Evaluation Summary of Maltol for Use as a Cigarette Ingredient

Maltol is naturally occurring substance in foods and has been used as a food flavoring and flavor-enhancing ingredient for over 60 years. U.S. Food and Drug Administration (FDA) lists maltol as generally recognized as safe (GRAS) as a synthetic flavoring substance or adjuvant (21 CFR § 172.515) . Maltol has been approved for use in foods by Joint FAO/WHO Expert Committee on Food Additives (JECFA),[1] Flavor and Extract Manufacturers Association (FEMA No. 2656)[2] and the Council of Europe (CoE No. 148).[3]

Maltol is slightly toxic in acute studies in animals when administered orally.[4-9] It is practically non-toxic dermally with no deaths observed when rabbits were treated at doses exceeding 5 g/kg.[4] Maltol is generally non-irritating and non-sensitizing to the skin.[4,10] Maltol did not produce irritation or sensitization reactions in human patch tests[11] and only one case report (allergic skin reaction to maltol in strawberry lip salve) was found in the literature to indicate any allergic potential.[12]

Absorption and metabolism studies indicate that maltol is relatively well absorbed in the gastrointestinal tract.[13-16] These studies also demonstrate maltol is rapidly and fairly completely absorbed in the gut and readily conjugated to the glucuronide or sulfate conjugate prior to urinary, and to a lesser extent, fecal elimination. Excretion is fairly rapid with over 64% present in the urine or feces within 24 hr.[14]

The findings from genetic toxicology testing suggests maltol is weakly mutagenic[17-19] and clastogenic[20,21] in bacterial and mammalian cell assays. However, repeat oral dosing in rats for three months with maltol decreased weight gain in female rats at doses of 500 and 1,000 mg/kg/day and males at 1,000 mg/kg/day. Kidney lesions described as dilated, acellular glomerular tufts and dilated corticomedullary tubules were observed in both sexes exposed to 1,000 mg/kg/day. No adverse effects were observed in either sex at 250 mg/kg/day.[5] In a subchronic feeding study in dogs early deaths and multiple organ pathology occurred at 500 mg/kg/day, but no adverse effects were found at 250 mg/kg/day with maltol.[5]

Furthermore, lifetime bioassays in multiple species with maltol or ethyl maltol have not resulted in increased tumor formation.[5] Dietary dosing of dogs and rats up to 200 mg/kg/day resulted in no significant increases in tumor formation in any tissue or organ. No other sign of toxicity on growth, clinical parameters or histopathological examinations of an extensive series of tissues and organs were observed in either species.[5] In mice, no increase in tumor incidence was found after dosing up to 400 mg/kg/day of maltol, but high dose males had degeneration of the testes and reduced liver weights.[22] Rats showed no effects other than a reduced weight gain at 400 mg/maltol after two years of feeding. In all of these long-term feeding studies, the no observed adverse effect level was 200 mg/kg/day.[23]

A three generation study reproduction study in rats demonstrated maltol is not a reproductive toxicant up to 400 mg/kg/day, with no effect on reproductive success or increase in external or gross organ abnormalities in the offspring.[24] Further reproductive studies in rats and dogs give no evidence of reproductive or developmental toxicity.[5]

Several studies have evaluated the ability of maltol to enhance aluminum absorption and retention in the bone and brain cells or to induce neurofibrillary tangles in brain cells.[25-27] Although the studies suggest that maltol can enhance absorption of aluminum and increased tangle formation in cultured brain cells, the toxicological significance of these findings is unknown.[28]

Maltol is currently used worldwide at levels below 100 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). Maltol may be applied to cigarette tobacco as an additive, flavoring, or flavoring agent, and as such, maltol may be subjected to pyrolysis-type reactions when smoked. Maltol may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

Purge and trap and pyrolysis studies were conducted by PM USA. The results of purge and trap studies, where maltol was heated to 100 °C, suggest that a portion of maltol would be expected to distill prior to the burning cone of the tobacco.[29] Additionally, pyrolysis studies conducted at higher temperatures offered further evidence that maltol would not be expected to pyrolyze extensively and would probably be delivered in the smoke relatively intact.[30]

Maltol was part of a PM USA testing program that was designed to evaluate the potential effects of 333 ingredients added to typical commercial blended test cigarettes on selected biological and chemical endpoints.[31-34] Three pairs of test cigarettes were produced, each containing different groups of ingredients. Maltol was added to two pairs at target levels of 19 ppm, 33 ppm, 58 ppm and 100 ppm. No significant effects were noted in cytotoxicity, mutagenic studies or in respiratory tract endpoints in 90-day rat inhalation studies. In addition, smoke chemistry studies from cigarettes containing a mixture of flavors including maltol did not significantly alter the smoke chemistry profile compared to control cigarettes. Based on the results of these studies, the authors concluded that these ingredients (including maltol) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing maltol in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of maltol as a single ingredient and at higher tobacco application levels. Published studies show there is no meaningful difference in the composition or toxicity of smoke from cigarettes with added ingredients (including maltol) compared to the smoke from cigarettes without added ingredients.[31-39] Based on the best available data, the ingredients used in PM USA and/or PMP SA cigarettes do not increase the overall toxicity of cigarette smoke.

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