SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

Opinion on Formaldehyde in Toy Materials.

1. Summary

1.1. Formaldehyde in toy materials was considered by the SAG-CS at their meetings in May and July 2021.[1]

1.2. Formaldehyde is a by-product of a number of industrial processes and is released into the air from plastic- and resin-based products. Chlorination and ozonation of drinking water can also cause the formation of formaldehyde through reaction with organic matter in the water.

1.3. Formaldehyde has been found to be carcinogenic in rats and mice via inhalation. The weight of evidence supports the hypothesis that sustained cytotoxic effects leading to chronic proliferation are the causal mechanism in nasal carcinogenicity. Ingestion through drinking water results in forestomach irritation and subsequent papillomas at the site of irritation in rodent studies, but it is unlikely that this endpoint is relevant to humans as humans do not have this organ, no dose-response relationship was observed, and no carcinogenicity has been observed in other organs. Formaldehyde can also be produced endogenously, humans can metabolise small amounts of formaldehyde, and there is likely to be a threshold for toxicity (WHO, 1993; EFSA, 2006)

1.4. Formaldehyde (CAS No 50-00-0) has a harmonised classification as a category 1B carcinogen under The Classification, Labelling and Packaging (CLP) regulation (ECHA, Summary of Classification and Labelling). A category 1B substance is presumed to have carcinogenic potential for humans based largely on evidence from animal studies. Formaldehyde also has a harmonised

[1] (SAGCS-052101 and SAGCS072103 link to papers and mins)

classification under CLP as a Category 2 Mutagen, Category 1B Skin Corrosive, Category 1 Skin Sensitiser and is classified as toxic when swallowed, inhaled or when in contact with the skin. The rationale for this harmonised classification can be seen in the Committee for Risk Assessment's (RAC) Opinion on the Proposed Harmonised Classification for Formaldehyde. (RAC, 2012).

1.5. Formaldehyde is not listed currently in Appendix C to Annex II of the Toy Safety Directive, which means it is currently not restricted in toys intended for use by children under 36 months or in other toys intended to be placed in the mouth (Directive 2009/48/EC). Pursuant to the CLP regulations, chemical substances classified as carcinogenic, mutagenic, or toxic for reproduction, such as formaldehyde, may be used up to a concentration of 0.1 %, which corresponds to 1000 mg/kg (content limit). A voluntary standard exists for organic chemical compounds in toys (EN 71-9) which specifies non-regulatory limits for formaldehyde in various toy materials (Table 1).

1.6. On 18th December 2018, the European Commission (EC) announced the introduction of formaldehyde restrictions for specific toy materials (Table 1) under the Toy Safety Directive.

Table 1. Summary of new formaldehyde restrictions in toy materials introduced by the EU Commission.

Toy Material	Current Voluntary Limit Value	Proposed Regulatory Limit Value	Formaldehyde Limit Type	Test Methods
Polymeric	2.5 mg/L	1.5 mg/L	Migration	EN 71-10:2005 EN 71-11:2005
Resin-bonded wood	80 mg/kg (total content)	0.1 mL/m^{3*}	Emission	EN 717-1:2004
Textile	30 mg/kg	30 mg/kg	Content	EN ISO 14184-1:2011
Leather	None	30 mg/kg	Content	EN ISO 17226-1:2008
Paper	30 mg/kg	30 mg/kg	Content	EN 645:1994 EN 1541:2001
Water-based	500 mg/kg	10 mg/kg	Content	EDQM Method

* 0.1 mL/m^3 or 1ppm = 0.124 mg/m^3 formaldehyde. Conversion factors can be found in Annex 1 to this paper.

2. Presentation and Discussion by the Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS)

2.1. Under the UK Toys (Safety) Regulations 2011/1881 (as amended)[2], chemicals that have been designated as either a carcinogen, mutagen or reproductive toxicant (CMR) can be used in toys so long as there is sufficient evidence to demonstrate that the likely use and exposure levels will not result in adverse effects on human health, that there is no suitable alternative and that the chemical is not banned in consumer products under REACH.

2.2. The SAG-CS were asked to consider whether the proposed levels in toys would have an impact on human health.

2.3. ***Health based guidance values***

2.3.1. More details on the health-based guidance values used to base the proposed regulatory limits can be found in the discussion paper from May 2021 (SAGCS-052101).

2.3.2. Briefly, the tolerable daily intake (TDI) for formaldehyde was set at 0.15 mg/kg bodyweight per day based on a 2-year oral study in rats by Til *et al.*, 1989 by the World Health Organisation (WHO) in their guidelines for drinking water quality (WHO, 1993) and has been confirmed by the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) of the European Food Safety Authority (EFSA, 2006).

2.3.3. In addition to an oral TDI value, the WHO has set an indoor air exposure limit for formaldehyde (WHO, 2010). A short term (30 minute) guideline indoor exposure limit of 0.1 mg/m^3 is recommended as preventing sensory irritation in the general population. This value was determined from an experimental study (Lang *et al., 2008)* in humans and is also protective for longer term health effects such as cancer endpoints.

2.3.4. Public Health England (PHE; now UK Health Security Agency - UKHSA) reviewed the data on formaldehyde in 2019 and concluded in their statement on "Indoor Air Quality Guidelines for selected Volatile Organic Compounds (VOCs) in the UK" that a long term (1 year) exposure limit of 0.01 mg/m^3 (10 µg/m^3) for formaldehyde should be adopted based on the US ATSDR long-term health-based guidance value of 10mg/m^3.

[2] The current UK regulations consist of the European Toy (Safety) Regulations (EC) 2011/1881 as amended by the UK SI 696/2019 Product Safety and Metrology (EU Exit) Regulations 2019. The full consolidated UK regulations will be available shortly.

2.4. ***General guidance***

2.4.1. Given that toys are not the only source of chemical exposure in children, the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) released an opinion in 2004, in which they set the maximum permitted contribution from toys as 10 % of the tolerable daily intake (TDI) (CSTEE, 2004). This percentage was confirmed twice by the Scientific Committee on Health and Environmental Risks (SCHER) in 2010 in its opinion on 'Risk from organic CMR substances in toys' and its opinion on 'Evaluation of the migration limits for chemical elements in toys'.

2.4.2. The SCHER Committee have also stated that CMR substances should not be present in toys and therefore levels should be as low as reasonably practicable (ALARP) (SCHER, 2007).

2.5. ***Polymeric toy materials***

2.5.1. Formaldehyde is used as a monomer in the manufacture of some polymeric materials used in toys. Children may therefore ingest formaldehyde when chewing and/or mouthing toys containing polymeric materials.

2.5.2. With a TDI of 0.15 mg/kg bodyweight per day set for formaldehyde by the WHO, a child with the body weight of 10 kg should not exceed 0.15 mg of formaldehyde per day from toys (in line with paragraph 2.4.1 above). With the assumption of a 100 ml daily ingestion of mouth saliva, a formaldehyde migration limit of 1.5 mg/L was recommended for polymeric toy materials.

2.5.3. Under the CLP regulations, 1B classified carcinogens such as formaldehyde may be present up to 0.1 % in the final product. This would convert to 1000 mg/kg and therefore the proposed level in toys is lower than the limit imposed by CLP.

2.5.4. Toy use could be considered analogous to food contact materials. Under EU 10/2011 Commission Regulation on plastic materials and articles intended to come into contact with food, certain plastics including melamine have a specific migration limit (SML) of 15 mg/kg food for formaldehyde. Again, the proposed limit in toys is lower than the migration level set for food contact materials.

2.6. ***Resin-bonded wood toy materials***

2.6.1. Formaldehyde is used in the manufacturing process of resin-bonded wood products such as plywood, medium-density fibre board and high-density fibre board. Formaldehyde resins include urea-formaldehyde, melamine-formaldehyde, phenol-formaldehyde, and polyacetal (polyoxymethylene – POM) resins. An emission limit of 0.1 mL/m^3 for formaldehyde was recommended. When the units of this limit are converted to mg/m^3, this limit of 0.124 mg/m^3 closely corresponds to the indoor air limit value established by WHO of 0.12 mg/m^3 (rounded down to 0.1 mg/m^3) [3] (WHO, 2010).

2.6.2. The ECHA RAC opinion (RAC, 2020) proposed a limit of 0.05 mg/m^3 in a range of consumer products but exclude items in scope of Directive 2009/48/EC on toys. This level suggested by RAC for consumer products in general is significantly lower than the proposed level in the SEAC opinion and those suggested by the EC in resin-bonded wooden toys of 0.1 mL/m^3 or 0.124 mg/m^3. The RAC do not disagree with the proposed levels for toys but suggest that indoor emission levels for household items should be lower in general thus reducing total exposure.

2.6.3. PHE (now UKHSA) reviewed the data on formaldehyde in 2019 and concluded in their statement on "Indoor Air Quality Guidelines for selected Volatile Organic Compounds (VOCs) in the UK" that a long term (1 year) exposure limit of 0.01 mg/m^3 (10 µg/m^3) for formaldehyde should be adopted based on the US ATSDR long-term health-based guidance value of 10mg/m^3.

2.7. ***Textiles, leather and paper toy materials***

2.7.1. Formaldehyde is used in the manufacture of textiles and can be present in toys containing textile materials. Formaldehyde has a harmonised classification as a class 1 skin sensitiser under CLP and dermal contact with formaldehyde may cause allergic contact dermatitis (OECD, 2002). The lowest threshold for contact dermatitis from formaldehyde was confirmed as 30 mg/kg by the Organisation for Economic Cooperation and Development (OECD) in 2002. This was based on the elicitation of allergic contact dermatitis in sensitised human subjects ranging from 30 ppm (w/w) for patch testing to 60 ppm (w/w) for products containing formaldehyde.

2.7.2. A content limit of 30 mg/kg formaldehyde in textile, leather and paper toy materials was recommended.

2.7.3. This was on the basis that exposure to toys produced with these materials is likely is to be similar to that of other materials considered.

[3] Annex 1 to this paper contains the calculation on which this conversion was based.

2.8. ***Water-based toy materials***

2.8.1. Formaldehyde can be used as a preservative in water-based toy materials such as inks, soap bubbles and dry materials that are intended to be mixed with water. It can also be produced as a result of other preservatives, such as bronopol in finger paints, reacting when used in aqueous media. A 10 mg/kg formaldehyde limit was recommended for water-based toy materials. The recommended limit is close to the lowest value that can be reliably determined by the EDQM method (method limit of quantification is 6 mg/kg) and takes account of formaldehyde traces that may be released by other preservatives.

2.8.2. Whilst it seems likely that the proposed limit is based on the ALARP principle and takes into account the limit of detection, it is calculated that a 10kg child exposed to 100ml of a water-based toy containing this level of formaldehyde would reach 10% of the TDI from this source. This is in line with the 100ml of saliva ingestion as mentioned above for polymeric toy materials.

3. **Conclusions**

Members agreed that they were content with the tolerable daily intake (TDI) set by the World Health Organization (WHO).

Members agreed that the limits of detection (LODs) and limits of quantification (LOQs) for the analytical methods were suitable when compared to the proposed limits for formaldehyde. They noted that the analytical limit of 16 mg/kg is quite close to that set for textile-based toy materials (30 mg/kg). Details of the methods of analysis can be found in Annex 2 to this opinion.

Members were content with the conversion of the formaldehyde emission limit of 0.1 mL/m^3 to 0.124 mg/m^3 (0.1 ppm) for resin-bonded wood toy materials (detailed in Annex 1).

Members acknowledged that there were now several recommended values for formaldehyde emission limits from authoritative bodies, namely 0.01 mg/m^3 from PHE (UKHSA) (as an indoor air quality limit), 0.05 mg/m^3 from RAC, or 0.124 mg/m^3 (0.1 mL/m^3) from WHO. Health Canada had also recommended a limit of 0.05 ppm (equivalent to 0.061 mg/m^3).

Following a review of these values, the SAG-CS considered that the proposed limits set for formaldehyde in water-based, polymeric, textile, leather and paper toys by the European Commission were a good first step in reducing potential exposure to formaldehyde. Going forward, Members considered that based on the indoor air quality guidelines from PHE (UKHSA), further reductions in exposure may be justified, but this would require a more detailed review. Therefore, in the short-term, the proposed reductions were agreed.

Based upon the Danish derogation for out-of-scope toy usage, members acknowledged that the limits to be set were for toy materials targeted at children under 36 months of age with mouthing and chewing expected. Members highlighted that future work in this area should include consideration of limits of formaldehyde in toy materials aimed at children older than 36 months, or not intended for mouthing/chewing.

Members noted that the endpoint of the pivotal study within the PHE (UKHSA) recommendation was asthma in children and acknowledged that further information may be required in order to set useful levels in toys. Members further acknowledged that the exposure scenario for the PHE (UKHSA) recommendation (building materials and vehicles) was different to that of children's toys.

SAG CS
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Abbreviations

AFC	Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food of the European Food Safety Authority
CLP	Classification Labelling and Packaging Regulations
CSTEE	Scientific Committee on Toxicity, Ecotoxicity and the Environment
DNEL	Derived No-Effect Level
DS	Dossier Submitter
ECHA	The European Chemicals Agency
EDQM	European Directorate for the Quality of Medicines & HealthCare of the Council of Europe
EPF	European Panel Federation
NOAEL	No Observed Adverse Effect Level
OECD	Organisation for Economic Cooperation and Development
POM	polyoxymethylene
RAC	ECHA Committee for Risk Assessment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SCHER	Scientific Committee on Health and Environmental Risks
SCOEL	Scientific Committee on Occupational Exposure Limits
SEAC	Committee for Socio-economic Analysis
TDI	Tolerable daily intake
WHO	World Health Organisation

References

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Directive 2009/48/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 June 2009 on the safety of toys- https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009L0048&from=EN

ECHA, Summary of Classification and Labelling- https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/55163 (Last Accessed September 2021)

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SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

SAGCS-072103. Formaldehyde in toy materials.

Conversion factors for formaldehyde from ml/m^3 to mg/m^3.

At 760 mmHg and 20 °C, 1 ppm = 1.249 mg/m^3 and 1 mg/m^3 = 0.801 ppm; at 25 °C, 1 ppm = 1.228 mg/m^3 and 1 mg/m^3 = 0.814 ppm.

Ideal gas calculation to verify:

mg/m^3 = ppm × (molecular weight/22.4) × (273/(273+Temp)) × (Atm Pressure/1013)
22.4 L = The volume of 1 mol at 1 atmospheric pressure at 0 °C
273 K = Thermodynamic temperature at 0 °C
1013 hPa = One atmospheric pressure = 760 mmHg

At 20 °C, mg/m^3 CH_2O = 0.1 x (30.026/22.4) x (273/273 + 20) x (1013/1013)
= 0.1 x 1.34 x 0.9317 x 1
= 0.125
At 25 °C, mg/m^3 CH_2O = 0.1 x (30.026/22.4) x (273/273 + 25) x (1013/1013)
= 0.1 x 1.34 x 0.9161 x 1
= 0.123

Note: It ultimately comes down to molecular weight divided by volume of 1 mole of gas at the two temps i.e. 30.03/24 L (@ 20 °C) and 30.03/24.4 L (@ 25 °C)

Between 20-25 °C, 0.1 ppm or 0.1 mL/m^3 equates to approximately 0.124 mg/m^3 CH_2O

Reference

Debra A. Kaden, Corinne Mandin, Gunnar D. Nielsen, and Peder Wolkoff (2010) Chapter 3. Formaldehyde in 'WHO Guidelines for Indoor Air Quality: Selected Pollutants'. Accessed online at https://www.ncbi.nlm.nih.gov/books/NBK138711/

SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

SAGCS-072103. Formaldehyde in toy materials

SAGCS-052101. Formaldehyde in toy materials – methods summary

Toy Material	**Current Limit Value (Voluntary Standard EN71-9)** *(Annex 1)*	**Proposed Regulatory Limit Value, and whether health (H) or analytically based (A)**	**Formaldehyde Limit Type**	**Test Methods***	**Basis of method**	**Detection capability, LoD, LoQ and comments on adequacy***	**Calibration curve lowest point stated/calculated**
Polymeric	2.5 mg/L	1.5 mg/L **H** this limit applies to the migrated test solution, e.g. 100 mL for polymeric materials, 15 mL for leather, liquids, clay or imitation tattoos (a)	Migration	EN 71-10:2005 EN 71-11:2005	A test portion is extracted with in most cases water and the formaldehyde determined by reaction with pentane-2,4-dione (acetyl acetone) and absorbance at	The validation report for the determination of formaldehyde migrated into an aqueous extract it was reported: LOD- 0.04mg/L LOQ- 0.06mg/L	1mg/mL

					410 nm against a calibration curve.	(probability error 1%)	
Resin-bonded wood	80 mg/kg (total content)	0.1 mL/m^3 This is technically equivalent to (b) 0.124mg/m^3	Emission	EN 717-1:2004	Test pieces of known surface area are placed in a chamber. Formaldehyde emitted and air sampled periodically drawing air through water, which absorbs the formaldehyde which is determined as above. The concentration of formaldehyde in the chamber atmosphere is calculated (mg/m^3). Sampling is periodically continued until the formaldehyde concentration in the chamber has reached a steady-state.	N/A	

Textile	30 mg/kg	30 mg/kg	Content	EN ISO 14184-1:2011	Formaldehyde is extracted with water at 40 °C and determined as above with a separate procedure to take account of any extracted colour	16mg/kg (<16mg/kg reported as not detectable when applying EN ISO 14184:2008)	15mg/kg
Leather	None	30 mg/kg	Content	EN ISO 17226-1:2008	Formaldehyde is separated and quantified by derivatisation and reversed-phase HPLC with known performance characteristics.	N/A	1µg/10mL Or 0.5mg/kg
Paper	30 mg/kg	30 mg/kg	Content	EN 645:1994 EN 1541:2001	The sample is torn or cut and extracted with water at 23 ± 2°C for 24 h, shaking occasionally. Formaldehyde determined by reaction with acetyl acetone as above with known performance characteristics	1mg/kg	0.00003mg/mL

					and, if limits are exceeded, a check procedure is used (scan of the UV-VIS spectrum and comparison with control)		
Water-based	500 mg/kg	10 mg/kg	Content	EDQM Method	Free formaldehyde is extracted with THF:water (9:1), and determined by derivatisation and reversed phase HPLC and UV detection at 354 nm. The identity of formaldehyde is confirmed by comparing UV spectra with reference samples. Only free formaldehyde is determined. Total formaldehyde, i.e. free formaldehyde and formaldehyde bound to the parent	LOD-3mg/kg LOQ- 6mg/kg	1.5mg/L

					preservative, can be determined using an HPLC method, based on derivatisation with acetyl acetone		

(a)- *The EU regulatory limit of 1.5 mg/L was proposed by ANEC in a paper to the EU toy Working Group applying the following rationale:*

The WHO Guidelines for Drinking-water Quality, 4th edition, 20114 (based on the background document "Formaldehyde in Drinking-water", 20055) consider a NOAEL of 260 mg/l appropriate. It corresponds to 15 mg/kg of body weight per day. Applying a safety factor of 100 results in a TDI of 1,5 mg/kg bw and day. A tenth of this value is 0,15 mg/kg. This NOAEL was also supported by the Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) related to "Use of formaldehyde as a preservative during the manufacture and preparation of food additives". It was concluded that the limit for formaldehyde as a monomer in EN 71-9 (2.5mg/L) should be lowered in line with acceptable NOAELs in this case 1.5mg/L.

(b)- *The restriction should be expressed as mg/m^3 as emission is usually measured and reported in these units. This is highlighted by the other existing emission restriction for toy materials namely formamide which is expressed as µg/m^3. As indicated later in the paper this will require a correction factor to be applied which if not stated could be calculated slightly differently. This should also be considered in light of other proposed EU restrictions for formaldehyde emission from consumer products under REACH where a limit of < 0.124 mg/m^3 (measured in the air of a test chamber) which corresponds to 0.1 mL/m^3 when converted under standard conditions.*

Limit of detection, LoD	A measured quantity for which the probability of falsely claiming the absence of a component in a material is β, given a probability α of falsely	Validation study, assessed from repeat analysis of blank or near blank samples as a multiple, usually between 3 and 5 (a multiplier of 3.3 is statistically

	claiming its presence. Default values for both α and β are usually 0.05. The term “sensitivity” is discouraged for ‘detection limit’.	valid) of the standard deviation to optimise avoidance of false negatives (α error) and false positives (β error). The aim of the LoD is to establish the concentration at which a user of the data can be confident (within defined limits) that the target analyte has been detected and the method used can distinguish this from a ‘blank’ response. Monitored as part of ongoing quality control
Limit of quantification, LoQ	The lower limit of the working range (‘*Terminology*…’, Not defined in VIM Informally LoQ can be regarded as the concentration at which the target analyte can be quantified with a given statistical probability.	Validation study, assessed from repeat analysis of blank or near blank samples as a multiple (usually 10) of the standard deviation. Both LoD and LoQ must be sufficiently below any applicable regulatory or specification limit to assure confidence, usually by a factor of 10 if possible. Monitored as part of ongoing quality control

Notes

General remarks:

The acetyl acetone method is well known with well characterised chemistry and the HPLC methods appear equally suitable with established performance characteristics and check procedure when required.