Input til høringssvar vedrørende ny opinion for salicylsyre

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MEMO

To **Miljøstyrelsen**

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SOCHR

Input til høringssvar vedrørende ny opinion for salicylsyre

DTU Fødevareinstituttet er d. 23. oktober 2018 blevet bedt om input til høringssvar vedrørende en ny SCCS opinion for salicylsyre. Høringsfristen er d. 14. november 2018 og arbejdet forventes udført under Miljøstyrelsens trækningsret.
Specifikt vil MST gerne vide om DTU Fødevareinstituttet har kommentarer til den konkrete opinion og om der er noget som ikke er omtalt tilstrækkeligt.
Ydermere vil MST gerne vide om DTU Fødevareinstituttet er enige med SCCS i at stoffet kan anvendes sikkert under de nævnte betingelser.
Som aftalt pr. e-mail 5.11.18 udarbejdes notatet på engelsk så det lettere kan bruges videre i EU sammenhæng. Eftersom salicylsyre er et af de stoffer som blev vurderet til at være hormonforstyrrende i liste-projektet under CEHOS (netop publiceret 31.11.18) vil vi henvise til den i vores svar.

I finder vores input til høringssvar herunder:
1. DK- EPA would like to know if DTU FOOD has any comments to the specific opinion and whether there is something that is not mentioned sufficiently in this opinion?

In the part **3.3.10 Special Investigations** where the endocrine disrupting properties of salicylic acid are briefly mentioned we find that this text needs to be elaborated.
Please consider including the following text **in 3.3.10**:
In a newly published report from the Danish Centre on Endocrine Disrupters researchers from the National Food Institute, Technical University of Denmark, and the University of Southern Denmark have evaluated that there is solid scientific evidence that salicylic acid is an endocrine disruptor (http://cend.dk/ed-liste.html). The evaluation was based on the new EU criteria for pesticides and biocides.

In this part of the opinion **3.3.10 Special Investigations** the study by Kristensen et al. 2011 was not included (see reference below):
Please consider including the following text **in 3.3.10**:
A study by Kristensen et al. found an increased risk of giving birth to sons with undescended testicles (cryptorchidism) in women taking more than one aspirin simultaneously. The second trimester appeared to be a particularly sensitive time.
Acetylsalicylic acid was administered to time mated Wistar rats in doses of 150, 200 and 250 mg/kg/day from GD 13 (Gestation Day) to 21 and Caesarean section was performed at GD21.

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Moreover, an *ex vivo* study where testis from male rat fetuses were incubated for 3 days in media with or without the test compounds was made.
These *in vivo* and *ex vivo* studies found that exposure to Acetylsalicylic acid lead to reduced levels of testosterone in the rat fetal testis by approximately 50% during the crucial early period of gestation when the male organs were forming. The effect was comparable to that caused by similar doses of e.g. some phthalates, which are recognized endocrine disrupters in EU.

Reference:

Kristensen DM, Hass U, Lesné L, Lottrup G, Jacobsen PR, Desdoits-Lethimonier C, Boberg J, Petersen JH, Toppari J, Jensen TK, Brunak S, Skakkebæk NE, Nellemann C, Main KM, Jégou B, Leffers H. Intrauterine exposure to mild analgesics is a risk factor for development of male reproductive disorders in human and rat. Hum Reprod. 2011 Jan;26(1):235-44. doi: 10.1093/humrep/deq323. Epub 2010 Nov 8.

In **3.6 DISCUSSION** it is written:
...
Developmental Toxicity
The report states: *SCCS agrees that salicylic acid can be considered as a developmental toxicant. Salicylic acid has been proposed for classification as Repr. 2; H361d (Suspected of damaging the unborn child) (ECHA 2016).*
The classification has to our knowledge been agreed upon in RAC. Please change the text accordingly to:
SCCS agrees that salicylic acid can be considered as a developmental toxicant. Salicylic acid has been **classified** as Repr. 2; H361d (Suspected of damaging the unborn child) (ECHA 2016).

This also needs to be clarified in **3.3.7.1 Fertility and reproduction toxicity** where it is written;
...not have significant effects on fertility and **is not classified as a reproductive toxicant.**

2. DK EPA would also like to know if DTU FOOD agrees with SCCS that the substance can be used safely under the mentioned conditions.

We would like to address the following comments:
1. Table 21. P. 50 in the opinion reports MOS (Margin of Safety) for aggregate systemic exposure to cosmetic products containing salicylic acid.
Here a MoS of 195 is calculated in a Probabilistic approach and a MoS of 50 by using the deterministic approach. The MoS on 195 could appear acceptable but do not take into account the possible exposure of salicylic acid from other sources (such as aspirin).
2. The report states:
The SCCS agrees that exposure to aspirin results in considerably larger doses of SA than the use as preservative in cosmetics. However, the use of a drug includes different risk- benefit considerations

than the use in cosmetics, and in recent times also the deliberate use of aspirin has been questioned by medical doctors. Therefore, the fact that aspirin results in much larger doses of salicylic acid cannot be used as an argument for the safety of SA.
Salicylic acid is also used as a preservative in food and as a biocide in some consumer products (see section 3.2.3). As no specific exposure data were made available to SCCS to assess exposure following these non-cosmetic uses, it was not possible to include them in the aggregated exposure scenarios.

DTU FOOD finds that the fact that SA is used both as a preservative in foods and cosmetics, as a biocide and in aspirin, leads to an increased risk of too high exposures for certain population groups. While we agree that the use of SA in drugs includes different risk-benefit considerations, we find that this exposure needs to be taking into account when determining safe exposure doses for other uses of SA. We are concerned that this combined exposure from many different sources may lead to a unacceptably high risk, as concomitant exposure to aspirin and cosmetic may lead to a too low MoS. DTU FOOD therefore finds that the opinion should take into account the aggregated exposure to SA from all available sources when calculating exposure. If there is a lack of some exposure data, DTU finds that this should be considered as uncertainty and reflected in the evaluation of the magnitude of the MoS.

3. DTU FOOD furthermore finds that the opinion should also take into account the exposure to other compounds having similar MoA as Salicylic acid (e.g. phthalates) and consider cumulative risk assessment of mixtures as stated in the EU report “State of the Art on Mixture Toxicity” (Kortenkamp et al. 2009).

Ref:
Kortenkamp, A & Backhaus, Thomas & Faust, M. (2009). State of the Art Report on Mixture Toxicity. Final Report http://ec.europa.eu/environment/chemicals/effects/pdf/report_mixture_toxicity.pdf