Green Ribbon Science Panel
Subcommittee #1 --- Chemical Identification and Prioritization

ATTACHMENTS

Attachment 1 --- Statutes
This document includes AB 1879 & SB 509 which provide the statutory mandates, authorities and scope for the regulations, and AB 289 which provides some limited data call-in authority for DTSC.

Attachment 2 --- Authoritative Bodies Lists Examples
This is a list of chemicals lists that have been established by other authoritative bodies.

Attachment 3 --- Prioritization Hazard & Exposure Factors Example
This document shows an approach to prioritization of chemicals (modeled on the DTSC draft regulations) that considers both hazard and exposure factors.

Attachment 4 --- Prioritization Exposure Factors Examples
This list is focused on exposure factors only; some taken from the DTSC draft regulations and some from stakeholder suggestions.

Attachment 5 --- Ranking Formula Approach Examples
This document shows several conceptual models for a ranking and/or weighted factor approach to prioritization (based on suggestions from stakeholders).

Attachment 6 --- USEPA Design for the Environment Alternatives Assessment Criteria for Hazard Evaluation (draft)
This model that includes a ranking process based largely on hazard considerations, and an approach to determining and applying "weight of evidence".

Attachment 7 --- Washington State Chemical Prioritization (presentation by Alex Stone)
Washington State's Children's Safe Product program uses a chemical prioritization process that includes both hazard and exposure factors.

Attachment 8 --- Reliable Information Definition Examples
This document essentially shows the approach to the data quality issue used in the DTSC draft regulations.

Attachment 9 --- OECD Guidance on Data Quality
This document sets forth the OECD approach to data quality (which is been suggested by some stakeholders).

Attachment 1-1

Statutes

AB 1879 (chap. 559, stat. 2008, Feuer)
SB 509 (chap. 560, stat. 2008, Simitian)

Health and Safety Code sections 25251 – 25257.1
Article 14. Green Chemistry

SB 509 **25251.** For purposes of this article, the following definitions shall apply:

(a) "Clearinghouse" means the Toxics Information Clearinghouse established pursuant to Section 25256.

(b) "Council" means the California Environmental Policy Council established pursuant to subdivision (b) of Section 71017[1] of the Public Resources Code.

(c) "Office" means Office of Environmental Health Hazard Assessment.

(d) "Panel" means the Green Ribbon Science Panel established pursuant to Section 25254

(e) "Consumer product" means a product or part of the product that is used, brought, or leased for use by a person for any purposes. "Consumer product" does not include any of the following:

(1) A dangerous drug or dangerous device as defined in Section 4022[2] of the Business of Professions Code.

(2) Dental restorative materials as defined in subdivision (b) of Section 1648.20[3] of the Business and Professions Code.

(3) A device as defined in Section 4023[4] of the Business of Professions Code.

(4) A food as defined in subdivision (a) of Section 109935[5].

(5) The packaging associated with any of the items specified in paragraph (1), (2), or (3).

(6) A pesticide as defined in Section 12753[6] of the Food and Agricultural Code or the Federal Insecticide, Fungicide and Rodenticide Act (7 U.S.C. Sec. 136 and following).

(7) Mercury-containing lights defined as mercury containing lamps, bulbs, tubes, or other electric devices that provide functional illumination.

(f) This section shall remain in effect only until December 31, 2011, and as of that date is repealed, unless a later enacted statute, that is enacted before December 31, 2011, deletes or extends that date.

SB 509 **25251.** For purposes of this article, the following definitions shall apply:

(a) "Clearinghouse" means the Toxics Information Clearinghouse established pursuant to Section 25256.

(b) "Council" means the California Environmental Policy Council established pursuant to subdivision (b) of Section 71017 of the Public Resources Code.

(c) "Office" means Office of Environmental Health Hazard Assessment.

(d) "Panel" means the Green Ribbon Science Panel established pursuant to Section 25254.

(e) "Consumer product" means a product or part of the product that is used, brought, or leased for use by a person for any purposes. "Consumer product" does not include any of the following:

(1) A dangerous drug or dangerous device as defined in Section 4022 of the Business of Professions Code.

(2) Dental restorative materials as defined in subdivision (b) of Section 1648.20 of the Business and Professions Code.

(3) A device as defined in Section 4023 of the Business of Professions Code.

(4) A food as defined in subdivision (a) of Section 109935.

(5) The packaging associated with any of the items specified in paragraph (1), (2), or (3).

(6) A pesticide as defined in Section 12753 of the Food and Agricultural Code or the Federal Insecticide, Fungicide and Rodenticide (7 United States Code Sections 136 and following).

(f) This section shall become effective on January 1, 2012.

AB 1879 **25252.** (a) On or before January 1, 2011, the department shall adopt regulations to establish a process to identify and prioritize those chemicals or chemical ingredients in consumer products that may be considered as being a chemical of concern, in accordance with the review process specified in Section 25252.5. The department shall adopt these regulations in consultation with the office and all appropriate state agencies and after conducting one or more public workshops for which the department provides public notice and provides an opportunity for all interested parties to comment. The regulations adopted pursuant to this section shall establish an identification and prioritization process that includes, but is not limited to, all of the following considerations:

(1) The volume of the chemical in commerce in this state.

(2) The potential for exposure to the chemical in a consumer product.

(3) Potential effects on sensitive subpopulations, including infants and children.

(b)(1) In adopting regulations pursuant to this section, the department shall develop criteria by which chemicals and their alternatives may be evaluated. These criteria shall include, but not be limited to, the traits, characteristics, and endpoints that are included in the clearinghouse data pursuant to Section 25256.1.

(2) In adopting regulations pursuant to this section, the department shall reference and use, to the maximum extent feasible, available information from other nations, governments, and authoritative bodies that have undertaken similar chemical prioritization processes, so as to leverage the work and costs already incurred by those entities and to minimize costs and maximize benefits for the state's economy.

(3) Paragraph (2) does not require the department, when adopting regulations pursuant to this section, to reference and use only the available information specified in paragraph (2).

AB 1879 **25252.5.** (a) Except as provided in subdivision (f), the department, in adopting the regulations pursuant to Sections 25252 and 25253, shall prepare a multimedia life cycle evaluation conducted by affected agencies and coordinated by the department, and shall submit the regulations and the multimedia life cycle evaluation to the council for review.

(b) The multimedia evaluation shall be based on the best available scientific data, written comments submitted by interested persons, and information collected by the department in preparation for adopting the regulations, and shall address, but is not limited to, the impacts associated with all the following:

(1) Emissions of air pollutants, including ozone forming compounds, particulate matter, toxic air contaminants, and greenhouse gases.

(2) Contamination of surface water, groundwater, and soil.

(3) Disposal or use of the byproducts and waste materials.

(4) Worker safety and impacts to public health.

(5) Other anticipated impacts to the environment.

(c) The council shall complete its review of the multimedia evaluation within 90 calendar days following notice from the department that it intends to adopt regulations. If the council determines that the proposed regulations will cause a significant adverse impact on the public health or the environment, or that alternatives exist that would be less adverse, the council shall recommend alternative measures that the department or

other state agencies may take to reduce the adverse impact on public health or the environment. The council shall make all information relating to its review available to the public.

(d) Within 60 days of receiving notification from the council of a determination of significant adverse impact, the department shall adopt revisions to the proposed regulation to avoid or reduce the adverse impact, or the affected agencies shall take appropriate action that will, to the extent feasible, mitigate the adverse impact so that, on balance, there is no significant adverse impact on public health or the environment.

(e) In coordinating a multimedia evaluation pursuant to subdivision (a), the department shall consult with other boards and departments within the California Environmental Protection Agency, the State Department of Public Health, the State and Consumer Services Agency, the Department of Homeland Security, the Department of Industrial Relations, and other state agencies with responsibility for, or expertise regarding, impacts that could result from the production, use, or disposal of consumer products and the ingredients they may contain.

(f) Notwithstanding subdivision (a), the department may adopt regulations pursuant to Sections 25252 and 25253 without subjecting the proposed regulation to a multimedia evaluation if the council, following an initial evaluation of the proposed regulation, conclusively determines that the regulation will not have any significant adverse impact on public health or the environment.

(g) For the purposes of this section, "multimedia life cycle evaluation" means the identification and evaluation of a significant adverse impact on public health or the environment, including air, water, or soil, that may result from the production, use, or disposal of a consumer product or consumer product ingredient.

AB 1879 **25253.** (a)(1) On or before January 1, 2011, the department shall adopt regulations pursuant to this section that establish a process for evaluating chemicals of concern in consumer products, and their potential alternatives, to determine how best to limit exposure or to reduce the level of hazard posed by a chemical of concern, in accordance with the review process specified in Section 25252.5. The department shall adopt these regulations in consultation with all appropriate state agencies and after conducting one or more public workshops for which the department provides public notice and provides an opportunity for all interested parties to comment.

(2) The regulations adopted pursuant to this section shall establish a process that includes an evaluation of the availability of potential alternatives and potential hazards posed by those alternatives, as well as an evaluation of critical exposure pathways. This process shall include life cycle assessment tools that take into consideration, but shall not be limited to, all of the following:

(A) Product function or performance.

(B) Useful life.

(C) Materials and resource consumption.

(D) Water conservation.

(E) Water quality impacts.

(F) Air emissions.

(G) Production, in-use, and transportation energy inputs.

(H) Energy efficiency.

(I) Greenhouse gas emissions.

(J) Waste and end-of-life disposal.

(K) Public health impacts, including potential impacts to sensitive subpopulations, including infants and children.

(L) Environmental impacts.

(M) Economic impacts.

(b) The regulations adopted pursuant to this section shall specify the range of regulatory responses that the department may take following the completion of the alternatives analysis, including, but not limited to, any of the following actions:

(1) Not requiring any action.

(2) Imposing requirements to provide additional information needed to assess a chemical of concern and its potential alternatives.

(3) Imposing requirements on the labeling or other type of consumer product information.

(4) Imposing a restriction on the use of the chemical of concern in the consumer product.

(5) Prohibiting the use of the chemical of concern in the consumer product.

(6) Imposing requirements that control access to or limit exposure to the chemical of concern in the consumer product.

(7) Imposing requirements for the manufacturer to manage the product at the end of its useful life, including recycling or responsible disposal of the consumer product.

(8) Imposing a requirement to fund green chemistry challenge grants where no feasible safer alternative exists.

(9) Any other outcome the department determines accomplishes the requirements of this article.

(c) The department, in developing the processes and regulations pursuant to this section, shall ensure that the tools available are in a form that allows for ease of use and transparency of application. The department shall also make every feasible effort to devise simplified and accessible tools that consumer product manufacturers, consumer product distributors, product retailers, and consumers can use to make consumer product manufacturing, sales, and purchase decisions.

AB 1879 **25254.** (a) In implementing this article, the department shall establish a Green Ribbon Science Panel. The panel shall be composed of members whose expertise shall encompass all of the following disciplines:

(1) Chemistry.

(2) Chemical engineering.

(3) Environmental law.

(4) Toxicology.

(5) Public policy.

(6) Pollution prevention.

(7) Cleaner production methods.

(8) Environmental health.

(9) Public health.

(10) Risk analysis.

(11) Materials science.

(12) Nanotechnology.

(13) Chemical synthesis.

(14) Research.

(15) Maternal and child health.

(b) The department shall appoint all members to the panel on or before July 1, 2009. The department shall appoint the members for staggered three-year terms, and may reappoint a member for additional terms, without limitation.

(c) The panel shall meet as often as the department deems necessary, with consideration of available resources, but not less than twice each year. The department shall provide for staff and administrative support to the panel.

(d) The panel meetings shall be open to the public and are subject to the Bagley-Keene Open Meeting Act (Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of Division 3 of Title 2 of the Government Code).

AB 1879 **25255.** The panel may take any of the following actions:

(a) Advise the department and the council on scientific and technical matters in support of the goals of this article of significantly reducing adverse health and environmental impacts of chemicals used in commerce, as well as the overall costs of those impacts to the state's society, by encouraging the redesign of consumer products, manufacturing processes, and approaches.

(b) Assist the department in developing green chemistry and chemicals policy recommendations and implementation strategies and details, and ensure these recommendations are based on a strong scientific foundation.

(c) Advise the department and make recommendations for chemicals the panel views as priorities for which hazard traits and toxicological end-point data should be collected.

(d) Advise the department in the adoption of regulations required by this article.

(e) Advise the department on any other pertinent matter in implementing this article, as determined by the department.

SB 509 **25256.** The department shall establish the Toxics Information Clearinghouse, which shall provide a decentralized, Web-based system for the collection, maintenance, and distribution of specific chemical hazard trait and environmental and toxicological end-point data. The department shall make the clearinghouse accessible to the public through a single Internet Web portal, and, shall, to the maximum extent possible, operate the clearinghouse at the least possible cost to the state.

SB 509 **25256.1.** On or before January 1, 2011, the office shall 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 the department 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 implementing this section.

SB 509 **25256.2.** (a) The department shall develop requirements and standards related to the design of the clearinghouse and data quality and test methods that govern the data that is eligible to be available through the clearinghouse.

(b) The department may phase in the access to eligible information and data in the clearinghouse as that information and data become available.

(c) The department shall ensure the clearinghouse is capable of displaying updated information as new data becomes available.

SB 509 **25256.3.** The department shall consult with other states, the federal government, and other nations to identify available data related to hazard traits and environmental and toxicological end-points, and to facilitate the development of regional, national, and international data sharing arrangements to be included in the clearinghouse.

AB 1879 **25257.** (a) A person providing information pursuant to this article may, at the time of submission, identify a portion of the information submitted to the department as a trade secret and, upon the written request of the department, shall provide support for the

claim that the information is a trade secret. Except as provided in subdivision (d), a state agency shall not release to the public, subject information supplied pursuant to this article that is a trade secret, and that is so identified at the time of submission, in accordance with Section 6254.7[7] of the Government Code and Section 1060[8] of the Evidence Code.

(b) This section does not prohibit the exchange of a properly designated trade secret between public agencies, if the trade secret is relevant and necessary to the exercise of the agency's jurisdiction and the public agency exchanging the trade secrets complies with this section. An employee of the department that has access to a properly designated trade secret shall maintain the confidentiality of that trade secret by complying with this section.

(c) Information not identified as a trade secret pursuant to subdivision (a) shall be available to the public unless exempted from disclosure by other provisions of law. The fact that information is claimed to be a trade secret is public information.

(d)(1) Upon receipt of a request for the release of information that has been claimed to be a trade secret, the department shall immediately notify the person who submitted the information. Based on the request, the department shall determine whether or not the information claimed to be a trade secret is to be released to the public.

(2) The department shall make the determination specified in paragraph (1), no later than 60 days after the date the department receives the request for disclosure, but not before 30 days following the notification of the person who submitted the information.

(3) If the department decides that the information requested pursuant to this subdivision should be made public, the department shall provide the person who submitted the information 30 days' notice prior to public disclosure of the information, unless, prior to the expiration of the 30-day period, the person who submitted the information obtains an action in an appropriate court for a declaratory judgment that the information is subject to protection under this section or for a preliminary injunction prohibiting disclosure of the information to the public and promptly notifies the department of that action.

(e) This section does not authorize a person to refuse to disclose to the department information required to be submitted to the department pursuant to this article.

(f) This section does not apply to hazardous trait submissions for chemicals and chemical ingredients pursuant to this article.

SB 509 **25257.1.** (a) This article does not limit and shall not be construed to limit the department's or any other department's or agency's existing authority over hazardous materials.

(b) This article does not authorize the department to supersede the regulatory authority of any other department or agency.

(c) The department shall not duplicate or adopt conflicting regulations for product categories already regulated or subject to pending regulation consistent with the purposes of this article.

End Notes

[1] Public Resources Code
71017. (a) "Council" means the California Environmental Policy Council.
(b) The council is hereby created and consists of the following members or their designees:
(1) The Secretary for Environmental Protection.
(2) The Director of Pesticide Regulation.
(3) The Director of Toxic Substances Control.
(4) The Chairperson of the State Air Resources Board.
(5) The Chairperson of the State Water Resources Control Board.
(6) The Director of the Office of Environmental Health Hazard Assessment.
(7) The Chairperson of the California Integrated Waste Management Board.

[2] Business and Profession Code
4022. "Dangerous drug" or "dangerous device" means any drug or device unsafe for self-use in humans or animals, and includes the following:
(a) Any drug that bears the legend: "Caution: federal law prohibits dispensing without prescription," "Rx only," or words of similar import.
(b) Any device that bears the statement: "Caution: federal law restricts this device to sale by or on the order of a ____," "Rx only," or words of similar import, the blank to be filled in with the designation of the practitioner licensed to use or order use of the device.
(c) Any other drug or device that by federal or state law can be lawfully dispensed only on prescription or furnished pursuant to Section 4006.

[3] Business and Profession Code
1648.20. (a) This article shall not apply to any surgical, endodontic, periodontic, or orthodontic dental procedure in which dental restorative materials are not used.
(b) For purposes of this article, "dental restorative materials" means any structure or device placed into a patient's mouth with the intent that it remain there for an indefinite period beyond the completion of the dental procedure, including material used for filling cavities in, or rebuilding or repairing the organic structure of, a tooth or teeth, but excluding synthesized structures or devices intended to wholly replace an extracted tooth or teeth, such as implants.

[4] Business and Profession Code
4023. "Device" means any instrument, apparatus, machine, implant, in vitro reagent, or contrivance, including its components, parts, products, or the byproducts of a device, and accessories that are used or intended for either of the following:
(a) Use in the diagnosis, cure, mitigation, treatment, or prevention of disease in a human or any other animal.
(b) To affect the structure or any function of the body of a human or any other animal.
For purposes of this chapter, "device" does not include contact lenses, or any prosthetic or orthopedic device that does not require a prescription.

[5] Health and Safety Code
109935. "Food" means either of the following:
(a) Any article used or intended for use for food, drink, confection, condiment, or chewing gum by man or other animal.
(b) Any article used or intended for use as a component of any article designated in subdivision (a).

[6] Food and Agricutural Code
12753. "Pesticide" includes any of the following:
(a) Any spray adjuvant.
(b) Any substance, or mixture of substances which is intended to be used for defoliating plants, regulating plant growth, or for preventing, destroying, repelling, or mitigating any pest, as defined in Section 12754.5, which may infest or be detrimental to vegetation, man, animals, or households, or be present in any agricultural or nonagricultural environment whatsoever.

[7] Government Code
6254.7. (a) All information, analyses, plans, or specifications that disclose the nature, extent, quantity, or degree of air contaminants or other pollution which any article, machine, equipment, or other contrivance will produce, which any air pollution control district or air quality management district, or any other state or local agency or district, requires any applicant to provide before the applicant builds, erects, alters, replaces, operates, sells, rents, or uses the article, machine, equipment, or other contrivance, are public records.

(b) All air or other pollution monitoring data, including data compiled from stationary sources, are public records.

(c) All records of notices and orders directed to the owner of any building of violations of housing or building codes, ordinances, statutes, or regulations which constitute violations of standards provided in Section 1941.1 of the Civil Code, and records of subsequent action with respect to those notices and orders, are public records.

(d) Except as otherwise provided in subdivision (e) and Chapter 3 (commencing with Section 99150) of Part 65 of the Education Code, trade secrets are not public records under this section. "Trade secrets," as used in this section, may include, but are not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information which is not patented, which is known only to certain individuals within a commercial concern who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know or use it.

(e) Notwithstanding any other provision of law, all air pollution emission data, including those emission data which constitute trade secrets as defined in subdivision (d), are public records. Data used to calculate emission data are not emission data for the purposes of this subdivision and data which constitute trade secrets and which are used to calculate emission data are not public records.

(f) Data used to calculate the costs of obtaining emissions offsets are not public records. At the time that an air pollution control district or air quality management district issues a permit to construct to an applicant who is required to obtain offsets pursuant to district rules and regulations, data obtained from the applicant consisting of the year the offset transaction occurred, the amount of offsets purchased, by pollutant, and the total cost, by pollutant, of the offsets purchased is a public record. If an application is denied, the data shall not be a public record.

[8] Evidence Code
1060. If he or his agent or employee claims the privilege, the owner of a trade secret has a privilege to refuse to disclose the secret, and to prevent another from disclosing it, if the allowance of the privilege will not tend to conceal fraud or otherwise work injustice.

AB 289 (chap. 699, stat. 2006, Chan)

Health and Safety Code sections 57018 – 57020

57018. (a) For purposes of Sections 57019 and 57020, the following definitions shall apply:

(1) "Analytical test method" means a procedure used to sample, prepare, and analyze a specific matrix to determine the identity and concentration of a specified chemical and its metabolites and degradation product. An analytical test method shall conform to the standards adopted by the National Environmental Laboratory Accreditation Conference.

(2) "Bioconcentration factor" means the concentration of a chemical in an organism divided by its concentration in a test solution or environment.

(3) "Chemical" has the same meaning as a chemical substance, as defined in Section 2602 of Title 15 of the United States Code.

(4) "Manufacturer" means a person who produces a chemical in this state or who imports a chemical into this state for sale in this state.

(5) "Matrix" includes, but is not limited to, water, air, soil, sediment, sludge, chemical waste, fish, blood, adipose tissue, and urine.

(6) "Octanol-water partition coefficient" means the ratio of the concentration of a chemical in octanol and in water at equilibrium and at a specified temperature.

(7) "State agency" means the State Air Resources Board, the Department of Toxic Substances Control, the Integrated Waste Management Board, the Office of Environmental Health Hazard Assessment, the State Water Resources Control Board, and the California Environmental Protection Agency. "State agency" does not include the Department of Pesticide Regulation.

57019. (a) The California Environmental Protection Agency shall coordinate all requests for information from manufacturers made pursuant to this section on behalf of the state agencies.

(b) In coordinating the requests made pursuant to this section, the California Environmental Protection Agency shall seek to accomplish the following objectives:

(1) Minimize or eliminate duplicate requests for the same or similar information.

(2) Coordinate with manufacturers of the same chemical to develop and submit the requested information in an equitable and resource-efficient manner.

(3) To the extent practicable minimize the cost burden on individual manufacturers.

(4) Maintain a record of requests made pursuant to this section.

(c) A state agency, before requesting any information from a manufacturer pursuant to subdivision (d), shall do all of the following:

(1) Post on its Internet Web site and the Internet Web site of the California Environmental Protection Agency an announcement that it seeks information pursuant to subdivision (d), including the chemical for which it seeks information, the type of information it is seeking, and the reason for seeking the information.

(2) Conduct a search for the information it seeks of all known public sources of information on the chemicals for which an announcement has been posted pursuant to paragraph (1). All known public sources include public and electronically searchable databases maintained by the federal government, state governments, and intergovernmental organizations.

(3) Make reasonable attempts to contact all manufacturers of chemicals listed for which an announcement has been posted pursuant to paragraph (1) to obtain any relevant information that may be held by those manufacturers but is not publicly available.

(4) Make reasonable attempts to consult with all manufacturers of chemicals listed for which an announcement has been posted pursuant to paragraph (1) to determine what additional information, if any, those manufacturers need to develop to assist the state agency in evaluating the fate and transport of those chemicals in the relevant matrices.

(5) Make reasonable attempts to consult with all manufacturers to evaluate the technical feasibility of developing the information requested by the agency.

(d) (1) A state agency may request a manufacturer to provide additional information on a chemical for which an announcement has been posted pursuant to paragraph (1) of subdivision (c).

(2) Upon request of a state agency, the manufacturer, within one year, shall provide the state agency with the additional information requested for the specified chemical.

(3) The information that the state agency requests may include, but is not limited to, any of the following:

(A) An analytical test method for that chemical, or for metabolites and degradation products for that chemical that are biologically relevant in the matrix specified by the state agency.

(B) The octanol-water partition coefficient and bioconcentration factor for humans for that chemical.

(C) Other relevant information on the fate and transport of that chemical in the environment.

(4) The manufacturer responding to a request pursuant to this subdivision shall collaborate and cooperate with the state agency making the request to the extent practicable for the following purposes:

(A) To ensure that the information being provided meets the needs of the state agency.

(B) To reduce disagreements over the information being provided.

(C) To decrease to the maximum extent possible the effort and resources the state agency must expend to verify and validate the information provided.

(e) The definitions in Section 57018 apply to this section.

(f) This section shall not be construed to limit the authority of a state agency to obtain information pursuant to any other provision of law.

57020. (a) Notwithstanding Section 6254.7 of the Government Code, if a manufacturer believes that information provided to a state agency pursuant to Section 57019 involves the release of a trade secret, the manufacturer shall make the disclosure to the state agency and notify the state agency in writing of that belief. In its written notice, the manufacturer shall identify the portion of the information submitted to the state agency that it believes is a trade secret and provide documentation supporting its conclusion.

(b) Subject to this section, the state agency shall protect from disclosure a trade secret designated as such by the manufacturer, if that trade secret is not a public record.

(c) Upon receipt of a request for the release of information to the public that includes information that the manufacturer has notified the state agency is a trade secret and that is not a public record, the following procedure applies:

(1) The state agency shall notify the manufacturer that disclosed the information to the state agency of the request, in writing by certified mail, return receipt requested.

(2) The state agency shall release the information to the public, but not earlier than 30 days after the date of mailing the notice of the request for information, unless, prior to the expiration of the 30-day period, the manufacturer obtains an action in an appropriate court for a declaratory judgment that the information is subject to protection under this section or for a preliminary injunction prohibiting disclosure of the information to the public and promptly notifies the state agency of that action. In order to prevent the state agency from releasing the

information to the public, the manufacturer shall obtain a declaratory judgment or preliminary injunction within 30 days of filing an action for a declaratory judgment or preliminary injunction.

(d) This section does not authorize a manufacturer to refuse to disclose to the state agency information required by Section 57019.

(e) Any information that a court, pursuant to this section, determines is a trade secret and not a public record, or pending final judgment pursuant to subdivision (c), shall not be disclosed by the state agency to anyone, except to an officer or employee of a city or county, the state, or the United States, or to a contractor with a city or county, or the state, and its employees, if, in the opinion of the state agency, disclosure is necessary and required for the satisfactory performance of a contract, for the performance of work, or to protect the health and safety of the employees of the contractor.

(f) The definitions in Section 57018 apply to this section.

Attachment 1-2

Authoritative Bodies Lists Examples

AUTHORITATIVE BODIES LISTS EXAMPLES

1. California Proposition 65 list of chemicals known to the state to cause cancer or developmental or reproductive effect.

2. International Agency for Research on Cancer, chemicals classified as Groups 1, 2A and 2B carcinogens.

3. National Toxicology Program (NTP) list of chemicals identified as known or reasonably anticipated to be human carcinogens in the Report on Carcinogens.

4. Carcinogens classified by Europe as Categories 1 and 2, or with Risk Phrases R45 (may cause cancer) or R49 (may cause cancer by inhalation).

5. NTP Center for Evaluation of Risks to Human Reproduction (CERHR), chemicals classified as posing “serious concern,” “concern” or “some concern” with regard to developmental or reproductive toxicity.

6. Chemicals classified by the European Commission as Reproductive Toxicity Categories 1 and 2, or in the hazard category for lactation effects (effects on or via lactation) or with Risk Phrases R60 (may impair fertility), R61 (may cause harm to the unborn child), and R64 (may cause harm to breastfed babies).

7. Chemicals identified as persistent, bioaccumulative, inherently toxic (PBT) by Environment Canada.

8. Chemicals identified by the European Commission as PBTs or vPvBs.

9. Chemicals on the State of Washington PBT list.

10. Oslo-Paris Convention Commission (OSPAR) list of substances of possible concern (includes the subset of chemicals for priority action).

11. U.S. EPA National Waste Minimization Program Priority Chemicals.

12. U.S. EPA Priority PBTs.

13. U.S. EPA Emergency Planning and Community Right to Know Act (EPCRA) PBTs.

14. U.S. EPA Toxic Release Inventory (TRI) List.

15. Chemicals classified by the European Commission as Category 1 or 2 endocrine disruptors.

16. Chemicals classified by the European Commission as Category 1 or 2 germ cell mutagens or with Risk Phrase R46 (may cause heritable genetic damage).

17. Japan International Center for Occupational Safety and Health list of mutagenic chemicals.

18. Chemicals classified by Europe as respiratory sensitizers or with Risk Phrases R42 (may cause sensitization by inhalation) and R42/43 (may cause sensitization by inhalation and skin contact).

19. Chemicals classified by Canada as inherently toxic to aquatic organisms.

20. Chemicals classified by the European Commission as hazardous to the aquatic environment.

21. Chemicals classified by the European Commission as hazardous to the ozone layer or with the Risk Phrase R59 (dangerous to the ozone layer).

22. Chemicals that have been identified by the California Toxic Air Contaminants Program.

23. Priority chemicals for biomonitoring under the California Environmental Contaminant Biomonitoring Program.

24. Chemicals with drinking water maximum contaminant levels established by the state of California or the US Environmental Protection Agency.

25. Chemicals for which water quality standards have been adopted by US Environmental Protection Agency or by any state or water quality authority under the Clean Water Act.

Attachment 1-3

Prioritization Hazard & Exposure Factors Examples

CHEMICAL PRIORITIZATION HAZARD & EXPOSURE FACTORS EXAMPLES

Factors to be considered:

1. Relative degree of threat posed by each chemical to public health or the environment based on consideration of:
    - Physical chemical hazards,
    - Adverse public health impacts,
    - Adverse ecological impacts,
    - Adverse air quality impacts,
    - Adverse water quality impacts, and
    - Adverse soil quality impacts.

2. Potential for consumers or environmental receptors to be exposed to the chemical in quantities that can result in adverse public health or environmental impacts.

3. Availability of "reliable information" to substantiate the threat(s) posed by the chemical, and the potential for exposures to the chemical.

4. Scope of federal and/or California State regulatory programs under which the chemical is regulated, and the extent to which these other regulatory requirements address the same public health and environmental threats and exposure pathways.

In evaluating the relative degree of threat and potential for exposures, priority should be given to those chemicals that:

1. Pose the greatest threat of adverse public health and environmental impacts,

2. Are most prevalently distributed in commerce and contained in products used by consumers, and

3. There is the greatest potential for consumers or environmental receptors to be exposed to the chemical in quantities that can result in adverse public health or environmental impacts.

The chemical prioritization process should proceed as follows:

1. Evaluation of chemicals based on the relative degree of threat and the availability of reliable information to substantiate the threat.

2. The initial prioritization should be adjusted based upon consideration of the potential for exposure and the availability of reliable information to substantiate the potential for exposure.

3. The prioritization should then be further adjusted based upon a determination of which (if any) threats and exposures are addressed by other federal and/or California State regulatory programs.

4. Chemicals assigned the highest priority at the conclusion of the first three steps should be placed on the List, except that the list should be limited in number based upon the availability of DTSC resources to evaluate consumer products containing these chemicals.

In evaluating the potential for harm that could result from potential exposures, consideration should be given to the type and severity of potential adverse impact(s) and the potency of the chemical(s) associated with the adverse impact(s) for both of the following:

1. Children, pregnant women and other sensitive subpopulations,

2. Environmental receptors, in particular, environmentally sensitive habitats and endangered and threatened species.

In evaluating the potential for exposure, consideration should be given to all of the following:

1. Reliable information demonstrating the occurrence, or potential occurrence, of public health and environmental exposures,

2. Information concerning the presence of the chemical in products commonly found in households, including the number of such of products, the frequency of use, and the concentration of the chemical in those products, and

3. Information showing how widely used the chemical is in products placed into the stream of commerce in California.

Attachment 1-4

Prioritization Exposure Factors Examples

PRIORITIZATION EXPOSURE FACTORS EXAMPLES

1. The chemical has been identified as a high production volume chemical by the USEPA, or there are large volumes of the chemical in commerce in California.

2. The chemical has been found through biomonitoring to be present in human bodily tissues or fluids.

3. The chemical has been found through sampling and analysis to be present in household dust, indoor air, drinking water, or elsewhere in the indoor environment.

4. The chemical has been found through monitoring to be present in fish, wildlife, or the natural environment.

5. The chemical is present in children's products.

6. The chemical is present in products used or present in the home.

7. The chemical is used in products resulting in potentially high exposure to sensitive subpopulations.

8. The chemical is used in dispersive product applications.

9. The chemical has the potential for long range transport.

10. The chemical has been found in California solid waste, wastewater or storm water streams in concentrations or volumes that present public health or environmental threats, or that require the expenditure of significant public funds.

Attachment 1-5

Ranking Formula Approach Examples

RANKING FORMULA APPROACH EXAMPLE

Example #1

Assign a numerical value (i.e., 1, 2, 3, 4) to various end-points (e.g., toxicological, environmental, use and exposure) for each chemical or product, and multiple these values to arrive at an overall ranking for each chemical or product:

Ranking Formula for Chemicals

Chemical Ranking Score = (Toxicity) x (Potential for Exposure) x (Persistence + Bioaccumulation)

Ranking Formula for Products

Product Ranking Score = (Chemical Ranking Score) x (Percentage of Chemical in Product) x (Potential for Exposure) x (Likelihood for Exposure to Sensitive Subpopulations or Environmental Receptors)

Sample definitions for the ranking formulas:

Toxicity - Toxicological endpoints are assigned a numerical value (e.g., 1-3) based on accepted toxicological classification. The sum of the endpoints would then give a total toxicity score.

Potential for Exposure - The potential for a human or environmental receptor to be exposed to the chemical via a relevant exposure pathway. This value would be expressed as a probability from 1 (low) to 10 (high).

Persistence or Bioaccumulation - Physical or chemical properties are assigned a numerical value similarly to the toxicological end-points. The sum of the endpoints would then give a total persistence or bioaccumulation scores.

Percentage of Chemical in Product - The percentage by weight of a chemical in a product.

Likelihood for Exposure to Sensitive Subpopulations - The probability that the potential for exposure would disproportionally affect sensitive human subpopulations or sensitive environmental receptors. This value would be expressed as a probability from 1 (low) to 10 (high).

Chemical Ranking Score - Chemicals above a specified ranking value would be placed on the chemicals list.

Product Ranking Score - Products above a specified ranking value would be placed on the products list.

Example #2

The same as example #1, with a weighting assigned to each factor used in the ranking formulas.

Example #3

- Give each chemical or product a High, Medium, or Low ranking for each factor.

- Give each chemical or product an overall High, Medium or Low ranking by adding up the individual factor rankings for the chemical or product:

  -- High, Medium and Low would each be assigned a numeric value (e.g., 3, 2, and 1, respectively).

  -- The individual factor rankings would be totaled using these numeric values, and then divided by the number of factors to arrive at an "average" ranking across all factors.

  -- This approach could also incorporate the weighted factor concept.

- All chemicals or products with an overall High ranking would be placed on the list.

Attachment 1-6

Design for the Environment Program

Alternatives Assessment Criteria for Hazard Evaluation

Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation

Draft
January 2011

Office of Pollution Prevention & Toxics
U.S. Environmental Protection Agency

The criteria within this document will be applied during upcoming DfE Alternatives Assessments. Lessons learned from the application of the criteria during those assessments will be incorporated into a finalized version.

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1. Introduction

The Design for the Environment (DfE) Program at the U.S. Environmental Protection Agency developed the Alternatives Assessment Criteria for Hazard Evaluation as a transparent tool for evaluating and differentiating among chemicals based on their concern for human health and environmental hazard. The Criteria will be applied in upcoming DfE Alternatives Assessments (for a current list of assessments to go: http://www.epa.gov/dfe/alternative_assessments.html). The Criteria could form the basis for decision-making by other organizations such as manufacturers, retailers, other government agencies, and non-governmental organizations.

DfE Alternatives Assessments are multi-stakeholder partnerships that evaluate a chemical of concern and its likely alternatives with the goal of "informing substitution" to safer alternatives. The assessments are intended to reduce the likelihood of the unintended consequences that might result if poorly understood alternatives were chosen. The Alternatives Assessment Criteria can be used to place chemicals on a continuum of relative hazard to inform decision making.

The criteria are robust and comprehensive, including consideration for human health and environmental hazards. For most endpoints, the criteria define “High,” “Moderate,” and “Low” concern. Authoritative sources – the United Nation’s Globally Harmonized System (GHS) for the Classification and Labeling of Hazard Substances and U.S. EPA programs – are the basis for these distinctions. In assigning a designation of Low, Moderate, or High concern for hazard, DfE uses the best information available, both experimental and modeled.

2. General Requirements

2. 1 Data for all relevant routes of exposure will be evaluated.

2.2. The GHS criteria and data evaluation approach, and EPA risk assessment guidance will be applied in the review of both no observed adverse effect levels/concentrations (NOAEL/NOAEC) and lowest observed adverse effect levels/concentrations (LOAEL/LOAEC). In general, NOAEL/NOAEC and LOAEL/LOAEC values are preferred over no observed effect levels/concentrations (NOEL/NOEC) and lowest observed effect levels/concentrations (LOEL/LOEC). When available and appropriate, the results of benchmark dose modeling will also be considered [1]. In reviews that include conflicting data, a weight of evidence evaluation will inform the hazard designation with a conservative approach aimed at the protection of human health and the environment. All reviews will include an assessment of potential impacts to vulnerable populations and life stages.

2.3 Use of existing data should follow the EPA HPV Challenge Program and OECD HPV Programme data adequacy guidelines: http://www.epa.gov/HPV/pubs/general/datadfin.htm.

2.4 When gathering data for evaluation under these criteria, a review of the open literature including published peer-reviewed studies and government reports as well as any confidential business information will be conducted.

2.5 Any known sensitivity of the test species or strain will be considered in the evaluation of data against these criteria.

Terms

3.1. **Acute aquatic toxicity** means the intrinsic property of a substance to be injurious to an organism in a short-term, aquatic exposure to that substance [2].

3.2. **Acute mammalian toxicity** refers to those adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours [3].

3.3. **Attribute**: The general property of the chemical that is being evaluated (e.g. acute mammalian toxicity, persistence).

3.4. The **benchmark dose (or concentration)** is the dose (or concentration) that is associated with a specific measure or change of a biological effect. The calculation of the benchmark dose (BMD) or concentration (BMC) generally represents the central estimate of the dose or concentration associated with some level of response above background. The lower limit of an on-side 95% confidence interval is generally applied to the BMD and BMC [1].

3.5. **Bioaccumulation** is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment, e.g., dietary and ambient environment sources. Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound and growth dilution [4].

3.6. **Biodegradation** is a process in which the destruction of the chemical is accomplished by the action of a living organism [5].

3.7. **Carcinogen** denotes a chemical substance or mixture of chemical substances which induces cancer or increases its incidence [6].

3.8. A **chemical** is identified by its Chemical Abstract Service (CAS) number.

3.9. **Chronic aquatic toxicity** means the intrinsic property of a substance to cause adverse effects to aquatic organisms during aquatic exposures which are determined in relation to the life-cycle of the organism [2].

3.10. **Criteria**: Endpoints and cutoffs for attribute information. Example: oral acute mammalian toxicity LD50 must be > 50 mg/kg. Data quality requirements (including acceptable test methods and information sources) are developed for all criteria.

3.11. **Dermal sensitizer**: A substance that will lead an allergic response following skin contact [7].

3.12. **Developmental toxicity**: Adverse effects in the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency [8].

3.13. **EC50**: Half maximal effective concentration.

3.14. **Endocrine activity** refers to a change in endocrine homeostasis caused by a chemical or other stressor from human activities (e.g., application of pesticides, the discharge of industrial chemicals to air, land, or water, or the use of synthetic chemicals in consumer products.)

3.15. An **endocrine disruptor** is an external agent that interferes in some way with the role of natural hormones in the body. An agent might disrupt the endocrine system by affecting any of the various stages of hormone production and activity, such as by preventing the synthesis of hormones, by directly binding to hormone receptors, or by interfering with the natural breakdown of hormones [9].

3.16. **Estimated concentration three (EC3)**: Estimated concentration of a test substance needed to produce a stimulation index of three in the local lymph node assay, a test used to evaluate dermal sensitization. [10]

3.17. **Genotoxicity**: The more general terms genotoxic and genotoxicity apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects [11].

3.18. An **ingredient** may be one chemical or a blend of multiple chemicals that are intentionally added.

3.19. **LC50:** Median lethal concentration.

3.20. **LD50:** Median lethal dose.

3.21. **LOAEL**: Lowest Observed Adverse Effect Level

3.22. **LOAEC**: Lowest Observed Adverse Effect Concentration

3.23. **LOEC**: Lowest Observed Effect Concentration

3.24. **LOEL**: Lowest Observed Effect Level.

3.25. **Mutagen**: The term mutagenic and mutagen will be used for agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms [11].

3.26. **Neurotoxicity**: An adverse change in the structure or function of the central and/or peripheral nervous system following exposure to a chemical, physical, or biological agent [12].

3.27. **NOAEL**: No Observed Adverse Effect Level

3.28. **NOAEC**: No Observed Adverse Effect Concentration

3.29. **NOEC**: No Observed Effect Concentration

3.30. **NOEL**: No Observed Effect Level

3.31. **Persistence**: The length of time the chemical can exist in the environment before being destroyed (i.e., transformed) by natural processes [13].

3.32. **Reproductive toxicity**: The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, 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 modifications in other functions that are dependent on the integrity of the reproductive systems [14].

3.33. **Respiratory sensitizer**: A substance that will lead to hypersensitivity of the airways following inhalation of the substance [7].

3.34. **Skin corrosion** is the production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours [15].

3.35. **Skin irritation** is the production of reversible damage to the skin following the application of a test substance for up to 4 hours [15].

3.36. **Stimulation Index (SI)**: A value calculated to assess the skin sensitization potential of a test substance that is the ratio of the proliferation in treated groups to that in the concurrent vehicle control group. [10]

3.37. **Suitable analog**: Suitable analogs will be based on a chemically (e.g., based on chemical structure) or biologically (e.g., based on metabolic breakdown, or likely

mechanistic/mode of action considerations) similar chemical. Guidance for identifying a suitable analog can be found in OECD *Series on Testing and Assessment No. 80 Guidance on Grouping of Chemicals* [16]. The analog used must be appropriate for the attribute being evaluated.

3.38. **Weight-of-evidence**: For the purposes of this document, weight-of-evidence refers to the process of considering the strengths and weaknesses of various pieces of information in reaching and supporting a conclusion concerning a property of the substance [17].

4. Toxicological Criteria

Evaluation of chemicals under these criteria will be based on the best available data. In general, DfE will use data in the following order of preference: 1) measured data on the chemical being evaluated, 2) measured data from a suitable analog, and 3) estimated data from appropriate models. EPA experts will evaluate the quality and reliability of both experimental and estimated data. The majority of measured data are expected to be from laboratory experiments. However, any available human data will be considered, e.g. Human Repeat Insult Patch Tests. In many cases, the evaluation of human data will require a qualitative assessment, since the criteria are primarily based on (non-human) animal studies. Human data may require appropriate review for ethical treatment of the subjects.

In the absence of measured data on the chemical being evaluated, measured data from a suitable analog and/or estimated data from computer models will be used. In the event that there are no suitable analogs, that suitable analogs lack measured data, and the substance, or its analog cannot be modeled, the hazard endpoint cannot be evaluated and will be designated "no data."

The links and references in this document are current as of the publication date of these Criteria. EPA will use the most recent version of each authoritative list, EPA data interpretation guidance, and test protocol when reviewing a chemical against these criteria. In the case where a GHS reference in this document is superseded by a more recent version, EPA may choose to update these Criteria to incorporate that newer version. EPA will consider all sources of developing information, such as the EPA Endocrine Disruptor Screening Program [18] or enhancements to estimation models such as EPI Suite™ [19] that occur over time. For convenience, a summary of DfE's Alternatives Assessment Criteria is located in the Appendix (see Table A1).

4.1. Human Health Effects

4.1.1. Acute Mammalian Toxicity

DfE's acute mammalian toxicity criteria differentiate compounds based upon a common measure of short term exposure toxicity, the median lethal dose or concentration (LD_{50} or LC_{50}), through oral, dermal, and respiratory routes. Chemical hazard designations will be made based upon the criteria in Table 1. These values were derived from the GHS criteria [20].

Table 1. Acute Mammalian Toxicity Criteria for Hazard Designation

Acute Mammalian Toxicity	Very High	High	Moderate	Low
Oral LD50 (mg/kg)	≤ 50	> 50 - 300	> 300 - 2000	> 2000
Dermal LD50 (mg/kg)	≤ 200	> 200 - 1000	> 1000 - 2000	> 2000
Inhalation LC50 (vapor/gas) (mg/L)	≤ 2	> 2 - 10	> 10 - 20	> 20
Inhalation LC50 (dust/mist/fume) (mg/L/day)	≤ 0.5	> 0.5 - 1.0	> 1.0 - 5	> 5

4.1.2. Carcinogenicity

These criteria are designed to determine whether a compound is known, presumed, or suspected to increase incidence of cancer, whether current data on carcinogenicity is equivocal, or whether adequate studies have been conducted to show no increase in cancer incidents. Carcinogenicity designations will be made according to the criteria in Table 2. Chemicals known, presumed, or suspected to be carcinogenic to humans according to the authoritative lists in Table 3 will be designated as High. When equivocal data or only positive structural alerts are present, a designation of Moderate will be used. The basis for Low concern may include negative carcinogenicity studies on the chemical being evaluated or negative studies on an analog and lack of structural alerts, in addition to mechanistic considerations.

Table 2. Carcinogenicity Criteria for Hazard Designation

Carcinogenicity	High	Moderate	Low
Carcinogenicity	Positive results	Equivocal results	Negative studies and no structural alerts

Table 3. Criteria and Authoritative Lists Used to Designate **High** Hazard for Carcinogenicity

Authoritative Body	Classifications for High Hazard Designation
Globally Harmonized System (GHS) [6]	Category 1A – Known to have carcinogenic potential for humans Category 1B – Presumed to have carcinogenic potential for humans Category 2 – Suspected human carcinogens
National Toxicology Program (NTP)	Known to be Human Carcinogen Reasonably Anticipated to be Human Carcinogen
U.S. Environmental Protection Agency (EPA)	(2005/1999) Carcinogenic to humans, Likely to be carcinogenic to humans, or Suggestive evidence of carcinogenic potential (1996) Known/Likely (1986) Group A – Human Carcinogen, Group B – Probable human carcinogen, or Group C – Possible human carcinogen
International Agency for Research on Cancer (IARC)	Group 1 – carcinogenic to humans Group 2A – probably carcinogenic to humans Group 2B – possibly carcinogenic to humans
EU CMR List [21]	Category 1 – Known to be carcinogenic to humans Category 2 – Should be regarded as if carcinogenic to humans Category 3 – Cause for concern for humans owing to possible carcinogenic effects
EU Risk Phrases [21]	R45: May cause cancer R49: May cause cancer by inhalation R40: Limited evidence of a carcinogenic effect *And all combination risk phrases containing one or more of the above.*

4.1.3. Mutagenicity/Genotoxicity

The Mutagenicity/Genotoxicity criteria classify compounds based upon capacity to cause gene mutations and/or chromosomal aberrations, whether current data are equivocal, or whether adequate studies have been conducted that show lack of mutagenic potential. Mutagenic/Genotoxic designations will be made according the criteria in Table 4. Those compounds showing positive results and/or categorized by one of the authoritative bodies in Table 5 will receive a High designation. When equivocal data or only positive structural data are present, a designation of Moderate will be used. A Low hazard designation will be assigned for chemicals with negative test data and no structural alerts.

Table 4. Mutagenicity/Genotoxicty Criteria for Hazard Designations

Mutagenicity/Genotoxicity	High	Moderate	Low
Mutagenicity/Genotoxicity	Positive results	Equivocal results	Negative for chromosomal aberrations and gene mutations, and no structural alerts.

Table 5. Criteria and Authoritative Lists Used to Designate **High** Hazard for Mutagenicity/Genotoxicity

Authoritative Body	Classifications for High Hazard Designation
Globally Harmonized System (GHS) [11]	Category 1A – Chemicals known to induce heritable mutations in germ cells of humans Category 1B – Chemicals which should be regarded as if they induce heritable mutations in the germ cells of humans Category 2 – Chemicals which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans
EU CMR List [21]	Category 1 – Substances known to be mutagenic to humans Category 2 – Substances which should be regarded as if they are mutagenic to humans Category 3 – Substances which cause concern for human owing to possible mutagenic effects
EU Risk Phrases [21]	R46: May cause heritable genetic damage R68: Possible risk of irreversible effects *And all combination risk phrases containing one or more of the above*

4.1.4. Reproductive and Developmental Toxicity

DfE's reproductive and developmental criteria classify compounds based upon the potential to cause adverse effects on reproductive capacity and/or subsequent development of the offspring through oral, dermal and respiratory exposure routes. In general, the NOAEL and LOAEL will be considered as a basis for evaluation. Chemical hazard designations will be made based upon the criteria in Table 6. These values were derived from the US EPA's Office of Pollution Prevention & Toxics criteria for HPV chemical categorization [22].

Table 6. Reproductive and Developmental Toxicity Criteria for Hazard Designations

Reproductive and Developmental Toxicity	High	Moderate	Low
Oral (mg/kg/day)	< 50	50 - 250	> 250
Dermal (mg/kg/day)	< 100	100 - 500	> 500
Inhalation (vapor/gas) (mg/L/day)	< 1	1 - 2.5	> 2.5
Inhalation (dust/mist/fume) (mg/L/day)	< 0.1	0.1 - 0.5	> 0.5

4.1.5. Neurotoxicity

DfE's neurotoxicity criteria will classify compounds based upon observed neurotoxic effects through oral, dermal, and respiratory exposure routes. Neurotoxic effects can be observed at multiple levels of organization within the nervous system, including neurochemical, anatomical, or behavioral, and across life stages. In general, NOAEL and LOAEL values will be considered as the basis for evaluation. Chemical hazard designations will be made based on the criteria in Table 7 which were derived from GHS criteria for Specific Target Organ Toxicity Repeated Exposure [23].

The dose values in Table 7 are to be applied to 90-day repeated dose studies. Dose values are tripled for chemicals evaluated in 28-day studies and similarly modified for studies of longer durations.

Table 7. Neurotoxicity Criteria for Hazard Designations

Neurotoxicity	High	Moderate	Low
Oral (mg/kg-bw/day)	< 10	10 - 100	> 100
Dermal (mg/kg-bw/day)	< 20	20 - 200	> 200
Inhalation (vapor/gas) (mg/L/6h/day)	< 0.2	0.2 - 1.0	> 1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)	< 0.02	0.02 - 0.2	> 0.2

4.1.6. Repeated Dose Toxicity

Chronic exposure will be evaluated with the results from repeated dose toxicity testing through oral, dermal, and respiratory routes. In general, the NOAEL and LOAEL will be considered as a basis for evaluation. Chemical hazard designations will be made based upon the criteria in Table 8 which were derived from the US EPA's Office of Pollution Prevention & Toxics criteria for HPV chemical categorization [22].

The dose values in Table 8 are to be applied to 90-day repeated dose studies. Dose values are tripled for chemicals evaluated in 28-day studies and similarly modified for studies of longer durations.

Table 8. Repeated Dose Toxicity Criteria for Hazard Designations

Repeated Dose Toxicity	High	Moderate	Low
Oral (mg/kg-bw/day)	< 10	10 - 100	> 100
Dermal (mg/kg-bw/day)	< 20	20 - 200	> 200
Inhalation (vapor/gas) (mg/L/6h/day)	< 0.2	0.2 - 1.0	> 1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)	< 0.02	0.02 - 0.2	> 0.2

4.1.7. Respiratory and Skin Sensitization

Evidence of whether repeated exposure to a chemical can induce an allergic response upon contact will be evaluated in DfE's sensitization criteria. Both dermal and respiratory sensitization will be considered. Chemical hazard designations will be made based upon the criteria in Table 9 which were derived from the GHS guidance values [7]. The GHS criteria for categorizing chemicals as Category 1A or 1B is given in Tables 10 and 11 respectively. For Respiratory Sensitization, designations of High, Moderate, and Low will not be used. Instead, a qualitative assessment of the available data will be prepared.

Table 9. Sensitization Criteria for Hazard Designations

Sensitization	High	Moderate	Low
Skin Sensitization	High frequency of sensitization in humans and/or high potency in animals (GHS Cat. 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Cat. 1B)	Adequate data available and not GHS Cat. 1A or 1B
Respiratory Sensitization	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of the available data will be prepared.		

Table 10. GHS Sensitization Criteria for **High** Hazard Designation

Assay	GHS Category 1A Criteria
Local lymph node assay	EC3 value ≤ 2%
Guinea pig maximization test	≥ 30% responding at ≤ 0.1% intradermal induction dose or ≥ 60% responding at > 0.1% to ≤ 1% intradermal induction dose
Buehler assay	≥ 15% responding at ≤ 0.2% topical induction dose or ≥ 60% responding at > 0.2% to ≤ 20% topical induction dose

Table 11. GHS Sensitization Criteria for **Moderate** Hazard Designation

Assay	GHS Category 1B Criteria
Local lymph node assay	EC3 value > 2%
Guinea pig maximization test	≥ 30% to < 60% responding at > 0.1% to ≤ 1% intradermal induction dose or ≥ 30% responding at > 1% dermal induction dose
Buehler assay	≥ 15% to < 60%responding at > 0.2% to ≤ 20% topical induction dose or ≥ 15% responding at > 20% topical induction dose

4.1.8. Eye and Skin Irritation/Corrosivity

Data on a chemical's ability to cause eye and skin irritation/corrosivity will be reviewed under these criteria. Hazard designations will be made based upon the criteria in Table 12. These criteria were derived from the OPP Acute Toxicity Categories [24].

Table 12. Irritation Criteria for Hazard Designations

Irritation/Corrosivity	Very High	High	Moderate	Low	Very Low
Eye Irritation/Corrosivity	Irritation persists for > 21 days or corrosive	Clearing in 8-21 days, severely irritating	Clearing in 7 days or less, moderately irritating	Clearing in less than 24 hrs, mildly irritating	Not irritating
Skin Irritation/Corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	Not irritating

4.1.9. Endocrine Activity

EPA will evaluate endocrine activity rather than characterize hazard in terms of "endocrine disruption". Evidence of a chemical having endocrine activity will be summarized in a narrative.

A) Data Resources

Endocrine activity can be defined as a change in endocrine homeostasis caused by a chemical or other stressor from human activities (e.g., application of pesticides, the discharge of industrial chemicals to air, land, or water, or the use of synthetic chemicals in consumer products.). Data that will be considered include:

- In vitro data such as hormone receptor binding assays or ex vivo assays
- In vivo data from studies of intact animals or wildlife (including aquatic organisms)
- Ethically conducted human studies
- In vivo short term exposures or altered (e.g., ovariectomized) animal models
- Structural similarity to known endocrine active substances using SAR tools such as AIM, QSAR, etc.
- Additional information gleaned from studies that are indicative of a chemical's endocrine system interactions, such as changes in hormone profiles or reproductive organ weights.

B) Criteria

Available data for each chemical will be evaluated for evidence of the presence of endocrine activity.

- If there are no data available to evaluate this endpoint, endocrine activity is unknown, untested and would be marked with a "ND" indicating the absence of information. (No Data)
- If data show evidence of endocrine activity then the chemical will be designated as potentially endocrine active, while noting caveats and limitations.
- If data conclude no evidence of activity (no binding, perturbation, or evidence of endocrine-related adverse effects) then the chemical will be designated as having no evidence of endocrine activity, noting caveats and limitations.

In consultation with EPA toxicologists and risk assessors, DfE will provide a summary statement of the available data, including the presence of equivocal or conflicting data and any limitations to the available data. The level of confidence in the assessment will be noted.

4.2. Environmental Toxicity and Fate

4.2.1. Aquatic Toxicity

Chemicals will be assigned hazard designations based on either the LC50 or EC50 values for acute aquatic toxicity, and lowest observed effect concentration (LOEC) for chronic aquatic toxicity. The criteria used for making chemical hazard designations are shown in Table 13. These values were derived from the EPA Office of Pollution Prevention and Toxics' (OPPT's) New Chemicals Program [25] and OPPT's criteria for HPV chemical categorization [22].

Table 13. Aquatic Toxicity Criteria for Hazard Designations

Aquatic Toxicity	Very High	High	Moderate	Low
Acute Aquatic Toxicity (LC50 or EC50) (mg/L)	< 1.0	1 - 10	> 10 - 100	> 100
Chronic Aquatic Toxicity (LOEC) (mg/L)	< 0.1	0.1 - 1	> 1 - 10	> 10

4.2.2. Environmental Persistence

Persistence designations will be based on ultimate degradation. In the absence of data on ultimate degradation, DfE will evaluate data on primary degradation of the compound and consider the potential for degradation products of concern. Environmental monitoring data may modify how a persistence designation is determined. If Ready Biodegradability test data are available but the chemical did not pass, the chemical is evaluated based on measured data for half-life.

In the absence of measured data on the substance of interest, DfE will evaluate data for suitable analogs and estimated values from models such as EPI Suite or SPARC [26]. Persistence designations will be made based upon the criteria in Table 14. These values were derived from OPPT's New Chemicals Program and the DfE Master Criteria, and reflect OPPT policy on PBTs [27-29]. For persistence in air, designations of High, Moderate, and Low will not be used. Instead, a qualitative assessment of available data will be prepared.

Table 14. Criteria for Persistence Designations

Environmental Persistence	Very High	High	Moderate	Low	Very Low
Persistence in water, soil or sediment	Half-life > 180 days or recalcitrant	Half life of 60 – 180 days	Half-life < 60 but ≥ 16 days	Half-life < 16 days OR passes Ready Biodegradability test not including the 10-day window.* No degradation products of concern.	Passes Ready Biodegradability test with 10-day window.* No degradation products of concern.
Persistence in air	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				

* See Ready Biodegradation test criteria [30-32].

4.2.3. Bioaccumulation

Data on the capacity for a compound to bioaccumulate will be evaluated. Environmental monitoring data will be considered when available. The criteria used to make bioaccumulation designations are shown in Table 15. These criteria were derived from OPPT's New Chemicals Program [27], and Arnot & Gobas 2006 [4].

Table 15. Criteria for Bioaccumulation Designations

Bioaccumulation	Very High	High	Moderate	Low
Bioaccumulation (BAF / BCF)	> 100,000	100,000 – 1,000	1,000 – 100	< 100
Log BAF/BCF	>5	5 - 3	3 – 2	< 2

When experimental BAF or BCF data are available:

1) If a measured log BAF or BCF is available and the value >2, apply the bioaccumulation criteria in Table 15.
2) If there are measured log BCF or log BAF values <2, consider application of the criteria on a case-by-case basis. For example, if there is a single measured log BCF <2, use the upper trophic BAF with metabolism from the BCFBAF model. If there are several measured values which all support a designation of low bioaccumulation potential, then the chemical will be designated as such.

When experimental BAF or BCF data are not available:

1) If there are no measured BCF or BAF values, consider the octanol-water (Kow) and octanol-air (Koa) partition coefficients. If a chemical has log Kow <2 and log Koa <5, it is given a low designation for bioaccumulation [ref Gobas 2006]; an estimated BAF or BCF is not needed. If no measured Kow and Koa values are available, they can be estimated from the EPI Suite models KOWWIN and KOAWIN or other models that may be available for these endpoints (e.g. SPARC).
2) If bioaccumulation is not Low after evaluating log Kow and log Koa as defined above, and there are no experimental bioaccumulation data, use estimated values (such as upper trophic BAF with metabolism from EPI Suite's BCFBAF model) and apply the bioaccumulation criteria in Table 15.

5. Test Methods and Data Interpretation

This section lists examples of test methods used to develop data from which hazard designations based upon the criteria in Section 4 will be made. In developing hazard designations we will consider both peer-reviewed, published studies as well as unpublished data. Published, peer-reviewed and guideline studies will be given the greatest weight.

5.1. Acute Mammalian Toxicity – Test Methods

- OPPTS Harmonized Guideline 870.1100: Acute oral toxicity [33]
- OPPTS Harmonized Guideline 870.1200: Acute dermal toxicity [34]
- OPPTS Harmonized Guideline 870.1300: Acute inhalation toxicity [35]
- OECD Test Guideline 420: Acute Oral Toxicity-Fixed Dose Method [36]
- OECD Test Guideline 423: Acute Oral Toxicity – Acute Toxic Class Method [37]
- OECD Test Guideline 425: Acute Oral Toxicity – Up-and-Down Procedure [38]
- OECD Test Guideline 402: Acute Dermal Toxicity [39]
- OECD Test Guideline 403: Acute Inhalation Toxicity [40]

5.1.1. Sources for Data Interpretation

- GHS Ch 3.1 Acute Toxicity [3]
- EU Dangerous Substances Directive, http://ecb.jrc.ec.europa.eu/documentation/. To access the list of substances carrying Risk Phrases, click on "CLASSIFICATION-LABELLING", then "DIRECTIVE 67-548-EEC", then "ANNEX I OF DIRECTIVE 67-548-EEC", and then either of the files listed as: "Annex I of Directive 67548EEC" [41]

5.2. Carcinogenicity – Test Methods

- OECD Test Guideline 451: Carcinogenicity Studies [42]
- OECD Test Guideline 453: Combined Chronic Toxicity/Carcinogenicity Studies [43]
- OPPTS Harmonized Guidelines 870.4200: Carcinogenicity [44]
- OPPTS Harmonized Guidelines 870.4300: Combined chronic toxicity/carcinogenicity [45]
- NTP 2 Year Study Protocol: "Specifications for the conduct of studies to evaluate the toxic and carcinogenic potential of chemical, biological and physical agents in laboratory animals for the National Toxicology Program" [46]

Alternative Test Methods for Carcinogenicity

- Modeled data from sources such as OncoLogic™ [47] are acceptable when data are unavailable.

5.2.1. Sources for Data Interpretation

- EU Dangerous Preparations Directive Article 6 and Annex II (1999/45/EC and subsequent updates/amendments) [48-50]
- EU Dangerous Substances Directive, http://ecb.jrc.ec.europa.eu/documentation/. To access the list of substances carrying Risk Phrases, click on "CLASSIFICATION-LABELLING", then "DIRECTIVE 67-548-EEC", then "ANNEX I OF DIRECTIVE 67-548-EEC", and then either of the files listed as: "Annex I of Directive 67548EEC" [41]
- GHS Ch 3.6 Carcinogenicity [6]
- Section 2, Hazard Assessment in Guidelines for Carcinogen Risk Assessment http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=439797 [51]
- Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens, available at: http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=160003 [52]

5.3. Genetic Toxicity – Test Methods

Per GHS [11], results from multiple, acceptable test methods must be used in conjunction for evaluation of genetic toxicity.

- OECD Test Guideline 471 (OPPTS 870.5100): Bacterial Reverse Mutation Test [53, 54]
- OECD Test Guideline 473 (OPPTS 870.5375): *In vitro* Mammalian Chromosome Aberration Test [55, 56]
- OECD Test Guideline 474 (OPPTS 870.5395): Mammalian Erythrocyte Micronucleus Test [57, 58]
- OECD Test Guideline 475 (OPPTS 870.5385): Mammalian Bone Marrow Chromosome Aberration Test [59, 60]
- OECD Test Guideline 476 (OPPTS 870.5300): *In vitro* Mammalian Cell Gene Mutation Test [61, 62]
- OECD Test Guideline 483 (OPPTS 870.5380): Mammalian Spermatogonial Chromosome Aberration Test [63, 64]
- OECD Test Guideline 486: Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *in vivo* [65]. This guideline does **NOT** substitute in the necessary minimum set for either the gene mutation or the chromosome aberration test.

5.3.1. Sources for Data Interpretation

- EU Dangerous Substances Directive, http://ecb.jrc.ec.europa.eu/documentation/. To access the list of substances carrying Risk Phrases, click on "CLASSIFICATION-LABELLING", then "DIRECTIVE 67-548-EEC", then "ANNEX I OF DIRECTIVE 67-548-EEC", and then either of the files listed as: "Annex I of Directive 67548EEC" [41]

- EU Dangerous Preparations Directive Article 6 and Annex II (1999/45/EC and subsequent updates/amendments) [48-50]
- GHS Ch 3.5 Germ Cell Mutagenicity [11]

5.4. Neurotoxicity – Test Methods

- OECD Test Guideline 424: Neurotoxicity Study in Rodents [66]
- OPPTS Harmonized Guideline 870.6200: Neurotoxicity screening battery [67]
- OECD Test Guideline 426: Developmental Neurotoxicity Study [68]
- OPPTS Harmonized Guideline: 870.6300 Developmental neurotoxicity study [69]

5.4.1. Sources for Data Interpretation

- Section 3, Hazard Characterization in *Guidelines for Neurotoxicity Risk Assessmen*t [12]
- GHS Ch. 3.9 Specific Target Organ Toxicity Repeated Exposure [23]

5.5. Repeated Dose Toxicity – Test Methods

- OECD Test Guideline 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents [70]
- OECD Test Guideline 409: Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents [71]
- OECD Test Guideline 411: Subchronic Dermal Toxicity: 90-day Study [72]
- OECD Test Guideline 413: Subchronic Inhalation Toxicity: 90-day Study [73]
- OPPTS Harmonized Guideline 870.3100: 90-Day oral toxicity in rodents [74]
- OPPTS Harmonized Guideline 870.3150: 90-Day oral toxicity in nonrodents [75]
- OPPTS Harmonized Guideline 870.3250: 90-Day dermal toxicity [76]
- OPPTS Harmonized Guideline 870.3465: 90-Day inhalation toxicity [77]
- OECD Test Guideline 407: Repeated Dose 28-day Oral Toxicity Study in Rodents [78]
- OECD Test Guideline 410: Repeated Dose Dermal Toxicity: 28-day Study [79]
- OECD Test Guideline 412: Repeated Dose Inhalation Toxicity: 28-day Study [80]
- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [81]
- OPPTS Harmonized Guideline 870.3050: Repeated dose 28-day oral toxicity study in rodents [82]
- OPPTS Harmonized Guideline 870.3200: 28-Day dermal toxicity [83]

5.5.1. Sources for Data Interpretation

- GHS Ch 3.9 Specific Target Organ Toxicity Repeated Exposure [23]

5.6. Reproductive and Developmental Toxicity – Test Methods

Fertility Test Methods

- OECD Test Guideline 415: One-Generation Reproduction Toxicity Study [84]
- OECD Test Guideline 416: Two-Generation Reproduction Toxicity Study [85]
- OPPTS Harmonized Guideline 870.3800: Reproduction and fertility effects [86]
- OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test [87]
- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [81]
- OPPTS Harmonized Guideline 870.3550: Reproduction/developmental toxicity screening test [88]
- OPPTS Harmonized Guideline 870.3650: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [89]

Developmental Toxicity Test Methods

- OECD Test Guideline 414: Prenatal Developmental Toxicity Study [90]
- OPPTS Harmonized Guideline 870.3800: Reproduction and fertility effects [86]
- OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test [87]
- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [81]
- OPPTS Harmonized Guideline 870.3550: Reproduction/developmental toxicity screening test [88]
- OPPTS Harmonized Guideline 870.3650: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [89]

5.6.1. Sources for Data Interpretation

- EU Dangerous Substances Directive, http://ecb.jrc.ec.europa.eu/documentation/. To access the list of substances carrying Risk Phrases, click on "CLASSIFICATION-LABELLING", then "DIRECTIVE 67-548-EEC", then "ANNEX I OF DIRECTIVE 67-548-EEC", and then either of the files listed as: "Annex I of Directive 67548EEC" [41]
- EU Dangerous Preparations Directive Article 6 and Annex II (1999/45/EC and subsequent updates/amendments) [48-50]
- GHS Ch 3.7 Reproductive Toxicity [91]
- Part A, Section 3, Hazard Characterization in *Guidelines for Reproductive Toxicity Risk Assessmen*t, http://www.epa.gov/ncea/raf/pdfs/repro51.pdf [14]
- Part A, Section 3, Hazard Characterization in *Guidelines for Developmental Toxicity Risk Assessmen*t, http://www.epa.gov/NCEA/raf/pdfs/devtox.pdf [8]

5.7. Skin Sensitization – Test Methods

- OECD Test Guideline 406: Skin Sensitization [92]
- OECD Test Guideline 429: Skin Sensitization: Local Lymph Node Assay [10]
- OPPTS Harmonized Guideline 870.2600: Skin Sensitization [93]

5.7.1. Sources for Data Interpretation

- EU Dangerous Substances Directive, http://ecb.jrc.ec.europa.eu/documentation/. To access the list of substances carrying Risk Phrases, click on "CLASSIFICATION-LABELLING", then "DIRECTIVE 67-548-EEC", then "ANNEX I OF DIRECTIVE 67-548-EEC", and then either of the files listed as: "Annex I of Directive 67548EEC" [41]
- EU Dangerous Preparations Directive Article 6 and Annex II (1999/45/EC and subsequent updates/amendments) [48-50]
- GHS Ch 3.4 Respiratory and Skin Sensitization [7]

5.8. Acute Aquatic Toxicity

Test Methods for Fish

- OECD Test Guideline 203: Fish, Acute Toxicity Test [94]
- OPPTS Harmonized Guideline 850.1075: Fish acute toxicity test, freshwater and marine [95]

NOTE – EPA may request that the test be carried out using semi-static renewal or a flow-through system with mean measured concentration. Any new testing should be done in consultation with EPA.

Test Methods for Aquatic Invertebrates

- OECD Test Guideline 202, Part 1, Daphnia sp., Acute Immobilisation Test [96]
- OPPTS Harmonized Guideline 850.1010: Aquatic invertebrate acute toxicity test, freshwater daphnids [97]
- OPPTS Harmonized Guideline 850.1035: Mysid acute toxicity test[98]

NOTE – EPA may request that the test be carried out using semi-static renewal or a flow-through system with mean measured concentration. Any new testing should be done in consultation with EPA. A 96-hour Mysid shrimp acute toxicity test can be used in place of a daphnid acute toxicity test when the latter is not available.

Test Methods for Algae

- OECD Test Guideline 201, Alga, Growth Inhibition Test (and biomass) [99]
- OPPTS Harmonized Guideline 850.5400: Algal toxicity, Tiers I and II (including growth inhibition and biomass) [100]

Alternative Test Methods, Acute Aquatic Toxicity

The following test methods may be considered, when relevant:

- OPPTS Harmonized Guideline 850.1085: Fish acute toxicity mitigated by humic acid [101]
- OPPTS Harmonized Guideline 850.1025: Oyster acute toxicity test (shell deposition) [102]
- OPPTS Harmonized Guideline 850.1045: Penaeid acute toxicity test [103]
- OPPTS Harmonized Guideline 850.1055: Bivalve acute toxicity test (embryo larval) [104]
- OPPTS Harmonized Guideline 850.4400: Aquatic plant toxicity test using *Lemna spp.* Tiers I and II [105]
- Modeled data from sources such as EPI Suite™ [19] are acceptable when data are unavailable.

5.8.1. Sources for Data Interpretation

- U.S. EPA Design for the Environment Program Master Criteria for Safer Ingredients [28]
- U.S. EPA EPI Suite™ [19]

5.9. Persistence

Data from experimental methods are generally preferred over estimations of persistence. It is noted that simulation tests are likely to better describe the biodegradability of a chemical in specific environmental conditions and may also contribute useful information to the review. Environmental monitoring data may modify how a persistence designation is determined.

Test Methods for Persistence

- OECD Test Guideline 301: Ready Biodegradability (sections A-F) [30]
- OECD Test Guideline 310: Ready Biodegradability – CO2 in sealed vessels [31]
- OPPTS Harmonized Guideline 835.3110: Ready biodegradability [106]
- If the compound degrades by more than 40% in 28 days during one of the Ready Biodegradability tests specified above or by more than 60% in one of the Inherent Biodegradability tests detailed in OECD Test Guidelines 302 (A-C) [107-109], then the half-life of a chemical is likely to be less than 60 days [110].
- OECD Test Guideline 303A (OPPTS 835.3240): Aerobic Sewage Treatment: Activated Sludge Units [111, 112]
- OECD Test Guideline 309 (OPPTS Harmonized Guideline 835.3190): Aerobic Mineralization in Surface Water - Simulation Biodegradation Test [113, 114]
- OECD Test Guideline 314: Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater (Note: TG 314 uses elements of OECD TG 301, 303A, 309, 310, and 311) [115]

- OPPTS Harmonized Guideline 835.3280–Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater [116]
- OPPTS Harmonized Guideline 835.3170 - Shake Flask Die-Away Test [117]
- OPPTS Harmonized Guideline 835.3180 - Sediment/Water Microcosm Biodegradation Test [118]

Other Methods of Degradation

On a case-by-case basis, DfE will consider other routes of degradation in the environment, such as hydrolysis or photolysis, and degradation in other relevant media, for example, soil or sediment. In evaluating such degradation studies, DfE will consider the relevance of that degradation pathway to the chemical in question as well as the significance of the degradation.

5.9.1. Sources for Data Interpretation

- U.S. EPA Design for the Environment Program Master Criteria for Safer Ingredients [28]
- U.S. EPA EPI Suite™ [19]
- SPARC [26]
- Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3 [119]
- OPPTS 835.0001 Principles and Strategies Related to Biodegradation Testing of Organic Chemicals under the Toxic Substances Control Act (TSCA) [120]

5.10. Bioaccumulation

A field-measured BAF (located in the literature) is the most preferred data for indicating bioaccumulation. Environmental monitoring data will be considered when available.

Alternative Test Methods for Bioaccumulation

When a field-measured BAF is not available, the following test methods may be used:

- OECD Test Guideline 305: Bioconcentration: Flow-through Fish Test [121]
- OPPTS Harmonized Guideline 850.1710: Oyster BCF [122]
- OPPTS Harmonized Guideline 850.1730: Fish BCF [123]
- Modeled data from sources such as EPI Suite™ [19] are acceptable when data are unavailable.

5.10.1. Sources for Data Interpretation

- U.S. EPA Design for the Environment Program Master Criteria for Safer Ingredients [28]
- U.S. EPA EPI Suite™ [19]
- SPARC [26]

6. Appendix

Table A1. Alternatives Assessment Criteria Quick Reference

Human Health Effects					
Acute Mammalian Toxicity	**Very High**	**High**	**Moderate**	**Low**	
Oral LD50 (mg/kg)	≤ 50	> 50 - 300	> 300 - 2000	> 2000	
Dermal LD50 (mg/kg)	≤ 200	> 200 - 1000	> 1000 - 2000	> 2000	
Inhalation LC50 (vapor/gas) (mg/L)	≤ 2	> 2 -10	> 10 - 20	> 20	
Inhalation LC50 (dust/mist/fume) (mg/L)	≤ 0.5	> 0.5 - 1.0	> 1.0 - 5	> 5	
Carcinogenicity		**High**	**Moderate**	**Low**	
		Positive results	Equivocal results	Negative studies and no structural alerts	
Mutagenicity/Genotoxicity		**High**	**Moderate**	**Low**	
		Positive results	Equivocal results	Negative for chromosomal abberations and gene mutations, and no structural alerts. Adequate data available.	
Reproductive and Developmental Toxicity		**High**	**Moderate**	**Low**	
Oral (mg/kg/day)		< 50	50 - 250	> 250	
Dermal (mg/kg/day)		< 100	100 - 500	> 500	
Inhalation (vapor, gas, mg/L/day)		< 1	1 - 2.5	> 2.5	
Inhalation (dust/mist/fume, mg/L/day)		< 0.1	0.1 - 0.5	> 0.5	
Neurotoxicity		**High**	**Moderate**	**Low**	
Oral (mg/kg-bw/day)		< 10	10 - 100	> 100	
Dermal (mg/kg-bw/day)		< 20	20 - 200	> 200	
Inhalation (vapor/gas) (mg/L/6h/day)		< 0.2	0.2 - 1.0	> 1.0	
Inhalation (dust/mist/fume) (mg/L/6h/day)		< 0.02	0.02 - 0.2	> 0.2	
Repeated Dose Toxicity		**High**	**Moderate**	**Low**	
Oral (mg/kg-bw/day)		< 10	10 - 100	> 100	
Dermal (mg/kg-bw/day)		< 20	20 - 200	> 200	
Inhalation (vapor/gas) (mg/L/6h/day)		< 0.2	0.2 - 1.0	> 1.0	
Inhalation (dust/mist/fume) (mg/L/6h/day)		< 0.02	0.02 - 0.2	> 0.2	
Sensitization		**High**	**Moderate**	**Low**	
Skin sensitization		High frequency of sensitization in humans and/or high potency in animals (GHS Cat. 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Cat. 1B)	Adequate data available and not GHS Cat. 1A or 1B	
Respiratory Sensitization	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				
Irritation/Corrosivity	**Very High**	**High**	**Moderate**	**Low**	**Very Low**
Eye Irritation/Corrosivity	Irritation persists for > 21 days or corrosive	Clearing in 8-21 days, severely irritating	Clearing in 7 days or less, moderately irritating	Clearing in less than 24 hrs, mildly irritating	Not irritating
Skin Irritation/Corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	Not irritating
Endocrine Activity	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				
Environmental Toxicity and Fate					
Aquatic Toxicity	**Very High**	**High**	**Moderate**	**Low**	
Acute Aquatic Toxicity (LC50 or EC50) (mg/L)	< 1.0	1 - 10	> 10 - 100	> 100	
Chronic Aquatic Toxicity (LOEC) (mg/L)	< 0.1	0.1 - 1	> 1 - 10	> 10	
Environmental Persistence	**Very High**	**High**	**Moderate**	**Low**	**Very Low**
Persistence in water, soil or sediment	Half-life > 180 days or recalcitrant	Half life of 60 – 180 days	Half-life < 60 but ≥ 16 days	Half-life < 16 days OR passes Ready Biodegradability test not including the 10-day window. No degradation products of concern.	Passes Ready Biodegradability test with 10-day window. No degradation products of concern.
Persistence in air (half-life days)	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				
Bioaccumulation (BAF / BCF)	**Very High**	**High**	**Moderate**	**Low**	
	> 100,000	100,000 – 1,000	1,000 – 100	< 100	

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Attachment 1-7

Washington State Chemical Prioritization

Presentation by Alex Stone

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Washington State Chemical Prioritization

Alex Stone
Safer Chemical Alternative Chemist

States' Chemical Legislation

Numerous states are passing chemical legislation including:

- Bans: DecaBDE (WA, ME, VT)
- Restrictions: Children's Safe Products Acts: (WA, ME, CT, MN)
- Broader Chemical Policy: Green Chemistry Initiative (CA)

Children's Safe Product Act

Washington Legislation Passed in April 2007

- Limited concentrations of lead, cadmium and phthalates in children's products
- Required identification of chemicals of high concern to children
- Included process on how to identify these chemicals

Federal Legislation

- Federal legislation passed in August 2007
- Preempted state authority to regulate lead and phthalates
- Did not preempt Washington's authority to require reporting on chemicals of high concern to children in products sold in WA
- Ecology currently working on list of chemicals of high concern to children for reporting

Universe of Chemicals

Toxics Substances Control Act List of Chemicals

- Currently believed to contain 80-100,000 chemicals
- As many as half may no longer be used in commerce
- Not easily accessible

Located other sources

- Canadian Domestic Substances List
- New Zealand Inventory of Chemicals in commerce
- Other smaller, authorative sources

Total chemicals-almost 40,000 chemicals

‘High Priority Chemicals’ (HPCs): (From legislation)

Section 2: Definitions

‘High priority chemical’ as identified by:

- **State agency**
- **Federal agency**
- **Accredited research university**
- **Other scientific evidence deemed authoritative**

One or more of the following criteria:

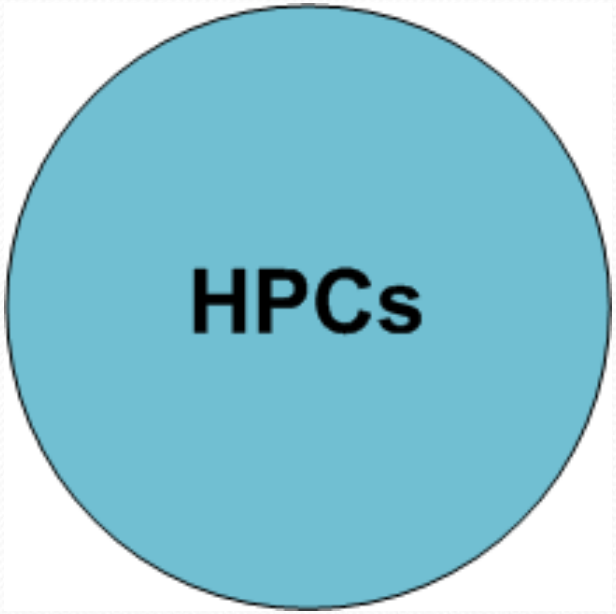
a) **Developmental toxin**

b) **Cause:**
   - **Cancer**
   - **Genetic damage**
   - **Reproductive harm**
   - **Endocrine disruptor**

c) **Damage:**
   - **Nervous system**
   - **Immune system**
   - **Organs**
   - **Other systemic toxicity**

d) **PBT**

e) **vPvB (very persistent & very bioaccumulative)**



HPC Sources:

United States: Federal

EPA TRI PBT Chemicals
EPA VCCEP
Nat. Waste Min. Prg. Priority Chem.
Nat. Tox Prg. Reproduction
Nat. Tox Prg. Carcinogens-Known
Nat. Tox Prg. Carcinogens-Suspected

IRIS Total
- IRIS 1986 Category A (known)
- IRIS 1986 Category B1 (probable-humans)
- IRIS 1986 Category B2 (probable-animal)
- IRIS 1986 Category C (possible)
- IRIS 1996 Known/likely
- IRIS 1999 Carcinogens
- IRIS 2005 Suggestive Evidence
- IRIS Oral RfD Critical Effects

Other

Grandjean Neurotoxins (developmental toxins)

United States: State

Prop 65-Total
- Prop 65 Cancer
- Prop 65 Developmental
- Prop 65 Female
- Prop 65 Male

WA PBTs

International

EU Endocrine Disruptors Cat 1
EU Endocrine Disruptors Cat 2
EU SVHC (Substances of Very High Concern)
EU PBTs
EU Chemicals identified for Risk Assessment
OSPAR Chemicals of Concern
OSPAR 1997 Chems for Priority Action
IARC Group 1 Known Carcinogens
IARC Group 2a Probable Carcinogens
IARC Group 2b Possible Carcinogens
Canadian PBiT list

Identify 'chemicals of high concern to children (CHCCs)': (From legislation)

Exposure Lists:

<u>Section 4:</u>

Identifying high priority chemicals of high concern for children after considering a child's or developing fetus's potential for exposure to each chemical.

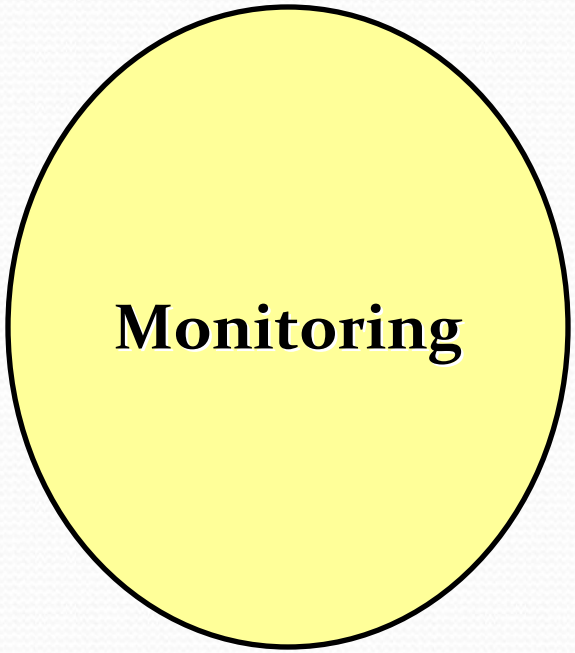
One or more of the following criteria:

Chemicals found in biomonitoring studies:

a) Humans
   - Umbilical cord blood
   - Breast milk
   - Urine
   - Other bodily tissues or fluids

b) Chemicals found in:
   - Household dust
   - Indoor air
   - Drinking water
   - Elsewhere in the home

c) Added or present in consumer product used or present in the home



Biomonitoring & Potential Exposure Lists

Established lists of chemicals in the four exposure areas:

1. **Biomonitoring**
2. **Indoor air and dust**
3. **Drinking water**
4. **Products**
    - **Children's products**
    - **Consumer products in general**

Biomonitoring & Potential Exposure Lists

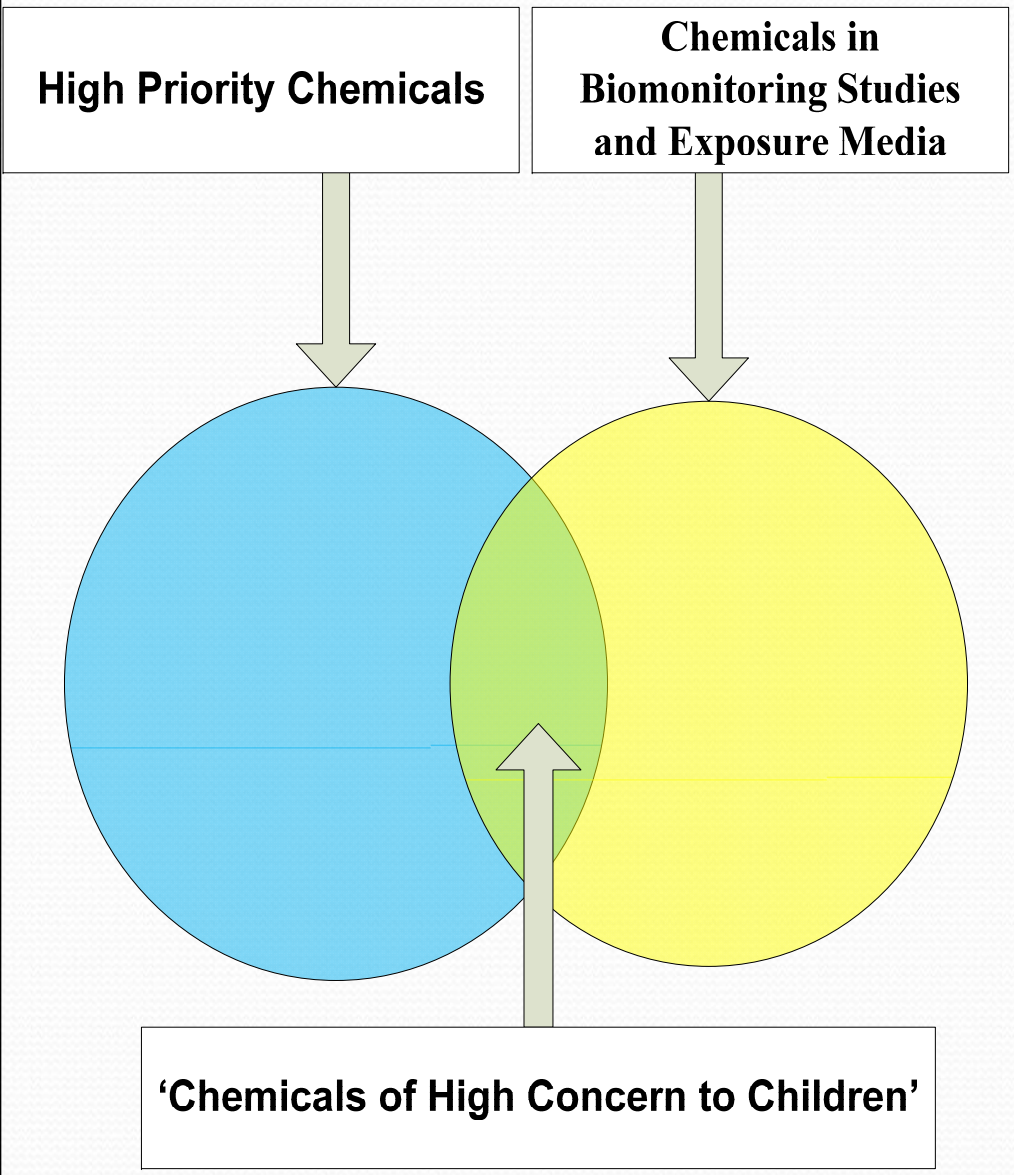
Chemicals added to lists from:

1. **Authoritative Sources**
   - **CDC's NHANES for <u>biomonitoring</u>**
   - **California Air Resources Board for <u>indoor air & dust</u>**
   - **EPA's drinking water program for <u>drinking water</u>**
   - **Danish Environmental Protection Agency and Dutch Food and Consumer Product Safety Authority for <u>products</u>**
2. **Original research published in peer-reviewed, scientific journals**

Number of Chemicals Associated with Information Sources

Information Sources	Number of Chemicals
Biomonitoring Studies	318
Indoor Air and House Dust	298
Drinking Water	285
Consumer Products	1,856
	2,757 (Total)
	2,293 (CAS)

CAS=Chemical Abstracts Service registry number.



High Priority Chemicals:

- **From authoritative sources**
- **With specific toxicities**

Biomonitoring & Potential Exposure Lists:

- **Chemicals found in:**
  - **Humans**
  - **Indoor Air and Dust**
  - **Drinking Water**
  - **Products**

CHCCs:

- **Intersection of two groups**

Conclusions:

- Can identify HPCs & CHCCs based upon current knowledge
- Transparent , flexible and easily understood process
- May have uses outside of current application
  - Process can be expanded to include other criteria (aquatic toxicity, worker health and safety, etc.)

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Attachment 1-8

Reliable Information Definition Examples

RELIABLE INFORMATION DEFINITION EXAMPLES

Reliable information means data, studies and other information that has been:

1. Scientifically peer-reviewed, or

2. Generated using one of the following:
   - US FDA Good Laboratory Practices,
   - US EPA's Harmonized Test Guidelines,
   - TSCA Testing Guidelines, or

3. Published in scientifically peer-reviewed literature, or

4. Published in final state or federal scientific reports, or

5. Published in a final report of the National Academy of Sciences, National Academy of Engineering, Institute of Medicine, or National Research Council, or

6. Published in final reports from specified California public health and environmental agencies, or

7. Developed, or reviewed and accepted, by a federal agency or a California State or local agency for compliance or other regulatory purposes, or

8. Generated according to valid accepted testing protocols in which the test parameters documented are based on specific testing guidelines or in which all parameters described are comparable to a guideline method, including:
   - OECD Guidelines for Testing of Chemicals,
   - OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring,
   - OECD Manual for Investigation of High Production Volume Chemicals,
   - REACH/ECHA Guidance on Information Requirements and Chemical Safety Assessment and Regulation (EC) No. 440/2008 of the European Parliament and the Council, and
   - Canadian Environmental Protection Act (CEPA) Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers, or

9. Qualitative or quantitative structural activity relationship model results based on guidelines provided in the OECD Manual for Investigation of High Production Volume Chemicals.

Reliable information demonstrating the occurrence, or potential occurrence, of public health and/or environmental exposures means all of the following that met the definition of reliable information:

1. Monitoring data that shows the chemical to be present in household dust, indoor air, drinking water, or on interior surfaces,

2. Monitoring data that shows the chemical to be present in, or released from, products used in or present in the home,

3. Environmental monitoring data, or environmental modeling results, that indicate environmental accumulation of a chemical,

4. California Environmental Contaminant Biomonitoring Program data, or other biomonitoring data, that show the chemical to be present in human organs, tissues or fluids,

5. Environmental monitoring data that shows the accumulation of the chemical in aquatic, avian, animal or plant species,

6. Exposure modeling that indicates exposure point concentration(s) associated with adverse public health or environmental impacts, and

7. Monitoring data indicating the presence of a chemical or its degradation products in California solid waste, wastewater or storm water streams collected or managed by California State or local agencies in concentrations or volumes that:
    - Present public health or environmental threats,
    - Require the significant expenditure of public funds to mitigate public health or environmental threats,
    - Significantly increase the costs of reusing or recycling materials containing the chemical, or
    - Interfere with the proper operation of solid waste, wastewater, or storm water treatment systems and may result in the discharge of the chemical to the environment.

Attachment 1-9

OECD Guidance on Data Quality

MANUAL FOR INVESTIGATION OF HPV CHEMICALS

CHAPTER 3: DATA EVALUATION

3.1 Guidance for Determining the Quality of Data for the SIDS Dossiers: (Reliability, relevance and adequacy)[1]

3.1.1 Introduction

1. There are approx. 5000 chemicals on the OECD List of High Production Volume Chemicals (last updated in 2004). The OECD HPV Chemicals Programme provides for an initial assessment of the potential human health and environmental hazards of a chemical.

2. The first step in the investigation of a HPV chemical is to collect and carry out a review to ensure that there is sufficient good quality information on each of the elements that make up the Screening Information Data Set (SIDS). This is necessary before deciding if additional testing is required for any given HPV chemical.

3. The purpose of this document is to provide basic guidance to industry, governments, and other interested parties on the first steps of a process, which ultimately ends in decisions about, whether existing data are sufficient to fill a SIDS data element.

4. The document is not intended to present all possible approaches which can be used to assess data quality but presents two tools, one already used by industry and another proposed by governments which is a more criteria driven approach for compiling and assessing the completeness of Screening Information Data Sets (SIDS) on HPV chemicals.

3.1.2 The Screening Information Data Set (SIDS)

5. The SIDS is used for making an initial hazard assessment on HPV chemicals and provides the basis for conclusions on potential human health and environmental hazards and recommendations on the need for further work.

6. In developing the SIDS, the OECD made maximum use of OECD Test Guidelines to establish the recommended test methods for the generation of new data on SIDS elements. Use of OECD Test Guidelines and OECD Principles of Good Laboratory Practice ensures that any newly generated test data is accepted under the OECD system of Mutual Acceptance of Data [see C(81)30 (Final)]. Data generated under this system is accepted between countries for assessment purposes without the need for repeat testing.

7. Consideration of all available existing information on an HPV chemical is important because, if it is judged to be of sufficient quality, there is no need for additional testing for that SIDS element, resulting in savings in resources, such as time, costs and laboratory animals.

3.1.3 The quality of existing data

8. The process of determining the quality of existing data takes into consideration three aspects - adequacy, reliability and relevance of the available information to describe a given SIDS element.

[1] This document was prepared by the OECD Secretariat based on the agreements reached in the OECD Existing Chemicals Programme up to December 2005.

These terms were defined by Klimisch et al. (1997) along the following lines:

- **Reliability** - evaluating the inherent quality of a test report or publication relating to preferably standardised methodology and the way the experimental procedure and results are described to give evidence of the clarity and plausibility of the findings;

- **Relevance** - covering the extent to which data and tests are appropriate for a particular hazard identification or risk characterisation; and

- **Adequacy** - defining the usefulness of data for hazard/risk assessment purposes. When there is more than one study for each SIDS element, the greatest weight is attached to the study that is the most reliable and relevant. Robust study summaries are prepared for the highest quality or "key"studies.

9. The guidance deals primarily with determining the reliability of data. This essentially relates to how the study was carried out. This information is needed to enable robust study summaries to be prepared and before relevancy and adequacy can be considered.

10. Careful consideration must be made of the quality of the study, the method, the reporting of the results, the conclusions drawn and the results in order to complete a robust study summary.

11. There are several reasons why existing study data may be of variable quality. Klimisch et al, 1997, have suggested the following:

- the use of different test guidelines (compared with today's standards);
- the inability to characterize the test substance properly (in terms of purity, physical characteristics, etc.);
- the use of crude techniques/procedures which have since become refined; and
- the fact that certain information may have not been recorded (or possibly even measured) for a given endpoint, but that it has since been recognized as being important.

12. The first step in assessing whether data gaps exist for an HPV chemical is to conduct a literature search and search of company records, as appropriate. The existing data identified in the search should then be reviewed to determine whether additional testing is necessary.

13. The identification of the need for additional testing may be considered at any stage of the data collection and review process including:

a) the initial determination of the quality of the data;
b) the preparation of robust study summary(ies) for most relevant and reliable study(ies) for each SIDS element; and
c) development of a test plan, if necessary.

14. In some cases the type of substance under investigation will result in the recommended SIDS test for a particular element being difficult or inappropriate to carry out, e.g. chemicals which are unstable in abiotic or biotic systems, chemicals with known explosive/flammable properties or volatile substances. In such cases the relevance of the study may be questionable.

15. Each study essentially will require a case by case consideration and for these reasons a quick look at the reliability of the studies may save time later when relevance and adequacy are considered. At least a minimal amount of information on the reliability of a given study needs to be known before proceeding to determine its relevance and adequacy for SIDS initial assessment purposes and before proceeding to

develop a robust study summary. The following guidance therefore provides two consistent approaches, which may be used as an initial or first screen.

3.1.4 Initial screen for reliability

16. The reliability of the data is a key initial consideration, which can be done relatively quickly to filter out unreliable studies and focus further resources on those considered most reliable. Without knowledge of how the study has been conducted all other considerations may be irrelevant. Two approaches have been proposed to assist the initial screening of study reports to set aside unreliable study data. Both are compatible and may be used either alone or together by a person compiling a SIDS Dossier and considering data quality.

17. One approach is that developed by **Klimisch et al. (1997)**. This approach was developed as a scoring system for reliability, particularly for ecotoxicology and health studies; however it may be extended to physicochemical and environmental fate and pathway studies. The other approach was developed in 1998 as part of the **US EPA HPV Challenge Programme**.

18. Klimisch et al. (1997), developed a scoring system which can be used to categorize the reliability of a study as follows:

> **1 = reliable without restrictions**: "studies or data...generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline...or in which all parameters described are closely related/comparable to a guideline method."
>
> **2 = reliable with restrictions:** "studies or data...(mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable."
>
> **3 = not reliable**: "studies or data...in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment."
>
> **4 = not assignable**: "studies or data....which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.)."

19. The use of Klimisch codes provides a useful tool for organising the studies for further review. E.g. it would allow the person reviewing the studies to focus on the most highly reliable study first to allow time to be devoted later to consider relevance and adequacy of the reliable studies only. Studies, which failed to meet essential criteria for reliability, would be set aside at the beginning. Provision has been made to add Klimisch scores into the information on specific studies in the SIDS Dossier [see Annex 1 to the Guidance for Developing Robust Study Summaries for SIDS Dossiers]. .

20. The second approach developed by the US EPA approach provides more information than the Klimisch system by describing the key reliability criteria for each type of data making up the SIDS Dossier (Table 1). These criteria address the overall scientific integrity and validity of the information in a study, i.e. reliability. This approach is consistent with the Klimisch approach - any study, which does not meet

the criteria in Table 1, would also not be assignable under the Klimisch system. Such studies may be however be considered later as supplementary information to the overall assessment of a particular SIDS element particularly if there is no single key study.

3.1.5 Determination of relevance and adequacy

21. The use of sound scientific judgment is the most important principle in considering relevance and adequacy. The studies that have passed the initial screen should be considered using the guidance used for assessing SIDS data elements and compiling robust study summaries [see Guidance for Developing Robust Study Summaries for SIDS Dossiers.]. These documents highlight aspects of the information that must be available in order for the study to be considered relevant and adequate for the SIDS initial assessment. At this stage it is expected that one or more key studies that best represent a particular SIDS element and whether robust study summaries can be prepared, will be identified.

22. The more detailed assessment of relevance and adequacy is very much related to preparing the SIDS Dossier (including robust study summaries, as appropriate). It can therefore be regarded as a second tier consideration.

3.1.6 Weight-of-the-Evidence Analysis

23. The use of tools for identifying reliable and relevant and adequate data to prepare robust study summaries helps to ensure that high quality data is used in the OECD HPV Chemicals Programme. They do not however remove the need for a weight-of-evidence analysis approach during the assessment of this data.

24. Similarly the assignment of Klimisch Codes for data reliability does not necessary mean that any extra weight should be given to these studies in the overall initial assessment, as there may be information from other studies on other elements which have an influence. Documentation prepared for the HPV Chemicals Programme will need to be explicit on the criteria, which have been applied to assess quality, rather than simply referencing a score.

25. Some HPV chemicals have been tested in a variety of studies that are beyond SIDS (e.g., neurotoxicity, fish chronic toxicity test, etc.), whereas the tests for the SIDS endpoint have not been carried out. In such cases, if a rationale can be presented to show that such non-SIDS tests adequately describe the SIDS element of concern, a new test for that particular endpoint may not be necessary.

26. Because of the nature of existing data, it is reasonable to expect that there will be some cases (for a given SIDS element) in which several studies - some of which may not have passed the initial screen may be collectively used to fill the element, thereby avoiding additional testing.

27. The pooling of several studies, one or more of which may be inadequate, to satisfy a specific SIDS element is another way that a weight-of-the-evidence analysis can be made. For example, there may be several repeated dose studies available on a particular chemical, none of which would be acceptable by itself due to some deficiency (i.e., low number of test animals/dose group, only one dose group in addition to control group, change in dose amount or frequency during the course of the study, etc.). Collectively, however, the different studies show effects in the same target organ at approximately the same dose and time. This could satisfy the repeated dose toxicity data element for SIDS.

Table 1: Initial Screening Criteria for data reliability by type of SIDS information items

Criteria	Required for following SIDS Information Items		
	P/Chem	**Env.Fate**	**Ecotox /Health**
Test Substance Identification (Adequate description of test substance, including chemical purity and identification/quantification of impurities to the extent available).	**X**	**X**	**X**
Temperature	**X**[1]	**X**	**X**
Full Reference/Citation	**X**	**X**	**X**
Controls[2]		**X**	**X**
Statistics With some exceptions (e.g., the *Salmonella*/Ames assays**)**			**X**
Species, strain, number, gender, & age of organism			**X**
Dose/conc. Levels		**X**	**X**
Route/type of exposure[3]			**X**
Duration of exposure		**X**	**X**

Footnotes to Table 1

1. For vapour pressure, octanol/water partition coefficient and water solubility values
2. All studies must have negative controls and some studies (e.g. biodegradation, Salmonella/Ames assay) must also have positive controls. If a vehicle is used in the administration of the test agent, vehicle controls should be established and reported. Exceptions may be allowed for acute mammalian toxicity studies.
3. The route/type of exposure (e.g., oral inhalation. etc for mammalian studies) or test system (static, flow-through, etc for ecotoxicity) must be reported.

3.1.7 Use of secondary data sources for physico-chemical endpoints

28. The primary concern for SIDS endpoints presented in submissions to the OECD HPV Chemicals Programme is that they should be accurate, reliable and valid. It is particularly important that accurate values are established for parameters such as the octanol-water partition coefficient, aqueous solubility and vapour pressure, which are required to predict environmental exposure and interpret ecotoxicity test data.

29. The reliability of data is demonstrated by the preparation of a Robust Study Summary, as detailed in Section 2.4.3. This provides information such as the identity of the test substance, the methodology used to make the measurement and whether this was performed to GLP standards. In order to obtain this information, reference should ideally be made to the primary data source, such as a published paper or test report[2]. Section 2.2.3, on existing SIDS data, states that "…as far as possible, original publications should be retrieved".

30. However, in the case of well-studied chemicals it may be acceptable to use values for physico-chemical parameters obtained from reliable secondary sources such as standard references, which are known to publish 'peer reviewed' data, i.e. the data available in the literature are critically evaluated and an appropriate, reliable value selected. It is appropriate to assign these sources of peer reviewed data a reliability code of (2), 'valid with restrictions', when considering reliability, since it is assumed that a variety of data sources have been consulted and the test methodology and identity of the test substance have been evaluated, and a reliable and representative value for the endpoint selected. Whether such a review process has been conducted should be stated in the introduction to the handbook or contained in the summary information for an on-line database.

31. Useful reference books and data compilations containing peer reviewed physico-chemical data (some of which are listed in Section 2.2.3) include:

- The Merck Index;
- The CRC Handbook of Chemistry and Physics;
- The IUPAC Solubility Data Series;
- Beilstein Database and;
- Illustrated Handbooks of Physical-Chemical Properties and Environmental Fate for Organic Chemicals.

32. Online databases such as the SRC PhysProp Database[3] and HSDB[4] on the TOXNET network are good sources of data and generally provide a reference for the value that they have selected. Because these database sources are usually secondary data sources themselves, the original data source should be checked and referenced rather than directly citing the database (or secondary data source without retrieving it). Databases such as these are valuable resources that should primarily be used as a source to highlight where data are available.

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[2] If the original data source is an 'old' reference it may be necessary to consider the following: (i) If the reference was published more than 20 years ago, then retrieval could require a lot of time or may not be possible; (2) Current GLP standards may not have been followed; and (3) Older publications may not have routinely provided information regarding the test substances, including the purity.

[3] Available on-line at http://esc.syrres.com/interkow/physdemo.htm. These data are also used to populate the 'Experimental Database' in the EPIWIN software suite

[4] Hazardous Substances Data Bank Available on-line via TOXNET at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

33. The issue of 'data recycling' and the potential for degrading the reliability of data for environmental assessment is an issue of growing concern in the scientific community[5] and reinforces the need for the preparation of a Robust Study Summary (RSS) from the primary data source as best practice.

34. When using data solely from secondary sources it is essential to construct a 'weight-of-evidence' approach (see Section 3.1.6) in order to establish that an appropriate value has been selected for the SIDS dataset. It is not normally acceptable to use a single, peer reviewed secondary source with no further supporting evidence. The SIDS Dossier should present values taken from multiple authoritative data sources, such as those detailed above, in addition to supporting data, such as manufacturing data, reliable QSAR predictions[6], and/or data from sources that may not have been peer reviewed, e.g. Vershueren's Handbook on Environmental Data. Values for physico-chemical properties taken from material safety data sheets (MSDSs) and all other company technical data can only be assigned a reliability rating of (4), unassignable, unless detailed information such as the experimental methodology and test substance are provided to enable the preparation of a RSS and an independent evaluation of the study's reliability.

35. When presenting values for physico-chemical parameters such as vapour pressure, Log Kow and water solubility from secondary sources the important factors to detail, if available, are: whether the value has been measured or estimated, the method of experimental determination or estimation[7]; the temperature at which the measurement/estimation was made and; a full reference/citation. If this is not clear in a handbook or data compilation whether a value has been determined experimentally or estimated then reference should be made to the primary source.

36. Some initial comments on the most common data sources for physico-chemical data are given in Table 2 below. However, it must be emphasised that it is difficult to draw general conclusions regarding the reliability of each data source for an individual parameter and reviewers should make every effort to ensure that the test substance identity, test method and result are reliable, in accordance with Chapters 2 and 3.

Table 2: Common sources for physico-chemical data

Source of physico-chemical data	Comments
Merck Index	Physical data are cited as found in the literature. When several alternate data values appear in the literature, the data is evaluated and representative selections are made; values are then reported with the corresponding source.
Hawley's Condensed Chemical Dictionary	This is a compendium of physical data that are taken to be 'reliable'; "where entries are incomplete, it may be presumed that no reliable data were provided by the reference system utilised". [References for values are not provided]

[5] See Renner R (2002) The Kow Controversy. Environmental, Science and Technology, v36, no. 21, pp. 411A-413A

[6] It should be demonstrated that the QSAR used to estimate a value is appropriate for the type of chemical under consideration (see Section 3.3). If the estimate generated by a QSAR calculation is considerably different to measured value(s) there should be some discussion of the difference, including whether the QSAR applied was appropriate or if the prediction is within the established/validated domain for the model that is being used.

[7] It is important that the methodology employed is appropriate to the particular test substance under consideration.

CRC Handbook of Chemistry and Physics	Data for physical constants have been taken from many sources, including both compilations and the primary literature. Where conflicts were found, the value deemed most reliable was chosen. [Reference sources are provided for selected properties such as solubility and Log Kow; these references are generally authoritative data compilations]
IUPAC Solubility Data Series	The Solubility Data Series is a project of the International Union of Pure and Applied Chemistry (IUPAC). Publication of the series began in 1979, its goal being to present a comprehensive and critical compilation of data on solubilities in all physical systems, including gases, liquids and solids.
Beilstein Database[8]	Beilstein organic substance records contain the critically reviewed and evaluated documents from the Beilstein Handbook of Chemistry as well as data from 176 leading journals in organic chemistry covering the period 1779 to present. [An exhaustive list of values and primary references are provided]
Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals (Mackay et al)	Physical properties such as melting and boiling point and density are obtained from commonly used handbooks. Other properties such as solubility, vapour pressure, Log Kow have been obtained from primary reference sources and handbooks. A range of referenced values are reported for each of these properties. Data have been evaluated and a selected 'best value' is given for each property and used in calculations of environmental distribution.
SRC PhysProp Database/ EPIWIN Experimental Database	For compounds with abundant data, values have been taken from databases that had already evaluated the data and selected a reliable value. For compounds with less data, values are selected based on a number of factors including the reliability of the source and details of the experimental methodology. [References are provided for all values, except those for melting point and boiling point, and it is clearly indicated whether values are experimental or estimated]
Yaws Chemical Properties Handbook	"Experimental and estimated values are provided in the compilation based on data source publications for organic compounds" [This handbook provides a list of primary references for each property but they are not assigned to particular values or compounds. It is, however, indicated whether data were determined experimentally or estimated]

[8] CrossFire Beilstein, Licensed by MDL Information Systems GmbH

HSDB on TOXNET	HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the data bank's scope. All data are referenced and derived from a core set of handbooks, government documents, technical reports and selected primary journal literature".
The Pesticide Manual (currently edited by C Tomlin and previously by CR Worthing).	The introduction to this book (12th Edition) and the discussion of the entries provides no indication that the data has been 'peer reviewed'. There is a brief discussion of vapour pressure (as an example phys-chem property) and it is stated that if there are conflicting values available then the lowest is chosen. A significant proportion of the data is provided directly by manufacturers and is therefore unlikely to have been subject to 'peer review'.
Sax's Dangerous Properties of Industrial Materials	The preface and introduction to this book (10th Edition) provide no indication that the physico-chemical data has been 'peer reviewed'. Physical properties are selected to be useful in evaluating the hazard of a material and designing its proper storage and use procedures. [References for values are not provided]
Bretherick's Handbook of Chemical Reactive Hazards	Several different sources are used. These include primary sources (generally specialist safety journals but also includes general chemical literature), secondary sources (selecting only reactive hazard data) and the direct reporting of incidents to the editors by readers. Full references are given where available. The introduction gives details of the scope and coverage.
Lange's Handbook of Chemistry	The preface to this book states that "every effort has been made to select the most useful and reliable information and to record it with accuracy" but no references are provided for the data presented and there are no indication as to how they were evaluated.
Fire Protection Guide on Hazardous Materials, National Fire Protection Association	No indication is provided on the sources of data or whether they have been 'peer reviewed'. Appendix C of the 12th Edition discusses the preparation of a revised form of the 'Hazardous Chemical Data Sheets' (NFPA 49) contained in this handbook and states that the primary source of information will be material safety data sheets. These are not generally regarded as authoritative sources of data for physico-chemical properties. [References for values are not provided]
Verschueren, K. Handbook on Environmental Data on Organic Chemicals.	A useful discussion is provided of the physico-chemical properties that are covered in Verchueren and how they can potentially be used in assessing environmental behaviour but there is no description of sources used to compile the reported data or how they were evaluated. Ranges rather than single values are sometimes presented for parameters such as water solubility and Log Kow. [References are not given for phys-chem values but they are provided for entries of biological effect levels, bioaccumulation and degradation rates]

Dust Explosions in the Process Industries (by R. Eckhoff)	No physico-chemical data relevant to the SIDS dataset are presented in this reference source other than experimental values for median particle diameter and particle size distribution of various dust types and classifications of flammability (these are non-SIDS endpoints).

3.1.8 Acceptance and use of studies from Industrial Bio-Test laboratories

Background

37. Industrial Bio-Test laboratories (IBT) was one of the largest independent testing facilities in the United States conducting a third of all toxicological testing in the United States before a routine inspection by FDA in 1976 uncovered numerous discrepancies between raw data and study reports, and gross deficiencies in study conduct. The problems were mainly associated with the sections conducting "non-acute" studies[9]. These shortcomings prompted the US FDA to initiate the regulation of laboratory testing, which ultimately led to the development of Good Laboratory Practice which was introduced in 1979. IBT was closed down in 1978.

38. In response to the concerns about the reliability of studies conducted by IBT, the US EPA introduced a legal requirement for study sponsors to audit the raw data and validate IBT studies submitted as part of pesticide registrations, particularly those considered to be pivotal to the regulatory decision making process. Spot-checking of the industry audits revealed some areas of concern leading the US EPA, in collaboration with the Canadian Health and Welfare Department, to set up a post-hoc audit program to formally check the validity of IBT studies. During this audit program, studies were reviewed to determine whether laboratory notes supported the information in the final report and to determine whether they met certain quality requirements (US-EPA, 1983). There is currently no information available as to whether similar concerns apply to environmental toxicity studies conducted by IBT. According to US EPA there is no information or documentation that the environmental toxicity studies were conducted at IBT. It is likely that IBT subcontracted these types of studies to the other facilities and submitted the final reports under its name.

39. Non-acute studies were identified as the main priority because the major discrepancies uncovered were in sections conducting chronic and multi-generation studies. Of the 867 non-acute studies reviewed under the audit programme, 618 were found to be invalid. Significant discrepancies and deficiencies were also noted in the acute toxicity studies; however, all focus was then on the repeated-dose, long-term studies that were mainly used for regulatory purposes. Problems were uncovered in studies conducted during the 1960's and until 1978. Thus studies collected during this period should be considered as problem studies.

40. The issue of whether results from the IBT studies can be used for regulatory purposes has been raised in a number of fora. There has been a somewhat inconsistent approach to the use of the IBT studies, from outright rejection to normal evaluation and use as with any other study. Below is a proposed structured approach to making the most appropriate use of IBT studies, taking into account the various

[9] Study types identified as potential problems:

- Sub-acute
- Sub-chronic
- Carcinogenicity
- Reproductive toxicity (including teratogenicity)
- Genotoxicity
- Neurotoxicity

factors detailed above. The general principles outlined could also be applied to studies from other test houses which are considered to be suspect.

Proposed approach

41. For studies conducted during the suspect period the assumption should be that they are potentially invalid and the findings unreliable. The exception to this is where a study has been formally audited by the regulatory authority and the audit did not uncover any problems, in which case it should be safe to consider the study as of sufficient reliability to be used. If the audit reveals significant problems which impact on the reliability of the findings then the study should be rejected.

42. There may be other factors which provide sufficient confidence to allow the data to be used. These should be considered on a case by case basis. It is also recommended that the issue is not just whether to use or reject the results from an IBT study, as it is considered that the data from an IBT study could be used in different ways depending on the level of confidence attached to it. For instance, data in which there is relatively high confidence could be used as a key study, supporting for example the derivation of a NOAEL or other limit, whereas if there is less confidence in the data it may still be used but down-graded to just supporting or weak evidence (as is often the case for old studies conducted using non-standard protocols). Of course, whenever an IBT study is used the problems and issues raised and a judgement on the reliability of the study (using a reliability score as well as a reliability rationale) should be clearly articulated in the assessment.

43. For example, a study audited only by the study sponsor and not by post-hoc programme might be considered less than totally reliable (given the concerns expressed by EPA on the industry audits which led to the initiation of the post-hoc audit programme) and therefore would only be used as supporting evidence.

44. Another important consideration is the consistency of the findings from the IBT study with findings from other studies that were conducted at reputable test houses at a later date to the IBT study (to rule out the possibility of data being manipulated by IBT to be consistent with existing data). Clearly if the findings are consistent (e.g. the same pathological findings, same target organ, similar dose-response relationship etc) then this would increase confidence in the IBT data, especially if the study has also been adequately audited. Expert judgement is required on a case by case basis to judge how those data should be used, but they may potentially be very useful, reproducing findings in other studies (and hence increasing confidence in the characterisation of that toxic effect of the chemical), or to consolidate a complete picture of the toxicological profile of a chemical, for instance by giving dose-response information at doses not covered by other studies.

45. In cases where there are no other studies available with which to compare, it is unlikely that an IBT study which has not been audited/ validated could be considered to provide anything more than weak evidence. Depending on the programme this situation may lead to a conclusion that there are data requirements. Where there is no independent audit/validation and the IBT study findings are inconsistent with other data then the study should be rejected.

46 In the absence of any information on the reliability of environmental studies signed by IBT, a similar strategy to that described above for the use of such studies is proposed.

Summary

47. In brief the proposed approach (for studies conducted during the suspect period) is:

- When the study has been audited in the EPA / FDA post-hoc programme

- Use the study as normal if no problems have been highlighted
- If minor issues that do not invalidate the data have been highlighted then use the study with care as supporting data
- If the audit reveals significant problems which impact on the reliability of the findings then the study should be rejected

- When the study has been audited by Industry
  - Use the study but use expert judgement to consider the reliability of the findings, for instance by comparing with findings from other studies conducted at a later date in reputable testing facilities
  - If the audit reveals significant problems which impact on the reliability of the findings then the study should be rejected

- When the study has not been audited
  - If the findings are consistent with a study conducted at a later date the study may be used but should be considered as weak evidence
  - If the findings are inconsistent with other studies or there are no other data with which to compare, reject the study

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