Intake Level and Risk Assessment of Butylated Hydroxyanisole and Butylated Hydroxytoluene as Food Additives (Overview)

The butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are synthetic phenolic antioxidants with high efficiency and low cost, which are widely used in the food and oil industry. The National Food Safety Standard for Uses of Food Additives (GB 2760-2014) stipulates that BHA and BHT can be used as antioxidants in food categories such as oils and fats, nuts, meat products, flavorings, ready-to-eat cereals, and puffed foods.

It has been shown that BHA and BHT can induce tumors in experimental animals. The International Agency for Research on Cancer (IARC) listed BHA and BHT as Group 2B carcinogens (possible human carcinogens) and Group 3 carcinogens (suspected human carcinogens), respectively, in 1987. Given that BHA and BHT are widely used in food production and processing as food additives in China, new toxicological data and related reports have triggered increasing public concern about their health effects, and no systematic risk assessment has yet been conducted in China. Their intake levels and risks are still unknown. Thus, it is necessary to conduct a risk assessment for food additives BHA and BHT. This project was proposed by National Experts Committee for Food Safety Risk Assessment in 2015, commissioned by the former National Health and Family Planning Commission, and implemented by the Secretariat of the National Experts Committee for Food Safety Risk Assessment.

1. Hazard Identification and Characterization of BHA and BHT

BHA is rapidly absorbed through the gastrointestinal tract and metabolized mainly in liver. Most of the BHA ingested by the body is excreted in the form of metabolites in the urine. Excessive BHA can accumulate in fat. The acute oral toxicity

of BHA is low. It was shown that long-term feeding of BHA at high doses could cause dysplasia, hyperkeratosis and hyperplasia of epithelial cells in the anterior gastric base of rats, which was considered to be correlated with the development of pathological hyperplasia, papilloma and squamous cell carcinoma in the anterior gastric region of rodents. However, no epidemiological evidence has been found for the carcinogenicity and other health effects of dietary intake of BHA in humans. In 1987, IARC listed BHA as a Group 2B carcinogen, and in 1989, JECFA set the Acceptable Daily Intake (ADI) for BHA at 0.5 mg/kg BW. Nevertheless, EFSA set the ADI at 1.0 mg/kg BW in 2011 based on the effect endpoints of BHA on growth retardation, lethality, and behavioral effects in rat offspring. Based on the concern about the potential carcinogenic risk of BHA, the ADI value of 0.5 mg/kg BW for BHA specified by JECFA was used in this evaluation.

BHT can be rapidly absorbed into the body through the gastrointestinal tract and is mainly distributed in the fat and liver. It can pass through the placental barrier into the fetus or be secreted into breast milk. The liver is the main organ of its metabolism. Most of the BHT is excreted in the form of metabolites in the urine. Its acute oral toxicity is low. The liver and the thyroid are the main target organs. The no-observed-adverse-effect level (NOAEL) for chronic oral exposure was 25 mg/kg BW for BHT-induced hyperthyroidism, increased adrenal weight, and hepatomegaly in rats. BHT was classified as a Group 3 carcinogen by IARC in 1987. Based on a NOAEL of 25 mg/kg bw/day from two 2-generation studies in rats and an uncertainty factor of 100 for the effects on reproductive organ and liver enzyme-induction, JECFA established an ADI value of 0.3 mg/kg BW for BHT in 1996. During the reassessment of BHT in 2012, EFSA adopted the ADI for BHT set by JECFA at 0.25 mg/kg BW based on the

NOAEL (25 mg/kg BW) derived from two 2-generation reproduction experiments in rats. The ADI value of 0.3 mg/kg BW established by JECFA for BHT was also used in this assessment.

2. Risk Assessment of Dietary Exposure to BHA and BHT

This assessment will be based on the stratified assessment principles of "Technical Guideline for Risk Assessment of Food Additives" for BHA and BHT。

2.1 Budget method

The estimate method uses the maximum human physiological limit of 0.1 L/kg BW for non-dairy beverages (equivalent to 6 L per day for a 60 kg body weight individual) and 0.05 kg/kg BW for foods (equivalent to 3 kg per day for a individual of 60 kg body weight) as the consumption levels for foods and beverages, and set the concentration of additives in foods and beverages as the maximum level allowed by regulation or reported in any food and beverage (the maximum use level for BHA and BHT in solid foods is 200 mg/kg). The proportion of solid foods containing additives is usually assumed to be 12.5%, and the theoretical maximum daily intake of BHA and BHT is 1.25 mg/kg BW for a standard body weight of 60 kg, both of which exceed the ADI values for BHA and BHT established by JECFA.

2.2 Theoretical maximum daily intake assessment

The theoretical dietary intake of BHA/BHT for Chinese residents was calculated based on the usage range of BHA and BHT in foods such as fats, oils, nuts, meat products, flavorings, ready-to-eat cereals and puffed foods as stipulated in GB 2760-2014 and based on the conservative assumption that BHA or BHT was added to all foods categories at its maximum use levels, taking into consideration the actual consumption data of foods to which BHA and BHT were allowed to be added in

China. The assessment results showed that the average theoretical daily dietary intake of BHA and BHT for the whole population in China were both 0.14 mg/kg BW, accounting for 27.6% and 46.0% of their ADI, respectively. At the high dietary consumption of P95, the theoretical intake of BHA for the whole population was about 81% of the ADI. However, the theoretical intake of BHT at high dietary consumption of P95 exceeded the ADI in varying degrees for all age groups.

Therefore, based on the maximum use levels of BHA and BHT in the food categories specified in GB 2760-2014, the average theoretical intake risk of dietary BHA and BHT for the Chinese population is acceptable, but there are different levels of theoretical intake risks of BHA/BHT for people in the lower age groups and for high consumers in other age groups. Due to the high conservativeness and uncertainty of the theoretical assessment, especially for high consumers, more accurate assessment of the population based on the actual BHA and BHT levels in foods is needed.

2.3 Risk assessment of dietary exposure to BHA and BHT based on their actual levels in food

The dietary intake risk of BHA and BHT in Chinese population was assessed based on the sampling results of national food safety supervision sampling project in 2016 that aimed to detect BHA and BHT in the main food categories from the market, using the consumption data of the corresponding food categories in Chinese population.

The results showed that:

1) The average daily intake of BHA from food samples for the whole population in China was 0.0004 mg/kg BW, only accounting for 0.1% of its ADI. Even at the

high food consumption level of P95, the BHA intake of the whole population was only 0.3% of ADI. The highest proportion of BHA intake from the food samples was 1.1% of ADI in all age groups. Among them, edible fats and oils were the most important source of dietary intake of BHA for the whole population and all age groups, accounting for 90.9% (87.9%-92.5%) of the total intake; followed by cookies 6.6% (4.4%-10.2%);

2) The results of the assessment of BHT showed that the average daily intake of BHT from the food samples for the whole population was 0.001 mg/kg BW, accounting for 0.3% of ADI. At high food consumption levels of P95, BHT intake was 0.6% of ADI for the whole population and 0.5% to 4.2% of ADI for all age groups. Edible fats and oils were the most important source of dietary intake of BHT for the whole population and all age groups, accounting for 86.4% (71.7%-88.0%) of their total intake; followed by instant rice and noodle products, accounting for 9.1% (6.5%-23.1%) of their total intake, cookies and fishery products accounting for 2.4% (1.6%-3.2%) and 2.1% (1.0%-2.7%).

Considering the theoretical maximum intakes of BHA and BHT for gum-based confectionery, food contact materials and unsampled foods, the average intakes of BHA and BHT for the whole population and all age groups could be theoretically increased to 21.6% and 5.6% of ADI, respectively. At the high food consumption level of P95, the intake levels of BHA and BHT for all age groups can increase to 22.4% and 8.7% of ADI, respectively. Therefore, according to the results of this assessment, the dietary risk of BHA and BHT intake for the whole population and different age groups in China was considered to be low.

3. Conclusions and Recommendations

Based on the results of this risk assessment, the following conclusions can be drawn:

(1) Based on the sampling data of BHA and BHT in food and considering the theoretical intake of BHA and BHT from other possible sources, the assessment results show that the dietary intake risk of BHA and BHT for the whole population and different age groups in China is at a low level.

(2) Edible fats and oils are the most important source of dietary intake of BHA and BHT in China, accounting for about 72% to 93% of BHA and BHT intake; followed by cookies and instant rice and noodle products.

Based on the assessment results, the National Experts Committee for Food Safety Risk Assessment recommends that:

Although the risk of dietary BHA and BHT intake in China is at a low level, manufacturers should still strictly implement the requirements of GB 2760-2014 for the use of BHA and BHT in fats and oils and other food categories to avoid excess of the scope and use level.