Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

Comments on the Scientific Committee on Consumer Safety (SCCS)'s opinion on the safety of aluminium in cosmetic products

Statement of the Norwegian Scientific Committee for Food Safety

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Contributors

Persons working for VKM, either as appointed members of the Committee or as *ad hoc* experts, do this by virtue of their scientific expertise, not as representatives for their employers. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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Background

On March 27, 2014, the Scientific Committee on Consumer Safety (SCCS) published their "Opinion on the safety of aluminium in cosmetic products" (SCCS/1525/14). This opinion is open for comments until 26 May 2014. In the opinion, the SCCS concludes 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". Further, the SCCS concludes *"Therefore internal exposure to aluminium after skin application should be determined using a human exposure study under use conditions"*.

On April 5, 2013, the Norwegian Scientific Committee for Food Safety (VKM) published the risk assessment entitled "Risk assessment of the exposure to aluminium through food and the use of cosmetic products in the Norwegian population". In this opinion, the total exposure to aluminium (Al) as a summation of the estimated dietary exposure and estimated exposure through the use of cosmetic products was calculated, and compared with the tolerable weekly intake (TWI) of 1 mg Al/kg bw/week established by EFSA (2008) and the provisional tolerable weekly intake (PTWI) of 2 mg Al/kg bw/week established by JECFA (2012).

The estimated dietary exposure to aluminium was based on national food consumption surveys for various age groups and the aluminium concentration in food on the Norwegian market. The additional contribution from the use of cosmetics was estimated as the systemic exposure dose (SED) from topical application of cosmetic products in different age groups. Lipstick/lip gloss, antiperspirants and a few brands of whitening toothpaste were considered the relevant sources of Al through cosmetics. For estimations of exposure to Al in the Norwegian population from cosmetics, occurrence data from cosmetic products on the Norwegian market were used. Dermal absorption of Al was based on the on skin penetration data from a human *in vitro* study by Pineau *et al.* (2012).

As the aluminium exposures from food and from the use of cosmetic products were estimated using different approaches the two estimates could not be directly compared. To sum up the two routes of exposures as total exposure, the dietary exposure was converted to a systemic exposure taking into account the low oral bioavailability (0.1%) of aluminium. Also, for comparison, the TWI set by EFSA (2008) was recalculated to a systemic TWI of 1 µg Al/kg bw/week, while the PTWI set by JECFA (2012) was converted to a systemic PTWI of to 2 µg Al/kg bw/week, assuming similar toxicity following oral and dermal exposure to aluminium. Please see the opinion for further details.

In its opinion in 2014, SCCS concluded for studies on dermal /percutaneous absorption that "The available studies are of poor quality and have not been carried out according to the current requirements. In the absence of any better data to estimate skin penetration of aluminium, the SCCS considers that aluminium absorption after dermal exposure is still very poorly understood. A conclusion on internal exposure to aluminium following cosmetic use cannot be drawn". This statement also included the study by Pineau *et al.* (2012) used by VKM in their risk assessment.

In this risk assessment from VKM, it was concluded that nine-year-old children, 13-year-old adolescents and adults may have an exposure to aluminium through the use of cosmetic products (lipstick/lip gloss, antiperspirants and/or whitening toothpaste) in addition to the contribution from food. The use of cosmetic products, in particular antiperspirants, contributed substantially to the total systemic exposure to aluminium. Both for adolescence and adults, the mean and high (95-percentile) total systemic exposures exceeded the systemic TWI and PTWI values in the standard scenarios (0.6% skin absorption, normal skin) and even more so in the worst case scenarios (10.7% skin absorption, stripped skin).

For persons using lipstick/lip gloss daily, the mean and high total systemic exposures varied from 0.51 to 1.4 µg Al/kg bw/week, depending on age group, in a standard scenario (0.6% skin absorption, normal skin). Only the total systemic exposure for 9-year-old children equaled (mean exposure) or exceeded (high exposure) the systemic TWI of 1 µg Al/kg bw/week. None of the estimated exposures exceeded the systemic PTWI of 2 µg Al/kg bw/week. In a worst case scenario (10.7% skin absorption, stripped skin), the mean and high total systemic exposures ranged from 4.5 to 14 µg Al/kg bw/week, depending on age group. The estimates exceeded both the systemic TWI and the systemic PTWI.

Adolescents and adults are assumed to use lipstick/lip gloss and/or antiperspirants on a daily basis. With the additional contribution from the use of lipstick/lip gloss and antiperspirants, the mean and high total systemic exposures varied from 30 to 50 µg Al/kg bw/week, depending on age group, in a standard scenario (0.6% skin absorption, normal skin). In a worst case scenario (10.7% skin absorption, stripped skin), the mean and high total systemic exposures ranged from 600 to 940 µg Al/kg bw/week, depending on age group. All the estimates exceeded the systemic TWI and the systemic PTWI. The additional use of whitening toothpaste containing aluminium did not contribute much to the total systemic exposure to aluminium in adults.

Terms of reference

In light of the opinion on the safety of aluminium in cosmetics from SCCS (SCCS, 2014), and with reference to the above explanations given in the letter from the Norwegian Food Safety Authority (dated April 29, 2014), VKM is requested to clarify the following points:

- Does VKM still think that the dermal penetration data generated by Pineau *et al.* (2012) can be used for estimation of systemic exposure dose (SED)? Please provide justification for the answer.
- Does VKM agree with the SCCS regarding the necessity of human (*in vivo*) dermal penetration data as a basis for risk assessment of aluminium in cosmetics?
- Does VKM have other comments pertaining to other aspects of the SCCS opinion?
- What, if any, consequences does VKM think the SCCS draft opinion has for its own risk evaluation of aluminium as published 5 April 2013?

Assessment

Question 1 from the Norwegian Food Safety Authority:
Does VKM still think that the dermal penetration data generated by Pineau *et al.* (2012) can be used for estimation of systemic exposure dose (SED)? Please provide justification for the answer.

In the risk assessment of Al performed in 2013, VKM used the SCCS's notes of guidance for the testing of cosmetic ingredients and their safety evaluation, as requested in the terms of reference from the Norwegian Food Safety Authority. The 7th revision of the guideline was used (SCCS/1416/11), which was adopted by SCCS December 14, 2010. In this guideline, Chapter 3-4.4 Dermal/percutaneous absorption on pages 32-34 was consulted and also included in Appendix 1 in VKM's risk assessment. In Chapter b. The SCCS "Basic criteria" in this guideline document a list of points that require special attention when performing *in vitro* studies of dermal absorption were given.

Regarding the dermal absorption of Al, VKM found that the study by Pineau *et al.* (2012) was the best available study at that time. Although not perfect according to the criteria set by SCCS, it was regarded as fulfilling most of the SCCS's requirements, and was therefore chosen for the estimations of SED in this opinion. Since it was regarded that this study did not significantly deviate from the protocol, the mean+1SD was used.

It is correct as SCCS states that mass balance analysis and recovery data were not included in this paper. However, VKM uses published scientific studies in the open literature for its risk assessments. Unless provided in the published papers by the authors or sometimes supplied by industry, data from other sources will most likely remain unknown and unavailable for use in risk assessments.

It is also correct as SCCS states that there was a large variability in measured aluminium. In the OECD Guidance Notes on Dermal Absorption, 2011, it is stated that results of *in vitro* dermal absorption studies can produce results that exhibit a degree of variability that is greater than that seen in many other types of studies used in human health risk assessments. Furthermore, this variability may not necessarily indicate poor experimental technique but be indicative of the physiological and biochemical inter-individual variability that exists in dermal absorption processes. When the degree of variability is high, as in Pineau *et al.* (2012), another value than the mean or possibly rejecting the study entirely should be considered. Since this study fulfilled most of the SCCS criteria for skin absorption, VKM chose not to reject the study. No other values than the mean were reported by Pineau *et al*., thus the mean values were used in VKM's opinion.

When a study fulfils all the basic SCCS criteria, the mean+1SD value should be used. In case of significant deviation from the protocol and/or very high variability, the mean+2SD should be used. Furthermore, the recommendation is "In case the results are derived from an

inadequate *in vitro* study, or no dermal absorption data is available, 100% dermal absorption is used." In VKM's opinion, the study by Pineau et al. (2012) fulfilled most of the SCCS's requirements and it was therefore used for the estimation of SED. Since the study by Pineau *et al.* (2012) did not fulfil all of the SCCS criteria for skin absorption of Al, VKM could have used the mean+2SD, or to be even more conservative, to use 100% dermal absorption. However, in VKMs opinion, already when using the mean+1SD the exposure to Al from cosmetics in comparison with exposure to Al from food, clearly indicated that cosmetic products, especially antiperspirants, and even more so if applied on non-intact skin, were a substantial source of exposure to Al.

In VKM's experience with risk assessments there is often a lack of good quality data or even lack of data at all, to perform one or more steps in the exposure or hazard characterizations. Whether the data are of sufficient quality to perform a risk assessment or not is a question to be discussed and decided upon in each case. In this assessment of exposure to aluminium from cosmetics, VKM decided that the study by Pineau et al. (2012) was of sufficient quality. Further, in VKM's view, it would be more useful to the risk managers and provide a better consumer protection to err on the side of caution than not to perform a risk assessment at all because of lack of data on skin absorption fulfilling all of SCCS's requirements.

At any time point the best available data should be used in risk assessments. If regarded necessary, risk assessments should be repeated when better data becomes available. VKM welcomes any new high quality data that can provide better estimates of human skin absorption of Al.

Question 2 from the Norwegian Food Safety Authority:
Does VKM agree with the SCCS regarding the necessity of human (*in vivo*) dermal penetration data as a basis for risk assessment of aluminium in cosmetics?

In the SCCS's guideline it is not stated that only human *in vivo* data should be used in risk assessments of cosmetics ingredients. On the contrary, much attention is given in this guideline document to criteria for performing *in vitro* skin absorption studies, stating that human skin from an appropriate site remains the gold standard. According to the OECD guideline no. 428 for skin absorption, either human skin or skin from other mammalians may be used.

It is not clear from the opinion from SCCS in 2014 whether a new human dermal absorption study should be an *in vivo* study, or how such a study should ideally be performed.

In VKM's opinion, the most important point is that in any new studies of skin absorption of Al the exposure situation should be as representative as possible of a real life situation for use of antiperspirants (regarding amounts applied, contact area and time etc.) preferably using skin from the armpit with intact sweat glands. All data necessary to evaluate the study quality and relevance, including data on mass balance and recovery, should be reported in the

published paper. VKM recommends that expertise on skin absorption experiments should be consulted to decide whether this goal of better, more realistic data, can be best achieved by human *in vitro* or *in vivo* experiments.

Question 3 from the Norwegian Food Safety Authority:
Does VKM have other comments pertaining to other aspects of the SCCS opinion?

VKM does not have any additional comments to the opinion from the SCCS.

Question 4 from the Norwegian Food Safety Authority:
What, if any, consequences does VKM think the SCCS opinion has for its own risk evaluation of aluminium as published April 5, 2013?

In VKM's opinion, the SCCS's opinion does not have any consequences for the risk assessment published by VKM on April 5, 2013.

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