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Last Name	First name	Organisation/company	E-mail	Country	Please specify:	Table of contents	Please indicate the line numbers of the text on which you comment, if appropriate	
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium		1.SUMMARY	Our comments are summarized in the attached document.	Based on the comment submitted, it is not possible for SCHEER to identify the specific issue(s) addressed in the comments. The reference to the Health Canada Report on food grades TiO2 is not sufficient as a comment. In addition, the Health Canada Report discusses food grade TiO2, which is quite different from pigmentary TiO2 used as coloring agent. However, similar to EFSA analysis of food grade TiO2, the Health Canada Report is now also discussed in the Opinion. Besides Health Canada Food Standards Agency (FSA) UK and Food Standards Australia and New Zealand commented on the EFSA Opinion on TiO2. These comments are now included in the opinion.
Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium		1.SUMMARY	All our comments are summarized in the attached document.	Based on the comment submitted, it is not possible for SCHEER to identify the specific issue(s) addressed in the comments. The reference to the Health Canada Report on food grades TiO2 is not sufficient as a comment. In addition, the Health Canada Report discusses food grade TiO2, which is quite different from pigmentary TiO2 used as coloring agent. However, similar to EFSA analysis of food grade TiO2, the Health Canada Report is now also discussed in the Opinion. Besides Health Canada Food Standards Agency (FSA) UK and Food Standards Australia and New Zealand commented on the EFSA Opinion on TiO2. These comments are now included in the opinion.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium		1.SUMMARY	Page 8, lines 49-50 Contrary to the uncertainties noted by EFSA, Health Canada recently joined the UK FSA in concluding that E171 in food is safe.	Based on the comment submitted, it is not possible for SCHEER to identify the specific issue(s) addressed in the comments. The reference to the Health Canada Report on food grades TiO2 is not sufficient as a comment. In addition, the Health Canada Report discusses food grade TiO2, which is quite different from pigmentary TiO2 used as coloring agent. However, similar to EFSA analysis of food grade TiO2, the Health Canada Report is now also discussed in the Opinion. Besides Health Canada Food Standards Agency (FSA) UK and Food Standards Australia and New Zealand commented on the EFSA Opinion on TiO2. These comments are now included in the opinion.

Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	kristin.lorenz@bfr.bund.de	Germany	1.SUMMARY	Oral exposure, p. 10 line 26-28: It is stated that "it cannot be concluded that finger paint, white colour pencils or lipstick/lip gloss can be used safely by children." This conclusion seems to be mainly driven by the high uncertainty regarding hazard characterisation with respect to immunotoxic, genotoxic and carcinogenic activity after oral exposure to TiO2. Does that mean that in view of SCHEER the conclusion is also appli-cable to all other toys and toy materials with a potential for oral exposure to TiO2 (either via direct ingestion or via mouthing; e.g. as indicated in Table 6.11, p. 35-36)? Or is the conclusion limited to the assessed toy products (i.e. finger paint, white pencil, lip gloss/lipstick)?	The conclusion is limited to the toys assessed as far as the information was available to the SCHEER. It cannot be excluded by SCHEER that other toys may be on the market with higher TiO2 content and a potential of higher oral exposures. However, as the scenario's evaluated are chosen as the worst case scenarios, it can be assumed that this is also true for other uses of TiO2 in toys in which oral exposure might occur.
Pronk	Marja	on behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	1.SUMMARY	It would be informative to add a paragraph on toxicokinetics to the summary.	The information on toxicokinectics is now included in the Summary and Opinion. The following text is added: "Regarding the toxicokinetics, it can be concluded that the systemic availability of TiO2 both oral and inhalation exporure is very low".
Lila	Arnola	TDMA	ali@cefic.be	Belgium	2.1 Background	Our comments on chapter 2.1 are summarized in Annex 2 attached.	This comment is related to the background information provided by the European Commission to the SCHEER. The SCHEER cannot answer comments to the background provided. The SCHEER is not able to change the text in a published mandate.
Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium	2.1 Background	Our comments on chapter 2.1 are summarized on Annex II attached.	This comment is related to the background information provided by the European Commission to the SCHEER. The SCHEER cannot answer comments to the background provided.The SCHEER is not able to change the text in a published mandate.

Fielding	Trevor	CEPE	t.fielding@cepe.org	Belgium	2.1 Background	Page 11, Lines 19-21 The European Artists' Colours Association (EuACA) is a Sector Group of CEPE, the European Council of the Paint, Printing Ink and Artists' Colours Industry, and represents over 20 companies who manufacture and supply Artists' Colours & related products to the market. These product lines include both powder paints and fingerpaints, hence our interest in this SCHEER study. We strongly contest the assertion that 'the vast majority of titanium dioxide placed on the market … contains 1% or more particles with an aerodynamic diameter of ≤ 10 µm'. Our members have confirmed that the vast majority of the TiO2 grades used in powder paints and fingerpaints sold into the European Toy industry for use by children do not contain 1% or more particles with an aerodynamic diameter of ≤ 10 µm. In other words, Note 10 in the harmonized classification for TiO2 (Annex VI of the CLP Regulation (EC) N° 1272/2008 with 14th ATP amendment EU 2020/217) applies to the grades used to manufacture these products by our members and, thus, these grades are not classified as Category 2 carcinogens by inhalation.	The text "vast majority" is present in the mandate as formulated by DG GROW of the EC, and is based on information from the Toy Industries of Europe. The SCHEER is not able to change the text in a published mandate. In addition, the mandate and the Opinion does not only deal with TiO2 pigments in paints only, but with toys in general. Information available shows that it is possible that toys contain more than 1% of particles with a MMAD below 10um. For such cases the SCHEER provided the risk assessment. SCHEER is not aware, or has not been informed about TiO2 pigmentary product composition for specific applications (e.g. paints) that would not be included in the requirements as indicated in the CLP Regulation.
Detcheverry	Mathilde	AVICENN	detcheverry.avicenn@gmail.com	France	3.SCIENTIFIC OPINION	Considering scientific publications compiled on our website https://veillenanos.fr/dossier/risques/risques-specifiques/risques-nanoparticules-tio2, AVICENN would like to thank Scheer for taking into account the ultrafine particles of TiO2 and for considering the fact that "the presence of an ultrafine fraction in the pigments cannot be excluded because measurement methods may not have evaluated primary particles and agglomerates. The weight of evidence for the absence of an ultrafine fraction is weak to moderate, based on limited data with medium consistency and medium quality. The data are provided by the toy industry while robust study reports on the measurement methods of the particle size distribution of TiO2 pigment used in toys are not available". AVICENN especially supports these statements: - "the inhalation exposures to ultrafine TiO2 released form casting kits, chalk, and powder paint can not be considered safe" - "it cannot be concluded that finger paint, white colour pencils and lipstick/lip gloss can be used safely by children".	Thank you for your support
BILLERET	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium	3.SCIENTIFIC OPINION	Page 13 line 44: TIE provided data on lip-gloss/lipstick for information. It was not anticipated (based on the inhalation exposure) that this product type would be considered for evaluation. As SCCS now has a mandate to further evaluate the safety of TiO2 in cosmetics, it is proposed that this exposure scenario is removed from the Opinion. Page 16 line 1: Can SCHEER comment on the apparent inconsistency between the conclusion that casting kits, chalk and powder paint are not safe when an ultrafine fraction is present, and the SCCS Opinion for cosmetics where face powders (that also contain and ultrafine fraction) are safe for use by consumers to 25% TiO2?	The SCHEER was asked for a risk assessment of TiO2 used in toys. SCHEER included also the possibility for oral uptake as SCHEER considers the lip-gloss/lipstick exposure scenario for this product sold as toys for childeren. Both this Opinion and the previous SCCS Opinion of 2020 (SCCS/1617/20) state that for pigmentary TiO2 there is no concern regarding inhalation exposure. However, the SCCS Opinion is based on specific pigments that are used in cosmetics. Regarding pigments used in toys, no specific information is available on the nanofractions. Therefore, the risk assessments for the possibility of the presence of a nanofraction was based on general information of ultrafine TiO2 in lack of more specific information on the composition of pigmentary TiO2. For safe use of TiO2 pigments in toys it is the responsibility of the producer to demonstrate the absence of a nanofraction in TiO2 pigments used in toys.
Beck	Giuliana	Eurocolour e.V.	beck@eurocolour.org		3.SCIENTIFIC OPINION	Section 3, especially question 2, page 17, line 13 and 18-21 In general, we would like to emphasize that while the initial goal of this evaluation was to assess the potential risk of titanium dioxide used in toys as a pigment in course of the classification of specific powder forms as potential carcinogen (cat. 2), the preliminary SCHEER Opinion focusses in many aspects solely on nanoparticles. However, as demonstrated be the titanium dioxide manufacturers , pigmentary grades as used in toys contain larger particles which do not fulfil the classification criteria. The SCHEER refers in its preliminary opinion on the safety of titanium dioxide in toys for the evaluation of the oral exposure to results from the EFSA opinion on the evaluation of titanium dioxide as E171 as food additive. SCHEER concludes that there are "uncertainties in the hazard characterization", especially for immunotoxic, genotoxic, and carcinogenic activities. However, we would like to emphasize two points regarding the transfer of EFSA's conclusion to toys. First of all, EFSA focusses in the respective section of their opinion solely on nanoparticles ("ultra fine particles" according to SCHEER's nomenclature). Macro-sized particles as used as colorants in toys are not included in the underlying studies. EFSA explicitly mentions that "overall negative results were obtained in genotoxicity studies with microsized TiO2 pigment" (see EFSA opinion, page 45). Therefore, it is hasty to consider the EFSA conclusion for the evaluation of the safety of pigmentary titanium dioxide particles in toys. Secondly, currently available studies do not fulfil the criteria to exclude all concerns, but they also give no reason for concerns. The food colourant E171 was the first to be evaluated based on the new EFSA Guidances for the evaluation of small particles (nanoparticles). The studies conducted by titanium dioxide manufacturers on genotoxicity did not meet the criteria laid down by this new guidance as the studies were started when the guidances were not published yet. Nevertheless, as stated in the Regulation (EU) 2022/63, EFSA did not identify a health concern about the safety of titanium dioxide. As soon as the substance evaluation under REACH is finalized, additional data might become available to resolve any uncertainties. Due to these reasons, we would like to propose a more differentiated evaluation of the oral exposure of titanium dioxide in toys as already demonstrated in the evaluation of t	Regarding pigments used in toys, no specific information was available to SCHEER on the nanofractions. Therefore, the risk assements for the possibility of the presence of a nanofraction was based on general information of ultrafine TiO2 in lack of more specific information on the composition of pigmentary TiO2. For safe use of TiO2 pigments in toys it is the responsibility of the producer to demonstrate the absence of a nanofraction in TiO2 pigments used in toys. As far as the information provided by the public consultation, data have been provided on size distribution based on weight. For a proper risk assessment, and demonstration of absence of an ultrafine fraction, the size distribution by number needs to be provided. Regarding the classification criteria, the information available to SCHEER indicates the presence of particles smaller than 10 micrometer above 1%. SCHEER agrees that although available studies do not give a reason for concern, the lack of data, specially regarding size distribution, warrant careful consideration by SCHEER and, therefore, SCHEER cannot exclude a concern. In the light of recent reports from several regulatory agencies, the SCHEER has reformulated and updated its Opinion concerning the genotoxicity of pigmentary TiO2.

Beck	Giuliana	Verband der Mineralfarbenindustrie e.V.	beck@vdmi.vci.de	Germany		3.SCIENTIFIC OPINION	Section 3, especially questions 2, page 17, line 13 and 18-21 In general, we would like to emphasize that while the initial goal of this evaluation was to assess the potential risk of titanium dioxide used in toys as a pigment in course of the classification of specific powder forms as potential carcinogen (cat. 2), the preliminary SCHEER Opinion focus-ses in many aspects solely on nanoparticles. However, as demonstrated be the titanium dioxide manufacturers , pigmentary grades as used in toys contain larger particles which do not fulfil the classification criteria. The SCHEER refers in its preliminary opinion on the safety of titanium dioxide in toys for the evaluation of the oral exposure to results from the EFSA opinion on the evaluation of titanium dioxide as E171 as food additive. SCHEER concludes that there are “uncertainties in the hazard characterization”, especially for immunotoxic, genotoxic, and carcinogenic activities. However, we would like to emphasize two points regarding the transfer of EFSA’s conclusion to toys. First of all, EFSA focusses in the respective section of their opinion solely on nanoparticles (“ultra fine particles” according to SCHEER’s nomenclature). Macro-sized particles as used as colorants in toys are not included in the underlying studies. EFSA explicitly mentions that “overall negative results were obtained in genotoxicity studies with microsized TiO2 pigment” (see EFSA opinion, page 45). Therefore, it is hasty to consider the EFSA conclusion for the evaluation of the safety of pigmentary titanium dioxide particles in toys. Secondly, currently available studies do not fulfil the criteria to exclude all concerns, but they also give no reason for concerns. The food colourant E171 was the first to be evaluated based on the new EFSA Guidances for the evaluation of small particles (nanoparticles). The studies conducted by titanium dioxide manufacturers on genotoxicity did not meet the criteria laid down by this new guidance as the studies were started when the guidances were not published yet. Nevertheless, as stated in the Regulation (EU) 2022/63, EFSA did not identify a health concern about the safety of titanium dioxide. As soon as the substance evaluation under REACH is finalized, additional data might become available to resolve any uncertainties. Due to these reasons, we would like to propose a more differentiated evaluation of the c	Regarding pigments used in toys, no specific information was available to SCHEER on the nanofractions. Therefore, the risk assements for the possibility of the presence of a nanofraction was based on general information of ultrafine TiO2 in lack of more specific information on the composition of pigmentary TiO2. For safe use of TiO2 pigments in toys it is the responsibility of the producer to demonstrate the absence of a nanofraction in TiO2 pigments used in toys. As far as the information provided by the public consultation, data have been provided on size distribution based on weight. For a proper risk assessment, and demonstration of absence of an ultrafine fraction, the size distribution by number needs to be provided. Regarding the classification criteria, the information available to SCHEER indicates the presence of particles smaller than 10 micrometer above 1%. SCHEER agrees that although available studies do not give a reason for concern, the lack of data, specially regarding size distribution, warrant careful consideration by SCHEER and, therefore, SCHEER cannot exclude a concern. In the light of recent reports from several regulatory agencies, the SCHEER has reformulated and updated its Opinion concerning the genotoxicity of pigmentary TiO2.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	3.SCIENTIFIC OPINION	Page 16 - Line 1: Can SCHEER comment on the apparent inconsistency between the conclusion that casting kits, chalk and powder paint are not safe when an ultrafine fraction is present, and the SCCS Opinion for cosmetics where face powders (that also contain and ultrafine fraction) are safe for use by consumers to 25% TiO2?	The SCHEER was asked for a risk assessment of TiO2 used in toys. SCHEER included also the possibility for oral uptake as SCHEER considers the lip-gloss/lipstick exposure scenario for this product sold as toys for children. Both this Opinion and the previous SCCS Opinion of 2020 (SCCS/1617/20) state that for pigmentary TiO2 there is no concern regarding inhalation exposure for the products evaluated. However, the SCCS Opinion is based on specific pigments that are used in cosmetics. Regarding pigments used in toys, no specific information is available on the nanofractions. Therefore, the risk assements for the possibility of the presence of a nanofraction was based on general information of ultrafine TiO2 in lack of more specific information on the composition of pigmentary TiO2. For safe use of TiO2 pigments in toys it is the responsibility of the producer to demonstrate the absence of a nanofraction in TiO2 pigments used in toys. The conclusion of the SCHEER on the inhalation exposure of ultrafine TiO2 particles is based on the margin of safety as presented in the Opinion, the MoS being below 25 for casting kits, chalk and powder paint. In addition, the SCCS Opinion (SCCS/1617/20) was dedicated to one specific TiO2 preparation, and cannot be considered applicable to all TiO2 preparations as used in cosmetics.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States	3.SCIENTIFIC OPINION	Page 13 - Line 44: The toy industry (Toy Industries of Europe) originally provided data on lipgloss/lipstick for information. It was not anticipated (based on the inhalation exposure) that this product type would be considered for evaluation. As SCCS now has a mandate to further evaluate the safety of TiO2 in cosmetics, it is proposed that this exposure scenario is removed from the Opinion. This is especially critical as the identified mechanism of action underpinning the classification of TiO2 as a Category 2 carcinogen is inflammation created by lung overload, a scenario to be found only in occupational, not consumer, settings; therefore, this route of exposure is irrelevant to toys.	The SCHEER answers the current mandate with the knowledge at this point in time. SCCS is involved in this Opinion. The exposure scenarios related to toys are distinct from the exposure scenarios to be considered by SCCS. Based on the information provided by the toys industry respiratory exposure by dust generated from several toys is likely. Therefore, the SCHEER also performs a risk assessment for an inhalation exposure by TiO2 pigments possibly released from toys.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium		3.SCIENTIFIC OPINION	Question 2 Page 14, Lines 37-40 We understand from expert colleagues from the TiO2 industry that a genotoxic effect in TiO2 (regardless of its form) has yet to be proven, and there is no clear Weight of Evidence to support the assertion in the study (question 2 lines 37-40). In addition, we are aware of a recent wide-ranging study by an independent panel of toxicologists assessing 330 separate scientific literature studies, that came to the conclusion that TiO2 is not directly genotoxic. We would suggest that, at minimum, references should be inserted into the Opinion document to clearly identify those in vitro and in vivo studies that support this assertion (for both ultrafine and non-ultrafine forms).	SCHEER has reevaluated the information regarding the possible genotoxicity of various forms of TiO2. The Opinion has been adapted according to the final conclusions of this reevaluation.

Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	3.SCIENTIFIC OPINION	Question 1 Page 13, Lines 8-11 Please note, as per our previous comment, that the vast majority of the TiO2 grades used in powder paints and fingerpaints sold into the European Toy industry for use by children do not contain 1% or more of particles having a mass median aerodynamic diameter of < 10 microns. We would therefore suggest that there was not any justification to run a specific risk assessment on these types of products within the scope of this study.	The text "vast majority" is present in the mandate as formulated by DG GROW of the EC, and is based from the Toy Industries of Europe. The SCHEER is not able to change the text in a published mandate. Information available shows that it is possible that toys contain more than 1% of particles with a MMAD below 10um. For such cases the SCHEER provided the risk assessment.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.2.11 Conclusions	p.24, line 2-4: The conclusion on the particle size of pigmentary TiO2 is unclear, as the mean presented (0.2-0.3 µm) does not fit the P10-P90 range given (5-45 µm). Do they actually deal with the same pigmentary TiO2 or is the one (the mean) what is generally found for e.g. food-grade TiO2, and the other (the P10-P90 range) for the much bigger pigmentary TiO2 used in toys? Or is this due to dual interpretation of the term 'particle': constituent particle vs aggregate/agglomerate? Please clarify. Note that this conclusion re-appears in sections 1 (Summary, p.8/l.30-32) and 3 (Scientific opinion – Question 1, p.13/l.16-18) of the draft opinion and should be made more clear there as well. p.24, line 12-13: From the data presented it indeed seems unlikely that an ultrafine fraction would be present in the pigmentary TiO2 used in toys. As to the WoE for the absence of an ultrafine fraction there is however some confusion, as in section 6.2.11 it is concluded to be 'weak to moderate' (as well as on p.8/l.37 and p.13/l.23 of the draft opinion), but in the section Weight of evidence (6.7.6.4, p.62/l.10) it is considered 'weak'. Please clarify/make consistent.	SCHEER has reevaluated the literature regarding size distributions and adapted the text on TiO2 particle sizes accordingly in section 6.2.9 Particle shape, particle size and distribution.
Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany	6.2.9 Particle shape, particle size and distribution	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. Aspect 1: Titanium dioxide used is not classified 6.2.9 Particle shape, particle size and distribution Chapter "particle size and distribution" The CLP classification of titanium dioxide as an inhalation carcinogen refers to the aerodynamic diameter of the particles. In the meantime, numerous titanium dioxide manufacturers have been able to prove that many titanium dioxide powders available on the market are non-classified (non-carcinogenic). Our members also only use non-classified titanium dioxide in toys. Thus, the concentration of particles with an aerodynamic diameter < 10 µm in the toy products is below 1 %. Please also see Annex 1 (Information on CLP classification) In addition, the pigment distribution reports of the titanium dioxide manufacturers show that even the ultrafine fraction (1-100nm) is only contained in negligible amounts in the titanium dioxide powders used. Please see Annex 2 (Information on particle size).	SCHEER is aware that many pigmentary TiO2 preparations may not contain particles with a size below 10 µm. However, the information received by SCHEER by various stakeholders indicates that the TiO2 pigments used in toys can contain a fraction above 1% with the size below 10 µm. It is for the manufacturer to demonstrate that the marketed product does not fulfil the requirements for the CMR classification. An example of the various figures is presented below: EWIMA-report: 0% below 0.1 µm TDMA-report 1: 0.001 - 1.29% below 10 µm TIE-report: ca 8% below 10 um and D50 16-23 and 14-20 µm TDMA: . The size of the primary particles of pigmentary TiO2 typically ranges from 100-250nm and for nano grades from 5-80nm.

Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.2.9 Particle shape, particle size and distribution	Our comments on chapter 6.2.9 are summarized in Annex 1 - part 2 attached.	SCHEER thanks TDMA for providing the information on the titaniun pigments used as food additive. The provided information in Annex 1-PArt 2 clearly show the presence of a nanofraction in the primary particle size analysis of Unitane O-220 by Electron Microscopy. SCHEER choose the subchronic Bermudez 2004 study as children are only exposed to pigments from toys for a limited timeframe. In addition, SCHEER wanted to know the risk of pure ultrafine TiO2 particles as part of its estimation of the total risk associated with the use of pigmentary TiO2.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.2.9 Particle shape, particle size and distribution	Our comments on chapter 6.2.9 are summarized in Annex 1 - part 1 attached.	SCHEER thanks TDMA for providing the information on the titaniun pigments used as food additive. Annex 1-Part-1 presents data for Uitane O-220 showing the presence of a nanofraction in this Unitane O-220 TiO2 preparation. SCHEER choose the subchronic Bermudez 2004 study as children are only exposed to pigments from toys for a limited timeframe. In addition, SCHEER wanted to know the risk of pure ultrafine TiO2 particles as part of its estimation of the total risk associated with the use of pigmentary TiO2.

Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium	6.2.9 Particle shape, particle size and distribution	Our comments on chapter 6.2.9 are summarized on Annex I (Part 2) attached.	SCHEER thanks TDMA for providing the information on the titaniun pigments used as food additive. The provided information in Annex 1-PArt 2 clearly show the presence of a nanofraction in the primary particle size analysis of Unitane O-220 by Electron Microscopy. SCHEER choose the subchronic Bermudez 2004 study as children are only exposed to pigments from toys for a limited timeframe. In addition, SCHEER wanted to know the risk of pure ultrafine TiO2 particles as part of its estimation of the total risk associated with the use of pigmentary TiO2.
Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium	6.2.9 Particle shape, particle size and distribution	Our comments on chapter 6.2.9 are summarized in Annex I (Part 1) attached.	SCHEER thanks TDMA for providing the information on the titaniun pigments used as food additive. Annex 1-Part-1 presents data for Uitane O-220 showing the presence of a nanofraction in this Unitane O-220 TiO2 preparation. SCHEER choose the subchronic Bermudez 2004 study as children are only exposed to pigments from toys for a limited timeframe. In addition, SCHEER wanted to know the risk of pure ultrafine TiO2 particles as part of its estimation of the total risk associated with the use of pigmentary TiO2.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	6.2.9 Particle shape, particle size and distribution	Particle size and distribution Page 23, Lines 11-20 Four pigments are listed under this section as being TiO2 grades used for the manufacture toys and toy material ('For four manufacturers of TiO2 used in toys and toy material, information was received regarding the particle size distribution of the pigmentary TiO2 '). A simple internet search reveals that none of these grades are pure TiO2 pigments. These grades are all pearlescent grades, where TiO2 has been combined with another substance (mica) to achieve certain visual effects, mainly used in the cosmetics sector. These grades should not be presented as 'standard' representative TiO2 types used to manufacture toys in general. The comments relating to particle distribution, and references these four grades should therefore be specifically placed in the context of cosmetic-related toy products (e.g. lip gloss). Information on other standard pure TiO2 grades used for e.g. fingerpaints could be included to improve the quality of this section of the Opinion.	The comment may be correct. SCHEER has included the information as received from the TIE and/or EWIMA. SCHEER is not responsible for the data. Other (reliable) data could not be obtained from the literature. Information provided at the public consultation contained data on a particle size measurement between 0,2 - 4 µm. In an added SDS of Ti-Pure™ Titanium Dioxide Pigment a particles size between 0,2 -0,4 µm was indicated, and a statement that the preparation did not contain particles below 10 µm in excess of 1%. Also, "internet" statements needs to be reliable. SCHEER considers reviewed scientific papers and so called grey literature (e.g (non) governmental reporst) to formulate its conclusions. Based on the comments, SCHEER has conducted a similar short internet search. However, this short internet search showed that information on size is not available in a number of manufactureres leaflets or SDS.

Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany	6.2.9 Particle shape, particle size and distribution	Particle size and distribution, p.23 line 13-20: Please consider to indicate the sample preparation as well as the analytical method or principle underlying the indicated particle size distribution of the listed TiO2 pigment products.	Limited information was available on the methods used. Text has been modiified. Text added: "as determined by laser diffraction".
Birkmann	Kathrin	TÜV Rheinland LGA Products GmbH	Kathrin.Birkmann@de.tuv.com	Germany	6.3. Application of TiO2 in toys	According to the table 6.3, a lot of different toys may contain > 1 % TiO2. However, the Opinion just mentions that polymeric materials practically do not pose a risk and investigates further very critical materials. What about the other materials like lacquer, dough, textiles and paper? Do they pose a risk concerning inhalation and/or oral exposure? Further, it it important to know that white pencils are not safe. What about other colours with less TiO2? It would be great if the conclusion could be extended to cover a broader range of toys resp. toy materials.	The risk assessment was based on the information available to the SCHEER, that clearly indicated a titanium oxide content of more than 1% in a number of toys. Only for polymeric materials the lack of migration of TiO2 out of the polimeric matrix was demonstrated. For the other materials mentioned in the comments, data was not available. There may be some misunderstanding as white colour pencil use is considered to pose a negligible risk and use is safe based on the Margins of Safety (MoS) calculated. So, if the use of white pencils is considered safe coloured pencils with less TiO2 should be considered safe as well. The conclusion is limited to the toys assessed as far as the information was available to the SCHEER. It cannot be excluded by SCHEER that other toys maybe on the market with higher TiO2 content and a potential of higher oral exposures. However, as the scenario's evaluated are chosen as the worst case scenarios, it can be assumed that this is also true for other uses of TiO2 in toys in which oral exposure might occur.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	6.3.1 Function and uses of TiO2 in toys	Page 25, lines 9-11 As per our previous comment, the four 'TiO2' grades mentioned in this report are not pure TiO2 pigments but are combined with mica, and thus should not be considered representat of the TiO2 grades used in toy products such as poster paints and fingerpaints.	The comment may be correct. SCHEER has included the information as received from the TIE and/or EWIMA. SCHEER is not responsible for the data. Other (reliable) data could not be obtained from the literature. Information provided at the public consultation contained data on a particle size measurement between 0,2 - 4 µm. In an added SDS of Ti-Pure™ Titanium Dioxide Pigment a particles size between 0,2 -0,4 µm was indicated, and a statement that the preparation did not contain particles below 10 µm in excess of 1%. Also, "internet" statements needs to be reliable. SCHEER considers reviewed scientific papers and so called grey literature (e.g (non) governmental reporst) to formulate its conclusions. Based on the comments, SCHEER has conducted a similar short internet search. However, this short internet search showed that information on size is not available in a number of manufactureres leaflets or SDS.

Jette	Borum	Schjerning Farver Denmark	jb@schjerning.dk	Denmark	6.3.2 Titanium content in toy materials	We have decided to remove the TIO2 from all fingerpaints. Since it has already been forbitten in food (6/8-2022) we are certain that it will also be forbitten in fingerpaints. We can not produce glossy school paint (CE marked) without TIO2 so hopefully it will still be allowed.	Thank you for this information. No change needed.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	6.3.4 Conclusions	Page 27, lines 2-9 As per our comments to sections 2.1 and 3, we strongly disagree with the assertion that the vast majority of TiO2 grades used to manufacture toys are classified as category 2 carcinogens in accordance with Annex VI of CLP - this is certainly not the case when considering fingerpaints or powder paints. We would suggest that such statements made to this effect in the Opinion should have been fully corroborated by other stakeholders prior to publication.	SCHEER has included the information on pigmentary TiO2 particle sizes as received from the TIE and/or EWIMA. SCHEER is not responsible for the data. Other (reliable) data could not be obtained from the literature. SCHEER considers reviewed scientific papers and so called grey literature (e.g (non) governmental reporst) to formulate its conclusions. Regarding the classification criteria, the information available to SCHEER indicates the presence of particles smaller than 10µm above 1%.
Dobel	Shima	Ministry of Environment of Denmark	sdo@mim.dk	Denmark	6.4 Exposure assessment	Overall, we do agree with the SCHEER on the exposure assessment as it takes both inhalation exposure and oral exposure into account. However, SCHEER has not considered additional possible exposure of TiO2 from other sources but the evaluation was strictly limited to toys and to materials. In general, we are of the opinion, that exposure of the same substance and substances with similar mode of action should be considered and taken into account when an exposure assessment is made. This should also be the case for TiO2.	In general SCHEER agrees that for a full risk assessment also other sources of exposure need to be considered. However, SCHEER was acting according its mandate that strictly limited the risk assessment to the application of TiO2 pigment in toys.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.4.2.1 Introduction	p.29, line 15-17: For the inhalation route, the scenarios as proposed by TIE have been adopted, but not the respective air concentrations/inhalation exposures because some parameters used by TIE were not agreed with. No arguments were however provided why SCHEER did not agree. I transparency it would further be helpful to present in the opinion also the TIE calculations for the inhalation exposure route.	The exposure calculations presented by TIE included several scenarios with different parameter settings. Since the SCHEER disagreed with the selection of the basic studies and how they were extrapolated for the exposure assessment, the SCHEER calculated the exposure based on the parameters as indicated in the text. It would be excessive to include also the TIE calculations, as they were not used for the RA. A further explanation is presented why SCHEER did not follow the TIE calculations and where SCHEER deviated from TIE. 6.4.2.1. Text has been modified as follows: "SCHEER follows the selection of exposure scenarios proposed by TIE. However, the SCHEER does not agree with some parameter choices for the TIE exposure calculations, e.g. the way the use amount was determined for some scenarios and how extrapolation was performed in cases where no specific data was available for the evaluated toys. Therefore, the SCHEER recalculated the respective air concentrations for the selected exposure scenarios as indicated in the calculations below."

Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany		6.4.2.2 Exposure scenarios – inhalation	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. Aspect 2: content of TiO2 in white colouring pencils 6.4.2.2. Exposure scenarios – inhalation, Table 6.7 In the exposure assessment on which the safety assessment is based, it is assumed that white colouring pencils contain up to 51 % titanium dioxide. There are indeed individual products that have a very high titanium dioxide content of 33 or 51 %. However, the majority of white colouring pencils contain significantly less titanium dioxide (usually below 25 %). We would therefore suggest that an exposure study should be performed with colouring pencils containing the most usual amount of titanium dioxide. Otherwise, the safety assessment could lead to a group of safe toys being considered unsafe due to isolated products containing higher amounts of titanium dioxide.	SCHEER uses a worst case scenario. So, if there are products on the market with 51% pigment content of TiO2, this is included in the worst case scenario. Coulored pencils have been considered safe regarding inhalation even on the basis of this worst case scenario. Therefore, no refinement is needed. For a refinement as proposed here, more data would need to be provided on the frequency of use of different kinds of pencils.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.2 Exposure scenarios – inhalation	Page 30 - Line 7: We believe the concern about particle release from chalk and crayons is unfounded. An historical U.S. CPSC staff report concludes that, despite measurable amounts of asbestos in sampled crayons, release is negligible in use. This may have an impact because TiO2 is a potential replacement for talc in crayons to avoid the possibility of asbestos contamination. CPSC staff report can be found here: https://www.cpsc.gov/s3fs-public/pdfs/crayons.pdf	SCHEER consider that particle release mechanisms of particulate pigments is quite different to that of fibers, so no change is needed in our opinion. Furthermore, the presented exposure calculations are based on recent reports and information submitted to SCHEER on particle release from crayons and chalk.
Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany		6.4.2.3 Exposure modelling – inhalation	p. 32 line 6: It is stated here that the symbol (a) as used in the equation in line 4 represents the "amount of TiO2 dispersed in the air". In the text on p. 31 line 38 it is written that the symbol (a) represents "the amount of product dispersed in the air". These seem to be different statements. Please check. Please check in addition the explanations for (ameas) on p. 32 line 19 and for (ascen) on p. 32 line 23. In our opinion the text on p. 31 line 38 seems to be correct while the legend of (a), (ameas), and (ascen) need amendment; otherwise it remains unclear why multiplication with the weight fraction of TiO2 would be required if the amount of TiO2 is already known. Or perhaps different legends/equations are required depending on the available data, i.e. whether filter loadings were analysed specifically for TiO2 or only generally for any particles. p. 33 line 2-3: The text "the weight fraction of the emitted TiO2 dust as measured for the chalks" seems to contradict the text provided on p. 34 line 19-21 "the calculations were based on an experiment with chalk where only particles in the air (PM2.5, PM10 and total suspended particulates) were measured." (i.e. no TiO2 dust was measured in the cited reference)". According to the information in the cited reference Goel et al., 2015 [1], the investigated chalks were unlikely to contain TiO2 in relevant amounts, as it had not been detected with the energy dispersive X-ray spectroscopy method applied for characterisation of the chalks. Please check. [1] Goel S, Patidar R, Baxi K, Thakur R (2015) Investigation of particulate matter performances in relation to chalk selection in classroom environment. Indoor and Built Environment, 26: 119-131. p. 33 Table 6.8: In Rasmussen et al., 2019 [2] the analytical result for PM10 concentration of adult body powder #1 at a distance of 53 cm is reported as 8.42 ± 6.71 mg/m³ for three replicates, i.e. there seems to be considerable variation between the individual measurement results. It is suggested to consider if the standard deviation could be respected in choosing Cair_meas, as the exposure assessment in the draft opinion aims for a conservative upper bou	SCHEER agrees with the comment and has changed the legend below the formula accordingly. Page 32 line 6. "α = amount of TiO2 product dispersed in the air." Page 32 line 19. αmeas = amount of product/PM10 fraction measured in the air Page 33 lines 2-3. SCHEER agrees with the comment. It is stated that the chalk without TiO2 is used as model to imitate the released from the chalk. To be checked. Text changed/added. " Since the experiment did not include, TiO2 containing chalks, in addition to the adjustment factor for V, an adjustment factor for the weight fraction wf of TiO2 in PM10 was used, with the assumption that the weight fraction of TiO2 in PM10 after release is the same as the weight fraction of the TiO2 in the solid chalk. " Page 33 Table 6,8. Answer to comment. "The chosen concentration represents the highest experimental concentration from 9 experiments with 3 products investigated at three different distances. Since the variation in measured air concentrations is mainly related to the variation in sprayed amounts, the median will be a better representative of the released amount, than median + standard deviation. Therefore the opinion is not changed. The weaknesses of the presented exposure calculations are acknowledged already in the WoE assessment."

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands		6.4.2.3 Exposure modelling – inhalation	p.33-34, scenario 2: For the chalk scenario (scenario 2) it is unclear how the realistic high air concentration of 2.11 µg/m3 has been calculated (in Table 6.8 no realistic high Cair_meas is given, only the upper bound Cair_meas; it can also not be found in Annexes III and IV). p.33-34, scenario 3: For the white colour pencil scenario (scenario 3), apparently 8 µg/m3 has been taken as realistic high Cair_meas (i.e., the median value for TiO2 < 10 µm from the dust release studies as presented in Table A-I.6). But that is not evident from the text or Table 6.8, as in the latter only the upper bound Cair_meas has been given (NB: mistakenly as 0.020 µg/m3 whereas it should be 20 µg/m3, according to Table A-I.6). The WoE for the exposure of scenario 3 is concluded to be 'strong' because 5 different pencils had been tested (p.33/l.15; also on p.62/l.20). There is some confusion though in the opinion on this, as Table 6.8 mentions '5 brands', Tables 6.9 and A-IV.1 'measurements for one pencil type', and Annex I presents data for 4 types of pencils (Table A-I.1) or 4 different products (Table A-I.6). Please clarify. p.33-34, scenarios 1 and 4: For the casting kit and powder paint scenarios (scenario 1 and 4, respectively), 1% release from the product use amounts is assumed (p.33/l.25-26), and the realistic high and upper bound ascen presented in Table 6.9 match with that percentage. However, in Table A-IV.1 in Annex IV different releases are given for the realistic high scenario (1%) and the upper bound scenario (10%). Please clarify/make consistent. NB: the upper bound use amount for casting kit is mistakenly given as 100 g in Table A-IV.1. According to p.33/l.28 this should be 1000 g.	For scenarios 2 and 3, respectively for chalk and white colour pencils, a reevaluation of the realistic and upper bound exposures was performed. For scenarios 2 and 3, in order to consistently derive the realistic and upper bound exposures the same parameters have been used in both scenarios, resulting in the same outcomes. Only for scenario 1 and 4, because of the large uncertainties, the parameter "product amount" differed between the realistic and upper bound scenarios. In the final risk assessment, only the upper bound scenario was considered. The number 0.02 has been corrected to 20. Comment regarding number of brands/pencils Table 6,8. Checked: four brands not five. Table A-I.1 should be 4 brands of pencils. Text corrected by adding brand names. Table A-I.6. Text corrected into brands/products. Thank you for the comment. The mistakes are corrected.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium		6.4.2.4 Conclusions on potential release of TiO2 into the air	page 34 line 10: The calculated air concentrations for the different scenarios are not differentiated by particle size. The exposure assumptions (and the subsequent MOS calculations), particularly for ultrafine particles makes the assumption that the TiO2 aerosol produced by the toy is equivalent to the test material used in the Bermudez 2004 study. Bermudez et al exposed the rat subjects to an aerosol of ultrafine TiO2 with an average particle size of 21nm. This is clearly over conservative and not justified when considering the likely particle size distribution of pigmentary TiO2 used in toys. Although the mean particle size in the study was 1.44um with a GSD of 2.60 as a result of agglomeration, the authors assumed that dis-agglomeration would occur in vivo. While this may be the case when the test material was nano sized to start with, in the case of toys the particle size distribution is significantly different, and this should be taken into account when estimating the exposure to ultrafine particles. Since the calculated MOS is only one order of magnitude less than 25, such an adjustment is justified.	The toxicity studies available indeed use a particle size that will be different from the particles sizes in toys. To allow a more accurate and less conservative worst case scenario for the risk assessment and increase the WoE, the SCHEER needs more information on the particles sizes of TiO2 in toys as well as toxicity studies with more relevant particle sizes. Based on the limited information provided, the presence of a nanofraction seems unlikely. However, SCHEER cannot exclude the presence of a nanofraction in the pigments. In its risk assessment, SCHEER therefore clearly distinguishes between possible effects of a nanofraction (ultrafine particles) and larger (fine) pigment particle sizes.
Kaufman	Alan	Affairs The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.4 Conclusions on potential release of TiO2 into the air	Page 34 - Line 10: The calculated air concentrations for the different scenarios are not differentiated by particle size. The exposure assumptions (and the subsequent MOS calculations), particularly for ultrafine particles assumes that the TiO2 aerosol produced by the toy is equivalent to the test material used in the Bermudez 2004 study. Bermudez et al exposed the rat subjects to an aerosol of ultrafine TiO2 with an average particle size of 21nm. This is clearly overly conservative and not justified when considering the likely particle size distribution of pigmentary TiO2 used in toys. Although the mean particle size in the study was 1.44um with a GSD of 2.60 (due to agglomeration), the authors assumed that dis-agglomeration would occur in vivo. While this may be the case when the test material was nano sized to start with, in the case of toys the particle size distribution is significantly different, and this should be considered when estimating the exposure to ultrafine particles. Since the calculated MOS is only one order of magnitude less than 25, such an adjustment is justified.	The toxicity studies available indeed use a particle size that will be different from the particles sizes in toys. To allow a more accurate and less conservative worst case scenario for the risk assessment and increase the WoE, the SCHEER needs more information on the particles sizes of TiO2 in toys as well as toxicity studies with more relevant particle sizes. Based on the limited information provided, the presence of a nanofraction seems unlikely. However, SCHEER cannot exclude the presence of a nanofraction in the pigments. In its risk assessment, SCHEER therefore clearly distinguishes between possible effects of a nanofraction (ultrafine particles) and larger (fine) pigment particle sizes.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium		6.4.2.5 Exposure scenarios –oral	Page 35 line 16: Finger paints must contain an embittering agent to prevent unintentional ingestion according to the harmonised and referenced standard EN71-7. Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly.	CEN TC 52 EN 71-7:2014+A3:2020 prescribes the use of embittering agents in finger paints to discourage ingestion via the mouth. "An embittering agent in accordance with the following list (see Table 4) shall be added in order to discourage and minimize the ingestion of paint." The text is changed accordingly to include this presence of an embittering agent. "The swallowing of finger paints is specifically discourage by addition of an embittering agents to the finger paints according to the European standard EN 71-7:2014+A3:2020." Based on recent information of CEN/TC 52, the exposure scenario for finger paint has been modified.

Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany		6.4.2.5 Exposure scenarios –oral	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. 6.4.2.5 Exposure scenarios – oral, Table 6.11 In the exposure assessment on which the safety assessment is based, it is assumed that white colouring pencils contain up to 51 % titanium dioxide. There are indeed individual products that have a very high titanium dioxide content of 33 or 51 %. However, the majority of white colouring pencils contain significantly less titanium dioxide (usually below 25 %). We would therefore suggest that an exposure study should be performed with colouring pencils containing the most usual amount of titanium dioxide. Otherwise, the safety assessment could lead to a group of safe toys being considered unsafe due to isolated products containing higher amounts of titanium dioxide.	SCHEER uses for its risk assessment a worst case scenario. So, if there are products on the market with 51% pigment content of TiO2, this figure is used for the risk assessment as it is indicated in the worst case scenario. Coulered pencils have been considered safe even on the basis of this worst case scenario. Therefore, no refinement is need For a refinement as proposed here, more data would need to be provided on the TiO2 content and frequency of use of different kinds of pencils.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.5 Exposure scenarios –oral	Page 38 - Line 5 and 6: The estimated frequency of exposure (2 x 8mg/day) is in contradiction with the way the Toy Safety Directive migration limits have been established (once a day for scraped-off materials). Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly.	SCHEER chose the twice-a-day exposure in the Opinion as an upper-bound worst case exposure scenario. The Opinion was not changed regarding this upper-bound scenario.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.5 Exposure scenarios –oral	Page 37 - Line 28 & 29: It shall be noted that white finger paint is uncommon, and most finger paints are primary colors that contain less than 1% TiO2 and rarely up to 4%. Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly.	This information provided previously by TIE indicate a TiO2 content up to 30% for finger paint Table 6,11 page 35. The respective scenarios use a worst case exposure approach, based on the information available, which is a conservative approach for risk assessment. Since no information is available on the actual distributions of use (and in addition these are not fixed) the scenario cannot be further refined.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.5 Exposure scenarios –oral	Page 37 - Line 26: Oral route of exposure is irrelevant based upon the rationale for classification of TiO2 for toy exposures, and is of questionable relevance even in occupational settings, where exposure is many orders of magnitude greater. Additionally, an Ad-Hoc group (led by the German BfR) to the European standardization Committee dealing with toy chemical safety standards (CEN/TC52/WG5) has recently worked on EN 71-7 related to toxicological risk assessment. Latest draft "concept on exposure estimation" provides a proposal for estimating systemic event exposure to substances due to the repeated use of finger paints. This document (CEN/TC52/WG5 N 1783 - November 2021) can be obtained directly from the secretariat of CEN/TC52. This document indicates "The mandatory use of embittering agents according to standard EN 71-7 on finger paints prevents repeated oral ingestion of finger paints; therefore, oral intake is not considered in systemic exposure due to repeated use of finger paints". It also indicates: "In the introduction of the standard EN 71-7:2014 it is stated that oral exposure to finger paints needs to be considered as well. Therefore, according to requirement 4.6 in EN 71- 7:2014, use of embittering agents is mandatory. A young child might explore the taste of finger paints upon first contact, which could eventually lead to systemic exposure following absorption in the oral mucosa or gastrointestinal tract. However, a child is not expected to try eating finger paint a second time due to the negative experience. Hence, repeated ingestion of finger paints is very unlikely. " On frequency of exposure, this document indicates: "RIVM assumes a use frequency of 100 events per year in its Toys Fact Sheet [RIVM 2002]. This value was supported by the Nordic Exposure Group for Health [Norden 2011] and used by the Danish EPA in its risk assessment of preservatives in toys [DK EPA 2014]. Scott and Moore estimated a use frequency of two times per week [Scott and Moore 2000]." Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly.	The text has been modified to include the use of an embittering agent in finger paints according to European standard EN 71-7:2014+A3:2020 (CEN, Brussels, Belgium). As the estimations for use are low (18 times per year or less), for the exposure b an acute and subchronic exposure. 6.4.2.6. Text changed accordingly However, the estimated total intake by Van Engelen et al. (2008) does not apply since 2014 as in EN 71-7:2014 an obligation was included to add an embittering agent to finger paints to limit and prevent uptake of finger paint by direct ingestion. It is likely that uptake of finger paint due to direct ingestion will be rather limited, as the bitter taste will result in avoiding oral uptake. More recent estimations for the possible uptake of finder paints containing an embittering agents propose an exposure frequency of 18 times per year for children 2 years of age (CEN/TC 52-WG5 N1682 20201127). SCHEER uses this proposal for estimating the oral exposure to pigmentary TiO2 for children 3.5 to 4.5 years of age. In view of the low frequency, SCHEER estimated both the effects of an acute and subchronic exposure. Single acute event: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, translating into for a 15kg child into a single acute exposure of 8 mg TiO2 per kg. Semi-chronic multiple events: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, 18 events per year results in 2160 mg per year, resulting in 5.9 mg per day, resulting in a dose of 0.39 mg per kg per day.

Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.4.2.5 Exposure scenarios –oral	Page 35 - Line 16: Finger paints must contain an embittering agent to prevent unintentional ingestion according to the harmonized and referenced standard EN71-7. Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly. See also comments above regarding the SCCS cosmetic opinion and the remote likelihood of lung overload from such products.	Text changed accordingly: The swallowing of finger paints is specifically discouraged by addition of an embittering agents to the finger paints according to the European standard EN 71-7:2014+A3:2020.
Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany		6.4.2.5 Exposure scenarios –oral	p. 35 table 6.11 (entries for polymeric materials): It is unclear why the potential for oral uptake of TiO2 via direct ingestion of polymeric toy material is indicated with “no” whereas the potential exposure via mouthing is indicated with “yes”. Ingestion of polymeric toy material may occur, e.g. because it was gnawed or bitten off during mouthing and, subsequently, swallowed. (Bite marks were observed during mouthing behaviour studies on polymeric toys, e.g. as reported in CEN/TR 16918:2015 [7]. In the opinion on estimates of the amount of toy materials ingested by children, SCHER elaborated that biting toys can result in the uptake of toy materials [8].) Likewise, mouthing of polymeric materials may occur. However, in the draft opinion it is reasoned that migration of TiO2 embedded in polymers is unlikely. This conclusion seems to hold true for both oral scenarios. Please check and/or provide rationale. [6] Safety of toys - Children´s mouthing behaviour in contact with toys; German version CEN/TR 16918:2015. [7] SCHER (Scientific Committee on Health and Environmental Risks), Final Opinion on estimates of the amount of toy materials ingested by children, 8 April 2016. https://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_170.p p. 35 table 6.11 (entries for solvent-based paints and water based paints): It is unclear why the potential for oral exposure to TiO2 via direct ingestion of these paint materials is indicated with “no”. Children might colour their hands or nails when using paints by purpose or by accident; subsequently, a small amount of this toy material might become available for oral exposure via hand-mouth contact. Please check and/or provide rationale.	Table 6,11. Polymeric materail. SCHEER agrees that children may bite of some polymeric metrial and then be exposed to the pigments included inthe polymer matrix. However, exposure to the pigment irself will only occur when the clolouring pigment is released from the p[olymer which does not seem to occur. So, in terms of direct exposure to the pigment this is not likely, therefore "no" was included in the table. So, a distinction was made between exposure to the TiO2 directly, or indirectly via TiO2 embedded in a matrix (e.g. a polymer, paper etcetera). Table 6,11 crayons. Exposure to the TiO2 present in crayons is possible by biting or scraping of material from the crayons by mouthing. Table 6,11 coating. Exposure to the TiO2 present in coatings is possible by biting or scraping of material from the coating by mouthing. The following text was added: **The mouthing may result in scraping or biting on the toy with a possible release of pieces of the toys including the TiO2 pigment, which may result in an indirect exposure.** Below table 6.11, the following paragraph was added: **For a number of products, a direct ingestion was considered not possible as the TiO2 pigment would be embedded within the matrix of the toys. However, oral uptake by scraping of material or biting on the products with release of pieces of the toys and thus oral uptake including the TiO2 pigment, which may or may not be freely available, remains possible.**
Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany		6.4.2.5 Exposure scenarios –oral	p. 35 table 6.11 (entries for wax crayons): p. 35 line 20-21: Ingestion of scraped-off material is not only relevant for toys intended to be placed in the mouth, but might also be relevant for toys put in the mouth despite not being intended for this purpose. For example, a small child might mouth on a plush toy (leading to ingestion of textile fibres becoming loose) or on a (painted) brick (leading to ingestion of gnawed off material). Please consider to include this information in the description of the direct ingestion exposure scenario. p. 35 table 6.11 (entries for coating): It is unclear why the potential for oral uptake of TiO2 via direct ingestion of coating is indicated with “no” whereas the potential exposure via mouthing is indicated with “yes”. Ingestion of coating material may occur, e.g. because it was gnawed or bitten off during mouthing and, subsequently, swallowed; this is acknowledged in the draft opinion on page 35, line 19: “In addition, some toys may have a layer of paint or other coating, or textile fibre that may easily be scraped or ripped off and swallowed”. Likewise, mouthing of toy’s coatings may occur. However, in the draft opinion it is reasoned that migration of TiO2 embedded in polymers is unlikely. This conclusion seems to be applicable to polymeric coatings in both oral scenarios. Please check and/or provide rationale. p. 35 table 6.11 (entries for dry paint tablets): It is unclear why the potential for oral uptake of TiO2 via direct ingestion of “dry paint tablets” is indicated with “no” whereas the potential exposure via mouthing is indicated with “yes”. If dry paint tablets are put in the mouth, pieces of them will likely break off or the tablet will partly dissolve or disperse in saliva. Thus, (parts of) the toy (i.e. the paint tablet) will be swallowed. In our point of view, this scenario rather falls into the category “direct ingestion” than “mouthing”. Please check and/or provide rationale. p. 35 table 6.11 (entries for paper): It is unclear why the potential for oral exposure to TiO2 via direct ingestion of the toy material “paper” is indicated with “no”. Studies on mouthing behaviour indicate that children frequen mouth objects made from paper and cardboard material (see references [3-6]). This can	Page 35 line 20-21: see answer to comment 47. Text added for explanation: The mouthing may result in scraping or biting on the toy with a possible release of pieces of the toys including the TiO2 pigment, which may result in an indirect exposure. 6,11, Coating: See #47 above. 6,11, dry paint tablets. See #47 above. 6,11, paper. To be added See #47 above. A distinction was made between exposure to freely available TiO2 directly, or indirectly via TiO2 embedded in a matrix (e.g. a polymer, paper etcetera).
Dobel	Shima	Ministry of Environment of Denmark	sdo@mim.dk	Denmark		6.4.2.5 Exposure scenarios –oral	The SCHEER asses that direct ingestion and mouthing mainly occur by children under 3 years. We do agree with SCHEER that children under 3 years are specially vulnerable due to the general exposure. However, children up to approximately 6 years of age is likely to put toys into the mouth. This was also assessed by the SCHEER in the opinion of squishy toys in 2021. Children up to 6 years should therefore be considered in a realistic worst case scenario due to the exposure of TiO2 to achieve a sufficient protection level.	SCHEER agrees with the comment, and has added this possibility in the text. For both exposure scenarios indicated above it should be realised that the exposure will not be limited to children up to three years of age, but also older children might be exposed due to direct ingestion or mouthing.

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.4.2.5 Exposure scenarios –oral	Of the three ways children can be orally exposed to TiO2 in toys, only scenarios for direct ingestion have been presented in the draft opinion. Not further addressing mouthing (as explained in section 6.4.2.6) seems justifiable, if the findings for migration of TiO2 from food contact/packaging materials (showing very low to absent migration potential) can indeed be extrapolated to toys. For indirect ingestion (via the mucocilliary route), however, no argument has been presented in sections 6.4.2.5/6 for not further addressing this route. It is only till section 6.7.3 (at the bottom of p.56) that this is sort of explained (however, without presenting evidence).	Text was added to section 6,4,2,5 indirect ingestion for further explanation. Text added in 6,4,2,5. indirect ingestion Inhalation exposure is expressed as TiO2 air concentration in µg/m3, and, as deposition is a fraction of the exposure dose, lung deposition and entry into the mucociliary escalator will likely be in the µg range as well. In contrast, oral exposure is determined by mg possibly released from the toy product. The contribution of the oral uptake due to the mucociliary escalator transport to the mouth can be considered to be very low to negligible compared to direct oral uptake, and is therefore not further considered in the oral exposure scenarios.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium	6.4.2.6 Exposure modelling-oral	Page 37 line 26: An Ad-Hoc group (led by the German BfR) to the European standardisation Committee dealing with toy chemical safety standards (CEN/TC52/WG5) has recently worked on EN 71-7 related to toxicological risk assessment. Latest draft "concept on exposure estimation" provides a proposal for estimating systemic event exposure to substances due to the repeated use of finger paints. This document (CEN/TC52/WG5 N 1783 - November 2021) can be obtained directly from the secretariat of CEN/TC52. This document indicates "The mandatory use of embittering agents according to standard EN 71-7 on finger paints prevents repeated oral ingestion of finger paints; therefore, oral intake is not considered in systemic exposure due to repeated use of finger paints". It also indicates: "In the introduction of the standard EN 71-7:2014 it is stated that oral exposure to finger paints needs to be considered as well. Therefore, according to requirement 4.6 in EN 71- 7:2014, use of embittering agents is mandatory. A young child might explore the taste of finger paints upon first contact, which could eventually lead to systemic exposure following absorption in the oral mucosa or gastrointestinal tract. However, a child is not expected to try eating finger paint a second time due to the negative experience. Hence, repeated ingestion of finger paints is very unlikely. " On frequency of exposure, this document indicates: "RIVM assumes a use frequency of 100 events per year in its Toys Fact Sheet [RIVM 2002]. This value was supported by the Nordic Exposure Group for Health [Norden 2011] and used by the Danish EPA in its risk assessment of preservatives in toys [DK EPA 2014]. Scott and Moore estimated a use frequency of two times per week [Scott and Moore 2000]." Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly. Page 37 line 28: It shall be noted that white finger paint is uncommon, and most finger paints are primary colours that contain less than 1% TiO2 and rarely up to 4%. Therefore, the exposure assumptions made in the draft Opinion should be revised accordingly. Page 38 line 5	Page 37 line 26: The text has been modified to include the use of an embittering agent in finger paints according to European standard EN 71-7:2014+A3:2020 (CEN, Brussels, Belgium). As the estimations for use are low (18 times per year or less), for the exposure both an acute and subchronic exposure. Text changed accordingly However, the estimated total intake by Van Engelen et al. (2008) does not apply since 2014 as in EN 71-7:2014 an obligation was included to add an embittering agent to finger paints to limit and prevent uptake of finger paint by direct ingestion. It is likely that uptake of finger paint due to direct ingestion will be rather limited, as the bitter taste will result in avoiding oral uptake. More recent estimations for the possible uptake of finder paints containing an embittering agents propose an exposure frequency of 18 times per year for children 2 years of age (CEN/TC 52-WG5 N1682 20201127). SCHEER uses this proposal for estimating the oral exposure to pigmentary TiO2 for children 3.5 to 4.5 years of age. In view of the low frequency, SCHEER estimated both the effects of an acute and subchronic exposure. Single acute event: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, translating into for a 15kg child into a single acute exposure of 8 mg TiO2 per kg. Semi-chronic multiple events: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, 18 events per year results in 2160 mg per year, resulting in 5.9 mg per day, resulting in a dose of 0.39 mg per kg per day. Page 37 line 28: This information provided previously by TIE indicate a TiO2 content up to 30% for finger paint Table 6,11 page 35. The respective scenarios use a worst case approach, based on the information available, which is a conservative approach for risk assessment. Since no information is available on the actual distributions of use (and in addition these are not fixed) the scenario cannot be further refined. The respective scenarios use a worst case approach, based on the information available, which is a conservative approach for risk assessment. Since there is no information is available on the actual distributions of use or TiO2 content the scenario cannot be refined, and there is also no need to do so.

Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany	6.4.2.6 Exposure modelling- oral	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. Aspect 4: Quantity intake pencil 6.4.2.6 Exposure modelling- oral Page 37-38, chapter "White colouring pencils" The opinion assumes that a child ingests 8 mg of a white colouring pencil (4.1 mg twice a day). In a study of a member company, the oral intake of water-soluble colouring pencils was investigated. Intensive licking was simulated by wiping the colouring pencil lead over a cloth. The result was that between 0.5 and 1.5 mg of the lead dissolved. In our opinion, the assumed 8 mg clearly exceeds the realistic intake of colouring pencils by children. Only when biting off the lead larger amounts could be ingested. However, these are not regular events. In addition, the titanium dioxide is bound in a solid matrix from which it does not dissolve directly and thus cannot be absorbed directly. We consider the assumption that a child bites off the pencil twice a day to be unrealistic.	These data were not (and are not) available to SCHEER. It should be realised that for the exposure scenarios worst case scenarios with exaggerated exposures are considered in the risk assessment. When we consider the 1.5 mg of the colouring pencil lead dissolved, and with a content of maximally 51% TiO2 present, the overestimation is approximately tenfold. This can be considered rather realistic for a worst case scenario.
Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany	6.4.2.6 Exposure modelling- oral	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. Aspect 3: Quantity intake finger paints 6.4.2.6 Exposure modelling- oral Page 37, chapter "finger paint" The SCHEER opinion states that children ingest 400 mg of finger paints per event. Accordi to van Engelen et al. (2008), this value is a rough estimate and needs further research. As worst-case scenario it is considered that finger paints are used once a day. This assumption seems unlikely high. Even Van Engelen et al (2008)* stated: "Similar to the ingestion default for dry, brittle, powder-like and pliable materials, an ingestion of 400 mg may occasionally occur, but not daily." From a rational point of view, combining these two estimated values multiplies the error of both. The result can neither present the reality, nor the reasonable worst case. Additionally, finger paints contain bittering substances. According to EN 71-7, a bittering agent must be added to finger paint in order to discourage and minimize the ingestion of paint. Therefore, the assumption of repeated oral intake of finger paints by children is unlikely. * Van Engelen JGM, Park MVDZ, Janssen PJCM, Oomen AG, Brandon EFA, Bouma K, Si AJAM, Van Raaij MTM (2008). Chemicals in Toys. A general methodology for assessment of chemical safety of toys with a focus on elements. RIVM report 320003001/2008, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands. (page 42)	The aspect of the addition of bittering agents to finger paints has been addressed. See #45, #46 and #51 Page 37 line 26: The text has been modified to include the use of an embittering agent in finger paints according to European standard EN 71-7:2014+A3:2020 (CEN, Brussels, Belgium). As the estimations for use are low (18 times per year or less), for the exposure both an acute and subchronic exposure. Text changed accordingly However, the estimated total intake by Van Engelen et al. (2008) does not apply since 2014 as in EN 71-7:2014 an obligation was included to add an embittering agent to finger paints to limit and prevent uptake of finger paint by direct ingestion. It is likely that uptake of finger paint due to direct ingestion will be rather limited, as the bitter taste will result in avoiding oral uptake. More recent estimations for the possible uptake of finder paints containing an embittering agents propose an exposure frequency of 18 times per year for children 2 years of age (CEN/TC 52-WG5 N1682 20201127). SCHEER uses this proposal for estimating the oral exposure to pigmentary TiO2 for children 3.5 to 4.5 years of age. In view of the low frequency, SCHEER estimated both the effects of an acute and subchronic exposure. Single acute event: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, translating into for a 15kg child into a single acute exposure of 8 mg TiO2 per kg. Semi-chronic multiple events: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, 18 events per year results in 2160 mg per year, resulting in 5.9 mg per day, resulting in a dose of 0.39 mg per kg per day.

Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany	6.4.2.6 Exposure modelling-oral	Scenario on white colouring pencils: In the draft opinion, it is assumed that an amount of 8 mg of the product (i.e. the pencil`s core) is ingested per event and that two events per day may occur. Hence, a total of 16 mg product might be ingested per day. In SCHER's final opinion on estimates of the amount of toy materials ingested by children [SCHER concluded the default ingestion amounts of 100 mg/d for dry, brittle, powder-like or pliable toy material, 400 mg/d for liquid or sticky toy material, and 8 mg/d for scraped-off toy material as appropriate. These assumptions form part of the basis on which the element migration limits in Annex II, part III, no. 13 of the Toy Safety Directive were derived. It is acknow-ledged that the SCHER opinion from 2016 elaborates on a rather generic differentiation of three categories of toy materials while in the current draft opinion on TiO2 toys several product specific scenarios are elaborated, providing the possibility to take specific properties of a toy into account (e.g. that only the pencil's tip is available for mouthing/direct ingestion while the most part of the pencils core is enclosed and not directly accessible). However, as a product specific scenario is elaborated in the draft opinion, it is suggested to reconsider the use of the terms "scraped material" (p. 37 line 37) and "scraped off toy material" (p. 38 line 8) in the rationale as its use here seems to differ a little bit from that in the SCHER opinion from 2016 as well as from that in the specifications of the Toy Safety Directive on element migration. Assumption of 15 kg of body weight for a child being 3.5 – 4.5 years old in the white colouring pencil scenario might not be the worst case. According to CEN ISO/TR 8124-8:2016 [8], the suitable starting age for colouring pencils (big and easy to grip) is indicated with 2 years; however, the TR mentions that even children in the age of 8 – 12 months might be able to scribble with colouring pencils. Hence, there is an indication that use of white colouring pencils might occur by children younger than 3.5 – 4.5 years. [7] SCHER (Scientific Committee on Health and Environmental Risks), Final Opinion on estimates of the amount of toy materials ingested by children, 8 April 2016. https://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_170.pdf. [8] Safety of toys - Part 8: Age determination guidelines (ISO/TR 8124-8:2016); German version CEN ISO/TR 8124-8:2016.	The intention is to identify material relased from a toy by mouthing. SCHEER considers "scraped material" and "scraped off material" adequate descriptions. These scraped off materials contain the chemical substance TiO2. The Toy Directive in Annex II, Part III, no 13, indicates the release or leakage of chemicals from the toys. This can be considered similar to the relase of chemicals from food contact materials (FCM). SCHEER considers this a different situation compared to toy material scraped off from a toy. the scraped off material has the same compostion matrix including TiO2 as the toy (pencil) itself. However, the scraped of piece has now a size that it can be ingested by the child.
Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany	6.4.2.6 Exposure modelling-oral	Scenario on finger paint: Assumption of 15 kg of body weight for a child being 3.5 – 4.5 years old in the finger paint scenario might not be the worst case. According to CEN ISO/TR 8124-8:2016 [8], the suitable starting age for finger paints is indicated with 2 years. In the US age determination guidelines [9] it is mentioned for the age group of 12 through 18 months old children that 'Finger painting with washable and non-toxic paint is appropriate at this age.' (p. 210). Furthermore, some individual finger paint products are marketed with a starting age of 1 year (based on information gathered during an online search in August 2021). In summary, there are several indications that use of finger paint might occur by or on children younger than 3.5 – 4.5 years. On the other hand, it might be of note that according to the standard EN 71-7 [10] embitteri agents need to be incorporated into finger paints to prevent (repeated) oral ingestion by sm children. Hence, assuming ingestion of 400 mg finger paint material per event might be unrealistic high. [8] Safety of toys - Part 8: Age determination guidelines (ISO/TR 8124-8:2016); German version CEN ISO/TR 8124-8:2016. [9] U.S. Consumer Product Safety Commission (CPSC): Age Determination Guidelines: Relating Consumer Product Characteristics to the Skills, Play Behaviors, and Interests of Children, 2020, CPSC Staff Document, https://www.cpsc.gov/s3fs-public/Draft%20Research%20Document%20for%20Updating%20Age%20Determination%20Guidelines%20for%20Toys.pdf?0ap6_dYUWpkLn.Bqc.S2qXpJJnr3LI3N [10] Safety of toys - Part 7: Finger paints - Requirements and test methods; German version EN 71-7:2014+A3:2020	The aspect of the addition of embittering agents to finger paints has been addressed, and text has been added accordingly. S #45, #46 and #51. Page 37 line 26: The text has been modified to include the use of an embittering agent in finger paints according to European Standard EN 71-7:2014+A3:2020 (CEN, Brussels, Belgium). As the estimations for use are low (18 times per year or less), for the exposure both an acute and subchronic exposure. Text changed accordingly However, the estimated total intake by Van Engelen et al. (2008) does not apply since 2014 as in EN 71-7:2014 an obligation was included to add an embittering agent to finger paints to limit and prevent uptake of finger paint by direct ingestion. It is likely that uptake of finger paint due to direct ingestion will be rather limited, as the bitter taste will result in avoiding oral uptake. More recent estimations for the possible uptake of finder paints containing an embittering agents propose an exposure frequency of 18 times per year for children 2 years of age (CEN/TC 52-WG5 N1682 20201127). SCHEER uses this proposal for estimating the oral exposure to pigmentary TiO2 for children 3.5 to 4.5 years of age. In view of the low frequency, SCHEER estimated both the effects of an acute and subchronic exposure. Single acute event: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, translating into for a 15kg child into a single acute exposure of 8 mg TiO2 per kg. Semi-chronic multiple events: uptake 400 mg with 30% TiO2 content results in an exposure of 120 mg, 18 events per year results in 2160 mg per year, resulting in 5.9 mg per day, resulting in a dose of 0.39 mg per kg per day.

Dobel	Shima	Ministry of Environment of Denmark	sdo@mim.dk	Denmark		6.4.2.6 Exposure modelling-oral	The assessment of oral exposure of TiO2 from finger paint is made for children of 3.5-4.5 years of age and therefore a bodyweight of 15 kg is used. Finger paint is likely used by children below 3 years and therefore a realistic worst case scenario should also be made for the most vulnerable child which will be children of 1-2 years of age. The exposure scenario TiO2 from finger paint is therefore not sufficiently protecting the smallest children.	See comments #45, #46, #51, and #55 above regarding use of finger paint and European Standard EN 71-7:2014+A3:2020 (CEN, Brussels, Belgium). SCHEER agrees that there is also a foreseeable use in younger children 1 to 2 years of age. Therefore, also a risk assessment exposure calculation was performed for a 10kg child. In addition, also the use of embittering agents in finger paint reduced the oral uptake. The text of the opinion was changed accordingly. Text added: As there is also a foreseeable use of finger paint for children below the age of 3, also an exposure calculation and risk assessment was performed for a child of 10 kg. The single acute event exposure for finger paint is 12 mg/TiO2/ kg bw for a 10 kg child. For the semi-chronic multiple events the dose is 5.9/10 = 0.59 mg tiO2/kg bw/day. This results in a MoS of 1695 for fingerpaint in a 10 kg child.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.5.2. Oral exposure	Page 41 - Line 29: Absorption data in the gastrointestinal tract (GIT) is based on pure particles. This is of limited relevance when evaluating exposure from toy materials such as white pencils as it ignores the matrix effect. Colored pencils are a mixture of clay fillers and approximately 15% paraffin wax which acts as a binder. TiO2 in the pencil will be contained within this homogeneous matrix. In 2000, the US Consumer Products Safety Commission investigated asbestos fibers in wax crayons and concluded that since the wax melts above body temperature the matrix would be intact, and no release of fibers would occur. While the proportion of wax is lower in pencils, the remaining matrix consists of compressed insoluble mineral clays suggesting a low probability of free TiO2 in the GIT.	The TiO2 released from toys is indeed considered to have a particulate nature as TiOs does not dissolve. Also the scraped off materials have a solid nature with the TiO2 embedded in the matrix. SCHEER agrees that there would be a low probability for particle release from these matrices used for toy manufacture. Based on the data available, the SCHEER concludes that the oral uptake is low. Industry did not provide data that allow a more quantitative conclusion regarding coloured pencils.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium		6.5.2.1. Introduction	Page 41 line 29: Absorption data in the GIT is based on pure particles. This is of limited relevance when evaluating exposure from toy materials such as white pencils as it ignores the matrix effect. Coloured pencils are a mixture of clay fillers and approximately 15% paraffin wax which acts as an anti-friction agent (lubricant). TiO2 in the pencil will be contained within this homogeneous matrix. In 2000, the US Consumer Products Safety Commission investigated asbestos fibres in wax crayons and concluded that since the wax melts above body temperature the matrix would be intact, and no release of fibres would occur. While the proportion of wax is lower in pencils, the remaining matrix consists of compressed insoluble mineral clays suggesting a low probability of free TiO2 in the GIT.	The TiO2 released from toys is indeed considered to have a particulate nature as TiO2 does not dissolve. Also the scraped off materials have a solid nature with the TiO2 embedded in the matrix. SCHEER agrees that there would be a low probability for particle release from these matrices used for toy manufacture Based on the data available, the SCHEER concludes that the oral uptake is low. Industry did not provide data that allow a more quantitative conclusion regarding coloured pencils.

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.5.4 Conclusions	p.42, line 40: To have an indication of what is 'relatively low', it would be helpful to present an (approxima percentage for the systemic availability after oral and inhalation exposure. This could then also be added to section 3 on p.14/l.20-21.	Text changed into: Estimations range from less than 0.5% of the exposure dose, (Geraets et al, 2014, Kreyling et al, 2017b, EFSA 2021), to approximately in the order of 0.001% (Health Canada 2022).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6 Toxicological evaluation	Based on the evaluation of toxicokinetic studies, the EFSA 2021 opinion on E171 indicated that steady state would be reached between 1.5 and 5 years. And consequently, that none of the rodent toxicity studies were long enough to cover the time needed to reach steady state. This may have impacted the interpretation of the toxicity study results. Although it is indicated in the SCHEER opinion that TiO2 particles may accumulate, the consequences for the interpretation of toxicity studies requires further attention in section 6.6.	This comment is valid for the oral studies only since inhalatory studies mainly relate to direct local effects (e.g. inflamation). The margin of the exposure in the oral studies also includes the uncertainty in the toxicokinectics of TiO2, including differences in lifespan between laboratory animals and humans.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 3 attached.	Annex 3 provides information on toxicokinetics of various Ti preparations. The information confirms the very low bioavailabilit Ti after oral exposure as already included in the Opinion. SCHEER has cited references from the public available literature accordingly. Bioavailability is also addressed in the Health Canada 2022 report that indicates a bioavailability in the order of 0,001% of the oral dose. Text added for clarification: Geraets et al., (2014) indicated organ levels in only a few of the orally treated animals just above the limit of detection with an overall estimation of 0.02% of the exposure dose recovered in all organs measured. Kreyling et al. (2017b) observed that approximately 0.6% of the administered dose passed the gastro-intestinal-barrier after one hour and about 0.05% were still distributed in the body after 7 days (Kreyling et al. 2017b). . In a recent evaluation by Health Canada (2022) systemic bioavailability after oral exposure was estimated to be in the order of 0.001% of the exposure dose (Health Canada 2022). Text added to conclusions: Estimations range from less than 0.5% of the exposure dose, (Geraets et al, 2014, Kreyling et al, 2017b, EFSA 2021), to approximately in the order of 0.001% (Health Canada 2022).

Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 13 attached.	The Annex 5 Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 12 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in annex 5-part 11 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 10 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized on Annex 5 part 9 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Arnola	Lilaj	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 8 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5-part 7 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 6 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized on Annex 5 - part 5 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 4 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5- part 3 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).

Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex 5 - part 2 attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Our comments on chapter 6.6.3 are summarized in Annex V (part 1) attached.	The Annex 5Part 1-13 contains the content of the Health Canada 2022 report on TiO2. As the Health Canada report was published after finalizing the SCHEER Opinion on TiO2 used as pigment in toys, the report was not considered previously. The Health Canada 2022 report is evaluated and its content where applicable, is now included in this Opinion. Now also included reports from Food Standards Agency UK (2022) and Food Standards Australia/New Zealand (2022).
Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium	6.6.3 Oral hazard of TiO2 pigment	Out comments on chapter 6.6.3 are summarized on Annex III attached.	Annex 3 provides information on toxicokinetics of various Ti preparations. The information confirms the very low bioavailabilit Ti after oral exposure as already included in the Opinion. SCHEER has cited references form the public available literature accordingly. Bioavailability is also addressed in the Health Canada report that indicates a bioavailability in the order of 0,001% of the oral dose. 6.5.2.2 Text added for clarification: Geraets et al., (2014) indicated organ levels in only a few of the orally treated animals just above the limit of detection with an overall estimation of 0.02% of the exposure dose recovered in all organs measured. Kreyling et al. (2017b) observed that approximately 0.6% of the administered dose passed the gastro-intestinal-barrier after one hour and about 0.05% were still distributed in the body after 7 days (Kreyling et al. 2017b). . 6.5.2.2 In a recent evaluation by Health Canada (2022) systemic bioavailability after oral exposure was estimated to be in the order of 0.001% of the exposure dose (Health Canada 2022). 6.5.4 Text added to conclusions: Estimations range from less than 0.5% of the exposure dose, (Geraets et al, 2014, Kreyling et al, 2017b, EFSA 2021), to approximately in the order of 0.001% (Health Canada 2022).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6.3 Oral hazard of TiO2 pigment	General comment: the overview of the oral hazard of TiO2 does not take the type of administration into account, whereas this can greatly affect the study outcome. Dietary studies in rodents showed no adverse effects (2-year bioassay by NCI 1979, Blevins et al. 2019, Warheit et al. 2015) whereas TiO2 dispersed in water given via drinking or oral gavage did induce adverse effect (Urrutia-Ortega et al. 2016, Bettini et al. 2017). Dispersing TiO2 in water vs. mixing with food can change the characteristics of the particles and affect bioavailability and toxicity. Unfortunately, most studies did not measure TiO2 uptake. Is the type of oral exposure from toys comparable to either TiO2 in food or TiO2 in drinking water as tested in the rodent studies? In the EFSA 2021 opinion on E171, uncertainty on the state of agglomeration on the absorption is indicated.	Probably uptake from toys is powder, pieces of toys in saliva. So, mixture of matrix (polymer/wax) and watery salive. 6.5.4 Text added to the conclusion section on toxicokinetics: It should be noted that studies on toxicokinetics usually use highly dispersed TiO2 solutions, that may differ in their exposure compared to TiO2 originating from toys, similar as the difference in exposure to food grade TiO2 with respect to the food composition in which the TiO2 is applied (Health Canada 2022). 6.6.4 text added as well: However, it should be noted that similar to studies on toxicokinetics usually use highly dispersed TiO2 solutions are used for toxicity studies, that may differ in their exposure compared to TiO2 originating from toys, similar as the difference in exposure food grade TiO2 with respect to the food composition in which the TiO2 is applied (Health Canada 2022).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6.5 Carcinogenicity	General comment: what about people/children with an inflammatory bowel disease (IBD)? The paper by Brand et al. 2020 describes the ongoing discussion on the possibility that TiO2 may exacerbate inflammation in patients with IBD (see Hummel et al. 2014, Lomer et al. 2004, Powell et al. 1996, Ruiz et al. 2017, all referenced in Brand et al. 2020).	Although this indeed may be an issue, in general risk assessments do not take into account disease states within the population. Hazard identification is performed in healthy animals. There is also no requirement to do so. 6.6.3.4 text added to show information on this possibility: This effect may have implications for children with diseases, such as was suggested for inflammatory bowel disease (IBD) as discussed in Brand et al. (2020).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6.5.2 Oral exposure	p.49, line1-3: Also in the paper from Braakhuis et al. 2021 an AOP is postulated for oral exposure to TiO2 leading to carcinogenicity. Intestinal uptake is suggested as initiating event. Available data indicate that some of the KE can be induced by TiO2 (intestinal uptake, ROS generation, oxidative stress, inflammation and hyperplasia).	Based on the comment, the text considering AOPs after oral TiO2 exposure has been modified as indicated below: 6.6.5.2 Brand et al. (2020) suggested that some of the key events (KEs) in the postulated AOPs for liver alterations and intestinal tumors can be induced by TiO2 after oral exposure in both rats and mice (e.g., intestinal uptake, ROS generation, oxidative stress, inflammation, and hyperplasia). Braakhuis et al. (2021) also identified a molecular initiating event (MIE), cell uptake, and a number of early KEs after oral TiO2 exposure in a postulated AOP such as ROS generation, oxidative stress and inflammation, although there was insufficient information on later events in the postulated AOP. In addition, more recently, AOPs for possible adverse outcomes were proposed for colorectal cancer, liver injury, reproductive toxicity, cardiac and kidney damage, as well as hematological effects (Rolo et al., 2022). These recents overviews have so far identified the presence of MIEs and KEs that fit the proposed AOPs. However, definitive experimental evidence for the final outcomes (including tumorigenicity) of these proposed AOPs is not yet available. Most of the available evidence supporting the AOPs relate to nanosized TiO2, and the influence of particle size within these AOPs is not known.

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6.5.5 Conclusions on carcinogenicity	p.49, line 39: The WoE for tumour induction in the GIT is in section 6.6.5.5 concluded to be 'absent to weak' (as well as on p.15/l.5 of the draft opinion), but in the section Weight of evidence (6.7.6.4, p.64/l.2) it is considered 'weak'. Please clarify/make consistent.	Changed to absent to weak in Section 6.7.6.4
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 7 attached.	Annex4 Part 1-7 comprise as a whole a report of an expert panel that described the WoE for the genotoxicity of TiO2, that has been recently published: Kirkland, D., Aardema, M.J., Battersby, Rü.V., Beevers, C., Burnett, K., Burzlaff, A., Czich, A., Donner, E.M., Fowler, P., Johnston, H.J., Krug, H.F., Pfuhler, S., Stankowski Jr., , L.F., A weight of evidence review of the genotoxicity of titanium dioxide (TiO_2), Regulatory Toxicology and Pharmacology 136 (2022) 105263. doi: https://doi.org/10.1016/j.yrtph.2022.105263. The SCHEER acknowledges and has evaluated the genotoxicity report submitted as comments during the public consultation. SCHEER noted a number of differences regarding the weight of evidence approach used in the report with the approach used by SCHEER. The main differences are regarding the following approach that was used by SCHEER: - Reliability - Klimisch (1997) giving 5 categories; - Relevance: 3 categories (High, Limited or Low); - More weight was given to study designs including observations confirming that cells were exposed to the nanoparticles. As a consequence, SCHEER included in its evaluation the following aspects: - In vitro micronucleus test - a higher weight was given to studies in which the uptake capability of the selected cell lines was demonstrated. A low weight was given to studies based on cell lines with high background micronuclei frequency (higher than 2%). - In vitro comet assay - the endpoint was included in WoE. - A lower relevance was given to studies performed using only excessively high concentrations i.e. higher than 100 µg/ml (because of aggregation/agglomeration and precipitation of the tested nanoparticles at high concentration). - Other genetic endpoints (direct DNA binding, phosphorylated form of H2AX, SCE, UDS etc.) were given a lower relevance however they were analysed. - The Ames test was not included in WoE evaluation. Considering these differences in evalution criteria of available data, differences in selection and scoring of particular studies, it is to be expected that there will be differences in the overall weight of evidence assessment. SCHEER acknowledges **lack of gene mutations induced by TiO_2** reported in the literature. However, in contrast to the conclusion by Kirkland et al (2022), SCHEER concluded in its assessment that **DNA damaging genotoxic activity** was demonstrated in several experimental studies for both ultrafine and non-ultrafine TiO2 forms. The text in the conclusions was modified to include the reference of Kirkland et al. 2022. "A gene mutation effect was not demonstrated although a genotoxic effect based on DNA damage by TiO2 in both ultrafine and non-ultrafine forms was demonstrated in several in vitro or in vivo studies. In a weight of evidence approach Kirkland et al., (2022) concluded that TiO2 did not have a direct mutagenic effect, while DNA damaging effects were excluded based on non-specific (secondary) effects like high cytotoxicity, and oxidative stress. More robust in vitro and in vivo genotoxicity studies were considered to be needed for definitive conclusions (Kirkland et al., 2022). SCHEER in this Opinion and previously by Elespuru et al., (2018) many studies were noted that did not meet a number of quality criteria for a valid test (Elespuru et al., 2018). Therefore, there exists uncertainty in the outcomes of these studies."
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 6 attached.	
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 5 attached.	
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 4 attached.	

Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 3 attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 2 attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized in Annex 4 - part 1 attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported in Annex IV (part 7) attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported in Annex 4 (part 6) attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported on Annex IV (part 5) attached.

Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported in Annex IV (part 4) attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported in Annex IV (part 3) attached.
Lilaj	Arnola	TDMA	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are reported in Annex IV (part 2) attached.
Lilaj	Arnola	Titanium Dioxide Manufacturers Association (TDMA)	ali@cefic.be	Belgium	6.6.6 Mutagenicity / genotoxicity	Our comments on chapter 6.6.6 are summarized on Annex 4 (part 1) attached.

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.6.6 Mutagenicity / genotoxicity	The paper by Elespuru et al. 2018 (https://doi.org/10.1093/toxsci/kfy100) is missing here. This paper gives a clear overview of what is needed for reliable genotoxicity testing of nanomaterials. Available studies are contradicting, probably because they differed in exposure route, concentration, duration and type of genotoxicity assay used. Also, internal distribution and/or cellular uptake has rarely been reported. There is a need for optimized and harmonized genotoxicity assays for testing nanomaterials (Elespuru et al. 2018). Taken together, the reliability of available genotoxicity testing is questionable.	SCHEER agrees on the uncertainties regarding genotoxicity results for TiO2 when certain quality criteria for genotoxicity testing are not met. The text on the Conclusions in 6.6.6.6 was modified accordingly: "However, there are also studies which were noted not to meet a number of criteria to a valid test (Elespuru et al., 2018). Therefore, there exists uncertainty in the outcomes of these studies". The text in the conclusions was modified to include the reference of Kirkland et al. 2022. "A gene mutation effect was not demonstrated although a genotoxic effect based on DNA damage by TiO2 in both ultrafine and non-ultrafine forms was demonstrated in several in vitro or in vivo studies. In a weight of evidence approach Kirkland et al., (2022) concluded that TiO2 did not have a direct mutagenic effect, while DNA damaging effects were excluded based on non-specific (secondary) effects like high cytotoxicity, and oxidative stress. More robust in vitro and in vivo genotoxicity studies were considered to be needed for definitive conclusions (Kirkland et al., 2022). SCHEER in this Opinion and previously by Elespuru et al., (2018) many studies were noted that did not meet a number of quality criteria for a valid test (Elespuru et al., 2018). Therefore, there exists uncertainty in the outcomes of these studies."
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	6.7.2. Previous risk assessments of TiO2	Page 54, lines 6-20 We would like to draw your attention to the fact that the Bermudez study was on a specific ‘catalytic’ grade of ultrafine TiO2 (P25), used for photocatalysis and UV filter applications. The nature and composition of this grade is entirely different and distinct from the grades and composition of TiO2 used to manufacture fingerpaints and powder paints, and thus its relevance to the current study should be questioned.	The toxicity studies available indeed sometimes use a particle size that will be different from the particles sizes of the TiO2 pigment used in toys. To allow a more accurate and **less worst case** risk assessment and increase the WoE, the SCHEER needs more information on the particles sizes of TiO2 as used in toys as well as toxicity studies with pigmentary TiO2 preparations with more relevant particle sizes.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium	6.7.3 Exposure assessment	Page 57 line 2: Aggregated exposure was considered for the three oral exposure scenarios. The above represents a daily direct ingestion of 400 mg of finger paint, 2x 8mg for white coloured pencil and 2 mg of lipstick. It is difficult to understand why aggregated exposure was retained. Taking into consideration the fact that finger paints must contain an embittering agent and the unlikely repeated oral exposure (see above comment for pages 35 and 37) a that lipsticks should not be considered (also considering the SCCS opinion for cosmetics), only the exposure from white colouring pencil (8mg per day – see comment for page 38) should be considered. Therefore, the exposure assumptions made in the draft Opinion sho be revised accordingly.	SCHEER agrees with the comments on the embittering agent that needs to be included in finger paints based on standard CEN 71-7. At appropriate location the text of the Opinion has been modified and the use of the embittering agents is now included in the Opinion. Accordingly, the exposure scenario for finger paints was modified. Also, the aggregated exposure was changed with new data for the exposure of TiO2 present in finger paints. SCHEER included also the possibility for oral uptake as SCHEER considers the lip-gloss/lipstick exposure scenario for this product sold as toys for childeren.
Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany	6.7.3 Exposure assessment	EWIMA (European Writing Instruments Manufacturer’s Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. Aspect 5: Aggregated exposure in case of oral ingestion 6.7.3 Exposure assessment Page 56, Table 6.13 The opinion assumes daily aggregated exposure from finger paints, white colouring pencils and lipstick. We consider this assumption to be very critical. On the one hand, the assumed events per day are very high (SCHEER opinion: finger paints 1x daily, white crayons 2x daily vs. Van Eeghen et. al (2008)* : Finger paints 1x per week, crayons 1x daily). Secondly, it is very unlikely that all these events occur at once. In our view, oral exposure to titanium dioxide from toys is overestimated. * Van Engelen JGM, Park MVDZ, Janssen PJCM, Oomen AG, Brandon EFA, Bouma K, Si AJAM, Van Raaij MTM (2008). Chemicals in Toys. A general methodology for assessment of chemical safety of toys with a focus on elements. RIVM report 320003001/2008, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands.	Based on the comments received, SCHEER has modified the exposure to finger paints and, consequently, also the aggregated exposure was changed (see comment #96). SCHEER agrees with the comments on the embittering agent that needs to be included in finger paints based on standard CEN 71-7. At appropriate location the text of the Opinion has been modified and the use of the embittering agents is now included in the Opinion. Accordingly, the exposure scenario for finger paints was modified. Also, the aggregated exposure was changed with new data for the exposure of TiO2 present in finger paints. SCHEER included also the possibility for oral uptake as SCHEER considers the lip-gloss/lipstick exposure scenario for this product sold as toys for childeren.

Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany		6.7.3 Exposure assessment	EWIMA (European Writing Instruments Manufacturer's Association) is a specialized industry and employers´ association. The association represents the interests of the most important manufacturers and suppliers of products of writing, drawing and creative design in form and colour. EWIMA is thankful for the opportunity to comment on the SCHEER preliminary opinion. 6.7.3 Exposure assessment, Page 56, lines 1-2 In the exposure assessment on which the safety assessment is based, it is assumed that white colouring pencils contain up to 51 % titanium dioxide. There are indeed individual products that have a very high titanium dioxide content of 33 or 51 %. However, the majority of white colouring pencils contain significantly less titanium dioxide (usually below 25 %). We would therefore suggest that an exposure study should be performed with colouring pencils containing the most usual amount of titanium dioxide. Otherwise, the safety assessment could lead to a group of safe toys being considered unsafe due to isolated products containing higher amounts of titanium dioxide.	SCHEER uses a worst case scenarion. So, if there are products on the market with 51% pigment content of TiO2, this is included in the worst case scenario. Coulored pencils have been considered safe even on the basis of this worst case scenario. Therefore, no refinement is need For a refinement as proposed here, more data would need to be provided on the frequency of use of different kinds of pencils.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.7.3 Exposure assessment	Page 57 - Line 2: Aggregated exposure was considered for the three oral exposure scenarios. The above represents a daily direct ingestion of 400 mg of finger paint, 2x 8mg for white colored pencil and 2 mg of lipstick. It is difficult to understand why aggregated exposure was retained. Taking into consideration the fact that finger paints must contain an embittering agent and the unlikely repeated oral exposure (see above comment for pages 35 and 37) that lipsticks should not be considered (also considering the SCCS opinion for cosmetics), only the exposure from white coloring pencil (8mg per day – see comment for page 38) should be considered. Therefore, the exposure assumptions made in the draft Opinion sho be revised accordingly.	Based on the comments received, SCHEER has modified the exposure to finger paints and, consequently, also the aggregated exposure was changed (see comment #96). SCHEER agrees with the comments on the embittering agent that needs to be included in finger paints based on standard CEN 71-7. At appropriate location the text of the Opinion has been modified and the use of the embittering agents is now included in the Opinion. Accordingly, the exposure scenario for finger paints was modified. Also, the aggregated exposure was changed with new data for the exposure of TiO2 present in finger paints. SCHEER included also the possibility for oral uptake as SCHEER considers the lip-gloss/lipstick exposure scenario for this product sold as toys for childeren.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands		6.7.3 Exposure assessment	p.56, line 30-31 / p.57, line 1-2: An aggregated oral exposure including the mucociliary route has not been considered for the reason that inhalation exposure, in general, is orders of magnitude lower than the oral exposure and consequently, that oral exposure due to the mucociliary escalator is negligible. Whereas that might be the case, it is noted that no evidence is presented to show that indeed inhalation exposure is orders of magnitude lower for the inhalation and oral scenarios at hand. Please elaborate on how this was established and how the comparison was made (on mg/kg bw basis?).	In general, the inhalation exposure is in the order of microgram/m3.air with deposition fraction in the airways and the lung of approximatelly 10% (0.1). The oral exposure is in the order of milligrams. Therefore, the contributions of the inhalation exposure to the aggregated oral exposure was not included (see table 6.12 and 6.13). 6.4.2.5 Text added Inhalation exposure is expressed as TiO2 air concentration in µg/m3, and, as deposition is a fraction of the exposure dose, lung deposition and entry into the mucociliary escalator will likely be in the µg range as well. In contrast, oral exposure is determined by mg possibly released from the toy product. The contribution of the oral uptake due to the mucociliary escalator transport to the mouth can be considered to be very low to negligible compared to direct oral uptake, and is therefore not further considered in the oral exposure scenarios.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium		6.7.4.2 PoD for inhalation	Page 57 line 30: Since toys that contain TiO2 are predominantly mixtures where agglomeration is highly plausible, we would question why the NOAEC of 0.5mg/m3 is used as the POD. Evidence shows that for cosmetics containing nanomaterials 'a user would be exposed to nanomaterial predominantly through nanoparticle-containing agglomerates larger than the 1–100-nm aerosol fraction' and 'Predominant deposition of nanomaterial(s) will occur in the tracheobronchial and head airways—not in the alveolar region as would be expected based on the size of primary nanoparticles.' (Potential for Inhalation Exposure to Engineered Nanoparticles from Nanotechnology-Based Cosmetic Powders, Nazerenko et al; (2012); Environmental Health Perspectives; 120; 6; pp885-892. The NOAEC for fine particles is therefore the most appropriate POD.	The information provided to SCHEER indicates that there is no nanofraction present in the TiO2 used as whitening pigment in toys. However, the data provided are limited. Therefore, SCHEER points at the uncertainty regarding the presence of nanoparticles in the TiO2 in toys. The SCHEER, therefore, assessed the risks based on NOAECs for both the nanofraction (1 mg/m3) and the fine fraction (10 mg/m3). A clear statement is made by SCHEER that when the absence of an NP fraction can be demonstarted the use of pigmentary TiO2 in toys is safe for all applications.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.7.4.2 PoD for inhalation	Page 57 - Line 30: Since toys that contain TiO2 are predominantly mixtures where agglomeration is highly plausible, we would question why the NOAEC of 0.5mg/m3 is used as the POD. Evidence shows that for cosmetics containing nanomaterials 'a user would be exposed to nanomaterial predominantly through nanoparticle-containing agglomerates larger than the 1–100-nm aerosol fraction' and 'Predominant deposition of nanomaterial(s) will occur in the tracheobronchial and head airways—not in the alveolar region as would be expected based on the size of primary nanoparticles.' (Potential for Inhalation Exposure to Engineered Nanoparticles from Nanotechnology-Based Cosmetic Powders, Nazerenko et al; (2012); Environmental Health Perspectives; 120; 6; pp885-892. The NOAEC for fine particles is therefore the most appropriate POD.	The information provided to SCHEER indicates that there is no nanofraction present in the TiO2 used as whitening pigment in toys. However, the data provided are limited. Therefore, SCHEER points at the uncertainty regarding the presence of nanoparticles in the TiO2 in toys. The SCHEER, therefore, assessed the risks based on NOAECs for both the nanofraction (1 mg/m3) and the fine fraction (10 mg/m3). A clear statement is made by SCHEER that when the absence of an NP fraction can be demonstarted the use of pigmentary TiO2 in toys is safe for all applications.

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.4.2 PoD for inhalation	The choice for PoDs of 0.5 and 10 mg/m3 and a threshold approach is supported, given that the AOP suggested for the induction of lung tumours points to a threshold for toxicity. It is acknowledged that also for the inhalation route there might be a potential risk for genotoxic but whether that will affect the threshold approach followed is not certain. NB: Such an acknowledgement is also present in section 6.7.7 of the draft opinion (p.64/l.33-35), but there it says 'the non-threshold approach followed'. This is a mistake, as the approach followed by SCHEER was threshold-based.	Thank you, mistake corrected.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.4.3 PoD for oral exposure	In section 6.7.4.3, the WoE for the oral hazard identification is concluded to be 'uncertain' due to uncertainties regarding potential immunotoxic, genotoxic and carcinogenic (and neurotoxic?, according to EFSA 2021) effects. In that respect, it is questionable whether it is appropriate to take as PoD for oral risk assessment a NOAEL for another endpoint (general toxicity, NOAEL of 1000 mg/kg bw/d) and to apply a threshold approach, as was done by SCHEER. The MOS calculations based on this PoD (in sections 6.7.6.2 and 6.7.6.3) may be given for illustrative purposes only, to have an indication in what range the MOSs would be in case the NOAELs for effects other than general toxicity are in the same order of magnitude and in case SCHEER's assumption that the AOP also for the oral route points to a threshold for toxicity (p.15/l.5-7) is correct. It is noted though that, according to the EFSA 2021 opinio on E171, the indications for immunotoxicity, inflammation as well as neurotoxicity occur at levels considerably below 1000 mg/kg bw/d.	It may be that the NOAEL for other toxicities may be lower than for the general toxicity of TiO2. However, as it is stated there is considerable uncertainty on these effects. This uncertainty goes both ways i.e. is there an effect or is there no effect. 6.7.4.3 Text added: For possible effects of TiO2 as E171 at lower doses, such as indications for immunotoxicity, inflammation as well as neurotoxicity, uncertainties were noted (EFSA 2021).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.5 Human Equivalent Concentrations (HEC)	- The exposure regimen for rats in the inhalation study (6h/d, 5d/wk) is different from that for humans (24h/d, 7d/wk). Given that the DAF is based on a comparison of deposition rates (and alveolar surface area) between rats and humans, the difference between 5 and 7 d/wk should be corrected for. Hence, the deposition rate calculated for rats based on the NOAEC of 0.5 mg/m3 (Table A-VI.1) is not 0.0043 m3/d, but 0.0031 m3/d, as also calculated in note (1) under that table (although there mistakenly the factor 5/7 was omitted in the formula). This correction will lower the calculated HECs by 5/7. - By assuming C x t = constant, time-adjusted HECs have been calculated for 10 and 60 minutes exposure duration. Whereas the 10 min HEC fits the inhalation exposure scenario and 4, it is not clear why for exposure scenarios 2 and 3 (45 min duration) 60 min HECs have been calculated instead of 45 min HECs. This should be corrected, resulting in 1.33-fold higher HECs. The two comments above also apply to Annex VI.	Thank you for the comment. Based on the comments, the figures were recalculated.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.6.1 Inhalation	p.61, line 1-11: The conclusions as to which inhalation scenarios show safe use (MOS > 25) or not (MOS < 25) are supported. It is noted that, although the actual MOS-values will change when making the appropriate corrections (x 5/7, for the difference between rat (5d/wk) and human exposure (7d/wk), and from 60 min HECs to 45 min HECs for scenarios 2 and 3), this will not affect the conclusions as to which scenarios show safe use, with the exception of the powder paint scenario without clearance in Table 6.18: correction will put the MOSs (now 27-29 and thus already of borderline concern) under 25.	The figures are corrected according to the comment above (comment 105).

Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.6.2 Oral exposure	Please see our comment on section 6.7.4.3, which also applies to sections 6.7.6.2 and 6.7.6.3.	It may be that the NOAEL for other toxicities may be lower than for the general toxicity of TiO2. However, as it is stated there is considerable uncertainty on these effects. This uncertainty goes both ways i.e. is there an effect or is there no effect. 6,7,4,3 Text added: For possible effects of TiO2 as E171 at lower doses, such as indications for immunotoxicity, inflammation as well as neurotoxicity, uncertainties were noted (EFSA 2021).
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.6.3 Aggregated exposure to TiO2 in different toys	Please see our comment on section 6.7.4.3, which also applies to sections 6.7.6.2 and 6.7.6.3.	It may be that the NOAEL for other toxicities may be lower than for the general toxicity of TiO2. However, as it is stated there is considerable uncertainty on these effects. This uncertainty goes both ways i.e. is there an effect or is there no effect. 6,7,4,3 Text added: For possible effects of TiO2 as E171 at lower doses, such as indications for immunotoxicity, inflammation as well as neurotoxicity, uncertainties were noted (EFSA 2021).

Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium		6.7.7 Final Conclusions	Page 66 line 5 and table 6.24: SCHEER indicates that it cannot be concluded that the described toy materials can be used safely by children. Impossibility to conclude on safe use should not lead to an opposite conclusion saying "not safe" as unsafe use does not appear to have been demonstrated. On 20 June 2022, Health Canada published a comprehensive report on the State of the Science of Titanium Dioxide (TiO) as a Food Additive, taking into account recent studies since the EFSA Opinion, and concluded that there was no evidence of adverse effects and did not identify any health concerns for the use of TiO We recommend SCHEER to take this report into consideration to revise the current SCHEER preliminary opinion. The report can be obtained from: https://www.canada.ca/en/health-canada/services/food-nutrition/reports-publications/titanium-dioxide-food-additive-science-report.html In addition, The European Commission issued a new mandate to SCCS to re-assess the safety of TiO2 with focus on genotoxicity and exposure via the inhalation and oral route (lip care, lipstick, toothpaste, loose powder, hair spray). https://health.ec.europa.eu/system/files/2022-06/sccs2022_q_007.pdf We are of the opinion that SCHEER should wait for the SCCS conclusions and take them into consideration prior to issue a final opinion on the use of TiO2 in toys. General comments to chapter 6.7.7 final conclusions, pages 64 to 66: The European Commission's mandate asked SCHEER to assess the use of TiO2 in toys in light of the inhalation exposure identified, and in light of the classification of titanium dioxide as carcinogenic category 2 after inhalation. It also required that safe toys and safe materials should be indicated. The Toy Safety Directive indicates that, when substances and mixtures classified as CMR by the CLP Regulation (EC) No 1272/2008 are contained in individual concentrations exceeding the CLP thresholds for their classification (1% for TiO2), a decision in accordance with Article 46(3) can be taken to permit a substance and its use via TSD Appendix A. The SCHEER preliminary opinion should make it clearer in its conclusion that it refers to the use/presence of CLP classified TiO2 in concentration exceeding 1% in toy materials. It	Valid point. The text in Table 6.24 has changed regarding the conclusion on ultrafine particles into: "safe use not determined conclusively". Regarding the genotoxicity of fine TiO2 particles, the Opinion was changed after an extensive reevaluation of the available literature. Regarding the hazard characterisation, some uncertainties remain. SCHEER is of the opinion that the lower particle sizes results in an increase in uncertainty of hazadous effects. However, a cut off point regarding size as a threshold for a possible hazardous effects could not be established. However, providing the absence of an ultrafine fraction can be demonstrated by an appropriate metodology, the use of fine pigmentary TiO2 resulting in possible oral exposure is considered safe. The SCHEER answers the current mandate to the knowledge at this point in time. SCCS is involved in this Opinion. The exposure scenarios related to toys are distinct from the exposure scenarios to be considered by SCCS. Comment on 6.7.7. Seeanswer 1 in the Opinion (page 13, lines 5-14): For these products, a specific risk assessment needs to be performed in view of the classification of TiO2 particles as carcinogen category 2 by inhalation with a limitation to respirable TiO2 particles.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	6.7.7 Final Conclusions	Page 66 - Lines 6, 7, and table 6.24: SCHEER indicates that it cannot be concluded that the described toy materials can be used safely by children. Not being able to conclusively determine that a use is safe is not logically equivalent to the converse conclusion that the use is "not safe", as convincing evidence of unsafe use does not appear to have been demonstrated. On 20 June 2022, Health Canada published a comprehensive report on the State of the Science of Titanium Dioxide (TiO) as a Food Additive (https://www.canada.ca/en/health-canada/services/food-nutrition/reports-publications/titanium-dioxide-food-additive-science-report.html), considering recent studies since the EFSA Opinion, and concluded that there was no evidence of adverse effects and did not identify any health concerns for the use of TiO_2.We recommend SCHEER to take this report into consideration to revise the current SCHEER preliminary opinion. In addition, The European Commission issued a new mandate to SCCS to re-assess the safety of TiO2 with focus on genotoxicity and exposure via the inhalation and oral route (lip care, lipstick, toothpaste, loose powder, hair spray). https://health.ec.europa.eu/system/files/2022-06/sccs2022_q_007.pdf We are of the opinion that SCHEER should wait for the SCCS conclusions and take them into consideration prior to issue a final opinion on the use of TiO2 in toys.	Valid point. The text in Table 6.24 has changed to: safe use not determined conclusively.
Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium		6.7.7 Final Conclusions	Page 64, lines 27-29 The final decision by ECHA's RAC Committee, and the subsequent harmonized classification of TiO2 as a category 2 carcinogen in the 14th ATP, clearly established the boundary for such as a classification relating to the content of particles with an aerodynamic diameter of 10 µm. Note 10 as part of the entry into CLP's Annex VI specifies that the classification as a category 2 carcinogen by inhalation only applies when the product in question contains 1% or more of such particles. For inhalation toxicity, one would need to get lung overload by chronic exposure to create the lung inflammatory effects that have been observed in rats only. We would strongly question whether this is even remotely feasible from children using Artists Colours products. There appears, however, to be much more of a focus within this Opinion on the content of ultrafine particles, rather than on whether the TiO2 grades used for the manufacture of toys and related products meet the requirements for category 2 carcinogen classification (by inhalation) or not. We would suggest that the latter should take much more prominence in the document, as ultimately this Opinion forms the basis for the decision as to whether a derogation under the TSD due to the presence of a category 2 CMR should be granted or not. Repeated references to ultrafine content are therefore confusing the situation. With regard to comments on genotoxicity effects relating to TiO2, we reiterate our previous comment that there are still studies underway to prove or disprove this, and thus the conclusions relating to possible effects due to oral exposure should be framed in this conte	The provided information regarding the size distribution of the pigmentary TiO2 used is toys is limited. Therefore SCHEER cannot exclude definitively the presence of a nanofraction in the pigmentary TiO2, as this was also observed for the pigmentary TiO2 (E171) used in food. The SCHEER furthermore argues that it is possible that toys contain TiO2 with an aerodynamic diamer of ≤ 10 um in a percentage above 1%. So, the SCHEER determined the risk for such products and it appeared that the content of ultrafine particles determines the risk. It is not clear why this is confusing, but the SCHEER has addressed this in the Opinion. Regarding the oral exposure and genotoxicity, now also the more recent reports of UK FSA committees, Health Canada and Food Standards Australia/New Zealand has been included in the Opinion. The classification in the CLP regulation indicates TiO2 independent whether this is a nanoform or large pigmentary form of TiO2.

Dobel	Shima	Ministry of Environment of Denmark	sdo@mim.dk	Denmark	6.7.7 Final Conclusions	Overall, the Ministry of Environment of Denmark agrees with the risk assessments made by SCHEER beside the remarks mentioned under the section on exposure scenario.	Thank you
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	6.7.7 Final Conclusions	In section 6.7.7, as well as in section 3 (p.15/l.47-48), it is concluded that for scenario 3 (white colour pencil) the WoE for particle size distribution of the TiO2 pigment used is 'wea It is not clear on what data that conclusion is based. Please clarify.	The information provided to SCHEER on the size distribution provided on the TiO2 pigment used in , is limited to two preparations from two manufacturers, whereas data in the literature were found. This affects the WoE and results in a weak WoE. See also under the paragraph on size distribution on Page 13 lines 16 - 26. During the public consultation for one TiO2 pigments, additional data on the size distribution was provided. This information has now been included in the Opinion. In the answer to Question 1 of the mandate text was added considereing additional information submitted at the public consultation period: Also for one product information was submitted indicating a size ranging from 0.2 µm to 4 µm. 6.2.9 section on Particle size and distribution The following thext was added: At the public consultation additional information was provided on Ti-Pure™ Titanium Dioxide Pigment (MSDS provided by Chemours) with an overall size between 0.2 µm – 4 µm, with a d(0.1): 0.274 µm, d(0.16) 0.32 µm, d(0.5) 0.541 µm, d(0.84) 0.96 µm, and d(0.9) 1.151 µm. The measurement range was 0.00% at 0.126 µm and 0.05% at 0.141 µm for the lower end, and 0.01% at 39.8 µm and 0.00%. at 44.6 µm at the high end.
Detcheverry	Mathilde	AVICENN	detcheverry.avicenn@gmail.com	France	ABSTRACT	Considering scientific publications compiled on our website https://veillenanos.fr/dossier/risques/risques-specifiques/risques-nanoparticules-tio2, AVICENN supports both statements: - Regarding inhalation exposure : "if an ultrafine fraction is assumed to be present, safe use is not indicated for the use of casting kits, chalk and powder paints" - Regarding oral exposure : "it cannot be concluded that finger paint, white colour pencil and lipstick/lip gloss can be used safely by children"	Thank you for your support
Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany	Annex I: Toys Industry data on release and content	For better traceability of the opinion and the calculation, it would be beneficial to know some more details of the analytics underlying the measured data on titan dioxide air concentrations. Therefore, SCHEER is kindly asked to consider whether the following information could be added: -Procedure of the sample preparation -Analytical method or analytical principle -Details on quality assurance such as blind values	The tests reports were made available to SCHEER. The test were performed by a certified test laboratory using both European and national recognised standards. The testing reports were evaluated by the SCHEER and considered to be reliable.

Dr. Lorenz	Kristin	German Federal Institute for Risk Assessment (BfR)	Kristin.lorenz@bfr.bund.de	Germany	Annex II: Formulas for the inhalation exposure scenario (evaporation)	Annex II elaborated on calculation formulas for inhalation exposure scenarios where evaporation needs to be considered. However, evaporation is not relevant for TiO2. Additionally, it seems that Annex II was not referenced in the main text of the draft opinion. Thus, Annex II can possibly be deleted.	SCHEER agrees with the comment and Annex II has now been deleted.
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands	Annex III: Calculation of scenario air concentrations	For the sake of transparency and completeness, please also present a table for the realistic high air concentrations.	The realistic high air and upper bound concentrations are presented in table 6.10 for exposure scenario 1 and 4. For convenience of the reader and further explanation, the parameters for the calculation of these values for the upper bound exposure are presented in Annex III.

Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	Annex VI: Calculation of the Human Equivalent Concentration (HEC)	Page 105 - Line 3: The Bermudez (2004) study is not included in the references.	Thank you. This reference has been added.	
Pronk	Marja	On behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands		Annex VI: Calculation of the Human Equivalent Concentration (HEC)	Please see our comments on section 6.7.5, which also apply to Annex VI. Additional comments: - For the sake of transparency and completeness, please also present: 1) tables with the calculations for the deposition rates and HECs belonging to the NOAEC of 10 mg/m3, similar to Tables A-VI.1 and A-VI.3 for the NOAEC of 0.5 mg/m3; 2) tables with MOS calculations for the upper bound exposures, similar to Tables A-VI.4-7 for the realistic high exposures. - In the box presented on p. 107, the correction factor for clearance is 6.7, not 6. - In Table A-VI.5 there seems to be a mistake in the MOS presented for 6-yr olds for scenario 3: the MOS should be around 100, not around 1000.	The tables as presented on the HECs in Annex VI are provided as additional information for the convenience of the reader about the origin of the data used in the calculations. SCHEER provided this information in order to illustrate the approach used for the risk assessment in this Opinion. The figure in the text box was corrected to 6.7. The figure in Table A-VI.5 was corrected to 99.5.	
Currier	Laura	EWIMA	laura.currier@ewima-isz.de	Germany		ASSESSMENT	With our previous contributions, we have commented on the different chapters individually. Finally, we would like to provide you with a pdf summarising the EWIMA comments.	SCHEER thanks EWIMA for the provided information on the CLP classification (Annex I) and the size distribution (Annex II). Both Annexes contain a MSDS sheet (provided by Chemours) with information on Ti-Pure™ Titanium Dioxide Pigment. In addition, Annex II contains measurement data that are now included in the section "Particle size and distribution".	

Pronk	Marja	on behalf of RIVM (Nat. Institute for Public Health and the Environment), The Netherlands	marja.pronk@rivm.nl	Netherlands		ASSESSMENT	- Health Canada recently completed a “state of the science” report on titanium dioxide (TiO2) as a food additive (Titanium dioxide (TiO2) as a food additive: Current science report - Canada.ca). In contrast to EFSA 2021, Health Canada’s position is that there is no conclusive scientific evidence that the food additive TiO2 is a concern for human health. It is important to cover this opposite position as well in the SCHEER opinion, because it may potentially affect the oral risk assessment, depending on how SCHEER weighs it against EFSA’s position. - ‘Constituent particles' is the preferred term over ‘primary particles’. - The term ‘particle’ is sometimes used for aggregate/agglomerate and sometimes for constituent particle or aerodynamic diameter. A consistency check and description of the term could provide clarity.	Reports of the UK FSA committees, Health Canada report and from Food Stanrads Australia/New Zealand were included in the Opinion. The text has been modified and the word "primary"was replaced by "constituent" where appropriate.
Geurdes	Han	GDS applied mathematics bv	han.geurdes@gmail.com	Netherlands		ASSESSMENT	My comments are directed to physical and chemical effects of titanium dioxide. It affects the chemical section of the SHEER document. However, I have written it as a response to the complete document as far as I thought relevant to what I would like to say. I employed the format of the SHEER document but with a scientific letter to the editor in mind.	We thank Dr. Geurdes for his comments regarding a possible interaction of TiO2 with the citric acid cycle. As was stated in the comments, for the moment this was a theorectical hypothesis. Also, in its literature evaluation, SCHEER did not find indications on this potential interaction. Therefore, the Opinion was not changed to include this possible activity of TiO2.
Billeret	Dominique	Toy industries of Europe	dominique.billeret@toyindustries.eu	Belgium		RECOMMENDATIONS FOR FUTURE WORK	Page 66 line 16: TIE would agree that more data is required. The exposure assumptions in the SCHEER draft opinion for air concentrations of TiO2 seem far in excess of the measured room air concentration in the SCCS Opinion on cosmetics which was 14ug/m3 (15 min TWA).	The SCHEER has used the release data for TiO2 as provided by TIE in the various study reports. SCHEER considers these reports data very reliable. Differences with data as used by the SCCS might be attributed to the different products evaluated.
Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	RECOMMENDATIONS FOR FUTURE WORK	Page 66 - Line 16: TA would agree that more data is required. The exposure assumptions in the SCHEER draft opinion for air concentrations of TiO2 seem far more than the measured room air concentration in the SCCS Opinion on cosmetics which was 14ug/m3 (15 min TWA).	The SCHEER has used the release data for TiO2 as provided by TIE in the various study reports. SCHEER considers these reports data very reliable. Differences with data as used by the SCCS might be attributed to the different products evaluated.

Fielding	Trevor	CEPE EuACA	t.fielding@cepe.org	Belgium	RECOMMENDATIONS FOR FUTURE WORK	Page 66, lines 12-17 As per our earlier comment, repeated mention of the ultrafine content confuses the issue. This is not the basis as to whether TiO2 is classified as a category 2 carcinogen or not, and we would recommend including reference to Note 10 in the Annex VI entry for TiO2 in the final Recommendations section. Our industry supports and welcomes the recommendation with regard to further migration studies, and studies on TiO2 release from toys and/or toy materials.	The classification in the CLP regulation indicates TiO2 independent whether this is a nanoform or large pigmentary form of TiO2. As the data on particle size distribution for the pigmentary TiO2 used in toys is rather limited, the presence of a nanofraction though unlikel, could not be excluded. Therefore SCHEER also evaluated the potentials risks associated with exposure from nanoparticles.
Billeret	Dominique	Toy Industries of Europe	dominique.billeret@toyindustries.eu	Belgium	REFERENCES	Page 67 line 39: The Bermudez (2004) study is not included in the references. (but mentioned on page 105 line 5	The reference has been added.

Kaufman	Alan	The Toy Association	akaufman@toyassociation.org	Other	United States of America	REFERENCES	Page 67 - Line 39: General Comments - The European Commission's mandate asked SCHEER to assess the use of TiO2 in toys in light of the inhalation exposure identified, and in light of the classification of titanium dioxide as carcinogenic category 2 after inhalation. It also required that safe toys and safe materials should be indicated. The Toy Safety Directive indicates that, when substances and mixtures classified as CMR by the CLP Regulation (EC) No 1272/2008 are contained in individual concentrations exceeding the CLP thresholds for their classification (1% for TiO2 of specific size), a decision in accordance with Article 46(3) can be taken to permit a substance and its use via TSD Appendix A. The SCHEER preliminary opinion should make it clearer in its conclusion that it refers to the use/presence of CLP-classified TiO2 in concentrations exceeding 1% in toy materials. It should also provide safe limits for CLP-classified TiO2 in toys where there is a likelihood of exposure.	See answer 1 in the Opinion (page 13, lines 5-14): For these products, a specific risk assessment needs to be performed in view of the classification of TiO2 particles as carcinogen category 2 by inhalation with a limitation to respirable TiO2 particles. Although the mandate asks for identification of categories of safe toys, the mandate does not require the derivation of safe limits.