German comments on the draft Non-Paper „Status of Hemp and Cannabis-derived ingredients in Cosmetics" and a potential mandate to SCCC

1) SCCS Mandate: Comments and toxicological data

We welcome that the Commission is considering to mandate the SCCS for the evaluation of cannabidiol (CBD), including residual levels of d9-tetrahydrocannabidiol (THC) in cosmetic products.

In order to be able to carry out a safety assessment for CBD and the traces of THC contained as impurities in cosmetic products, we consider it necessary that toxicological data, in particular on dermal uptake, are submitted or – if not available – generated.

According to observations of the German market surveillance authorities, "CBD cosmetics" are available on the market increasingly, seemingly to circumvent the food law regulations by the declaration as cosmetic products. This applies in particular to products that are intended to be placed in contact with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours. For these products an oral uptake seems likely.

As it can be assumed that oral care products containing CBD are swallowed, we consider it necessary that this is also taken into account in the toxicological assessment.

At the Bavarian competent authority „Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit (LGL)", a gel for application to the skin with a CBD content of 4661.7 mg/kg (= 0.46 %) was toxicologically evaluated. In the context of hazard identification and hazard characterisation, the following statement was made with respect to the toxicity of CBD: "...Cannabidiol (CBD) has only a low acute toxicity. This is reflected by the LD50 values determined for i.v. administration in experimental animals: 50, 242, > 254 or 212 mg/kg bw in mice, rats, dogs or monkeys (1).

The Committee on Toxicity of the United Kingdom (COT UK; 2, 3) points out that CBD has only a low bioavailability (< 10%) in oral fasting intake. For oral intake of CBD with food, a mean bioavailability of 14-25% is indicated (2, 3).

With regard to absorption via skin, the COT UK assumes that the systemic availability with dermal application is probably less than 10 % of the systemic availability with oral absorption.

This assumption is supported e.g. by the results of the study by Bartner et al. (4) on beagle dogs, which were orally administered 10 or 20 mg CBD/kg bw and day (CBD dissolved in an oil) and the same dose of CBD was applied to the skin of their auricles via a cream.

The authors found a relative bioavailability of CBD of 8.6% at the lower dosage and 9.9% at the higher dosage when applied to the skin compared to oral administration. The low systemic availability of CBD in dermal application is explained by the high lipophilicity of CBD (log Kow/log P-value of approx. 6). Therefore CBD accumulates in the stratum corneum of the skin of humans and laboratory animals and does not penetrate into deeper skin layers where absorption into the bloodstream would be possible (4)...".

References:

1. European Medicines Agency (EMA, 2019): Assessment Report Epidyolex: https://www.ema.europa.eu/en/documents/assessment-report/epidyolex-epar-public-assessment-report_en.pdf
2. Committee on Toxicity, COT UK Tox /2020/62: Potential adverse effects associated with exposure to cannabidiol (CBD) by inhalation https://cot.food.gov.uk/sites/default/files/2020-11/TOX-2020-62%20Cannabidiol%20inhalation.pdf
3. Committee on Toxicity (COT, UK, 2020): CBD Update: https://cot.food.gov.uk/sites/default/files/tox202002cbd.pdf
4. Bartner L.R. et al.: Pharmocokinetics of cannabidiol administered by 3 delivery methods at 2 different dosages to healthy dogs. Can. J. Vet. Res. 82: 178-183, (2018) https://pubmed.ncbi.nlm.nih.gov/30026641/

In addition to the literature cited above in the toxicological assessment, the toxicological expert of the LGL refers to further publications on the dermal

effects of CBD and potential risks associated with the topical application of CBD:

- Deutsche Apotheker Zeitung (DAZ) 47/2016: Cannabidiol in Dermatika: https://www.deutsche-apotheker-zeitung.de/daz-az/2016/daz-47-2016/cannabidiol-in-dermatika
- Baswan S. et al.: Therapeutic Potential of Cannabidiol (CBD) for Skin Health and Disorders . Clinical, Cosmetic and Investigational Dermatology 13 (2020): 927 – 942: CCID_A_286411 927..942 (nih.gov) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7736837/
- Gupta A.K. et Talukder M.: Cannabinoids for skin diseases and hair regrowth. J. Cosmet. Dermatol. 20 (2021): 2703 – 2711: https://pubmed.ncbi.nlm.nih.gov/34363728
- COT UK 2020 Paper: TOX/2020/23: COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT: Potential risks from use of topically applied CBD-containing cosmetic products: https://cot.food.gov.uk/sites/default/files/tox202023topicalcbdforwebsite.pdf

We would also like to refer to the following link of the Swiss BLV:

- https://www.blv.admin.ch/blv/de/home/lebensmittel-und-ernaehrung/rechts-und-vollzugsgrundlagen/bewilligung-und-meldung/bewilligung/cannabis-cannabidiol.html

2) Comments on Non-Paper

Irrespective of the findings in this Non-paper, it might be advisable to adapt the specific wording in Annex II No. 306 of Regulation (EU) 1223/2009 or to make it more precise. The entry currently reads:

" ***Narcotics, natural and synthetic: All substances listed in Tables[1] I and II of the Single Convention on narcotic drugs of 1961***."

[1] The term 'Tables' refers to 'Schedules' of the Singe Convention of 1961

The considerations included in the draft Non-paper are based on the understanding that "only" narcotics as defined in the Single Convention on Narcotic Drugs signed in New York in 1961 are meant here and thus only narcotics as defined in the Single Convention are to be regarded as prohibited substances.

The decision of the Administrative Court of Schleswig dated from 25.1.2021 – 1 B 171/20, reads:

"The statement of the European Court of Justice that cannabidiol is not an 'narcotic drug' for trade in agricultural products between the Member States on the basis of the statement of the referring court does not change the specific regulation for cosmetic products in Regulation (EC) No. 1223/2009. In its opinion, the competent authority „Landesamt Berlin-Brandenburg“ rightly refers to the specific wording of Annex II No. 306 of Regulation (EC) No. 1223/2009, according to which narcotic is any substance listed in Tables I and II of the Single Convention on Narcotic Drugs signed in New York on 30 March 1961. Due to the fact that the Regulation refers directly to Table I of the Single Convention, all substances listed there are still prohibited in cosmetic products – i.e. also the flowers or fruits of the cannabis plant, cannabis resin as well as cannabis extracts and tinctures. Whether the definition of narcotic substance within the meaning of the Single Convention is fulfilled is not relevant due to the direct reference of Regulation (EC) No. 1223/2009 to the mentioned Tables."

With regard to CosIng, we propose to check the entries on cannabis and its ingredients for consistency.