Evaluation Summary of Carob Bean Extract for Use as a Cigarette Ingredient

Carob bean extract is Generally Recognized As Safe (GRAS) by U.S. Food and Drug Administration for direct food additive in accordance with 21 CFR § 182.20.[1] The Flavor and Extract Manufacturers Association (FEMA No. 2243)[2] and the Council of Europe (CoE No. 120)[3] also approve carob bean extract for food use.

Carob bean extract is a product delivered in a tincture of alcohol (generally 20-25% carob in 55-77% alcohol) or other fluids.[4] The extract is derived from milled seeds of the fruit pod of *Ceratonia siliqua Leguminosae,* a large evergreen tree native to the Middle East region and to the southern part of the Mediterranean. It is extensively cultivated for the seeds and fruit in Cyprus, Greece, Syria, Spain and Italy.[5] The carob tree (also referred to as the locust tree) can reach heights of 33 feet and is well adapted to arid farming conditions.[6]

A thorough search of the literature on carob bean failed to reveal significant information regarding the potential toxicity of carob bean extract. Since carob bean gum is used extensively in food manufacturing, most of the relevant published literature data involved studies conducted with carob bean gum. This summary therefore includes data derived from studies with carob bean gum. The relevance of the results of testing with carob bean gum to those that might be produced by carob bean extract is unknown.[4]

Carob bean gum is chemically defined as a 1,4-galactomannan polymer and biologically characterized as an indigestible polysaccharide hydrocolloid.[7] Carob bean gum moves through the small intestine and arrives in the lower bowel largely undigested.[8-10] Although decreases in serum glucose and cholesterol have been associated with ingestion of large amounts of carob bean gum by experimental animals,[11-14] the research information speaks to a secondary mechanism on these findings – through a reduction in gastric emptying and perhaps peristalsis, thereby delaying or retarding their absorption.[13]

The toxicology studies with carob bean gum further support the inert nature of this molecule. Acute toxicity studies in several species did not show any evidence of oral toxicity at doses up to 10 g/kg.[15-17] Subchronic toxicity studies of dose level in rodents up to 10% were unremarkable.[16-18] Similarly, dogs receiving up to 10% (7,500 mg/kg/day) of carob bean gum admixed in the diet for 30 weeks showed no evidence of a compound-related toxicity.[19] Lifetime bioassay studies in rats and mice with up to 5% (2,500 mg/kg/day for rats and 7,500 mg/kg/day for mice) dietary exposure to carob bean gum did not evoke any meaningful evidence that galactomannan possessed a carcinogenic (or a long-term toxicological) potential.[16,20] Mutagenicity studies were negative[17,21-23] and no chromosomal damage has been demonstrated.[17,23] Teratology studies were performed in four species (rats,[24] mice,[24] hamsters[25] and rabbits[25]) gave no suggestion of a teratogenic effect at levels of 910–1,300 mg/kg, although maternal toxicity was evident in rabbits and mice at the highest doses.[24,25]

Carob bean gum has similarly low toxicity in humans. Several clinical studies have failed to show that oral ingestion of carob bean gum has any adverse sequelae.[12,26,27] There is clinical data to support claims of a decrease in serum cholesterol and a blunting of the glucose-tolerance test following oral ingestion of carob bean gum, but whether this is directly related to a carob bean gum effect on gastrointestinal peristalsis or a consequence of the physical nature of the

hydrocolloid structure is not known.[12,28-31] The impact of these serum biochemical findings has not been readily embraced by the medical community because carob bean gum is not normally a recommended dietary approach to correcting even marginal increases in plasma cholesterol levels or fasting glucose swings.[4]

The only finding of consequence occurred with carob bean flour, a material derived from the unrefined whole ground seed. There are reports of an allergic response to extensive inhalation exposure to this flour.[32-35] It is not known if this response is a rare occurrence. However, it does follow a pattern that has been noted with inhalation exposure to other proteinaceous materials, including soy protein.[4]

Carob bean extract is currently used worldwide at levels below 5,000 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). Carob bean extract may be applied directly to the tobacco during cigarette manufacturing as a tobacco flavoring material, and as such, may be subject to pyrolysis-type reactions. Carob bean extract may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

As suggested by the purge and trap studies conducted by PM USA,[36] carob bean extract would not be expected to extensively distill at 100°C. Pyrolysis analysis at temperatures up to 900°C suggested that carob bean extract would pyrolyze extensively.[37]

Carob bean extract was a part of the PM USA ingredient testing program that was designed to evaluate the potential effects of ingredients added to typical commercial blended test cigarettes on selected biological and chemical endpoints. Carob bean extract was added to test cigarette tobacco at target concentrations of 1,500 ppm, 4,500 ppm, or 7,000 ppm, and did not increase the mutagenic response of Salmonella bacteria to smoke condensate preparations.[38] Similarly, at the same target concentrations, the cytotoxic response of mouse embryo BALB/c 373 cells treated with mainstream smoke condensate preparations (particulate and gas vapor phase) was not altered by carob bean extract addition.[39] There were also no effects on any smoke constituents which correlated with the level of carob bean extract added to the cigarette tobacco on and equal TPM or tar basis.[40] The biological effects of inhaling smoke from cigarettes with carob bean extract was assessed in Sprague-Dawley rats exposed nose-only to smoke for 6 hrs/day, 7 days/week for 13 weeks. The results of the smoke inhalation studies indicated that the addition of carob bean extract to cigarette tobacco at target levels up to 7,000 ppm did not discernibly alter the biological effects normally associated with smoke exposure in rodents.[41]

The results of this evaluation of carob bean extract involving a review of published information and internal studies, suggests that addition of carob bean extract as a cigarette ingredient at the current use levels does not discernibly alter the biological effects normally associated with cigarette smoke.

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