5.0×10^{-5} $(\mu g/m^3)^{-1}$.

In this example, aggregate risk ranges from two to six cancer cases. The smallest city, City C, has the highest maximum ambient concentration, but the lowest aggregate risk.

The aggregate risk calculation for City A is [(6 x 5,000) + (3 x 20,000) + (0.5 x 50,000)] x 5.0×10^{-5} = 5.75.

The aggregate risk calculation for City B is [(3 x 10,000) + (1 x 50,000) + (0.1 x 200,000)] x 5.0×10^{-5} = 5.

The aggregate risk calculation for City C is [(7 x 1,000) + (5 x 5,000) + (1 x 10,000)] x 5.0×10^{-5} = 2.1.

Individual risks calculated from concentrations

Where the concentration is given in terms of micrograms per cubic meter ($\mu g/m^3$), the individual risk is calculated as follows: Individual Risk = $\mu g/m^3$ x unit risk factor.

For example, an ambient concentration of coke oven emissions has been measured at 1.613 $\mu g/m^3$. Coke oven emissions have a unit risk factor of 6.2×10^{-4} $(\mu g/m^3)^{-1}$. What is the individual risk associated with this concentration?

The individual risk = (1.613 $\mu g/m^3$) x 6.2×10^{-4} $(\mu g/m^3)^{-1}$ = 1.0×10^{-3}.

Where the concentration of a pollutant is given in terms of parts per billion by volume (ppbv), the individual risk can be calculated.

The individual risk = ppbv x unit risk factor x molecular weight divided by 24.45 L/mole at 25°C.

As another example, acetaldehyde has a unit risk factor of 2.2×10^{-6} and a molecular weight of 44.05. If an ambient concentration of 2.52 ppbv has been measured, what is the individual risk?

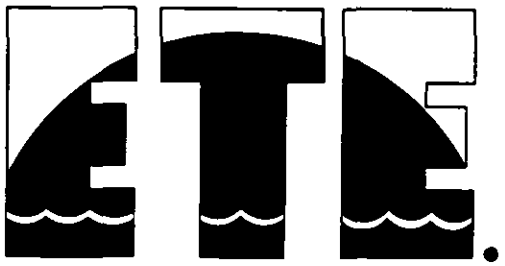
The individual risk = (2.52) x (2.2 x 10^{-6}) x (44.05) divided by 24.45 = 1.0×10^{-5}.

The equation for calculating individual risk from a given concentration in terms of ppbv can be simplified for each pollutant as: The individual risk = ppbv x factor.

The factor in this equation is equal to the unit risk factor of the pollutant multiplied by its molecular weight divided by 24.45 L per mole at 25° C. Table 1 presents these factors for 28 pollutants.

Gerald Rich is senior field editor for Pollution Engineering. He is a registered professional engineer and a registered environmental professional. He has extensive experience with governmental regulations and environmental consulting.

RESPONSIBILITY FOR A CLEAN ENVIRONMENT IS YOUR BUSINESS. YOUR OPPORTUNITY TO FULFILL IT IS



THE ENVIRONMENTAL TECHNOLOGY EXPO

CONFERENCE AND EXPOSITION

April 8–11, 1991

McCormick Place East
Chicago, Illinois

It's finally happened. One event, one investment in the Environmental Technology Expo (ETE) is all you need to serve many industrial markets for your pollution abatement and control technology. Developed in response to the emerging pollution abatement and control industry, it is a broad-based marketplace for suppliers who offer solutions for air pollution, water pollution, solid waste management, hazardous waste management, and recycling.

Exposition highlights include:

▲ Qualified attendance by engineers and managers responsible for industrial pollution control and abatement—the people who must make critical investment decisions to comply with government regulations and public demand.

▲ A hands-on, up-to-the-minute Conference focused on regulations/legislation, new technology, and applications.

▲ Sponsorship by national and international publications and associations, including *Pollution Engineering* magazine.

▲ Co-location with the National Plant Engineering & Maintenance Show and the National Design Engineering Show, providing an extended attendee base of 50,000 engineers and managers.

▲ Chicago location near major Midwest industries and providing a convenient transportation hub for all national and international participants.

RESERVE YOUR EXHIBIT SPACE TODAY.

As a supplier of pollution abatement technology, you cannot ignore industry's demand for your solutions—and you can't ignore your best opportunity to respond to this demand. Plan to exhibit at ETE, the one event that puts you at the heart of the pollution abatement and control marketplace.

For more information on exhibiting or attending ETE, contact: Jill Vanderlin, Show Manager
Cahners Exposition Group • Cahners Plaza • 1350 East Touhy Avenue • P.O. Box 5060 • Des Plaines, IL 60017-5060 • Telephone: (708) 299-9311 • FAX: (708) 635-1571