Committee for Risk Assessment (RAC)

Committee for Socio-economic Analysis (SEAC)

Opinion

on an Annex XV dossier proposing restrictions on

Substances in single-use baby diapers

ECHA/RAC/RES-O-0000007017-78-01/F

ECHA/SEAC/[Opinion N°(same as opinion number)]

Adopted

16 September 2021

16 September 2021

RES-O-0000007017-78-01/F

[Date]

[SEAC opinion number]

Opinion of the Committee for Risk Assessment

and

Opinion of the Committee for Socio-economic Analysis

on an Annex XV dossier proposing restrictions of the manufacture, placing on the market or use of a substance within the EU

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular the definition of a restriction in Article 3(31) and Title VIII thereof, the Committee for Risk Assessment (RAC) has adopted an opinion in accordance with Article 70 of the REACH Regulation and the Committee for Socio-economic Analysis (SEAC) has adopted an opinion in accordance with Article 71 of the REACH Regulation on the proposal for restriction of

Chemical name(s): **Substances in single-use baby diapers**

EC No.: **-**

CAS No.: **-**

This document presents the opinions adopted by RAC and SEAC and the Committee's justification for their opinions. The Background Document, as a supportive document to both RAC and SEAC opinions and their justification, gives the details of the Dossier Submitters proposal amended for further information obtained during the consultation and other relevant information resulting from the opinion making process.

PROCESS FOR ADOPTION OF THE OPINIONS

France has submitted a proposal for a restriction together with the justification and background information documented in an Annex XV dossier. The Annex XV report conforming to the requirements of Annex XV of the REACH Regulation was made publicly available at https://echa.europa.eu/restrictions-under-consideration on **21 December 2020**. Interested parties were invited to submit comments and contributions by **21 June 2021**.

ADOPTION OF THE OPINION

ADOPTION OF THE OPINION OF RAC:

Rapporteur, appointed by RAC: **Veda VARNAI**

Co-rapporteur, appointed by RAC: **Sonja KAPELARI**

The opinion of RAC as to whether the suggested restrictions are appropriate in reducing the risk to human health and/or the environment was adopted in accordance with Article 70 of the REACH Regulation on **16 September 2021**.

The opinion takes into account the comments of interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The opinion of RAC was adopted **by consensus**.

ADOPTION OF THE OPINION OF SEAC

Rapporteur, appointed by SEAC: **Simon COGEN**

Co-rapporteur, appointed by SEAC: **Marit MÅGE**

The draft opinion of SEAC

The draft opinion of SEAC on the proposed restriction and on its related socio-economic impact has been agreed in accordance with Article 71(1) of the REACH Regulation on **9 September 2021.**

The draft opinion takes into account the comments from the interested parties provided in accordance with Article 69(6)(a) of the REACH Regulation.

The draft opinion takes into account the socio-economic analysis, or information which can contribute to one, received from the interested parties provided in accordance with Article 69(6)(b) of the REACH Regulation.

The draft opinion was published at https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e1840698d5 on **15 September 2021**. Interested parties were invited to submit comments on the draft opinion by **14 November 2021**.

The opinion of SEAC

The opinion of SEAC on the proposed restriction and on its related socio-economic impact was adopted in accordance with Article 71(1) and (2) of the REACH Regulation on **[date of adoption of the opinion]**. **[**The deadline for the opinion of SEAC was in accordance with Article 71(3) of the REACH Regulation extended by **[number of days]** by the ECHA decision **[number and date]]**[1].

[The opinion takes into account the comments of interested parties provided in accordance with Article[s 69(6) and][5] 71(1) of the REACH Regulation.**] [**No comments were received from interested parties during the consultation in accordance with Article[s 69(6) and][3] 71(1)**]**[6].

[1] Delete the unnecessary part(s)

The opinion of SEAC was adopted **by [consensus.][a simple majority]** of all members having the right to vote. [The minority position[s], including their grounds, are made available in a separate document which has been published at the same time as the opinion**.]**[6].

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Tables

1. OPINION OF RAC AND SEAC

The restriction proposed by the Dossier Submitter is:

Substances	Conditions of the restriction
Formaldehyde (CAS Number: 50-00-0) Polychlorobiphenyls (DL-PCBs and NDL-PCBs)[2] Polycyclic aromatic hydrocarbons (PAHs) Polychlorinated dibenzo-p-dioxins (PCDDs) Polychlorinated dibenzofurans (PCDFs) The PAHs, PCDDs, PCDFs, and DL-PCBs involved in this restriction are listed in the table 1.	1. Shall not be placed on the market, after the 01/01/2024, in any of the disposable baby diapers such as: ○ **Traditional baby diapers,** ○ **Diaper pants** or **training pants** for toilet-training the child, ○ **Night diapers**, intended for children over three years of age, in order to help them with toilet training at night, ○ **Swimming diapers**, used when babies/children are engaging in water activities. Intended to be used for children and infants, if, the substances migrate in a concentration equal to or above the limits specified in paragraph 2. 2. For the entire articles listed in paragraph 1, the following substances should not migrate in a concentration equal to or greater than the limits specified below: i. Formaldehyde in individual migration limit equal to or greater than **0.42 mg/kg of diaper** for all the entire articles specified in paragraph 1. ii. The sum of the quantified PCDDs, PCDFs, and DL-PCBs in a migration limit equal to or greater than **0.0017 ng_{TEQ}[3]/kg of diaper** for all the entire articles specified in paragraph 1. iii. The sum of the quantified PCBs in a migration limit equal to or greater than **112 ng/kg of diaper** for all the entire articles specified in paragraph 1. iv. The sum of the detected or quantified PAHs in a migration limit equal to or greater than **0.023 ng_{TEQ}/kg of diaper** for all the entire articles specified in paragraph 1.

[2] DL-PCBs (dioxin like) PCBs and NDL-PCBs (non-dioxin-like) PCBs

[3] TEQ used are the ones from WHO 2005, please refer to Annex B

3. Paragraphs 1 to 2 shall apply without prejudice to the application of any stricter restrictions or existing regulations.

4. Paragraphs 1 to 2 shall not apply to

i. Re-usable diapers

ii. Incontinence diapers as defined as a medical device in the sense of the regulation EU 2017/745

5. An analytical method developed using extraction by urine simulant in a whole diaper shall be used as the test method for demonstrating the conformity of articles to paragraphs 1 and 2. A standardized method needs to be defined.

The restriction shall apply 24 months after its entry into force.

Table 1 List of substances that are involved in this restriction proposal

Group of substances	Substance name	CAS Number	EC number
Formaldehyde	formaldehyde	50-00-0	200-001-8
PAHs	benzo[*c*]fluorene	205-12-9	205-908-2
	benz[*a*]anthracene	56-55-3	200-280-6
	cyclopenta[*c,d*]pyrene	27208-37-3	-
	Chrysene	218-01-9	205-923-4
	5-methylchrysene	3697-24-3	-
	benzo[*e*]acephenanthrylene	205-99-2	205-911-9
	benzo[*k*]fluoranthene	207-08-9	205-916-6
	benzo[*j*]fluoranthene	205-82-3	205-910-3
	benzo[*e*]pyrene	192-97-2	205-892-7
	benzo[*def*]chrysene	50-32-8	200-028-5
	dibenz[*a,h*]anthracene	53-70-3	200-181-8
	indeno[1,2,3-*c,d*]pyrene	193-39-5	205-893-2
	benzo[*g,h,i*]perylene	191-24-2	205-883-8
	dibenzo[*def,p*]chrysene	191-30-0	205-886-4
	naphtho[1,2,3,4-*def*]chrysene	192-65-4	205-891-1
	benzo(*r,s,t*)pentaphene	189-55-9	205-877-5
	dibenzo[*b,def*]chrysene	189-64-0	205-878-0
PCDDs	2,3,7,8-tetrachlorodibenzo[*b,e*][1,4]dioxin; 2,3,7,8-TCDD	1746-01-6	217-122-7
	1,2,3,7,8-pentachlorodibenzo-*p*-dioxin; 1,2,3,7,8-PeCDD	40321-76-4	-

	1,2,3,4,7,8-hexachlorodibenzo-*p*-dioxin; 1,2,3,4,7,8-HxCDD	39227-28-6	-
	1,2,3,6,7,8-hexachlorodibenzo-*p*-dioxin; 1,2,3,6,7,8-HxCDD	57653-85-7	-
	1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin; 1,2,3,7,8,9-HxCDD	19408-74-3	-
	1,2,3,4,6,7,8-heptachlorodibenzo-*p*-dioxin; 1,2,3,4,6,7,8-HpCDD	35822-46-9	-
	octachlorodibenzo-*p*-dioxin; OCDD	3268-87-9	-
PCDFs	2,3,7,8-tetrachlorodibenzofuran; 2,3,7,8-TCDF	51207-31-9	-
	1,2,3,7,8-pentachlorodibenzofuran; 1,2,3,7,8-PeCDF	57117-41-6	-
	2,3,4,7,8-pentachlorodibenzofuran; 2,3,4,7,8-PeCDF	57117-31-4	-
	1,2,3,4,7,8-hexachlorodibenzofuran; 1,2,3,4,7,8-HxCDF	70648-26-9	-
	1,2,3,6,7,8-hexachlorodibenzofuran; 1,2,3,6,7,8-HxCDF	57117-44-9	-
	2,3,4,6,7,8-hexachlorodibenzofuran; 2,3,4,6,7,8-HxCDF	60851-34-5	-
	1,2,3,7,8,9-hexachlorodibenzofuran; 1,2,3,7,8,9-HxCDF	72918-21-9	-
	1,2,3,4,6,7,8-heptachlorodibenzofuran; 1,2,3,4,6,7,8-HpCDF	67562-39-4	-
	1,2,3,4,7,8,9-heptachlorodibenzofuran; 1,2,3,4,7,8,9-HpCDF	55673-89-7	-
	octachlorodibenzofuran; OCDF	39001-02-0	-
PCBs	All the PCBs (DL and NDL are included in the scope of the restriction)		-

1.1. THE OPINION OF RAC

RAC considers that the proposed restriction on **substances in single-use baby diapers** is not justified because the risk could not be demonstrated for formaldehyde and PCDD/Fs/DL-PCBs and could not be characterised for PAHs and NDL-PCBs.

RAC has formulated its opinion on the proposed restriction based on an evaluation of the information related to:

- the identified risk;
- the options identified to reduce the risk;
- the comments submitted by interested parties, as well as;
- other available information as recorded in the Background Document.

1.2. THE OPINION OF SEAC

See SEAC opinion.

2. SUMMARY OF THE PROPOSAL AND OPINION

2.1. Summary of the proposal

The restriction proposal aims at reducing health risks associated in the assessment of the Dossier Submitter with the wearing of single-use baby diapers by children and infants under the age of three.

Diapers are made of several materials whose purpose is to absorb and retain the child's urine and faeces, thus keeping their skin cleaner and dryer. Since the 1990s, single-use baby diapers have been used by more than 90% of families in most of the European Union countries. Estimates of the total number of single-use baby diapers used per baby before the age of toilet training range from 3800 to 4800.

The Dossier Submitter reports that formaldehyde, polycyclic aromatic hydrocarbons (PAHs), polychlorinated dibenzo-p-dioxins (dioxins or PCDDs), polychlorinated dibenzofurans (furans or PCDFs) and polychlorobiphenyls (PCBs) have been detected and/or quantified in single-use baby diapers through analytical tests using extraction with a urine simulant. These substances are either classified for carcinogenicity, mutagenicity and skin sensitisation according to the CLP Regulation (formaldehyde), investigated for their carcinogenic potential (PAHs), or associated with various health effects, including toxic effects, adverse reproductive, mutagenic, genotoxic and endocrine effects (PCDD/Fs, PCBs). This indicates the potential exposure of children and infants wearing these articles to the named groups of substances and the potential for various health effects.

The materials used for the production of baby diapers can include hazardous substances in the form of impurities/contaminants. The Dossier Submitter carried out analytical research in order to identify which substances could pose a risk for babies and infants under the age of three, since this population is particularly vulnerable to adverse effects of exposure to chemicals and should therefore be protected from hazardous substances.

Based on the results of investigations of diaper samples, which were presented in a report published by the French Agency for Food, Environmental and Occupational Health and Safety (ANSES, 2019), further analyses were carried out on diapers sold on the French market, using an experimental urine simulant methodology to extract the substances of concern from the diaper samples. Using these results as the basis for a quantitative risk assessment, the Dossier Submitter selected the substances to be included in the scope of the restriction proposal (i.e., formaldehyde, PAHs, PCDDs/Fs, DL-PCBs).

The Dossier Submitter concluded that the risks from formaldehyde, PAHs, PCDD/Fs, and/or PCBs in single-use baby diapers are not adequately controlled. An analysis of several risk management options (RMOs) was therefore conducted to identify the most appropriate measure to address the risk and to define the scope and conditions of the restriction proposal. The Dossier Submitter further concluded that a restriction under REACH is the most appropriate RMO. Two restriction options were further analysed in the impact assessment. They both aim at limiting the migration of substances in single-use baby diapers placed on the market but differ with respect to which substances are included.

The restriction options further assessed by the Dossier Submitter were:

- **Restriction option 1 (RO1):** Limiting the migration of formaldehyde, the sum of 17 detected or quantified PAHs, the sum of quantified PCDD/Fs and DL-PCBs and the sum of quantified PCBs.

- **Restriction option 2 (RO2):** Limiting the migration of all the substances and sum of substances listed in RO1 and all the congeners of the PAHs, PCDD/Fs and DL-PCBs.

A quantitative risk assessment was performed for each of the substances detected or quantified, based on which the Dossier Submitter considers these substances to have the potential to induce adverse effects in babies if present in single-use baby diapers that come into contact with the skin.

On the basis of an analysis of the effectiveness, practicality and monitorability of RO1 and RO2, and the impact assessment performed, RO1 was proposed by the Dossier Submitter as the preferred restriction option.

2.2. Summary of the opinion

RAC concurred, in general, with the Dossier Submitter that the substances in the scope of the proposal might have the potential to induce adverse effects in babies if they are present[4] (or are present above certain concentrations) in single-use baby diapers that come (directly or indirectly via e.g., urine) in contact with the skin.

RAC considered that the separate grouping approaches for PAHs, for PCDDs/Fs and DL-PCBs and for PCBs (DL and NDL) were well justified. NDL-PCBs were not included in the ANSES (2019) study. Nevertheless, RAC considered that inclusion of these substances in the assessment (within the group of total PCBs) was justified due to their hazardous properties and since it is known that humans are always exposed to complex mixtures of PCBs comprising both DL-PCBs and NDL-PCBs.

In terms of the hazard assessment:

- **Formaldehyde**: RAC considered that the internal DNEL of 0.075 mg/kg/day derived by the Dossier Submitter is highly uncertain with respect to its relevance to a dermal route of exposure, which in the view of the Committee is the only relevant exposure route for this restriction proposal. In RAC's view, systemic effects of formaldehyde exposure via the dermal route are unlikely, and local effects, i.e., skin sensitisation, are more relevant.

- **PAHs**: RAC agreed with the Dossier Submitter's choice of carcinogenicity as the most critical long-term human health effect. It also supported the Dossier Submitter's approach to derive a DMEL (at a 10^{-6} risk level) of 4 pg/kg bw/day for PAH mixtures based on dermal studies (Schmähl et al., 1977; Fhl, 1997) assessed by BAuA (2010), and of 6 pg/kg bw/day for BaP alone based on dermal carcinogenicity data for benzo[a]pyrene (BaP) obtained in mice (Knafla et al., 2006), with the application of

[4] RAC notes that for some of the long-term effects mentioned above (related to PAH exposure), no threshold could be derived.

Toxic Equivalency Factor (TEFs).

- **PCDDs/Fs/DL-PCBs**: RAC supported the Dossier Submitter's approach to derive an internal DNEL based on an epidemiological study in children (Minguez-Alarcon et al., 2017). RAC considered that the selected critical effect (fertility) is relevant and sensitive and agreed with the proposed internal DNEL of 0.3 pg_{TEQ}/kg bw/day. However, RAC noted that the uncertainties in the critical study are substantial, and that they are expected to lead to a lower (more conservative) DNEL than necessary.

- **PCBs (DL and NDL)**: RAC concurred with the Dossier Submitter's approach to use oral data from long-term toxicity studies in monkeys and agreed with the proposed internal DNEL of 20 ng/kg bw/day. RAC considered that the critical effects chosen (immunotoxicity supported by neurobehavioral changes) are sensitive and relevant for humans, and that the critical studies are reliable and well reported.

RAC identified significant uncertainties/shortcomings in the reported risk assessment, as follows:

- Methodology used for the extraction, detection and quantification of substances from single-use diapers:
    - Whilst the Committee supported the use of the urine simulant extraction method in principle, it noted that the method requires further validation (e.g., representativeness of extraction time and volumes), and harmonisation to ensure its repeatability/reproducibility and relevance for use in risk assessment.
    - Further consideration should be given to prevent samples from being contaminated (e.g., replacement of manual steps in the extraction protocol; avoiding keeping the diaper in open containers overnight during the extraction period) and adequate control of any contamination by the use of blank sample analysis.
    - There is a lack of information on blanks in the first set of analyses (ANSES, 2019) and the blanks were not subtracted in the second set of analyses (performed in 2019), affecting the reliability of the results.
    - For PAHs, an adequate explanation was not provided as to why the results (including LoDs/LoQs) quantified by SCL and DGCCRF/INC are orders of magnitude lower in the 2019 analytical campaign compared to the 2018 campaign.
    - For PAHs, the lowest limit of detection (LoD) used is orders of magnitude greater than the proposed migration limits. Therefore, it is not known how many samples were above/below the proposed migration limits. In addition, such a high LoD in relation to the limit value would also make the implementation of the restriction proposal challenging because interested parties (enforcement, industry) would not know if a diaper is compliant with the restriction requirements or not.
    - The levels of dioxins, furans and PCBs determined by the urine simulant (water-based solution) extraction method were reported by the Dossier Submitter to exceed the risk threshold, while these substances, although highly lipophilic, were detected at lower concentrations or even not detected

after solvent-based extraction of shredded diaper samples (ANSES, 2019); this lack of consistency raises uncertainties about the reliability of the urine simulant extraction or analytical methodology.

- The measurement of PCDD/Fs in samples could potentially be caused by contamination from laboratory water (background amounts of PCDD/Fs, which can regularly be detected in laboratory water of accredited laboratories that are specialised in dioxin/furan analyses, are within the concentration ranges that would be required to determine the levels of PCDD/Fs in the proposed restriction) questioning the reliability of the data.

- Daily exposure/dose calculation:
  - There are concerns regarding serious overestimation of the levels of extractable substance compared to a realistic worst-case scenario of conditions of use, primarily due to a two order of magnitude larger volume of urine simulant extracted from a diaper sample (220 to 250 mL) compared to the volume that is expected during actual conditions of use (1 to 2 mL). Also, the volume of urine simulant used in the Dossier Submitter's calculations was two to three times greater than it is normally expected for two months to 12 months old babies.
- Risk characterisation:
  - RAC does not support the use of an allocation factor of 10% of the risk characterisation ratio (to account for aggregate exposure from different routes) for substances with local dermal effects (formaldehyde and PAHs). For other substances with systemic effects (for instance, those caused by PCDD/Fs and PCBs), the use of an allocation factor of 10% has not been sufficiently justified by the Dossier Submitter.

In conclusion, and after considering the shortcomings and uncertainties identified above, RAC is of the opinion that the EU-wide risk for babies and infants wearing single-use diapers has not been demonstrated for the substances in the scope of the Annex XV dossier.

For **formaldehyde**, RAC concludes that risk of skin sensitisation is a more appropriate assessment endpoint in diapers than the systemic effects proposed by the Dossier Submitter and that exposure to formaldehyde via diapers would be likely to be 20 times below reported elicitation thresholds for sensitisation (see section 3.1.4). RAC also notes that as formaldehyde has a harmonised classification as a skin sensitiser it would be restricted in single-use diapers by means of the proposed restriction on skin sensitisers under REACH[5]; as such no further action for formaldehyde would appear to be necessary.

For **PCDD/Fs** and **DL-PCBs**, RAC undertook a sensitivity analysis of the Dossier Submitter's exposure assessment using more realistic conditions of use and concluded that risks for the endpoints assessed by the Dossier Submitter would be unlikely to occur from the wearing of

[5] The restriction proposes to restrict the use of all substances classified as skin sensitisers according to the CLP Regulation, as well as a list of disperse dyes, in various articles, including single-use baby diapers. The opinion was adopted in September 2020 and, at the time of writing, a decision by the European Commission is still pending. More information on this restriction proposal can be found here: https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e182446136

single-use baby diapers because the assumptions used by the Dossier Submitter (and their inherent uncertainties) would tend to result in significant overestimates of exposure and risk. Nevertheless, RAC notes that the size of the allocation factor used for the risk characterisation is a critical uncertainty in determining whether a risk would occur for certain sub-populations (i.e., formula-fed infants) and that the Dossier Submitter did not assess the potential for risks via all potentially relevant endpoints (e.g., via endocrine disruption). Therefore it is not possible to conclude that there are no potential risks from these substances in single-use diapers based on the available assessment (see section 3.1.4).

For **PAHs**, RAC concluded that the available analytical data are of insufficient quality for a reliable exposure assessment, which means that risks cannot be reliably characterised (see section 3.1.4).

For **NDL-PCBs**, there are no analytical data upon which to base an assessment. Therefore, similarly to PAHs, RAC cannot conclude whether NDL-PCBs in diapers pose a risk or not (see section 3.1.4).

RAC points out that the degree of uncertainty associated with this proposal is greater than other, apparently similar, restriction proposals such as that for skin sensitising substances[6] where there was epidemiological data indicating the scale of the risks (and health impacts) that were not adequately controlled. For the restriction proposed on single-use baby diapers, there is no epidemiological data demonstrating an association between health effects and the wearing of diapers. On this basis, a simple comparison between these two restrictions is not possible. In the case of the skin sensitisers proposal, it was considered reasonable for RAC to support the introduction of concentration limits for a broad range of substances with a harmonised classification (as skin sensitisers), despite an absence of validated analytical methods, as it was not the analytical data that was underpinning the restriction, but the harmonised classification and the associated epidemiological data. The opinion of RAC on the skin sensitisers proposal noted that "*for most of the targeted skin sensitisers in the scope of this restriction proposal, the concentration limits, are far below the highest approximated concentrations in textile and leather at point of sale. Therefore, the risks from these substances are not adequately controlled for these uses*". As a general principle, there is an important difference between justifying a restriction based on analytical data of exposure (e.g. chemicals in single-use baby diapers) and restrictions to address widespread health concerns which require analytical methodology to be developed for the purpose of enforcement (e.g. the skin sensitisers proposal). The availability of reliable exposure data is comparatively more important in the former case, than the latter.

RAC is of the opinion that the following information (by the Dossier Submitter or other bodies) would be needed to address the identified (main) uncertainties concerning the exposure:

- Detailed information about
    - sample preparation;
    - analytical quality control and assurance information (including the use of blank

[6] Restriction on the placing on the market of textile, leather, hide and fur articles containing skin sensitising substances, ECHA (2020): https://echa.europa.eu/de/registry-of-restriction-intentions/-/dislist/details/0b0236e182446136

samples) for analytical data.

In addition, if the risks of substances in single-use baby diapers are reconsidered in the future (i.e., not as part of the opinion development on this Annex XV dossier) the following topics should be elaborated in order to minimise the uncertainties:

- appropriate rewet factor;
- evaluation of direct exposure;
- reproducibility and relevance (to reasonably foreseeable conditions of use) of urine simulant extraction methodology;
- justification for the use of (and value for) an allocation factor

RAC notes that until the uncertainties/shortcomings concerning the restriction proposal on single-use baby diapers are resolved, the voluntary action by industry (the EDANA Stewardship Programme for Absorbent Hygiene Product) could further reduce the concentration of the substances in the scope of the proposed restriction (and also of other substances like phthalates, organotins, metals), in all single-use diapers placed on the European market. However, RAC does not see voluntary action as a substitute for a restriction under REACH should the risk from specific substances be adequately demonstrated. According to comments made by industry, currently about 85% of European single-use diaper manufacturers follow this programme, although this has not been confirmed by RAC. RAC notes that industry´s voluntary action has not been evaluated by RAC in terms of the migration limits it specifies or how effectively the member companies have implemented these limits, nor how it deals with imports of diapers.

RAC points out that the substances in the scope of the restriction proposal should be kept to a level as low as possible/feasible, and preferably not be present at all. RAC notes that the POPs (Persistent organic pollutants) regulation already covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed.

3. JUSTIFICATION FOR THE OPINION OF RAC AND SEAC

3.1. IDENTIFIED HAZARD, EXPOSURE/EMISSIONS AND RISK

Justification for the opinion of RAC

3.1.1. Description of and justification for targeting of the information on hazard(s) and exposure/emissions) (scope)

Summary of proposal:

This restriction proposal aims at minimising health risks associated with the wearing of single-use baby diapers by children and infants under the age of three. Single-use diapers are placed on the market and according to the Dossier Submitter can contain formaldehyde, polycyclic aromatic hydrocarbons (PAHs), polychlorinated dibenzo-p-dioxins (dioxins or PCDDs),

polychlorinated dibenzofurans (furans or PCDFs) and/or polychlorobiphenyls (PCBs).

In 2019, ANSES published a report on the risks associated with the presence of hazardous substances in single-use baby diapers and made recommendations for risk reducing measures. Analyses were carried out in a survey of 19 diaper samples (2018) and 32 samples (2019), reportedly including the best-selling products on the French market. The analytical laboratory developed and applied an experimental urine simulant methodology to extract the substances of concern from diaper samples. A quantitative health risk analysis was then performed based on the various analyses undertaken by the SCL and the INC, including solvent extractions in shredded whole diapers or diaper parts (SCL, 2017; INC, 2017 and 2018; Group'Hygiène, 2018), extractions with a urine simulant in shredded whole diapers (SCL, 2017), and extractions with various urine simulants in whole diapers (SCL, 2018; Group'Hygiène, 2018). The quantitative health risk analysis was first undertaken using a "worst-case" scenario in order to rapidly eliminate substances posing no health risks. In this scenario, parameters corresponding to a new-born with a very low body weight (2.6 kg) who is changed very frequently (12 times per day), with 100% dermal absorption, were used. In cases when the toxic reference value was exceeded, a "realistic" approach (a scenario whose parameters were intended to replicate commonly encountered actual conditions of use) was implemented separately for six age groups of children (0-6, 6-12, 13-18, 19-24, 25-30, 31-36 months). For the substances below the toxic reference value, the Dossier Submitter considered the possibility of an increase above the toxic reference value due to aggregate exposure via various exposure routes. Using these results as the basis for a quantitative risk assessment, they selected the substances to be included in the proposed restriction.

According to the Dossier Submitter, the risk calculations for the substances detected or quantified in the migration tests using whole diapers, showed that for children aged 0 to 36 months it is not possible to rule out a health risk associated with the routine wearing of single-use diapers for: formaldehyde, the sum of 17 PAHs, the sum of PCDD/Fs and DL-PCBs, the sum of PCBs.

Based on these results, the Dossier Submitter concluded that the risk from formaldehyde, PAHs, PCDD/Fs, and/or PCBs in single-use baby diapers is not adequately controlled, and proposed the substances listed in Table 1 to be included in the scope of a restriction (RO1). Non-dioxin-like PCBs (NDL-PCBs) were not measured in single-use baby diapers. However, these substances are included in the scope of the proposed restriction since it is commonly known that when DL-PCBs can be quantified, NDL-PCBs are also likely to be present. NDL-PCBs have also been quantified in similar articles, i.e., in incontinence diapers (UFC Que Choisir, 2019).

Hazardous properties of the substances within scope

Formaldehyde has a harmonised EU classification for carcinogenicity, mutagenicity and skin sensitisation according to the CLP Regulation. Furthermore, formaldehyde has been restricted in toys, in other articles and is proposed to be restricted for its skin sensitisation property in single-use baby diapers in the skin sensitisers restriction proposal according to REACH.

PAHs have been investigated for their carcinogenic potential and many share the same genotoxic mechanism of action. The PAHs addressed by this restriction proposal have a harmonised or a self-classification for carcinogenicity under the CLP regulation. Furthermore, some of these PAHs have been examined by RAC and SEAC for a restriction under REACH

when present in granules and mulches used in synthetic turf pitches, or in loose forms at playgrounds and other sports facilities (ECHA 2019).[7]

PCDD/Fs and **DL-PCBs** have been targeted as potentially requiring restriction due to their potential to cause various adverse health effects, including hepatic, immunological, neurological, metabolic and endocrine toxic effects, adverse reproductive effects, mutagenicity effects and genotoxic effects.

Proposed migration limits are shown in Table 2.

Table 2 Proposed migration limits

Substance/group of substances	Proposed migration limit
Formaldehyde	
Formaldehyde	**0.42 mg/kg of diaper**
PCDDs/PCDFs/PCBs	
Sum of the quantified PCDDs/Fs/DL-PCBs **in TEQ**[1]	**0.0017 ng_{TEQ}/kg of diaper**
Sum of the quantified total PCBs	**112 ng/kg of diaper**
PAHs	
The sum for the detected or quantified PAH **in TEQ**[2]	**0.023 ng_{TEQ}/kg of diaper**

[1] TEQ from WHO 2005; [2] The Dossier Submitter selected TEFs for 17 PAHs from the existing TEFs defined by various organisations (OEHHA, 1993 revised in 2015; INERIS, 2003; AFSSA, 2003; DFG, 2008 cited in BfR, 2009b; US EPA, 2010) (Table 39 in the Background Document)

RAC conclusion(s):

Children, particularly infants, are especially vulnerable to the adverse effects of exposure to chemicals. Formaldehyde, PAHs, PCDDs (dioxins), PCDFs (furans), and PCBs (dioxin-like (DL) and non-dioxin-like (NDL)) possess various acute and chronic hazardous properties.

The risk posed by these substances was assessed quantitatively by the Dossier Submitter using a risk quotient approach. For substances with a threshold effect (formaldehyde, PCDD/Fs and DL-PCBs), and for substances with a non-threshold effect (PAHs), the risk level was characterised by means of a RCR, which is the ratio between the daily exposure dose and the appropriate internal DNEL or dermal DMEL (the latter expressed for PAHs at the 10^{-6} risk level). The numerical value of this ratio was used to determine whether or not the dose received exceeded the DNEL or DMEL. Daily exposure dose was based on the concentration of the chemical extracted with a urine simulant from a whole diaper, considering the weight

[7] More information on this restriction proposal can be found here: https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e181d5746d

of the diaper, the volume of urine simulant used for the extraction, the frequency of diaper changes, the fraction absorbed by the skin, and the body weight of a child.

RAC concurs, in general, with the Dossier Submitter that these substances might have the potential to induce adverse effects in babies if present[8] (or present above certain concentrations) in single-use baby diapers that come (directly or indirectly via e.g., urine) in contact with the skin. RAC also generally agrees with the Dossier Submitter that for the above substances, long-term effects are more relevant for this restriction proposal than acute effects, since the latter generally occur at higher exposure levels compared to long-term effects. However, RAC concludes that regarding formaldehyde, skin sensitisation would be a more relevant critical effect for this restriction proposal than long-term systemic effects observed in animal experiments (e.g., nephrotoxicity, reduced body weight gain).

The details concerning long-term hazardous effects of the substances/groups of substances listed above and the derived migration limits are dealt with in section 3.1.1.

RAC considers that the separate grouping approaches for **PAHs**, for **PCDDs/Fs and DL-PCBs** and for **PCBs** (DL and NDL) are well justified (see section *"Key elements underpinning the RAC conclusion"* below).

NDL-PCBs were not included in the ANSES (2019) study. RAC, nevertheless, considers that inclusion of these substances in the assessment (within the group of total PCBs) is justified due to their hazardous properties and since it is known that humans are always exposed to complex mixtures of PCBs comprising both DL-PCBs and NDL-PCBs.

RAC notes that there is very limited information available for the risk assessment of hazardous chemicals in baby diapers and a quantitative risk assessment for the chemicals in the scope (which are present at the levels of impurities in diaper samples on the EU market) is technically challenging and is associated with numerous uncertainties. It should also be noted that none of these substances are intentionally used in single-use baby diapers, but they are rather residues or contaminants (see *"Key elements underpinning the RAC conclusion(s)"* for further discussion).

Based on the above, RAC considers that this restriction proposal represents a precautionary approach, aiming to minimise exposure of children to hazardous chemicals in the scope. However, due to the uncertainties and shortcomings related to the exposure assessment and risk characterisation, RAC concludes that the EU-wide risk for babies and infants wearing single-use diapers has not been demonstrated for the substances in the scope of the Annex XV dossier.

For **formaldehyde**, RAC concludes that risk of skin sensitisation is a more appropriate assessment endpoint in diapers than the systemic effects proposed by the Dossier Submitter and that exposure to formaldehyde via diapers would be likely to be 20 times below reported elicitation thresholds for sensitisation (see section 3.1.4). RAC also notes that as formaldehyde has a harmonised classification as a skin sensitiser it would be restricted in single-use diapers by means of the proposed restriction on skin sensitisers under REACH as

[8] RAC notes that for some of the long-term effects mentioned above (related to PAH exposure), no threshold could be derived.

such no further action for formaldehyde would appear to be necessary.

For **PCDD/Fs** and **DL-PCBs**, RAC has undertaken a sensitivity analysis of the Dossier Submitter's exposure assessment using more realistic conditions of use and concludes that risks for the endpoints assessed by the Dossier Submitter would be unlikely to occur from the wearing of single-use baby diapers because the assumptions used by the Dossier Submitter (and their inherent uncertainties) would tend to result in significant overestimates of exposure and risk. Nevertheless, RAC notes that the size of the allocation factor used for risk characterisation is a critical uncertainty in determining whether a risk would occur for certain sub-populations (i.e., formula-fed infants) and that Dossier Submitter did not assess the potential for risks via all potentially relevant endpoints (i.e., via endocrine disruption). Therefore, it is not possible to conclude that there are no potential risks from these substances in single-use diapers based on the available assessment (see section 3.1.4).

For **PAHs**, RAC concludes that the available analytical data are of insufficient quality for a reliable exposure assessment, which means that risks cannot be reliably characterised (see section 3.1.4).

For **NDL-PCBs**, there are no analytical data upon which to base an assessment. Therefore, similar to PAHs, RAC cannot conclude whether NDL-PCBs in diapers pose a risk or not (see section 3.1.4).

Fragrances, volatile organic compounds (VOCs), pesticides, and skin sensitisers (except those already included in the scope due to their other hazardous properties) were not included in the scope of this restriction proposal. Since they were not assessed by the Dossier Submitter, RAC cannot evaluate the appropriateness of the Dossier Submitter's decision to not include these substances in the scope of the restriction proposal.

Key elements underpinning the RAC conclusion(s):

Formaldehyde, and many of the PAHs, have a harmonised classification, making them relevant for this restriction proposal. Most of the substances in the other groups do not have harmonised classifications. They are either self-classified by industry, or there is no classification related to human health, but their hazardous properties have been recognised by different international bodies (e.g., WHO, IARC, ATSDR; see section 3.1.2. below).

Grouping of PAHs is well justified. Many PAHs share the same genotoxic mechanism of action. From the 17 PAHs included in the scope of the proposal, eight are classified as Carc. 1B (H350) according to CLP Regulation (EC 1272/2008), benzo[d,e,f]chrysene is also classified as Muta 1B (H340) and chrysene as Muta. 2 (H341), and further three substances are proposed to be classified as Muta. 2 (H341) and Carc. 1B (H350) by RAC.

Grouping of PCDDs, PCDFs and DL-PCBs: PCDDs (dioxins) and PCDFs (furans) are grouped under the term PCCD/Fs. PCCD/Fs form a group of 210 theoretical compounds or congeners: there are 75 possible PCDDs and 135 possible PCDFs (EFSA, 2018[9], Jaspers et al., 2014). Seven PCCDs and ten PCDFs are bioaccumulative in animals and humans. Human

[9] Risk for animal and human health related to the presence of dioxins and dioxin-like (DL-)PCBs in feed and food, adopted 14 June 2018; doi: 10.2903/j.efsa.2018.5333.

exposure to dioxins and furans has been associated with a variety of adverse effects, including skin disorders (e.g., chloracne), hepatotoxicity, immunotoxicity, reproductive toxicity and carcinogenicity.

All DL-PCB and many NDL-PCB congeners accumulate in humans and animals[10] (Larsen et al., 2014). Human studies have identified associations between exposure to PCB mixtures and adverse immunological, reproductive, neurological and dermatological effects and cancer, and studies in primates showed adverse effects related to exposure to commercial mixtures of PCBs (WHO, 2003; ATSDR, 2000).

Grouping PCDDs/Fs and DL-PCBs is justified since both DL-PCBs and relevant PCDD/Fs are known to bind to the intracellular aryl hydrocarbon receptor (AhR) (EFSA, 2018). In addition, there are strong indications in epidemiological studies that fertility is declining due to exposure to these groups of substances. With regard to endocrine disrupting properties, it is noted that some PCDDs/Fs and PCBs are on the TEDX (The Endocrine Disruption Exchange Inc[11]) and the Sin List (Substitute It Now[12]).

Grouping of PCBs (DL-PCBs and NDL-PCBs): Joint FAO/WHO Expert Committee on Food Additives (JECFA) recognised that there are similarities in some of the reported effects for NDL-PCBs, and a risk estimation for combined exposure has been recommended (WHO, 2016). Some of the NDL-PCBs have hybrid activity, showing both dioxin-like and non-dioxin-like toxicity[13]. International bodies have identified seven 'indicator' PCBs that can be used to characterise the presence of PCB contamination. Six of these seven are NDL-PCBs and one is a DL-PCB (WHO, 2016). Also, it should be noted that humans are always exposed to complex mixtures of both DL-PCBs and NDL-PCBs, whose relative contribution to toxicity is unclear (WHO, 2016). RAC, therefore, agrees with the proposed grouping of these substances.

Available human and animal data provide very limited information for the assessment of health risk from hazardous chemicals present in baby diapers

There are some human studies that investigated whether disposable diapers' use in babies could be linked to increased risk for testicular cancer, but they did not study potential risk posed by specific substances in diapers. Rather, they were concerned with increased scrotal temperature due to diaper use (Møller, 2002; Partsch et al., 2000), and did not find the evidence for the association between use of disposable baby diapers and increased risk of

[10] A subgroup of 12 PCB congeners that are non-ortho or mono-ortho chlorine substituted and contain at least four chlorine substituents can easily adopt a coplanar structure and show toxicological properties similar to tetrachlorodibenzo-p-dioxin (TCDD) and other PCDD/Fs. This subgroup is termed DL-PCBs. Due to their lipophilic properties and poor degradation they accumulate in the food chain and in the human body (EFSA, 2018).

[11] https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list

[12] https://sinlist.chemsec.org

[13] Primary toxic action of NDL-PCBs is not via AhR binding, but it is proposed to be rather via agonistic effect on nuclear hormone receptors (the constitutive androstane receptor, CAR, and pregnane X receptor, PXR) (Larsen et al., 2014). Other potential mechanisms, such as activation of ryanodine receptors (RyRs; which play a crucial role in calcium signalling and neurotoxicity), are proposed as well, but are not as much explored as NDL-PCBs effects on nuclear hormone receptors (WHO, 2016).

testicular cancer later in life (Møller, 2002).

Animal data do provide information on the hazardous properties of the substances within the scope of the proposed restriction, but typically at doses that are markedly higher than real-life exposure levels via diapers, and predominantly using the oral exposure route in adult animals.

3.1.2. Information on hazard(s)

Summary of proposal:

For this restriction proposal, information on hazard properties was retrieved by the Dossier Submitter from published literature, reports and REACH registrations (in accordance with ECHA guidance on information gathering ECHA, 2012b).

Formaldehyde has a harmonised classification for carcinogenicity, mutagenicity, skin corrosion and skin sensitisation according to the CLP Regulation (skin corrosion category 1B, skin sensitisation category 1, mutagenicity category 2, carcinogenicity category 1B). Given the targeting of this restriction proposal, only effects observed following oral or dermal exposure were addressed.

PAHs have been investigated for their carcinogenic potential and many PAHs share the same genotoxic mechanism of action. Given the targeting of this restriction proposal, only mutagenicity and carcinogenicity were addressed.

In humans, brief exposure to high levels of PCDD/Fs may result in skin damage. Long-term exposure is associated with hepatic, immunological, neurological, metabolic and endocrine effects. It should be noted that PCDD/Fs are among the first 12 POPs (persistent organic pollutants) included in the Stockholm Convention in 2001.

Brief skin contact with PCBs causes local irritation, while repeated or prolonged contact may result in skin damage. Long-term exposure is associated with hepatic, immunological, neurological, metabolic and endocrine effects. PCBs like PCDD/Fs are also among the first 12 POPs covered the Stockholm Convention in 2001 (meaning they are known to be Persistent Organic Pollutants and regulated as such). Given the targeting of this restriction proposal, only effects observed following oral or dermal exposure were addressed.

For each chemical/group of chemicals, the human health reference values (HRVs) established by national (ANSES, US EPA, ATSDR, OEHHA, Health Canada, RIVM), European (EFSA, JECFA, ECHA) and international (WHO) organisations were identified, focusing on those developed for a chronic duration of exposure, which is regarded as most relevant in view of the context of this restriction proposal.

Since, dermal HRVs were not available except for PAHs, the Dossier Submitter chose chronic oral HRVs for formaldehyde, PCDD/Fs/DL-PCBs and total PCBs. After the selection of an HRV, the value was corrected for oral bioavailability in order to derive an internal dose (DNEL or slope factor) linked to the selected HRV.

DMEL were set for non-threshold effects of PAHs, while for other substances/groups of substances with threshold effects DNELs were set (see Table 3).

Table 3 Critical effects and DN(M)EL derivation for substances in the scope

Chemicals	HRV	Source	Value	Critical effect; species	Oral abs. (%)	internal DNEL/DMEL/TDI
Formaldehyde	Oral chr.	WHO/IPCS (2005)	TDI: 0.15 mg/kg/day	stomach irritation, nephrotoxicity; rats	50	0.075 mg/kg/day
PAHs	Der mal carc.	BAuA (2010) Knafla et al. (2006)	Slope factors	skin tumours; mice	NA	0.004 ng/kg/day for PAHs mixture 0.006 ng/kg bw/day for BaP
PCDD/Fs, DL-PCBs	Oral chr.	EFSA (2019)	TDI: 0.3 pg/kg bw/day	fertility effects; humans	100	0.3 pg/kg/bw/day
total PCBs (DL and NDL)	Oral chr.	WHO (2002b)	TDI: 20 ng/kg bw/day	immunotoxicity, neurobehavioral effects; monkeys	100	20 ng/kg bw/day

DL: dioxin like; NDL: non-dioxin-like; TDI: tolerable daily intake

RAC conclusion(s):

The Dossier Submitter retrieved detailed information on hazard properties from published literature, reports and REACH registrations, in accordance with ECHA guidance on information gathering (ECHA, 2012b).

RAC agrees that in the absence of toxicity data via the dermal route, an internal DNEL can be derived from the available oral (dietary) data (in line with Guidance on information requirements and chemical safety assessment, Chapter R.8, ECHA 2012).

Formaldehyde: RAC considers that the internal DNEL of 0.075 mg/kg/day derived by the Dossier Submitter from an oral chronic HRV based on histologically observed gastric changes and nephrotoxicity in rats is highly uncertain with respect to its relevance to a dermal route of exposure, which is the only relevant exposure route for this restriction proposal. Systemic effects of formaldehyde exposure via the dermal route are unlikely because:

- it is not well absorbed via the skin, and dermal absorption is limited to the cell layers immediately adjacent to the point of contact (ECHA, 2019);
- formaldehyde is rapidly metabolised at the site of initial contact and therefore distribution of formaldehyde to more distant organs is not likely, except from exposure to high concentrations (ECHA, 2019);
- there is no convincing evidence of formaldehyde-induced carcinogenic effects at distant sites or via routes of exposure other than inhalation;
- formaldehyde is present in diapers as an impurity, and high concentrations are not expected (2.75 mg/kg was the highest concentration found among 51 samples analysed by the SCL (Service Commun des Laboratoires)).

In such circumstances, local effects, i.e., skin sensitisation, is more relevant than systemic effects.

PAHs: RAC agrees with the critical effect chosen for PAHs since carcinogenicity is generally known to be the most critical long-term human health effect associated with PAH exposure (ECHA, 2019). The Dossier Submitter's approach is to derive a DMEL (at a 10^{-6} risk level) of 4 pg/kg bw/day for PAH mixtures based on dermal studies (Schmähl et al., 1977; Fhl, 1997) assessed by BAuA (2010), and of 6 pg/kg bw/day for BaP alone based on dermal carcinogenicity data for benzo[a]pyrene (BaP) obtained in mice (Knafla et al., 2006), with application of TEFs. RAC agrees with this approach as it considers the dermal route (which is the relevant route for this restriction proposal), and available carcinogenicity data on PAHs following dermal exposure.

PCDDs/Fs/DL-PCBs: The data on the dermal toxicity of these substances is rather limited. Therefore, RAC supports the Dossier Submitter's approach to derive an internal DNEL based on an epidemiological study in children (Minguez-Alarcon et al., 2017), in which the primary source of exposure to this group of substances was via diet, with dermal absorption, inhalation, and hand-to-mouth transfer from contaminated dust and soil as additional exposure routes. RAC considers that the selected critical effect (fertility) is relevant and sensitive, the critical study is well conducted and reported, with transparent methodology of HRV derivation, and agrees with the proposed internal DNEL of 0.3 pg_{TEQ}/kg bw/day. However, RAC notes that the uncertainties in the critical study are substantial, and that they are expected to lead to a lower (i.e., overprotective) DNEL than necessary.

PCBs (DL and NDL): Since a dermal HRV derived by another EU or non-EU regulatory body is not available, RAC concurs with the Dossier Submitter's approach to use oral data from long-term toxicity studies in monkeys and agrees with the proposed internal DNEL of 20 ng/kg bw/day. RAC considers that the critical effects chosen (immunotoxicity supported by neurobehavioral changes) are sensitive and relevant for humans, and that the critical studies are reliable and well reported.

Key elements underpinning the RAC conclusions

These are explained in detail and discussed in Annex I to the opinion.

3.1.3. Information on emissions and exposures

Summary of proposal:

Since the 1990s, single-use baby diapers have been used by more than 90% of families in most of the European Union (EDANA, 2011). Following chemical analysis performed in France (DGCCRF/INC, the French National Consumer Institute) and SCL (Service Commun des Laboratoires), single-use baby diapers have been reported as containing various hazardous chemicals that may impair the health of babies wearing/using these articles. Three types of analyses[14] were performed with single-use baby diapers.

The analyses were performed on 51 different diapers that were available on the French market between 2017 and 2019. The Dossier Submitter reported the exposure level according to the ECHA R.15 guidance, meaning that they calculated the Q95 of the distribution of the 51

[14] Solvent extraction on shredded diapers, solvent extraction on shredded parts of diapers and simulant urine migration tests on shredded whole diapers and on whole diapers.

samples. The following approach was chosen:

- if the substance was not detected, the LoD was retained,
- if the substance was detected, the LoQ was retained,
- if the substance was quantified, the concentration was retained.

The assessment of the exposure to chemical substances released by single-use baby diapers in urine simulant would ideally be based on the presence in single-use baby diapers and information on migration of the substance to skin during use. The parameters needed to perform the assessment of exposure to chemicals were, for most of them, available to the Dossier Submitter (concentration in a urine simulant, frequency of use, body weight, diapers weight, skin absorption). The assessment of exposure relies on the calculation of a daily exposure dose, which is the quantity of a substance to which a population (children between zero and three years of age here) is exposed on a daily basis. The daily exposure dose is expressed in mg/kg bw/day.

The dermal route of exposure was the one considered in this assessment, and more specifically exposure in the diaper area.

The equation for the daily exposure dose for each chemical individually is:

$$\textbf{daily exposure dose} = (C_{diaper} \times W \times F \times Abs_{skin}) / BW$$

where:

- C_{diaper}: concentration of the chemical (in mg/kg of diaper) extracted with a urine simulant from a whole diaper, in relation to the weight of the diaper (W), taking into account the extracted simulant volume (V) [$C_{diaper} = C_{urine\ simulant} \times V_{urine\ simulant} / W$]
- W: average weight of a diaper (kg)
- F: frequency of use (number/day)
- Abs_{skin}: fraction absorbed by the skin (%)
- BW: body weight of a child (kg)

For PCDD/Fs and DL-PCBs, exposure was assessed using toxic equivalency factors (TEFs) indicating the toxicity of all congeners having the same mechanism of toxicological action as the "Seveso" dioxin (2,3,7,8-TCDD), considered the most toxic. Exposure was therefore expressed in toxic equivalent quantities (TEQs). For PAHs, BaP was considered as a marker of PAH exposure and carcinogenic effects (WHO-IPCS, 1998), and the toxicity of other PAHs were estimated based on toxic equivalency factors (TEFs). The Dossier Submitter selected TEFs for 17 PAHs from the existing TEFs defined by various organisations (OEHHA, 1993 revised in 2015; INERIS, 2003; AFSSA, 2003; DFG, 2008 cited in BfR, 2009b; US EPA, 2010), and they are shown in Table 39 (*TEFs proposed by various organisations for PAHs*) in the Background Document.

Consequently, the calculation of the daily exposure dose is then:

$$\textbf{daily exposure dose}_{TEQ} = (C_{diaper} \times W \times F \times Abs\ skin \times TEF) / BW$$

24 hours was selected as an appropriate time frame for exposure.

The Dossier Submitter assumed a dermal absorption rate of 50%[15] to calculate exposure.

The values of the parameters used by the Dossier Submitter to perform the exposure assessment (and calculate the daily exposure dose) are gathered in Table 4 below.

Table 4 Values of the parameters used in the exposure assessment

Parameter	Realistic conservative approach		
	Value		Reference
Weight of a diaper by age group (W)	0-6 months exclusive	23.1 g	Group Hygiène (2019) *via* personal communication
	6-12 months inclusive	31.0 g	
	13-18 months inclusive	31.0 g	
	19-24 months inclusive	31.0 g	
	25-30 months inclusive	46.3 g	
	31-36 months inclusive	46.3 g	
Daily frequency of use (average) (F)	0-6 months exclusive	7.98	UK Environment Agency, 2005b (average daytime frequency + one diaper/night)
	6-12 months inclusive	6.66	
	13-18 months inclusive	6.75	
	19-24 months inclusive	5.95	
	25-30 months inclusive	5.85	
	31-36 months inclusive	4.70	
Dermal absorption rate (Abs_{skin})	50%		ANSM (2010)
Body weight (BW)	0-6 months exclusive	5.2 kg	BEBE-SFAE (2013)
	6-12 months inclusive	7.5 kg	
	13-18 months inclusive	9.6 kg	
	19-24 months inclusive	10.9 kg	
	25-30 months inclusive	12.0 kg	
	31-36 months inclusive	12.0 kg	

RAC conclusion(s):

RAC concurs with the Dossier Submitter that frequent use of single-use baby diapers over a longer period of time could lead to exposure of children and infants to hazardous substances should they be present as impurities - particularly where exposure occurs under occlusive conditions. RAC further notes that babies often suffer from baby rash, which might enhance the absorption of substances from diapers.

RAC agrees with the Dossier Submitter that any hazardous substances present in diapers could be either directly released or extracted by urine absorbed from the diapers while wearing them. Due to the effect of urine migration, even substances from the inner parts of the diapers could potentially migrate to the outer layer and come into contact with a baby's skin.

[15] During opinion development the Dossier Submitter revised the dermal adsorption rate from 100% to 50% in response to feedback from RAC.

RAC considers that using a urine simulant for extraction is representative of indirect exposure to diaper core constituents (which are not in direct contact with the skin but in the presence of urine could migrate to the top sheet), but that direct exposure is not adequately addressed in the exposure scenario, especially regarding the extraction of lipophilic substances which could come into direct contact with the baby's skin.

Namely, RAC concurs with the Dossier Submitter that using a urine simulant to detect and/or quantify the concentration of the hazardous substances in the scope of the proposed restriction (which might be able to migrate from the diaper) provides a better representation of actual use, compared to solvent extraction but notes that the method requires additional validation and standardisation. RAC also generally supports the Dossier Submitter´s approach to base their quantitative deterministic exposure assessment on urine simulant extraction, using the following parameters:

- the absorption fraction,
- the frequency of use,
- body weight of the babies,
- diapers weight and
- the concentration of the substances of interest in the urine simulant extracted from the diaper under predefined conditions.[16]

RAC considers that most of the exposure variables selected by the Dossier Submitter are well explained and, in general, realistically reflect the population's habits and children's body weight. However, RAC considers that the way these variables were used in daily exposure dose calculation led to a clear overestimation of exposure, particularly due to the disparity in the "rewet" factor (quantity of urine refluxed from a diaper) assumed by the Dossier Submitter for their calculations and those reported by industry.

Regarding the results of diaper sample analysis undertaken by SCL and DGCCRF/INC, RAC recognises major uncertainties/shortcomings described in the section *"Key elements underpinning the RAC conclusion(s)"*. RAC considers that these uncertainties and shortcomings seriously impede the reliability of the exposure assessment for the substances of concern.

Key elements underpinning the RAC conclusion(s):

A. Exposure scenario parameters

The first studies on composition of single-use diapers were performed by the INC (French

[16] Briefly, whole diapers are soaked with urine simulant and placed in oven at 37 °C for 16 hours. 200 mL of urine simulant is added to a diaper, for 3 times (600 mL total), with 30-minute rest period between each addition. The simulant is recovered by gentle pressing at room temperature (for 5 to 10 minutes) in a stainless-steel container, and 220 to 250 mL are recovered.

National Consumer Institute)[17] and by the French Joint Laboratory SCL (Service Commun des Laboratoires)[18] in 2016, 2017 and 2018, using solvent extraction for screening chemicals in 19 of the best-selling commercial single-use diapers on the French market (see ANSES report (2019).

SCL also performed migration tests with shredded whole diapers in 2017 and whole diapers in 2018, using a urine simulant for both of these migration studies on the same 19 single-use diapers.

The analyses in 2018 were carried out by soaking entire single-use diapers with urine simulant for 16 hours at a temperature of 37 °C as described in Annex B.9.2.2. of the Background Document, noting that about 220 to 250 mL of the 600 mL urine simulant added was recovered by pressing the diaper. In 19 single-use diapers analysed, formaldehyde was quantified or detected in 13 diapers, PAHs were detected but not quantified in 16 diapers, PCDD/Fs, and DL-PBCs were quantified in all diapers (see Table 5).

Table 5 Quantities of chemicals extracted by urine simulant in relation to diaper weight; second exploratory study (SCL, 2018)

Anonymised products	Formaldehyde (mg/kg)	Total DL-PCBs (ng/kg)	Total PCDD/Fs (ng/kg)	benzo[e]pyrene (mg/kg)	benzo[a]pyrene (mg/kg)	benzo[b]fluoranthene (mg/kg)	dibenzo[a,h]anthracene (mg/kg)	5-methylchrysene (mg/kg)	Chrysene (mg/kg)	benzo[g,h,i]perylene (mg/kg)	benzo[k]fluoranthene (mg/kg)	Benzo[j]fluoranthene (mg/kg)
1	3.57	35.67	0.43	-	-	-	-	-	-	-	-	-
2	1.86	30.80	0.3	<LQ= 2	-	-	-	-	-	-	-	-
3	-	34.03	0.67	-	<LQ= 2.21	-	-	-	-	-	-	-
4	1.66	13.76	0.09	-	-	<LQ= 1.82	<LQ= 0.54	-	-	-	-	-
5	-	6.04	0.13	<LQ= 1.58	-	-	-	-	-	-	-	-

[17] Pesticides, PAHs, dioxins and furans, fragrances and volatile organic compounds (VOCs), heavy metals, nonylphenol, octylphenol and nonylphenol monoethoxylates were screened by INC.

[18] Pesticides, PAHs, dioxins, furans, DL-PCBs, phthalates, organotins, VOCs, fragrances and azoic dyes were screened by SCL.

6	1.23	11.44	0.06	-	-	-	-	<LQ= 1.7	-	-	-	-
7	2.91	34.84	0.83	<LQ= 2.2	-	-	-	-	-	-	-	-
8	-	7.39	0.84	<LQ= 1.93	-	<LQ= 1.93	-	-	-	-	-	-
9	1.99	379.6	1.36	<LQ= 3.26	-	-	-	-	-	-	-	-
10	1.15	43.40	0.16	<LQ= 1.36	-	-	-	-	<LQ= 1.36	<LQ= 1.36	-	-
11	1.62	36.94	0.36	-	<LQ= 1.92	-	-	-	-	-	-	-
12	4.98	29.94	0.64	<LQ= 1.72	-	<LQ= 1.72	-	-	-	<LQ= 1.72	-	-
13	7.18	20.38	0.30	<LQ= 1.71	-	<LQ= 1.71	-	-	-	-	-	-
14	4.66	27.24	0.25	-	-	-	-	-	-	-	-	-
15	7.5	25.71	0.12	<LQ= 2.28	-	-	-	-	-	<LQ= 2.28	-	-
16	-	20.73	0.04	-	-	<LQ= 2.08	-	-	-	<LQ= 2.08	-	-
17	-	12.13	0.07	<LQ= 2.01	-	<LQ= 2.01	-	-	-	<LQ= 2.01	<LQ= 2.01	<LQ= 2.01
18	ND (LQ=1 .07)	12.48	0.06	-	<LQ= 1.77	-	-	-	-	-	-	-
19	1.10	8.76	0.06	-	-	-	-	-	-	-	-	-

ND: not detected; The results in the table correspond to the concentrations extracted in the urine simulant without considering the volume recovered (200 to 250 mL).

In addition to the analyses in 2018, SCL performed a follow-up study in 2019 with 32 single-use diapers. The results of both of these studies are included in Table 6. RAC notes that due to lack of information it is not clear whether the diaper brands analysed by the SCL are representative for the whole EU/EEA. However, RAC notes that the most important manufacturers produce diapers in different countries of Europe and might therefore not only use the same materials for the different production sites but also sell their diapers in several countries in Europe.

Table 6 Aggregated results from the 2018 and 2019 studies on migration of substances, using urine simulant extraction from whole diaper (according to Table 51, Background Document)

Substance	No of Analyses**	Detection / quantification for number	LoD* (Range)	LoQ* (Range)	Substance	No of Analyses**	Detection / quantification for	LoQ* (Range)

		of diapers					**number of diapers**	
Formaldehyde (mg/kg of diaper)	**51**	quantified No = 22; detected No = 17	0.269 – 0.742	0.403 - 2.75	**DL-PCBs (ng/kg of diaper)**	**51**	quantified	
PAHs (mg/kg of diaper)	**51**	detected, not quantified			PCB 77		quantified No = 40	0.038 - 2.72
benzo[e]pyrene		detected No = 10		0.499 -0.836	PCB 81		quantified No = 2	0.048 – 0.072
benzo[a]pyrene		detected No = 4		0.649 - 0.81	PCB 123		quantified No = 40	0.022 – 0.051
benzo[b]fluoranthene		detected No = 6		0.627 - 0.763	PCB 118		quantified No = 51	0.749 -9.119
dibenzo[a,h]anthracene		detected No = 2		0.198	PCB 114		quantified No = 31	0.0309 – 0.291
5-methylchrysene		detected No = 1		0.623	PCB 105		quantified No = 51	0.3063 – 5.232
chrysene		detected No = 1		0.499	PCB 126		quantified No = 3	0.011 – 0.069
benzo[g,h,i]perylene		detected No = 5		0.499 – 0.836	PCB 167		quantified No = 32	0.0073 – 0.919
benzo[k]fluoranthene		detected No = 1		0.737	PCB 156		quantified No = 47	0.0449 – 1.857
benzo[j]fluoranthene		detected No = 1		0.737	PCB 157		quantified No = 17	0.0114 -0.412
Benzo[a]anthracene		detected No = 4		0.0004 – 0.001	PCB 169		quantified No = 3	0.0068 – 0.06
PCDFs (ng/kg of diaper)	**50**	quantified			PCB 189		quantified No = 23	0.0051 – 0.353
1,2,3,6,7,8 HxCDF		quantified No = 7		0.0004 –	**PCDDs (ng/kg of**	**51**	quantified	

				0.015	**diaper)**			
2,3,4,6,7,8 HxCDF		quantified No = 13		0.0007 – 0.031	1,2,3,4,6 ,7,8 HpCDD		quantified No = 48	0.0017 - 0455
1,2,3,4,6,7,8 HpCDF		quantified No = 43		0.0008 – 0.059	OCDD		quantified No = 48	0.0032 – 0.372
OCDF		quantified No = 43		0.0008 – 0.078	1,2,3,6,7 ,8 HxCDD		quantified No = 5	0.0004 – 0.015
2,3,7,8 TCDF		quantified No = 2		0.0006 6	1,2,3,4,7 ,8 HxCDD		quantified No = 2	0.0039 – 0.0047
1,2,3,7,8 PeCDF		quantified No = 1		0.0039	1,2,3,7,8 ,9 HxCDD		quantified No = 2	0.0051 – 0.0097
2,3,4,7,8 PeCDF		quantified No = 9		0.0007 – 0.015				
1,2,3,4,7,8 HxCDF		quantified No = 4		0.0027 – 0.013				
1,2,3,7,8,9 HxCDF		quantified No = 2		0.0056 – 0.0067				
1,2,3,4,7,8,9 HpCDF		quantified No = 4		0.0067 – 0.014				

* The concentrations indicated in the table have been transformed from the concentration measured in ng of substance per mL of urine simulant into the concentration of mg or ng of substance/kg of diaper according to the volume of urine simulant added in the diaper (660 mL) and the volume of urine simulant extracted (220 to 250 mL) which is different for each diaper examined.
With regard to PAHs, there are uncertainties about the values presented, including whether the values are LoDs or LoQs.
** RAC notes that several diaper samples of the same brand could be included in these tests. RAC notes that there is an inconsistency in the numbers on detected/quantified analytes provided by the Dossier Submitter which could not be solved during the opinion making process.

Table 7 Concentrations of substances in the scope in two SCL studies (2018 and 2019)

	Formaldehyde [mg/kg]	Sum PAHs (TEQ) [mg/kg]	Sum PCDDs (TEQ) [ng/kg]	Sum PCDFs (TEQ) [ng/kg]	Sum DL-PCBs (TEQ) [ng/kg]
SCL (2018), 19 samples					
Lowest value	0.015	**0.377**	0.0001	0.0004	0.300
Median value	0.609	**0.587**	0.0010	0.0021	0.302
95th percentile	2.644	**1.372**	0.0055	0.0060	0.303
SCL (2019), 32 samples					
Lowest value	0.110	**0.0002**	0.0001	0.0001	0.300
Median value	0.425	**0.0004**	0.0003	0.0006	0.301
95th percentile	1.106	**0.0009**	0.0019	0.0039	0.301

Population to be included in the scope: In this restriction proposal, the health risk assessment was undertaken for children aged from birth to 36 months included. Since, according to the UK Environment Agency data (2005b), by that age about 5% of children still wear diapers, the age range covered by the restriction proposal seems reasonable. Six age groups were described by the Dossier Submitter, to account for the babies' weight and psychomotor development. However, the Dossier Submitter decided to calculate the RCR using the parameters related to babies aged between zero to six months, as for this category of age, the ratio bodyweight/weight is the lowest and so the RCR will be the worst case over the six classes of age.

Contact between single-use baby diapers and skin: RAC agrees with the Dossier Submitter that the exposed skin area is 100% covered by a diaper material.

Exposure duration: RAC supports a 24-hour period as an appropriate time frame for exposure duration for substances with a threshold effect (formaldehyde, PCDD/Fs, PCBs), given that exposure is expected throughout the day until the child or the infant is fully toilet trained. This scenario is applicable also for bioaccumulative PCDD/Fs and DL-PCBs, since EFSA's CONTAM Panel in TDI derivation for these substances applied a toxicokinetic model which considers bioaccumulative property of a substance (EFSA, 2018).

Child body weight: The Dossier Submitter's rationale to use the data from the BEBE-SFAE study (2013) is well explained (Table 4). RAC notes the Dossier Submitter used 25th percentile of the body weight for each age group. The 3rd percentile could have also been considered since "normal growth/weight relationship" for babies and children up to three years is in the range of 3rd to 97th percentile according to the WHO Child Growth Standards[19]. However, the 25th percentile is commonly used in exposure assessments.

[19] WHO MULTICENTRE GROWTH REFERENCE STUDY GROUP, Mercedes de Onis et al.: Acta Paediatrica 95 (Suppl 450) (2006).

Absorbed fraction by the skin: For all substances in the scope, the Dossier Submitter assumed 50% absorption rate as a choice to calculate exposure for babies including preterm babies.

Until a child is toilet trained, the diaper area is a warm, occlusive (although nowadays highly breathable diapers are used) and moist environment with ideal kinetic conditions facilitating the percutaneous absorption of substances. Compromised skin conditions, such as diaper dermatitis, a common skin disorder in babies, contact dermatitis, or prematurity could potentially increase dermal penetration of chemicals. The diaper area contains not only skin but mucous membranes as well. Due to these reasons, it is often recommended that a safety assessment of ingredients used in the diaper area is based on an assumption of 100% dermal penetration (Felter et al., 2017; *Agence nationale de sécurité du médicament et des produits de santé* (ANSM))[20]. However, this "default value" approach with 100% absorption rate has been criticised recently (e.g. Felter et al., 2017; Dey et al., 2016) as follows:

- Significant decrease in the incidence and severity of diaper dermatitis has been observed over the past few years (ANSM, 2010) due to improved design of single-use diapers and of wipes, use of barrier emollients, and improved general skin care of infants. Diaper rash is generally an episodic inflammatory reaction, with a mean duration of 2 to 3 days, and it affects only a portion of total diaper skin area.

- RAC also notes that although prematurity could play a role, it is assumed that premature neonates born after 34 weeks of gestational age generally have dermal barrier functions similar to full-term neonates and babies up to six months of age (CIR, 2014). In infants of less than 34 weeks of gestational age, rapid epidermal cell differentiation occurs in the first few weeks of life and, structurally, the skin of the most immature infants resembles that of full-term infants by several weeks (two to four weeks) (Kalia et al., 1998). Only for early gestation premature infants (23 to 25 week of gestational age), the authors found that complete development of a fully functional stratum corneum can require significantly longer than four weeks (Kalia et al., 1998).

- Although it has been shown that genital mucous membranes rapidly absorb chemicals without metabolising them (Nicole et al., 2014), they represent only a small fraction of the total diaper area.

- Regarding physiological differences between infant and adult skin, SCCS (2018) states that in full-term newborns and infants "the skin possesses all skin structures of adult skin, and anatomically these structures do not undergo dramatic changes after birth" and "the dermal absorption in skin of newborns is similar to that observed in adult skin, when the skin is intact". Similarly, EFSA considers that "age-dependent differences in skin properties and functions do not require a separate approach for children and adults when determining absorption values" (EFSA, 2011, 2012). Higher surface area/body weight ratio, which is up to 2.3-fold higher in newborns than in adults (changing to 1.8- and 1.6-fold at 6 and 12 months, respectively) is considered

[20] Manufacturers of products intended to be used for infants, including diapers and wet wipes, often start with an assumption of 100% chemical absorption in the diaper area (Felter et al., 2017).

to be covered by the intraspecies assessment factor of 10 (SCCS, 2018).

- Dermal penetration and systemic bioavailability of chemicals following dermal exposure could be affected by age-dependent enzymatic biotransformation in the skin[21] (CIR, 2014). However, this issue is largely unexplored. Both under-estimation and over-estimation of systemic bioavailability in infants compared to adults is possible, depending on a substance (SCCS, 2018).

RAC points out that in the most recent (10th) revision of the SCCS guidance for the testing of cosmetic ingredients and their safety evaluation (SCCS, 2018), it is noted that "a tiered quantitative approach to take the potential for diaper rash into consideration when doing a safety evaluation for products used in the diaper area has been proposed by Felter et al. (Felter et al., 2017)". Based on the published literature on diaper rash and data from Procter and Gamble (P&G) unpublished clinical studies, Felter et al. (2017) proposed that the following conservative assumptions should be made when evaluating the potential impact of diaper rash on the integrity of the skin barrier:

- An infant experiences diaper rash ~6 days/month (20% of the time).
- When rash is present, it involves 25% of the total surface area of the diapered skin.
- When rash is present, 60% is assumed to be mild and 40% is assumed to be moderate to severe.

The authors state that "these assumptions are based on the high end of values in the published data as well as P&G's extensive clinical database. While difficult to quantify, each assumption is conservative; when taken together, the overall degree of conservatism is compounded". The tiered approach proposed by the authors could be summarised as follows:

- for substances with dermal absorption of 50% or higher, there is no impact on the overall exposure assessment;
- for substances that have a low degree of dermal penetration (10%), the impact is less than two-fold; and
- for substances with a very low degree of dermal penetration (1%), the impact is less-than four-fold. It is recommended that for such compounds, an explicit consideration of the impact of diaper rash be considered.

For these reasons, and considering the comments provided in the consultation, RAC supports a lower default dermal absorption rate of 50% as proposed by the Dossier Submitter. This value is recommended by the Scientific Committee on Consumer Safety (SCCS). RAC notes that substance-specific dermal absorption data should be preferred over a default value. However, this approach is not feasible since data for dermal absorption of chemicals in infants (or suckling animals) are lacking.

Exposure frequency: The number of diapers used per day is influenced by the age of the child, the size of the diaper, the type of diaper used, the country and cultural habits. It ranges, on average, from seven per day at birth to five per day at the age of 2.5 years. Analysing the

[21] The metabolic capacity of liver enzyme systems matures rapidly in the neonates, achieving, or even exceeding, adult capacities mostly within about 6 months to 1 year after birth. If development of enzymatic systems in the skin parallels development in the liver, many enzyme systems in the skin will be fairly mature by about six months of age (CIR, 2014).

data gathered through the call for evidence and literature search (Tables 58 and 59 in Annex B.9.4.6. of the Background Document), the Dossier Submitter decided to use the data from a robust study undertaken in 2002 to 2003 in the United Kingdom in more than 2 000 households (Table 64 in Annex B.9.4.6. of the Background Document; Table 4 in this opinion). RAC supports this choice.

Baby diaper weights: Since the average weight of a single-use baby diaper decreased by almost 50% since the 1980s, the Dossier Submitter gathered new data through the call for evidence and literature search (Tables 61 and 62 in Annex B.9.4.7. of the Background Document) and decided to use the most recent data available from a European industrial association (Group'Hygiène, 2019, via personal communication) (Table 4 in this opinion). The weights of premature babies' diapers could not be considered in the weight of diapers by age group due to lack of available data.

Nevertheless, during the consultation on the Annex XV report it was proposed that the actual weight of diapers is lower (comment #3165) than the values selected by the Dossier Submitter. In addition, it was noted that diapers are not made or marketed for a specific age group (comment #3176). Diapers are developed/designed for specific body weight intervals. Besides, diapers made for the same weight interval can vary substantially in weight between producers and models. RAC, therefore, notes some minor uncertainties about the diaper weight.

B. Extraction method with urine simulant

The extraction method as described by the DS was still being developed during the assessment reported by ANSES (2019) and is not yet standardised or validated. Additional concerns were raised during the consultation[22] regarding a two orders of magnitude overestimation of the levels of extractable substance compared to a realistic worst-case scenario of use.

RAC notes that according to comments received during the consultation (e.g., #3135, #3166, #3167), the volume of urine simulant extracted from a (diaper) sample (220 to 250 mL) might be two orders of magnitude larger than would be expected in reality (1 to 2 mL). A laboratory test provided by industry shows that a diaper (size 4) loaded with 220 mL of urine (which represents four episodes of urination, 55 mL each time), results in a small amount of liquid extracted (0.7 mL), imitating a baby of about 10 kg body weight, sitting on the diaper) (rewet factor). That means that approximately 35% of the urine simulant was extracted from

[22] **Comment #3166 (Industry)**: Some of the exposure parameters selected lead to unrealistic situations: A baby 0 to 6 months does not urinate 4.700 mL of urine per 24 hours; The principle of a baby diaper is to pick up baby's urine and hold it according to the dry-keeping mechanism, and diapers do not release 200 mL of urine. An average overnight diaper is "loaded" with approx. 210 mL (not 600 mL) and only releases up to 2 mL back the skin (known as rewet in the industry).
Comment #3167 (MSCA): "… the analysis of extractable chemicals was carried out with whole diapers soaked in artificial urine, incubated at 37 degrees Celsius for 16 hours, during which an additional 3*200 mL of urine was added. Extraction was performed thereafter by pressing out excess urine. In combination with a use frequency of 4.7 to 7.98 diapers per day, this would correspond to a urinary output of around 3000 to 5000 mL depending on age, which largely exceeds children's actual daily urinary output (approximately 200 to 600 mL per 24 hours, depending on age). This is not realistic and likely overestimates the levels of extractable substance compared to a realistic scenario of use. Moreover, the incubation time should for a realistic scenario, considering the diaper use frequency, be between 3 to 5 hours, depending on the age of the child."

single-use diapers in the SCL analyses (2018, 2019), while only less than 1% of the baby's urine was extracted from a diaper under industry laboratory conditions (e.g., 0.25% found by Rai et al., 2009; 0.32 to 0.66% obtained by Dey et al., 2016).

The Dossier Submitter considered 24 hours to be an appropriate time frame for risk calculation. Over this period of time, however, only a frequency of two diaper changes should be used in the exposure assessment due to the fact that in the exposure scenario diapers were soaked over 16 hours with the urine simulant. RAC notes that the Dossier Submitter provided a sensitivity analysis considering a diaper change of two in 24 hours (this topic is further elaborated in section 3.1.5). However, the volume of urine simulant used to soak a diaper sample during one extraction period was 600 mL. Therefore, even with two "diaper changes per day" used in the calculation, the total urine simulant volume is 1 200 mL, while daily urine output for babies aged 2 to 12 months is only 400 to 600 mL. This leads to overestimation by a factor of two to three. On the other hand, it is not known whether the urinary simulant extraction of the substances in the scope of proposed restriction follows a linear function or whether the extraction capacity is reduced over time. Namely, if a majority of extraction happens at the beginning of extraction period, two extraction periods of 16 hours each (two "diaper changes per day") would yield lower amounts of extracted substances compared to more frequent extraction periods of shorter duration (e.g., 4 times 6 hours extraction period).

Urinary output in infants: RAC notes that the urinary output of babies aged between zero and six months varies (see Table 8 below). However, RAC considers that the amount used in the exposure estimate is overly conservative and not sufficiently realistic (see paragraph above).

Table 8 Reference values for urinary output (*Guide pratique des analyses médicales*, 4th edition), see Background Document

Age group	Urinary output (mL/24 hours)
Newborn	15 - 60
Two weeks	100 - 300
One to two months	250 - 450
Two to 12 months	400 - 600
Two to four years	500 - 800

C. Daily exposure dose calculation

The daily exposure dose calculation considered only the substances extracted with the urine simulant, since the objective was to measure the quantity of impurities/contaminants that is not retained in the diaper´s core. The Dossier Submitter, however, did not specifically consider transfer of substances in diapers to baby skin via direct skin contact. DGCCRF/INC and SCL analysed certain relevant substances (i.e., PAHs, PCDD/Fs and PCBs, but not

formaldehyde)[23] in shredded diaper parts by solvent extraction (ANSES, 2019), but these data were not used by the Dossier Submitter for exposure and risk assessment. In the opinion of RAC, this introduces an uncertainty in the exposure (and risk) assessment of lipophilic substances (PAHs, dioxins, furans, PCBs). Namely, in comparison to the extraction with water-based solutions (baby's urine and urine simulant), these substances could be expected to be more efficiently absorbed during direct contact with baby's skin, especially considering that baby's skin is often treated with a lotion and that some diapers' topsheet may also be treated with a lotion.

In the Background Document, a relatively new method for calculating direct contact transfer and reflux has been used (Dey et al., 2016) to simulate exposure to hazardous substance by wearing of diapers (Prolonged Exposure Rewet Method in Diapers, PERMID). This is based on gravimetry where collagen is used to mimic skin, considering:

- the pressure a child may apply to a diaper,
- a representative urine load during diaper wear,
- the gap between urine voids,
- exposed surface area,
- and diaper wear time.
-

Diaper topsheet-lotion transfer was used as a model for direct transfer of substances to skin from the topsheet. Indirect contact (rewet) was calculated as a fraction of total liquid load that resurfaces back to the topsheet after absorption due to applying pressure on the absorbent material. This pressure was measured in 174 children between the ages of two weeks and 56 months, in four positions (sitting up straight, lying on the stomach, lying on the back, and falling on the buttocks).

For direct contact, 4% transfer was calculated after three hours of wear, 3% after six hours of wear, and 4.3% after a night. For indirect contact, an average reflux factor of 0.46% (range 0.32 to 0.66%) was adopted, considering that 50% of the diaper surface area (since in real conditions of use the applied pressure from the baby will not be on 100% of the diaper surface area at all times). These results are in line with earlier report by Rai et al. (2009) (0.25%), as well as with the values claimed by the industry during the consultation period (e.g., comments #3165, 3166).

RAC considers that 4.3% for direct contact and 0.66% for indirect contact (rewet) could represent realistic worst-case values and uses them in the sensitivity analysis for the risk characterisation (Tables 11 to 13 in section 3.1.4).

D. Uncertainties/shortcomings in the exposure assessment concerning the analytical method

[23] Dioxins and furans were found in outer/inner diaper layer, and in other diaper parts, except the core. PAHs (benzo[b]fluoranthene, benzo[a]anthracene, indeno[1,2,3- c,d]pyrene, benzo[g,h,i]perylene) were detected in the elastics. Health thresholds were not exceeded for children aged 0 to 36 months in the ANSES risk assessment in these 23 diaper samples (ANSES, 2019).

RAC considers that there are major uncertainties regarding the results of the diaper sample analysis undertaken by SCL and DGCCRF/INC, especially related to PAHs and other lipophilic substances (e.g., dioxins, furans, PCBs). These include:

- Overall, it has not been possible to confirm the reliability of the analytical data.

- The sample preparation and extraction method with urine simulant is not yet standardised and validated. This introduces further uncertainty into the exposure assessment, especially considering major uncertainties related to exposure scenario (e.g., disparity in the rewet factor between the Dossier Submitter's proposal and information provided by the industry). RAC notes that uncertainties in the analytical method required to assess the risk and justify a restriction is much more critical than the availability of a standard method needed for the purpose of enforceability (which could be developed later on during implementation).

- In 2019, three blank tests were performed. The values for PCDD/Fs and DL-PCBs obtained from the blank samples were not subtracted from those obtained in the diaper extraction tests. According to the Dossier Submitter, there is no European harmonisation with regard to the removal of blanks. RAC considers that lack of information on blanks in the first set of analyses (ANSES, 2019) and not accounting for background concentrations of dioxins and furans in the second set of analyses (performed in 2019) is a methodological shortcoming.

- Concerning PAHs, it is not clear why the measured values are orders of magnitude lower in 2019 compared to the 2018 analysis (Table 7). RAC notes that the LoDs/LoQs were three orders of magnitude lower for the 2019 analysis compared to the 2018 analysis. The Dossier Submitter noted that the analytical method was the same in 2018 and 2019 and suggested that there might have been improvements in the manufacture of diapers since EDANA has started developing an industry guidance on trace substances (Codex™ see section 3.3.) in 2017. However, according to industry, no such extensive changes in the quality of materials occurred in this short timeframe.

- For PAHs, the LoD of the methods used in the analyses was between 0.03 and 0.1 mg/L, and the LoQ was between 0.1 and 0.4 mg/L, while the migration limits proposed for PAHs is 0.023 ng_{TEQ}/kg. Although a simple comparison between the LoD of the analytical method to the proposed migration limit is not possible, it is obvious that the difference is several orders of magnitude (when calculated by the Dossier Submitter, the lowest value in the dataset of measured values for PAHs in diaper samples was 100 ng/kg). It is unknown whether the real values were above or below the proposed limits.

- The levels of dioxins, furans and PCBs determined by the urine simulant (water-based solution) extraction method exceeded the DNELs, while these substances, although highly lipophilic, were detected at lower concentration or even not detected by solvent-based extraction from shredded diaper samples (ANSES, 2019).

- Background concentrations of PCDD/Fs can regularly be detected in the water supplies of accredited laboratories that are specialised in dioxin/furan analyses (comment #3165). These background amounts fluctuate over time and are within the concentration ranges that would be required to determine the levels of PCDD/Fs at the

limits proposed in the Annex XV dossier. This can introduce a high risk of "false positive" detections.

- The extraction protocol has several manual steps and keeping the diaper in open containers overnight (for extraction with urine simulant) could introduce contamination. The artificial urine used is made of several ingredients, which also increase the risk of introducing contamination (and demands the strict use of method blanks).

The exact magnitude of the uncertainties and shortcomings regarding the analytical method is unclear, however the reliability of the analytical results is likely to be severely affected by the described uncertainties.

In addition, RAC notes an inconsistency[24] in the number of analytes presented by the Dossier Submitter.

Table 9 The main uncertainties/shortcomings incl. the effect of concern and the level of concern

Uncertainties/shortcomings	Effect on concern	Level of concern
Uncertainties and shortcomings concerning the analytical method	↑↓	Very high
Use of the exposure variables in the daily exposure dose calculation, particularly the disparity in the "rewet" factor (baby's urine refluxed from a diaper):	↓	High (approximately two orders of magnitude overestimation)
Lacking assessment of direct exposure - especially regarding extraction of lipophilic substances which could come into direct contact with baby's skin;	↑	Medium

3.1.4. Characterisation of risk(s)

Summary of proposal:

Given that most of the estimated exposure levels are above the calculated limits for adverse effects, the Dossier Submitter concludes that the risk from the substances in the scope of the restriction is not adequately controlled.

For substances with a threshold effect, meaning formaldehyde, PCDD/Fs and DL-PCBs, and for substances with a no-threshold effect (mainly genotoxic carcinogens, in this restriction dossier, PAHs), the risk level is expressed by the RCR, which is the ratio between the daily

[24] The number of quantified analytes for PCDDs/Fs and DL-PCBs is not consistent in the documents provided by the Dossier Submitter.

exposure dose and the appropriate internal DNEL or dermal DMEL, expressed for **10^{-6} risk level**. The numerical value of this ratio is used to determine whether or not the dose received exceeds the $DNEL_{in}$ or $DMEL_{dermal}$.

RCR = daily exposure dose/$DNEL_{in}$ or $DMEL_{dermal}$.

The numerical value of the RCR is interpreted as follows: an RCR greater than 1 means that the toxic effect may occur, without being possible to predict its likelihood of occurrence in the exposed population, whereas an RCR lower than 1 means that no toxic effect is theoretically expected in the exposed population provided that the exposure to the substance is only due to the single-use baby diaper.

Single usable baby diapers are not the only source of babies´ exposure to substances. The Dossier Submitter states that the intake of chemicals from single-use baby diapers is small in comparison with that from other sources, such as food, air, drinking-water and other consumer products. So, some consideration is needed as to the proportion of the DNEL that may be allowed from different sources.

The approach of using an allocation factor ensures that the total daily intake from all sources does not exceed the DNEL. For example, an allocation of 10% of the TDI to the intake of formaldehyde from toys was used to derive a migration limit for formaldehyde in toys (Commission Directive (EU) 2019/1929 of 19 November 2019 amending Appendix C to Annex II to Directive 2009/48/EC[25]). According to RIVM (2008), this allocation factor was already used in 1984 by the Scientific Advisory Committee to examine the toxicity and ecotoxicity of chemical compounds to propose thresholds for metals (report EU 12964 EN not available) (RIVM, 2008).

The possibility of cumulative exposure through other sources (environmental, food, etc.) leading to an increase in the total daily exposure dose cannot be ruled out, meaning that the exposure to the chemicals in the scope of this Annex XV dossier is likely not to be limited to diapers only. Therefore, the Dossier Submitter decided to limit the share allocated to single-use baby diapers to 10% of the DNEL/DMEL.

The limits in single-use baby diaper were therefore calculated using the following equation:

$$\mathbf{C_{diaper} = RCR \times 10\% \times BW \times DNEL_{in}} \text{ or } DMEL_{dermal} \mathbf{/ (W \times F \times Abs_{skin} \times TEF)}$$

With:

- $DNEL_{in}$: internal DNEL (mg/kg bw/d)
- $DMEL_{dermal}$: dermal DMEL (mg/kg bw/d)
- BW: body weight of a child (kg)
- W: weight of a diaper (kg)
- F: frequency of use per 24h (number/24h)
- Abs_{skin}: fraction absorbed by the skin (%)

[25] COMMISSION DIRECTIVE (EU) 2019/1929 of 19 November 2019 amending Appendix C to Annex II to Directive 2009/48/EC of the European Parliament and of the Council for the purpose of adopting specific limit values for chemicals used in certain toys, as regards formaldehyde: https://eur-lex.europa.eu/legalcontent/EN/TXT/HTML/?uri=CELEX:32019L1929&from=EN

- TEF: toxic equivalent factor (only used for PCDD/Fs and DL-PCB and PAHs)
- C_{diaper}: migration limit of the chemical extracted with a urine simulant from a whole diaper, in relation to the weight of the diaper considering the extracted simulant volume (mg/kg of diaper)

The concentration of the **available** substance expressed in mg/kg of diaper cannot be directly measured. It is proposed to be determined after extraction of said substance from a whole diaper with a urine simulant. It is thus related to the weight of the diaper, and to the extracted simulant volume. The migration limit of available substance expressed in mg/kg of diaper can thus be transformed into a limit concentration of the **available** substance expressed in mg/L of urine simulant using the following equation:

$C_{urine\ simulant}$ [mg/mL urine simulant] = ($C_{diaper\ simulant}$ [mg/kg diaper] x weight of the diaper [kg]) / extracted volume [mL]

The Dossier Submitter chose to report the concentration level detected/quantified according to the ECHA R.15 guidance, meaning that the Dossier Submitter calculated the 95th percentile of the distribution of the 51 samples, including a default for those below LoD and/or LoQ. Indeed, for this calculation, the LoD was retained, if the substance was not detected. The LoQ was retained, if the substance was detected and if the substance was quantified the quantified concentration was retained.

Using the formula

CL_{diaper} = RCR x 10% x DN(M)EL x BW / (W x F x Abs_{skin} x TEF)

the Dossier Submitter calculated the migration limits in single-use baby diapers.

Formaldehyde

Migration limit (mg/kg diaper) = 0.1 x 0.075 X 5.2 /(0.0231 X 7.98 X 50%) = **0.42 mg/kg**

The sum of PAHs

Migration limit (ng_{TEQ}/kg diaper) = 1 X 0.1 X 0.004 X 5.2 /(0.0231 X 7.98 X 50%) = **0.023 ng_{TEQ}/kg**

The sum of PCDD/Fs/DL-PCBs

Migration limit (ng $_{TEQ}$/kg diaper) = 1 X 0.1 X 0.0003 X 5.2 /(0.0231 X 7.98 X 50%) = **0.0017 ng $_{TEQ}$/kg**

The sum of the total PCBs

Migration limit (mg/kg diaper) = 1 X 0.1 X 2.10^{-5} X 5.2 /(0.0231 X 7.98 X 50%) = **112 ng/kg**

Table 10 Calculated migration limits for the substances in scope (according to Table 71 in the Background Document)

Substance/group of substances	Proposed migration limit
Formaldehyde	
Formaldehyde	**0.42 mg/kg of diaper**[3]
PCDDs/PCDFs/PCBs	
Sum of the quantified PCDD/Fs **in TEQ**[1]	**0.0017 ng_{TEQ} /kg of diaper**
Sum of the quantified total PCBs	**112 ng/kg of diaper**
PAHs	
The sum for the detected or quantified PAH **in TEQ**[2]	**0.023**[4] **ng_{TEQ} /kg of diaper**

[1] TEQ from WHO 2005; [2] The Dossier Submitter selected TEFs for 17 PAHs from the existing TEFs defined by various organisations (OEHHA, 1993 revised in 2015; INERIS, 2003; AFSSA, 2003; DFG, 2008 cited in BfR, 2009b; US EPA, 2010) (Table 39 in the Background Document)
[3] This migration limit is proposed to cover all categories of ages and all sizes of diapers available on the market.
[4] Final value, corrected in the last version of the report by the Dossier Submitter following RAC's indication as there was a calculation mistake.

RAC conclusion(s):

RAC supports the Dossier Submitter´s approach to calculate the risk for the population in the scope of the Annex XV dossier (children aged between zero to 36 months), based on the most vulnerable group within this population (babies aged between zero to six months).

RAC concurs with the Dossier Submitter to express the risk level by the risk characterisation ratio (RCR) for substances with a threshold effect (formaldehyde[26], PCDD/Fs and DL-PCBs) as well as for substances with no-threshold (carcinogenic) effect. The RCR is therefore the ratio between the daily exposure dose and the appropriate internal $DNEL_{in}$ or $DMEL_{dermal}$, **expressed at 10^{-6} risk level**.

Nevertheless, RAC notes that:

- there are significant uncertainties related to the analyses of diaper samples carried out by DGCCRF/INC and SCL (in 2018 and 2019), especially regarding PAHs, PCDDs/Fs and DL-PCBs (i.e., all lipophilic substances in the scope), as already described in section 3.1.3. "*Information on emissions and exposures"*;
- there is likely overestimation in the daily estimated dose, and consequently the RCRs calculated by the Dossier Submitter, due to two orders of magnitude higher rewet factor and approximately 4-times higher volume of urine simulant used in diaper

[26] In this Annex XV dossier, the carcinogenic effects of formaldehyde were not considered since via the dermal route the skin sensitising effects are of relevance but not the carcinogenic ones.

samples' extraction, compared with realistic volume of urine output in babies of that age;

- for PAHs, since the lowest LoD is orders of magnitude higher than the proposed migration limits, it is not known how many samples were above/below the proposed limits - such a high LoD in relation to the limit value makes the restriction proposal rather meaningless because interested parties (enforcement, industry) would never know if a diaper is in line with restriction requirements or not;
- RAC does not support the use of an allocation factor for the calculation of risk (to account for aggregate exposure from different exposure routes) for the local dermal effects (formaldehyde and PAHs); for other effects (PCDD/Fs and PCBs), the value of an allocation factor of 10% is not considered to be sufficiently justified by the Dossier Submitter.

RAC concurs with the Dossier Submitter that other studies that analysed contaminants in baby diapers are either old and do not adequately reflect the present manufacturing process of diapers; the extraction methods used (solvent extractions) differed from the one recommended in the present restriction proposal (urine simulant extraction); or are too limited in reporting the study methodology.

Taking these issues into consideration, RAC concludes the following for the risk characterisation for substances in the scope of the proposed restriction:

Formaldehyde: In contrast to the Dossier Submitter's calculation, the sensitivity analysis performed by RAC showed RCR values below 1, with or without the allocation factor of 10%. However, RAC considers that skin sensitisation is probably the most sensitive critical effect following dermal exposure to formaldehyde in any case. Although this critical effect has not been assessed by the Dossier Submitter, an illustrative example calculated by RAC does not indicate a risk for skin sensitisation. RAC, therefore, concludes that the risk posed by formaldehyde has not been demonstrated by the Dossier Submitter. It should be also pointed out that formaldehyde in single-use diapers is within the scope of the proposed restriction on skin sensitisers in textiles (ECHA, 2020).

PAHs: Similar to the Dossier Submitter's analysis, RAC's sensitivity analysis showed RCR values several orders of magnitude above 1, both for direct and indirect exposure. The allocation factor was not applied, since local effect, i.e. skin tumorigenesis, was the critical effect. Nevertheless, RAC has identified significant uncertainties related to the PAH analyses performed by DGCCRF/INC and SCL (described in section 3.1.3. and *"Key elements underpinning the RAC conclusions"* below), due to which the risk for babies from exposure to PAH substances in single-use diapers cannot be characterised at present.

PCDDs/Fs/DL-PCBs. In contrast to the Dossier Submitter's calculation, RAC's sensitivity analysis showed RCRs below 1 for indirect exposure, direct exposure, and for the sum of RCRs for indirect and direct exposure. Allocation factor to the RCR could be justified for this group of substances, as discussed in *"Key elements underpinning the RAC conclusions"* in this section. However, RAC considers that the precise value of the allocation factor (i.e., 10%) is not sufficiently justified by the Dossier Submitter and points out that RCRs from mother's milk are two orders of magnitude higher than from diapers (EFSA, 2018). Considering uncertainties related to analyses performed by DGCCRF/INC and SCL (section 3.1.3 above), and the fact that the contribution of diapers to PCDDs/Fs/DL-PCBs exposure is negligible compared to

exposure from human milk, RAC concludes that presently available evidence is not reliable enough to justify a restriction for this group of substances.

NDL-PCBs were not analysed by DGCCRF/INC and SCL in diaper samples, so the risk has not been characterised.

Overall, RAC concludes that due to the high level of uncertainties related to the exposure assessment and risk characterisation of the substances in the scope of this restriction proposal, **the EU-wide risk for babies and infants wearing single-use diapers has not been demonstrated for the substances in the scope of the Annex XV dossier.**

For **formaldehyde**, RAC concludes that risk of skin sensitisation is a more appropriate assessment endpoint in diapers than the systemic effects proposed by the Dossier Submitter and that exposure to formaldehyde via diapers would be likely to be 20 times below reported elicitation thresholds for sensitisation. RAC also notes that as formaldehyde has a harmonised classification as a skin sensitiser it would be restricted in single-use diapers by means of the proposed restriction on skin sensitisers under REACH as such no further action for formaldehyde would appear to be necessary.

For **PCDD/Fs** and **DL-PCBs**, RAC has undertaken a sensitivity analysis of the Dossier Submitter's exposure assessment using more realistic conditions of use and concludes that risks for the endpoints assessed by the Dossier Submitter would be unlikely to occur from the wearing of single-use baby diapers because the assumptions used by the Dossier Submitter (and their inherent uncertainties) would tend to result in significant overestimates of exposure and risk. Nevertheless, RAC notes that the size of the allocation factor used for risk characterisation is a critical uncertainty in determining whether a risk would occur for certain sub-populations (i.e. formula-fed infants) and the that the Dossier Submitter did not assess the potential for risks via all potentially relevant endpoints (i.e. via endocrine disruption). Therefore, it is not possible to conclude that there are no potential risks from these substances in single-use diapers based on the available assessment.

For **PAHs**, RAC concluded that the available analytical data are of insufficient quality for a reliable exposure assessment, which means that risks cannot be reliably characterised.

For **NDL-PCBs**, there are no analytical data upon which to base an assessment. Therefore, similar to PAHs, RAC cannot conclude whether NDL-PCBs in diapers pose a risk or not.

In order to address the highlighted uncertainties and enable a reliable risk assessment in an updated restriction proposal, several aspects could be considered:

- The simulated urine extraction method clearly has potential (above solvent extraction) but needs standardising with more realistic exposure assumptions;
- Suitable low and consistent limits of detection and quantification are needed for the analysis of the substances of concern and should include method validation within the range to be analysed and appropriate analytical and extraction method blanks;
- Realistically, further measurement campaigns showing consistent results would be needed to provide a strong basis upon which to base a risk assessment in support of a restriction proposal;

- Further investigations do not necessarily apply only to the substances in the scope of this restriction proposal but also to other hazardous substances, including fragrances, VOCs and pesticide residues;
- The use of allocation factors would need to be carefully justified.

RAC considers that the time required to obtain this information will be determined by:

a) the development of more sensitive analytical methods, bearing in mind the very low levels of derived DN(M)ELs for PAHs as well as PCDDs/Fs and PCBs set by the Dossier Submitter's restriction proposal and;
b) The standardisation of the simulated urine extraction method.

The potential consequences of inaction while this information is being generated are difficult to predict. The very limited human data available do not indicate an increased risk from testicular carcinoma in adult life associated with single-use diaper wearing during infancy (e.g., Møller, 2002), but they are not considered sufficient to conclude that there is no risk regarding carcinogenic effects of PAHs in single-use baby diapers. Similarly, there is generally a lack of human data on endocrine-disrupting effects of environmental contaminants (such as PCDDs/Fs/DL-PCBs at a very low levels of exposure.

RAC, however, thinks that the implementation of EDANA´s Stewardship Programme[27] for all manufacturers/importers of diapers in the EU/EEA could alleviate somewhat the potential consequences of inaction until the aforementioned information is generated. But, as discussed above, RAC has not evaluated the scheme in detail.

Key elements underpinning the RAC conclusion(s):

Considering 95th percentile of measured concentrations of substances in 51 diaper samples (SCL 2018, 2019), frequency of diapers' change (7.98), diaper weight (0.0231 kg), skin absorption (0.5) and baby's body weight (5.2 kg) for the class of age from zero to six months, the Dossier Submitter calculated daily exposure dose (DED) and RCR values ("DS" – "RCR 10%", Tables RCR1 - 3).

$$DED_{0\text{-}6} = (C_{diaper} \times F \times W \times Abs_{skin}) / BW$$

$$RCR_{0\text{-}6} = DED / DNEL$$

RAC notes that the sensitivity analyses were provided by the Dossier Submitter in order to address the uncertainties related to the frequency of diaper change considered in the exposure scenario. However, the sensitivity analyses were not performed by the Dossier Submitter regarding the rewet factor.

[27] https://www.edana.org/how-we-take-action/edana-stewardship-programme-for-absorbent-hygiene-products

Sensitivity analysis by RAC:

1) using the same 95th percentile values which were used by the Dossier Submitter in their analysis;
2) applying a rewet factor of 0.66% (as a realistic worst-case value from the PERMID method described by Dey et al., 2016), instead of 35% extracted urine simulant volume applied by the Dossier Submitter;
3) applying 2 instead of 7.98 diaper changes, in order to stay within the range of expected daily urinary output of babies during the first year of life (i.e., 400 to 600 mL per 24h);
4) adding direct transfer of 4.3% (as a realistic worst-case value from the PERMID method described by Dey et al., 2016) for substances for which data for solvent extraction from shredded diaper parts were available in the ANSES report (2019; Table 55). Only diaper parts that could be in direct contact with baby's skin were considered (e.g., top sheet, elastic parts; Rai et al., 2009)[28].

In the calculations performed by RAC, the volume of urine simulant per day was not corrected to more realistic values, i.e., volume of urine simulant in these calculations is 2 to 3 times higher than it is normally expected for two months to 12 months old babies. This more conservative approach allows for other uncertainties, e.g., for potential variability of rewet factor or uncertainty whether the urinary simulant extraction of the substances in the scope of this restriction proposal follows a linear function or whether the extraction capacity is reduced over time.

Regarding the allocation factor of 10% for the calculation of risk, RAC acknowledges that different exposure routes and sources (food, ambient air, cosmetic products, objects and toys) might contribute to the uptake of substances in the scope of the Annex XV dossier. However, RAC considers that the Dossier Submitter's approach to use an allocation factor of 10% for the calculation of risk is not sufficiently justified. The extent of the share depends on the substance, on the route which is considered in the exposure scenario (e.g., dermal route) and the approach chosen for the hazard assessment (e.g., dermal slope for PAHs). Thus, RAC considers that an allocation factor is not justified for formaldehyde and PAHs, for which local effects are the most relevant ones for this restriction proposal. For substances like PCDDs/Fs and PCBs for which systemic effects (reprotoxicity, immunotoxicity) were considered critical, an allocation factor is justified (Costopoulou et al., 2013; EFSA, 2017). However, in RAC's opinion, the Dossier Submitter has not provided sufficient documentary evidence regarding why an allocation of the total daily intake (TDI) to 10% from diapers reflects a reasonable level of exposure.

<u>Formaldehyde</u>

When a rewet factor of 0.66% was applied in RAC's sensitivity analysis, RCRs were well below 1, either with 2 or 8 diaper changes. Direct contact could not be calculated since there were

[28] INC and SCL calculated daily exposure dose (DED) according to formula DED = ($C_{shredded\ material}$ x W x F x T x Abs)/BW, where $C_{shredded\ material}$ is the highest concentration of the chemical extracted with a solvent from shredded diaper parts (mg/kg of the diaper); W is the average weight of the diaper part (kg); F is the frequency of use (12 per day); T is transfer to the skin (100%); Abs is fraction absorbed by the skin (100%); and BW is body weight of a child (2.6 kg). RAC recalculated these values using 8 instead of 12 diaper changes per day, body weight of 5.2 kg instead of 2.6 kg, and 50% absorption via the skin.

no data available in ANSES report for formaldehyde in diaper parts.

Table 11 Risk characterisation for formaldehyde, calculated by the Dossier Submitter and by RAC (sensitivity analysis)

Substance(s)	Rewet factor	95th percentile (mg/kg)	Frequency of diaper change/day	Diaper weight (kg)	Skin abs.	Body weight (kg)	DED (mg/kg bw/day)	DN(M)EL	RCR	RCR 10%
Formaldehyde										
DS	35%	1.77	8	0.0231	0.5	5.2	0.03132	0.075	**0.42**	**4.18**
	35%	1.77	2	0.0231	0.5	5.2	0.00785	0.075	**0.10**	**1.05**
Rapps										
Indirect contact	0.66%	0.033	8	0.0231	0.5	5.2	0.00059	0.075	**0.008**	**0.08**
	0.66%	0.033	2	0.0231	0.5	5.2	0.00015	0.075	**0.002**	**0.02**

DED = daily exposure dose; RCR 10% = RCR with 10% allocation factor applied; DS = Dossier Submitter

Regarding the allocation factor, the Dossier Submitter argues that an allocation of 10% of the TDI to the intake of formaldehyde (due to its carcinogenic effect) was used to derive a migration limit for formaldehyde in toys (Commission Directive (EU) 2019/1929 of 19 November 2019 amending Appendix C to Annex II to Directive 2009/48/EC). However, this cannot be extrapolated to this restriction proposal as RAC is of the opinion that local effects, i.e., skin sensitisation, is probably the most sensitive critical effect following dermal exposure to formaldehyde. This critical effect has not been assessed by the Dossier Submitter.

Just as an illustration for a possible approach to risk characterisation based on skin sensitisation, RAC compared skin exposure to formaldehyde in diapers with the elicitation threshold for formaldehyde (20.1 µg/cm^2; Flyvholm et al., 1997) used in the proposed restriction on skin sensitisers in textiles (ECHA, 2020). RAC calculated skin exposure to formaldehyde in diapers as a ratio between:

- formaldehyde content extracted by urine simulant during 24h (based on 95th percentile of formaldehyde concentration measured in diaper samples by SCL and DGCCRF/INC), i.e., 326 µg/day;[29] and
- skin area in contact with diaper (287 cm^2) according to ECHA, 2017 and Boniol et al., 2008);

obtaining the value of: 326 µg/day / 287 cm^2 = 1.1 µg/cm^2.

This value is approximately 20 times lower than the elicitation threshold of 20.1 µg formaldehyde/cm^2. RAC considered that elicitation threshold value (Flyvholm et al., 1997) has been obtained in adults and not in infants, and that diaper dermatitis, a common problem in children, is considered to increase the risk for allergic sensitisation (e.g., Sweeney et al. 2021). Nevertheless, it is considered that the use of elicitation instead of induction dose (which is expected to be higher than elicitation dose) in the calculation, alleviates these uncertainties. RAC also points out that formaldehyde in single-use baby diapers is within the scope of the proposed restriction on skin sensitisers in textiles (ECHA, 2020).

[29] C_{diaper} (95th percentile) x frequency of diaper changes x diaper weight = 1.77 mg/kg x 7.98 x 0.023 kg = 0.326 mg/day

PAHs

Even when applying a rewet factor of 0.66%, 2 diaper changes, and no allocation factor (since the local effect, i.e., skin tumorigenesis, was the critical effect) in RAC's sensitivity analysis, RCR was several orders of magnitude above 1 for indirect contact. For direct contact (PAHs were detected/quantified in elastic parts of diapers by solvent extraction; ANSES, 2019), RCR was also several orders of magnitude above 1. The sum of RCRs for direct and indirect exposure were approximately 4 orders of magnitude above 1.

Table 12 Risk characterisation for PAHs, calculated by the Dossier Submitter and by RAC (sensitivity analysis)

Substance(s)	Rewet factor/ Direct transfer	95th percentile (mg/kg)	Frequency of diaper change/day	Diaper weight (kg)	Skin abs.	Body weight (kg)	DED (mg/kg bw/day)	DN(M)EL	RCR
PAHs, sum	Rewet factor								
DS	35%	1.080	8	0.0231	0.5	5.2	0.01914	4.00E-09	4783815
	35%	1.080	2	0.0231	0.5	5.2	0.00480	4.00E-09	1198951
Rapps	Rewet factor								
Indirect contact	0.66%	0.020	8	0.0231	0.5	5.2	0.00036	4.00E-09	90209
	0.66%	0.020	2	0.0231	0.5	5.2	0.00009	4.00E-09	22609
	Direct transfer								
Direct contact	4.3%	0.141	8	0.00012007	0.5	5.2	1.3E-05	4.00E-09	3246

DED = daily exposure dose; DS = Dossier Submitter

Nevertheless, RAC recognises several significant uncertainties related to PAHs analyses performed by DGCCRF/INC and SCL, mainly described in section 3.1.3. above. In the sensitivity analysis, the 95th percentile was calculated based on the data from both sets of measurements (from 2018 and 2019). It should be stressed that in the analysis carried out in the year 2019, only 4 out of 32 samples had detectable level of one PAH (benzo[a]anthracene). Since the lowest LoD in 2019 analysis (100 ng/kg) is four orders of magnitude higher than the proposed migration limit for PAHs (0.023 ng/kg), it is not known whether the true quantity (if any) of non-detected PAHs were above or below the proposed migration limits.

RAC considers that due to these uncertainties, the risk for babies from exposure to PAH substances in diapers cannot be characterised at present.

PCDDs/Fs/DL-PCBs

When applying a rewet factor of 0.66%, 2 diaper changes, and no allocation factor, RAC's sensitivity analysis showed RCRs below 1 for indirect exposure, direct exposure (furans were detected/quantified by solvent extraction in topsheet layer and other diaper parts, excluding diaper's core which is not in direct contact with baby's skin; ANSES, 2019), and for the sum of RCRs for indirect and direct exposure.

Table 13 Risk characterisation for PCDDs/Fs/DL-PCBs, calculated by the Dossier Submitter and by RAC (sensitivity analysis)

Substance(s)	Rewet factor/ Direct transfer	95th percentile (mg/kg)	Frequency of diaper change/day	Diaper/ diaper part weight (kg)	Skin abs.	Body weight (kg)	DED (mg/kg bw/day)	DN(M)EL	RCR
PCDD/Fs/DL-PCBs	Rewet factor								
DS	35%	3.1E-07	8	0.0231	0.5	5.2	5.53E-09	3.00E-10	18.4
	35%	3.1E-07	2	0.0231	0.5	5.2	1.38E-09	3.00E-10	4.6
Rapps									
Indirect contact	0.66%	5.9E-09	8	0.0231	0.5	5.2	1.04E-10	3.00E-10	0.35
	0.66%	5.9E-09	2	0.0231	0.5	5.2	2.61E-11	3.00E-10	0.09
	Direct transfer								
Direct contact	4.3%	5.5E-08	8	0.001-0.006	0.5	5.2	1.6E-10	3.00E-10	0.52
							Sum RCR for 8 changes =		0.87
							Sum RCR for 2 changes =		0.61
PCDD/Fs/DL-PCBs in breastfed infants with average human milk consumption (EFSA 2018)							3.29E-08	3.00E-10	110
PCDD/Fs/DL-PCBs in breastfed infants with high human milk consumption (EFSA 2018)							4.93E-08	3.00E-10	164
Mean exposure via infant formula (Infant TDS, ANSES 2016)							2.00E-10	3.00E-10	0.67

DED = daily exposure dose; DS = Dossier Submitter

Allocation factor to the RCR could be justified for this group of substances, as discussed above. However, RAC considers that the precise value of the allocation factor (i.e., 10%) is not sufficiently justified by the Dossier Submitter. For example, allocation factor for diapers is expected to differ several orders of magnitude between breastfed infants and infants fed with infant formula (Table RCR3). Namely, according to EFSA report (2018), the RCR from mother's milk is two orders of magnitude higher than from diapers.

Considering the uncertainties related to analyses performed by DGCCRF/INC and SCL (described in section 3.1.3. above), and the fact that the contribution of diapers to PCDDs/Fs/DL-PCBs exposure is negligible compared to dietary sources, i.e., human milk, RAC concludes that presently available evidence is not substantial (or reliable) enough to justify a restriction proposal for this group of substances.

NDL-PCBs were not analysed by DGCCRF/INC and SCL in diaper samples, so the risk for these substances has not been characterised.

3.1.5. Evidence if the risk management measures and operational conditions implemented and recommended by the manufactures and/or importers are not sufficient to control the risk

Summary of proposal:

For all the chemicals in the scope of the restriction proposal, the migration limits are far below the highest limits found in single-use baby diapers at point of sale. Therefore, the Dossier Submitter concludes that the risks associated with these substances are not adequately controlled. Hence, lowering the concentrations of these chemicals in single-use baby diapers, so that they comply with the migration limits proposed, is considered to significantly reduce the risk. The limits proposed are considered to adequately protect infants and children under the age of three.

RAC conclusion(s):

RAC notes that none of the substances in the scope of the Annex XV dossier are intentionally added to diapers according to information provided by industry. Although a risk for babies has not been demonstrated for formaldehyde, PCDDs/Fs/DL-PCBs and cannot be characterised for PAHs and NDL-PCBs, RAC is of the opinion that each of these substances should be kept to a level as low as possible/feasible[30] in single-use baby diapers, and preferably not be present at all. RAC notes that the POPs (Persistent organic pollutants) regulation already covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed.

Key elements underpinning the RAC conclusion(s):

According to information provided by industry, e.g., comment #3165, "formaldehyde, PCDD/Fs and DL-PCBs, PCBs and PAHs are not intentionally added" to single-use baby diapers. They are impurities and according to information obtained during the consultation, there is no clear knowledge where these substances come from. According to comment #3162, source of contaminates could be raw materials, oils, glues, wetness indicator, pigments, etc. However, it is also noted that the source for PCCDs/Fs and PCBs are most likely from cellulose (comment #3208).

3.1.6. Evidence if the existing regulatory risk management instruments are not sufficient

Summary of proposal:

At EU level, baby diapers are subject to the general safety requirements defined by European legislation related to consumer goods. A European regulatory framework specific to babies' diapers does not exist. In 2019, ANSES published a report on the risks associated with the presence of hazardous substances in single-use baby diapers and made recommendations for risk reducing measures (ANSES, 2019).

There is no epidemiological data demonstrating an association between health effects and the wearing of diapers. However, hazardous chemicals have been found in single-use baby diapers. Based on the results of the tests and the literature data, a quantitative health risk assessment was undertaken for single-use baby diapers according to realistic scenarios. This assessment showed cases of the health thresholds being exceeded for several substances. Therefore, the Dossier Submitter concludes that it is not possible to rule out a health risk associated with the repeated wearing of single-use diapers and recommends regulatory actions to be taken.

RAC conclusion(s):

RAC is of the opinion that the EU-wide risk for babies and infants wearing single-use diapers has not been demonstrated for the substances in the scope of the Annex XV dossier.

[30] Feasibility refers in to technical (incl. analytical methods) and economic feasibility.

Nevertheless:

- for **PCDD/Fs and DL-PCBs**, RAC notes that the Dossier Submitter did not assess the potential for risks via all potentially relevant endpoints (i.e., via endocrine disruption) therefore, it is not possible to conclude that there are no potential risks from these substances in single-use diapers based on the available assessment (see section 3.1.4).

- for **PAHs**, RAC concludes that the available analytical data are of insufficient quality for a reliable exposure assessment, which means that risks cannot be reliably characterised (see section 3.1.4).

- for **NDL-PCBs**, there are no analytical data upon which to base an assessment. Therefore, similar to PAHs, RAC cannot conclude whether NDL-PCBs in diapers pose a risk or not (see section 3.1.4).

RAC acknowledges that there is no binding EU wide regulation which deals with migration limits of hazardous substances like formaldehyde, PAHs, PCDDs/Fs and PCBs in disposable baby diapers.

With regard to formaldehyde, RAC refers, however, to its opinion on the Annex XV dossier on skin sensitisers in textiles, leather, fur and hide articles (skin sensitising substances in textiles – ECHA,2020) which would very likely address the risk of this substance to induce allergic effects in the population addressed by the restriction proposal if adopted. Systemic effects of formaldehyde via the dermal route are highly unlikely according to RAC.

Key elements underpinning the RAC conclusion(s):

The potential risks associated with EU manufactured or imported single-use baby diapers articles containing the chemicals of concern need to be addressed on a Union-wide basis since exposure takes place in all Member States.

3.2. JUSTIFICATION IF ACTION IS REQUIRED ON AN UNION WIDE BASIS

Justification for the opinion of SEAC and RAC

Summary of proposal:

At EU level, baby diapers are subject to the general safety requirements defined by European legislation related to consumer goods. There is no regulatory framework specific to babies' diapers in the EU.

According to the Dossier Submitter, one of the primary reasons to act on a Union-wide basis is the cross-boundary human health problem: a risk from exposure exists in all Member States and because trans-boundary trade between Member States exists. A Union-wide regulatory measure would also ensure a harmonised high level of protection for human health across the Union.

RAC conclusion(s):

Single-use baby diapers are produced, marketed, transported and used throughout the EU, traded between Member States and also imported from outside Europe. As such, any action aiming to reduce the exposure of children to hazardous substances in single-use diapers should be taken on a Union-wide basis. The substances in the scope of the restriction proposal should be kept to a level as low as possible/feasible, and preferably not be present at all. RAC notes that the POPs (Persistent organic pollutants) regulation already covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed.

Furthermore, based on the key principles of ensuring a consistent level of protection across the Union and of maintaining the free movement of goods within the Union, RAC supports the view that any necessary action to further reduce the substances in the scope of the restriction proposal should be taken. These substances are either classified for carcinogenicity, mutagenicity and skin sensitisation according to the CLP Regulation (formaldehyde), investigated for their carcinogenic potential (PAHs), or associated with various health effects, including toxic effects, adverse reproductive effects, mutagenicity effects, genotoxic effects and endocrine effects (PCDD/Fs, PCBs), see section 3.1. in this opinion.

SEAC conclusion(s):

Key elements underpinning the SEAC and RAC conclusions:

The Dossier Submitter presents two reasons to justify acting on a union-wide basis:

A. Severity and extent of health risks

While no epidemiological data exists that shows an association between health effects and the wearing of diapers, the Dossier Submitter does contend that there is a risk of exposure to several hazardous substances present in single-use baby diapers above health thresholds. Additionally, children and infants' sensitivity to chemical exposure is known to be higher when compared to adults. The Dossier Submitter estimates that about 90% of European babies (about 14.5 million) wear only single-use diapers.

As stated before, the available human and animal data provides very limited information for the assessment of health risks from the hazardous chemicals present in baby diapers. RAC notes that it is very difficult (and therefore very unlikely) that associations will be found in epidemiological data to demonstrate such a health risk for babies/children posed by the substances in the scope of this restriction proposal. Hazardous substances in modern diapers are mostly at very low levels, while health effects like cancer, adverse reproductive effects, mutagenicity effects, genotoxic effects and endocrine effects are complex, multifactorial adverse effects, mostly with a long latency period. These factors demand very large sample size to obtain adequate statistical power, and there is still an issue of uncontrolled/unrecognised confounding factors. Lack of human evidence, therefore, cannot exclude the risk, especially regarding non-threshold effects, such as genotoxic carcinogenicity or endocrine disruption. Consequently, it is necessary to keep these substances to a level as low as possible/feasible in such articles, and preferably not be present at all. RAC notes that the POPs (Persistent organic pollutants) regulation already covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed.

B. Free movement of goods

Single-use baby diapers, both imported and manufactured, circulate freely throughout the EU. If action is still deemed necessary by the Commission, despite the scientific uncertainties raised by RAC, it should be taken on a union-wide basis to have a harmonised treatment of these goods within the EU and to avoid competitive distortion.

3.3. JUSTIFICATION WHETHER THE SUGGESTED RESTRICTION IS THE MOST APPROPRIATE EU WIDE MEASURE

Justification for the opinion of SEAC and RAC

Scope including derogations

Justification for the opinion of RAC

Summary of proposal:

The intention of the proposed restriction is to minimise health risks associated with the wearing of single-use baby diapers on children and infants under the age of three. The restriction proposal covers finished single-use baby diapers which are placed on the market for children and infants under the age of three.

The articles covered by the restriction proposal are the following:

- Single-use baby diapers,
- Single-use baby diaper pants or training pants for toilet-training the child,
- Single-use night diapers intended for children over three years of age, in order to help them with toilet training at night,
- Single-use swimming diapers used when babies/children are engaging in water activities.

The articles not covered by the current restriction proposal are the following:

- Re-usable diapers: Unlike single-use baby diapers, reusable diapers can be re-used after being worn and washed. Different types of re-usable diapers exist with all or only some parts of them that can be re-usable.
- Incontinence diapers: Incontinence diapers are articles made of various materials which objectives are to absorb and contain urines and (faeces) from incontinence persons while keeping their skin dry. Incontinence diapers are regulated by the regulation EU 2017/745 (Medical Devices).

The following REACH restriction options were considered by the Dossier Submitter:

- Restriction option 1 (RO1): Limiting concentrations of migration of formaldehyde, the sum of detected or quantified 17 PAHs, the sum of quantified PCDD/Fs and DL-PCBs, the sum of quantified PCBs.
- Restriction option 2 (RO2): Limiting concentrations of migration of all the substances and sum of substances listed in RO1 and all the congeners of the PAHs, PCDD/Fs and

DL-PCBs.

The following risk management options were briefly considered, but not assessed further by the Dossier Submitter:

- Labelling requirements: Harmonised classification of substances according to the CLP regulation entails requirements, such as labelling, but would require a long process given that not all substances in the scope have harmonised classification. Since labelling does not force companies to replace the substances of concern, it is likely to have a smaller economic impact on the EU diaper sector, in comparison to a total ban or a REACH restriction limiting the concentration.
- Identification as SVHC according to REACH Article 57 and subsequent authorisation: SVHC identification and the authorisation system are designed for risk management of one substance at a time and it would be a very time consuming, and therefore inefficient, process to regulate the risks taking each possible hazardous chemical in single-use baby diapers. Moreover, the requirements for authorisation only apply to articles produced in the EU.
- Harmonised classification of substances under CLP (EC) No 1272/2008: similar challenges as for labelling above.
- Other legislations:
    - The General Product Safety Directive (GPSD) (EC) No 2001/95: Under this legislation consumer products that pose an acute health risk in various Member States, e.g., because of a specific chemical substance, may become temporarily restricted by a Commission Decision. This type of restriction, however, provides only short-term solutions that apply one year at a time awaiting permanent regulations. It does not directly apply in EU Member States, but must be implemented through national legislation, and does thus not imply a full harmonisation. Moreover, the GPSD deals with acute health risk while the concerns raised by the substances in the scope of this assessment are related to chronic health effects.
    - The Medical Device Regulation (EU) No 2017/745: Incontinence diapers are considered as medical device according to the regulation (EU) 2017/745. However, a single-use baby diaper cannot be considered a medical device because it is not an article used to achieve a function that the human body could not achieve anymore.
    - Childcare articles: Single-use baby diapers can be considered as childcare articles according to the definition in Directive 76/769/EEC. However, this definition does not imply any limitation regarding the chemicals to be used except for the phthalates that are restricted in childcare articles under REACH.
- Development of a specific EU product legislation covering single-use baby diapers: The development of a specific single-use baby diaper regulation is considered possible in the long-term only. Given the current conditions, the risks with chemicals in single-use baby diapers can be addressed under existing chemical regulations (meaning the restriction under REACH regulation). If a specific baby diapers regulation is further developed, existing restrictions could be integrated in that act.

- Voluntary actions: The Scientific Committee on Consumer Safety (SCCS) could be asked to develop an opinion on these chemicals, which could then be sent to industry as a guide to ensure safer single-use baby diapers. However, such a guide would not be mandatory for industry and would not include enforcement measures for the authorities to control if single-use baby diapers put onto the market follow the recommendations.

RAC conclusion(s):

RAC agrees in principle with the Dossier Submitter in the consideration that a restriction under REACH, Article 69 would be the most appropriate risk management option for substances in the scope of the Annex XV dossier which pose a risk for babies and children under the age of three.

However, since the risk for babies from formaldehyde, and PCDDs/Fs/DL-PCBs wearing single-use baby diapers, has not been demonstrated and cannot be characterised for PAHs and NDL-PCBs, RAC is of the opinion that it has not been demonstrated that a restriction is the most appropriate measure.

In the meanwhile, the already existing EDANA Stewardship Programme for Absorbent Hygiene Products[31] - a voluntary action by industry - could ensure a standard throughout the EU/EEA in dealing with impurities/contaminants. However, RAC does not see this as any substitute for a restriction under REACH should the risk be adequately demonstrated. This programme may help to further reduce the concentration of the substances in the scope of the Annex XV dossier – but also of other substances like phthalates, organotins, metals - in all single-use diapers put on the European market. As indicated by industry orally, 85% of the European manufacturers comply to this programme, however, that means that, still, a number of producers of single-use baby diapers does not follow this programme. In addition, RAC points out that importers may not be addressed by the Stewardship Programme at all.

The POPs (Persistent organic pollutants) regulation covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed. RAC therefore considers that there is a concern related to the proposed restriction being counter to the objectives of the existing POPs regulation.

With regard to the articles covered by the scope, RAC considers that this topic is clear but it is not possible to support any of the two risk options (RO1 or RO2) considered by the Dossier Submitter due to the uncertainties and shortcomings related to the exposure assessment and risk characterisation.

RAC notes that no derogations were claimed during the commenting period, probably due to the fact that the same "base material" might be used for all the different diapers listed in the scope of the restriction proposal.

Key elements underpinning the RAC conclusion(s):

RAC is of the opinion that based on the information in the Annex XV dossier and its Annex,

[31] https://www.edana.org/how-we-take-action/edana-stewardship-programme-for-absorbent-hygiene-products/the-edana-absorbent-hygiene-product-stewardship-programme-codex

none of these RMOs would be more efficient than a restriction under REACH, Article 69 if the substances in the scope of the Annex XV dossier pose a health risk for babies and children.

In the following RAC briefly describes why the other RMO mentioned by the Dossier Submitter are not considered to be more efficient than a restriction under REACH:

Introduction of labelling requirements for disposable baby diapers on the EU market containing formaldehyde, PAHs, PCDDs/Fs and or PCBs without any restriction: RAC considers that labels on disposable diapers might not be an appropriate measure in order to reduce a health risk for babies and children because labels would not force manufacturers to reduce the concentration of the substances in the scope of the Annex XV proposal in single-use diapers.

Identification as SVHC according to REACH Article 57 and subsequent authorization: The Authorisation process in the EU only applies to the use of a chemical during its incorporation into an article. Since the substances in the scope of the Annex XV dossier are not intentionally added, Authorisation is not considered to be an appropriate RMO by RAC.

Harmonised classification of substances under CLP (EC) No 1272/2008: Although harmonised classification is an important tool to "identify" substances of high concern, it does not protect babies and children from exposure to the substances in the scope of the Annex XV dossier. Therefore, RAC does not consider classification to be an appropriate RMO concerning impurities in disposable baby diapers.

Other legislation:
Legislations like the General Product Safety Directive (EC) No 2001/95 apply to disposable baby diapers. However, since such a general regulation does neither include information on maximum concentration levels of any impurities nor does it regulate specific (concentration/migration) limits of hazardous substances, it might contribute to address the problem only partially.

RAC notes that a regulatory framework to babies' diapers, which tackles specific concentration/migration limits on hazardous substances in these products, has not yet been implemented in the EU. RAC considers, however, that a restriction under REACH might result in lower administrative burden than the development of a specific EU product regulation in respect to specific migration/concentration limits.

Although RAC acknowledges that the POPs regulation is solvent and not urine based, the regulation addresses the content of impurities on PCBs.

Voluntary actions:
A review of 47 studies on voluntary agreements between governments or government bodies and individual businesses or industry groups concluded that, if properly implemented and monitored, voluntary agreements can be effective (Bryden and al., 2013). Although RAC considers that the effectiveness of voluntary agreement in general is highly uncertain and therefore this option, in absence of complementary legislation, is usually not feasible in terms of risk management, RAC points out that according to comment #3165 (industry) EDANA member companies have adhered to the guidance values set in the Codex™ related to EDANA´s Stewardship Programme. Due to the lack of existing legislation which covers migration limits for PAHs, PCDDs/Fs in single-use baby diapers, it would make sense to use the Codex™ until a specific legislation exists. However, RAC points out that it has not

evaluated the migration limits listed in the Codex™ or how effectively the member companies have implemented these limits, since such evaluations are not in its remits.

Justification for the opinion of SEAC

See SEAC opinion

3.3.1. Effectiveness in reducing the identified risks

Justification for the opinion of RAC

Summary of proposal:

RO1 (the proposed restriction covering formaldehyde, the sum of detected or quantified 17 PAHs, the sum of quantified PCDD/Fs and DL-PCBs, and the sum of quantified PCBs) is considered to be the most efficient restriction option in terms of risk reduction capacity. The migration limits proposed are deemed to adequately protect children and infants against adverse effects caused by the chemicals of concern. It is considered that RO1 would protect at least 90% of European babies (i.e., 14.5 million babies) from being exposed to hazardous chemicals contained in their diapers every year within the EEA31. The lack of harmonised analytical method may be an issue. However, and due to current research by industry to put in place a harmonised analytical method, the Dossier Submitter is confident that this will be in place before the end of the transitional period proposed (24 months).

RAC conclusion(s):

RAC notes that the effectiveness in reducing the risks cannot be assessed due to the uncertainties related to the exposure/risk characterisation.

Since RAC considers that for formaldehyde local effects, i.e., skin sensitisation, is more relevant than systemic effects (as pointed out in section 3.1.2.), these effects would be very likely covered by the proposed restriction on skin sensitising substances in textiles.

Key elements underpinning the RAC conclusion(s):

RAC notes that any action to reduce the substances in the scope of the restriction proposal would be appreciated since they are in general known to cause health effects like cancer, adverse reproductive effects, mutagenicity effects, genotoxic effects, endocrine effects and skin sensitisation. Therefore, it is necessary to keep these substances to a level as low as possible/feasible in such articles, and preferably not be present at all. RAC notes that the POPs (Persistent organic pollutants) regulation already covers the unintentional presence of PCBs in all articles, including diapers, and, as such, no PCB content above the detection limit would be allowed.

With regard to formaldehyde, RAC points out that formaldehyde in single-use baby diapers is within the scope of the proposed restriction on skin sensitisers in textiles (ECHA, 2020), see section 3.1.4. *"Key elements underpinning the RAC conclusion(s)".*

3.3.2. Socio-economic impact

Justification for the opinion of SEAC

3.3.2.1. Costs

See SEAC opinion

3.3.2.2. Benefits

See SEAC opinion

3.3.2.3. Other impacts

See SEAC opinion

3.3.2.4. Overall proportionality

Summary of proposal:

The proposed restriction will bring benefits to society due to the avoided health impacts of adverse effects on babies' health even though their magnitude could not be accurately assessed. Potentially very severe, variable and latent diseases affecting their quality of life over their lifetime are expected to be avoided in babies at older ages and in their adulthood such as cancers, suspected endocrine disruption, reprotoxic effects, etc. Given the widespread use of single-use baby diapers, the Dossier Submitter considers that the proposed restriction is expected to prevent 90% of European babies (i.e. 14.5 million babies) from being exposed to hazardous chemicals contained in their diapers every year. Due to uncertainties and a lack of data, the benefits could not be quantified but a break even analysis was performed by the Dossier Submitter to evaluate proportionality of the proposal.

RAC conclusion(s):

RAC notes that from a risk point of view, the uncertainties related to the restriction proposal's exposure and risk assessments are such that a risk for babies has not been demonstrated for formaldehyde and PCDDs/Fs/DL-PCBs, and cannot be characterised for PAHs and NDL-PCBs.

Key elements underpinning the RAC conclusion(s):

The uncertainties and shortcomings described in sections 3.1.3 and 3.1.4 do not allow RAC to conclude that a risk has been demonstrated; in its absence, the full implementation of the EDANA programme aimed at limiting the use of hazardous substances may contribute to further reduce any potential risk. However, RAC does not see this as any substitute for a restriction under REACH should the risk be adequately demonstrated.

3.3.2.5. Uncertainties in the proportionality section

Give the relevant uncertainties here and summarise in the separate section at the end of the justification.

3.3.3. Practicality, incl. enforceability

Justification for the opinion of RAC and SEAC

Summary of proposal:

Difficulties are expected from a technical and/or economic standpoint regarding the analytical feasibility for testing and monitoring capacity of the restriction. For now, no standardised analytical method exists using an extraction by urine simulant in a whole diaper. Considering that companies, laboratories but also EU enforcement services will have to build this new analytical method, even define a CEN standard, the transitional period of 24 months is considered by the Dossier Submitter as necessary.

RAC and SEAC conclusion(s):

RAC concludes that the following issues should be considered to ensure the practicality of the proposed restriction:

- the LoQ of the respective analytical method should be below the limit values of the restriction for all substances in scope; and
- the development of a standardised methodology will facilitate the achievement of harmonised results given the specific sampling method proposed for this restriction.

Key elements underpinning the RAC and SEAC conclusion(s):

According to the Forum's advice, the scope of the restriction would be enforceable. However, the LoQ of the respective analytical method should be below the limit values of the restriction for all the substances regulated. The relation LOQ ≤0.3 *Limit Value should be satisfied.

Table 14 Current LoD/LoQs for the substances in the scope of the Annex XV proposal

Substances	LoD	LoQ	LV	LoQ ≤0.3 LV
PAHs	Between 0.03 and 0.1 mg/kg	Between 0.1 and 0.4 mg/kg	0.023 ng/kg (0.000000023 mg/kg)*	no
Dioxins, furans & DL-PCBs	From 0.002 to 1 ng/kg regarding the test sample	From 0.002 to 1 ng/kg regarding the test sample	0.0017 ng_{TEQ}/kg*	no
Total PCBs	From 0.05 to 3.2 ng/kg according to the test sample	From 0.05 to 3.2 ng/kg according to the test sample	112 ng/kg	yes
Formaldehyde	0.11 mg/kg	0.35 mg/kg	0.42 mg/kg	no

* In the Forum advice, the Forum considered the limit values proposed by the Dossier Submitter at that time. However, after the Forum advice had been developed, the Dossier Submitter updated the limit values for PAHs from 0.034 ng/kg to 0.023 ng/kg and for dioxins & furans & DL-PCBs from 1 700 ng_{TEQ}/kg to 0.0017 ng_{TEQ}/kg. With this update, the relation LOQ ≤0.3 *Limit Value is no longer satisfied for dioxins & furans & DL-PCBs (it would have been

with the originally proposed limit value of 1 700 ng_{TEQ}/kg).

Based on this analysis, it can be concluded that:

- For PAHs the limit value should be set between 0.3 and 1.3 mg PAH/kg considering the currently achievable LoQs.
- For formaldehyde the limit value should be set to at least 1.16 mg formaldehyde/kg considering the currently achievable LoQs.
- For dioxins, furans and DL-PCBs the limit value should be set between 0.0067 and 3.3 ng/kg considering the currently achievable LoQs.
- For the sum of total PCBs, the proposed limit value should be enforceable considering the currently achievable LoQs.

The Forum also points out that the development of a standardised methodology will facilitate the achievement of harmonised results given the specific sampling method proposed for this restriction.

Concerning practicality, the Forum is of the opinion that the restriction would be practical.

3.3.3.1. Monitorability

Justification for the opinion of RAC and SEAC

Summary of proposal:

The implementation of this restriction proposal will imply testing and controls costs for industry and authorities (see the section on costs for more information). Nevertheless, by the time being, no harmonized analytical method is available based on urine simulant although EDANA is currently working on the establishment of guidelines for all Absorbent Hygiene Products (AHPs) with a common analytical method that may help the stakeholders defining, before the end of the transitional period, a harmonized analytical method. In conclusion, to enable the monitoring of the results of the implementation of the proposed restriction, a harmonized method should be developed during the transitional period.

RAC and SEAC conclusion(s):

RAC notes that the restriction should in principle be monitorable in general if appropriate analytical methodologies are developed.

Key elements underpinning the RAC and SEAC conclusion(s):

The discussion on monitorability is in this case intimately linked to the practicality, including enforceability, of the proposed restriction. Please refer to that section of the opinion for a more in-depth discussion. The conclusions for this section can be found above.

3.4. UNCERTAINTIES IN THE EVALUATION OF RAC AND SEAC

3.4.1. RAC

Summary of proposal:

The Dossier Submitter has listed and described a number of uncertainties. These can be categorised as follows:

Human health hazard assessment: Formaldehyde: The route-to-route extrapolation is questionable because observed effects are correlated with the route of exposure. These are only local effects. Systemic toxicity has not been demonstrated. PAHs: Dermal DNEL calculated by ECHA and expressed in µg/cm²/d but not usable to perform the daily exposure dose calculation. The daily exposure dose calculation could have been done if data on surface weight had been made available to the Dossier Submitter.

Exposure assessment: Test method: SCL tests with entire diapers, extraction with a urine simulant. Representative of normal use enabling the chemicals actually extracted by urine to be identified. Skin Absorption: The Dossier Submitter decided to use a value of 50% for skin absorption assuming that baby skin can be damaged and enhance the penetration. The approach was adopted by the SCCS and ANSM for products for the buttocks area due to the frequency of skin diseases in the diaper area in babies.

Risk assessment: Risk characterisation: The calculations to generate migration limits are based on worst case scenarios.

Analysis of Alternatives: The identification of the contamination sources for the chemicals of concern has been difficult due to lack of data. Link between FSC certification to get TCF pulp claimed by industry to be a problem to switch to TCF pulp. According to experts consulted, FSC certification is linked to sustainable forest management and not wood transformation.

Human health impact assessment:The human health impact assessment has not been quantified and monetised due to uncertainties (no prevalence/incidence data, all DNEL/DMEL used in the risk assessment were derived based on oral route studies, dose-response relationships available for some substances in the scope only built on animal studies, etc.).

Analytical feasibility: No harmonised test method is available for now.

RAC conclusion(s):

In the following table the uncertainties/shortcomings recognised by RAC are listed:

Table 15 Main uncertainties and shortcomings concerning the Annex XV dossier

Part of the underlying assessment	Identified uncertainty			Priority	Summary of contribution to uncertainty about results of the assessment
	No.	Description of uncertainty	Input/ Methodology		

Exposure assessment	1	Uncertainties and shortcomings concerning the analytical method (see section 3.1.3, D)	I/M	Very high	>30%
	2	Use of the exposure variables in the daily exposure dose calculation, particularly the disparity in the "rewet" factor (baby's urine refluxed from a diaper)	M	High	15% (approximately two orders of magnitude overestimation)
	3	It is not clear why PAHs concentrations in diapers (including LoDs/LoQs) are orders of magnitude lower in 2019 compared to 2018 analysis performed by SCL and DGCCRF/INC	I/M	High	10%
	4	Lacking assessment of direct exposure - especially regarding extraction of lipophilic substances which could come into direct contact with baby's skin	M	Medium	5-10%
Risk characterisation	5	For PAHs, the lowest LoD is orders of magnitude higher than the proposed migration limits - it is not known how many samples were above/below the proposed limits	M	High	10%
	6	Allocation factor should not be used for the calculation	M	High	10%

		of risk (to account for aggregate exposure from different exposure routes) for the local dermal effects (formaldehyde and PAHs); for other effects (PCDD/Fs and PCBs), the value of an allocation factor of 10% is not sufficiently justified by the Dossier Submitter			
	7	A cumulative risk assessment (exposure to a mixture of substances present in diapers and from other sources relevant for children up to three years of age) was not presented in the Annex XV dossier.	I	Medium	5%
Hazard assessment	8	Uncertainties related to epidemiological study in Russian children (stated in section 3.1.2, "Key elements underpinning the RAC conclusion(s)") - overestimation of the DNEL expected	M	High	10%
	8	Local skin sensitisation of formaldehyde was not assessed	I	Low	<1% Skin sensitising effects very likely addressed in the REACH restriction concerning skin sensitisers in textiles.

	9	Limited information on dermal toxicity for PCDDs/Fs/DL-PCBs	I	Low	<5%
	10	Health risk assessment is based on studies using a limited set of PCB mixtures, so when the pattern of PCB congeners is different from the commercial mixtures, another approach could be preferable; however, NDL-PCBs have not been analysed in diapers, so the pattern of congeners is unknown	M	Low	<5%

RAC is of the opinion that the following information (by the Dossier Submitter or other bodies) would be needed to address the identified (main) uncertainties concerning the exposure:

- Detailed information about
    - sample preparation;
    - analytical quality control and assurance information (including the use of blank samples) for analytical data.

In addition, if the risks of substances in single-use baby diapers are reconsidered in the future (i.e., not as part of the opinion development on this Annex XV dossier) the following topics should be elaborated in order to minimise the uncertainties:

- appropriate rewet factor;
- evaluation of direct exposure;
- reproducibility and relevance (to reasonably foreseeable conditions of use) of urine simulant extraction methodology;
- justification for the use of (and value for) an allocation factor.

According to industry, further reduction of the LoD/LoQ for the substances included in the scope of the restriction proposal, particularly for PAHs, would require several years (certainly much longer than the two years proposed as transitional period).

However, as previously mentioned, RAC notes that a methodologically different approach could also be used to deal with hazardous substances in single-use baby diapers in a restriction proposal.

Key elements underpinning the RAC conclusion(s):

Key elements concerning the different topics are already described in the respective sections above.

3.4.2. SEAC

Summary of proposal:

SEAC conclusion(s):

Add conclusion of SEAC.

Key elements underpinning the SEAC conclusion(s):

Add analysis that justifies the conclusion given above[12]

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3.6. ANNEX I

Key elements underpinning the RAC conclusions on information on hazards

Formaldehyde

Although formaldehyde is classified for mutagenicity and carcinogenicity, these effects were not seen as critical in the Dossier Submitter's assessment. Since the data on sub-chronic or chronic toxicity of formaldehyde following dermal exposure is limited, the Dossier Submitter chose an oral chronic HRV based on histological changes in the stomach (hyperplasia, hyperkeratosis, ulceration, chronic gastritis) and renal papillary necrosis in male rats exposed to 82 mg/kg bw/day for 2 years via drinking water (Til et al., 1989). At this dose level decreased food and liquid intake, and decreased body weight gain were observed. Applying a factor of 10 for interspecies variability and a factor of 10 for interindividual variability to the NOAEL of 15 mg/kg bw/day, a toxicity reference value (TRV) of 0.15 mg/kg bw/day is derived (or 2.6 mg/L drinking water). Four organisations proposed chronic threshold TRVs based on the same critical effect, the same key study and the same uncertainty factors: ECHA (2017; in the assessment of formaldehyde as a biocidal substance), the US EPA (1990), Health Canada (2001), WHO/IPCS (2005) and ATSDR (1999). It should be noted, therefore, that all these TRVs were based on systemic effects following oral exposure, which in the case of formaldehyde are not as relevant as local skin effects, i.e. skin sensitisation.

On the estimated TRV of 0.15 mg/kg bw/day, the Dossier Submitter applied a factor of 0.5 (based on experimental data on formaldehyde toxicokinetics) to correct for oral bioavailability. The resulting chronic **internal DNEL of 0.075 mg/kg/day** for the general population was, thus, derived. The Dossier Submitter considers that the selected HRV is applicable to children between birth and three years of life and points out that studies during gestation were taken into account by WHO/IPCS in 2005 for the establishment of the TRV.

RAC agrees with the Dossier Submitter to consider the non-mutagenic and non-carcinogenic toxic effects as a point of departure. Namely, as concluded previously by RAC (2012; 2020), formaldehyde is a mutagen and (local) carcinogen, inducing tumours at the site-of-contact after inhalation (nasal tissue) but not at distant sites, and there is no convincing evidence of formaldehyde-induced carcinogenic effects at distant sites or via routes of exposure other than inhalation. Regarding mutagenicity, DNA-protein crosslinks (DPX) are eliminated by spontaneous hydrolysis and/or other DNA repair mechanisms and do not accumulate during prolonged exposure to formaldehyde. Additionally, adduct formation was generally shown to be formaldehyde concentration dependent (RAC, 2020).

The TRV used by the Dossier Submitter covers two types of critical effects: one is local (at the site of first contact, i.e., histological changes in the stomach[32]) and the second one is

[32] The histopathological changes in stomach included papillary epithelial hyperplasia in the forestomach, frequently accompanied by hyperkeratosis located on the limiting ridge or in its vicinity, and focal ulcerations; chronic atrophic gastritis in the glandular stomach, in some cases with inflammatory process involving the entire mucosa, and with ulceration. In some rats, bulky plugs of necrotic tissue, inflammatory exudate, mucus and feed particles were seen attached to the damaged mucosa.

systemic (renal effect[33]), and they were observed at the same oral dose level (82 mg/kg bw/day) in Til et al. (1989) study. It is unclear if the systemic effects are primary, i.e., directly resulting from formaldehyde or its metabolites, or secondary to local lesions and inflammatory reactions (ECHA, 2019). The Dossier Submitter decided to derive a systemic reference dose to protect from potential internal effects following prolonged exposure to low concentrations of the active substance. Whereas renal effects are systemic effects which may not be solely as a consequence of local effects, the Dossier Submitter choose to derive an internal DNEL as a conservative approach to assessing the risk.

RAC agrees with the Dossier Submitter that the local effects observed after oral exposure are of questionable relevance for this restriction proposal, considering that dermal route is a relevant exposure route in the restriction's exposure scenario. This is in line with ECHA Guidance (2012) which states that "for DNELs covering local inhalation and local dermal effects route-specific data need to be available". If oral data are selected for deriving internal DNEL, an emphasis should be put on systemic effects induced by exposure to formaldehyde (e.g., nephrotoxicity), noting that there is an uncertainty whether these effects are just a consequence of local effects. Namely, it is unclear, whether formaldehyde induces primary systemic effects in mammals. Formaldehyde is not classified for STOT RE (or STOT SE). As stated in the Annex B.5.3.6. of the Background Document, in experimental studies, formaldehyde induced toxic effects only at the site of first contact after oral or dermal exposure, and general signs of toxicity occurred secondary to these local lesions. No systemic toxicity was observed following repeated exposure to formaldehyde in animals and humans according to NICNAS (2006), and renal toxicity is not unequivocally recognised in humans or in animal studies (ATSDR, 1999; Gelbke et al., 2019)[34].

In ECHA's assessment of formaldehyde as a biocidal substance (under Regulation (EU) No 528/2012) (ECHA, 2017), it was considered that the submitted repeated dose studies had deficiencies in reporting with respect to organs other than those that come into direct contact with formaldehyde. These deficiencies severely constrained any independent evaluation of systemic toxicity of formaldehyde after repeated administration. It remained unclear if any systemic effect was primary, i.e., directly resulting from formaldehyde or its metabolites, or

[33] The study authors relate decreased food intake and, consequent, decreased body weight gain in top dose animals, to rejection of the drinking water solution (bad palatalability due to high formaldehyde concentration in the solution).

[34] Renal effects have been observed in repeated toxicity studies performed by Til et al. (1988, 1989), and also, at very high dose (5000 mg/L drinking water) in rats in Tobe et al. study (1989). Also, some more recently published studies (which quality, however, has not (yet) been assessed) found renal toxicity following exposure to formaldehyde via oral (Bansal and Uppal, 2011), inhalation (Ramos et al., 2017) or intraperitoneal route (Bakar et al., 2015; Morsy, 2018) in rats and rabbits.
Regarding human data, four cases of nephrotic syndrome after exposure to toxic concentrations of formaldehyde in newly built homes were reported (Breysse et al, 1994). However, the authors found that these patients shared a particular HLA type on the major histocompatibility complex and speculated that the patients were genetically susceptible to "triggering" of immune reactions by formaldehyde exposure. This has not been confirmed by other studies (Formaldehyde. Micromedex, IBM Corporation 2021; Breysse et al, 1994).
Gelbke and co-workers (2019), who performed an assessment of safe exposure levels for potential migration of formaldehyde into food, consider that available literature indicates that formaldehyde could be nephrotoxic. As a potential mechanism, sustained metabolic acidosis produced by formic acid (the first-step metabolite in formaldehyde metabolism), has been proposed (Gelbke et al., 2019). The authors' position is that "as potential long-term consequences of mild, non-life threatening chronic acidosis are unknown and determination of blood pH does not belong to the standard toxicological repertoire, a conservative derivation of safe exposure levels has to consider such a possibility".

secondary to local lesions and inflammatory reactions. This uncertainty was reflected by derivation of a systemic reference dose to protect from potential internal effects following prolonged exposure to low concentrations of the active substance. It was considered that the overall NOAEL of 15 mg/kg bw/day for subacute, subchronic and chronic oral exposure based on stomach lesions, renal papillary necrosis and reduced body weight gain observed in rats in the Til et al. study (1989), provides the relevant starting point for derivation of oral and systemic reference doses, regarding dietary exposure to formaldehyde. By setting a default assessment factor of 100 and considering an oral absorption of 100%, a value of 0.15 mg/kg bw/day was defined for acute, medium-term and long-term Acceptable Exposure Level (ECHA, 2017). However, it was also pointed out that "due to the high reactivity of formaldehyde, local effects dominate the toxicity profile of the substance" and that "irritation of the skin and sensitisation were observed following dermal administration of doses considerably lower than the oral NOAEL forming the basis for the Systemic Reference Dose". This has been also pointed out in ECHA's assessment of worker exposure to formaldehyde and formaldehyde releasers, as well as the fact that formaldehyde is an endogenous substance at relatively high concentrations (i.e., about 2.6 mg/L in the blood; total body content of 1.82 mg/kg bw) (ECHA, 2019c; EFSA, 2014).

It should be also noted that toxicokinetic differences between oral and dermal exposure route are unclear but could be significant regarding quantitative differences in formaldehyde-metabolising enzymes (e.g., formaldehyde dehydrogenase, "The Human Protein Atlas" https://www.proteinatlas.org/ENSG00000197894-ADH5/tissue).

To conclude, it is considered that for formaldehyde, local effects (i.e., skin sensitisation), are more relevant than systemic effects for this restriction proposal. Namely, due to formaldehyde's high reactivity at the site of first contact, local effects dominate the toxicity profile of the substance, and skin irritation and sensitisation were observed following dermal administration of doses considerably lower than the oral NOAEL.

PAHs

Although some PAHs (primarily those with a low molecular weight) induce systemic non-carcinogenic threshold effects (mainly kidney, liver and blood disorders) for which HRVs have been established, the Dossier Submitter chose carcinogenicity as a critical effect for PAHs: eight out of 17 PAHs included in the scope of the Annex XV dossier are classified as category 1B (H350) carcinogens; many PAHs share the same genotoxic mechanism of action; and carcinogenicity was chosen as a critical effect in the Annex XV dossier on PAH in granules and mulches used in synthetic turf pitches (ECHA, 2019) as well as in the Annex XV dossier for eight PAHs in consumer articles (BAuA, 2010).

Considering the dermal route as the relevant route for this restriction proposal, and that carcinogenicity data on PAHs following dermal exposure are available, the Dossier Submitter decided to derive a DMEL based on dermal carcinogenicity data.

Several dermal DMELs or cancer slopes built on animal data have been derived by regulatory bodies or are available in the open literature (Sullivan et al., 1991, cited by Knafla et al., 2011; LaGoy and Quirck, 1994; Hussain et al., 1998; Knafla et al., 2006; Knafla et al., 2011; BAuA, 2010; ECHA 2018). Considering the unit of the slope factor (per surface of treated area) and the exposure data available, the Dossier Submitter considered that slope factors derived by Sullivan et al. (1991), Laroy and Quirck (1994) and Knafla et al. (2011; which was

used to establish a dose-response relationship for the carcinogenicity of CTPHT, ECHA, 2018b) were not appropriate for use in this restriction proposal. The Dossier Submitter also did not choose the slope factor derived by Hussain et al. (1998) because of the lack of information on the method of derivation.

The Dossier Submitter, therefore, decided to calculate two DMELs, at a 10^{-6} risk level, from the following reports/studies:

- **DMEL of 4 pg/kg bw/day** for **PAHs mixture**, based on dermal studies (Schmähl et al., 1977; Fhl, 1997) assessed by **BAuA (2010)**, in which BaP was applied as a component of PAHs mixture (most conservative DMEL of the range);
- **DMEL of 6 pg/kg bw/day** for **BaP alone**, derived from **Knafla et al. (2006)**, in which only BaP was dermally applied.

In the restriction of PAHs in consumer products, BAuA (2010; restriction entry 50 of Annex XVII to REACH: Polycyclic aromatic hydrocarbons in articles supplied to the general public) derived several dermal DMELs for BaP using T25 or BMD calculations. Only the studies in which BaP was administered as the component of a mixture of PAHs were used. For each of the selected studies (where appropriate) T25, BMD_{10}, and $BMDL_{10}$ estimates were used as dose descriptors, and DMELs were calculated applying both the 'Large Assessment Factor' and the 'Linearised' approach (the latter at both the 10^{-5} and 10^{-6} risk levels and using the 'Probit' as well as the 'Multistage Cancer' algorithms for curve fitting). BAuA (2010) noted that the Multistage Cancer model is the approach recommended by the REACH IR/CSA guidance, and excluded from further calculations the very low values obtained by the Probit approach. When only dermal studies were considered, the following DMEL ranges for PAHs mixture were derived by BAuA:

- range for linearised approach, 10^{-5} risk level: 35 – 115 pg/kg bw/day;
- range for linearised approach, 10^{-6} risk level: 4 - 12 pg/kg bw/day;
- range for large assessment factor: 99 – 323 pg/kg bw/day.

The Dossier Submitter choose the BMD approach because this approach is based on modelling of the experimental data considering all available information on the dose response curve whereas T25 is calculated from one data point on the dose-response curve. The Dossier Submitter choose BMDL as the dose descriptor because it is the lowest statistically significantly increased incidence that can be measured in most studies and would normally require little or no extrapolation outside the observed experimental data.

Knafla et al. (2006) proposed a dermal slope factor of 25 cases per mg/kg bw/day for BaP, based on seven relevant dermal carcinogenesis animal studies (studies based on a two-stage model of carcinogenesis, i.e., initiation–promotion, were not considered). This cancer slope factor was developed using the benchmark dose approach and the linearised multistage model. An average dermal cancer slope factor of 0.55 cases per µg/animal/day was then converted to a dose-equivalent slope factor of 25 cases per mg/kg bw/day, based on an adult mouse body weight of 45 g.

In order to derive a DMEL, both in BAuA (2010) calculations and in case of Knafla et al. (2006) slope factor, allometric scaling factor (7 for mice) was applied, as well as a bioavailability factor in order to account for the assumption of 50% absorption across all routes in animal experiments using organic solvents as vehicle *vs.* 20% absorption in the human exposure situation (dermal absorption from a sweat matrix). Since a linearised approach was applied

(with a standard high-to-low extrapolation factor), no additional assessment factors were used, in line with ECHA Guidance (ECHA, 2012).

The toxicity of other PAH substances was estimated based on toxic equivalency factors (TEFs).

RAC agrees with the Dossier Submitter's DMEL derivation but regarding the use of TEFs notes that either the EFSA PAH8 or the REACH-8 PAHs approach would have been preferred to be in line with previous restrictions.

In the available animal studies with dermal exposure to PAHs, systemic tumours were not investigated, so the potential for induction via the dermal route could not be adequately assessed. Nevertheless, as stated in ECHA 2018b, "based on current knowledge dermal exposure in humans is related with cancers in areas of first contact with the body and its effect is rather local than systemic", and "limited evidence exists that PAHs may induce tumours at sites other than at the site of application, i.e., other than respiratory tract cancers after inhalation exposure or skin cancers after dermal exposure". RAC also notes that since the DMELs derived by the Dossier Submitter are two orders of magnitude lower than DMELs derived from oral studies using the same approach (i.e., Multistage Cancer modelling, linearised approach, 10^{-6} risk level) (BAuA, 2010; US EPA, 2017), they are expected to also be protective of the potential risk of systemic tumour development in dermally exposed individuals.

PCDD/Fs and PCBs (DL-PCBs and NDL-PCBs)

These substances have no harmonised classification in the EU presently, but TCDD was classified as reprotoxic category 1B by the Chemical Management Center of Japan National Institute of Technology and Evaluation. Some of these substances are self-classified in the EU (predominantly for repeated toxicity). The hazards and risks they pose to human and animal health were reviewed within various risk assessment frameworks and by various international committees (ATSDR, 1998; ATSDR, 2000; ATSDR, 2004 cited in Danish EPA, 2014; Danish EPA, 2014; DGS, 1998; EFSA, 2018; IARC, 1997, 2016; INERIS, 2006; INRS, 2007, 2016; INSERM, 2000; OSAV, 2016; US EPA, 1992; WHO, 2016).

There are no available dermal HRVs derived by any EU or non-EU regulatory bodies. Data on chronic and sub-chronic dermal toxicity in animals exist, but they would first require a thorough analysis in order to decide whether they are appropriate enough for deriving a dermal DNEL.

Since PCDD/Fs and DL-PCBs have similar hazard profile (including hepatotoxicity, epithelial effects, immunotoxicity, reproductive toxicity), the Dossier Submitter decided to select the same critical effect for these substances.

Although several organisations proposed non-threshold oral HRVs for these substances (based on carcinogenicity, i.e., liver tumours), the Dossier Submitter decided to use a chronic threshold HRV. Namely, carcinogenic effects of PCDD/Fs and DL-PCBs are considered to have thresholds, since they are not linked to mutagenic effect or to DNA binding. Also, carcinogenic effects of dioxins/DL-PCBs are observed at higher doses than for other toxic effects (IARC, 2012).

A number of chronic HRVs for dioxins, furans, and DL-PCBs, or only for the most hazardous substance in this class, 2,3,7,8-TCDD, were derived (Table 47 in Annex B.5.12.12.1). All these

HRVs, except that of the US EPA and EFSA values, were based on animal studies. Only EFSA's and the US EPA HRVs are based on epidemiological data. The Dossier Submitter considers that in line with ECHA Guidance (Chapter R.8; ECHA, 2012), epidemiological data should be favoured over animal data, and proposes to use EFSA's HRV since it is more recent (from 2018), and it is described clearly and transparently.

EFSA's CONTAM Panel reviewed the data from experimental animal and epidemiological studies and decided to base the human risk assessment on effects observed in humans and to use animal data as supportive evidence. The critical effect observed in human and animal data was on semen quality, following pre- and postnatal exposure. The strongest associations were between the exposure to TCDD during infancy/prepuberty and impaired semen quality, observed in the Seveso population (Mocarelli et al., 2008, 2011) and in the Russian Children's Study (Minguez-Alarcon et al., 2017). The CONTAM Panel selected the Russian Children's Study as a critical study[35].

The Russian Children's Study is a cohort study in 516 boys who were enrolled at age 8 to 9 years and followed for up to 10 years. At 18 to 19 years, 133 young men provided 1 or 2 semen samples, which were analysed for volume, sperm concentration and motility. The results showed that higher quartiles of TCDD and PCDD TEQs were associated with lower sperm concentration, total sperm count, and total motile sperm count (p-trends ≤ 0.05 in linear mixed models), compared with the lowest quartile. Similar associations were observed for serum PCDD TEQs with semen parameters. Although there was no significant association between NDL-PCBs and semen parameters, the association between TCDD and semen parameters became slightly stronger after adjustment for NDL-PCBs. Serum PCBs, furans, and total TEQs were not associated with semen parameters.

NOAEL of 7.0 pg WHO_{2005}-TEQ/g fat in blood sampled at age 9 years based on PCDD/F-WHO_{2005}-TEQs was defined, as median serum level for the sum of PCDD/F- WHO_{2005}-TEQ in the lowest quartile (at which sperm parameters were within the reference range). Using toxicokinetic modelling and considering the exposure from breastfeeding and a twofold higher intake during childhood, the CONTAM Panel established a **TWI** of 2 pg WHO_{2005}-TEQ/kg bw/week (**0.3 pg** WHO_{2005}-TEQ**/kg bw/day**). Although this TWI is based on findings on PCDD/F-WHO_{2005}-TEQ only, the CONTAM Panel concluded that the TWI should apply to the sum of PCDD/Fs and DL-PCBs.

Among available studies on oral absorption of PCDD/Fs and PCBs, the Dossier Submitter selected an oral absorption fraction based on McLachlan (1993) study, rounded to 100%. In this study more than 90% absorption rates were found for TCDD, penta- (2,3,4,7,8-PeCDF, 1,2,3,7,8-PeCDD) and hexa-substituted congeners (1,2,3,4,7,8- HxCDF, 1,2,3,6,7,8-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,7,8,9-HxCDD) in a

[35] Contrary to the Seveso studies, in the Russian Children's Study also other PCDD/Fs and DL-PCBs were analysed. Concentrations of TCDD were much lower in the Russian Children's Study than those in the Seveso study. The effects on semen parameters were observed at much lower TCDD levels in the Russian study compared to the Seveso Cohort study. TEQs in Seveso had to be estimated from other studies. In contrast to the two Seveso studies, the Russian Children's Study included two semen samples for most participants. The Russian Children's Study had the advantage of a very narrow age range (18 to 19 years), while the Seveso studies had a broader age range, and the analyses had to be adjusted for age. The reference group in Seveso study (healthy blood donors) may in some respects are not directly comparable with the men from Seveso. In the Seveso studies, semen was collected at home, while in the Russian Children's Study semen was collected in the laboratory.

nursing infant, by determining 12-day mass balance (the difference between the total intake with breast milk and the excretion in the faeces present in the mother's milk). This value is almost identical to 97% oral absorption used in the calculations of EFSA CONTAM Panel. **Internal DNEL**, therefore, remained identical to DNEL of **0.3 pg_{TEQ}/kg bw/day**.

The Dossier Submitter decided to use TEQ concept for PCDD/Fs and DL-PCBs, based on different toxic equivalency factors (TEFs), with "Seveso" dioxin (2,3,7,8-TCDD), as the most toxic congener, assigned a value of 1. TEF values have been defined in 1998 and revised in 2005 by the WHO for PCDD/Fs and PCB-DL (Van den Berg et al., 2006). The Dossier Submitter retained the values of TEF from WHO 2005 (Figure 16 in the Annex B.5.12.12.3.). RAC notes that uncertainties related to TEF concept are identified by EFSA (please see below).

EFSA's HRV is considered applicable to children between the ages of zero and three years since the modelling considered the much higher exposure during infancy from both breast milk and food. Also, according to the CONTAM Panel, derived TWI should be protective towards all endpoints identified by the CONTAM Panel assessment (other reprotoxic effects and higher TSH levels in new-borns).

RAC notes that the data on dermal toxicity of PCDD/Fs and DL-PCBs is rather limited. Therefore, **RAC concurs with the Dossier Submitter's approach to derive internal DNEL based on an epidemiological study in Russian children** (Minguez-Alarcon et al., 2017), in which the primary source of exposure to PCDD/Fs and DL-PCBs was diet, with dermal absorption, inhalation, and hand-to-mouth transfer from contaminated dust and soil as additional exposure routes (Burns et al., 2009).

The uncertainties are well analysed and described in the EFSA report (EFSA, 2018). Some of the uncertainties are around:

- the use of WHO2005-TEFs for all species;
- the studies indicate that the current TEFs require re-evaluation; in particular, PCB-126, which contributes most to the DL-PCB-TEQ level, may be less potent in humans than indicated by the TEF-value of 0.1;
- true exposure in epidemiological study being higher or lower than the estimate of exposure;
- true outcome in epidemiological study more or less prevalent than the estimate of the outcome;
- confounding by other factors;
- low number of epidemiological studies on the critical endpoint at low exposure;
- exposure to other compounds which may impair semen quality;
- uncertainty regarding critical window for effect on semen quality outcome.

Additionally, as pointed out by the authors of the Russian Children's Study, the boy's median serum total TEQ concentrations were relatively high compared to data from the US and Germany, which makes it difficult to investigate the effects of very low exposures.

RAC agrees with the Dossier Submitter that the study is well conducted and reported, with transparent methodology of HRV derivation. The uncertainties are, however, substantial, and although their magnitude cannot be defined, they are expected to lead to a lower (i.e., overprotective) DNEL than necessary.

Total PCBs (DL- and NDL-PCBs)

As stated in the previous section above (3.1.1), the NDL-PCBs have different toxicological activity compared with the DL-PCBs and PCDDs/PCDFs, so the Dossier Submitter considered that a DNEL for total PCBs cannot be the same as the one derived for PCDD/Fs and DL-PCBs.

The Dossier Submitter presented the HRVs for PCBs developed by several international regulatory bodies (Health Canada, RIVM, WHO, ATSDR, US EPA), with values ranging from 0.01 to 0.13 µg/kg bw/day (Annex B.5.12.12.1). Three organisations proposed the same chronic threshold TRV of 0.02 µg/kg/day for PCBs, based on the same critical effect and the same key study: ATSDR (2000), RIVM (2001) and WHO (2003). Only the choice of assessment factors differed between these three organisations (more details are in the Annex B.5.12.12.1). The Dossier Submitter adopted this HRV (0.02 µg/kg/day) since it was established in accordance with high quality standards and considered a set of consistent studies. This HRV is considered applicable to children between the ages of zero and three years.

Applying the same oral absorption factor of 100% as the one used for PCDD/Fs/DL-PCBs, **internal DNEL of 0.02 µg/kg/day** has been derived.

Since in deriving this HRV, it was considered that the limitations of human studies (limited exposure data; inconsistency among some results; the presence of confounding factors, such as co-exposure to dioxins) make it impossible to use them as a basis for quantitative risk estimation, animal data were used for the risk characterisation. Tryphonas et al. (1989, 1991) studies were chosen as critical studies since they were long-term studies (5 years); relatively large number of animals was used (13 to 16 monkeys per group); monkey is a good model for humans; and experimental design and data analysis were good. Female *Rhesus* monkeys receiving daily doses of Aroclor 1254 for several months showed a dose-related increase in liver weight and decreases in the IgG and IgM immunoglobulin response to a sheep red blood cell challenge. No NOAEL was found so the lowest dose studied, 5 µg/kg bw/day, was identified as the LOAEL. Using an uncertainty factor of 300 (factor of 3 for interspecies variation, 10 for intraspecies variation, and 10 for extrapolation from a LOAEL to a NAEL), a **TDI of 0.02 µg/kg bw/day** was derived for mixtures of PCBs. Slight changes in neurobehavioral tests observed at 7.5 µg/kg bw/day (the only dose level tested) in developmental neurotoxicity study in *Cynomolgus* monkeys (Rice and Hayward, 1997), support this TDI, especially for infants[36].

No OECD or EU test method is currently available to investigate immunotoxicity. In Chapter R.8; ECHA (2012) it is stated that the "Health Effects Test Guidelines OPPTS 870.7800 Immunotoxicity" can be referred to. Tryphonas et al. (1989, 1991) studies methodologically deviate from this Guideline (e.g., method of IgM analysis[37]). Nevertheless, the tested outcome (T-cell-dependent antibody response in a form of antibody production against sheep red blood

[36] The PCB mixture given to the monkeys in this study was engineered to mimic the congener pattern in mother's milk.

[37] In Tryphonas et al. (1989, 1991) studies, serum dilutions were reacted with SRBC in the microplate haemolytic complement assay. Titers (IgM) were expressed as the reciprocal of the highest serum dilution showing a 50% haemolysis. On the other hand, in this type of test, anti-SRBC plaque-forming cell (PFC) assay or enzyme-linked immunosorbent assay (ELISA) are usually performed, to determine the effects of the test substance on either splenic IgM PFC response, or serum IgM levels (Health Effects Test Guidelines OPPTS 870.7800; Lebrec et al., 2011; Ladics, 2007).

cells, SRBC) is a well-known model in immunotoxicity assessment, including non-human primates (Lebrec et al., 2011), and "became the cornerstone of recent guidelines for assessing the potential immunotoxicity of xenobiotics" (Ladics, 2007). Immunological changes were also observed in human populations exposed to PCBs and manifested as increased infection rates and changes in circulating lymphocyte populations (WHO, 2003).

The assessment factor of 3 for interspecies variation is based on observations from an oral Aroclor study, which confirmed non-human primates as among the most sensitive species (WHO, 2003). This factor is supported by allometric scaling factor of 2 for Rhesus monkeys (Chapter R.8; ECHA, 2012).

For LOAEL to NAEL extrapolation, an assessment factor of 10 was used (no explanation is provided in WHO 2003 document why a maximum value of 10 was selected). Although the Benchmark dose (BMD) approach, which is preferred over the LOAEL-NAEL extrapolation by ECHA Guidance (2012), was not used, RAC considers that factor of 10 is justified, considering a shape of the dose-response curve (i.e., very steep at lower doses, Figure 1).

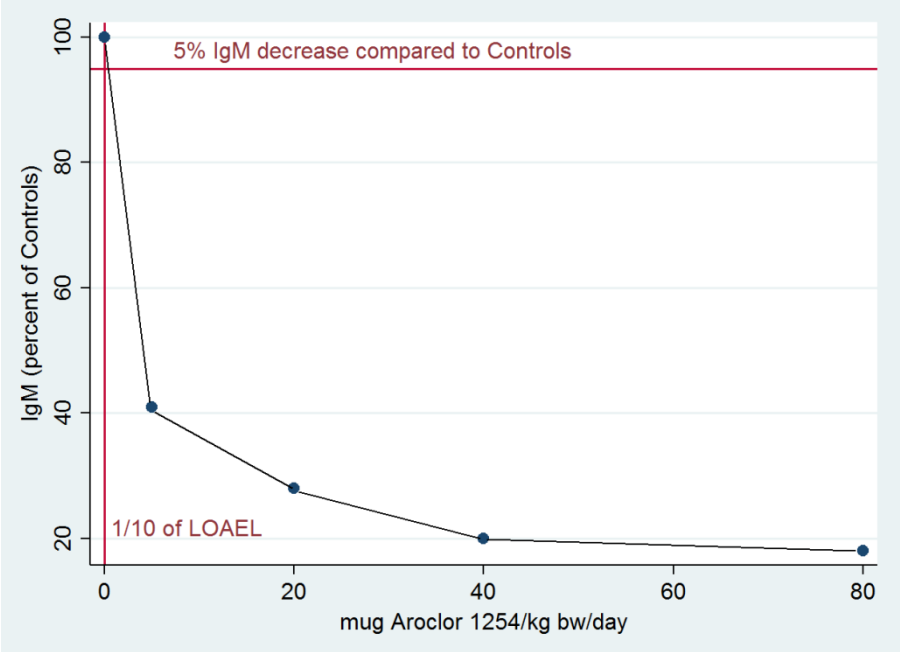

Figure 1: Dose-response curve for anti-sheep red blood cells IgM changes following oral exposure to Aroclor 1254 in monkeys in Tryphonas et al. (1991) study

IgM values are presented as percent of control values, averaged for four assessment periods (once a week during 4-week period following secondary immunisation with SRBC injected on 55th month of the study). **5% IgM decrease compared to Control** corresponds to BMD5, proposed to be comparable to a NOAEL (ECHA Guideline, 2012). **1/10 of LOAEL** represents a value of LOAEL (5 µg/kg bw/day) on which assessment factor of 10 (for LOAEL to NAEL extrapolation) has been applied. As stated in WHO (2003) report, the health risk assessment is based on studies using a limited set of PCB mixtures, mostly Aroclors 1242 and 1254, so when the pattern of PCB congeners is different from the commercial mixtures, another approach could be preferable. RAC notes, however, that NDL-PCBs have not been analysed in diapers, so the pattern of congeners is unknown.

RAC concurs with the Dossier Submitter's approach to deriving a DNEL for this group.