MCCP: are medium-chain chlorinated paraffins of concern for humans?

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Received: 20 November 2019 / Accepted: 17 February 2020 / Published online: 26 February 2020
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Chlorinated paraffins (CP) represent polychlorinated alkanes (empirical formula: $C_nH_{2n+2-x}Cl_x$) with a degree of chlorination between 30 and 70%. Based on the carbon chain lengths, a classification into short-chain CP (SCCP, C_{10-13}), medium-chain CP (MCCP, C_{14-17}) and long-chain CP (LCCP, C_{18-30}) has been introduced. In general, CP are mixtures consisting of up to 200 congeners and belong to the group of UVCB (substances of unknown or variable composition, complex reaction products or biological materials). Known applications of CP are, for instance, the serving as pressure additives in the metal working industry, as plasticizers in the polyvinyl chloride (PVC) production, as additives to rubber, paints and lacquers, adhesive sealants and other polymer material, such as polyurethane, and as lubricants and flame retardants. In 2013, the estimated annual production of MCCP (CAS: 85535-85-9) in China, being the main producer, is 600,000 tons (Gluege et al. 2018).

Due to its persistent, bioaccumulative and toxic (PBT) properties, SCCP (CAS: 85535-84-8) are categorized as SVHC (Substance of Very High Concern), thereby meeting also the criteria for very persistent/very bioaccumulative (vPvB) substances according to REACH. SCCP are also listed in Annex I of the Persistent Organic Pollutant (POP) Regulation (EU No. 2019/1021) and uses are no longer permitted. Exemptions are uses of SCCP as such or preparations and articles with SCCP contents below 1% (w/w) and 0.15% (w/w), respectively. Restrictions on some uses (metal working/fat liquoring of leather, Entry Annex XVII of REACH Regulation) of SCCP are in place since 2009. It seems likely that both production and distribution of SCCP will further decrease in the future. MCCP most likely have been served in the majority of its uses as alternative to

SCCP. Quantification of CP in ground soil can support this presumption. Accordingly, concentrations of SCCP in soil decreased from 1989 to 2014, while it increased for MCCP (Bogdal et al. 2017).

Currently, MCCP are not categorized as SVHC. However, MCCP are listed on the “Community Rolling Action Plan” (CoRAP) and so-called Risk Management Option Analyses (RMOAs) will be developed to clarify the concerns with regard to potential PBT and reprotoxic properties of MCCP.

The main difference between MCCP and SCCP are their chain lengths, assuming that similarities and differences of their properties depend on this parameter. Based on the degree of chlorination of the components, MCCP are classified according to the CLP Regulation as Lact. (“may cause harm to the breast-fed children”), Aquatic Acute 1 (“very toxic to aquatic life”), and Aquatic Chronic 1 (“very toxic to aquatic life with long lasting effects”). In addition, the label EUH066 is mandatory and indicates that “repeated exposure may cause skin dryness or cracking” of the skin. Until today, it is assumed that consumer exposure is generally very low and that dermal uptake may occur only if leather clothes are treated with MCCP.

However, recent publications show that the consumer can be exposed to considerable levels of MCCP. CP have been detected as contaminants in fish collected in the Rhône river basin (Labadie et al. 2019), in fish from the North and Baltic Sea (Reth et al. 2005), in salmon (aquaculture as well as wild) and trout (Kraetschmer et al. 2018). Using consumption data, the EFSA estimated mean lower bound (LB) and upper bound (UB) exposure levels of SCCP across surveys and age groups between 1.9 and 35 ng/kg b.w. per day. For MCCP, mean LB and UB exposures (95th percentile) are between 3.2 and 59 ng/kg b.w. per day (EFSA Draft 2019). Importantly, Kraetschmer et al. (2019) showed that the concentration of CP exceeded that of polychlorinated biphenyls (PCB) and hexabromocyclododecanes (HBCDD) in virtually all fish samples. This indicated that CP are among the dominant substances in this matrix. In addition, vitamin E dietary supplements, based on palm oil, can be a source of MCCP (Sprengel et al. 2019). A mean dietary uptake of up to 38 µg/

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person per day (range of 12–112 µg/person) is calculated by the authors, if the dietary supplements are used according to the recommendations as printed on the package. Consumer products, such as baking ovens may contain CP (Gallistl et al. 2018) and an average concentration of 12.6 mg MCCP/g surface fat is detected at the inside of the baking chamber. Ten out of 21 ovens contained MCCP in a range of 1.9–93 mg/g surface fat. Studies are needed to validate whether or not these CP may contribute to the contamination of food, while being prepared in these kinds of ovens. Contamination of food may also occur by the use of hand blenders (BfR 2016; Yuan et al. 2017). Yuan and co-workers calculated a daily oral uptake of 3 µg MCCP per person. An ADME study showed that intestinal absorption of SCCP occurs (Geng et al. 2016) and MCCP are detected in human breast milk samples ($n = 60$) at a range of 9.6–903 ng/g lipid weight with a median of 115.4 ng/g (Hilger et al. 2011).

House dust also contains CP (Shang et al. 2019; Wong et al. 2017). Friden et al. (2011) reported up to 18 µg CP per gram house dust in Swedish households and, based on these data, calculated a mean intake of 1 µg CP per day by air and dust. Indoor air is filtered in kitchen hoods which function as “lipophilic traps” and a mean concentration of 3.5 µg CP/g surface fat has been reported (Bendig et al. 2013). Plastic sport courts and synthetic turf may also contain CP (Cao et al. 2019). In summary, the data published in the literature point to an ubiquitous exposure of consumers against CP via oral, inhalation as well as dermal routes.

Degradation of CP may occur at and above temperatures of 200 °C (Perkons et al. 2019; Xin et al. 2017), an observation which indicates that MCCP may serve as precursor compounds of those SCCP that are listed in the POP Regulation. At temperatures between 200 and 400 °C, cyclization and aromatization of CP may occur instead, thereby likely leading to the generation of polychlorinated biphenyls (Xin et al. 2018).

Several subchronic toxicity studies have been performed with MCCP [for summaries, see The Danish Environmental Protection Agency (2013) and EFSA Draft (2019)]. These studies identified liver, kidney and the thyroid gland as main target organs for SCCP and MCCP. Furthermore, postnatal effects such as decreased pup survival and internal bleedings (haemorrhages) are observed for MCCP. In 2008, a NOAEL of 23 mg/kg b.w. per day is derived (ECHA 2008) based on increased kidney weights, a value also confirmed by the Scientific Committee on Health and Environmental Risks (EC SCHER 2008). Using Benchmark Dose Modeling, the EFSA derived a NOAEL of 36 mg/kg b.w. per day for MCCP (EFSA Draft 2019) in 2019. CP are most likely non-genotoxic. Until recently, data on SCCP have been used to fill data gaps in the assessment of MCCP. Since SCCP are shown to increase the incidence of tumours in rats and mice and are legally classified as Carcinogen, category 2

(Annex VI of CLP Regulation), this raises a similar concern for MCCP according to its carcinogenic potential. Unfortunately, no carcinogenicity studies are available for MCCP, yet. Furthermore, studies show that SCCP (Gong et al. 2018) and MCCP (Poon et al. 1995) affect the thyroid gland and its hormones in rodents. While Gong et al. (2018) reported disturbances of serum hormone levels of T3, T4 and TSH without any histological changes for SCCP, Poon and et al. (1995) reported MCCP induced histological changes of the thyroid, only. For the purpose to fully characterize potential hazards on human health (via identifying similarities and differences of individual congeners, concerns for neurodevelopmental disturbances based on changes of thyroid hormones, carcinogenicity, etc.) and to assess potential risks for consumers, the current toxicological and exposure databases related to MCCP are rated insufficient. Therefore, we conclude a need for further data generation in the following fields associated to the health concern of CP:

- validated analytical methods for the detection of CP (in food and food contact materials)
- data on the occurrence in food and monitoring of CP in food
- data on the occurrence in consumer products and exposure scenarios
- health effects of different congeners of CP in potential target organs of humans.

Acknowledgements Open Access funding provided by Projekt DEAL.

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