APPENDIX C
GLOSSARY

Acute hazard or toxicity — see Health hazard.

Added risk — The difference between the cancer incidence under the exposure condition and the background incidence in the absence of exposure; AR = P(d) - P(O).

Adequacy — When applied to an intervention, the ratio of the expected number of potentially preventable cases to the number of cases that would occur in the absence of an intervention.

Adverse event (outcome) —Premature death or morbidity.

Analytic horizon —The time period over which the costs and benefits of health outcomes that occur as a result of the intervention are considered.

Attributable risk — The theoretical reduction in the rate or number of cases of an adverse outcome that can be achieved by elimination of a risk factor.

Audience — The consumer of the study results. Defined as policy decision makers, program decision makers, or others such as patients, health-care workers, media, other researchers, and the general public.

Averaging-out-and-folding-back — In decision analysis, a series of mathematical computations of probability values multiplied by utility estimates and summed to average out the expected value of the branches leading out of each chance node. The results are then folded back from right to left until a value is found for each decision option.

Baseline comparator — One of the alternative prevention strategies in a decision analysis. May be either the existing-program/strategy alternative or a no-program/strategy alternative, if no program exists at the time of the intervention.

Benefit-cost ratio — A mathematical comparison of the benefits divided by the costs of a project or intervention. When the benefit-cost ratio is greater than 1, benefits exceed costs.

Benign — Not malignant; remaining localized.

Bioassay — The determination of the potency (bioactivity) or concentration of a test substance by noting its effects in live animals or in isolated organ preparations, as compared with the effect of a standard preparation.

Bioavailability — The degree to which a drug or other substance becomes available to the target tissue after administration or exposure.

Carcinogen — An agent capable of inducing a cancer response.

Carcinogenesis — The origin or production of cancer, very likely a series of steps. The carcinogenic event so modifies the genome and/or other molecular control mechanisms in the target cells that these can give rise to a population of altered cells.

Case-control study — An epidemiologic study that looks back in time at the exposure history of individuals who have the health effect (cases) and at a group who do not (controls), to ascertain whether they differ in proportion exposed to the chemical under investigation.

Chance node— In a decision tree, an event which occurs as a consequence of the decision but over which one has no control. Usually drawn as a circle.

Chronic effect — An effect that remains manifest after some time has elapsed from initial exposure. See also Health Hazard.

Chronic exposure — Continuous or multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's lifetime.

Chronic hazard or toxicity — see Health hazard.

Chronic study — A toxicity study designed to measure the (toxic) effects of chronic exposure to a chemical.

Cohort — Any defined group of persons selected for a special purpose or study.

Cohort study — An epidemiologic study that observes subjects in differently exposed groups and compares the incidence of symptoms. Although ordinarily prospective in nature, such a study is sometimes carried out retrospectively, using historical data.

Confounder — A condition or variable that may be a factor in producing the same response as the agent under study. The effects of such factors may be discerned through careful design and analysis.

Consumer market studies — The determination of the value of nonmarket resources from reference to similar commodities for which a market exists in the context of estimating willingness-to-pay (WTP) values of health outcomes.

Contingent valuation studies — The use of surveys of individuals conducted in the context of a hypothetical market situation to elicit consumer valuation of goods and services. Used to estimate the willingness-to-pay (WTP) values of health outcomes.

Control group — A group of subjects observed in the absence of agent exposure or, in the instance of a case/control study, in the absence of an adverse response.

Cost — A measure of what must be given up to acquire or produce something. Economic costs can be differentiated in the following manner:

- total cost (TC) Sum of the costs of producing a particular quantity of output.
- fixed cost (FC) Costs which do not vary with the quantity of output in the short run, e.g., rent, utilities, and administrative salaries.
- variable cost (VC) Costs which vary with the level of output and which responds proportionately to change in volume of activity.
- average cost (AC) The total cost divided by the total output. Reported as the cost per unit of output.
- marginal cost (MC) The additional cost of an intervention to produce one additional unit of output. An intra program measure.
- incremental cost (IC) When interventions are ranked in ascending order of effectiveness, the additional cost to the next most effective intervention of producing another unit of output. An interprogram measure.
- incidence-based See incidence-based cost.
- prevalence-based See prevalence- based cost.

Cost analysis — The process of estimating the cost of prevention activities, also called cost identification.

Cost-benefit analysis (CBA) — A type of economic analysis in which all costs and benefits are converted into monetary (dollar) values and results are expressed as either the net present value or the dollars of benefits per dollars expended.

Cost-effectiveness analysis (CEA) — An economic analysis in which all costs are related to a single, common effect. Results are usually stated as additional cost expended per additional health outcome achieved. Results can be categorized in one of or all of the following ways:

- average cost-effectiveness The total cost of an intervention divided by the health outcomes produced by that intervention.

- marginal cost-effectiveness The additional cost incurred by an intervention to produce an additional unit of the health outcome.

- incremental cost-effectiveness When strategies are ranked in order of effectiveness, the additional cost incurred by the next most effective strategy to produce an additional unit of the health outcome.

Cost-of-illness (COI) methodology — An approach to estimate the costs of a health intervention in which two types of costs are collected: the direct medical and nonmedical costs associated with the illness and the indirect costs associated with lost productivity due to morbidity or premature mortality.

Cost-utility analysis (CUA) — A type of cost-effectiveness analysis in which benefits are expressed as the number of life years saved adjusted to account for loss of quality from morbidity of the health outcome or side effects from the intervention. The most common measure in CUA is the quality-adjusted life year (QALY)

Critical effect — The first adverse effect, or its known precursor, that occurs as the dose rate increases.

Decision analysis — An explicit, quantitative, systematic approach to decision making under conditions of uncertainty.

Decision node — In a decision tree, the first point of choice, usually drawn as a box.

Decision tree models — A graphic representation of how possible choices in a decision analysis relate (stochastically) to the possible outcomes.

Delphi process — An iterative consensus process used to determine the "best estimate" of professionals in the field. This process is often used in decision analysis to estimate the probability that an event will occur or the valuation of costs and benefits of outcomes when there is insufficient data in the published literature.

Developmental toxicity — The study of adverse effects on the developing organism (including death, structural abnormality, altered growth, or functional deficiency) resulting from exposure prior to conception (in either parent), during prenatal development, or postnatally up to the time of sexual maturation.

Direct costs — The measure of the resources expended for prevention activities or health care (compare with indirect cost).

- direct medical costs The measure of the resources for medical treatment (e.g., the cost of a physician visit).

- direct nonmedical costs Those costs incurred in connection with a health intervention or illness, but which are not expended for medical care itself (e.g., the transportation costs associated with a physician visit).

Discounting — A method for adjusting the value of future costs and benefits to an equivalent value today to account for time preference and opportunity cost, i.e., a dollar today is worth more than a dollar a year from now (even if inflation is not considered).

Discount rate — The rate at which future costs and benefits are discounted to account for time preference. See social discount rate or real discount rate.

Distributional effects — The manner in which the costs and benefits of a preventive strategy affect different groups of people in terms of demographics, geographic location, and other descriptive factors.

Dose-response relationship — A relationship between the amount of an agent (either administered, absorbed, or believed to be effective) and changes in certain aspects of the biological system (usually toxic effects), apparently in response to that agent.

Effectiveness — The improvement in health outcome that a prevention strategy can produce in typical community-based settings.

Efficacy — The improvement in health outcome that a prevention strategy can produce in expert hands under ideal circumstances.

Efficiency — A measure of the relationship between inputs and outputs in a prevention strategy. Efficiency goes beyond effectiveness of a prevention strategy by attempting to identify the maximum health output achievable for a set amount of resources.

Endpoint — A response measure in a toxicity study.

Etiologic fraction — The proportion of cases in the exposed group presumably attributable to the exposure, appropriate only if the exposed group has a higher risk of disease then the unexposed group.

Excess fraction — The fractional excess caseload produced by an exposure.

Excess lifetime risk — The additional or extra risk incurred over the lifetime of an individual by exposure to a toxic substance.

Expected utility — The sum of the products of the preference ranking, i.e., utility for an outcome and the probability that the outcome will occur for all the possible outcomes of a prevention strategy.

Expected utility theory — The dominant theory of individual behavior under conditions of uncertainty based on the assumption that, given different alternatives, the alternative with the outcome that has the highest expected utility should be chosen.

Expected value — The sum of the products of the value of outcomes and the probability of the outcome occurring for all possible outcomes of a prevention strategy.

Extra risk — The added risk to that portion of the population that is not included in measurement of background tumor rate:

$$ER(d) = [P(d) - P(O)]/[1-P(O)].$$

Extrapolation — An estimation of a numerical value of an empirical (measured) function at a point outside the range of data which were used to calibrate the function. The quantitative risk estimates for carcinogens are generally low-dose extrapolations based on observations made at higher doses. Generally one has a measured dose and measured effect.

Frank-effect level (FEL) — Exposure level which produces unmistakable adverse effects, such as irreversible functional impairment or mortality, at a statistically or biologically significant increase in frequency or severity between an exposed population and its appropriate control.

Guidelines for Carcinogen Risk Assessment — U.S. EPA guidelines intended to guide Agency evaluation of suspect carcinogens in line with statutory policies and procedures. See FR 33992-34003, September 24, 1986.

Health condition — A specific medical characterization of a health outcome over a period of time.

Health hazard (types of) —

1. Acute toxicity: The older term used to describe immediate toxicty. Its former use was associated with toxic effects that were severe (e.g., mortality) in contrast to the term “subacute toxicity” that was associated with toxic effects that were less severe. The term “acute toxicity” is often confused with that of acute exposure.

2. Allergic reaction: Adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one.

3. Chronic toxicity: The older term used to describe delayed toxicity. However, the term "chronic toxicity" also refers to effects that persist over a long period of time whether or not they occur immediately or are delayed. The term "chronic toxicity" is often confused with that of chronic exposure.

4. Idiosyncratic reaction: A genetically determined abnormal reactivity to a chemical.

5. Immediate versus delayed toxicity: Immediate effects occur or develop rapidly after a single administration of a substance, while delayed effects are those that occur after the lapse of some time. These effects have also been referred to as acute and chronic, respectively.

6. Reversible versus irreversible toxicity: Reversible toxic effects are those that can be repaired, usually by a specific tissue's ability to regenerate or mend itself after chemical exposure, while irreversible toxic effects are those that cannot be repaired.

7. Local versus systemic toxicity: Local effects refer to those that occur at the site of first contact between the biological system and the toxicant; systemic effects are those that are elicited after absorption and distribution of the toxicant from its entry point to a distant site.

Health outcome — The spectrum of human health states that can result from an exposure; also a change in morbidity or mortality.

Health-related event (HRE)— Adverse health condition.

Health state — A health condition at a specific point in time.

Health utility — The measure assigned to quality of life.

Health utility index — A multifaceted measure of utility in which different utility functions (e.g., physical function, role function, social-emotional function, and other coexisting health problems) are weighted and combined to determine an overall preference for a particular outcome.

Incidence — The number of new cases of a disease within a specified period of time.

Incidence-based cost — The total lifetime cost of new cases of a disease or injury that occur during a certain period of time.

Incidence rate — Measure of the frequency of new cases of disease in a particular population, which occurred during a specified period of time.

Incremental analysis — A type of comparative analysis used to examine the relationship between the differences in costs and benefits (whether measured in monetary, natural, or quality-adjusted units)'between two or more prevention strategies.

Incremental cost — The additional cost of producing one more additional unit of output by an alternative intervention.

Incremental cost-effectiveness — See cost-effectiveness.

Indirect cost — The resources forgone either to participate in an intervention or as the result of a health condition (e.g., earnings forgone because of loss of time from work).

Individual risk — The probability that an individual person will experience an adverse effect. This is identical to population risk unless specific population subgroups can be identified that have different (higher or lower) risks.

Interspecies dose conversion — The process of extrapolating from animal doses to equivalent human doses.

Intangible cost — Cost, such as pain and suffering, for which assigning a monetary value is difficult.

Lowest-observed-adverse-effect level (LOAEL) — The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Lowest-effect level (LEL) — Same as LOAEL.

Malignant — Tending to become progressively worse and to result in death if not treated; having the properties of anaplasia, invasiveness, and metastasis.

Marginal analysis — A type of analysis that examines the additional cost required to produce an additional unit of output by a prevention strategy.

Marginal cost — See cost.

Marginal cost-effectiveness — See cost-effectiveness.

Margin of Exposure (MOE) — The ratio of the no observed adverse effect level (NOAEL) to the estimated exposure dose (EED).

Meta-analysis — A systematic, quantitative method for combining information from multiple studies in order to derive the most meaningful answer to a specific question.

Model — A mathematical function with parameters which can be adjusted so that the function closely describes a set of empirical data. A “mathematical” or “mechanistic” model is usually based on biological or physical mechanisms, and has model parameters that have real world interpretation. In contrast, “statistical” or “empirical” models are curve-fitting to data where the math function used is selected for its numerical properties. Extrapolation from mechanistic models (e.g., pharmacokinetic equations) usually carries higher confidence than extrapolation using empirical models (e.g., logit).

Modifying factor (MF) — An uncertainty factor which is greater than zero and less than or equal to 10; the magnitude of the MF depends upon the professional assessment of scientific uncertainties of the study and database not explicitly treated with the standard uncertainty factors (e.g., the completeness of the overall data base and the number of species tested); the default value for the MF is 1.

Multiattribute utility (MAL) model — In a cost-utility analysis (CUA), the mathematical combining of the utility functions and weights for each dimension into one single function.

Net present value (NPV)— The sum that results when the discounted value of the costs of a prevention strategy are deducted from the discounted value of the benefits of the strategy

No-observed-adverse-effect level (NOAEL) — An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered as adverse, nor precursors to adverse effects. In an experiment with several NOAELs, the regulatory focus is primarily on the highest one, leading to the common usage of the term NOAEL as the highest exposure without adverse effect.

No-observed-effect level (NOEL) — An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control.

Opportunity cost — The value of the resources used in providing a specific set of health-care services valued in terms of forgone alternative uses.

Outcome measure — The final health consequence, e.g., cases prevented, quality-adjusted life years, of an intervention.

Physiologically based pharmacokinetic (PBPK) model — Physiologically based compartmental model used to quantitatively describe pharmacokinetic behavior.

Policy decision makers — Elected officials, agency heads, state and local public health officials, and others responsible for setting public health policy.

Population attributable risk — The incidence of a disease or condition in a population that is associated with exposure to the risk factor.

Premature mortality —(1) Any preventable death; (2) Deaths that occur before a specified age, most often age 65, or the average life expectancy of a certain population.

Prevalence — The number of instances of a given disease or condition in a given population at a designated time.

Prevalence-based cost — The cost associated with the existing cases of disease or injury that occur during a specified time period.

Preventable fraction — The proportion of an adverse health outcome that potentially can be eliminated as a result of a prevention strategy.

Prevented fraction — The proportion of an adverse health outcome that has been eliminated as a result of a prevention strategy.

Prevention — The promotion and preservation of health, the restoration of health when it is impaired, and the minimization of suffering and distress.

- primary prevention An intervention to reduce risk or exposure to prevent occurrence of disease or injury.

- secondary prevention An intervention to detect and treat a disease before it becomes clinically apparent.

- tertiary prevention An intervention implemented after a disease or injury is established to prevent sequelae or to minimize suffering.

Prevention effectiveness — The systematic assessment of the impact of public health policies, programs, and practices on costs and health outcomes.

Principal study — The study that contributes most significantly to the qualitative and quantitative risk assessment.

Productivity loss — The value of output not produced due to morbidity or premature mortality.

Program decision makers — Users of the results of prevention-effectiveness studies who are responsible for decisions about prevention programs.

Program evaluation — An assessment of the processes, impacts, and outcomes of intervention programs, with particular attention paid to the purposes and expectations of stakeholders of the program.

Proportionate mortality ratio (PMR) — The number of deaths from a specific cause and in a specific period of time per 100 deaths in the same time period.

Prospective study — A study in which subjects are followed forward in time from initiation of the study. This is often called a longitudinal or cohort study.

q1* — Upper bound on the slope of the low-dose linearized multistage procedure.

Quality-adjusted life years (QALY)— A frequently used outcome measure in cost utility analysis that incorporates the quality or desirability of a health state with the duration of survival. The quality of life is integrated with the length of life by using a multiplicative formula.

Quality of well-being (QWB)— A health utility index widely used for cost utility analysis.

Rank and scale — A method of valuing utilities whereby outcomes are ranked in order of best to worst and then are assigned numerical values.

Reference Concentration (RfC) — An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime.

Reference Dose (RfD) — An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Relative risk — The ratio of the incidence rate for persons exposed to a factor to the incidence rate for those not exposed.

Risk — The likelihood that a person having specified characteristics (e.g., high blood cholesterol, failure to wear seat belts) will acquire a specified disease or injury.

Risk assessment — The determination of the kind and degree of hazard posed by an agent, the extent to which a particular group of people has been or may be exposed to the agent, and the present or potential health risk that exists due to the agent.

Risk management — A decision-making process that entails considerations of political, social, economic, and engineering information with risk-related information to develop, analyze, and compare regulatory options and to select the appropriate regulatory response to a potential chronic health hazard.

Risk ratio — The ratio of the risk among persons with specific risk factors compared to the risk among persons without the risk factors.

Safety — An assessment of the level and acceptability of risk of adverse outcomes that occur as a result of a prevention technique in the context of a specific prevention strategy and disease or injury outcome.

Sensitivity analysis — Mathematical calculations that isolate factors involved in a decision analysis or economic analysis to indicate the degree of influence each factor has on the outcome of the entire analysis.

- one-way sensitivity analysis When only one value is changed.
- multiway sensitivity analysis When several values are changed simultaneously.

Slope Factor — The slope of the dose-response curve in the low-dose region. When low-dose linearity cannot be assumed, the slope factor is the slope of the straight line from 0 dose (and 0 excess risk) to the dose at 1% excess risk. An upper bound on this slope is usually used instead of the slope itself. The units of the slope factor are usually expressed as 1/(mg/kg-day).

Societal perspective — The perspective of society as a whole. Economic analyses which take a societal perspective include all benefits of a program regardless of who receives them and all costs regardless of who pays them.

Stakeholder — An individual or organization with an interest in an intervention or outcome.

Standard gamble — In cost utility analysis, a lottery-based approach to determining the utility of a particular outcome.

Standardized mortality ratio (SMR) — The ratio of observed deaths to expected deaths.

Subchronic exposure — Multiple or continuous exposures occurring usually over 3 months.

Subchronic study — A toxicity study designed to measure effects from subchronic exposure to a chemical.

Systemic effects — Systemic effects are those that require absorption and distribution of the toxicant to a site distant from its entry point, at which point effects are produced. Most chemicals that produce systemic toxicity do not cause a similar degree of toxicity in all organs, but usually demonstrate major toxicity to one or two organs. These are referred to as the target organs of toxicity for that chemical.

Technology — Techniques, devices, drugs, or procedures used to reduce the risk of an adverse health outcome.

Terminal node — In a decision tree, the end point of each sequence of events representing a health outcome. Usually represented by a rectangle.

Threshold — The dose or exposure below which a significant adverse effect is not expected. Carcinogens are thought to be non-threshold chemicals, to which no exposure can be presumed to be without some risk of adverse effect.

Threshold analysis — A type of sensitivity analysis that identifies the conditions (e.g., the values of variables) that would have to exist for the expected value or expected utility of two interventions to be equivalent. Threshold analysis is often used to identify the "switch points" at which cost savings begin or end and to indicate the point at which a different decision should be made.

Time frame — The specified period in which the intervention strategies are actually applied.

Time trade-off — A method of eliciting utilities from an individual perspective based on the willingness to trade time for health.

Utility — In decision analysis, a quantitative measure of the strength of a preferred outcome.

Uncertainty factor — One of several, generally 10-fold factors, used in operationally deriving the Reference Dose (RfD) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure; and (4) the uncertainty in using LOAEL data rather than NOAEL data.

Unit Risk — The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water, or 1 µg/cu.m in air.

Upper bound — An estimate of the plausible upper limit to the true value of the quantity. This is usually not a statistical confidence limit.

Weight-of-evidence for carcinogenicity — The extent to which the available biomedical data support the hypothesis that a substance causes cancer in humans.

Willingness-to-pay (WTP)— A method of measuring the value an individual places on reducing risk of death and illness by estimating the maximum dollar amount an individual would pay in a given risk-reducing situation.