SCCS/1644/22
Final version
CORRIGENDUM 21 March 2023

Scientific Committee on Consumer Safety

SCCS

OPINION

on the safety of aluminium in cosmetic products

- Submission III -

The SCCS adopted this document
by written procedure on 1 February 2023

- CORRIGENDUM adopted in plenary meeting on 21 March 2023 -

ACKNOWLEDGMENTS

Members of the Working Group are acknowledged for their valuable contribution to this Opinion. The members of the Working Group are:

For the preliminary version

SCCS members
Dr U. Bernauer
Dr L. Bodin
Prof. Q. Chaudhry (SCCS Chair)
Prof. P.J. Coenraads (SCCS Vice-Chair and Chairperson of the WG)
Prof. M. Dusinska
Dr J. Ezendam
Dr E. Gaffet
Prof. C. L. Galli
Dr B. Granum
Prof. E. Panteri
Prof. V. Rogiers (SCCS Vice-Chair)
Dr Ch. Rousselle
Dr M. Stepnik
Prof. T. Vanhaecke
Dr S. Wijnhoven

SCCS external experts
Dr N. Cabaton
Dr A. Koutsodimou
Prof. W. Uter
Dr N. von Goetz (Rapporteur)

For the final version

SCCS members
Dr U. Bernauer
Dr L. Bodin
Prof. Q. Chaudhry (SCCS Chair)
Prof. P.J. Coenraads (SCCS Vice-Chair and Chairperson of the WG)
Prof. M. Dusinska
Dr J. Ezendam
Dr E. Gaffet
Prof. C. L. Galli
Prof. E. Panteri
Prof. V. Rogiers (SCCS Vice-Chair)
Dr Ch. Rousselle
Dr M. Stepnik
Prof. T. Vanhaecke
Dr S. Wijnhoven

SCCS external experts
Dr N. Cabaton
Dr A. Koutsodimou
Prof. W. Uter
Dr N. von Goetz (Rapporteur)

This Opinion has been subject to a commenting period of eight weeks after its initial publication (from 30 May to 25 July 2021). Comments received during this period were considered by the SCCS. For this Opinion, main changes occurred in the following sections: 3.1, 3.2.4.1 SCCS comment under Table 4A, 3.2.4.4 SCCS comment under Tables 10 and 10A, 3.2.4.5 SCCS comment under Figure 2, 3.2.4.6. SCCS comment under Table 15A, 3.2.4.7. SCCS comment under Table 17, 3.4 incl. Table 18, discussion, conclusion as well as the reference list.

A corrigendum has been adopted on 21 March 2023 adding a note explaining that "AP" means "antiperspirant" under Table 6 of the Applicant.

All Declarations of Working Group members are available on the following webpage:
Register of Commission expert groups and other similar entities (europa.eu)

1. ABSTRACT

The SCCS concludes the following:

1. In light of the new data provided, does the SCCS consider Aluminium compounds safe when used in cosmetic products other than deodorants, antiperspirants, lipsticks and toothpastes? In the event that the estimated exposure to Aluminium from cosmetic products is found to be of concern, SCCS is asked to recommend safe concentration limits for each category.

The SCCS considers that aluminium compounds are safe when used

- in non-sprayable product categories at the maximum levels indicated in Tables 4 and 6; and
- in sprayable products, at the maximum levels indicated in Table 4, provided that the percentage of particles/droplets with a diameter of less than 10 µm does not exceed 20% of the total aerosolised particles/droplets. Since the Applicant's data submission indicated that aluminium is not used in sunscreen aerosol sprays, this Opinion does not cover sunscreen aerosol sprays.

2. Does the SCCS have any further scientific concerns regarding the use of relevant Aluminium compounds in cosmetic products taking into account the newly submitted information on aggregate exposure to Aluminium from cosmetics, medicines (e.g. antacids) and food intake?

As aluminium does not belong to substances classified as CMR 1A or B, only exposure from cosmetic uses was considered in this safety assessment with the exposure assessment based on maximum use levels for cosmetic ingredients.

However, the submission also provided a scenario where realistic exposure from non-cosmetic sources of aluminium (food and pharmaceuticals) was aggregated along with exposure from cosmetics at use levels from the year 2016. From this scenario, it can be deduced that contribution to aluminium exposure from food may be at a similar order of magnitude to that from cosmetics used for the safety assessment. Considering the conservative nature of the estimates, the aggregate exposure to aluminium from cosmetic and non-cosmetic sources may exceed safe limits for consumers at the highest exposure ranges.

Keywords: SCCS, revision, scientific opinion, aluminium, submission III, Regulation 1223/2009

Opinion to be cited as: SCCS (Scientific Committee on Consumer Safety), Opinion on the safety of aluminium in cosmetic products - Submission III, preliminary version of 6 May 2022, final version of 1 February 2023, Corrigendum 21 March 2023, SCCS/1644/22

About the Scientific Committees
Two independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.
These Committees are: the Scientific Committee on Consumer Safety (SCCS) and the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) and they are made up of scientists appointed in their personal capacity.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Agency (EMA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCCS
The Committee shall provide Opinions on questions concerning health and safety risks (notably chemical, biological, mechanical and other physical risks) of non-food consumer products (for example cosmetic products and their ingredients, toys, textiles, clothing, personal care and household products such as detergents, etc.) and services (for example: tattooing, artificial sun tanning, etc.).

Scientific Committee members
Ulrike Bernauer, Laurent Bodin, Qasim Chaudhry, Pieter Jan Coenraads, Maria Dusinska, Janine Ezendam, Eric Gaffet, Corrado Lodovico Galli, Eirini Panteri, Vera Rogiers, Christophe Rousselle, Maciej Stepnik, Tamara Vanhaecke, Susan Wijnhoven

Contact
European Commission
Health and Food Safety
Directorate B: Public Health, Cancer and Health security
Unit B3: Health monitoring and cooperation, Health networks
L-2920 Luxembourg
SANTE-SCCS@ec.europa.eu

PDF ISSN 1831-4767 ISBN 978-92-68-19396-9 doi:10.2875/404299 EW-AQ-24-013-EN-N

The Opinions of the Scientific Committees present the views of the independent scientists who are members of the committees. They do not necessarily reflect the views of the European Commission. The Opinions are published by the European Commission in their original language only.

SCCS - Opinions (europa.eu)

TABLE OF CONTENTS

2. MANDATE FROM THE EUROPEAN COMMISSION

Background

Aluminium (Al) and Al compounds are used in a variety of cosmetic products, predominantly in deodorants, antiperspirants, lipsticks and toothpastes. Several Al compounds are regulated in different entries of the Cosmetics Regulation (EC) No 1223/2009[1].
In 2013, a risk assessment issued by the Norwegian Scientific Committee for Food Safety reported that cosmetic products, and in particular antiperspirants, constitute a significantly larger contribution to the total systemic Al exposure compared to diet at least for the Norwegian population that was used in the study. As a result, SCCS was mandated to evaluate the possible risk for human health arising from the presence of Al in cosmetics. The assessment was based on products and aluminium compounds that contributed to the highest consumer's exposure, namely antiperspirants/deodorants, toothpastes and lipsticks.
In its Opinion SCCS/1525/14, the SCCS concluded that, due to the lack of adequate data on dermal penetration, the requested risk assessment could not be performed[2]. In 2016, industry submitted a new safety dossier to address the dermal penetration and the fate of Al (after skin application) based on a human exposure study. At its plenary meeting on 3 March 2020, the SCCS adopted its final Opinion SCCS/1613/19[3] and in March 2021 an addendum to this Opinion was published[4].
In the addendum, the SCCS concluded that the use of aluminium compounds is safe at the following equivalent aluminium concentrations up to:

- 6.25% in non-spray deodorants or non-spray antiperspirants
- 10.60% in spray deodorants or spray antiperspirants
- 2.65% in toothpaste, and
- 14% in lipstick

In addition, the SCCS stated "…*the systemic exposure to aluminium via daily applications of cosmetic products does not add significantly to the systemic body burden of aluminium from other sources. Exposure to aluminium may also occur from sources other than cosmetic products, and a major source of aluminium in the population is the diet. This assessment has not taken into account the daily dietary intake of aluminium".*
Following the discussion at the Cosmetics Working Group held on 25 June 2020 and in light of the comments received on the use of Al compounds in a variety of products other than deodorants, antiperspirants, lipsticks and toothpastes, the Commission considered opportune to request from industry to submit additional information on the 'other product categories' and on the aggregate exposure not only from cosmetics.
In March 2021, industry submitted a dossier focusing on the aggregate exposure to aluminium concerning the European population when considering the use of cosmetics and personal care products, medicines (e.g. antacids) and dietary intake.

The current request is based on the dossier submission III by the Applicant in order to demonstrate the safe use of aluminium in product categories other than deodorants, antiperspirants, lipsticks and toothpastes, as well as concerning the aggregate exposure. The current submission includes in particular additional data and considerations on the MoS calculation and aggregate exposure from cosmetics, medicines and food intake.

[1] Annex III (entry 50 - Aluminium Zirconium Chloride Hydroxide, and entries 189, 190, 192 - hair dyes), in Annex IV (entries 117, 118, 119, 150 - colorants) and Annex VI (entry 27a – coating for UV-filter).
[2] "*Aluminium is a known systemic toxicant at high doses. The SCCS is of the opinion that due to the lack of adequate data on dermal penetration to estimate the internal dose of aluminium following cosmetic uses, risk assessment cannot be performed. Therefore, internal exposure to aluminium after skin application should be determined using a human exposure study under use conditions*" (Opinion SCCS/1525/14).
[3] SCCS (Scientific Committee on Consumer Safety), Opinion on the safety of aluminium in cosmetic products, preliminary version of 30-31 October 2019, final version of 03-04 March 2020, SCCS/1613/19, link.
[4] https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_248.pdf

Terms of reference

1. *In light of the new data provided, does the SCCS consider Aluminium compounds safe when used in cosmetic products other than deodorants, antiperspirants, lipsticks and toothpastes? In the event that the estimated exposure to Aluminium from cosmetic products is found to be of concern, SCCS is asked to recommend safe concentration limits for each category.*

2. *Does the SCCS have any further scientific concerns regarding the use of relevant Aluminium compounds in cosmetic products taking into account the newly submitted information on aggregate exposure to Aluminium from cosmetics, medicines (e.g. antacids) and food intake?*

3. OPINION

During the commenting period, the Applicant has provided a new exposure calculation with adjusted factors for inhalation. The draft Opinion was updated with the submitted Tables which have received the same number as the original Table together with an A for transparency.

3.1 CHEMICAL AND PHYSICAL SPECIFICATIONS

Physicochemical properties of aluminium compounds that can generally be used as cosmetic ingredients have been summarised in Annex I of the previous SCCS Opinion (SCCS/1613/19). These encompass aluminium compounds in water-soluble and water-insoluble form. The water-soluble Al-containing compounds form are simple inorganic salts, simple organic salts, aluminium benzoate, and chlorohydrates, which can be used in skin care products. Water-insoluble aluminium containing ingredients can be minerals, glasses and clays, aluminium lakes, carbohydrates, fatty acid salts, which are typically added to cosmetic products as bulking agents, coloured pigments, and sometimes as mild abrasives.

The new submission presents an industry survey that indicates the substances actually in use along with their amounts. The INCI names and CAS numbers of these substances are given in Tables 2 and 3 of this Opinion. The respective physicochemical properties of the substances can be retrieved from Annex 1 of SCCS/1613/19.

On the basis of available information on solubility (Annex 1 of SCCS/1613/19), the SCCS agrees that aluminium citrate may exhibit the highest bioavailability amongst the Al salts assessed in this Opinion.

3.2 EXPOSURE ASSESSMENT & TOXICOKINETICS

3.2.1 Function and uses

Taken from the previous Opinion (SCCS/1613/19):

Antiperspirants

Aluminium salts in antiperspirants, such as aluminium chlorohydrate, form insoluble aluminium hydroxide polymer gel plugs within sweat ducts to temporarily prevent sweat reaching the surface of the skin. These substances are soluble at very low pH in the formulation; however, once applied on the skin they form chemically inert complexes with basic components of sweat and skin. The relatively high molecular weight of the compounds, low 'Log P' and positive charge limit the potential for skin penetration through the *stratum corneum*. Moreover, absorption across the skin is further minimised by the formation of protein complexes in the outermost layers of the *stratum corneum* (Hostynek, 2003). These chemical properties limit the systemic delivery of aluminium via the intake skin.

Lipsticks

Aluminium colloidal colorant 'lakes' are mainly used in lipsticks. Colloidal colourants are prepared under aqueous conditions by reaction between aluminium oxide and the organic pigments in order to make them insoluble. Aluminium oxide is usually freshly prepared by reaction of aluminium sulphate or aluminium chloride with sodium carbonate or sodium bicarbonate or aqueous ammonia. Due to the complex molecular structures and high molecular weights of organic lakes, the aluminium represents only a small part of the weight of the raw material of which the extractable (bioaccessible) part will represent only a fraction.

Toothpastes

Insoluble minerals are used in toothpastes mainly to act as mild abrasives and to provide shine/gloss benefit through the polishing of the enamel. They are also used to improve rheology in striped toothpastes. Toothpastes may also contain aluminium colloidal colourant "lakes" and pigments.

New submission:

In reply to a request of the European Commission regarding Al-content of 'other cosmetic products' than antiperspirants, lipsticks and toothpastes, the Applicant has submitted a report that includes the findings of a market survey on Al-containing products.

According to the Applicant, this company survey inquired in seven large multi-national companies for the total volume of products sold in Europe in 2016 (and toothpaste data from one company from 2020), whether or not the products included an aluminium containing ingredient, and the concentration values of aluminium and its compounds in the product formulations. The inclusion criteria were ingredients where aluminium comprised at least 0.01% of the material, and formulations where the aluminium containing ingredient was present in at least 0.01% in the formulation. Regarding the tonnage data, the criteria were products where at least 10 kg were placed on the market in 2016 within the EEC+5 region.

In total, around 5300 formulations were identified that contained Al-compounds as ingredients. A total of 51 different Al-compounds were identified. The reason why Al-compounds are used in these different product categories is because, like *e.g.* Aluminium Starch Octenylsuccinate, they may absorb oil, sweat or odour. Furthermore, they may function as pigments and thickening agents (https://cosmeticsinfo.org/aluminum). Table 1 lists the number of reported formulations for different product categories.

Table 1: Number of unique formulations containing one or more Al-ingredients per product category

	Product as labelled in the model	Number of unique formulas
1	AfterShave	12
2	BarSoap	7
3	BodyLotion	102
4	BodySpray	3
5	DeoRollOn – Gel	37
6	DeoRollOn – RollOn	358
7	DeoRollOn – Stick	145
8	DeoRollOn – Wipes	0
9	DeoSpray – Anti-Perspirant	435
10	DeoSpray – Pump	27
11	EaudeParfum, EaudeToilette	3
12	EyeLiner	217
13	EyeShadow	728
14	FaceMoisturizer	378
15	HairSpray	6
16	HairStyling	45
17	HandCream	16
18	Lipstick	1346
19	LiquidHandSoap	0
20	LiquMakeupFoundation	979
21	MakeupRemover	33
22	Mascara	60
23	Mouthwash	0
24	RinseoffConditioner	93
25	Shampoo	181
26	Showergel	13
27	Toothpaste	68

Representativeness

According to the Applicant, the survey on occurrence and amount of Al-ingredients used in cosmetic products was conducted with the Al-consortium.
According to the Applicant, the Al consortium members represent approximately 40% of the EU market share based on retail value (source: Euromonitor 2016, data made available to the SCCS) and include some of the highest market shares. Of the total of the more than 389 companies represented, 370 (95%) have below 1% market share and 343 (88%) below 0.1% of the market share. The mean market share is below 0.2% for the non-consortium members. Therefore, the consortium believes that this Al Consortium data is representative of the EU marketplace. In addition, when comparing to subsequent years, the market share of the consortium members remains stable and within the same range as 2016.

SCCS comment
Based on the data presented, the SCCS considers the presented survey as largely representative for the aluminium-containing ingredients and aluminium-containing products on the European market.

3.2.2 Dermal / percutaneous absorption

The data related to dermal/percutaneous absorption were assessed and commented upon by the SCCS in the previous Opinion on Aluminum (SCCS/1613/19). Below is a brief summary.

Dermal absorption was calculated from an exposure study with 6 female volunteers after application of 0.75 g antiperspirant per axilla on 100 cm^2, respectively. The antiperspirant contained Aluminum-Chlorhydrate which had been doped with radioactive ^{26}Al and the volunteers were biomonitored for ^{26}Al in 24h-urine (TNO, 2019). This yielded a skin absorption value of 0.00052%. Combined with the Al found in the feces in the same study (0.0014%), this yields an overall percentage of bioavailable Al of 0.00192%.

SCCS comment
The respective dermal absorption percentage of 0.00192% was used in the presented exposure calculation. This is considered a valid absorption value. Due to occlusion and formulation characteristics of antiperspirants, the dermal absorption for antiperspirants is considered to be a conservative value that is also valid for the other cosmetic products addressed in this opinion.

3.2.3 Other studies on toxicokinetics

Toxicokinetic studies were reviewed in SCCS/1613/19, and were summarised as follows:

Oral absorption: EFSA (2008) concluded that a value of 0.3% oral bioavailability was appropriate to use in human risk assessment for soluble aluminium in drinking water (*i.e.* without food) and 0.1% with food.

Lung absorption: Taken together, all available data suggest that absorption of aluminium from lung deposits in the blood is low. For the purposes of lung exposure modelling and risk assessment, a conservative value for aluminium uptake by the lung is 3% (Jones & Bennett, 1986; DeVoto & Yokel, 1994).

SCCS comment
The SCCS considers that oral bioavailability of 0.1% is an appropriate value for use in risk assessment for indirect ingestion after removal from the upper respiratory tract by the mucociliary elevator.

Regarding inhalation, as reported in the SCCS/1613/19, a conservative value for aluminium uptake by the lung of 3% is an appropriate value for use in risk assessment. From the upper respiratory tract, no data on bioavailability is available, but since mucociliary clearance will lead to expectorate or swallowing of the Al trapped in that part of the body, intestinal resorption values of 0.1 or 0.3% can be used (EFSA, 2008).

3.2.4 Calculation of SED/LED

The Applicant has submitted a comprehensive report on single product and aggregate exposure to Al via cosmetics, as well as an aggregate assessment of Al in cosmetics, medicines (antacids) and food. The assessment is based on a survey among the European industry that included 7 large producers.

3.2.4.1 Concentrations in cosmetics

According to the Applicant, the aluminium concentration data reported in this section were collected in the company survey. Six companies provided comprehensive data on Al use across a range of cosmetic products for the year 2016. An additional company provided comprehensive data on Al use in toothpastes for the year 2020. The seven companies

participating in the project identified 51 different Al-ingredients that were present in cosmetic products sold in the European market.

The results of the survey showed that 21 Al-ingredients were uniquely reported by a single company, thus exhibiting a unique aluminium concentration data point, provided by that company. These single data points, listed in Table 2, were used as constants in the exposure model, meaning that these 21 Al-ingredients always had the same concentration of aluminium as reported by the company using it.

Table 2: Aluminium ingredients with constant aluminium concentration values

#	INCI NAME	CAS #	Aluminium Concentration in Ingredient
1	ALUMINA /SYNTHETIC RUBY POWDER	1344-28-1 / 1333-84-2	52.93%
2	ALUMINIUM HYDROXIDE SULPHATE	1332-73-6 / 21645-51-2 / 8011-94-7	19.26%
3	ALUMINIUM LACTATE	18917-91-4	9.17%
4	ALUMINIUM ZIRCONIUM PENTACHLOROHYDRATE	57158-29-9 / 173762-83-9	8.40%
5	ALUMINUM TRISTEARATE	637-12-7	3.08%
6	ALUMINUM BENZOATE	555-32-8	6.91%
7	ALUMINUM CALCIUM SODIUM SILICATE	1344-01-0	14.81%
8	ALUMINUM DIMYRISTATE	56639-51-1	5.41%
9	ALUMINUM DISTEARATE	300-92-5	4.42%
10	ALUMINUM POWDER	7429-90-5	100.00%
11	ALUMINUM SILICATE	1327-36-2	24.73%
12	CARMINE (COCHINEAL LAKE)	1390-65-4	21.50%
13	KAOLIN	1332-58-7	5.23%
14	Montmorillonite	10043-67-1	7.80%
15	RED 21 LAKE	15086-94-9 / 548-26-5 / 15876-39-8	6.20%
16	RED 22 LAKE	548-26-5	12.80%
17	RED 40 LAKE	68583-95-9 / 25956-17-6	24.70%
18	RED 7 LAKE	5281-04-9	22.60%
19	SAPPHIRE POWDER	1317-82-4	52.90%
20	SODIUM POTASSIUM ALUMINUM SILICATE	12736-96-8	11.75%
21	TOURMALINE	1317-93-7	20.70%

According to the Applicant, 30 additional Al-ingredients were reportedly used by more than one company and, as the individual companies use different raw materials, multiple concentration values were reported for these raw materials. Table 3 reports the summary statistics of the aluminium concentrations reported for these Al-ingredients. Concentration values were reported as a list of single values or as ranges. Ranges were treated by the exposure model as uniform distributions and the model randomly selected a single value from the distribution whenever it was required.

Table 3: Summary statistics of aluminium concentrations in aluminium-ingredients with multiple values

#	INCI NAME	CAS #	Aluminium Concentration in Ingredient			
			Min	Max	Mean	# of reported concentrations
1	ALUMINA	1344-28-1	0.35%	0.69%	0.52%	2
2	ALUMINIUM, ZINC, MAGNESIUM AND CALCIUM STEARATES	7047-84-9	3.40%	3.70%	3.55%	2 (2 uniforms)
3	ALUMINUM CHLORIDE	7446-70-0 / 7784-13-6	10.00%	12.00%	11.09%	2 (1 uniform)
4	ALUMINUM CHLOROHYDRATE	1327-41-9	12.20%	30.90%	21.30%	14 (5 uniforms)
5	ALUMINUM HYDROXIDE	21645-51-2	1.19%	34.60%	11.57%	4
6	ALUMINUM SESQUICHLOROHYDRATE/ DIALUMINIUM CHLORIDE PENTAHYDROXIDE?	12042-91-0	11.50%	25.50%	18.48%	4 (2 uniforms)
7	ALUMINUM STARCH OCTENYLSUCCINATE	9087-61-0	0.16%	50.00%	27.85%	8 (1 uniform)
8	ALUMINUM STEARATE	7047-84-9	3.00%	7.83%	5.42%	2
9	ALUMINUM ZIRCONIUM OCTACHLOROHYDRATE	57158-29-9 / 98106-55-9	10.21%	10.21%	10.21%	2
10	ALUMINUM ZIRCONIUM TETRACHLORHYDRATE GLY	134910-86-4	14.50%	15.50%	15.33%	3 (1 uniform)
11	ALUMINIUM ZIRCONIUM TRICHLOROHYDREX GLY	134375-99-8	15.48%	17.80%	16.64%	2
12	BENTONITE	1302-78-9	9.00%	10.80%	9.90%	2
13	BLUE 1 LAKE/ ACID BLUE 9 ALUMINUM LAKE	68921-42-6	0.02%	31.50%	15.63%	4
14	CALCIUM ALUMINUM BOROSILICATE/ GLASS	65997-17-3	1.79%	13.20%	4.16%	5
15	MAGNESIUM ALUMINUM SILICATE	1327-43-1 / 12511-31-8	7.00%	18.82%	11.61%	3

#	INCI NAME	CAS #	Aluminium Concentration in Ingredient			
			Min	Max	Mean	# of reported concentrations
16	MAGNESIUM ALUMINUM SILICATE (ARGILLA)	12199-37-0	1.40%	21.00%	8.40%	3 (2 uniforms)
17	MICA	12001-26-2	0.04%	21.20%	11.72%	59 (6 uniforms)
18	PERLITE	93763-70-3	7.40%	8.20%	7.80%	2
19	POTASSIUM ALUM	10043-67-1 / 7784-24-9	3.95%	6.25%	5.10%	2
20	POTASSIUM ALUMINIUM SULPHATE	10043-24-9 / 7784-24-9	5.68%	10.44%	8.06%	2
21	PUMICE	1332-09-8	6.60%	7.14%	6.78%	3
22	RED 28 LAKE	18472-87-2	24.70%	29.68%	27.53%	4
23	RED 30 LAKE	2379-74-0	20.76%	41.40%	27.99%	3
24	RED 33 LAKE	3567-66-6	30.10%	31.60%	30.85%	2
25	SILICA/KAOLIN	1332-58-7	19.30%	23.80%	21.33%	3
26	SYNTHETIC FLUORPHLOGOPITE	12003-38-2	4.62%	6.41%	5.52%	2
27	TITANIUM DIOXIDE COATED WITH ALUMINIUM OXIDE	1344-28-1	1.56%	26.50%	7.34%	5
28	ULTRAMARINES	101357-30-6	13.00%	16.70%	15.47%	3
29	YELLOW 5 LAKE	12225-21-7	23.00%	39.70%	30.10%	5
30	YELLOW 6 LAKE FD&C	12227-60-0 / 15790-07-5 / 2783-94-0 / 174514-58-0	0.47%	24.50%	12.49%	2

By combining % Al in the ingredient with % of Al-ingredient used in the product, the Applicant derived distributions for the concentration values for each product category included in the exposure assessment (see Table 4) and for the product categories not included in the exposure assessment (see Table 6).

Table 4: Min, max and mean values of the reported concentrations of aluminium in each product type and category included in the exposure assessment.

	Product as labelled in the model	# of Al-ingredients identified across the product types	Aluminium concentrations (%) in products		
			Min	Max	Mean
1	AfterShave	1	0.00%	2.15%	0.59%
2	BarSoap	2	0.00%	0.07%	0.01%
3	BodyLotion	10	0.00%	3.81%	0.21%
4	BodySpray	1	1.10%	1.18%	1.12%
5	DeoRollOn – Gel	7	0.00%	6.18%	1.70%
6	DeoRollOn – RollOn	12	0.00%	5.63%	1.45%
7	DeoRollOn – Stick	9	0.00%	7.73%	1.05%
8	DeoRollOn – Wipes	0	0.00%	0.00%	0.00%
9	DeoSpray – Anti-Perspirant	8	0.00%	3.24%	0.32%
10	DeoSpray – Pump	5	0.00%	4.88%	1.17%
11	EaudeParfum, EaudeToilette	2	0.01%	0.05%	0.03%
12	EyeShadow	19	0.11%	43.31%	6.24%
13	EyeLiner	16	0.01%	15.76%	2.28%
14	FaceMoisturizer	19	0.00%	10.59%	0.69%
15	HairSpray	1	0.00%	0.00%	0.00%
16	HairStyling	7	0.00%	1.19%	0.10%
17	HandCream	2	0.00%	0.86%	0.30%
18	Lipstick	19	0.00%	14.62%	1.60%
19	LiquidHandSoap	0	0.00%	0.00%	0.00%
20	LiquMakeupFoundation	17	0.01%	6.59%	0.43%
21	MakeupRemover	14	0.00%	10.59%	0.62%
22	Mascara	11	0.00%	3.13%	0.53%
23	Mouthwash	0	0.00%	0.00%	0.00%
24	RinseoffConditioner	6	0.00%	7.14%	0.12%
25	Shampoo	7	0.00%	7.14%	0.45%
26	Showergel	7	0.00%	0.89%	0.13%
27	Toothpaste	6	0.00%	3.18%	0.07%

The product formulations reported in the company survey contain from 1 to 10 different Alingredients in combination. The products that contain the highest average number of Alingredients per product type are Lipstick with 3.6 Al-ingredients per formula; the formula with the absolute highest number of Al-ingredients (10) is also a lipstick. Lipsticks are followed by EyeShadow (2.55 Al-ingredients per formula) and LiquMakeupFoundation (1.88 Al-ingredients per formula). The averages of the these and all other product types are presented in Table 5. The data collected in the company survey capture the co-occurrence of different Alingredients in the same product formulations; this information was incorporated in the exposure model.

Importantly, Table 4 represents those formulations reported to include aluminium containing ingredients, with the exception of Mouthwash, LiquidHandSoap, and Deo-wipes, which contain none. Although the minimum is rounded to 0.00% in the table, this reflects formulations containing low levels of aluminium (given the inclusion criteria discussed

above, the theoretical minimum for a formulation that includes 0.01% of an ingredient that contains 0.01% aluminium would be 0.000001%).
Table 5: Average number of Al-ingredients per formula per product type

	Product as labelled in the model	Average # Al-ingredients per formula
1	AfterShave	1
2	BarSoap	1
3	BodyLotion	1.12
4	BodySpray	1
5	DeoRollOn – Gel	1.27
6	DeoRollOn – RollOn	1.25
7	DeoRollOn – Stick	1.12
8	DeoRollOn – Wipes	0
9	DeoSpray – Anti-Perspirant	1.1
10	DeoSpray – Pump	1.26
11	EaudeParfum, EaudeToilette	1
12	Eyeliner	1.49
13	EyeShadow	2.55
14	FaceMoisturizer	1.28
15	HairSpray	1
16	HairStyling	1.11
17	HandCream	1
18	Lipstick	3.6
19	LiquidHandSoap	0
20	LiquMakeupFoundation	1.88
21	MakeupRemover	1.39
22	Mascara	1.42
23	Mouthwash	0
24	RinseoffConditioner	1.1
25	Shampoo	1.11
26	Showergel	1.23
27	Toothpaste	1.13

Table 6: Min, max and mean values of the reported concentrations of aluminium in each product type and category that is **NOT** included in the exposure calculations.

Product Type	# of Al-ingredients included in the product type	Aluminium concentrations (%) in products		
		Min	Max	Mean
Other products with and without AP	3	0.00001%	2.794%	0.832%
Shaving products	1	0.09410%	0.094%	0.094%
Nail varnish	11	0.00223%	3.618%	0.166%
Eye contour products	7	0.00007%	1.290%	0.153%
Sun cream/lotion	10	0.00209%	8.403%	0.467%
Sun cream/lotion pump spray	2	0.33208%	0.332%	0.332%
Hair Color and Perms	2	0.00006%	0.002%	0.000%
Lip care products: Lip balm	3	0.00001%	0.606%	0.119%
Other products	17	0.01278%	15.887%	3.943%
Other products - Decoloration	2	0.00668%	4.760%	0.818%
Other products - oxidative coloration	2	0.01837%	0.120%	0.054%
Talc	1	0.01330%	0.013%	0.013%

According to the Applicant, the category "other products with and without AP" includes products for sweat control on hands and feet that are not considered daily use products frequently used by consumers. AP stands for "antiperspirant".

Also, data on occurrence of Al in cosmetics was derived for product categories included in the assessment (see Table 7) and those not included in the exposure assessment (Table 8).

Table 7: Product categories that can potentially contain Al and were included in the exposure assessment: Quantities sold in Europe in 2016 and relative occurrence of aluminium-containing products

	Product as labelled in the model	Quantity of all products sold (tonnes)	Quantity of products with aluminium sold (tonnes)	Occurrence
1	AfterShave	2,379.73	88.15	3.70%
2	BarSoap	42,259.45	983.45	2.33%
3	BodyLotion	75,047.33	21,872.97	29.15%
4	BodySpray	20,025.64	62.60	0.31%
5	DeoRollOn – Gel	975.33	959.83	98.41%
6	DeoRollOn – RollOn	16,980.30	15,751.75	92.76%
7	DeoRollOn – Stick	3,848.38	2,764.84	71.84%
8	DeoRollOn – Wipes	0.02	-	0.00%
9	DeoSpray – Anti-Perspirant	56,680.32	48,360.40	85.32%
10	DeoSpray – Pump	1,738.97	735.26	42.28%
11	EaudeParfum, EaudeToilette	3,927.52	0.31	0.01%
12	EyeLiner	69.79	41.82	59.92%
13	EyeShadow	116.49	116.28	99.82%
14	FaceMoisturizer	21,060.00	5,353.81	25.42%
15	HairSpray	40,048.88	19.79	0.05%
16	HairStyling	41,859.15	1,293.27	3.09%
17	HandCream	4,685.26	569.42	12.15%
18	Lipstick	298.02	261.30	87.68%
19	LiquidHandSoap	29,321.13	-	0.00%
20	LiquMakeupFoundation	2,516.76	2,284.24	90.76%
21	MakeupRemover	56,284.66	501.96	0.89%
22	Mascara	821.92	132.81	16.16%
23	Mouthwash	10,555.08	-	0.00%
24	RinseoffConditioner	148,701.36	8,470.45	5.70%
25	Shampoo	428,111.81	67,911.38	15.86%
26	Showergel	352,998.42	1,038.42	0.29%
27	Toothpaste*	76,634.45	19,632.27	25.62%

* One company shared Toothpaste data from 2020 and not 2016.

Table 8: Product categories that can potentially contain Al and were **NOT** included in the exposure assessment: Quantities sold in Europe in 2016 and relative occurrence of aluminium-containing products

Product type	Quantity of all products sold (tons)	Quantity of products sold (tons) with aluminium	Occurrence
Other products with and without AP	207.29	143.63	69.29%
Body hair removal products	36.43	0	0.00%
Shaving products	35,184.80	0.57	0.00%
Eye liner & Eye pencil	69.79	41.82	59.92%
Nail varnish	613.27	190.09	31.00%
Eye contour products	242.23	99.33	41.01%
Sun cream/lotion	11,690.92	3398.42	29.07%
Sun cream/lotion aerosol spray	1,733.24	0	0.00%
Sun cream/lotion pump spray	5,454.00	55.12	1.01%
Hair Color and Perms	30,299.49	987.11	3.26%
Lip care products: Lip balm	493.72	124.44	25.20%
Other products	3,697.65	206.20	5.58%
Other products - Decoloration	8,763.56	850.52	9.71%
Other products - oxidative coloration	23,888.04	1661.23	6.95%
Talc	296.38	18.49	6.24%
Toners/astringents	1,970.74	0	0.00%

Additional information provided by the Applicant upon request (05.11.2021)
Upon request of the SCCS, the Applicant has stated that the beach products (*i.e.*, sunscreen lotion) and other product categories listed in Tables 6 and 8 were not part of the Creme model because they are only used periodically. Importantly, the additional exposure from the excluded cosmetic product categories listed in Tables 5 and 7 are a minor contribution to the aggregate and total daily exposure to aluminium. The Applicant has further provided a deterministic exposure assessment for sunscreens (Table 9):

Table 9: Daily exposure estimate of aluminium. (Deterministic exposure calculations for sunscreen products combined with probabilistic assessment)

	Maximum / Day	Mean / Day
Aluminium in Product	8.40%	0.47%
Quantity of Product Per Day (g)	18	18
Dermal Absorption from SCCS Opinion	0.00192%	0.00192%
Systemic Exposure (µg/person)	29.04	1.61
Systemic Exposure (µg/kg bw/day)	0.484	0.03
MOS	375	6692
Proportion of PTWI	27%	1%
Probabilistic exposure All Sources P95 from Creme Report (µg/kg bw/day)	0.1631	0.1631
Total systemic body burden: Sunscreen + Probabilistic (µg/kg bw/day)	0.6471	0.1900
MOS (total systemic body burden)	278	947

Additional information provided by the Applicant after public consultation (22.09.2022)

A new scenario 1b has been calculated by the Applicant. According to the Applicant, scenario 1b is similar to Scenario 1 as it assumes 100% of cosmetic products contain Aluminium and concentrations are represented as single maximum values for each product. For a few products, the concentrations used in Scenario 1b are higher than the concentrations used in Scenario 1 and so it provides a more conservative estimate of exposure. The concentrations for Scenario 1b are shown in Table 4A.

Table 4A: Values of the concentrations of aluminium in each product type and category for Scenario 1b.

	Product as labelled in the model	Aluminium concentrations (%) in products in Scenario 1b
1	AfterShave	2.15%
2	BarSoap	4%
3	BodyLotion	3.81%
4	BodySpray	1.18%
5	DeoRollOn – Gel	6.18%
6	DeoRollOn – RollOn	5.63%
7	DeoRollOn – Stick	7.73%
8	DeoRollOn – Wipes	0%
9	DeoSpray – Anti-Perspirant	3.24%
10	DeoSpray – Pump	4.88%
11	EaudeParfum, EaudeToilette	0.05%
12	EyeShadow	43.31%
13	EyeLiner	15.76%
14	FaceMoisturizer	10.59%
15	HairSpray	0.15%
16	HairStyling	6.7%
17	HandCream	0.86%
18	Lipstick	14.62%
19	LiquidHandSoap	0.89%
20	LiquMakeupFoundation	23%
21	MakeupRemover	10.59%
22	Mascara	3.13%
23	Mouthwash	0%
24	RinseoffConditioner	7.14%
25	Shampoo	7.14%
26	Showergel	0.89%
27	Toothpaste	3.18%

SCCS comment

The SCCS considers the term "constant aluminium levels" in the header of Table 2 as confusing. The understanding of SCCS is that Table 2 lists Aluminium ingredients with one single concentration reported by one company that was subsequently used in the model as a point value. Likewise, the SCCS regards the title of Table 3 as confusing. The SCCS understands that Table 3 reports Al ingredients with a range of aluminium concentrations reported in industry survey (several companies).

The SCCS further understands that 'Al-concentrations' of Al-containing cosmetics ingredients mentioned in Tables 2 and 3 represent the Al-contents in terms of the stochiometric ratios of Al in these ingredients.

It is unclear to the SCCS why a range of Al-contents ('Al-concentrations') in the Al-ingredient for some of the Al-ingredients may result from the defined stoichiometry of the chemical substance (e.g. for potassium aluminium sulphate in Table 3). However, the SCCS has calculated the Al-contents based on stoichiometry and found that the Al-content in the maximal value was not underestimated by using the ranges provided by the Applicant. Therefore, risk assessment based on exposure calculations with these maximum values is considered valid.

Some products had been excluded from the aggregate exposure assessment (see Tables 6, 8) without explanation in the submitted report. Upon request, the Applicant has submitted the explanation and an additional deterministic exposure assessment of sunscreens. The assessment using the maximum Al level possible (Table 9) is considered valid by the SCCS.

The SCCS considers that sunscreen products should be included in the assessment, because on a seasonal basis they are used regularly, even daily, and because the high amounts applied may represent a considerable source for exposure. Furthermore, the presence probability of aluminium in sunscreens (*i.e.* the fraction of products that contain the substance) is 30%, which cannot be considered negligible.

Some of the products that have not been considered may also be used on a regular basis (shaving products, eyeliner, eye contour products and lip care products). However, for these products the exposure potential is low and the tonnage of Al-containing products sold is also low. Therefore, their contribution to dermal exposure can be considered as negligible and therefore these products can be considered safe for use.

In scenario 1b the Applicant has used higher concentrations for the product categories BarSoap, HairStyling, LiquidHandSoap and LiquMakeupFoundation. Since no reasoning for the new concentrations were given, the new values were not accepted by the SCCS. The SCCS will use the dermal and oral exposure values of the original report for its assessment.

Inhalation exposure was not calculated by the Applicant for sunscreens products. Therefore, this opinion considers only sunscreen lotions and creams, and not sunscreen products that may result in exposure of the lung.

3.2.4.2 Frequency of use and co-use

The frequency of application and co-use data for cosmetic products are available from Kantar Worldpanel, except for Mascara, Eye Shadow, Eye Liner and Makeup Remover. Kantar data on product usage frequency (at the resolution of one hour) were collected from consumer product consumption surveys from 2007 and 2008 for France, Germany, Spain, and the United Kingdom. In the case of Mascara, Eye Shadow, Eye Liner and Makeup Remover, frequency of use data is available from two studies (Bremmer, 2006a; Biesterbos, 2013). The Biesterbos study was based on 516 Dutch subjects (302 females, 210 males).

3.2.4.3 Amount per use

According to the Applicant, amount per use data comes from the Colipa studies (for Deo Roll-On (Gel, Roll-On, Stick), Deo Spray (Anti-Perspirant, Pump), cosmetics and toothpaste)) and additional data from the CTFA studies for certain cosmetics. The following is a set of abbreviations used here for the data sources mentioned above:

- COLIPA1: "European consumer exposure to cosmetic products, a framework for conducting population exposure assessments." (Hall *et al.*, 2007)
- COLIPA2: "European consumer exposure to cosmetic products, a framework for conducting population exposure assessments Part 2." (Hall *et al.*, 2010)
- CTFA1: "Exposure data for cosmetic products: lipstick, body lotion, and face cream." (Loretz L., *et al.*, 2005)
- CTFA2 "Exposure data for personal care products: hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. (Loretz *et al.,* 2006)
- CTFA3 "Exposure data for cosmetic products: facial cleanser, hair conditioner, and eye shadow." (Loretz *et al.*, 2008)

The amounts for Bar Soap products were taken from the publication of Comiskey *et al.* (2017), who report the amounts used for showering and washing hands. For conservative reasons, the exposure model was based upon the amounts of Bar Soap products used for showering as they are significantly higher than the amounts related to hand washing. The amounts for Liquid Hand Soap were derived from Ficheux *et al.* (2016), which is a study about the amount per use of cosmetic products consumed at home by the French adult, child and baby populations.

The amounts of Deo Spray products reported in COLIPA 1 only apply to pressurised (propellant-driven) sprays, since the amount used/day includes propellants. For Deo Spray-Pump products, lower values should be applied; in accordance with the consortium, it was decided to use the amounts of the DeoRollOn products as a proxy.

The amounts for Mascara, Eye liner and Make-up remover products come from Biesterbos *et al.* (2012).

3.2.4.4 Retention and bioavailability factors

According to the Applicant, users of cosmetic products may be exposed to aluminium via three different routes: the dermal route, which is applicable to all cosmetics, the inhalation route, which is applicable to spray products only, and the oral route, which is applicable to lipsticks and toothpastes only. These routes require three different sets of bioavailability and retention factors.

In the exposure report by the Applicant, dermal retention factors for personal care products vary depending on the product type with leave-on, non-spray products (e.g. body lotion) set at 100% and rinse-off products (e.g. Shampoo) conservatively set at 1% by default. The dermal retention factors for Toothpaste and Mouthwash are set l to 5% and 10%, respectively; these are the values set by the SCCS guidelines (SCCS 2012-2018).

According to the Applicant, the dermal retention factor for DeoSpray products is based on findings from the literature, where it has been shown that, of the amount of spray that is directed to the skin, only 23.5% actually lands on the skin (Steiling *et al.*, 2012). The dermal retention factor for HairSpray is set at 10%, which means that 10% of sprayed

product remains on the scalp (Api *et al.*, 2008, SCCS 2012-2018). According to Comiskey *et al.* (2017), 80% of EaudeToilette and EaudeParfum are retained on the skin.

A single aluminium percutaneous absorption factor of 0.00192% is assumed for all products applied to the skin. This is the dermal absorption percentage derived in the most recent SCCS opinion on aluminium (SCCS, 2020).

Bioavailability factors are the proportion of a substance which enters the circulation when it comes into contact with the body and are used to estimate the internal exposure from the external exposure. For toothpaste, mouthwash, and lipsticks, which may be partly or totally ingested, the model used an oral bioavailability value of aluminium of 0.1%, as per food and beverages. The amount of foods and antacids absorbed by the GI tract depends on the oral circulation through the GI tract. EFSA (2008) reports an oral bioavailability value of approximately 0.3% for Al in drinking water and less than 0.1% for Al in food and beverages.

Table 10 presents a summary of the used penetration, retention and bioavailability factors.

Table 10: Summary of assessment factors used in the exposure assessment

Product	Dermal retention factor	Dermal penetration factor	Adjusted Inhalation factor	Lung Bioavailability Factor (RF[a])	Upper airways factor (NRF[b])	Ingestion factor	Oral bioavailability factor
Food and beverages						100%	0.1%
Water						100%	0.3%
Antacids						100%	0.1%
AfterShave	100%	0.00192%					
BarSoap	1%	0.00192%					
BodyLotion	100%	0.00192%					
BodySpray	100%	0.00192%					
DeoRollOn – Stick	100%	0.00192%					
DeoRollOn – RollOn	100%	0.00192%					
DeoRollOn – Gel	100%	0.00192%					
DeoRollOn – Wipes	100%	0.00192%					
DeoSpray – Anti-Perspirant	23.5%	0.00192%	0.892%	3% (20%)	0.1% (80%)		
DeoSpray – Pump	23.5%	0.00192%	0.892%	3% (2%)	0.1% (98%)		
EaudeParfum EaudeToilette	80%	0.00192%	0.234%	3% (2%)	0.1% (98%)		
EyeShadow	100%	0.00192%					
Face Moisturizer	100%	0.00192%					
HairSpray	10%	0.00192%	1.047%	3% (20%)	0.1% (80%)		
HairStyling	10%	0.00192%					
HandCream	100%	0.00192%					
Lipstick	0%	0.00192%				100%	0.1%
LiquidHandSoap	1%	0.00192%					
LiquMakeupFoundation	100%	0.00192%					
Mascara	100%	0.00192%					
Mouthwash	10%	0.00192%				10%	0.1%
RinseoffConditioner	1%	0.00192%					
Shampoo	1%	0.00192%					
Showergel	1%	0.00192%					
Toothpaste	5%	0.00192%				5%	0.1%
EyeLiner	100%	0.00192%					
MakeupRemover	1%	0.00192%					

[a] Respirable Fraction

[b] Non-Respirable Fraction

According to the Applicant, Table 10A shows a summary of the factors used in Scenario 1b with the Inhalation factor column derived from RIFM 2-box modelling using the more conservative inhalation parameters discussed in the preliminary SCCS opinion 2022 and outlined in Table 12A below (chapter 3.2.4.5). It should be noted that a substantial amount of formulation lands on skin, so assuming that 100% is available for inhalation is not realistic.

Table 10A: Summary of Factors used in Scenario 1b

Product	Dermal retention factor	Dermal penetration factor	Inhalation factor	Lung Bioavailability Factor (RF[a])	Upper airways factor (NRF[b])	Ingestion factor	Oral bioavailability factor
Food and beverages						100%	0.1%
Water						100%	0.3%
Antacids						100%	0.1%
AfterShave	100%	0.00192%					
BarSoap	1%	0.00192%					
BodyLotion	100%	0.00192%					
BodySpray	100%	0.00192%					
DeoRollOn – Stick	100%	0.00192%					
DeoRollOn – RollOn	100%	0.00192%					
DeoRollOn – Gel	100%	0.00192%					
DeoRollOn – Wipes	100%	0.00192%					
DeoSpray – Anti-Perspirant	23.5%	0.00192%	**1.208%**	3% (20%)	0.1% (80%)		
DeoSpray – Pump	23.5%	0.00192%	**1.208%**	3% (2%)	0.1% (98%)		
EaudeParfum EaudeToilette	80%	0.00192%	**1.213%**	3% (2%)	0.1% (98%)		
EyeShadow	100%	0.00192%					
Face Moisturizer	100%	0.00192%					
HairSpray	10%	0.00192%	**1.204%**	3% (20%)	0.1% (80%)		
HairStyling	10%	0.00192%					
HandCream	100%	0.00192%					
Lipstick	0%	0.00192%				100%	0.1%
LiquidHandSoap	1%	0.00192%					
LiquMakeupFoundation	100%	0.00192%					
Mascara	100%	0.00192%					
Mouthwash	10%	0.00192%				10%	0.1%
RinseoffConditioner	1%	0.00192%					
Shampoo	1%	0.00192%					
Showergel	1%	0.00192%					
Toothpaste	5%	0.00192%				5%	0.1%
EyeLiner	100%	0.00192%					
MakeupRemover	1%	0.00192%					

[a] Respirable Fraction

[b] Non-Respirable Fraction

SCCS comment

In the original submission, the Applicant cites Steiling *et al.* 2012 to support a dermal retention of 23.5% to be used for reducing inhalation exposure. The cited value is the P90 for dermal load from an experimental study, which could be used as reasonable worst case for dermal exposure. However, subtracting an upper percentile value for dermal load from the total available amount will not result in a conservative value for inhalation and therefore cannot be used for deriving an adjustment factor for inhalation. Hence, the SCCS considered the" adjusted inhalation factors" for DeoSpray-antiperspirant and DeoSpray-pump in the original submission not valid.

In the new submission the Applicant has now provided an exposure assessment based on the upper bound of 100% for inhalation (see below). Therefore, the "adjusted inhalation factors" for DeoSpray-antiperspirant and DeoSpray-pump presented in Table 10A can now in principle be accepted. However, the transfer rate between Box 1 and Box 2 of the inhalation model is still very high (see chapter 3.2.4.5.)

Regarding Eau de Toilette, Eau de Parfum and HairSpray, Comiskey et al, 2017 cite an internal report that is not available to the SCCS. Therefore, the 80% dermal retention factor

cannot be evaluated. Hence, the SCCS considered also the ”adjusted inhalation factors“ for Eau de Toilette, Eau de Parfum and HairSpray in the original assessment not valid.
In the new submission the Applicant has provided an exposure assessment based on the upper bound of 100% for inhalation (see below). Therefore, the “adjusted inhalation factors” for Eau de Toilette, Eau de Parfum and HairSpray presented in Table 10A can now be accepted.

3.2.4.5 Inhalation exposure

According to the Applicant, the exposure model developed by Creme Global, utilised in the exposure study, requires several inputs. Among them, there is the output obtained from a separate computational model, called the 2-box model, that returns the fraction of aluminium inhaled by the consumer of a spray product. Since higher tier experimental data on each individual spray product were not available, estimates of the contribution from lung exposure rely on conservative computational model predictions.

According to the Applicant, the inhalation route is applicable only to spray products: DeoSpray – Anti-Perspirant, DeoSpray-Pump, EaudeParfum, EaudeToilette, HairSpray. Cosmetic spray products (HairSpray, DeoSpray, EaudeToilette and EaudeParfum) are directed to the skin and may also be incidentally inhaled. After dermal exposure, a percentage of the product remains on the skin once applied (dermal retention factor). For inhalation exposure, a percentage of the amount of product that is released is available to be inhaled; this percentage is calculated as 100% minus the dermal retention factor. An ‘inhalation factor’ is proposed to calculate the percentage of chemical released into the atmosphere that is available for inhalation. The inhalation factor depends on the product and is based on calculations using the 2-box model. The dermal retention factors and the inhalation factors are shown in Table 11.

Table 11: Dermal retention and inhalation factors

Product	Dermal Retention Factor (DRF)	% Available for Inhalation (1-DRF)	Inhalation Factor (IF)[d]	Adjusted Inhalation Factor (IF x (1- DRF))
DeoSpray, Anti-Perspirant and Pump	23.5%[a]	76.5%	1.167%	0.892%
HairSpray	10%[b]	90%	1.163%	1.047%
EaudeToilette, EaudeParfum	80%[c]	20%	1.171%	0.234%

[a] Steiling et al., 2012
[b] Api et al., 2008
[c] Comiskey et al., 2017
[d] Calculated via 2-box model

According to the Applicant, the ‘adjusted inhalation factor’ is a multiplication of the ‘inhalation factor’ (calculated by the 2-box model) and the ‘% available for inhalation’ for a specific product. As an example, we know that for DeoSpray 76.5% of the product that is released from the can is available for inhalation. The Inhalation Factor for DeoSpray (as calculated by the 2-box model) is 1.167%, which means that 1.167% of the product that is released into a room may be inhaled by the user. And as only 76.5% of it is available for inhalation, this results in an Adjusted Inhalation Factor of 0.892% for DeoSpray (*i.e.* 0.892% of the total amount of product released from the can may be inhaled by the user).

Some aerosol spray products, called in the model “DeoSpray – Anti-Perspirant”, can be classified as “compressed”. This describes a technology which reduces the quantity of propellant in the can and, proportionately, reduces the spray rate to ensure equivalent

product release (and hence consumer exposure) compared to standard dilute aerosols over the same duration of spray (Unilever 2015). The cosmetic companies participating in the company survey reported whether their aerosol spray products are compressed and, if so, the size of the spray rate reduction compared to standard dilute aerosols. Given that the Creme model uses exposure data for standard aerosols, the higher concentration of aluminium in the compressed product would lead to an artificially high modelled consumer exposure. In order to account for the reduced spray rate in the Creme model, the percentage of spray rate reduction is used by the exposure model as a multiplier of the aluminium concentrations to adjust exposure for compressed products. The percentages of spray rate reduction reported in the company survey are in the range 53-68%.

For aluminium, a lung bioavailability value of 3% is reported (DeVoto & Yokel, 1994), which has been considered in this 2-box model. It is generally considered that the cut-off value for droplets/particles to reach the deep lung, and be available for absorption, is <10 µm (Steiling et al, 2014). This is known as the 'respirable fraction'. Determination of what proportion of a sprayed product is considered as the respirable fraction is based on particle size measurements. Industry data demonstrates that for aerosol spray product, approximately 20% of the spray particles are <10 µm (unpublished industry data). The remaining 80%, known as the non-respirable fraction (or inhalable fraction) is likely deposited in the upper respiratory tract (nasopharyngeal and tracheobronchial region). For this fraction, mucociliary clearance leads to expectoration or swallowing of the aluminium trapped in the upper respiratory tract, and hence the oral absorption value of 0.1% can be applied (EFSA, 2008).

For the calculation of inhalation exposure, the Applicant used a 2-box model based on the work of Nicas & Mark (2014) and Sahmel *et al.* (2009).

Figure 1: The two-box model described in terms of relevant parameters, with descriptions of parameters (inset)

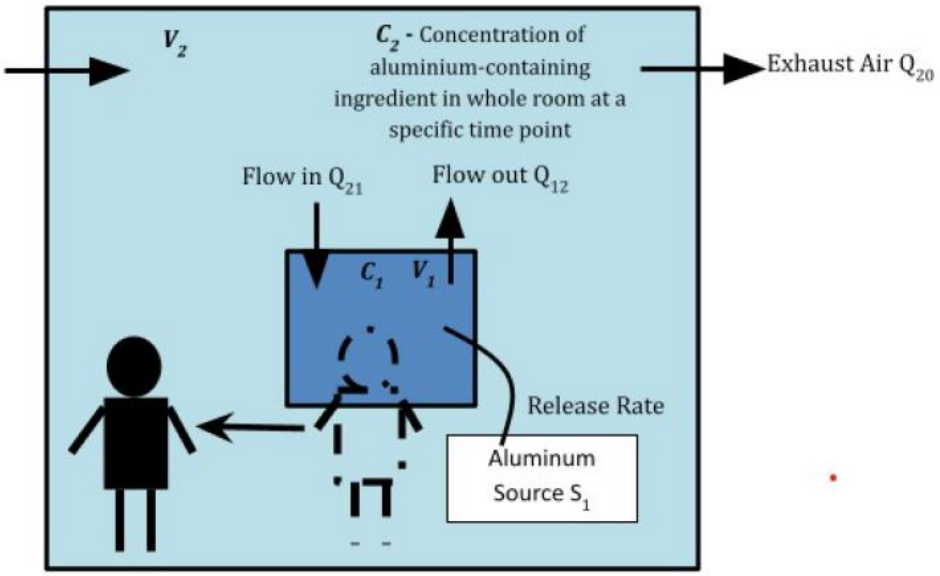


Figure 4: Two-box model described in terms of relevant parameters, with description of parameters (inset).

Where:

C_1 – aluminium concentration in air in box 1
C_2 – aluminium concentration in air in box 2
S_1 – source of aluminium used in box 1
Q_{12} – airflow from box 1 to box 2 (m^3/min)
Q_{21} – airflow from box 2 to box 1 (m^3/min)
Q_{02} – airflow from external world to box 2 (m^3/min) (see Section 3.2.)
Q_{20} – airflow from box 2 to external world (m^3/min)
V_1 – volume of box 1 (m^3)
V_2 – volume of box 2 (m^3)

Mathematically, the mass balance can be described by:

$$\text{Zone 1} : V_1 \, (dC_1/dt) = S_1 + Q_{21}C_2(t) + Q_{01}C_0 - (Q_{12} + Q_{10})\, C_1(t)$$

$$\text{Zone 2} : V_2 \, (dC_2/dt) = S_2 + Q_{12}C_1(t) + Q_{02}C_0(t) - (Q_{21} + Q_{20})\, C_2(t)$$

The following parameter values were used for calculating the inhalation factor for input into the Crème model.

Table 12: Parameters used for calculating the inhalation factor for input into the Crème model

Parameter	Value
Zone 1 volume (V1)	2 m^3 [e]
Time in zone 1 (t1)	2 min[e]
Zone 2 volume (V2)	10 m^3 (bathroom)[b, e]
Time in zone 2 (t2)	10 min[e]
Air Flow (Zone 1 -> Zone 2)	7.24 m^3/min[c]
Air Flow (Zone 2 -> Outside)	0.1 m^3/min[c]
Human inhalation rate (IR)	13.1 L/min[d]
Emission Duration	0.17 min (DeoSpray)[a], 0.24 min (HairSpray)[a], 0.08 min (EaudeParfum, EaudeToilette)[a]

[a] Bremmer et al., 2006a
[b] Bremmer et al., 2006b
[c] ECHA, 2016
[d] Salem & Katz, (2006) & Finley et al. (1994)
[e] Rothe et al., 2011

Table 12A: Parameter values used for the calculation of the inhalation factor (via the 2 box model) in Scenario 1b

Parameter	Value
Zone 1 volume (V1)	2 m^3 [e]
Time in zone 1 (t1)	2 min[e]
Zone 2 volume (V2)	10 m^3 (bathroom)[b, e]
Time in zone 2 (t2)	10 min[e]
Air Flow (Zone 1 -> Zone 2)	7.24 m^3/min
Air Flow (Zone 2 -> Outside)	**0 m^3/min**
Human inhalation rate (IR)	13.1 L/min
Emission Duration	0.17 min (DeoSpray)[a], 0.24 min (HairSpray)[a], 0.08 min (EaudeParfum, EaudeToilette)[a]
% Available for inhalation	**100% DeoSpray** **100% Hairspray** **100% EaudeParfum, EaudeToilette**

[a] Bremmer et al., 2006a
[b] Bremmer et al., 2006b
[c] ECHA, 2016
[d] Salem & Katz, (2006) & Finley et al. (1994)
[e] Rothe et al., 2011

According to the Applicant, the 2-box model requires also as input the quantity of aluminium which is released into the air each minute. This value is calculated by multiplying the product's spray rate (mg/min), the emission duration (min) and aluminium concentration (%) in the product. These three parameters are also used to calculate the total amount of aluminium released (TAR). The TAR is used to estimate the inhalation factor which corresponds to the fraction of TAR that is inhaled during the exposure event, *i.e.* the model divides the total exposure by the TAR. In doing so, the model cancels out the effect of product's spray rate and aluminium concentration on the result; these two parameters can be varied but the inhalation rate remains unchanged. However, dividing the total exposure by the TAR does not completely cancel out the effect of the emission duration. The longer the length of the emission duration, the more product is released into the air and is available for inhalation by the user before the larger product particles, under the effect of gravity, drop towards the floor, exit the area surrounding the user's head, and are no longer available for inhalation. The 2-box model can calculate the exposure per unit of bodyweight by dividing the total exposure by the bodyweight. However, the model is used here to estimate the fraction of product that is typically inhaled by an adult, regardless of their bodyweight. The bodyweight was considered in the Crème model.

Table 13 contains the list of the inhalation exposure inputs used to estimate the inhalation exposure to the spray products, together with the references to the scientific literature. All these factors are applied to the exposure levels as multipliers, as explained in detail in this section.

Table 13: Inhalation input parameters

Inhalation Factor	DeoSpray – Anti-Perspirant	DeoSpray – Pump	EaudeParfum, EaudeToilette	HairSpray
Adjusted Inhalation factor	0.892%	0.892%	0.234%	1.047%
Respirable fraction (<10 µm) (RF)[d]	20%	2%	2%	20%
Lung Bioavailability Factor for Aluminium[a]	3%	3%	3%	3%
Non-respirable fraction (NRF), calculated as 1-RF	80%	98%	98%	80%
Oral bioavailability (to account for Al from upper airways[b])	0.1%	0.1%	0.1%	0.1%
Compression factor[c]	53-68%	NA	NA	NA

[a] DeVoto & Yokel, 1994
[b] EFSA, 2008
[c] Values submitted in the company survey
[d] Based on particle size measurements (unpublished company data).

In the following, the step-wise approach used by the Applicant is described:

Step 1: the model selects each diary and retrieve the list of cosmetic products used each day. For example, the diary of subject #1 on the first day report the use of an "DeoSpray – Anti-Perspirant" deodorant and of body lotion.

Step 2: the model randomly selects one of the formulas used in "DeoSpray – Anti-Perspirant" deodorants reported by the companies. The amount sold of each formula is used as a statistical weight to determine the frequency with which each formula is selected. Let's assume that the model selects formula F7, that was reported by company A, which contains 10% of MAGNESIUM ALUMINUM SILICATE (ARGILLA) and 15% of ALUMINUM CHLOROHYDRATE.

Step 3: the model goes in the ingredient list of company A and retrieves the aluminium concentrations related to the two aluminium ingredients used in formula F7. In case the company reported a range of aluminium concentrations, the model randomly selects a number within the range. Let's assume in this case the concentration 2% of aluminium concentration MAGNESIUM ALUMINUM SILICATE (ARGILLA) and 12.7% to ALUMINUM CHLOROHYDRATE

Step 4: the model calculates the total aluminium concentration in formula F7 as the sum of the products between the concentration of the aluminium ingredients in the formula times the concentration of aluminium in each ingredient, as shown the following equation:

Total-Al-concentration ($_C$) = 10% * 2% + 15% * 12.7% = 2.105%

Step 5: the model calculates the exposure level of aluminium by entering the total aluminium concentration in equation (1). Let's assume that the selected "DeoSpray – Anti-Perspirant" deodorant is a compressed one with compression factor equal to 53%, the used amount is 1.43 g (or 1,430 mg), which is the applied daily amount of spray deodorant recommended as default value in exposure assessments by the SCCS 10th notes of guidance (SCCS 2018), and the bodyweight of the subject is 60 kg. Then the resulting exposure level is calculated as

$$E(\frac{mg}{kg}) = \frac{1430(mg) \times 0.892\% \times 53\% \times 2.105\%}{60\,kg} = 0.002372$$

Step 6: the exposure level *E* calculated in the previous step is then split into its respirable and non-respirable components. The respirable component is equal to *E* multiplied times the respirable fraction *RF* and the lung bioavailability factors *BL* which are equal to 20% and 3%, respectively (see Table 25).

$$E_{respirable}(\frac{mg}{kg}) = E \times RF \times BL = 1.42E-05$$

The non-respirable component is instead equal to *E* multiplied by the non-respirable fraction *NF* and the upper respiratory tract bioavailability factor *BUA* which are equal to 80% and 0.3%, respectively (see Table 25).

$$E_{non-respirable}(\frac{mg}{kg}) = E \times NF \times BUA = 5.69E-06$$

Step 7: the model repeats the above steps for each consumption event of the subject where a "DeoSpray – Anti-Perspirant" deodorant has been used. Then calculate the total respirable and non-respirable exposure levels and divide them by 7 (this is the number of days recorded in each diary) to calculate the average daily exposure.

The aluminium concentration for each product type is assigned at subject level, i.e. the model assumes that the subject uses the same product over the week hence the concentration does not change. For example, if a subject reported the usage of "DeoSpray – Anti-Perspirant" deodorant in three events, the model assigns the same aluminium concentration to all the three events.

The model analyses the exposure to aluminium as a single chemical, thus removing the dependence on source of the ingredient. Information about the exposure to each aluminium ingredient is stored by the model but not analysed.

Additional information provided by the Applicant after public consultation (22.09.2022)

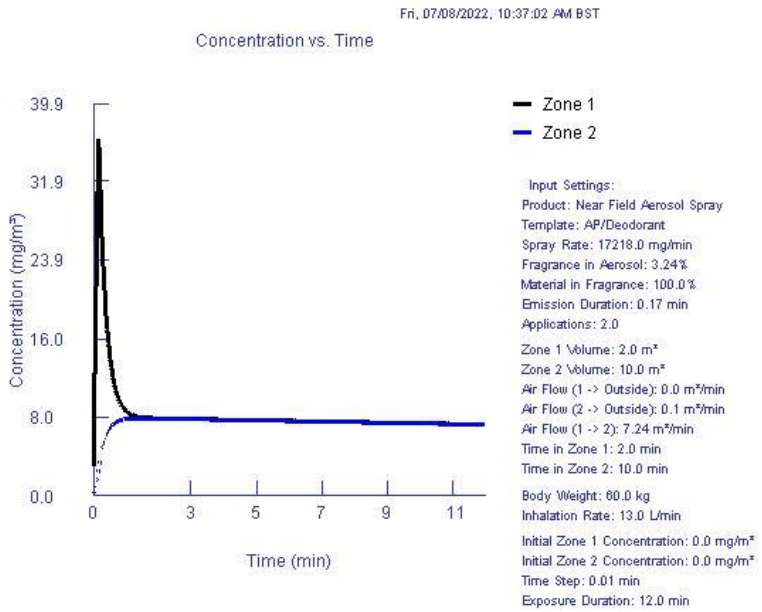
Scenario 1b uses more conservative parameters in the Two-box model and therefore more conservative inhalation parameters which adds an additional layer of conservatism. These values are given in Table 12A.

Table 12A: Parameter values used for the calculation of inhalation factor (via the 2-box model) in Scenario 1b

Parameter	Value
Zone 1 volume (V1)	2 m^3 [e]
Time in zone 1 (t1)	2 min[e]
Zone 2 volume (V2)	10 m^3 (bathroom)[b, e]
Time in zone 2 (t2)	10 min[e]
Air Flow (Zone 1 -> Zone 2)	7.24 m^3/min
Air Flow (Zone 2 -> Outside)	**0 m^3/min**
Human inhalation rate (IR)	13.1 L/min
Emission Duration	0.17 min (DeoSpray)[a], 0.24 min (HairSpray)[a], 0.08 min (EaudeParfum, EaudeToilette)[a]
% Available for inhalation	**100% DeoSpray** **100% Hairspray** **100% EaudeParfum, EaudeToilette**

[a] Bremmer et al., 2006a
[b] Bremmer et al., 2006b
[c] ECHA, 2016
[d] Salem & Katz, (2006) & Finley et al. (1994)
[e] Rothe et al., 2011

Figure 2: Output graph from RIFM-2 box model with zone 1 to zone 2 ventilation rate set to 7.24 m^3/min



SCCS comment
In the calculations of inhalation exposure, a very high airflow from zone 1 to zone 2 has been assumed, without support by literature (the reference cited (ECHA, 2016) does not report the respective value, neither can it be found in the references cited therein). However, based on the SCCS Notes of Guidance (11th Revision, SCCS/1628/21), a conservative approach is warranted, with the assumption of no ventilation. This means that the inhalation factor used in the submission dossier is too low.

A reference for the compression factor used in step 5 is not given.

The Applicant cites unpublished industry data for the assumption that approximately 20% of the spray particles are <10 µm for aerosol spray products. This data is not available to the SCCS and therefore cannot be evaluated.

The procedure for deriving the factor "available for inhalation" is questionable, since the experiments used to derive the dermal absorption rate aimed at deriving a worst case for dermal exposure. As explained in the comments on bioavailability, subtracting a worst-case dermal exposure from the total 100% does not result in conservative estimates for inhalation. A conservative estimate for inhalation would *e.g.* result from subtracting a lower estimate for dermal exposure. In consequence, the SCCS does not accept the respective factor "available for inhalation" (1-DRF) proposed in Table 11, and the proposed inhalation parameters in Table 13.

During the commenting period, the Applicant has submitted a new exposure calculation for a scenario designated as scenario 1b. In this calculation, the availability for inhalation was set to 100% and the ventilation to outside was set to zero. This results in more conservative estimates for inhalation exposure to the sprayable products. The SCCS considers that the transfer rate between the Box 1 and 2 is still too high, because - as also illustrated by the Figure submitted by the Applicant - the substance is completely distributed into Box 2 within less than 2 min. This means that the assumption of 2 min in Box 1 as suggested by Rothe *et al.,* 2011 is not observed. Therefore, for deodorant as the most important contributor an additional exposure term was added by the SCCS for the first 2 min in Box 1 based on the 2-Box model submitted in an earlier submission (see below).

3.2.4.6 Exposure calculations and Scenarios for cosmetics

According to the Applicant, a tiered approach that starts from a deterministic model up to a fully probabilistic model was used to assess the exposure to aluminium contained in personal care products, foods and medications (antacids). The aim was to estimate the total amount of aluminium to which humans are exposed from all these various sources. This amount is otherwise known as aggregate exposure.
The Creme Global model was used as the main tool to assess aggregate exposure to aluminium. The Creme tool was run first in a deterministic tier 1 mode, which simply summed the P95 exposure values for the individual products to obtain the aggregate exposure, and then in a Tier 2, probabilistic mode, to estimate the impact of the two approaches on the exposure levels related to cosmetic products.

The Creme Global model is based on the following equation for calculating the daily chemical exposure for a group of cosmetic products i and a single subject j:

$$E_{ij} = \frac{F_{ij} \times A_{ij} \times X_i \times C_{ij}}{7 \times BW_j} \quad (1)$$

Where each term on the right-hand side can be a fixed estimate or drawn from a distribution and each term is understood as follows:

E_{ij} is the systemic/internal exposure in subject j to aluminium from product group I [µg/kg/day]
F_{ij} is the frequency of applications/consumption events by subject j of product group I [day-1] during the seven-day Kantar survey.
A_{ij} is the amount used by subject j per application/consumption event of product group i [µg]
X_i represents the exposure factors, reported in Section 3.9, for product group i [%] multiplied one by each other. These are independent of the subject.

C_{ij} is the concentration of aluminium in product group i [unitless] assigned to subject j, BW_j is the consumer's bodyweight [kg]

A group of products is one for which all included products are considered equivalent. For example, various brands and colours of lipstick, etc. are assessed together under the product group lipstick.

Aggregate aluminium exposure for each individual subject is estimated by

$$SE_j = \sum_{i=1}^{n} E_{ij} \quad (2)$$

Where:

SE_{ij} is the total (or aggregated) systemic/internal exposure to aluminium from all products [µg/kg/day] for subject j
E_{ij} is the systemic/internal exposure to aluminium from product group i [µg/kg/day] for subject j

The population-level exposure can then be calculated from the individual subject-level exposures. The population can be defined in two ways. The first is the Total Population, *i.e.* all subjects in the survey, and the other is the Exposed Population, *i.e.* only those consumers who are exposed to aluminium. Given that there are two potential populations that can be used to characterise exposure, an immediate question posed is to determine which one is most appropriate. One guiding principle is that for aggregate exposure resulting from multiple sources that are used by most of the population (e.g. all categories of cosmetics and personal care products or most foods in the diet), then exposure is well represented by the Total Population. However, if exposure is due to a small number of products or is due to an infrequently occurring substance, then the Exposed Population is likely the more appropriate set to use. This is so that there is not inappropriate dilution of exposure statistics by the inclusion of large number of zero values in their calculation.

Then the population daily exposure (PE) can be written as:

$$PE = Stat(E_1, E_2, \ldots, E_N) \quad (4)$$

where Ej is the daily exposure for individual j, and the Stat() function is typically something like the 95th percentile.

The main differences in the values of the model parameters that were used in the three scenarios are summarized in Table 14.

Table 14: Summary of the differences in value of the main model parameters used in the three scenarios

Table 18: Summary of the differences in value of the main model parameters used in the three scenarios.

	Product as labelled in the model	Conservative, screening analysis based on single value estimates at P95 for cosmetics		Probabilistic model		
		Scenario 1 Max Concentration	Scenario 1 Occurrence	Scenarios 2 & 3 Concentration	Scenario 2 Occurrence	Scenario 3 Occurrence
1	AfterShave	2.150%	100%	Distribution (see Table 6)	100%	30%
2	BarSoap	0.070%				35%
3	BodyLotion	3.810%				30%
4	BodySpray	1.180%				5%
5	DeoRollOn – Stick	7.730%				75%
6	DeoRollOn – RollOn	5.630%				95%
7	DeoRollOn – Gel	6.180%				100%
8	DeoRollOn – Wipes	0.000%				80%
9	DeoSpray – AP	3.240%				90%
10	DeoSpray – Pump	4.876%				100%
11	EaudeParfum, EaudeToilette	0.050%				40%
12	EyeShadow	43.310%				100%
13	FaceMoisturizer	10.590%				35%
14	HairSpray	0.000%				5%
15	HairStyling	1.190%				15%
16	HandCream	0.860%				30%
17	Lipstick	14.620%				90%
18	LiquidHandSoap	0.000%				50%
19	LiquMakeupFoundation	6.590%				95%
20	Mascara	3.130%				35%
21	Mouthwash	0.000%				60%
22	RinseoffConditioner	7.140%				35%
23	Shampoo	7.140%				40%
24	Showergel	0.890%				50%
25	Toothpaste	3.18%				55%
26	EyeLiner	15.760%				60%
27	MakeupRemover	10.590%				25%
28	Food and drinking water	see Table 10	100%			100%
29	Antacids	see Table 12	100%			100%

Deterministic calculation for Scenario 1:

Based on point estimates of each parameter of the model, the exposure was calculated by multiplying the factors as in equation (1) above for each product individually; however, the calculation cannot be carried out at subject level but only at population level.
The point estimates of the different factors are worst-case estimates (upper percentiles of the value distributions). Creme Global, in accordance with the Aluminium Consortium, decided to use as default values for the model parameters:

- the maximum concentration value of aluminium in each product category
- the 95th percentiles of the value distributions retrieved from the above-mentioned surveys and databases for all the other parameters.
- set the aluminium occurrence equal to 100% for each product category.

To calculate the systemic exposure in a deterministic model, a basic method is to simply sum up the population exposures from the individual products as:

$$SE = Stat(E_1) + Stat(E_2) + \ldots + Stat(E_M) \quad (5)$$

where the Stat(Ei) terms are the population exposure statistics for a single product Ei. The expectation here was that the sum of these statistics would provide a good estimate of the corresponding statistic for the aggregate statistic for the systemic exposure. However, for most statistics, there is little mathematical reason to suggest that this summation would be a good estimate.

The model analysed the exposure to aluminium as a chemical from each formulation, by taking into consideration all ingredients which might contribute aluminium to the formulation, thus removing the dependence on the source of the ingredient. Information about the exposure to each Al-ingredient was stored by the model but not analysed. Equation (1) was used to estimate the dermal and oral exposure levels.
The oral route is applicable to lipsticks and toothpaste products which can be ingested. In this case, the Xi factor corresponds to the oral bioavailability factor.

Table 15: Summary statistics of the exposure to Al from the use of cosmetics per route of exposure for the three different scenarios provided by the Applicant

Route	Statistics	Exposed Population			Total Population		
		Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3
Dermal	Count	104780	104780	101364	104836	104836	104836
	Mean*	0.01657	0.002565	0.001727	0.01656	0.002562	0.001663
	P50*	0.01004	0.001087	0.0004282	0.01003	0.001085	0.0003614
	P95*	0.0529	0.0102	0.007553	0.05283	0.01019	0.007370
Ingestion	Count	95760	95760	61064	104836	104836	104836
	Mean*	0.03174	0.0006820	0.0006595	0.02861	0.0006146	0.0003831
	P50*	0.02617	0.0002215	0.0001798	0.02342	0.0001711	2.65e-05
	P95*	0.07635	0.002450	0.002386	0.07404	0.002314	0.001617
Inhalation Non-Respirable	Count	73328	73328	48984	104836	104836	104836
	Mean*	0.002787	0.000932	0.001324	0.00192	0.0006423	0.0005856
	P50*	5.4e-06	3.80e-06	0.0002713	2.3e-06	1.1e-06	0.0
	P95*	0.013054	0.004840	0.005737	0.01089	0.003906	0.003656
Inhalation Respirable	Count	73328	73328	48984	104836	104836	104836
	Mean*	0.019	0.006355	0.008920	0.013084	0.004383	0.003944
	P50*	3.4e-06	6.14e-06	0.0007796	1.43e-06	8.0e-07	0.0
	P95*	0.09735	0.03445	0.04123	0.0804	0.02746	0.02528
Total Systemic (Combined Oral, Dermal & Inhalation)	Count	104780	104780	101413	104836	104836	104836
	Mean*	0.06024	0.00821	0.006820	0.06018	0.008200	0.006577
	P50*	0.04486	0.002665	0.001384	0.0448	0.002659	0.001219
	P95*	0.1671	0.03647	0.03317	0.1671	0.03647	0.03238

* Units for Mean, P50 and P95 are µg/kg bw/day.

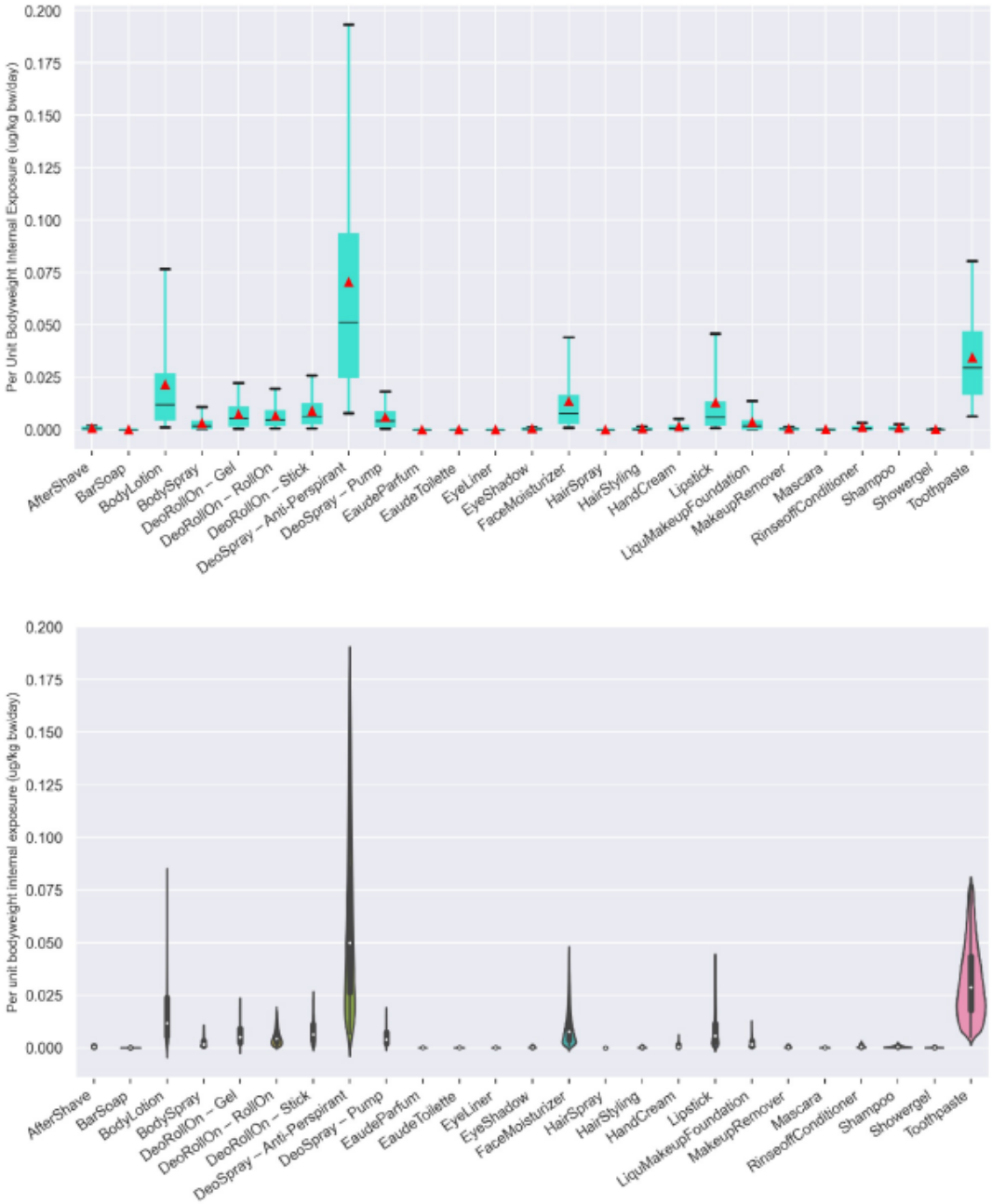


Figure 1: Distribution of internal exposure levels per cosmetic product, scenario 1

In a previous dossier (Cosmetics Europe, 2016), the Applicant had provided a deterministic 2-Box-Model calculation for the systemic body burden of aluminium via the lung. When aluminium chlorohydrate was used in spray/aerosol antiperspirants, a 2-Box exposure model was used. The 2-Box model calculation was performed using the input parameters given in Table 16.

Table 16: Parameter values used for the calculation of lung exposure in the 2-Box model (Cosmetics Europe, 2016)

		Reference
Distribution volume at time point 1 (V1)	2 m^3	Rothe *et al.*, 2011
Exposure time 1 (t1)	2 min	Rothe *et al.*, 2011
Distribution volume at time point 2 (V2)	10 m^3	Rothe *et al.*, 2011
Exposure time 2 (t2)	10 min	Rothe *et al.*, 2011
Human breath minute volume (BR)	13.1 l/min	Finley *et al.*, 1994; Salem & Katz, 2006
Mean human body weight (BW)	60 kg	SCCS (2015), 9th notes of guidance
Airborne Fraction (AF)*	76.5%	Steiling et al., 2012
Respirable Fraction (<10 µm) (RF)	20%	based on particle size measurements (unpublished company data) The cut-off value for droplets/particles reaching the deeper lung is set as <10 µm - SCCS (2015), 9th notes of guidance
Non-Respirable fraction (NRF)	80%	The inhaled Al that is trapped in the upper respiratory tract (and does not reach the deeper lung) is also considered
Lung deposition rate	20%	Lippmann (1977)
Gas exchange factor	75%	Rothe *et al.*, 2011
Concentration of Al in spray formulation incl. propellant (C)	2.86%	Maximum value reported by industry
Amount sprayed per day (A)	6.1 g	Hall *et al.*, 2007 (6.1 g is the 90th percentile value of daily deo/ap spray usage (including the propellant and solvent)
Bioavailability of Al from alveoli	3%	DeVoto & Yokel, 1994
Bioavailability of Al from upper airways	0.3%	EFSA J (754), 1-34, 2008 (typical value for oral bioavailability)

* It should be noted that ACH is not a volatile substance and the fraction that is present on the skin would not become volatile and be available for inhalation.

Calculation of the substance amount relevant for exposure (EA)

The amount of Al that will be available for inhalation after spraying is calculated as follows:

EA [g] = A [g] x C [%] x AF [%] x RF [%]/NRF [%]

The Applicant further calculated the systemic exposure dose for aluminium upon inhalation as follows:

For the respirable fraction:
EA [g] = A [g] x C [%] x AF [%] x RF [%]
EA resp = 6.1 g x 0.0286 x 0.765 x 0.2 = 0.02669 g

For the non-respirable fraction:
EA [g] = A [g] x C [%] x AF [%] x NRF [%]
EA non-resp = 6.1 g x 0.0286 x 0.765 x 0.8 = 0.10677 g

Calculation of the Exposure Dose (ED)
The inhaled amounts (IM) at time point 1 and 2 (IM 1/2, 2/10 min) are calculated with the following formula:
IM 1/2 [mg] = (EA [mg] / V1/2 [l]) x BR [l/min] x t1/2 [min]

For the respirable fraction:
first 2 minutes: IM 1 [mg] = (26.69 / 2000) x 13.1 x 2 = 0.350
following 10 minutes: IM 2 [mg] = (26.69 / 10000) x 13.1 x 10 = 0.350

For the non-respirable fraction:
first 2 minutes: IM 1 [mg] = (106.77 / 2000) x 13.1 x 2 = 1.399
following 10 minutes: IM 2 [mg] = (106.77 / 10000) x 13.1 x 10 = 1.399

The ED is then calculated as follows:
ED(inhal) [mg/kg bw/d] = (IM 1 + IM 2 mg) / BW [kg]
ED(resp) [mg/kg bw/d] = (0.350 + 0.350) / 60 = 0.01167
ED(non-resp) [mg/kg bw/d] = (1.399 + 1.399) / 60 = 0.04663
ED(total) [mg/kg bw/d] = 0.01167 + 0.04663 = 0.0583

Thus, the total amount of Al exposure via inhalation within 12 minutes after spraying of an antiperspirant spray in a 10 m^3 room according to this calculation is 0.0583 mg/kg bw/day.

Additional information provided by the Applicant after public consultation (22.09.2022)

Calculations with scenario 1b result in exposure estimates highlighted in Table 18A.

Table 15A: Summary statistics of the exposure to Al from the use of cosmetics per route of exposure for the four different scenarios provided by the Applicant

Route	Statistic	Exposed Population				Total Population			
		Scenario 1	Scenario 1b	Scenario 2	Scenario 3	Scenario 1	Scenario 1b	Scenario 2	Scenario 3
Dermal	Count	104780	**104780**	104780	101364	104836	**104836**	104836	104836
	Mean*	0.01657	**0.01858**	0.002565	0.001727	0.01656	**0.01857**	0.002562	0.001663
	P50*	0.01004	**0.01102**	0.001087	0.0004282	0.01003	**0.011**	0.001085	0.0003614
	P95*	0.0529	**0.05988**	0.0102	0.007553	0.05283	**0.05987**	0.01019	0.007370
Ingestion	Count	95760	**95760**	95760	61064	104836	**104836**	104836	104836
	Mean*	0.03174	**0.03179**	0.0006820	0.0006595	0.02861	**0.02866**	0.0006146	0.0003831
	P50*	0.02617	**0.02611**	0.0002215	0.0001798	0.02342	**0.02342**	0.0001711	2.65e-05
	P95*	0.07635	**0.07683**	0.002450	0.002386	0.07404	**0.07471**	0.002314	0.001617
Inhalation Non-Respirable	Count	73328	**73328**	73328	48984	104836	**104836**	104836	104836
	Mean*	0.002787	**0.003756**	0.000932	0.001324	0.00192	**0.00259**	0.0006423	0.0005856
	P50*	5.4e-06	**1.712e-04**	3.80e-06	0.0002713	2.3e-06	**1.58e-05**	1.1e-06	0.0
	P95*	0.013054	**0.01761**	0.004840	0.005737	0.01089	**0.01473**	0.003906	0.003656
Inhalation Respirable	Count	73328	**73328**	73328	48984	104836	**104836**	104836	104836
	Mean*	0.019	**0.02592**	0.006355	0.008920	0.013084	**0.01786**	0.004383	0.003944
	P50*	3.4e-06	**7.25e-04**	6.14e-06	0.0007796	1.43e-06	**9.74e-06**	8.0e-07	0.0
	P95*	0.09735	**0.13124**	0.03445	0.04123	0.0804	**0.10971**	0.02746	0.02528
Total Systemic (Combined Oral, Dermal & Inhalation)	Count	104780	**104780**	104780	101413	104836	**104836**	104836	104836
	Mean*	0.06024	**0.0677**	0.00821	0.006820	0.06018	**0.06767**	0.008200	0.006577
	P50*	0.04486	**0.04785**	0.002665	0.001384	0.0448	**0.04781**	0.002659	0.001219
	P95*	0.1671	**0.19911**	0.03647	0.03317	0.1671	**0.19906**	0.03647	0.03238

* Units for Mean, P50 and P95 are µg/kg bw/day.

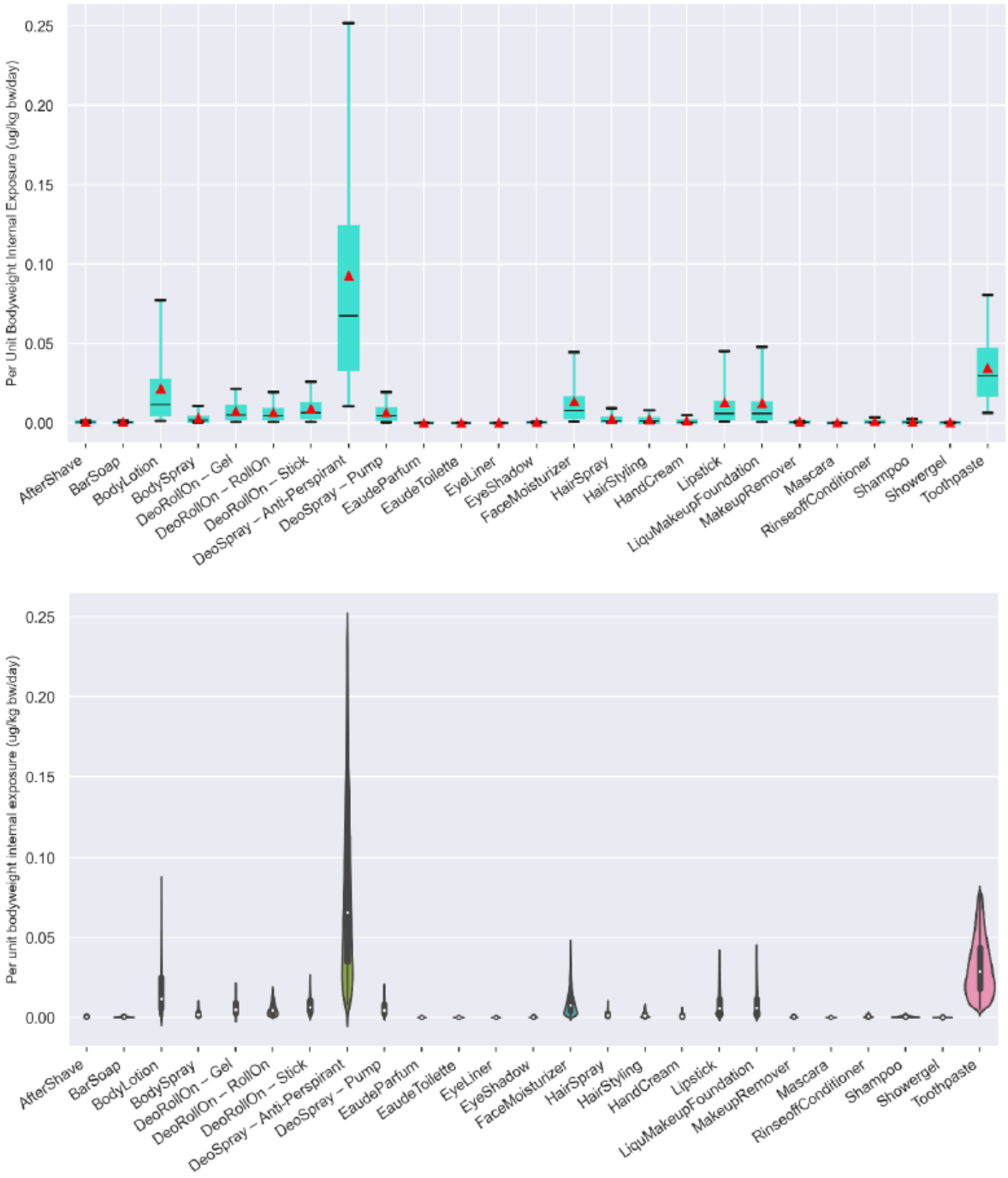


Figure 15A Distribution of internal exposure levels per cosmetic product, scenario 1b

SCCS comment

Of the presented scenarios, only Scenario 1 can be accepted according to the SCCS Notes of guidance (SCCS/1628/21), because Scenarios 2 and 3 use distributions for the concentrations in products and not the maximum levels. Scenario 3 in addition uses occurrence data that may change over time.

The SCCS in principle accepts the new inhalation exposure estimates calculated for Scenario 1b for sprayable products. However, since the transfer rate from Box 1 to Box 2 results in

less than 2 min residence time of the substance in Box 1 for the most relevant product deodorant, the SCCS adds an exposure estimate for the first 2 min based on the calculations in a previous dossier. For the other sprayable products this amount is considered to be covered by other conservatisms in the assumptions.

Adding up the respirable and non-respirable amounts from the first 2 min yields 1.749 mg, divided by 60 kg and with an AF of 100% instead of 76.4% (which is not accepted due to derivation from a dermally conservative value) yields 0.038 mg/kg BW /day.

However, since in Scenario 1b maximal amounts were changed for some product categories without justification, for dermal and oral exposure SCCS will use the original exposure assessment from Scenario 1 and derive the aggregate exposure over routes by adding the inhalation contribution from Scenario 1b.

3.2.4.7 Aggregate exposure with food and antacids

According to the Applicant, concentrations of aluminium in food were defined based on the 2006 UK Total Diet Study (Rose, *et al.*, 2010) which outlines aluminium concentration levels in 20 food groups, based on measurements. The 20 food groups were defined from the British Total Diet Study for Monitoring Food Constituents from 1981 (Peattie, 1983). Drinking water is the only food group not studied in Peattie, 1983. The aluminium concentration value of drinking water has been retrieved from the EU Drinking Water Directive 98/83/EC of 3 November 1985, which set a concentration limit of 0.2 mg/L. The WHO Drinking Water Guidelines (WHO, 2011) explain that it is reasonable to expect municipal drinking water treatment plants to contain between 0.1-0.2 mg/L. Estimates of aluminium in foods are for the element itself rather than an Al-ingredient, so a breakdown by Al-ingredient was not required.

According to the Applicant, the concentrations of aluminium in antacids are drawn from Micromedex data (Webb, 2000) and individual product websites. The Al-amount in one dosing ranges from 48.5 – 207 mg for different products.

Frequency of use and co-use in food was taken from the Dutch (DNFCS), Irish (NSIFCS) and UK (NDNS) national dietary surveys. The NSIFCS and NDNS surveys are 7-day semi-weighed food diaries and the DNFCS comprises 2 non-consecutive 24-hour diaries. Co-use of foods is automatically taken care of in the food consumption diaries.

Frequency of use data for antacids was not identified for European consumers and so US data was used as a proxy. Frequency of use data of antacids comes from a 30-day weighted US National Health and Nutrition Examination Survey (NHANES) 2007-2008 survey on supplement use. The results are based on a representative sample of 10,537 people in the US. Antacids are independent of all other products because the model does not assume any correlation between the consumption of antacids and the consumption of foods and cosmetics. Also, not all the subjects were considered as antacid-consumers by the model; only those subjects randomly matched with antacid-consumer subjects from the NHANES survey were considered as such. Hence, it is useful to contrast exposure estimates for the general population, which models less than 5% of consumers using antacids, and the 'exposed population' which assumes that antacid use is 100%.

The data of aluminium concentrations in food and drinking water are presented for aluminium as a standalone chemical not bounded to any specific compound, while antacids may contain different Al-ingredients. To make sure that the results obtained from all the different sources are comparable, the analyses must be carried out on the final concentrations of aluminium in every media.

The calculation of the exposure levels related to foods and antacids follows the same process previously described for cosmetics. The only difference is in the equation to calculate the exposure levels; exposure from foods and antacids must take in account other factors so equation (1) is to be substituted with two proper equations.
The aluminium exposure levels from food are calculated as

$$E_{ij} = \frac{F_{ij} \times A_{ij} \times X \times C_{ij}}{n \times BW} \quad (6)$$

Where each term on the right-hand side can be a fixed estimate or drawn from a distribution
and each term is understood as follows:
Eij is the systemic/internal exposure to aluminium from food group i [µg/kg/day]
Fij is the frequency of consumption events of food group i [day^{-1}] during the survey of length n days
Aij is the amount consumed at each consumption event of food group i [µg]
X is the oral bioavailability factor [%]
Cij is the concentration of aluminium in food group i [unitless]. Food groups according to the Applicant were: Bread, Miscellaneous cereals, carcass meat, offal, meat products, poultry, fish, oils and fats, eggs, sugars &
BW is the consumer's bodyweight [kg]

The aluminium exposure levels from antacids are calculated as:

$$E_{ij} = \frac{F_{ij} \times A_{ij} \times X \times C_{ij} \times P_{ij}}{30 \times BW} \quad (7)$$

Where each term on the right-hand side can be a fixed estimate or drawn from a distribution and each term is understood as follows:
Eij is the systemic/internal exposure to aluminium from antacid of brand i [µg/kg/day]
Fij is the frequency of consumption events of antacid of brand i [day^{-1}] during the survey of length 30 days
Aij is the recommended serving size of antacid of brand i [µg]
X is the oral bioavailability factor [%]
Pij is the occurrence of aluminium in antacid of brand i [unitless]
Cij is the concentration of aluminium in antacid i [unitless]
BW is the consumer's bodyweight [kg]

Table 17: Summary statistics of the internal exposure to Al per route for Scenario 1

Route	Statistics	Exposed Population				
		Ingestion	Dermal	Inhalation Respirable	Inhalation Non-Respirable	Total
All Ingested Al**	Count	104836	0	0	0	104836
	Mean*	0.1175	0.0000	0.0000	0.0000	0.1175
	P95*	0.1966	0.0000	0.0000	0.0000	0.1966
Antacids	Count	4264	0	0	0	4264
	Mean*	0.2341	0.0000	0.0000	0.0000	0.2341
	P95*	1.0391	0.0000	0.0000	0.0000	1.0391
Cosmetics	Count	95760	104780	73328	73328	104780
	Mean*	0.03174	0.01657	0.01899	0.002786	0.06023
	P95*	0.07636	0.05288	0.09733	0.01306	0.16715
Food	Count	104836	0	0	0	104836
	Mean*	0.0749	0.0000	0.0000	0.0000	0.0749
	P95*	0.1253	0.0000	0.0000	0.0000	0.1253

* Units for Mean and P95 are µg/kg bw/day.

** "All Ingested Al" is the combination of exposure from food, from antacids and from ingested cosmetics.

Conclusions by the Applicant:

• Food is the principal overall source of exposure to aluminium for the majority of the population.

• The population cohort taking antacids have the highest exposure to aluminium.

• Probabilistic estimates (Scenario 2 and 3) indicate that cosmetics contribute no more than 7-9% of mean aggregate exposures to aluminium, and 20-23% of P95 aggregate exposures, suggesting cosmetics are a minor source of aggregate consumer exposure.

• While the output of this exposure estimate suggests that inhalation exposure (primarily of aerosol deodorants) appears to be the main route of exposure to aluminium from cosmetics, the 2-Box model methodology is very conservative and overestimates inhalation exposure. There is scope to further refine this estimate with experimental measurements if needed.

• Overall, the margin of safety relative to the point of departure identified by the SCCS is sufficiently protective (4900 for Scenario 2, P95).

• In the context of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) tolerable weekly intake (TWI) of 2 mg/kg bw/week, which is equivalent to an internal systemic exposure of 1.8 µg/kg bw/day, total consumer exposure represents a small contribution to the tolerable intake, with cosmetics making a minor contribution of less than 0.5% (mean) and 2% (95th percentile) of the tolerable intake.

SCCS comment
The SCCS notes that food may contribute to the aggregate exposure to aluminium in the same order of magnitude as cosmetics, when the conservative estimate for cosmetics using maximum use levels is compared to the aggregate estimates for food. Pharmaceuticals such as antacids may contribute to a higher proportion but are consumed by only a small fraction of the population under different risk-benefit considerations.

3.3 TOXICOLOGICAL EVALUATION

The data related to toxicological evaluation were assessed and commented upon by the SCCS in the previous Opinion (SCCS/1613/19). Only SCCS' comments and main conclusions are included in this section.

General toxicity

The toxicological evaluation is focused on the toxicity of aluminium compounds relevant to the risk assessment of cosmetic ingredients containing aluminium. There is an extensive body of literature on the health effects and toxicity of aluminium; a number of extensive reviews and authoritative evaluations were published before 2014 (WHO IPCS 1997; Krewski *et al.*, 2007; ATSDR, 2008; EFSA, 2008; FAO/WHO JECFA 2007; Environment Canada & Health Canada 2010; AFSSAPS 2011; FAO/WHO JECFA, 2012; VKM 2013; Willhite *et al*., 2014). For the 2017 SCHEER Opinion on aluminium in toys, a literature search covering the period from 01/01/2008 until 31/01/2017 was performed. The evaluation by JECFA (2011) was based on new data which included a developmental toxicity study specifically evaluating neurobehavioural endpoints (Poirier *et al*., 2011). The LOAELs identified in these studies were consistent with the body of data reviewed previously by other committees; however, the oral developmental toxicity study in rats provided a suitable and robust NOAEL for risk assessment (30 mg/kg bw/day). By applying the standard uncertainty factor of 100 to this NOAEL and considering the bioavailability of aluminium citrate, the JECFA considered it appropriate to revise the PTWI (provisional tolerable weekly intake) upward to 2 mg/kg bw/week. This new data by the JECFA Committee therefore supersedes its earlier Opinions in 2008 and does not contradict the 2008 EFSA Opinion. The SCCS agrees on the NOAEL of 30 mg/kg bw/day used by JECFA for risk assessment.

Irritation/sensitisation

Local dermal effects have been observed when aluminium compounds (10% [w/v] chloride, nitrate) have been applied to the skin of mice, rabbits and pigs over five-day periods (once per day) including epidermal damage, hyperkeratosis, acanthosis and microabcesses (Lansdown, 1973). In this study, these effects were not observed with aluminium acetate, hydroxide or chlorohydrate compounds (SCCS/1626/20 Final version Addendum to the scientific opinion SCCS/1613/19 on the safety of aluminium in cosmetic products (lipstick) - Submission II).

Aluminium compounds are widely used in antiperspirants without acute harmful effects to the skin. Some people, however, may be unusually sensitive to topically-applied aluminium compounds. Skin irritation has been reported in human subjects following the application of aluminium chloride hexahydrate in ethanol used in a high-dose (20% ACH) formulation for the treatment of axillary or palmar hyperhidrosis (excessive sweating) (Ellis and Scurr, 1979; Goh, 1990; Reisfeld & Berliner, 2008) and after use of a crystal deodorant containing alum (Gallego *et al.,* 1999).

Although some high-strength antiperspirants used in hyperhidrosis treatments, using aluminium chloride, have been associated with irritation of the axilla, the long history of cosmetic antiperspirant use would suggest that irritation of the axilla is uncommon. There are several examples of cosmetic product formulations that include raw materials that are irritant in isolation, yet acceptable amongst consumers (e.g. surfactants, menthol).

With respect to skin sensitisation, the SCCS agrees that the available animal studies show that aluminium compounds used in antiperspirants are not skin sensitising. There is limited evidence that aluminium compounds can cause contact allergy in humans. However, taking into account the widespread use of these compounds, the SCCS considers this to be a rare phenomenon.

Mutagenicity/Genotoxicity

The most commonly reported mode of genotoxic action is induction of oxidative stress by aluminium ions. The other suggested MoA is inhibition by Al ions of proteins involved in mitotic spindle function. Hence, an existence of a threshold mechanism for Al ions can be assumed. Considering all the data, the SCCS is of the opinion that under the scenarios of dermal exposure in cosmetics, aluminium is not likely to pose a risk of genotoxic effects. The SCCS is aware of the request addressed by ECHA for a combined *in vivo* mammalian erythrocyte micronucleus test and an *in vivo* mammalian Comet assay with additional specific investigation on oxidative DNA damage in rats by oral route, using aluminium sulphate.

Carcinogenicity

Carcinogenicity studies in animals have been reviewed by the SCCS and were summarised in the Annex of the previous Opinion ((SCCS/1525/14, Revision of 18 June 2014). There was no indication of carcinogenicity at high dietary doses (up to 850 mg Al/kg bw/day) in animal studies, and the SCCS considers that carcinogenicity is not expected at exposure levels that are achieved via cosmetic use.

The new submission comprised only a new exposure assessment, not a new toxicological evaluation. Therefore, only the study selected previously for the safety assessment (Poirier et al, 2011) is reported here in detail, all other studies are summarised and discussed in preceding Opinions, notably in SCCS/1613/19. Only the final SCCS statement taken from discussion of the previous Opinion is reported here for transparency.

Since the last SCCS Opinion 1613/19, two additional papers on the effects of aluminium chloride on chromosomal integrity in mammalian cells have been published, continuing the work of Sappino *et al.* (2012) and Mandriota (2016).
In the study by Mandriota *et al*. (2020) normal mouse mammary epithelial cells after long-term culture in the presence of aluminium chloride formed tumours and metastases when injected into syngeneic and immunocompetent BALB/cByJ mice. As was shown by the authors $AlCl_3$ rapidly increased chromosomal structural abnormalities in the cultured cells.
In the second study by Tenan *et al.* (2021) in V79 hamster lung fibroblasts exposed to aluminium dose-dependent increases in DNA double strand breaks, and chromosome numerical abnormalities (aneuploidy) as well as arrest in the G2/M phase of the cell cycle, were observed. Additionally, during mitosis, abnormal multipolar mitotic spindles were detected.
Additionally, García-Alegría *et al.,* 2020 investigated aluminium chloride alone and in co-treatment with MNU in female Sprague Dawle rats. They treated rats with 1mL (2000mg/L) of aluminium solution 5 days per week and sampled blood at 5, 10, and 15 days of exposure. They found significant time dependent increase in micronucleus induction as well as DNA damage measured by the comet assay. However, only one concentration of

aluminium chloride was used with three exposure time points. In study of Jalili *et al*., 2020 acute exposure to aluminium chloride induced slight but non-significant oxidative DNA damage in peripheral blood lymphocytes. No increase of micronuclei in both bone marrow cells and in colon was observed.
Based on analysis of the whole series of 4 articles by the same group as well as additional literature, the SCCS acknowledges that aluminium ions may disturb structural and functional features of chromosomal material in the cells; however, the potential of the ions to induce such effects in the organism after exposure to cosmetic products is still unknown and rather implausible. There is no additional data available to support a link between skin penetration of aluminium and the occurrence of genotoxic effects at relevant exposure conditions. Based on the actual available information the SCCS is of the opinion that there is no concern for carcinogenicity in the context of use in cosmetics.

Fertility and reproduction toxicity

Poirier *et al.*, 2011, reported a 12-month neuro-developmental toxicity study of aluminium citrate. The study in Sprague-Dawley rats was conducted according to a double-blind, vehicle-controlled randomised design by exposing offspring to aluminium citrate in-utero, through lactation, and then via drinking water post-weaning. The study was conducted according to Good Laboratory Practice (GLP) and was conducted to distinguish between cumulative neurodegenerative and cognitive changes from aberrant neural development alterations. Three dose levels were used: 30, 100, 300 mg Al/kg bw/day, in addition to control groups that received either water or a sodium citrate solution (27.2 g/L) compared to 27.2 g sodium citrate/L in the control group. Aluminium citrate was selected for the study since it is the most soluble and bioavailable aluminium salt. It is also the salt which is likely to be formed readily in the body when absorbed aluminium reacts with endogenous citrate. Pregnant dams (n=20 per group) were exposed to aluminium citrate from gestational day 6 through lactation, and then the offspring (n = 80 per group) were exposed post-weaning until postnatal day 364.
Aluminium citrate was generally well tolerated in the dams at all doses, except the high dose (300 mg Al/kg bw/day) where diarrhoea occurred in 8 of the treated dams. In high-dosed pups, the main toxic effects were observed in the urinary tract (damage and the formation of calculi (chalky secretions blocking the urinary tract)), resulting in high mortality in the male offspring (see Table 3 below). This caused a differential response in female and male pups. High-dose males were euthanised on study day 98 because of excessive clinical signs (including weight loss, diarrhoea, mild dehydration and poor hair coat).

In the same study, Poirier also evaluated the relative distribution of aluminium following repeated oral administration of various aluminium salts. Sprague–Dawley rats (n= 5 per sex per group) were orally gavaged with formulations of aluminium citrate, sulphate, nitrate, chloride and hydroxide, each delivering a dosage of 30 mg/kg body weight aluminium. Control animals were similarly dosed with deionised water. Animals were dosed daily for either 7 days or 14 days, followed by blood and organ collection. The distribution and concentrations of aluminium present in different tissues and organs, were measured by ICP Mass Spectrometry. From this analysis, concentrations in the blood were much lower than those that distributed heterogeneously into other tissues and organs, in both females and males. The authors state that 'of the few significant differences, concentrations of aluminium were highest for the aluminium citrate treatment.' The authors further conclude from their data that 'bioavailability of the three Al salts (chloride, sulfate and nitrate) and the Al hydroxide looks much lower than that of the Al citrate'.

However, as ^{26}Al was not used as a tracer, it is not possible to know the absolute oral bioavailability of the administered dose.

SCCS comment
Based on the results of this neurodevelopmental toxicity study, the SCCS derives a NOAEL of 30 mg/kg bw/day, which will be used for MoS calculation. This is in line with SCHEER (2017), where the same NOAEL from the same study was used to derive migration limits for Al in toys.

Furthermore, on the basis of available information on solubility (Annex 1 of SCCS/1613/19), the SCCS agrees that aluminium citrate can be regarded as the most bioavailable of the Al salts assessed in this Opinion. Therefore, the derived NOAEL can be regarded as a worst case for all aluminium salts discussed in this Opinion.

Human data

The SCCS considers that aluminium is a known neurotoxicant in animals. Circumstantial evidence has linked this metal with several neurodegenerative disorders, like Alzheimer's disease (Miu and Benga, 2006; Percy *et al.*, 2011), Parkinson's diseases (Oyanagi, 2005) and other chronic neurodegenerative diseases (Bondy, 2010), but no causal relationship has yet been proven.

3.4 SAFETY EVALUATION (including calculation of the MoS)

The new submission comprised only a new exposure assessment, not a new toxicological evaluation. Some new scientific studies on genotoxicity, which have become available lately, have been evaluated by the SCCS, but do not change the general picture. Therefore, the toxicological assessment, selected NOAEL and point of departure derived in SCCS/1613/19 remain valid.

Based on the results of the neurodevelopmental toxicity study on rats with aluminium citrate (Poirier *et al*., 2011), the SCCS derived a NOAEL of 30 mg aluminium citrate/kg bw/day. After adjustment for the rat oral bioavailability (0.6%) of aluminium citrate (Poirier *et al.,* 2011, Zhou *et al.,* 2008), the systemic exposure at the NOAEL is estimated to be **180 µg Al/kg bw/day**. This value is used as a point of departure for the safety assessment and MoS calculation.

The provided exposure report included an aggregate exposure assessment of all Cosmetic categories containing aluminium at maximum levels (Scenario 1). The respective aggregate estimate is considered valid as aggregate value for all assessed product categories, for which the main exposure routes are dermal and oral exposure. The deterministic assessment to aluminium in sunscreens needs to be added to this aggregate assessment.

Table 18: Calculation of aggregate exposure and MoS for aluminium-containing cosmetics

Product type	Systemic Exposure (internal dose) µg Al/kg bw/day	Remarks	MOS based on POD of 180 µg Al/kg bw/day
Dermal from exposure report	0.053	P95, exposed population, Table 15	3403
Dermal sunscreen lotion, deterministic	0.484	Deterministic calculation, max. content, NoG, Table 9	372
Oral from exposure report	0.076	P95, exposed population, Table 15	2358
Inhalation from addendum (respirable + non-respirable)	0.149	P95, exposed population, Table 15A	1209
Inhalation for deodorant first 2 min	0.03		4718
Aggregation over routes	**0.800**		**225**

SCCS conclusion
Under the assumption that approximately 20% of the spray particles are <10 µm for aerosol spray products, the SCCS considers that Al is safe for use in antiperspirant and deodorant products (spray and non-spray) and all other product categories.

3.5 DISCUSSION

Physicochemical properties

Physicochemical properties of aluminium compounds that can generally be used as cosmetic ingredients have been summarised in Annex I of the previous SCCS Opinion (SCCS/1613/19). These encompass aluminium compounds in water-soluble and water-insoluble form. The water-soluble Al-containing compounds form are simple inorganic salts, simple organic salts, aluminium benzoate, and chlorohydrates, which can be used in skin care products. Water-insoluble aluminium containing ingredients can be minerals, glasses and clays, aluminium lakes, carbohydrates, fatty acid salts, which are typically added to cosmetic products as bulking agents, coloured pigments, and sometimes as mild abrasives.

The new submission presents an industry survey that indicates the substances actually in use along with their amounts. The INCI names and CAS numbers of these substances are given in Tables 2 and 3 of this Opinion. The respective physicochemical properties of the substances can be retrieved from Annex 1 of SCCS/1613/19.

On the basis of available information on solubility (Annex 1 of SCCS/1613/19), the SCCS agrees that aluminium citrate may exhibit the highest bioavailability amongst the Al salts assessed in this Opinion.

Exposure assessment & Toxicokinetics

The SCCS understands that the 'Al-concentrations' of Al-containing cosmetics ingredients mentioned in Tables 2 and 3 represent the Al-contents in terms of the stochiometric ratios of Al in these ingredients.

It is unclear to the SCCS why a range of Al-contents ('Al-concentrations') in the Al-ingredient for some of the Al-ingredients may result from the defined stoichiometry of the chemical substance (*e.g.* for potassium aluminium sulphate in Table 3). However, the SCCS has calculated the Al-contents based on stoichiometry and found no underestimation of Al-content in the upper bound (max value). Therefore, risk assessment based on exposure calculations with these maximum values is considered valid.

Some products had been excluded from the aggregate exposure assessment (see Tables 5, 7) without explanation in the submitted report. Upon request, the Applicant has submitted the explanation along with additional deterministic assessment of dermal exposure from sunscreen creams and lotions. The assessment using the maximum Al level possible is considered valid by the SCCS.

The SCCS considers that sunscreen products should be included in the assessment, because on a seasonal basis they are used regularly, even daily, and due to the high amount applied may present a large exposure source. Furthermore, the presence probability of aluminium in sunscreens is 30%, which cannot be considered negligible.

Some of the products that have not been considered may also be used regularly (shaving products, eyeliner, eye contour products and lip care products). However, for these products the exposure potential is low and the tonnage of Al-containing products sold is also low. Therefore, their contribution to dermal exposure can be considered as negligible and these products can be considered safe for use.

Scenario 1 can be accepted according to the SCCS Notes of guidance (SCCS/1628/21), but not Scenarios 2 and 3, because these use distributions for the concentrations in products and not the maximal levels. Scenario 3 in addition uses occurrence data that can be specific in time.

The SCCS notes that food may contribute to the aggregate exposure to aluminium in the same order of magnitude as cosmetics, when deterministic estimates are compared across the sectors food, pharmaceuticals and cosmetics. Pharmaceuticals such as antacids may contribute to a higher degree but are consumed by only a small fraction of the population under different risk-benefit considerations.

Toxicological Evaluation

The new submission comprised only a new exposure assessment, not a new toxicological evaluation. Some new scientific studies on genotoxicity, which have become available lately, have been evaluated by the SCCS, but do not change the general picture. Therefore, the toxicological assessment, selected NOAEL and point of departure derived in SCCS/1613/19 remain valid.

Based on the results of the neurodevelopmental toxicity study, the SCCS derived a NOAEL of 30 mg/kg bw/day. After adjustment for the rat oral bioavailability (0.6%) of aluminium

citrate, the systemic exposure at the NOAEL is estimated to be 180 µg Al/kg bw/day. This value is used as a point of departure for the safety assessment and MoS calculation.

4. CONCLUSION

1. In light of the new data provided, does the SCCS consider Aluminium compounds safe when used in cosmetic products other than deodorants, antiperspirants, lipsticks and toothpastes? In the event that the estimated exposure to Aluminium from cosmetic products is found to be of concern, SCCS is asked to recommend safe concentration limits for each category.

The SCCS considers that aluminium compounds are safe when used

- in non-sprayable product categories at the maximum levels indicated in Tables 4 and 6; and
- in sprayable products, at the maximum levels indicated in Table 4, provided that the percentage of particles/droplets with a diameter of less than 10 µm does not exceed 20% of the total aerosolised particles/droplets. Since the Applicant's data submission indicated that aluminium is not used in sunscreen aerosol sprays, this Opinion does not cover sunscreen aerosol sprays.

2. Does the SCCS have any further scientific concerns regarding the use of relevant Aluminium compounds in cosmetic products taking into account the newly submitted information on aggregate exposure to Aluminium from cosmetics, medicines (e.g. antacids) and food intake?

As aluminium does not belong to substances classified as CMR 1A or B, only exposure from cosmetic uses was considered in this safety assessment with the exposure assessment based on maximum use levels for cosmetic ingredients.

However, the submission also provided a scenario where realistic exposure from non-cosmetic sources of aluminium (food and pharmaceuticals) was aggregated along with exposure from cosmetics at use levels from the year 2016. From this scenario, it can be deduced that contribution to aluminium exposure from food may be at a similar order of magnitude to that from cosmetics used for the safety assessment. Considering the conservative nature of the estimates, the aggregate exposure to aluminium from cosmetic and non-cosmetic sources may exceed safe limits for consumers at the highest exposure ranges.

5. MINORITY OPINION

/

6. REFERENCES

AFSSAPS (2011). Agence Française de Sécurité Sanitaire des Produits de Santé. Evaluation du risque lié à l'utilisation de l'aluminium dans les produits cosmétiques, 43 pages (report in French).

Alejandro Monserrat García-Alegría, Agustín Gómez-Álvarez, Iván Anduro-Corona, Armando Burgos-Hernández, Eduardo Ruíz-Bustos, Rafael Canett-Romero, Humberto González-Ríos, José Guillermo López-Cervantes, Karen Lillian Rodríguez-Martínez, Humberto Astiazaran-Garcia Genotoxic Effects of Aluminum Chloride and Their Relationship with N-Nitroso-N-Methylurea (NMU)-Induced Breast Cancer in Sprague Dawley Rats Toxics. 2020 Apr 20;8(2):31. doi: 10.3390/toxics8020031.

Api A.M., Basketter D.A., Cadby P.A., Cano M.F., Ellis G., Gerberick G.F., Griem P., McNa mee P.M., Ryan C.A., Safford R. (2008). Dermal sensitization quantitative risk assessment (QRA) for fragrance ingredients. Regulatory toxicology and pharmacology: RTP, 52(1), 3–23. doi:10.1016/j.yrtph.2007.10.008

ATSDR (2008). Toxicological profile for aluminium. Atlanta GA.: U.S. Department of Health and Human Services, Public Health Service. pp357.

BfR (2020). New studies on antiperspirants containing aluminium: impairments to health unlikely as a result of aluminium uptake via the skin, BfR Opinion No 030/2020 of 20 July 2020, https://doi.org/10.17590/20200813-130651

Biesterbos, J., T Dudzina, C Delmaar, M Bakker, F Russel, N von Goetz, P Scheepers, N Roeleveld. Usage patterns of personal care products: important factors for exposure assessment. Food and Chemical Toxicology 55 (2013) 8–17.

Bondy SC. (2010). The neurotoxicity of environmental aluminium is still an issue. Neurotoxicology. 2010 Sep;31(5):575-81.

Bremmer, H.J., Prud homme de Lodder, L.C.H., van Engelen, J.G.M., 2006a. Cosmetics Fact Sheet to assess the risk for the consumer. Updated version for ConsExpo 4. RIVM report 320104001/2006. https://www.rivm.nl/bibliotheek/rapporten/320104001.pdf

Bremmer, H.J., Prud homme de Lodder, L.C.H., van Engelen, J.G.M., 2006b. General Fact Sheet – Limiting conditions and reliability, ventilation, room size, body surface area. Updated version for ConsExpo 4, RIVM report 320104002/2006
http://www.rivm.nl/bibliotheek/rapporten/320104002.pdf

Comiskey D., Api A.M., Barrett C., Ellis G., McNamara C., O'Mahony C., Robison S.H., Rose J., Safford B., Smith B., Tozer S., 2017. Integrating habits and practices data for soaps, cosmetics and air care products into an existing aggregate exposure model. Regulatory Toxicology and Pharmacology, 88:144-156

Carthew *et al.* 2002 Safety Assessment for Hair-Spray Resins: Risk Assessment Based on Rodent Inhalation Studies, International Forum for Respiratory Research, Volume 14, 2002 - Issue 4. https://doi.org/10.1080/08958370252871023

Cosmetics Europe, 2016. Dossier on the Human Safety Evaluation of Aluminium in Cosmetic Products. For Submission to the Scientific Committee on Consumer Safety

DeVoto, E., Yokel, R.A., 1994. The biological speciation and toxicokinetics of aluminium. Environ Health Perspect. Nov; 102(11): 940-51.

ECETOC, 2016. Guidance for Effective Use of Human Exposure Data in Risk Assessment of Chemicals. Technical Report No. 126. Brussels, November 2016. Technical Report no.126 - Guidance for Effective Use of Human Exposure Data in Risk Assessment of Chemicals - ECETOC

ECHA 2016. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.15: Consumer exposure assessment. Version 3.

EFSA 2008. Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC). Safety of aluminium from dietary intake. The EFSA Journal. 6(7); 754: 1-34

Environment Canada & Health Canada (2010) Priority substances list assessment report follow up to the state of science report 2000: aluminium chloride, aluminium nitrate, aluminium sulphate. Available at https://www.ec.gc.ca/lcpecepa/default.asp?lang=En&n=491F0099-1

Ficheux A.S., Chevillotte G., Wesolek N., Morisset T., Dornic N., Bernard A., Bertho A., Romanet A., Leroy L., Mercat A.C., Creusot T., Simon E., Roudot A.C., 2016. Consumption of cosmetic products by the French population second part: Amount data. Food and Chemical Toxicology, 90, pp. 130-141

Finley, B., Proctor, D., Scott, P., Harrington, N., Paustenbach, D., Price, P., 1994. Recommended distributions for exposure factors frequently used in health risk assessment. Risk Anal. 14, 533-553

Hall B., Tozer S., Safford B., Coroama M., Steiling W., Leneveu-Duchemin M.C., McNamara C., Gibney M. 2007. European consumer exposure to cosmetic products, a framework for conducting population exposure assessments. Food and Chemical Toxicology.

Hall B., Steiling W., Safford B., Coroama M., Tozer S., Firmani C., McNamara C., Gibney M. 2010. European consumer exposure to cosmetic products a framework for conducting population exposure Part 2. Food and Chemical Toxicology.

JECFA (2007). Aluminium from all Sources, including Food Additives. Safety evaluation of certain food additives and contaminants: Prepared by the sixty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series. 58: 119-207. http://apps.who.int/iris/bitstream/10665/43645/1/9789241660587_eng.pdf

JECFA (2012). Aluminium-containing food additives (addendum). Safety evaluation of certain food additives and contaminants: Prepared by the seventy-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series. 65: 3-86. http://whqlibdoc.who.int/publications/2012/9789241660655_eng.pdf

Joint FAO/WHO Expert Committee on Food Additives (JECFA) report TRS 996-JECFA 74/7 (2011 update) Evaluation of Certain Food Additives and Contaminants. Chapter 3, Section 3.1.1. http://apps.who.int/iris/bitstream/10665/44788/1/WHO_TRS_966_eng.pdf#page=18

Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, Kacew S, Lindsay J, Mahfouz AM, Rondeau V. J (2007) Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. Toxicol Environ Health B Crit Rev.10 Suppl 1:1-269.

Lippmann M, (1977) Regional deposition of particles in the human respiratory tract, In: Handbook of Physiology, Section 9: Reactions to Environmental Agents, Lee DHK, Falk HL, Murphy SD, Giger SR (eds), American Physiological Society, Bethesda, MD, 213.

Loretz, L.J., Api A.M., Barraj L.M., Burdick J., Dressler W.E., Gettings S.D., Han Hsu H., Pan Y.H., Re T.A., Renskers K.J., Rothenstein A., Scrafford C.G., Sewall C. 2005. Exposure data for cosmetic products: lipstick, body lotion, and face cream. Food and Chemical Toxicology.

Loretz, L.J., Api A.M., Barraj L., Burdick J., Davis de A., Dressler W., Gilberti E., Jarrett G., Mann S., Laurie Pan Y.H., Re T., Renskers K., Scrafford C., Vater S. 2006. Exposure data for personal care products: Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. Food and Chemical Toxicology.

Loretz L.J., Api A.M., Babcock L., Barraj L.M., Burdick J., Cater K.C., Jarrett G., Mann S., Pan Y.H., Re T.A., Renskers K.J., Scrafford C.G. 2008. Exposure data for cosmetic products: Facial cleanser, hair conditioner, and eye shadow. Food and Chemical Toxicology.

Mandriota SJ, Tenan M, Nicolle A, Jankowska JD, Ferrari P, Tille JC, Durin MA, Green CM, Tabruyn S, Moralli D, Sappino AP. Genomic Instability Is an Early Event in Aluminium-Induced Tumorigenesis. Int J Mol Sci. 2020 Dec 7;21(23):9332. doi: 10.3390/ijms21239332.

Meech, 2011. Study report. Project Zoom Antipersipirant Aerosol: Antiperspirant Simulated Use Evaluation. Study DS090138. Unilever

Meek M.E., Boobis A.R., Crofton K.M., Heinemeyer G., Van Raaij M., Vickers C. Risk assessment of combined exposure to multiple chemicals: A WHO/IPCS framework. Regulatory Toxicology and Pharmacology (2011), doi: 10.1016/j.yrtph.2011.03.010

Miu AC, Benga O (2006). Aluminium and Alzheimer's disease: a new look. Alzheimers 10 (2-3):179-201.

Nicas, Mark. (2014). Estimating exposure intensity in an imperfectly mixed room. American Industrial Hygiene Association Journal; June 1996; 57:6:542.

Oyanagi K. (2005). The nature of the parkinsonism-dementia complex and amyotrophic lateral sclerosis of Guam and magnesium deficiency. Parkinsonism Relat Disord. 11, Suppl 1: S17-23.

Peattie, M.E., Buss D.H., Lindsay D.G., Smart G.A., 1983. Reorganisation of the British Total Diet Study for Monitoring Food Constituents from 1981. Food and Chemical Toxicology 21, pp. 503-507.

Pégah Jalili, Sylvie Huet, Rachelle Lanceleur, Gérard Jarry, Ludovic Le Hegarat, Fabrice Nesslany, Kevin Hogeveen, and Valérie Fessard Genotoxicity of Aluminum and Aluminum Oxide Nanomaterials in Rats Following Oral Exposure Nanomaterials (Basel). 2020 Feb; 10(2): 305. Published online 2020 Feb 11. doi: 10.3390/nano1002030 PMCID: PMC7075173 PMID: 32053952

Poirier J, Semple H, Davies J, Lapointe R, Dziwenka M, Hiltz M and Mujibi D. (2011). Double-blind, vehicle-controlled randomized twelve-month neurodevelopmental toxicity study of common aluminium salts in the rat. Neuroscience. 193: 338-362.

Reisfeld R, Berliner KI (2008) Evidence-based review of the nonsurgical management of hyperhidrosis. Thorac Surg Clin. 18(2):157-66.

Rose, M., Baxter, M., Brereton, N. & Baskaran, C., 2010. Dietary exposure to metals and other elements in the 2006 UK total Diet Study and some trends over the last 30 years. Food Additives and Contaminants 27 (10), pp. 1380 - 1404

Rothe, H., Fautz, R., Gerber, E., Neumann, L., Rettinger, K., Schuh, W., Gronewold, C., 2011. Special aspects of cosmetic spray safety evaluations: principles on inhalation risk assessment. Toxicol. Lett., 205 (2011), pp. 97-104

SCCS (Scientific Committee on Consumer Safety), Opinion on the safety of aluminium in cosmetic products, preliminary version of 30-31 October 2019, final version of 03-04 March 2020, SCCS/1613/19

Salem, H., Katz, S.A., 2006. Inhalation Toxicology, 2nd ed. CRC Taylor & Francis, BocaRaton, USA (ISBN-10: 0849340497)

Sahmel J, Unice K, Scott P, Cowan D, 1Paustenbach D (2009). The use of multizone models to estimate an airborne chemical contaminant generation and decay profile: Occupational exposures of hairdressers to vinyl chloridein hairspray during the 1960s and 1970s. Risk Analysis, Vol. 29, No. 12, 1699-1725.

Scientific Committee on Consumer Safety (SCCS). 2012. The SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation – 8th revision.

Scientific Committee on Consumer Safety, 2015. The SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation 9th revision. SCCS/1564/15

Scientific Committee on Consumer Safety, 2015. The SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation 10th revision. SCCS/1602/18

Schwarz *et al.* 2018, A methodology for the assessment of inhalation exposure to aluminium from antiperspirant sprays, Archives of Toxicology volume 92, pages1383–1392(2018) https://doi.org/10.1007/s00204-017-2151-2

Singal, M., Pandian, M., Joachim, F., Corea, N., Jones, L., & Smith, L. (2010). Estimating Inhalation Exposure to Fragrance Materials in Air Freshening Products using a Two-Zone Residential Indoor Air Dispersion Model. 2010 Society of Toxicology 49th Annual Meeting & ToxExpo. SaltLake City, Utah.

Steiling W., Buttgereit P., Hall B., O'Keeffe L., Safford B., Tozer S., Coroama M., 2012. Skin Exposure to deodorants/antiperspirants in aerosol form. Food and Chemical Toxicology, pp. 2206-2215.

Steiling, W., Bascompta, M., Carthew, P., Catalano, G., Corea, N., D'Haese, A. & Singal, M. (2014). Principle considerations for the risk assessment of sprayed consumer products. Toxicology letters, 227(1), 41-49.

Tenan MR, Nicolle A, Moralli D, Verbouwe E, Jankowska JD, Durin MA, Green CM, Mandriota SJ, Sappino AP. Aluminum Enters Mammalian Cells and Destabilizes Chromosome Structure and Number. Int J Mol Sci. 2021 Sep 1;22(17):9515. doi: 10.3390/ijms22179515.

TNO 2019 Final Assessment of bioavailability of aluminium in humans after topical application of a representative antiperspirant formulation using a [26Al] microtracer approach. 09-05-2019. Study report R10508. Study commissioned by the Cosmetics Industry via Cosmetics Europe, 09-05-2019

Unilever 2015. Making Compressed Commonplace, Technical White Paper. http://www.compresseddeodorants.com/assets/content/uk/Compressed_white_paper_22-02-2016.pdf

VKM 2013 Norwegian scientific Committee for Food Safety, Risk assessment of the exposure to aluminium through food and the use of cosmetic products in the Norwegian population, 5 April 2013

Webb, S., 2000. Overview on Human Exposure to Aluminium. Procter & Gamble EMEA. Scientific & regulatory affairs.

Willhite CC, Karyakina NA, Yokel RA, Yenugadhati N, Wisniewski TM, Arnold IMF, Momoli F, Krewski D (2014) Systematic review of potential health risks posed by pharmaceutical, occupational and consumer exposures to metallic and nanoscale aluminium, aluminium oxides, aluminium hydroxide and its soluble salts. Criticl reviews in Toxicology, 44:sup4, 1-80.

World Health Organization, 2011. Chemical fact sheets. Retrieved at https://www.who.int/water_sanitation_health/publications/2011/9789241548151_ch12.pdf#Page=5

WHO IPCS (International Programme on Chemical Safety) (1997). Aluminium. Environmental Health Criteria 194. United Nations Environment Programme. Geneva: World Health Organization, pp. 1–214. Available at: http://www.inchem.org/documents/ehc/ehc/ehc194.htm

Zhou Y, Harris WR, Yokel RA (2008) The influence of citrate, maltolate and fluoride on the gastrointestinal absorption of aluminium at a drinking water-relevant concentration: A 26Al and 14C study. J Inorg Biochem;102(4)798–808.

7. GLOSSARY OF TERMS

See SCCS/1628/21, 11th Revision of the SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation – from page 181.

8. LIST OF ABBREVIATIONS

See SCCS/1628/21, 11th Revision of the SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation – from page 181.