

MOU Listing Criteria for Chemicals of Concern in Children's Products

Overview

Categories and criteria below are based upon models developed for alternative assessment and product certifications. The main source is the USEPA Safer Choice Master Criteria (https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf) which references various worldwide criteria for the listing of hazardous chemicals: e.g., EU CMR (carcinogen, mutagen, reproductive) listing, United Nations GHS (globally harmonized system) and for carcinogens IARC and NTP. We also refer to lists of carcinogens and reproductive hazards kept by California under Proposition 65.

Toxicity/Hazard Assessment

The various hazard properties a chemical may be tested for are listed below, along with toxicology criteria for judging whether a property represents a low, medium, high or very high level of concern. Where there are substantial datagaps which prevent ranking, a moderate level of concern is applied.

- 1) Persistence in body/environment: what is potential for chemical to be retained, have a long term body burden, be transferred to next generation via breast milk/placenta or be persistent in environment
 - No concern:
 - o body t_{1/2} -- < 12 hr (e.g., common solvents, modern pesticides, many pharmas);
 - o environmental: volatile (e.g., formaldehyde, benzene)
 - Low concern:
 - o body t_{1/2} -- 13 hr to 2 days (permethrin);
 - o environmental: semi-volatile, log Kow 1-2
 - Moderate concern:
 - o body t_{1/2} -- 3 days to 2 wk (TBBPA, deca-BDE);
 - o environmental: semi-volatile, log Kow 3-4
 - High concern:
 - o body t_{1/2} -- 2 wk – 2 months (e.g., mercury, lead)
 - o environmental: semi-volatile, log Kow > 4-5
 - Very high concern:
 - o body t_{1/2} -- > 2 months (PCBs, PFAS, dioxins, penta-BDE, HBCD)
 - o environmental: semi-volatile, log Kow > 5

- 2) Acute toxicity: potential for chemical to be immediately hazardous; more relevant for cleaning products, glues and other items a child may contact in concentrated form or large quantity.

Guidelines below are for oral route; guidance for other dose routes available at EPA Safer Choice website.

- No concern: no lethality in acute testing
 - Low concern: oral LD₅₀ > 2000 mg/kg (USEPA Safer Choice/GHS guidance)
 - Moderate concern: oral LD₅₀ 200 – 2000 mg/kg (e.g., malathion, other pesticides)
 - High Concern: LD₅₀ 10-200 mg/kg (e.g., parathion)
 - Very high concern: LD₅₀ <10 mg/kg (cyanide, sarin)
- 3) Repeat Dose Toxicity (Endocrine/Immunotox/Neurotox/Target Organs): potential for chemical to decrease function of a variety of systems or to damage organs from multiple days of dosing, usually at least 1 month. The cutpoints below are based upon 90 day studies, with higher cutpoints advised by USEPA Safer choice for shorter periods.
- No concern: no or minimal effects from 90 day to chronic study
 - Low concern: toxicity only at >100 mg/kg/d (USEPA/GHS)
 - Moderate concern: toxicity at 10- 100 mg/kg/d or severe effects at 100 to 1000 mg/kg/d
 - High concern: toxicity at <10 mg/kg/d or severe effects at < 100 mg/kg/d
 - Very high concern: toxicity <1 mg/kg/d or severe effects at < 10 mg/kg/d
- 4) Genotoxicity: this includes mutagenicity and clastogenicity, in vitro and in vivo test systems. These are largely predictive and mechanistic studies which can add to the weight of other endpoints (e.g., equivocal carcinogenicity) but are less important if other testing fails to show effects (no cancer or developmental effects). Genotoxic carcinogens are known to be more potent in early life (placental and 0-2 years postnatal) than adult.
- No concern: negative in mutagen and clastogen tests
 - Low concern: positive in sporadic testing, only at cytotoxic levels
 - Moderate concern: mixed results in genotoxicity testing (chloroform)
 - High concern: primarily positive results and/or listed as genotoxic on EU CMR list or GHS list (e.g. glyphosate, nitrosamines, benzo(a)pyrene)
 - Very high concern: positive in vitro results with evidence for genotoxicity in humans; listed as genotoxic as above.
- 5) Reproductive and Developmental Toxicity: highly relevant to early life windows of vulnerability, with relevance to some endocrine disruptor endpoints. Limited information on postnatal exposure provided in reproductive test.
- No concern: no reproductive or developmental effects in repro/devel studies
 - Low concern: toxic effect level > 250 mg/kg/d (USEPA/GHS) and not on EU CMR or Cal Prop 65 lists and no evidence of greater vulnerability of early life stage compared to adult
 - Moderate concern: toxic level 50 to 250 mg/kg/d and not listed as above; no evidence of greater early life vulnerability

- High concern: toxicity at 5 to 50 mg/kg/d or listed on EU or Cal lists or evidence for greater early life vulnerability
 - Very high concern: toxicity at < 5 mg/kg/d, listed as above and evidence for greater early life vulnerability.
- 6) Cancer: carcinogens can be more potent in early life than at older ages, especially mutagenic carcinogens.
- No concern: no positive tumor findings in animal or epi studies
 - Low concern: Equivocal evidence in at least one study, not listed by EU CMR, Cal Prop 65, NTP, EPA, IARC
 - Moderate concern: Clear evidence in at least one study, not listed as above
 - High concern: Clear evidence in multiple studies, listed on at least one list
 - Very high concern: chemical is also a mutagen or if there is substantial evidence in humans as well as animals.

Framework for Toxicology Criteria

A chemical's overall hazard characterization is low, medium or high based upon the highest ranking in any one toxicology category. Only chemicals with a high level of concern for toxic effects will be considered for MOU listing (i.e., it must have at least one toxic property that is of high concern).

To further prioritize these substances for MOU listing, a hazard ranking score will be developed which is the sum of all categories as follows:

- No concern =0 points
- Low concern =1 points
- Moderate concern =2 points
- High concern =3 points
- Very High concern = 4 points
- (NOTE: a very high for reproductive/developmental or carcinogens = 5).
- NOTE: toxicology areas where there is a substantial lack of data are given a moderate concern (2 point) score so as not to discount an endpoint on the basis of key datagap.

Maximum possible toxicology score = 25

Exposure Criteria

Exposure is judged based upon the likelihood for the chemical to be present in a children's product. This takes into account direct and indirect evidence with a risk-based quantitative consideration used to

further prioritize and rank chemicals. A final category is for chemicals which are not in products that are designed for children but to which children can receive frequent exposure due to direct contact or because they contribute to indoor air or house dust (e.g., air fresheners, couches, sun tan lotion).

1. Is there direct evidence that the chemical is currently in children's products
 - E.g., testing or reporting in databases such as that maintained by Washington State
 - (YES = 20 points, NO = 0 points)?
2. Is there indirect evidence that the chemical might be in children's products?
 - Chemical is widely used in commerce/other household products (2 points)
 - Chemical is not banned from children's products (2 points)
 - Chemical is found in house dust (2 points)
 - Chemical is found in indoor air (2 points)
 - Chemical is found in children's biomonitoring studies at levels > adults (2 points)
 - (Total up to 10 points but these point counts are used only if first question is "No" such that these auxiliary questions are the main evidence for children's exposure.)
3. Is the amount of chemical exposure in children within range of a health benchmark?
 - Screening risk evaluation to show order of magnitude estimate of exposure relative to a health benchmark from toxicity assessment (YES doubles response from #1 ie 2)
4. Is the chemical currently in products children frequently contact but not designed for children?
 - Qualitative support for overall score, no points

Summary of Framework for Exposure Criteria

For a chemical to be of high exposure concern and prioritized for MOU listing it must have a Yes answer to either Q#1 or Q#2. Highest priority is given to those chemicals which are Yes to Qs 1, 2 and 3. Given that product testing data are limited, indirect evidence may be helpful to support a finding of chemical presence in children's products. The quantitative approach in Q#3 will help to further prioritize chemicals based upon their levels in a child's environment. Yes answer to #1 is worth 20 points; if the answer to #1 is no, then a yes answer to #2 is worth up to 10 points with each subcategory of evidence adding 2 points. A yes answer to #3 doubles the total from #1 or #2. A yes answer to #4 does not add points but indicates an area of children's exposure that needs further examination.

Maximum Exposure Score = 40 points

Final Listing Criteria:

Chemicals must be of high toxicology concern (high ranking for at least one toxicology endpoint) and high exposure concern (yes answer to Q 1 or 2) to be considered for MOU listing. Further prioritization is accomplished by calculating the total rank score as follows:

Total Rank Score = Hazard Rank Score * Exposure Rank Score (maximum possible = 1000 points)

There is no cutoff for how high the total rank score must be for MOU listing of the chemical. Rather, the total rank score will be used to rank chemicals against each other and thus demonstrate which are the highest chemicals of concern to children from consumer products. The goal is to develop a short list of 3-5 chemicals at first, with the possibility of adding more later.

MOU Listing of Chemicals of Concern to Children

