Letter to the Editor

Risk Assessment of MOAH and MOSH in Infants and Young Children*

ZHU Lei[1], ZHANG Hong[1], CHEN Yan Fen[2], PAN Jing Jing[2], LIU Ai Dong[1], PAN Feng[1], ZHANG Jian Bo[1,#], and ZHONG Huai Ning[2,#]

Mineral oil hydrocarbons (MOH) in food may come from both contamination and various intentional uses in food production. MOH is widely used in food contact materials and food additives. It comprises complex mixtures, including straight and branched open-chain alkanes (paraffins), largely alkylated cycloalkanes (naphthenes), and it can be collectively classifiable as mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH)[1]. The Joint FAO/WHO Expert Committee on Food Additives (JECFA), European Food Safety Authority (EFSA) and the German Federal Institute for Risk Assessment (BfR) conducted a number of toxicological and risk assessment studies on MOH[2-4]. Animal studies have shown that MOSH can lead to deposits and inflammatory effects in the liver of a certain rat strain. In 2012, EFSA demonstrated that MOAH comprise carcinogenic compounds and may accumulate in human tissues and form microgranuloma[3]. But up to now, there is no comprehensive study on MOH risk assessment for the Chinese population. This study was done to assess the risk posed by MOSH and MOAH to Chinese infants and young children aged 0-36 months, which are the most sensitive population. Considering the different dietary patterns and the relevant National Safety Standards, we divided the population into 0–6-month infants, 7–12-month follow-up infants, and 13–36-month young children.

Food consumption data were obtained from the China Food Consumption Survey in 2015 using non-consecutive 3 day–24 h dietary recall interviews. We obtained consumption data from 20,722 subjects: 4,185 0–6 month infants, 3,038 7–12 month follow-up infants, and 13,499 13–36 month young children. According to food consumption data, the main food of infants and young children below 36 months of age included formula for infants and young children, complementary foods for infants and young children, and drinking water. These three food categories had their sub-categories; Infant and young children formula included infant formula, follow-up formula, and young children formula. Complementary foods for infants and young children included rice flour, pasty canned food, noodles, and biscuits. Drinking water included mineral water, bottled water, and tap water.

A total of 230 infant and young children foods including 115 samples of infant and young children formula, 76 samples of complementary foods for infants and young children, and 39 samples of drinking water were collected from online shopping, supermarkets, local markets and the manufacturers directly covering different origins, as well as 12 domestic brands and 15 imported brands.

The food was extracted as described by S. Biedermann-Brem[5,6]. Twenty g solid food or 50 mL liquid food, with 60 μL internal standard solution and 150 mL hexane (50 mL hexane for liquid food), were extracted overnight at 60 °C. Decanted extracts were re-concentrated five times before analysis. Blank samples were treated as the above procedures. Silver silica gel preparation was derived according to the research of Fiselier[7]. Upon opening of the valve to dry the sorbent, 1.5 mL of sample was loaded to the top of the packed bed. The following 5.5 mL (n-hexane) fraction containing MOSH and the next 15 mL (n-hexane/dichloromethane, 4:1 v/v) fraction containing MOAH were collected in two tubes, respectively. The fractions were concentrated to 1 mL and then analyzed by GC-FID or GC-MS.

Point-estimation was used as the exposure assessment method in this study. Daily intake from individual food was calculated by multiplying consumption data of individual food with corresponding MOAH or MOSH concentration in

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1. China National Centre for Food Safety Risk Assessment, Beijing 100022, China; 2. Guangdong Inspection and Quarantine Technology Centre, Guangzhou 510623, Guangdong, China

food. The total daily intakes of MOAH or MOSH were gotten by adding up all daily intakes from all types of food. The formula of daily intake from individual food was as below:

$$Exp = \frac{F \times C}{BW} \quad (1)$$

Where *Exp* denoted dietary intake of MOAH or MOSH (μg/kg bw/d), *F* denoted consumption of food (g/d); *C* denoted concentration of MOAH or MOSH in food (mg/kg); *BW* referred to body weight of target population (kg).

The formula of total daily intake was as below:

$$Exp_t = Exp_i + Exp_c + Exp_d \quad (2)$$

Where Exp_t denoted the total daily intake of MOAH or MOSH for infants and young children aged 0–36 months; Exp_i, Exp_c and Exp_d, denoted daily intake of MOAH or MOSH from infant and young children formula, complementary foods for infant and young children, as well as drinking water respectively.

In this study, typical consumers and brand loyalty consumers were selected as two representative populations. For typical consumers, the total daily intake of MOAH or MOSH was gotten by summing up mean daily dietary intake from all types of food. To avoid overestimation, mean daily dietary intake from complementary foods for infant and young children was selected for calculation of dietary intake of brand loyalty consumers. So for brand loyalty consumers, the total daily intake of MOAH or MOSH was gotten by summing up maximum daily dietary intake from infant and young children formula, mean daily dietary intake from complementary foods for infant and young children as well as maximum daily dietary intake from drinking water.

According to EFSA's Scientific Opinion, MOAH may be carcinogenic and mutagenic. Hence, it is impossible to establish a Reference Point (RP) upon which to base a margin of exposure (MOE) calculation, which would normally be the approach for the risk characterization of MOAH[3]. No toxicological data is available that would permit the assessment and derivation of the limit values for MOAH[3]. The drafted revised version of BMEL Ordinance of Consumer Goods set 0.5 mg/kg as the SML for MOAH (C_{16}-C_{35}) migrated from recycling paper and paperboard behind a functional barrier[8]. This study used this SML as the threshold in MOAH evaluation.

JECFA has set several ADIs for mineral oil based on toxicity studies. But in 2012, the seventy-sixth meeting of JECFA withdrew the established temporary group ADI because it was impossible to establish an ADI based on external dose in the absence of information on the relative accumulation potential of classes II and III mineral oils in humans compared with rats[9]. In the absence of toxicological studies on MOSH, it is inappropriate to establish a health based guidance value for MOSH. So EFSA decided to use Margin of Exposure (MOE) approach and selected the highest NOAEL (No Observed Adverse Effect Level) below the lowest LOAEL (Lowest Observed Adverse Effect Level) as an RP for MOSH exposure scenario. MOE is calculated by dividing NOAEL by EDI (Estimated Dietary Intake). So MOE approach was used in risk characterization of MOSH in this study. MOAH and MOSH levels in formula samples for infants and young children were in the range of no detection to 17.35 mg/kg, as well as no detection to 27.34 mg/kg. The non-detection rates of MOAH and MOSH were 78.01% and 81.68%, respectively. In accordance with the principles of WHO[10], sensitivity analyses were done by assigning all non-detected values to 0 and the limit of detection (LOD), and then the change in exposure estimates were evaluated. As the change between the two results was negligible, we assumed the non-detection values to be LOD by the worst-case principle. The detailed data are shown in Table 1. MOAH and MOSH in all drinking water samples were not detected. Because MOH was insoluble in water, all levels in drinking water samples were set to 0.

Seven kg, 9 kg, and 13 kg were chose as the body weight of the three populations. The detailed estimates of dietary exposure to MOAH and MOSH were shown in Table 2. According to the table, the dietary exposure to MOAH and MOSH in most cases of infants at 0–6 months was the highest among the three populations.

The dietary intake of MOSH of infants and young children in China and Europe were compared. The data of Europe was from the assessment made by EFSA[3]. The detailed data are shown in Table 3. From the comparison, the mean dietary intake of Europeans was higher than that of the Chinese. But the P_{95} dietary intake of 0–12 month infants in China was higher than that of the same group in Europe. Because of the high consumption of the population of 0–12 month infants in China, their MOSH exposure should therefore be of particular concern.

There were some uncertainties in exposure assessment in this study. First, some consumed food categories were not involved. For example, breast milk was the main food of breast-fed infants below 12 months. But breast milk was not included in this study because of the difficulty of obtaining samples. It may lead to underestimation. For some young children aged 12–36 months, the dietary pattern was similar to that of adults. But we included only three food categories for this population, and this may similarly lead to underestimation. Second, the number of food samples may be increased to improve the representation of this study in future work.

We used 0.5 mg/kg as the migration limit in risk characterization of MOAH according to the BMEL Ordinance draft[8]. The over-limit quantities and over-limit ratio for MOAH concentration in food was calculated. The results illustrate that follow-up infant formula, noodles, infant formula, and young-children formula were the main contributors to dietary intake of MOAH for Chinese infants and young children and thus needed more attention. Moreover, it should be noted that the migration limit from the BMEL Ordinance draft has no toxicological base; it should be improved in future work.

The MOE to MOSH for three populations were calculated using the RP of 19 mg/kg bw per day, in accordance with the recommendations of EFSA[3]. The MOEs for typical consumers (mean) of 0–6 months infants, 7–12 months follow-up infants, and 13–36 months young children were 1025.36, 922.33, and 1625.32, respectively. The MOEs for brand loyalty consumer of the three populations were 12.61, 15.78, and 23.87, respectively. P95 of MOE for the three populations were 43.90, 53.97, and 102.81, respectively. Hence, MOE in brand loyalty consumers,

Table 1. Levels of MOAH and MOSH in Food for Infants and Young Children

Substance	Food Category	Numbers of Samples	Numbers of Non-detectable Samples	Levels in Food (mg/kg)			
				Min	Mean	P_{95}	Max
MOAH	Infant formula	42	32	0.5	1.23	5.46	6.65
	Follow-up infant formula	38	21	0.5	1.34	3.3	17.35
	Young children formula	35	26	0.5	0.86	2.27	2.27
	Rice flour	19	19	0.5	0.5	0.5	0.5
	Pasty canned food	17	17	0.5	0.5	0.5	0.5
	Noodle	17	12	0.5	0.65	1.25	1.25
	Biscuits	23	23	0.5	0.5	0.5	0.5
MOSH	Infant formula	42	31	1	4.77	24.27	25.22
	Follow-up infant formula	38	30	1	3.99	3.3	17.35
	Young children formula	35	24	1	3.94	15.3	17.12
	Rice flour	19	19	1	1	1	1
	Pasty canned food	17	17	1	1	1	1
	Noodle	17	12	1	6.04	27.34	27.34
	Biscuits	23	23	1	1	1	1

Table 2. Detailed Estimated Dietary Exposure to MOAH and MOSH (μg/kg bw per day)

Population	Typical Consumers (Mean)		Brand Loyalty Consumers		P_{95}		Max	
	MOAH	MOSH	MOAH	MOSH	MOAH	MOSH	MOAH	MOSH
0-6 months infants	4.99	18.53	876.85	1968.27	104.22	432.79	901.72	2242.63
7-12 months follow-up infants	6.25	20.60	696.45	1204.41	105.59	352.02	721.20	1478.51
13-36 months young children	2.90	11.69	461.52	795.92	45.18	184.81	478.44	982.30

Table 3. The Dietary Intake of MOSH of Infants and Young Children in China and Europe (mg/kg bw per day)

Population	Europe		China	
	Mean	P_{95}	Typical consumer (Mean)	P_{95}
0-6 months infants	0.038-0.18	0.13	0.019	0.43
7-12 months follow-up infants	0.038-0.18	0.13	0.021	0.35
13-36 months young children	0.083-0.19	0.18-0.26	0.012	0.18
Breast-fed infants (0-6 months)	0.29-0.32	0.43-0.48 (high consumption)	-	-

P_{95} MOE of 7–12 months follow-up infants, and 13–36 months young children were below 100. These exposure scenarios were considered to be of particular concern. The findings indicated that the contamination of food for infants and young children was universal and may potentially pose a risk to 0–36 months infants and young children, as well as affect the brand loyalty of consumers. More systematic toxicological studies on MOAH and MOSH and more types of food consumed are anticipated to optimize the results of this study.

Measures should be taken by enterprises, especially manufacturers of formula for infants and young children, to control MOAH and MOSH contamination of food.

[#]Correspondence should be addressed to ZHANG Jian Bo, researcher, Tel: 86-10-52165425, Fax: 86-10-52165424, E-mail: jianbozhang@cfsa.net.cn; ZHONG Huai Ning, researcher, Tel: 86-20-87004041, Fax: 86-20-38290551, E-mail: marco_zhong@iqtc.cn

Biographical note of the first author: ZHU Lei, female, born in 1980, associate researcher, majoring in safety standard and evaluation of food contact materials.

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