A Tiered Approach for Assessing Children's Exposure

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Recently, intense attention has been given to children's health issues, particularly in the use of consumer products. Because of this attention, researchers have been planning and initiating studies specifically aimed at developing both toxicology data and exposure data directed to improve our understanding of industrial and consumer product chemical impacts on children's health. To ensure that this research is focused on the highest priority chemicals, we present a methodology for determining and prioritizing the higher hazard chemicals and scenarios for which children could be disproportionately or highly exposed. This tiered approach includes a screening step for initial chemical selection, a hazard assessment based on no- or lowest-observed-adverse-effect levels, and a margin of exposure (MOE) calculation. The initial chemical screen focuses on the chemical presence in specific media that are special to children, such as foods children regularly eat and drink, residential or school air, products children use, and soil and dust in and around residences. Data from the literature or from models serve as the initial exposure estimate. This methodology would allow us to focus on those chemicals to which children are most exposed that are also associated with, potentially, the highest risk. Use of the MOE calculation allows for comparison among chemicals, prioritization of chemicals for evaluation and testing, and identification of significant data gaps. *Key words*: assessment, chemical, children, exposure, exposure factors, health, margin of exposure, tiered. *Environ Health Perspect* 108:469–474 (2000). [Online 11 April 2000]

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There is a distinct need to further evaluate how and the extent to which children are exposed to chemicals. As compared to adults, children may be more exposed, less exposed, or exposed the same to a chemical. The differences are chemical- and situation-specific (*1*), but the literature regarding those differences with respect to chemical response is limited at present. There are substances and chemical classes for which the scientific literature contains relatively robust (but not yet definitive and complete) data for children's health impact, with lead (*2*) and pesticides (*3*) as examples. Although we know significant details about some substances and can build on that knowledge, there is a need to broaden and deepen our knowledge regarding both the exposures of children to chemicals and the effect of those chemicals on children of all developmental stages. At present, the list of potential substances to evaluate for exposure evaluation and toxicology testing is very long. Only a fraction of the chemicals in commerce have full data sets including reproductive and developmental toxicity testing. Hence, selecting the candidate substances for further testing is very important, both for maximizing the new knowledge yield and for the efficient use of testing resources.

We believe that all interested parties, i.e., regulators, industry, academia, the general public, and children, will benefit from an efficient process to *a*) identify the chemicals that result in exposure to children, *b*) analyze their risk, and *c*) target further action on them in a priority order. We propose a tiered assessment process to help achieve that identification and prioritization. In the initial tier, the available (and possibly limited) data would be used for a first level of prioritization. We believe that in general, high biologic activity (from basic toxicology testing) and potential high exposure present an appropriate start for the first level of prioritization for further testing by a battery designed to improve our understanding of potential adverse effects on children. This initial screen may assign an unduly high or low priority for a given chemical. However, we lack the detailed data regarding the chemical's hazard to children that would support a robust prioritization, and if the robust data were available, we perhaps would not need further data on that chemical.

By understanding the activities and physiology of children we can better classify children's exposure potential. That understanding will help support recommendations regarding hazard testing, other data needs, risk assessments, and risk management strategies. As the data set builds in rigor, subsequent selection may become more tailored to specific children's health protection needs.

A Tiered Approach

Chemicals that pose hazards to children based on potential high exposure or due to the unique sensitivity of children should be given higher priority for chemical industry attention. All potential chemicals that children are exposed to cannot be evaluated simultaneously. Exposure assessments are typically conducted in a stepwise (tiered) process. We suggest that a tiered approach is also appropriate for children's exposure, but specific differences of children must be considered in the process, to the extent information to do so is available. We recommend a three-stage tiered approach.

Tier 1: chemical selection. This initial tier would serve as a screen to select the first-pass priority chemicals for a margin of exposure (MOE) evaluation. The tier has exposure and hazard components. The exposure component includes five criteria in which chemicals are selected if they are present in or expected to be present in foods children regularly eat and drink, residential or school air, products children use, soil and dust in and around residences, or tissues of children. The hazard component, in which chemicals are selected if they have a moderate or high hazard based on their no-observed-adverse-effect levels (NOAEL) or lowest-observed-adverse-effect levels (LOAEL), is also considered within this tier and is described below. Both of these criteria should be met to move to the next tier.

Tier 2: initial MOE. This tier will calculate an initial (conservative) MOE using hazard data from tier 1 and default, or readily available, exposure concentration data. MOE comparisons are well known and used in risk characterizations. MOE concentrations are simply defined as MOE = NOAEL/exposure. If the MOE is high (> 1,000), the chemical is judged not to be present at sufficient levels, and no further action is required. If the MOE is low (< 100–1,000), then a chemical would move to the next tier.

Tier 3: refined MOE. Using more refined exposure data from modeling or more specific exposure assessments, this tier

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will recalculate the MOE. As noted previously, if the MOE is high (> 1,000), no further action is required. If the MOE is low (< 100–1,000), this MOE value can then be used to prioritize (on a relative scale) the chemicals for future study or risk reduction measures. Factors such as the fate and transport characteristics and the bioavailability of the chemical should be explicitly considered (to the extent possible) in determining the refined exposure.

Tiers 2 and 3 are crucial elements of this process and allow the user to move beyond mere "present in" selection criteria and to characterize the potential children's exposure relative to hazard. This tiered system results in a prioritized list of chemicals that are judged to be present at sufficient levels so that further data gathering or risk management action is warranted. We recognize that an MOE approach may overestimate potential hazard in some cases and underestimate it in others. Nevertheless, this approach will significantly enhance the likelihood that the chemicals that have the greatest potential to impact children's health (because of a combination of high toxicity and exposure) are identified. The approach also provides a simple process to easily reevaluate chemicals as new data become available.

Identifying Sufficient Levels of Exposure

When assessing possible health risks of chemicals to children, both the potential hazard and estimated exposure must be assessed. This requires the definition of "present at sufficient levels." The range of chemicals to evaluate, and the range of their potential hazards, precludes any fixed numeric criteria for exposure. Thus, the following criteria are intended for use in a relative manner for prioritization.

Recommended exposure criteria for assessing children's exposure. In light of the information regarding exposure potential, these criteria are designed to capture those chemicals that present a high or disproportionate exposure to children. As such, the criteria are very targeted. Sufficient data should be available to obtain this information in current databases and in the literature. When suitable measured exposure data are available in the literature, they may be the main basis for the assessment. In other cases, various modeling approaches may be followed, as described in the tiered process. For each of these criteria and for the aggregated exposure, the determined exposure should be compared to a hazard level.

Present at sufficient levels in foods children regularly eat and drink. This criterion combines data on intake rates (ingestion rates and types of food) and media concentrations. There are data to indicate that children tend to eat a less variable diet than adults and different foods than adults (*3,4*). As such, specific foods may be targeted for assessment. These include breast milk, formula, dairy products (milk and cheese), fruit juices, and others. Drinking water is also considered part of this category. An important requirement is that the concentration data collected be for food as eaten or prepared, not the raw material. Additionally, the concentration in food as eaten should be found in sufficient quantities that would cause a high exposure or disproportionate exposure to children.

Present at sufficient levels in the air children breathe, including residential or school air. Children spend a considerable amount of time indoors in home, school, or day-care environments. Also, children's indoor and outdoor activities are different from those of adults. Children spend more time on the floor or close to the ground, where air concentrations of chemicals could be higher. This factor, coupled with the slightly higher inhalation rate (per kilogram of body weight) for children, could result in highly or disproportionately greater exposure of children as compared to adults. However, such a case is likely to be true for only a limited number of chemicals. Presence in indoor air alone is not an adequate criterion because it is not linked to a sufficient level nor is it sufficiently selective. This criterion could be narrowed even further by evaluating the data and determining if certain chemicals have high concentrations in school or residential indoor air or if they are found in higher concentrations near the floor than in other parts of a room.

Present at sufficient levels in products children use and having physical–chemical properties that allow for transfer. This criterion includes those chemicals that are found at potentially significant levels on or in children's toys and other products used for children. The chemical must also have the ability to migrate from the product to the child under typical and reasonably severe use conditions. A chemical that is irreversibly bound to a toy or product should not be included because the exposure concentration during use of the toy is negligible and thus the exposure pathway for such a chemical is not complete.

A chemical's migration potential may be considered qualitatively by assessing its physical–chemical properties or may be considered quantitatively using migration studies or models. The result of the assessment would be an exposed concentration as compared to the source concentration.

Present at sufficient levels in soil and dust in and around residences. A potential exposure pathway for young children is ingestion of soil or dust either directly or incidentally (mouthing of dirt or dust-covered hands or toys) and inhalation of chemicals volatilizing from floor dust or soil. This activity is not typically associated with adults or older children but is designed to capture an area that could provide disproportionate exposure to smaller children. Consideration of a chemical's fate and transport properties will assist in determining if volatilization is likely. For chemicals adhered to soil, the bioavailability or dermal absorption factor should be included when calculating exposed concentration.

Present at sufficient levels in the tissues of children. This criterion captures those chemicals that are found in measurable quantities in blood, urine, and tissues of children. These biomarkers of exposure do not necessarily indicate a hazard, but may highlight chemicals or chemical precursors that require additional attention. By following and tracking the research at such organizations as the Centers for Disease Control and Prevention (Atlanta, GA) and the Agency for Toxic Substances and Disease Registry (Atlanta, GA), new biomarkers of exposure can be considered.

Establishing the MOE

Minimal toxicology data must exist on a chemical to determine its potential hazard. For example, data from acute, subacute, subchronic, and mutagenicity studies could be used to determine hazard potential for the initial prioritization. Chemicals that demonstrate moderate to high hazard potential in these studies would proceed to the next level. Values for moderate to high hazard potential are well established within the scientific and regulatory toxicology community [e.g., the detailed descriptions used under the European Union Labeling Guidelines (*5*)].

In assessing hazard, NOAELs or LOAELs from acute, subacute, and subchronic studies should be used as a starting point. As mentioned, there may be difficulties arising from this process because of a shortage of toxicology data that specifically address children's-health-relevant end points. However, for relative prioritization, and until more relevant test data become available, we suggest this NOAEL/LOAEL approach. If supporting data exist, different NOAELs or LOAELs could be established for the pertinent developmental stages. We believe that these hazard values (based on the most relevant available studies) should be used rather than U.S. Environmental Protection Agency (EPA) or state-established reference dose (RfD) or reference concentration (RfC) values.

EPA RfD/RfCs have been developed for roughly 500 chemicals. They may represent a fairly well characterized subset of chemicals,

where data supported RfC or RfD development. However, this is a small proportion of chemicals to which children could be possibly exposed. Reliance on RfD or RfC values as a hazard indicator may inappropriately focus on these chemicals, ignoring potential hazards to children from other chemicals. More chemical-specific NOAELs/LOAELs exist than RfD/RfC values, and they are readily identified from available studies. As more chemicals are tested as part of testing initiatives [i.e., the EPA high-production-volume chemicals testing program (*6*)], these values will be readily available, possibly more quickly than new RfCs or RfDs. Using NOAELs/LOAELs from these emerging studies will allow us to quickly assess a potential hazard to children. Finally, RfD/RfC values incorporate uncertainty factors to account for potential differences in susceptibility in extrapolating animal results to predict potential adult human risk. It is unclear if these uncertainty factors will be sufficient or appropriate for extrapolating animal results to potential risks to children.

Refining the Assessment of Exposure to Children

The EPA *Guidelines for Exposure Assessment* (*7*) provide all of the basic approaches needed to assess exposures, including those of children. However, there are specific aspects about a child's physiology and activities that allow for unique exposure patterns. This means that the EPA guidance needs to be supplemented by: *a*) further commentary and information on the application of the approaches to children; *b*) specific data relevant to children, such as age-specific exposure factors; and *c*) delineation of relevant exposure scenarios for children. Research is ongoing in many of these areas. When this information is available or can be developed, the exposure assessment can be refined. The exposure assessment refinement will be needed at some point in the process of risk assessment. The refinement could be conducted either before or after the development of additional toxicology data. We propose that refined assessments be conducted as part of the final prioritization process of chemicals to be subject to additional toxicology testing.

The EPA guidelines suggest three approaches for quantifying exposure: *a*) the exposure can be measured at the point of contact while it is taking place; *b*) the exposure can be estimated by performing a scenario evaluation, which separately evaluates concentration and the contact variables (time, rate, and receptor); or *c*) the exposure can be reconstructed using biomarkers of exposure to estimate external dose.

All three approaches are useful in understanding and refining assessments of exposure to children. Good science requires that the methods and data of an exposure assessment clearly support the conclusion within known or stated bounds. The American Industrial Health Council *Exposure Factors Sourcebook* (*8*) provides an overview of good exposure assessment practice. This practice includes methods for properly developing an exposure assessment plan. Hawkins et al. (*9*) present a method for ensuring consistency and quality in an exposure assessment, and most importantly, one whose results will satisfy the study objective.

Delineating age ranges. Children's activities and physiologic status change substantially from birth to maturity. By also understanding a material's uses, and by understanding age-specific activity patterns, we can gain an improved understanding of the potential for exposure. This will lead to a more appropriate screening of materials with potential age-specific and activity-specific elevated exposure. Many published sources provide children's specific exposure factors, and more continue to appear (*3,4,10–29*). Table 1 presents a general listing of age brackets and activities relevant to the age category that could impact exposure. A combination of physiologic maturity and developmental behavioral patterns are involved in susceptibility and exposure. We suggest the Table 1 age brackets as suitable surrogates for physiologic maturity and age-related patterns.

For persistent environmental contaminants, it may be appropriate for the exposure assessment to cross several or all age brackets. This would be needed if the chemical body burden rose as the child aged because of a long biologic half-life. There should be an understanding about the half-life in relevant age brackets because metabolic and physiologic differences may impact the half-life of a chemical in children.

Additionally, sensitivity to a specific agent may vary with physiologic maturity stages. This will also determine what age brackets are important for the exposure and risk assessment process. Growth rates are greatest at infancy and puberty, but factors other than growth rate may be important. The National Research Council (*3*) mentioned puberty as a potentially sensitive period for agents that would interfere with normal reproductive system maturation. For general use, we suggest a breakdown that would split out toddlers from young children (Table 1). However, either finer breakdown or further lumping together may be appropriate depending on the chemical use scenario to be assessed. In summary, children should not be treated as one group, and differences in physiology and activity patterns should be considered whenever possible.

Determining complete exposure pathways. Good exposure assessment practice integrates complete exposure via all relevant media and all relevant pathways (*30*). However, for the best use of available resources, it is most important to focus on those pathways that lead to high or incrementally greater exposure in children. Not all pathways will lead to high or disproportionate exposure for all materials. The characterization of important pathways should be tailored to the particular use circumstances.

The first stage is to determine the relevant pathways. Next, those pathways should be carefully characterized. This characterization should consider such factors as *a*) transport/degradation/fate before reaching the target age group, *b*) bioavailability via the pathway and media, *c*) uptake and elimination of the bioavailable fraction, and *d*) direct and indirect transport and exposure pathways.

For dermal exposure to a contaminant in soil, the EPA guidelines for exposure assessment (*7*) consider adjustments for soil adherence, bioavailability, dermal permeation, absorption, etc.

In addition to the dermal pathways, other pathways should be evaluated for completeness. For example, a chemical that is present in a child's toy does not necessarily mean that the child is exposed, even if mouthing or teething occurs. There needs to be a mechanism for transport from the source (toy or product) to the receptor (child). This is necessary for all pathways and all media. Consideration of factors such as migration potential, bioavailability, and actual use patterns will help determine if an exposure pathway is truly complete.

Inclusion of likely misuse scenarios. Children in younger age brackets have neither the ability to understand nor the judgment to follow use instructions on consumer products, which is why many products—including all pesticides—are labeled "keep out of reach of children." Accidental misuses of home medications or cleaning products are well-known examples of children's home safety issues. Childproof and child-resistant closures on many products emerged as a means to reduce the potential for misuse by children. Accidental ingestion is an extreme case of potential misuse. There is a need to evaluate likely and less severe misuses of products either by children or by adults. For example, a hard surface cleaner for the consumer market has a presumed application frequency and rate, possibly once a day for counter tops in kitchens and bathrooms. The exposure evaluation could consider a potential misuse involving more frequent/more extensive use or heavier application rates, such as daily use to clean an entire nursery's tile floor. This would then possibly affect the

dermal exposure potential of an infant playing on that hard surface soon afterward, or could impact the air concentration portion of the exposure assessment. Although such a misuse scenario could indicate elevated exposure, comparison to the NOAEL and calculation of the MOE would be required before deciding if this potential elevation reaches a significant level.

Level of detection. There is a need to specifically address how nondetection should be handled when assessing large data sets of measured concentrations. If an existing data set is used, it must satisfy data quality objectives (DQOs) specific to the use of the data. The data set should be relevant and adequate to supply the precision needed for the intended use (*7*). Often, the most problematic issue is that available data were generated using a level of detection not low enough for the intended use. The level of detection in this analysis should be lower than the hazard level described previously. If the level of detection is higher than the hazard level, assumptions should be made regarding the actual concentration in the samples (e.g., one-half the detection limit) or additional data obtained with a lower detection limit.

Fate and transport. Detection of a chemical in measurable quantities in soil, food, or consumer products does not necessarily indicate that a child is exposed to that chemical. For an exposure pathway to be complete, there needs to be a mechanism for migration of the chemical from the medium to the child. Ingestion is an obvious mechanism. However, for other exposure pathways, the transfer may have other complexities. Aspects such as bioavailability of the chemical once inside the body are important to consider but are not explicitly addressed here. This paper deals primarily with exposure potential, which is characterized as the amount of a chemical at the environment/body interface.

A chemical's physical–chemical properties can be used to predict the ease of transfer from one medium to another. Chemicals with high vapor pressures and Henry's Law constants are more likely to migrate to air than to any other media. Chemicals with high octanol–water partition coefficients are likely to bind readily (and perhaps irreversibly) to organic matter in soils and lipids in foods. For chemicals of this type, ingestion and perhaps dermal exposure will play a role. Often, only one or two exposure pathways will drive a risk assessment. Consideration of physical–chemical properties will focus the assessor on the most important pathways, resulting in a more cost effective, yet still adequately protective, analysis.

Other exposure pathways are not as passive as dermal absorption. For example, assessment of chemical migration from a child's toy during mouthing and teething requires consideration of the extra energy in the system and the transfer media (saliva). These active scenarios could lead to higher estimates of migration as compared to a slow diffusion into quiescent liquids. This would result in a higher exposed concentration in the active scenario than in the passive one. It is also possible that no plausible amount of extra energy could remove the chemical from the original matrix. In that case, the exposed concentration would be zero.

For chemicals found in food, there is a need to identify changes in chemical concentration that occur during food preparation. The National Research Council (*3*) notes that the highly processed foods that dominate infant and toddler diets are generally greatly reduced in pesticide residues. The preparation process may remove certain contaminants or free others. Also, higher concentrations may be found in food parts not typically eaten, e.g., shells, rinds, etc. Thus, it is important to consider chemical concentrations in foods as used, not as produced or as initially applied.

Modeling alternatives. In the absence of good measured data, which are preferable, mathematical models can be used to quantify the migration potential of a chemical. There are models for evaluating the migration of chemicals in soils and groundwater to indoor air, drinking water wells, and ambient air. Models are also useful in assessing

Table 1. Summary of exposure aspects typically relevant to particular age brackets.

	Age brackets				
Activity, factor	0–6 months[a]	6 months–2 years[b]	2–5 years	5–12 years	13+ years
Inhalation					
Indoor environment					
Home[c]	✓	✓	✓	✓	✓
Day care	✓	✓	✓	–	–
School	–	–	–	✓	✓
Recreational	?	✓	✓	✓	✓
Workplace	–	–	–	–	✓
Other					
Transportation[d]	✓	✓	✓	✓	✓
Outdoor	✓	✓	✓	✓	✓
Parental/sibling secondary (indirect) exposure[e]	✓	✓	✓	✓	?
Ingestion					
Breast milk	✓	✓	–	–	–
Formula	✓	✓	?	–	–
Foods	✓	✓	✓	✓	✓
Water and beverages	✓	✓	✓	✓	✓
Bath water[f]	✓	✓	✓	–	–
Pica	✓	✓	?	–	–
Dental preparations[g]	?	✓	✓	?	–
Oral exploration/ingestion					
Fingers/hands/toes[h]	✓	✓	✓	–	–
Toys[i]	✓	✓	✓	–	–
Surfaces[j]	✓	✓	✓	–	–
Dermal contact					
Indoor surfaces[k]	✓	✓	✓	✓	✓
Outdoor surfaces[l]	✓	✓	✓	✓	✓
Abrasions[m]	✓	✓	✓	✓	✓
Indirect: pets[n]	✓	✓	✓	✓	✓
Miscellaneous[o]	✓	✓	✓	✓	✓
Clothing/fabric treatments/residues	✓	✓	✓	✓	✓
Child-care products					
Shampoos/soaps	✓	✓	✓	✓	✓
Skin preparations	✓	✓	✓	✓	✓
Medications	✓	✓	✓	✓	✓
Excreta contact[p]	✓	✓	–	–	–

[a]Up to extensive crawling age. [b]Because of oral exploration, crawling (frequency/extent of skin exposure), and relative food/water/air consumption rates, this age bracket (toddlers) may often present the highest of the children's total exposure potentials. [c]Room-use pattern, duration spent in home, or proximity to specific sources. [d]Time spent in transportation environment. [e]Extent, frequency of close contact, materials desorbed from clothing or in exhaled breath, or in proximity to other's product use. [f]Incidental ingestion greater than school age and older. Surfactants may enhance bioavailability. [g]Younger ages more ingestion than for older ages. [h]Transfer from surfaces, etc. [i]As transfer agents for contaminants on carpet, bedclothes, or other surfaces. Toys may also act as solid-phase extraction media for some low-volatility chemicals. [j]Crib rails, tables, counters, or floors/carpets. [k]Crib surfaces, tables, counters, or floors/carpets. [l]Soil, lawns, or other vegetation. [m]May lead to enhanced uptake in some conditions. [n]Children may have longer/closer contact than adults and a greater extent of dermal and hand to mouth transfer (flea control agents, lawn care products, carpet treatments, etc.). [o]Art/craft supplies, toys, or clothing/fabric treatments/residues. [p]Excreta may contain parent compound or relevant metabolites, and contribute primarily via dermal uptake (note dermal layer may be episodically nonintact), with occasional prolonged contact.

indoor air concentrations from consumer products. Often the models are packaged as stand-alone computer programs; other times they are mathematical representations solved with spreadsheet calculations. Table 2 provides a summary of some modeling tools useful in estimating exposure concentrations from different media.

Sources of data and methods for exposure assessment. If an existing data set is to be used for an exposure assessment, the data set should be evaluated to ensure that it is relevant and adequate to support the requirements of the assessment (*4*). In short, the evaluation should consider the relevance of the data set, the adequacy of the data, any data gaps, combinations of exposure, and the iterative approach.

The U.S. EPA (*7*) states that when making inferences from a data set, the assessor must establish a clear link between the data and the inference. (The inference is a generalization that goes beyond the data contained in the original data set.) Factors to consider when determining relevance include the time period of the original data collection, the analytical techniques, and the detection limits used (e.g., do they satisfy DQOs?), and the population sampled.

The number of samples and the accuracy of the data will determine if the data set is adequate for the intended assessment. This is determined by evaluating the analytical methods used, the analytical data reports, any censored data sets, and data for blank samples.

In many cases, the use of an existing data set will result in the identification of data gaps. The EPA (*7*) recommends the following approaches (used singly or in combination) to support the existing data: new data can be collected; the scope of the assessment can be narrowed; conservative assumptions can be used; models can be used to estimate values and characterize uncertainty; or surrogate data may be used.

For chemicals that affect the same target organs and have the same mode of action, it may be useful to perform a cumulative exposure assessment that considers multiple chemicals and multiple routes of exposure. Consideration of pharmacokinetic interactions (such as receptor binding and competition) when data are available will result in a more accurate assessment of target organ dose. For single chemical assessments, aggregating the exposure over time and location is appropriate.

MOE analyses should include an iterative (stepwise) process. This provides an efficient use of information and resources. First, an initial (conservative) MOE should be calculated using readily available hazard data and default or readily available exposure concentration data. If the MOE is high, no further action is required. If the MOE is low, the MOE should be refined using data from more specific exposure assessments or modeling.

Conclusion

To maximize the efficiency of exposure assessments and generate data that are needed and applicable to children's health, criteria for chemical selection should not be overly inclusive. We suggest that a tiered assessment for prioritization will help achieve the most valuable information in the most effective manner. We recommend the following criteria regarding children's exposure:

- present at sufficient levels in foods children regularly eat and drink
- present at sufficient levels in residential or school air
- present at sufficient levels in products children use and having physical–chemical properties that allow for transfer
- present at sufficient levels in soil and dust in and around residences
- present at sufficient levels in tissues of children.

In combination with an MOE approach and using the most relevant available toxicology data, priorities for further assessment (exposure and/or toxicology) can be established and appropriate risk management actions taken.

Table 2. Examples of possibly useful exposure models.

Model name	Author/sponsor	Summary
AMEM (Arthur D. Little Migration Estimation Model) (*31*)	U.S. EPA, A.D. Little	Estimates monomer migration from a polymer
API DSS (American Petroleum Institute Decision Support System) (*32*)	American Petroleum Institute	Estimates chemical migration from soil and groundwater
ASTM risk-based corrective action and materials (*33,34*)	American Society for Testing and Materials	Set of equations to estimate leaching potential and volatilization potential of chemicals in soil
CALTOX (*35*)	California EPA	Multimedia model to estimate direct and indirect exposure via many pathways
CONSEXPO (*36*)	Dutch National Institute of Public Health and Environmental Protection, The Netherlands	Consumer exposure model for inhalation, ingestion, and dermal pathways
Dermal (*37*)	U.S. EPA	Estimates dermal penetration
MCCEM (*38*)	U.S. EPA	Indoor air models
SCIES (Screening Consumer Inhalation Exposure Software) (*39*)	U.S. EPA	Estimates indoor air concentration from consumer products
THERdbASE (Total Human Exposure Risk database and Advanced Simulation Environment) (*40*)	U.S. EPA	Multipathway multimedia model and database

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