Organisation for Economic Co-operation and Development

ENV/JM/MONO(2019)29

Unclassified **English - Or. English**

6 September 2019

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

CONSIDERATIONS WHEN ASSESSING CHILDREN'S EXPOSURE TO CHEMICALS FROM PRODUCTS

Series on Testing and Assessment
No. 310

JT03450673

SERIES ON TESTING AND ASSESSMENT

NO. 310

CONSIDERATIONS WHEN ASSESSING CHILDREN'S EXPOSURE TO CHEMICALS FROM PRODUCTS

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

Environment Directorate
ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT
Paris 2019

About the OECD

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 36 industrialised countries in North and South America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several countries with special status at the OECD, and from interested international organisations, attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

The Environment, Health and Safety Division publishes free-of-charge documents in eleven different series: **Testing and Assessment**; **Good Laboratory Practice and Compliance Monitoring**; **Pesticides**; **Biocides**; **Risk Management**; **Harmonisation of Regulatory Oversight in Biotechnology**; **Safety of Novel Foods and Feeds; Chemical Accidents; Pollutant Release and Transfer Registers; Emission Scenario Documents;** and **Safety of Manufactured Nanomaterials.** More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (www.oecd.org/chemicalsafety/).

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

This publication is available electronically, at no charge.

Also published in the Testing and Assessment link

For this and many other Environment, Health and Safety publications, consult the OECD's World Wide Web site (www.oecd.org/chemicalsafety/)

or contact:

OECD Environment Directorate,
Environment, Health and Safety Division
2 rue André-Pascal
75775 Paris Cedex 16
France

Fax: (33-1) 44 30 61 80

E-mail: ehscont@oecd.org

OECD Environment, Health and Safety Publications

Foreword

Children exhibit specific habits and practices that may result in exposure scenarios not considered for other population groups. In addition, there are physiological differences between children and adults, affecting the exposure assessment methodologies. Presently, there is often no structured and harmonised approach for determining when to include a separate children's exposure assessment within risk assessments for chemicals in products.

A survey conducted by the OECD's Working Party on Exposure Assessment (WPEA, formerly Task Force on Exposure Assessment (TFEA)) in 2011 showed a gap in exposure assessment methodologies aimed at children [ENV/JM/MONO(2013)20] (OECD, 2013[1]). Specifically, the survey revealed the need of risk assessors for a general and harmonised approach to aid the decision whether to include a risk assessment for children, as well as the need to identify specific exposure factors or situations accounting for the difference between children and adults, and this called for a set of specific default values for exposure scenarios relevant to children.

Subsequently, the TFEA held a Workshop on Children's Exposure to Chemicals in 2013 in Utrecht, the Netherlands, with the primary aim to make recommendations on when a child-specific exposure assessment needs to be performed [ENV/JM/MONO(2014)29] (OECD, 2014[2]). The second aim of this Workshop consisted of eliminating scenarios for some product groups that are not relevant for children. A reason for elimination can be that children do not use, or are not exposed to specific products or articles. However, it is also possible that the exposure assessment for adults already covers the exposure/risk for children. The third aim of the Workshop was to make progress on additional guidance or tools for assessing the risks of chemicals to children's health.

As a result of the workshop, experts developed a children's exposure decision tree to guide the risk assessor in determining whether a separate assessment for children is necessary, although further modifications would be needed following the investigation of a number of case studies. The decision tree was further adjusted based on the input at the 6th TFEA meeting in 2014 in Tokyo, Japan.

The sub-group, led by the Netherlands and composed of members representing Australia, Canada, Denmark, France, Germany, Italy, Japan, Sweden, the US and the Business and Industry Advisory Committee to the OECD (BIAC), was formed to further revise and finalise the decision tree. This document was produced mainly on the basis of the case studies conducted by the National Institute for Public Health and the Environment (RIVM) of the Netherlands, and input from other sub-group members. The drafting of this document was supported by valuable comments by the WPEA and Working Group on Pesticides.

This document was prepared under the supervision of the WPEA and published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology of the OECD.

Table of contents

Tables

Figures

Abbreviations and acronyms

ADME	Absorption, Distribution, Metabolism and Excretion
AS	Active Substance
BPA	Bisphenol A
CEN	European Committee for Standardization
DEHP	Diethylhexylphthalate
EC	European Commission
ECHA	European Chemicals Agency
E-FAST	Exposure and Fate Assessment Screening Tool
EFSA	European Food Safety Authority
EU	European Union
HEEG	Human Exposure Expert Group
MCPA	2-methyl-4-chlorophenoxyacetic acid
MoE	Margin of Exposure
MoS	Margin of Safety
NOAEL	No-Observed Adverse Effect Level
PBDEs	Polybrominated diphenyl ethers
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RCR	Risk Characterisation Ratio
RIVM	National Institute for Public Health and the Environment
SVOC	Semi-Volatile Organic Compounds
SCCS	Scientific Committee on Consumer Safety
SOPs	Standard Operating Procedures
US EPA	United States Environmental Protection Agency
VOC	Volatile Organic Compounds
WHO	World Health Organization

Executive Summary

This document aims to enhance awareness for inclusion of children's exposure in risk assessments when relevant and presents a children's exposure decision tree that facilitates such decisions. The decision tree can be used to identify if a separate exposure assessment is needed with regard to children, and also aims to identify whether the exposure assessment conducted for adults already provides an acceptable level of safety of children.

The focus of this document is on 'industrial chemicals', and targeted at 'consumer products'. However, other types of products may also be covered, as such definitions can differ between countries. The key point of the document is to create awareness on child-specific exposure. It is important to realise that legislations can also differ between countries, including existing requirements on whether to perform child-specific exposure and risk assessments. Exposure via food or the environment is regarded as background exposure in this document.

The functionality of the decision tree is to raise awareness of children's exposure to chemicals from products as well as to identify differences between adults' and children's exposure estimates illustrated by three case studies. The decision tree may be helpful in initiating the development of a guidance on how to perform a child-specific exposure assessment.

1. Introduction

1.1. Background and Objectives

Humans of every age can be exposed to chemicals from products through different routes (i.e. orally, dermally or via inhalation). To assess the risk of these substances it is essential to estimate the level of exposure. Therefore, in addition to physicochemical and hazard information on the substance concerned, the magnitude, duration and frequency of exposure, along with the characteristics of the exposed individual are required (Cohen Hubal, Moya and Selevan, 2008[3]; van Engelen and Prud'homme de Lodder, 2007[4]; Wolterink, Van Engelen and Van Raaij, 2007[5]). Special attention in this respect needs to be given to the differences in exposure profiles between adults and children (Armstrong et al., 2000[6]; Cohen Hubal et al., 2000[7]; Samet, 2004[8]). In addition to physiological differences which affect the characteristics of the exposed individual, habits and practices of infants and children significantly differ from those of adults, for example mouthing and crawling behaviour (ter Burg, Bremmer and Van Engelen, 2007[9]; Tulve et al., 2002[10]; Xue et al., 2010[11]). These differences can result in enhanced exposure to toxic substances as compared to adults and thus emphasise the need to take children into account when performing an exposure assessment.

Specific factors or characteristics influencing children's exposure need to be taken into account when performing a risk assessment (Cohen Hubal et al., 2000[7]; Armstrong et al., 2002[12]; WHO, 2011[13]). There is a gap regarding exposure assessment methodologies aimed specifically at children, and a need of risk assessors for a general and harmonised approach to aid the risk assessment for children, and to identify specific exposure factors or situations accounting for the difference between children and adults [ENV/JM/MONO(2013)20]. Such an approach should be helpful to decide whether a child-specific exposure assessment needs to be performed, or to eliminate scenarios for some products that are not relevant for children. A reason for elimination can be that children do not use these products, or indirect exposure to chemicals from these products is highly unlikely to occur. It is also possible that the exposure assessment for adults already covers the exposure for children. The decision tree in this document can be helpful for deciding when the inclusion of a child-specific exposure or risk assessment is warranted.

This document aims to create awareness of child-specific exposure to chemicals in products. This attention is not new (Chance and Harmsen, 1998[14]; Armstrong et al., 2000[6]; Wolterink, Piersma and van Engelen, 2002[15]), but children's specific characteristics in relation to exposure assessment are still overlooked in many risk assessment procedures (Chance and Harmsen, 1998[14]; Tyshenko et al., 2007[16]; OECD, 2013[1]). The decision tree can be used as a practical guidance to decide whether a separate exposure assessment for children is needed. It draws the attention to both physiological and behavioural differences in specific exposure scenarios where those are relevant.

1.2. Sources of Exposure of Relevance

The focus of this document is on 'industrial chemicals', and targeted at 'consumer products'. However, as the definitions of interpretation of such terms can differ between countries, this focus is not very strict. In addition, the key point of the document is raising awareness on child-specific exposure, which goes beyond the boundaries between specific product-related (regulatory) categories. It is important to realise that legislations can also differ between countries, and that requirements on whether to perform child-specific exposure studies may already exist. Needless to say, the decision tree is not to be used in order to raise awareness in those cases. This document also presents cases for illustration purposes, including secondary exposure to a herbicide, which is a plant protection product. For such product-specific regulations, children exposure is often already being assessed (but therefore these are valuable examples to illustrate differences between adults and children with respect to exposure in a regulatory setting). Therefore, the focus of this document is on exposure to chemicals from products which can be (economically) consumed, i.e. which are potentially present in the everyday life of children. There are other additional sources as well via which children can be exposed to chemicals, and which can be very child-specific, too. These include exposure via food (e.g. mother milk, specific dietary habits) or via the environment (e.g. eating contaminated soil). As an example, infant exposure to dioxin-like chemicals can be much higher because of the consumption of mother's milk (Lorber and Phillips, 2002[17]). Another example is the exposure to lead, which is strongly absorbed by soil and can be ingested by children during child-specific hand-to-mouth behaviour, while adult exposure via this route is considered less relevant (Landrigan and Garg, 2002[18]). However, with the focus on 'industrial chemicals' targeted at 'consumer products', exposure via food and environment are regarded as background exposure in this document.

1.3. Definition of a "Child"

The term "child" refers to human from the entire period upon birth and until adulthood. As this definition depends on the definition of age of majority, which differs largely throughout countries and cultures (from 15 years up to 21 years), this document uses the World Health Organization (WHO) definition of a child (up to 21 years of age), with the sub-classification according to the WHO classification which classifies a neonate as less than 1 month of age, an infant as 1 month to 1 year, a toddler as 1 to 2 years, early childhood as 2 to 6 years, middle childhood as 6 to 11 years, early adolescence as 11 to 16 years, and late adolescence as 16 to 21 years (Cohen Hubal et al., 2014[19]). Depending upon the objectives of the risk assessment, and the framework and program under which the exposure assessment is developed, countries may use different approaches for evaluating children's exposure and resulting risk, and may use specific age groupings in assessing exposure. It is important to realise that for some countries, the unborn child or prenatal period is assumed to be protected within the risk assessment for the adult/general population, while other countries may develop specific assessments addressing in utero exposure, as appropriate. In this document, however, no earlier life stages than the neonatal stage, nor pregnant women are concerned where "child-specific" is meant.

1.4. Physiological Characteristics

Differences in physiology of children compared to adults can affect the exposure, such as a higher body surface to body weight ratio, a relatively bigger head, and a higher breathing rate and air intake, as well as a relatively higher intake of water and calories (on body weight basis). Additional to these differences, there are also physiological differences in toxicokinetics further affecting internal exposure. Difference in Absorption, Distribution, Metabolism and Excretion (ADME) characteristics can occur because of e.g. an increased dermal permeability, a higher gastric pH, different digestive enzymes and bacterial flora, and differences in metabolizing enzymes (Bearer, 1995[20]; Chance and Harmsen, 1998[14]; Cohen Hubal et al., 2000[7]; Cresteil, 1998[21]; Felter et al., 2015[22]; Narciso et al., 2017[23]; Wolterink, Piersma and van Engelen, 2002[15]). Such factors could considerably affect the internal exposure to and the effects of a certain chemical. Furthermore, the effect of the exposure may be different because of differences in toxicodynamics, e.g. an immune system with higher level of tissue proliferation and differentiation, and not yet fully developed organs such as brain, liver and kidney (Hayashi, 2009[24]). This is also relevant where comparisons of Margin of Safety (MoS) values are being made in order to decide whether the MoS for adult exposure is protective enough for children. Although all these factors are highly relevant for a risk assessment, the physiological factors in this document are limited to children specific differences affecting exposure assessment calculations, such as breathing volume per day (Arcus-Arth and Blaisdell, 2007[25]), body weight or body surface to body weight ratio. For instance, where air concentrations of a certain chemical are concerned, it is important to realise that often no correlation for body weight is made, which leads to an underestimation of the internal exposure of children compared to adults. As this document is only focused on exposure assessment, specific differences in toxicokinetics and toxicodynamics are not addressed in this document. Such differences are beyond the focus of the decision tree which is to be regarded as a first tier for child-specific exposure assessment.

1.5. Behavioural Characteristics

In addition to physiological differences, differences in behaviour of children compared to adults can affect their exposure (Moya, Bearer and Etzel, 2004[26]). Each age group has its own physiological and behavioural characteristics, which can be relevant for the exposure assessment (Firestone et al., 2007[27]; Neal-Kluever et al., 2014[28]). For example, small children have high hand-to-mouth activities and grow rapidly. Compared to adults, children are much more likely to engage in mouthing behaviour, which is defined as behaviour including all activities in which objects, including fingers, are touched by the mouth or put into the mouth except for eating and drinking, and includes licking, sucking, chewing and biting (Groot, Lekkerkerk and Steenbekkers, 1998[29]). Especially children less than 2 years of age show much higher frequencies of mouthing (Tulve et al., 2002[10]). A distinction between hand- and object-to-mouth contacts can be made (CEN, 2015[30]; ter Burg, Bremmer and Van Engelen, 2007[9]; Xue et al., 2007[31]; Xue et al., 2010[11]). OECD (2019[32]) provides key considerations and good practices for addressing potential risk from direct object mouthing [ENV/JM/MONO(2019)24]. Because of mouthing, children can be exposed orally to chemicals to which adults only are exposed dermally, and therefore child-specific exposure assessment may include an additional oral route of exposure.

Furthermore, children often spend more time indoors, and live closer to the ground, i.e. breathe and play close to the floor, especially children that cannot walk yet. This may result in specific exposure scenarios, e.g. dermal and respiratory exposure to chemicals from products, including house dust, present on the floor whereupon infants crawl (Ferguson, Penney and Solo-Gabriele, 2017[33]; Roberts and Dickey, 1995[34]). This child-specific behaviour could lead to relevant, increased and/or additional exposure for children. At adolescence ages, factors such as smoking, high use of make-up and personal care products, or different environments can lead to changed exposures (Cohen Hubal et al., 2014[19]).

2. Decision Tree

The decision tree (Figure 1) is presented as a flow chart containing questions concerning exposure assessment that will lead to an answer if a separate children's exposure assessment should be conducted. Background information for each step is provided below. In case of uncertainty whether "Yes" or "No" is to be answered (i.e. unknown), "Yes" will be a safe option, i.e. when it does not reflect the actual situation it will be the conservative choice, leading to an outcome in which an exposure assessment for children has to be performed.

2.1. Question 0 (Q0): What is the objective of the risk assessment, what is the framework?

At a starting point for applying the decision tree (Figure 1), the objective of the risk assessment has to be considered because the decisions and assumptions in the risk assessment depend heavily on the objective. Examples of different objectives are:

- a preventive risk assessment for one substance in one single product; or
- a substance within a legal framework such as Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), the European Cosmetics Directive or the Canadian Environmental Protection Act (1999)[1] as part of the Chemicals Management Plan.

2.2. Question 1 (Q1): Is this product intended for use by consumers?

The purpose of this question is to separate the exposure to industrial chemicals via consumer products from occupational exposure. If a product is not intended for use by consumers, it is unlikely (i.e. assuming young children are not present at an occupational setting) that (young) children will be primarily exposed to chemicals from these products.

2.3. Question 1a (Q1a): Could consumers come into contact with this product?

Although a product might not be intended for use by consumers, secondary exposure can still occur and a separate children exposure assessment can still be needed. Examples are a plant protection product for professional use and children residing closely to the field of application and coming into contact with the spray drift, or the use of a professional cleaning agent in a school, day-care or hospital. If the public cannot come into contact with a product because of reasons such as that it is an intermediate during production or will be incorporated into another product, it is expected that this product only leads to exposure at the workplace, and in general no consumer exposure assessment is needed. Additionally, one could ask whether the exposure at an occupational setting would result in exposure of

[1] https://laws-lois.justice.gc.ca/eng/acts/C-15.31/section-93.html

children via breathing air, drinking water, playing in soil or with dust contaminated with a chemical; however these environmental sources are regarded as background exposure in this document.

2.4. Question 2 (Q2): Is this product specifically meant for children?

Products such as toys and children's clothing are specifically designed for use by children. Therefore, a child-specific exposure assessment is automatically required. Note that in the regulations of certain countries, a child-specific exposure assessment may also be required for various products not directly meant for children, e.g. direct exposure to toothpaste, sunscreen, body lotions, or indirect exposure to paint, cleaning agents, and building materials.

2.5. Question 3 (Q3): Is the contact direct?

Direct contact involves exposure with the substance directly when using the product. For instance, the application of a hair spray on a person, yourself or a child, in both cases is assumed to be direct exposure. Also contact with a substance from a carpet cleaner when using it is assumed to be direct exposure. Contact with a substance from the cleaned carpet, however, is assumed to be indirect or secondary exposure. Indirect, secondary exposure to a chemical could be of importance for children's risk assessment (see next question).

2.6. Question 4 (Q4): Does indirect exposure occur?

Indirect exposure generally refers to any exposure that does not involve direct contact with substances when using a product. Indirect or secondary exposure can occur after a product is used and might be due to child-specific behaviour, e.g. certain mouthing behaviour, crawling on a cleaned floor and playing in a room that has been painted. Even if the product is not meant for use by children, exposure to consumer products may also occur during product use if the child is in the same room or in the near vicinity (bystander exposure) while the product is being used by an adult. Indirect exposure may also occur if the child is spending time in an area where the product is present or was used (e.g. a painted wall or a cleaned surface). Indirect exposure to commercial, professionally applied products may also occur (e.g. chemicals in treated wood products for playgrounds, artificial turf, pesticides on fields).

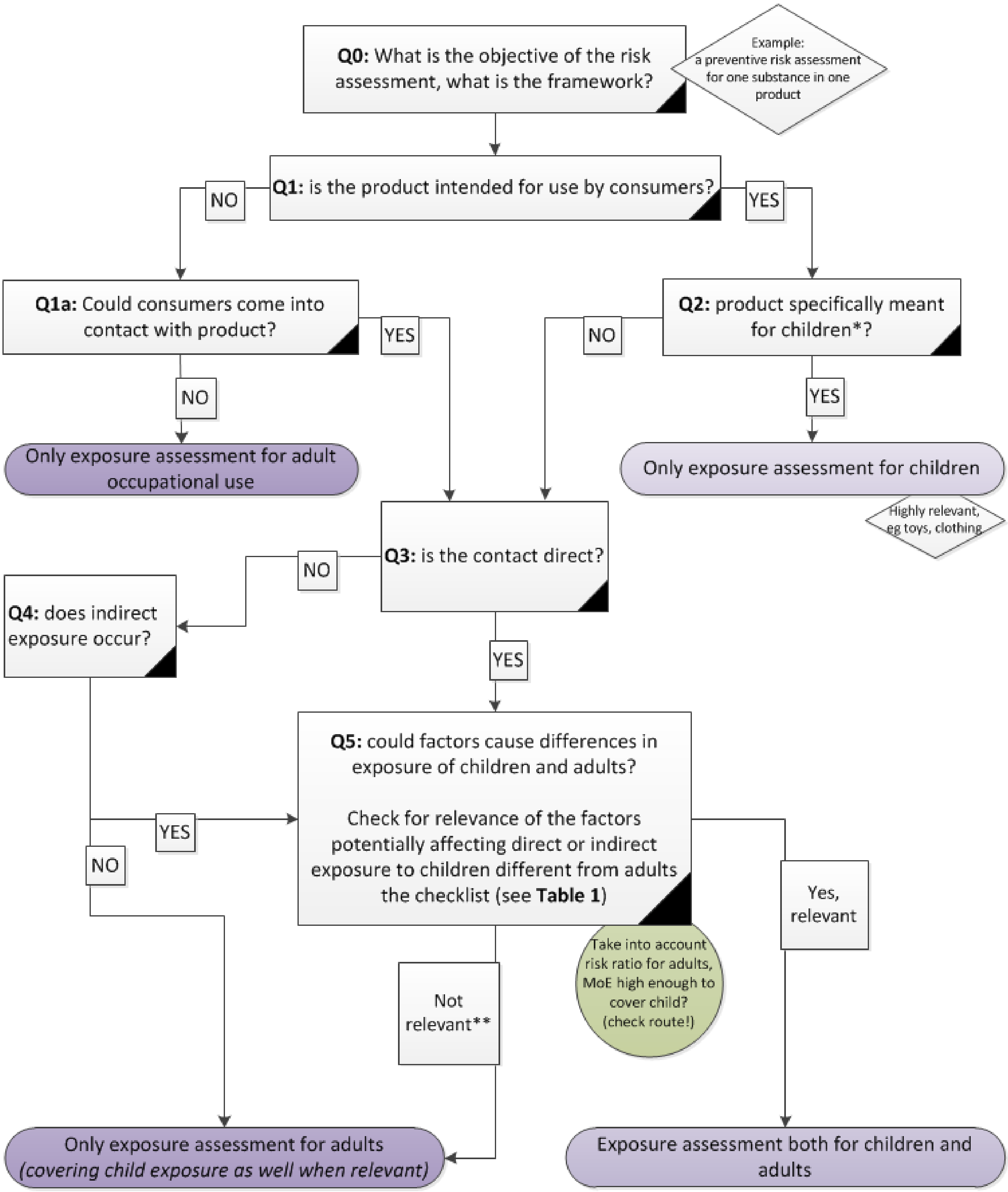
2.7. Question 5 (Q5): Could the factors cause differences in exposure of children and adults?

Differences between adults and children in certain factors can lead to differences in exposure. Question 5 in Figure 1 directs to a checklist (Table 1) to help identify whether relevant direct or indirect exposure for children is different from adults for different exposure routes. For example, as the breathing rate of children is higher compared to adults, (high) vapour pressure of a chemical could result in a relative higher internal exposure for children via inhalation. Also, infants tend to mouth products, and have higher hand-to-mouth contact rates and therefore the potential leaching of a chemical from a product could result in a relative higher oral exposure for children. Furthermore, for dermal exposure the crawling behaviour of children can lead to a higher exposure compared to adults and should be taken into account when assessing a substance that is used to clean floors, for example. These examples of factors listed in the checklist (Table 1) for relevance of indirect/direct exposure to children (different from adults) can help decide whether a child-specific exposure assessment is needed. Table 1 is not exhaustive, but contains examples meant as a starting point for expert judgement, and can be expanded.

The decision tree (Figure 1) leads a risk assessor to a decision whether exposure assessments are needed for both adults and children, or whether an assessment for adults or children only would suffice. In some cases, an exposure (or risk) assessment for adults could indicate that children would also be protected. In other words, the exposure or risk assessment performed for adults could provide a basis in order to decide that conducting an exposure assessment for children is not necessary. This might, for example, occur if the Margin of Exposure (MoE) or MoS for adults is sufficiently large enough or the Risk Characterisation Ratio (RCR) is sufficiently low enough. Needless to say, whether this ratio is acceptable to draw such a conclusion is highly dependent on e.g. the specific product and its use, the exposure factors and the related routes of exposure taken into account. E.g. when a certain MoE for adults is higher than 10 000 or 100 000, it is very likely to cover an acceptable exposure for children as well. But the conclusion whether an exposure assessment for adults covers the exposure for children should be drawn very carefully, and will often only be clear after calculating rather than deciding beforehand. Naturally, for further risk assessment and MoS ratios between adults and children, toxicokinetic and toxicodynamic differences between adults and children could also be of importance (e.g. other toxicological reference values).

The decision tree is intended to make the risk assessor aware of relevant differences in exposure between adults and children. It is not intended to be used as a fixed protocol. It should also be noted that following the path of the decision tree might result in different conclusions compared to the inclusion of child-specific exposure assessment in specific regulatory frameworks, or guidances. As an illustration, a few examples are provided on how to deal with certain child-specific differences, which usually concerns the use of other values for physiological factors such as body weight, dermal surface area or breathing rate (Armstrong et al., 2002[12]; ter Burg, Bremmer and Van Engelen, 2007[9]). With regard to breathing rate, for example, according to Armstrong et al. (2002[12]) the air intake of a child (<1 year) is 2.3 times the adult intake rate, and therefore if exposed to the same air concentrations, child exposure can be estimated as 2.3 times higher when compared to the adult exposure value in mg/kg bw (i.e. the internal dose). Alternatively, if an adult assessment has been done and the MoE is deemed sufficiently high, the adult assessment may cover children as well. If a child (<1 year) is only exposed due to passive presence in the house, it can be considered safe if the risk assessment for the active user indicates low risk. For example, inhalation exposure estimates based upon the Exposure and Fate Assessment Screening Tool (E-FAST) model indicated that the passive exposure of children with the highest air intake rate on a body weight basis (< 1 year old) were similar to that of older children (16-19 years) actively using the substance (Zaleski, Pavkov and Keller, 2007[35]).

Figure 1. Decision tree to raise awareness of children's exposure to chemicals from products



* The WHO defines a child as a person up to 21 years of age.
** Exposure for children is different from adults because of behaviour or anthropometric characteristics, but adult exposure (very likely) exceeds that of children and the MoE for adults is high enough to cover child exposure.

Table 1. Checklist with examples (not exhaustive) of child-specific physiological and behavioural characteristics and related exposure factors per route of exposure causing differences in exposure of children compared to adults

Child-specific difference and effect in exposure scenario	Related exposure factors
Inhalation	
Higher breathing rate and surface area for absorption (relative to body weight) resulting in higher internal exposure via inhalation (per kg bw)	Vapour pressure of a chemical
Crawling behaviour or lower body height resulting in a lower personal breathing zone if stratification is expected in room air (air intake at lower position, possibly closer to surfaces)	Emission from product, Semi-Volatile Organic Compounds (SVOCs)
Exposure pattern, e.g. a child generally spends more time indoors leading to a higher magnitude, duration, or frequency of exposure to indoor air. Smoking behaviour in older children.	Presence in specific buildings (home, day-care, school), etc.
Oral	
Higher intake (relative to body weight) leading to a higher exposure via the oral route (per kg bw)	
Oral exploration and mouthing resulting in additional, or higher exposure via the oral route	Leaching from product
Dermal	
Crawling behaviour, larger surface area (relative to body weight) and relatively bigger head, all leading to higher exposure via the dermal route (per kg bw)	Ability of migration to skin, contact to textile, clothing, flouring, etc.
Exposure pattern, e.g. a child lays/plays more on the grass or ground, sleeps longer in bed, all leading to higher magnitude, duration, or frequency of exposure via the dermal route (per kg bw). high use of cosmetics and personal care products in older children	Ability of migration to skin, contact to textile, matrasses, ground, grass, flouring, etc.

Note: This table is not exhaustive but meant as a starting point to trigger expert judgement.

3. Case Studies

The decision tree results in four possible outcomes (the purple text boxes with rounded corners in Figure 1):

1. "**Only exposure assessment for adult occupational use**" when consumers do not come into contact with a product (environmental background exposure as defined in this document is not taken into account);
2. "**Only exposure assessment for children**" when consumer products are specifically meant for children such as children's clothing, toys or personal care products intended for use specifically by or for children (e.g. baby wipes or children's toothpaste);
3. "**Only exposure assessment for adults (which covers child exposure as well, when relevant)**" when consumer products are meant for adults and no direct or indirect exposure of children occurs (e.g. for car engine coolant), or in the case that direct or indirect exposure of children potentially occurs but the factors listed in the checklist (Table 1) would not be expected to cause relevant differences in exposure between children and adults (i.e. adult internal dose is higher, or MoE is sufficiently high enough – in case this is known), and adult exposure assessment most probably covers children exposure as well; or
4. "**Exposure assessment both for children and adults**" when consumer products are meant for children and adults, and direct or indirect exposure does occur and the factors listed in the checklist (Table 1) could result in differences in exposure of children and adults.

Outcome 1 and 3 only requires an exposure assessment for adults, whereas outcome 2 and 4 requires a specific assessment for children. With regard to outcome 3, a consumer product not specifically meant for children, leading to direct or indirect contact, but without any factors potentially resulting in relevant differences in exposure of children and adults (Table 1) would mean that the adult exposure scenario would also cover children's exposure. This might be relevant for a situation where a child is in a bystander situation, and therefore might have an exposure different than the adult because of behavioural or anthropometric characteristics, but still the adult exposure assessment most probably covers the exposure assessment of a child (e.g. for application of rubber solution for a flat tyre or shoe polish). The use of consumer products for which no direct nor indirect contact for children is foreseen (e.g. adding car engine coolant fluid) would also lead to outcome 3. Naturally, children's clothing or toys would are examples of products leading to outcome 2, requiring a specific assessment for children. Outcome 4 requires an exposure assessment both for children and for adults.

Three cases are presented below leading to outcome 4 requiring an exposure assessment for both children and adults, and illustrating both the performance of the decision tree and various differences between adult and children's exposure. Case 1 (two types of hair spray) illustrates differences between adult and child exposure and shows the influence of Volatile Organic Compounds (VOC) and non-VOC products on this exposure. Case 2 (kitchen cleaner spray) illustrates the additional dermal exposure through table top contact. Case 3 (a pesticide in a public park) demonstrates different dermal exposure factors for children of two age groups and additional oral exposure for infants.

3.1. Case 1: two types of hair spray

3.1.1. Scenario

This scenario includes exposure to two different types of hair spray, which are common consumer products intended for adults, but for which (young) children's indirect exposure is considered reasonably foreseeable.

3.1.2. Decision tree

- Q0: The framework consists of an exposure assessment to investigate the potential differences in exposures between adults and (young) children from the use of two consumer products (hair sprays) intended for adults. This includes whether adult exposures typically cover potential exposures of children, and the roles of various routes of exposure, as well as differences between VOCs and non-VOCs as constituents in products.
- Q1: Yes. These hair sprays are intended to be used by consumers.
- Q2: No. These products are not specifically meant for use by children.
- Q3: No. Children are not directly exposed to hair spray. Unless (young) adolescents are using hair spray by themselves (see Q5).
- Q4: Yes. Indirect dermal or inhalation exposure of (younger) children might occur during application (when being in the same room), but also post-application exposure might occur. Post-application exposure may include dermal exposure via crawling, oral exposure via hand-to-mouth contact or direct object mouthing for toddlers. In addition, dermal exposure may occur from contact with surfaces were hair spray has accumulated or from contact with adults who have used the product.
- Q5: Possibly. The factors listed in the checklist for direct/indirect exposure might cause differences in all routes of exposure, in this case the crawling and mouthing behaviour, the higher breathing rate and overall relatively lower body weight. Therefore, an exposure assessment for both adults and children is recommended. Note that in case (young) adolescents are using hair spray by themselves (see answer to Q3), they may show different behaviour in the use of hair spray leading to another exposure scenario. In consequence, different outcomes may be obtained for different age-classes of children.

3.1.3. Exposure assessment

The exposure during application was calculated for both products using ConsExpo 4.1 factsheets and the spray model from ConsExpo 4.1 (Delmaar and Bremmer, 2009[36]). The exposure during the post-application scenario was calculated using US EPA residential Standard Operating Procedures (SOPs) for pesticide exposure (US EPA, 2012[37]) and the ConsExpo 4.1 cosmetics factsheet (Bremmer, Prud'homme de Lodder and van Engelen, 2006[38]). Toddlers were assumed to be present at locations where exposures were estimated, i.e. during product use and post application. For the calculations, 100% bioavailability was assumed for all routes of exposure (dermal, oral, inhalation), which should be noted that it is conservative with regard to recommended default values by various organisations (e.g. by European Food Safety Authority (EFSA) et al. (2017[39]) and the Scientific Committee on Consumer Safety (SCCS) (2018[40])). For VOCs, 100% evaporation was assumed, and therefore no dermal exposure for VOC scenarios is considered. Inhalation is assumed to be the predominant route of exposure. Default values for exposure parameters were based on realistic worst-case scenarios leading to an (assumed protective) conservative exposure outcome. Calculations were performed without residue depletion during exposure duration, applying the well-mixed box scenario during application. The result of the exposure calculations is presented in Table 2.

Table 2. Calculated integrated doses to hair spray for toddlers and adults

Product	Integrated dose *(µg/kg bw/day)*		Factor difference	Drive
	Toddler	Adult	Toddler/Adult	
Hair spray (non-VOC)	0.88	142	0.01	Dermal exposure
Hair spray (VOC)	22	11	**2.00**	Inhalation exposure

Note: Exposure resulting from direct exposure during application by the adult and post application exposure, and passive exposure of the toddler during application and post-application exposure is presented. The factor difference between toddler and adult (higher exposures for toddlers in bold) is given, and the driver indicates the exposure route which is mainly responsible.

The results (Table 2) show a great difference between the estimated integrated doses for toddlers and adults. For non-VOC hair spray the calculated dose of toddlers of 0.88 µg/kg bw/day was more than 160 times lower (rounded factor difference of 0.01 in Table 2) compared to the dose estimate for adults, because of the non-inclusion of scalp contact. For VOC hair spray, however, inhalation is the only driver resulting in a 2-fold higher exposure of toddlers compared to adults.

In this example, the use of the adult estimate for the non-VOC containing hair spray could be assumed to be protective of children. In contrast, for VOCs in hair spray, exposure doses among children are higher than those of adults because of the higher breathing rate in addition to a lower body mass for children compared to adults (unless the ConsExpo 4.1 two-box model is used where the breathing zone air concentration may be higher for the adult user than the child bystander).

3.2. Case 2: Kitchen Cleaner Spray

3.2.1. Scenario

This scenario includes exposure to a kitchen cleaner spray, which is a common (non-VOC) consumer product not intended for use by (young) children but for which indirect children's exposure is considered reasonably foreseeable.

3.2.2. Decision tree

- Q0: The framework consists of an exposure assessment to investigate the difference in exposure between adults and children from the use of a kitchen cleaner spray, including whether adult exposures typically cover potential exposures of children, and the roles of various routes of exposure.

- Q1: Yes. Kitchen cleaner spray is intended to be used by consumers.
- Q2: No. This product is not specifically meant for use by children.
- Q3: No. Children are not exposed to kitchen spray cleaner through direct use (there might be an exception as young children sometimes assist their parents with cleaning. Older children might perform the whole cleaning by themselves).
- Q4: Yes. Indirect exposure might occur during application of the product, and additional post-application for children is foreseen (dermal exposure via crawling, oral exposure via hand-to-mouth or direct object mouthing).
- Q5: Possibly. Factors as listed as examples in the checklist for direct/indirect exposure (Table 1) might cause differences in exposure of children and adults. In addition to larger body surface area (relative to body weight), also behavioural aspects (crawling) could potentially lead to higher dermal exposure, and additional oral exposure because of exploration/mouthing for the infant. Therefore, exposure assessments for both adults and children are recommended.

3.2.3. Exposure assessment

The exposure during application was calculated by using ConsExpo 4.1 factsheets and the spray model from ConsExpo 4.1 (Delmaar and Bremmer, 2009[36]). Exposure during the post-application scenario was calculated using US EPA residential SOPs for pesticide exposure (US EPA, 2012[37]) and the ConsExpo 4.1 cleaning products factsheet (Prud'homme de Lodder, Bremmer and van Engelen, 2006[41]). Toddlers were assumed to be passively exposed post-application by hand-to-mouth contact and dermal surface contact behaviour, while adults were assumed to be exposed during application. For the calculations, as in the previous case, conservatively 100% bioavailability was assumed for all routes of exposure (dermal, oral, inhalation). Default values for exposure parameters were based on realistic worst-case scenarios leading to an (assumed protective) conservative exposure outcome. Calculations were performed without residue depletion during exposure duration, applying the well-mixed box scenario during application. The results of the exposure calculations are presented in Table 3.

Table 3. Calculated integrated doses to kitchen spray cleaner for toddlers and adults

Product	Integrated dose (*μg/kg bw/day*)		Factor difference	Drive
	Toddler	Adult	Toddler/Adult	
Kitchen spray cleaner	161	0.78	**206**	Dermal exposure

Note: Exposure dose resulting from exposure during application by the adult, and post-application passive exposure of the toddler is presented. The factor difference between toddler and adult (higher exposures for toddlers in bold) is given, and the driver indicates the exposure route that is mainly responsible.

The calculated exposure estimate of toddlers of 161 μg/kg bw/day was over 200 times higher compared to adults (Table 3), which mainly results from table top dermal contact and the resulting dermal surface contact.

3.3. Case 3: A pesticide in a public park

3.3.1. Scenario

This scenario includes a post-application exposure after application of a liquid lawn herbicidal product intended for professional use, containing the active substance 2-methyl-4-chlorophenoxyacetic acid (MCPA). Bystander application during application is not considered. It is assumed that after treatment of a public park, a family with children enters the lawn to relax, a child in its early childhood playing in the grass and an infant being allowed out of the carriage for some time to crawl in the grass.

3.3.2. Decision tree

- Q0: The framework is a regulatory context for authorisation of a pesticide to the market.
- Q1: No. This product is not intended for use by consumers.
- Q1a: Yes. Consumers can come into contact with the product after use.
- Q3: No. Contact with the product is not through direct use.
- Q4: Yes. Indirect exposure might occur because of contact with the treated lawn after application of the product.
- Q5: Possibly. Factors as are listed as examples in the checklist for direct/indirect exposure (Table 1) might cause differences in exposure of children and adults. In addition to the higher body surface to body weight ratio, also behavioural aspects could potentially lead to higher dermal exposure (crawling) and additional oral exposure because of exploration/mouthing for the infant. Therefore, exposure assessments for both adults and children are recommended.

3.3.3. Exposure assessment

In the current regulatory risk assessment of plant protection products, this exposure scenario has been covered by several exposure models, e.g. the harmonised EFSA OPEX model within the EU (EFSA, 2014[42]). However, the exposure assessment in this case is performed using the "Secondary exposure to lawn pesticides methodology" described by RIVM (Prud'homme de Lodder, Bremmer and van Engelen, 2006[43]). This model has no legal status at this moment, but illustrates the differences in exposures for two age groups of children including differences in physiology as well as in behaviour. For this example, the proposed application rate is 1.8 kg active substance per area (ha). Dermal exposures resulting from contact with the treated lawn after application of the product are calculated for three different age groups (infant, child and adult), using specific default factors for body weight, transfer coefficient and contact duration (Table 4) (Prud'homme de Lodder, Bremmer and van Engelen, 2006[43]). Note that other exposure models can use different default factors. In addition to the dermal exposure, oral exposure is also calculated for the infant to account for the exploration/mouthing behaviour by children of this age. This is calculated as a default fraction (10%) of the dermal exposure (Prud'homme de Lodder, Bremmer and van Engelen, 2006[43]).

Table 4. Default values for risk assessment factors for calculating dermal absorption by specific age groups in the present example

	Infant (10.5 months)	child (4 years)	adult (lying in the grass)
body weight *(kg)*	8.69	15	63
transfer coefficient *(m^2/hr)*	0.7	1	1.3
contact duration *(hr/day)*	1.5	3	3

Source: (Prud'homme de Lodder, Bremmer and van Engelen, 2006[43])

The internal dose in this example has been calculated using a dermal absorption factor of 2.5% for the active substance MCPA (EC, 2008[44]). For oral absorption, a default value of 100% has been used. The calculated internal dose for children (4 years) of 0.68 mg MCPA/day, or 45 µg MCPA/kg bw/day, is 3.2-fold higher than the calculated internal dose of adults of 14 µg MCPA/kg bw/day (Table 5). The calculated internal dose for infants of 1.16 mg MCPA/day, or 133 µg MCPA/kg bw/day, is 9.5-fold higher than the calculated internal dose of adults of 14 µg MCPA/kg bw/day (Table 5). This illustrates there is a factor ~10 difference between the calculated internal dose of infants compared to adults to the active substance because of contact with the treated lawn in a park with MCPA. One could argue that this difference for infants is mainly caused by the additional exposure route accounting for the exploration/mouthing behaviour by infants, which is calculated using a default value of 100%. However, even when the oral absorption default of 100% would have been refined and replaced by experimentally determined factors of 55-78% (EC, 2008[44]), still the calculated total internal dose would be 84 µg MCPA/kg bw/day, 6-fold higher than the calculated internal dose of adults.

Table 5. Internal dose of infants, children and adults as a result of post-application exposure because of lawn-treatment in a public park

Route	Infant (10.5 months)		Child (4 years)		Adult (lying in the grass)	
	Internal dose		Internal dose		Internal dose	
	mg AS/ day	µg AS/kg bw/day	mg AS/ day	µg AS/kg bw/day	mg AS/ day	µg AS/kg bw/day
Oral	0.95	109	n.a.	n.a.	n.a.	n.a.
Dermal	0.21	24	0.68	45	0.88	14
Total	**1.16**	**133**	**0.68**	**45**	**0.88**	**14**

Note: The internal dose is calculated using the Secondary exposure to lawn pesticides methodology described by the RIVM (Prud'homme de Lodder, Bremmer and van Engelen, 2006[43]) for the application of a liquid lawn pesticide containing 1.8 kg Active Substance (AS)/ha. The dislodgeable fraction is 5%. "n.a." stands for not applicable.

Plant protection products are usually highly regulated and their risk assessment often already takes into account the exposure of children. The exposure assessment in this case was modelled using a model which illustrates differences in exposure not only between children and adults, but also between children of different age groups (te Biesebeek et al., 2019[45]). Other models which are currently used in a regulatory risk assessment of plant protection products use different methodologies and often different default values for factors affecting the outcome of these models.

4. Discussion and Conclusion

This document aims to create awareness of child-specific exposure to chemicals, which is not new. Armstrong and co-workers already published earlier a methodology to determine and prioritise chemicals to and scenarios in which children could be disproportionately or more highly exposed (Armstrong et al., 2000[6]; Armstrong et al., 2002[12]). These publications were aimed at selecting relevant substances to which children are exposed and prioritisation of the substances by a MoE approach. Later, other literatures with attention to child-specific exposure in chemical risk assessments also appeared (Samet, 2004[8]; Cohen Hubal, Moya and Selevan, 2008[3]; Makris et al., 2008[46]; Landrigan and Goldman, 2011[47]; Felter et al., 2015[22]; Narciso et al., 2017[23]).

The definition of children (age, physiological characteristics but also their activities) differs between different countries or legal frameworks as has been discussed in this document. For instance, the first outcome ("only exposure assessment for adult occupational use") assumes children are not present at an occupational setting. This assumption, however, should be assessed for representativeness of the situation being addressed, as teens can perform tasks in some occupational settings (e.g. retail or professional kitchens), or within certain branches at certain times (e.g. holiday work or seasonal employment). In addition, it does not consider indirect exposure of children via transfer from adults exposed in the workplace, e.g. via mother's milk, clothing or breath. In many regions, the laws have already eliminated many of these exposures at the industrial level (i.e. when handling lead/heavy metals workers must use overalls and facilities must be provided to shower prior to leaving the site).

The decision tree presented in this document provides further support in choosing whether estimating additional exposures for children is needed and highlights considerations in which situations assessment of exposure for children is needed. Together with the examples of factors in its checklist, the decision tree draws the attention to both physiological and behavioural differences between adults and children in exposure scenarios where those are relevant. It is noted that child-specific differences in toxicokinetics and toxicodynamics should also be taken into account when performing risk assessments aimed at children.

The focus of this document is on 'industrial chemicals', and targeted at 'consumer products'. However, also for other types of products exposure to children may be of concern, as definitions can differ between countries. The key point of the document is to create awareness on child-specific exposure. This has been illustrated by different examples (cases) in this document. It is important to realise that legislations can also differ between countries, including existing requirements on whether to perform child-specific exposure assessments (e.g. the European Union (EU) Guidance on pesticides exposure assessment of operators, workers, residents and bystanders for plant protection products (EFSA, 2014[42]), or the EU Guidance on the Biocidal Products Regulation (ECHA, 2017[48])). Some countries define specific products (e.g. toothpaste, sunscreen, body lotions, paint, cleaning agents and building materials) for which direct or indirect exposure to children needs to be assessed, regardless of whether the product is intended to be used by children. The decision tree, however, aims to create awareness if actual exposure occurs. For consumer products specifically meant for children (outcome 2 of the decision tree), the exposure of children is evident, for instance in case of children's clothing or toys. However, this does not automatically mean that children are considered within the exposure assessment for such products. For example, under the (more general) REACH legislation it is up to the registrant's judgment if and when to include a child in the exposure assessment for chemicals used in textile or clothing.

The decision tree is focussed on consumer products and as such does not cover specific exposure routes such as exposure via food products or the environment, that are regarded as background in this document. However, such media could be relevant with regard to child-specific exposures, e.g. especially indoor air, mother's milk, dust, soil and water used in infant formula. Alternatively, some countries use more direct considerations whether child-specific exposure assessment is required, i.e. whether children and adults encounter products/media in the same manner (same use patterns and locations). If the only differences are based upon child-specific physiology, it could be possible to estimate child exposure from adult exposure by multiplying adult exposure by a ratio. If this ratio is small compared to the MoE, the adult exposure estimation may be sufficient. When behavioural differences are concerned, including e.g. the presence at specific locations (e.g. schools or day cares) a child-specific exposure scenario can be determined.

For a lot of products, the decision tree will usually lead to outcome 4 ("Exposure assessment both for children and adults"). Also, when no direct exposure for children takes place, indirect exposure is often likely to occur, and in this situation there are usually factors of which examples are listed in the checklist (Table 1) causing differences in exposure of children compared to adults. The importance of conducting exposure assessments for both adults and children is illustrated in the cases. Whether an exposure assessment for adults will be protective enough to cover the exposure for children will depend on the product, chemical, routes, exposure factors involved and the MoE. The MoE for adults might be large enough to assume that children will be covered as well. Many different factors are illustrated in the cases described. Case 1 (the two types of hair spray), for instance, illustrates that the volatile or non-volatile character of the product could lead to a decision whether a children specific exposure assessment is necessary. The kitchen cleaner spray case (case 2) illustrates that crawling behaviour of toddlers contributes greatly to the exposure. Case 3 (a pesticide in a public park) illustrates, apart from physiological differences, the importance of the additional contribution of mouthing behaviour of toddlers to the exposure.

When a child-specific exposure assessment is necessary according to the decision tree, the subsequent issue is how to perform such an exposure assessment (provided no regulatory requirements or guidance is already present). Although many suggestions and cases can be found in literatures, general guidance with respect to this topic is absent. In some cases only changing the calculation factors (e.g. body weight, surface area and breathing rate) of specific variables mentioned in the checklist might be sufficient, in such a way the calculation is applicable to children when only physiological differences are of importance (e.g. with certain clothing, or specific personal care products). In order to do so, one needs to know the differences in physiological factors for children compared to adults e.g. body weight, skin surface and breathing rate (see e.g. the work by Cohen and co-workers or other sources (Cohen Hubal et al., 2000[7]; ECHA, 2017[48]; HEEG, 2013[49]; te Biesebeek et al., 2014[50]; US EPA, 2011[51])). However, usually behavioural differences are concerned, and preferably a child-specific exposure scenario should be determined. Additional routes of exposure might be necessary to add to the exposure estimation (Cohen Hubal, Moya and Selevan, 2008[3]). Here, one should decide as well for what specific child, i.e. of what age(s), an exposure assessment should be performed (e.g. in Case 3 both an infant as well as a 4-year old child were considered). The US EPA's exposure factors handbook incorporates child-specific information with regard to exposure assessment (US EPA, 2011[51]), and superseded the US EPA's child-specific exposure factors handbook (US

EPA, 2008[52]). Together with the US EPA's child-specific exposure scenarios examples (US EPA, 2014[53]), the handbook offers general children's activity patterns and exposure factors from a number of published studies, along with approaches in order to address different exposure routes and dose estimates in some specific contexts (US EPA, 2011[51]; US EPA, 2014[53]). For children specific differences related to behavioural differences such as crawling or mouthing, one may need additional information (e.g. duration and frequency of behaviour) but such scenarios are much less defined (te Biesebeek et al., 2014[50]; ter Burg, Bremmer and Van Engelen, 2007[9]; van Engelen and Prud'homme de Lodder, 2007[4]; Wolterink, Van Engelen and Van Raaij, 2007[5]). It should also be considered that default values for parameters vary case by case and/or are substance specific (e.g. dermal absorption, transfer efficiency, use frequency and surface residual) and product specific (e.g. rates of emission, leaching and their application (surface area)). Consequently, such exposure assessment might also contain many uncertainties because behaviour such as crawling and mouthing is highly variable (Xue et al., 2007[31]; Xue et al., 2010[11]). Chemicals for which child-specific exposure assessment is performed in scientific literature are e.g. Polybrominated diphenyl ethers (PBDEs) (Ionas et al., 2016[54]), Bisphenol A (BPA) (Healy et al., 2015[55]), Diethylhexylphthalate (DEHP) (Ginsberg, Ginsberg and Foos, 2016[56]) and parabens (Gosens et al., 2011[57]; Gosens et al., 2014[58]).

The issues highlighted above will serve to improve exposure and risk assessments for children of all life stages.

References

Arcus-Arth, A. and R. Blaisdell (2007), “Statistical Distributions of Daily Breathing Rates for Narrow Age Groups of Infants and Children”, *Risk Analysis*, Vol. 27/1, pp. 97-110, http://dx.doi.org/10.1111/j.1539-6924.2006.00862.x. [25]

Armstrong, T. et al. (2000), “A tiered approach for assessing children’s exposure”, *Environmental Health Perspectives*, Vol. 108/6, pp. 469-474, http://dx.doi.org/10.1289/ehp.00108469. [6]

Armstrong, T. et al. (2002), “A tiered approach to assessing children’s exposure: a review of methods and data”, *Toxicology letters*, Vol. 127/1-3, pp. 111-9, http://www.ncbi.nlm.nih.gov/pubmed/12052648. [12]

Bearer, C. (1995), “How are children different from adults?”, *Environmental Health Perspectives*, Vol. 103/suppl 6, pp. 7-12, http://dx.doi.org/10.1289/ehp.95103s67. [20]

Bremmer, H., L. Prud’homme de Lodder and J. van Engelen (2006), *Cosmetics Fact Sheet. To assess the risks for the consumer. Updated version for ConsExpo 4*, RIVM report 320104001/2006, https://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. [38]

CEN (2015), *Children’s mouthing behaviour in contact with toys*, CEN/TR 16918:2015. [30]

Chance, G. and E. Harmsen (1998), “Children are different: environmental contaminants and children’s health”, *Canadian Journal of Public Health*, Vol. 89 Suppl 1, pp. S9-13, S10-5, http://www.ncbi.nlm.nih.gov/pubmed/9654786. [14]

Cohen Hubal, E. et al. (2014), “Identifying important life stages for monitoring and assessing risks from exposures to environmental contaminants: Results of a World Health Organization review”, *Regulatory Toxicology and Pharmacology*, Vol. 69/1, pp. 113-124, http://dx.doi.org/10.1016/j.yrtph.2013.09.008. [19]

Cohen Hubal, E., J. Moya and S. Selevan (2008), “A lifestage approach to assessing children’s exposure”, *Birth Defects Research Part B: Developmental and Reproductive Toxicology*, Vol. 83/6, pp. 522-529, http://dx.doi.org/10.1002/bdrb.20173. [3]

Cohen Hubal, E. et al. (2000), “Children’s exposure assessment: a review of factors influencing Children’s exposure, and the data available to characterize and assess that exposure”, *Environmental Health Perspectives*, Vol. 108/6, pp. 475-486, http://dx.doi.org/10.1289/ehp.108-1638158. [7]

Cresteil, T. (1998), “Onset of xenobiotic metabolism in children: Toxicological implications”, *Food Additives and Contaminants*, Vol. 15/suppl, pp. 45-51, http://dx.doi.org/10.1080/02652039809374614. [21]

Delmaar, J. and H. Bremmer (2009), *The ConsExpo Spray Model. Modeling and experimental validation of the inhalation exposure of consumers to aerosols from spray cans and trigger sprays*, RIVM report 320104005/2009, https://www.rivm.nl/bibliotheek/rapporten/320104005.pdf. [36]

EC (2008), "Review report for the active substance MCPA", No. SANCO/4062/2001-final, http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.ViewReview&id=196. [44]

ECHA (2017), *Guidance on the Biocidal Products Regulation. Volume III Human Health - Assessment and Evaluation (Parts B+C)*, ECHA-17-G-27-EN, http://dx.doi.org/10.2823/143042. [48]

EFSA (2014), *Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products*, http://dx.doi.org/10.2903/j.efsa.2014.3874. [42]

EFSA; Buist, Harrie; Craig, Peter; Dewhurst, Ian; Hougaard Bennekou, Susanne; Kneuer, Carsten; Machera, Kyriaki; Pieper, Christina; Court Marques, Daniele; Guillot, Gilles; Ruffo, Federica; Chiusolo, Arianna (2017), *Guidance on dermal absorption*, http://dx.doi.org/10.2903/j.efsa.2017.4873. [39]

Felter, S. et al. (2015), "Assessment of health risks resulting from early-life exposures: Are current chemical toxicity testing protocols and risk assessment methods adequate?", *Critical Reviews in Toxicology*, Vol. 45/3, pp. 219-244, http://dx.doi.org/10.3109/10408444.2014.993919. [22]

Ferguson, A., R. Penney and H. Solo-Gabriele (2017), "A Review of the Field on Children's Exposure to Environmental Contaminants: A Risk Assessment Approach", *International Journal of Environmental Research and Public Health*, Vol. 14/3, http://dx.doi.org/10.3390/ijerph14030265. [33]

Firestone, M. et al. (2007), "Identifying Childhood Age Groups for Exposure Assessments and Monitoring", *Risk Analysis*, Vol. 27/3, pp. 701-714, http://dx.doi.org/10.1111/j.1539-6924.2007.00918.x. [27]

Ginsberg, G., J. Ginsberg and B. Foos (2016), "Approaches to Children's Exposure Assessment: Case Study with Diethylhexylphthalate (DEHP)", *International Journal of Environmental Research and Public Health*, Vol. 13/7, http://dx.doi.org/10.3390/ijerph13070670. [56]

Gosens, I. et al. (2014), "Aggregate exposure approaches for parabens in personal care products: a case assessment for children between 0 and 3 years old", *Journal of Exposure Science & Environmental Epidemiology*, Vol. 24/2, pp. 208-214, http://dx.doi.org/10.1038/jes.2013.33. [58]

Gosens, I. et al. (2011), *Aggregate exposure assessment of chemicals in consumer products. Exposure to parabens in cosmetics in children as a case study*, RIVM letter report 320015005/2011, https://rivm.openrepository.com/bitstream/handle/10029/256932/320015005.pdf?sequence=3&isAllowed=y. [57]

Groot, M., M. Lekkerkerk and L. Steenbekkers (1998), *Mouthing behaviour of young children: an observational study*, Wageningen Agricultural University, http://agris.fao.org/agris-search/search.do?recordID=NL2012063697. [29]

Hayashi, Y. (2009), "Scientific basis for risk analysis of food-related substances with particular reference to health effects on children.", *The Journal of toxicological sciences*, Vol. 34 Suppl 2, pp. SP201-7, http://www.ncbi.nlm.nih.gov/pubmed/19571470. [24]

Healy, B. et al. (2015), "Bisphenol A exposure pathways in early childhood: Reviewing the need for improved risk assessment models", *Journal of Exposure Science & Environmental Epidemiology*, Vol. 25/6, pp. 544-556, http://dx.doi.org/10.1038/jes.2015.49. [55]

HEEG (2013), *Default human factor values for use in exposure assessments for biocidal products*, https://echa.europa.eu/documents/10162/21664016/recom_14+_default+human_factor_values_biocidal+products_en.pdf/88354d31-8a3a-475a-9c7d-d8ef8088d004. [49]

Ionas, A. et al. (2016), "Children's exposure to polybrominated diphenyl ethers (PBDEs) through mouthing toys", *Environment International*, Vol. 87, pp. 101-107, http://dx.doi.org/10.1016/j.envint.2015.11.018. [54]

Landrigan, P. and A. Garg (2002), "Chronic effects of toxic environmental exposures on children's health", *Journal of Toxicology. Clinical Toxicology*, Vol. 40/4, pp. 449-456, http://www.ncbi.nlm.nih.gov/pubmed/12216997. [18]

Landrigan, P. and L. Goldman (2011), "Children's Vulnerability To Toxic Chemicals: A Challenge And Opportunity To Strengthen Health And Environmental Policy", *Health Affairs*, Vol. 30/5, pp. 842-850, http://dx.doi.org/10.1377/hlthaff.2011.0151. [47]

Lorber, M. and L. Phillips (2002), "Infant exposure to dioxin-like compounds in breast milk", *Environmental Health Perspectives*, Vol. 110/6, pp. A325-332, http://dx.doi.org/10.1289/EHP.021100325. [17]

Makris, S. et al. (2008), "A lifestage-specific approach to hazard and dose-response characterization for children's health risk assessment", *Birth Defects Research Part B: Developmental and Reproductive Toxicology*, Vol. 83/6, pp. 530-546, http://dx.doi.org/10.1002/bdrb.20176. [46]

Moya, J., C. Bearer and R. Etzel (2004), "Children's behavior and physiology and how it affects exposure to environmental contaminants", *Pediatrics*, Vol. 113/4 Suppl, pp. 996-1006, http://www.ncbi.nlm.nih.gov/pubmed/15060192. [26]

Narciso, L. et al. (2017), "The juvenile toxicity study as a tool for a science-based risk assessment in the children population group", *Reproductive Toxicology*, Vol. 72, pp. 136-141, http://dx.doi.org/10.1016/j.reprotox.2017.06.188. [23]

Neal-Kluever, A. et al. (2014), "Infant toxicology: State of the science and considerations in evaluation of safety", *Food and Chemical Toxicology*, Vol. 70, pp. 68-83, http://dx.doi.org/10.1016/j.fct.2014.05.003. [28]

OECD (2019), *Estimating Mouthing Exposure in Children - Compilation of Case Studies*, OECD [ENV/JM/MONO(2019)24]], http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2019)24&doclanguage=en. [32]

OECD (2014), *Report on OECD workshop on children's exposure to chemicals*, OECD [ENV/JM/MONO(2014)29], http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)29&doclanguage=en. [2]

OECD (2013), *Assessing the risk of chemicals to children's health: an OECD-wide survey*, OECD [ENV/JM/MONO(2013)20], http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)20&doclanguage=en. [1]

Prud'homme de Lodder, L., H. Bremmer and J. van Engelen (2006), *Assessment of secondary exposure to lawn pesticides*, RIVM SIR report 09709A00. [43]

Prud'homme de Lodder, L., H. Bremmer and J. van Engelen (2006), *Cleaning Products Fact Sheet. To assess the risks for the consumer*, RIVM report 320104003/2006, https://www.rivm.nl/bibliotheek/rapporten/320104003.pdf. [41]

Roberts, J. and P. Dickey (1995), "Exposure of children to pollutants in house dust and indoor air", *Reviews of Environmental Contamination and Toxicology*, Vol. 143, pp. 59-78, http://www.ncbi.nlm.nih.gov/pubmed/7501867. [34]

Samet, J. (2004), "Risk assessment and child health", *Pediatrics*, Vol. 113/4 Suppl, pp. 952-956, http://www.ncbi.nlm.nih.gov/pubmed/15060187. [8]

SCCS (2018), *The SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation. 10th revision*, SCCS/1602/18, https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_224.pdf. [40]

te Biesebeek, J. et al. (2014), *General Fact Sheet. General default parameters for estimating consumer exposure - Updated version 2014*, RIVM Report 090013003/2014, https://www.rivm.nl/bibliotheek/rapporten/090013003.pdf. [50]

te Biesebeek, J. et al. (2019), *Modellen om de humane blootstelling aan gewasbeschermingsmiddelen te berekenen: een stand van zaken [Models to calculate human exposure to plant protection products: a state of affairs]*, RIVM Briefrapport 2019-0031, https://www.rivm.nl/bibliotheek/rapporten/2019-0031.pdf. [45]

ter Burg, W., H. Bremmer and J. Van Engelen (2007), *Oral exposure of children to chemicals via hand-to-mouth contact*, RIVM report 320005004/2007, https://www.rivm.nl/bibliotheek/rapporten/320005004.pdf. [9]

Tulve, N. et al. (2002), "Frequency of mouthing behavior in young children", *Journal of Exposure Science & Environmental Epidemiology*, Vol. 12/4, pp. 259-264, http://dx.doi.org/10.1038/sj.jea.7500225. [10]

Tyshenko, M. et al. (2007), "Regulatory and Nonregulatory Strategies for Improving Children's Environmental Health in Canada", *Journal of Toxicology and Environmental Health, Part B*, Vol. 10/1-2, pp. 143-156, http://dx.doi.org/10.1080/10937400601034613. [16]

US EPA (2014), *Child-Specific Exposure Scenarios Examples*, EPA/600/R-14-217F, Washington DC, https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=262211. [53]

US EPA (2012), *Standard Operating Procedures for Residential Pesticide Exposure Assessment*, Office of Pesticide Programs, https://www.epa.gov/sites/production/files/2015-08/documents/usepa-opp-hed_residential_sops_oct2012.pdf. [37]

US EPA (2011), *Exposure Factors Handbook 2011 Edition*, EPA/600/R-09/052F, Washington DC, https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252. [51]

US EPA (2008), *Child-Specific Exposure Factors Handbook*, EPA/600/R-06/096F, Washington DC, https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=199243. [52]

van Engelen, J. and L. Prud'homme de Lodder (2007), *Non-food products: How to assess children's exposure?*, RIVM report 320005005/2007, https://www.rivm.nl/bibliotheek/rapporten/320005005.pdf. [4]

WHO (2011), *Summary of Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals*, https://www.who.int/ceh/publications/health_risks_exposure_chemicals/en/. [13]

Wolterink, G., A. Piersma and J. van Engelen (2002), *Risk assessment of chemicals: What about children?*, RIVM report 613340005/2002, https://www.rivm.nl/bibliotheek/rapporten/613340005.pdf. [15]

Wolterink, G., J. Van Engelen and M. Van Raaij (2007), *Guidance for assessment of chemical risks for children*, RIVM report 320012001/2007, https://www.rivm.nl/bibliotheek/rapporten/320012001.pdf. [5]

Xue, J. et al. (2007), "A Meta-Analysis of Children's Hand-to-Mouth Frequency Data for Estimating Nondietary Ingestion Exposure", *Risk Analysis*, Vol. 27/2, pp. 411-420, http://dx.doi.org/10.1111/j.1539-6924.2007.00893.x. [31]

Xue, J. et al. (2010), "A meta-analysis of children's object-to-mouth frequency data for estimating non-dietary ingestion exposure", *Journal of Exposure Science & Environmental Epidemiology*, Vol. 20/6, pp. 536-545, http://dx.doi.org/10.1038/jes.2009.42. [11]

Zaleski, R., K. Pavkov and L. Keller (2007), "Methyl ethyl ketone safety characterization for infants and children: assessment in the USEPA voluntary children's chemical evaluation program", *Human Ecological Risk Assessment*, Vol. 13/4, pp. 747-772, http://dx.doi.org/10.1080/10807030701456585. [35]