This is a pre-regulatory proposal that is being published for stakeholder discussion and public comment. It may change significantly prior to any formal regulatory proceeding.

These draft regulations would be added to the regulations currently being proposed by the Department of Toxic Substances Control (DTSC) for the Green Chemistry Program. The Office of Environmental Health Hazard Assessment (OEHHA) and DTSC are working collaboratively on these proposed regulations in order to ensure that they are compatible with the regulations and process DTSC has already developed for the Green Chemistry Program.

OEHHA is required by SB 509 (Simitian, 2007) to evaluate and specify the hazard traits and environmental and toxicological end-points and any other relevant data that are to be included in the clearinghouse. The office shall conduct this evaluation in consultation with DTSC and all appropriate state agencies, after one or more public workshops, and an opportunity for all interested parties to comment. The office may seek information from other states, the federal government, and other nations in developing this information.

OEHHA has conducted three public workshops related to hazard traits and endpoints and has conducted significant research into existing definitions, endpoints and other relevant information in the development of this draft regulation. Many of the provisions of this draft regulation are taken directly from working definitions and methodologies used by well-respected scientific organizations such as the World Health Organization’s International Agency for Research on Cancer and the National Toxicology Program.
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1. **Preamble** – This section was adopted by the Office of Environmental Health Hazard Assessment under the authority of Health and Safety Code section 25252(b)(1). This regulation will facilitate the implementation of the Green Chemistry Program by specifying hazard traits, environmental and toxicological endpoints and other relevant data to be included in the Toxics Information Clearinghouse that will be created by the Department as required by Health and Safety Code section 25256.

2. **Definitions – for purposes of this Section only:**
   a. “Adverse effect” means a biochemical change, functional impairment, or pathologic lesion that negatively affects the performance of the whole organism, or reduces an organism’s ability to respond to an additional environmental challenge.
   b. “Adverse environmental effect” means a significant change that negatively affects an ecosystem or ecosystem component at the system, community, assemblage, population, species, or individual level.
   c. “Authoritative organization” means a state, national, international or non-governmental entity whose scientific findings on the safety, risks or hazards of chemical agents are relied upon by state, national and international governments and their supporting public health and environmental entities in regulating or otherwise protecting human health or the environment from threats posed by those chemical agents. Organizations that satisfy the definition of “authoritative organization” are the following:
      i. OEHHA, DTSC and other State of California Boards, Departments, Offices or Agencies
      ii. The National Academy of Sciences, including the National Research Council and the Institute of Medicine
      iii. Departments or Agencies of the United States federal government, including but not limited to: the Consumer Product Safety Commission, Environmental Protection Agency, Food and Drug Administration, National Toxicology Program, National Institute of
Environmental Health Sciences, National Institutes of Health, National Institute of Occupational Safety and Health, the Occupational Safety and Health Administration, and the Department of Transportation.

iv. Canadian government agencies including Environment Canada and Health Canada

v. Governmental bodies within the European Union, including the European Chemicals Agency

vi. World Health Organization, including the International Agency for Research on Cancer

vii. The United Nations and organizations within the United Nation.

d. A “chemical substance” is a chemical, chemical compound, a chemical mixture, elemental material, particulate matter or fiber, or radioactive agent; its metabolites or degradation by-products.

e. A “Class One” chemical is identified as having a specific hazard trait when there is a strong body of evidence indicating that the chemical substance has the specific toxicological hazard trait. Methods for identifying chemicals as having a Class One hazard trait can be found in subsection 4(a).

f. A “Class Two” chemical is identified as having a hazard trait when there is a lesser body of evidence than for a specific Class One identification. Methods for identifying chemicals as having a Class Two hazard trait can be found in subsection 4(B).

g. “Department” or “DTSC” means the Department of Toxic Substances Control.

h. “Document” is a report, memo, list or other written material released in paper or electronic form.

i. “Environmental endpoints” are measured or otherwise observed adverse environmental effects in ecological systems, or components of ecological systems, or non-human organisms within ecological systems.

j. “Exposure potential characteristic” means an inherent property of a chemical substance that contributes to the likelihood of significant human or environmental exposure, in general or in scenarios that can be used to estimate exposures in specific situations.

k. “Hazard traits” are properties of chemicals that fall into broad categories of toxicity, adverse environmental effects, physical hazards, or exposure potential characteristics.

l. “Mechanistic similarity” means that a chemical substance acts on a biological system in a manner similar to other chemicals that induce toxicological or environmental effects associated with a specific hazard trait.
m. “Not Classifiable” means that there is insufficient scientific evidence available to classify a chemical as having a “Class One” or “Class Two” hazard trait.

n. “OEHHHA” means the Office of Environmental Health Hazard Assessment within the California Environmental Protection Agency

o. “Other relevant data” means chemical, physical, biochemical or other data indicative of one or more hazard traits.

p. “Toxicological endpoints” are those measured or otherwise observed adverse effects in biological systems that may indicate the presence of one or more hazard traits.

q. “Well conducted scientific studies” means studies published in the open literature or submitted to a local, state, national or international government agency, using methods and analyses which are scientifically valid according to generally accepted principles

r. “Wildlife” means all non-human undomesticated animals present in the environment.

3. Specific Hazard Traits, and Endpoints and Other Relevant Data – Hazard traits are defined in this subsection within the following groupings: Toxicological (human health) hazards, environmental hazards, exposure potential hazards and physical hazards. A specific chemical substance may be identified as having a specific hazard trait of Class One, or Class Two type, or there may be inadequate information on the chemical available to make an identification, in which case the chemical would be viewed as not classifiable. Criteria for assigning a chemical substance a Class One or Class Two designation for a specific hazard trait are set out in subsection 4.

a. Toxicological hazard traits – these hazard traits affect human health. These include, but are not limited to the following:

i. Carcinogenicity

   1. The carcinogenicity hazard trait is defined as the occurrence of increased incidence, reduced latency, or increased severity or multiplicity in neoplasia following exposure to a chemical substance.

   2. Endpoints include, but are not limited to those indicating malignant and benign neoplasia of alimentary, cardiovascular,
endocrine, genital, hematopoietic, integumentary, musculoskeletal, nervous, respiratory, special senses, and urinary systems as well as any other systemic neoplastic lesions observed in human or animal studies.

3. Other relevant carcinogenicity data includes but are not limited to: data on mechanisms of carcinogenesis such as exposure-related modifications to the physiology or response of cells, tissues and organs (e.g., mitogenesis, compensatory cell division, hyperplasia) or in the signaling pathways used by cells to manage critical processes related to increased risk for cancer; changes in key cellular structures at the molecular level such as mutation and other genotoxicity endpoints; epigenetic changes associated with increased cancer risk; structural similarity to other chemicals with the carcinogenicity hazard trait.

ii. Cardiovascular toxicity

1. The cardiovascular toxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the heart or the vascular system following exposure to a chemical substance.

2. Cardiovascular toxicity endpoints include but are not limited to those indicating: structural effects associated with necrosis, degeneration, proliferation, or inflammation of the heart or vasculature, damage to the blood vessel walls that may result in lesions leading to atherosclerosis or hypertension; functional effects including adverse changes in the ability of the cardiovascular system to maintain homeostasis, supply appropriate nutrients, metabolites, respiratory gases, or hormones, or in its ability to remove waste products or foreign material, changes in rhythmicity or contractility of the heart, hypo- or hyper- tension, impaired ability to regulate tissue pH or body temperature; vascular effects including alteration of vascular reactivity or vessel dilation or contraction.

3. Other relevant cardiovascular toxicity data include but are not limited to: in vitro measures of cardiovascular toxicity such as cytotoxicity to isolated vascular endothelial cells; structural or
mechanistic similarity to other chemicals with the cardiovascular toxicity hazard trait.

iii. Dermatotoxicity

1. The dermatotoxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the skin including its barrier properties and its ability to maintain heat, fluid, or electrolyte homeostasis following exposure to a chemical substance.

2. Endpoints include but are not limited to those indicating: systemic reactions, allergic sensitization, allergic reactions, acute or subacute irritation, or photosensitivity.

3. Other relevant dermatotoxicity data include, but are not limited to: in vitro measures of dermatotoxicity such as toxicity to isolated skin or skin cells; and structural or mechanistic similarity to other chemicals with the dermatotoxicity hazard trait.

iv. Developmental toxicity

1. The developmental toxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the developing organism following exposure to a chemical substance. Developmental toxicity can result from an exposure of either parent that occurs prior to conception, during prenatal development, or postnatally before the time of sexual maturation.

2. Endpoints for developmental toxicity include but are not limited to those indicating: death of the developing organism, structural abnormality, altered growth, functional deficiency or other adverse effect on the developing organism. These observations in animals or humans can be manifested at any point in the lifespan of the organism or its offspring.

3. Other relevant data include but are not limited to: mechanistic data at the molecular level such as genotoxicity or epigenetic toxicity, or at the cellular, organ, or organism level; structural or mechanistic similarity to other chemicals with the developmental toxicity hazard trait.
v. Endocrine toxicity

1. The endocrine toxicity hazard trait is defined as the occurrence of adverse effects following exposure to a chemical substance on the structure or function of the endocrine system (often referred to as endocrine disruption), and includes metabolic syndrome.

2. Endocrine toxicity endpoints include but are not limited to those indicating: observations of adverse effects on endocrine organs; adverse perturbations of the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, metabolism, reproduction, development or behavior; any other interactions with hormone receptors or receptor processes to mimic, enhance or inhibit action of a natural hormone on the target organ system.

3. Other relevant data include but are not limited to: binding of a chemical substance or its metabolites to hormones or hormonal receptors or inhibition of hormone synthesis in silico or in vitro experimental models; induction of hormone metabolic enzymes; structural or mechanistic similarity to other endocrine toxicants.

vi. Epigenetic toxicity

1. The epigenetic toxicity hazard trait is defined as heritable changes in gene expression or gene function that do not involve changes in the DNA sequence, following exposure to a chemical substance.

2. Epigenetic toxicity endpoints include, but are not limited to those indicating: toxicity in humans or animals associated with epigenetic mechanisms such as chemically induced DNA methylation, histone modification, nucleosome remodeling, or non-coding RNA. Chemically induced epigenetic endpoints may be observed in an exposed individual or its offspring.

3. Other relevant epigenetic toxicity data include but are not limited to: in vitro or other data indicative of chemically induced DNA methylation, histone modification, nucleosome remodeling, non-coding RNA or other epigenetic mechanisms;
structural or mechanistic similarity to other epigenetic toxicants.

vii. Genotoxicity

1. The genotoxicity hazard trait is defined as the occurrence of a substance-induced change, heritable at the cellular level, to the DNA sequence following exposure to a chemical substance.

2. Genotoxicity endpoints include but are not limited to those indicating: DNA strand breaks, mutations in genes, chromosomal aberrations, sister chromatid exchange, aneuploidy, or polyploidy in humans, animals, or cell lines.

3. Other relevant data include but are not limited to: data on DNA adduct formation, protein-adduct formation; structural similarity to other genotoxicants; electrophilic potential.

viii. Immunotoxicity

1. Immunotoxicity is defined as adverse effects on the components or function of the immune system following exposure to a chemical substance.

2. Endpoints include but are not limited to: allergic sensitization such as anaphylactic hypersensitivity, antibody-dependent cytotoxic hypersensitivity, complex mediated hypersensitivity, or delayed type hypersensitivity; changes in immune cell numbers such as leukocytopenia, leukocytosis, granulocytopenia, granulocytosis, lymphopenia, or lymphocytosis; suppression or enhancement of the immune response; changes in specific immunoglobulins with no obvious explanation; changes in immune organ weights; and initiation or exacerbation of auto immunity.

3. Other relevant immunotoxicity data include but are not limited to: altered immune function following neurosensitization, mechanisms of heightened immune response due to high chemical reactivity/antigenicity; changes in number or behavior of specific classes of regulatory effector cells.
ix. Hematotoxicity
   1. The hematotoxicity hazard trait is defined as the occurrence of adverse effects on blood or blood forming tissues following exposure to a chemical substance.
   2. Hematotoxicity endpoints include, but are not limited to those indicating: alterations in the number, types or lifetime of circulating blood cells; decrease in the oxygen transporting capacity of hemoglobin; increase or decrease in blood clotting activity resulting from interference in platelet response or function or other causes.
   3. Other relevant data include but are not limited to: in vitro measures of toxicity in isolated blood cells or blood forming tissues; structural or mechanistic similarity to other hematotoxicants.

x. Hepatotoxicity and digestive system toxicity
   1. The hepatotoxicity and digestive system toxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the liver, gall bladder, and gastrointestinal tract following exposure to a chemical substance.
   2. Endpoints include, but are not limited to those indicating: liver damage, hepatitis, cholestasis, vascular changes, and steatosis, gall bladder disease, and inflammation or hyperplasia of the gastrointestinal epithelium
   3. Other relevant hepatotoxicity and gastrointestinal toxicity data include but are not limited to those indicating: possible liver damage, excretion of pro-inflammatory cytokines, induction of xenobiotic metabolizing enzymes or generation of reactive metabolites; disruption of glucose or glycogen metabolism; impaired or unbalanced serum protein production; structural or mechanistic similarity to other chemicals with this hazard trait.

xi. Musculoskeletal toxicity
   1. The musculoskeletal toxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the musculoskeletal system, including bones, muscles,
cartilage, tendons, ligaments, joints and connective tissue following exposure to a chemical substance.

2. Musculoskeletal toxicity endpoints include but are not limited to those indicating: arthritis, decreased joint movement; changes in mineral content of bone; osteomalacia; osteoporosis bone malformation or other skeletal growth disorders; abnormal bone mass or density indices; tooth loss; fibromyalgia; adverse muscle or neuromuscular function.

3. Other relevant musculoskeletal toxicity data include but are not limited to: in vitro observations indicative of musculoskeletal toxicity; structural or mechanistic similarity to other chemicals with the musculoskeletal toxicity hazard trait.

xii. Nephrotoxicity and other toxicity to the urinary system

1. The nephrotoxicity hazard trait is defined as adverse effects on the structure or function of the kidney and components of the urinary system following exposure to a chemical substance.

2. Endpoints for evaluating nephrotoxicity or other toxicity to the urinary system include, but are not limited to those indicating: abnormal urine volume or chemistry; alterations in glomerular filtration rate or tubular re-absorptive capacity; pathological changes to the kidney; formation of calculi in the ureter or bladder; muscular or epithelial damage in the urinary bladder.

3. Other relevant renal toxicity data include, but are not limited to: outcomes of in vitro tests for nephrotoxicity; structural or mechanistic similarity to other chemicals with the nephrotoxicity hazard trait.

xiii. Neurotoxicity

1. The neurotoxicity hazard trait is defined as the occurrence of adverse effects on the components or function of the central or peripheral nervous system following exposure to a chemical substance. Function includes neurochemical, neurophysiological, or behavioral effects.

2. Endpoints include, but are not limited to those indicating: pathological changes in the central or peripheral nervous systems; abnormal electrical activity of the central or
peripheral nervous systems, altered neurochemical synthesis, storage, secretion and uptake, impairments in neuromuscular control, mood disorders; behavioral changes; impaired cognition.

3. Other relevant neurotoxicity data include but are not limited to: in vitro indicators of neurotoxicity in isolated nervous system cells; structural or mechanistic similarity to other neurotoxicant.

xiv. Ocular toxicity
1. The ocular toxicity hazard trait is defined as adverse changes to the components or function of the visual system following exposure to a chemical substance.
2. Endpoints include but are not limited to those indicating: iris, conjunctival, lens or corneal damage; abnormal reaction to light; damage to the eye lids or nictitating membranes; functional or structural damage to the retina; damage to or induction of functional abnormalities to the ocular portions of the central nervous system.
3. Other relevant ocular toxicity data include, but are not limited to physicochemical properties such as pH and chemical reactivity; data on dermal irritancy or corrosivity; structural or mechanistic similarity to other chemicals with the ocular toxicity hazard trait.

xv. Ototoxicity
1. The ototoxicity hazard trait is defined as the occurrence of adverse effects on the structure or function of the inner ear or the vestibulo-cochlear nerve, which could result in temporary or permanent disturbances of hearing, balance, or both following exposure to a chemical substance.
2. Endpoints include, but are not limited to those indicating: hearing impairment; abnormal balance; changes to cellular components of the inner ear; change in auditory response or electrical activity in the auditory areas of the brain.
3. Other relevant data include but are not limited to: in vitro indications of ototoxicity; structural or mechanistic similarity to other chemicals with the ototoxicity hazard trait.
xvi. Reactivity in biological systems

1. The reactivity in biological systems hazard trait is defined as the occurrence of rapid reactions with molecules in the body that lead to alterations in critical molecular function and ultimately adverse health outcomes.

2. Endpoints include, but are not limited to those adverse health effects resulting from covalent binding or oxidation of cellular macromolecules, generation of reactive oxygen species or oxidative stress, or catalytic generation of hydroxyl radicals.

3. Other relevant data include but are not limited to measurements of covalent binding to or oxidation of DNA, lipids or proteins, and detection of reactive species in cell culture.

xvii. Reproductive toxicity

1. The reproductive toxicity hazard trait is defined as the occurrence of adverse effects on the reproductive system or function of females or males following exposure to a chemical substance.

2. Endpoints of reproductive toxicity include but are not limited to those indicating: adverse alterations to the female or male reproductive organs, the related endocrine system, pregnancy outcomes, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or other modifications that compromise the integrity of the reproductive system or function in animals or humans.

3. Other relevant data include but are not limited to: data on endocrine disruption, genotoxicity, in vitro measures of the capacity of a chemical to damage the function or structure of germ cells such as sperm or oocytes or cells critical for reproductive function such as Sertoli and Leydig cells in males; structural or mechanistic similarity to other reproductive toxicants.
xviii. Respiratory toxicity

1. The respiratory toxicity hazard trait is defined as an adverse change in the structure or function of the respiratory tract following exposure to a chemical substance, including respiratory tract injury or decreasing the ability of the lungs to function in gas exchange.

2. Endpoints include but are not limited to those indicating: irritation of the respiratory epithelium; pathological changes to the airway or other lung structures; airways hyper-reactivity; altered lung function; asthma; airways remodeling; increased respiratory infections.

3. Other relevant data include but are not limited to: In vitro evidence for respiratory toxicity such as increased inflammatory cytokine expression in airway cells; particle size distribution inclusive of respirable particles, fibrous nature; long half-life in the lung; chemical reactivity; redox potential; structural or mechanistic similarity to other respiratory toxicant.

b. Environmental Hazard Traits – these hazard traits affect the environment. These include, but are not limited to the following:

i. Wildlife survival impairment

1. The wildlife survival impairment hazard trait is defined as the occurrence of increased incidence of death, disease or other biological impairment, following exposure to a chemical substance that significantly decreases the potential for wildlife survival in the environment.

2. Endpoints include, but are not limited to those indicating: death, endpoints of toxicity listed for the toxicological hazard traits above, non-specific toxicity, behavioral impacts, or increased disease susceptibility observed in experimental or field studies.

3. Other relevant survival impairment data include but are not limited to: mechanistic or structural similarity to other chemicals that impair wildlife survival; mechanistic data listed for toxicological hazard traits above, or correlative data from field studies linking chemical exposure with community- or
ecosystem-level impacts, loss of biodiversity including genetic diversity, or impacts on endangered or threatened species.

ii. Wildlife reproductive impairment

1. The wildlife reproductive impairment hazard trait is defined as the occurrence of adverse effects on the reproductive system or sexual function of wildlife following exposure to a chemical substance that may reduce reproductive capacity in the environment.

2. Endpoints include, but are not limited to those indicating: reductions in production of vitellogenin, gamete maturation, physiological or behavioral impacts on mating or spawning, fecundity, viable offspring or parental caretaking observed in animal or field studies; induction of abnormal sex ratios or appearance of unexpected intersexual anatomical or behavioral characteristics in the laboratory or in a wild population.

3. Other relevant reproductive impairment data include but are not limited to: mechanistic or structural similarity to other chemicals that impair wildlife reproduction; exposure related perturbations of the hypothalamic–pituitary–gonadal axis; agonism of the aryl hydrocarbon receptor; binding or disruption of the function of the estrogen or androgen receptors; toxicogenomic responses associated with reproductive impairment, or related data as described under the reproductive or endocrine toxicological hazard traits above. Correlative data from field studies linking exposure to a chemical substance with reductions in animal reproduction are also considered relevant.

iii. Wildlife developmental impairment

1. The wildlife developmental impairment hazard trait is defined as the occurrence of adverse effects on the structure or function of the developing organism following exposure to a chemical substance.

2. Endpoints include, but are not limited to those indicating: exposure related abnormalities in body form, metamorphosis,
behavior (hyperventilation, atypical locomotion) or morphometrics (e.g., weight, length).
3. Other relevant developmental impairment data include but are not limited to: mechanistic or structural similarity to other chemicals that impair wildlife development; data on mechanisms of mammalian developmental toxicity (described above) or those specific to nonmammalian wildlife (e.g., signaling control of metamorphosis).

iv. Wildlife growth impairment
1. The wildlife growth impairment hazard trait is defined as the occurrence of adverse changes in absolute growth, proportional growth (e.g., organ to body ratio) or growth rate following exposure to a chemical substance.
2. Endpoints include, but are not limited to those indicating: abnormalities in length, weight (body or organ), condition index, body surface area or growth rate observed in animals.
3. Other relevant growth impairment data includes but are not limited to: mechanistic or structural similarity to other chemicals that impair wildlife growth; mechanistically based markers of data on growth retardation.

v. Non-target phytotoxicity
1. The non-target phytotoxicity hazard trait is defined as unwanted detrimental deviations from the normal pattern of appearance, growth, or function of plants following exposure to a chemical substance. The phytotoxic response may occur during germination, growth, differentiation, or maturation of plants, and may be of a temporary or long-term nature.
2. Endpoints include, but are not limited to those indicating: adverse effects on growth habit, yield, or quality of plants or their commodities.
3. Other relevant phytotoxicity impairment data include but are not limited to: mechanistic or structural similarity to other phytotoxicants.
vi. Loss of genetic diversity, including biodiversity
   1. The loss of genetic diversity hazard trait is defined as adverse
      change in the genetic make-up of a species, community,
      assemblage or ecosystem following exposure to a chemical
      substance
   2. Endpoints include, but are not limited to those indicating:
      changes in the locational distribution of species, or the genetic
      make-up of resident populations of individual species.
   3. Other relevant data include but are not limited to: in silico
      predictions of changes in genetic diversity; high species
      specific acute toxicity.

vii. Eutrophication
   1. The eutrophication hazard trait is defined as the occurrence,
      following a chemical substance release, of excessive plant
      growth in water bodies resulting from excessive plant nutrients
      that stimulate excessive plant growth.
   2. Endpoints include, but are not limited to those indicating: low
      dissolved oxygen content, or hypoxia.

c. Exposure potential hazard traits
   i. Ambient ozone formation
      1. The ambient ozone formation hazard trait is defined as the
         capacity for chemicals such as volatile organic compounds
         and oxides of nitrogen to generate photochemical smog and
         ozone and other oxidants indoors.
      2. A chemical’s propensity to form ozone can be indicated by
         photochemical and other reactivity to form ozone and other
         oxidants. A chemical substance has this hazard trait if it or its
         breakdown products meets the definition of photoreactivity as
         determined by the Air Resources Board protocol.
   
   ii. Bioaccumulation
      1. The bioaccumulation hazard trait is defined as the propensity
         for an agent to be sequestered in organisms or parts of an
organism following exposure. The concentration of the agent is greater in the organism than in its surrounding environment.

2. A substance has this hazard trait if it, its metabolite or environmental degradation product has a bioaccumulation factor greater than 2000, a log octanol water coefficient greater than or equal to 4, has been shown to bioaccumulate in animal or human tissues, or when it inhibits an efflux transporter.

iii. Environmental persistence
   1. The environmental persistence hazard trait is defined as the propensity for a substance to exist in the environment for a long time period subsequent to its release.
   2. A chemical substance has this hazard trait if it, or its environmental degradation product has the following half-lives in the environment: marine water – greater than 60 days; fresh or estuary water – greater than 40 days; marine sediment – greater than 180 days; ambient air – greater than 2 days; soil – greater than 6 months.

iv. Global warming potential
   1. The global warming potential hazard trait is defined as the propensity to be a greenhouse gas, that is, to absorb infra-red radiation in the atmosphere, and thereby contribute to the general warming of the planet.
   2. Criteria and methods used by the California Air Resources Board to identify greenhouse gases will be used to evaluate this hazard trait.

v. Lactational or transplacental transfer
   1. The lactational or transplacental transfer hazard trait is defined as the ability of a chemical substance to transfer from the mother’s tissues into breast milk or across the placenta.
   2. A chemical’s propensity for lactational or transplacental transfer can be indicated by studies measuring the chemical substance in mother’s milk or crossing the placenta into fetal circulation, or by physical-chemical properties associated with movement into mother’s milk or across the placenta.
vi. Mobility in environmental media
1. The mobility in environmental media hazard trait is defined as the capacity of a chemical substance for rapid movement in the environment.
2. A chemical substance has this trait if rapid or broad environmental mobility has been reported in the scientific literature, if it is volatile, water soluble, or possesses other physico-chemical characteristics predisposing to ease of movement through environmental compartments such as air, water, and soil.

vii. Particle size or fiber dimension
1. The particle size or fiber dimension hazard trait is the existence of a chemical substance in the form of nano-, ultrafine, fine or respirable particles or fibers or the propensity for it to form into such small-sized particles or fibers with use or environmental release.
2. A chemical substance has this hazard trait if it is in particle form in the respirable size range (less than or equal to 10 micrometers in mass median aerodynamic diameter (MMAD)), in the fine particle size range (less than or equal to 2.5 micrometers MMAD), in the ultrafine or nanoparticle size range (less than or equal to 0.1 micrometers in MMAD), or exists as a fiber with at least a 3:1 aspect ratio and a diameter less than or equal to 3 micrometers.
3. Other relevant data related to this hazard trait include but are not limited to: particle size distribution, surface area, aspect ratio, surface coatings, and surface charge.

viii. Persistence in biota
1. The biopersistence hazard trait is defined as the propensity for a substance to exist in the biota (including humans) for a long time period subsequent to its release.
2. Chemicals that have the following half-lives are considered biopersistent: humans – greater than one month; other species – greater than 0.1% of their lifespan.
ix. Stratospheric ozone depletion potential
   1. This hazard trait is defined as the capacity for a chemical substance to deplete stratospheric ozone, and thereby contribute to higher levels of ultraviolet B radiation reaching the earth’s surface.
   2. Any chemical substance or its environmental degradation product has this hazard trait if it is characterized as such by the California Air Resources Board or the United States.

x. Toxic environmental transformation
   1. The toxic environmental transformation hazard trait is defined as the potential for a chemical substance to be transformed environmentally to a form that is more toxic or more persistent.
   2. A chemical substance has this hazard trait if such transformations are observed in the field or laboratory or reliably predicted through structure activity analyses.

d. Physical hazard traits – these hazard traits may affect human health or the environment. These include, but are not limited to the following:

i. Explosivity
   1. The explosivity hazard trait is defined as a hazard that results from chemical reaction that produces gas at such a temperature and pressure and at such a speed as to cause damage to the surroundings.
   2. Chemicals substances that have this hazard trait are those materials meeting the criteria for being defined or otherwise classified as explosive, pyrotechnic, or organic peroxide substances or mixtures by the U.S. Department of Transportation.

ii. Flammability
   1. The flammability hazard trait is defined as hazards due to substances that ignite under certain conditions, causing burns or fire.
   2. Chemicals substances that have this hazard trait are those materials meeting the criteria for being defined or otherwise classified as flammable gases, aerosols, liquids, solids, pyrophoric liquids, pyrophoric solids, self-heating material, substances or mixtures which, in contact with water, emit flammable gases, or organic peroxides by the U.S.
iii. Nanomaterial hazard trait
   1. The nanomaterial hazard trait is defined as hazards due to a chemical substance having greater toxicity when in nanoparticle form than in bulk form.
   2. Nanoparticles or nanosized fibers, that are particles that are 100 nm or less in any dimension, or would be defined as nanoparticles according to section 3.c.vi, may have this trait.

iv. Oxidization
   1. The oxidization hazard trait is defined as hazards due to substances that, generally by yielding oxygen, cause, or contribute to, the combustion of other material.
   2. Chemical substances that have this hazard trait are those materials meeting the criteria for being defined or otherwise classified as an oxidizer by the U.S. Department of Transportation.

v. Self-reactive substances and mixtures
   1. The self-reactive hazard trait is defined as hazards due to thermally unstable liquid or solid substances or mixtures liable to undergo a strongly exothermic decomposition even without participation of oxygen (air).
   2. Chemicals substances that have this hazard trait are those meeting the criteria for being defined or otherwise classified as having such properties by the U.S. Department of Transportation.

vi. Radioactivity
   1. The radioactivity hazard trait is defined as hazards due radioactive decay.
   2. Chemical substances have this hazard trait if they are radioactive elements or isotopes or if they contain radioactive elements or isotopes.
4. **Sources and methodologies for identifying toxicological and environmental hazard traits** – The following sources or methodologies shall be used to identify and classify the hazard traits of specific chemical substances.

   a. A chemical substance has a specific Class One hazard trait if one or more of the following apply:
      
      i. A document of an authoritative organization identifies or otherwise indicates that the chemical substance, or its metabolite or environmental degradation product poses a hazard trait as defined in subsection 3.
         1. The document must either discuss studies that identify the hazard, use studies identifying this hazard as a basis for a hazard identification, dose-response assessment or risk assessment, or include the chemical substance, its metabolite or environmental degradation product on a list of substances identified or regulated based on a hazard trait as defined in subsection 3.
      ii. At the request of DTSC, OEHHA may determine whether or not a chemical substance, its metabolite or environmental degradation product has a Class One hazard trait, except for carcinogenicity, developmental or reproductive toxicity, based on the weight of the available scientific evidence, including data suggesting lack of effect, from:
         1. well conducted scientific studies that show exposure to the chemical substance, metabolite or environmental degradation product induces a toxicological endpoint or endpoints for the hazard trait; and
         2. other relevant data from well conducted scientific studies.
      3. In the event the chemical substance has insufficient scientific evidence to make this determination, OEHHA may determine whether or not the chemical has the related Class Two hazard trait, or whether the chemical should be considered not classifiable.

   b. A chemical substance has a specific Class Two hazard trait, if it does not meet the criteria for Class One in subsection 4(a) above, but one or more of the following apply:
i. A document of an authoritative organization identifies the chemical substance, its metabolite or environmental degradation product as possibly having one or more of the hazards defined in subsection 3, and discusses well-conducted studies supporting the possibility that the chemical substance possesses the hazard trait.

ii. At the request of DTSC, OEHHA may determine that a specific chemical substance, its metabolite or environmental degradation product poses the Class Two hazard trait, based on the weight of the evidence, including scientific data indicating lack of effect, from:
   1. a well conducted scientific study that indicates exposure induces a toxicological endpoint or endpoints for this hazard trait, and
   2. other relevant data from well conducted scientific studies.

iii. In the event the chemical substance has insufficient scientific evidence to make this determination, the chemical shall be considered not classifiable.

c. For purposes of this section, a chemical substance is classified as a Class One Hazard Trait for carcinogenicity if one or more of the following apply to the chemical substance, its metabolite or environmental degradation product:
   i. It is known to the state to cause cancer under Title 27 California Code of Regulations, section 27001 (Proposition 65).
   ii. It is identified by the U.S. Environmental Protection Agency as being “Carcinogenic to Humans” or “Likely to Be Carcinogenic to Humans” or has been classified as a Group A, B1 or B2 carcinogen.
   iii. It is classified in Group 1, 2A or 2B by the International Agency for Research on Cancer.
   iv. It is identified as a carcinogen under the California Toxic Air Contaminant or Public Health Goal programs.
   v. It is classified as “known to be” or “reasonably anticipated to be” a human carcinogen by the U.S. National Toxicology Program.
   vi. It is identified or otherwise recognized as a known or potential carcinogen in a report by the National Academy of Sciences' National Research Council or Institute of Medicine.
   vii. It is otherwise recognized as a known or potential carcinogen by California, other states, the United States or other nations.
d. A chemical substance has a Class Two hazard trait for Carcinogenicity if it does not meet the criteria in subsection 5(c) for having the Carcinogenicity (Class One) Hazard Trait but one or more of the following apply to the chemical substance, its metabolite, or environmental degradation product:
   i. It is identified by the U.S. Environmental Protection Agency as having “Suggestive Evidence of Carcinogenic Potential,” or as being in Group C.
   ii. It is identified as having limited evidence of carcinogenicity in animals by the International Agency for Research on Cancer.
   iii. It is otherwise identified by the OEHHA as a suspected carcinogen or as an agent with carcinogenic potential.
   iv. It is otherwise recognized as a suspected carcinogen by California, other states, the United States or other nations.
   v. It has the Genotoxicity (Class One) Hazard Trait.
   vi. At the request of DTSC, OEHHA may determine whether or not it has the Carcinogenicity (Class Two) Hazard Trait, based on the weight of the evidence, including data indicating lack of effect, according to the methods in subsection 4(b)(ii). This evidence includes, but is not limited to:
      1. Whether or not it meets the criteria for being classified as having “Suggestive Evidence of Carcinogenic Potential” by the U.S. EPA or “limited evidence of carcinogenicity” in animals by the International Agency for Research on Cancer.
      2. Strong indications of carcinogenicity from validated Quantitative Structure Activity Relationship programs such as those used by U.S. Environmental Protection Agency to evaluate the potential toxicity of new or existing chemicals.
      3. Mechanistic or other relevant data as described by the International Agency for Research on Cancer.
      4. Adequate evidence for the classification based on induction of responses in medium or high throughput or cell-, tissue- or whole organism- based assays perturbing known physiological, biochemical or other pathways involved in carcinogenesis (such as a specific endocrine disruption pathway).
      5. In the event the chemical substance has insufficient scientific evidence to make this determination, the chemical shall be considered not classifiable.
e. A chemical substance has the Developmental Toxicity (Class One) Hazard Trait if one or more of the following apply to it or its metabolite or environmental degradation product:
   i. It is identified as known to the state to cause reproductive toxicity with developmental toxicity denoted as an endpoint in Title 27 California Code of Regulations section 27001 (Proposition 65).
   ii. It is identified as having “clear evidence of adverse effects” for developmental toxicity in laboratory animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction.
   iii. It is identified as a developmental toxicant under the California Toxic Air Contaminant or Public Health Goal programs.
   iv. It is identified in the NIOSH Pocket Guide to Chemical Hazards as having teratogenic or other developmental effects as a symptom.
   v. It is identified as a known or potential developmental toxicant or having the capacity to cause developmental toxicity in a report by the National Academy of Sciences’ National Research Council or Institute of Medicine.
   vi. It is otherwise recognized by California, other states, the United States or other nations as a developmental toxicity hazard.

f. A chemical substance has the Developmental Toxicity (Class Two) Hazard Trait if it does not meet the criteria for having the Developmental Toxicity (Class One) Hazard Trait but one or more of the following apply to it, its metabolite, or environmental degradation product:
   i. It is identified as having “some evidence of adverse effects” or “limited evidence of adverse effects” for developmental toxicity in laboratory animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction,
   ii. It is classified as having limited evidence of carcinogenicity by the International Agency for Research on Cancer, with a clear statement that the chemical substance may induce transplacental carcinogenesis noted in an IARC Monograph on the Evaluation of Carcinogenic Risks to Humans
   iii. It is otherwise recognized as a suspected developmental toxicant by California, other states, the Federal government or other nations.
iv. At the request of DTSC, OEHHA may determine whether or not the chemical, in accordance with the methods in subsection 4(a)(ii), the Developmental Toxicity (Class Two) Hazard Trait because:

1. It has strong indications of the developmental toxicity hazard trait from validated Quantitative Structure Activity Relationship programs such as those used by U.S. Environmental Protection Agency to evaluate the potential toxicity of new or existing chemicals,

2. It has a Genotoxicity (Class One) or Endocrine Toxicity (Class One) Hazard Trait with mechanisms of genotoxicity or endocrine disruption likely to be involved in developmental toxicity.

3. It has “supportive studies,” as described by the National Toxicology Program, indicating possible developmental toxicity.

4. It induces responses in high or medium throughput, whole organism or other assays perturbing known physiological, biochemical or other pathways involved in developmental toxicity.

5. It meets the criteria for being identified as having some evidence of developmental toxicity in animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction,

6. In the event the chemical substance has insufficient scientific evidence to make this determination, the chemical shall be considered not classifiable.

g. A chemical substance has the Reproductive Toxicity (Class One) Hazard Trait if one or more of the following apply to it or its metabolite or environmental degradation product:

i. It is identified in Title 27 California Code of Regulations, section 25001(Proposition 65) as known to the state to cause reproductive toxicity with, at a minimum, male or female reproductive toxicity denoted as an endpoint,

ii. It is identified as having "clear evidence of adverse effects" for reproductive toxicity in male or female laboratory animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction,
iii. It is identified as being a male or female reproductive toxicant under the California Toxic Air Contaminant or Public Health Goal programs,

iv. It is identified as a known or potential male or female reproductive toxicant or having the capacity to cause reproductive toxicity in a report by the National Academy of Sciences’ National Research Council or Institute of Medicine,

v. It is identified in the NIOSH Pocket Guide to Chemical Hazards with having reproductive organs as the target organ or as having sterility or other reproductive effects in the symptoms field, or

vi. It is otherwise recognized as a male or female reproductive hazard by California, other states, the United States or other nations.

h. A chemical substance has the Reproductive Toxicity (Class Two) Hazard Trait if it does not meet the criteria for having the Reproductive Toxicity (Class One) Hazard Trait but one or more of the following apply to it, its metabolite, or environmental degradation product:

i. It is identified as having “some evidence of adverse effects” or “limited evidence of adverse effects” for reproductive toxicity in laboratory animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction,

ii. It is otherwise recognized as a suspected reproductive toxicant by California, other states, the Federal government or other nations

iii. At the request of DTSC, OEHHA may determine whether or not the chemical, in accordance with the methods in section (4)(a)(ii), has the Reproductive Toxicity (Class Two) Hazard Trait because:

   1. It has strong indications of the reproductive toxicity hazard trait from validated Quantitative Structure Activity Relationship programs such as that used by U.S. Environmental Protection Agency to evaluate the potential toxicity of new or existing chemicals,

   2. It has “supportive studies,” as defined by the National Toxicology Program, indicating possible male or female reproductive toxicity

   3. It has a Genotoxicity (Class One) or Endocrine Toxicity (Class One) Hazard Trait with mechanisms of genotoxicity or endocrine disruption likely to be involved in reproductive toxicity.

   4. It induces responses in high or medium throughput, whole organism or other assays perturbing known physiological,
biochemical or other pathways involved in male or female reproductive toxicity, or
5. It meets the criteria for being identified as having some evidence of reproductive toxicity in animals or humans by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction.
6. In the event the chemical substance has insufficient scientific evidence to make this determination, the chemical shall be considered not classifiable.

i. A chemical substance has a hazard trait in accordance with subsections 4(a through g) above, unless the DTSC or OEHHA, based on current scientific information, makes a determination that the chemical substance does not have the hazard trait, and publishes that determination.