Evaluation Summary of Cocoa for Use as a Cigarette Ingredient

Cocoa is the basis of chocolate flavoring and is the confection of choice in the United States, representing nearly half of the total candy consumption. Cocoa extract is also consumed at high levels, placing it among the top 16% of food ingredients when ranked according to consumption.[1,2] Cocoa powder, cocoa butter, and cocoa liquor are all products of the same fruit from the cacao tree, a member of the family *Sterculiaceae*, most often *Theobroma cacao* L. and rarely, *T. pentagona* or *T. spherocarpa.*[3] Cocoa is regulated as a food by the U.S. Food and Drug Administration (21 CFR § 163.110 thru 21 CFR § 163.155).

Cocoa butter is unlikely to be toxic at average human consumption levels due to the low reported toxicities of the individual fatty acids contained in the butter.[4-6] The high content of long chain fatty acids (oleic and stearic acids) in cocoa butter have been linked to their hypocholesterolemic effects in study animals.[7,8]

Animal studies of cocoa powder toxicity have related its effects to the amount of theobromine contained in the cocoa.[3,6,9-11] Theobromine is considered the most relevant pharmacologically active agent contained in cocoa powder.[11,12] Animal studies have indicated that theobromine is toxic to Sertoli cells of the testes in rats.[13,14] In comparison to other commonly consumed methylxanthines, caffeine and theophylline, theobromine has a low potency in regards to its effects on cytosolic calcium levels, adenosine receptor antagonism and inhibition of phosphodiesterases.[11,12] Theobromine is not considered to be a stimulant of the central nervous system as are caffeine and theophylline.[11,15-22]

Results of reproductive studies in rats and rabbits indicate that high levels of theobromine are required in order to reduce the reproductive viability in these animals. The amounts of cocoa required to reach these same levels of theobromine in humans far surpasses its average daily consumption.[23-28] A two year toxicity study found no evidence of carcinogenesis in rats fed diets of up to 5.0% cocoa powder.[29]

Cocoa is currently used worldwide at levels below 9,000 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). As such, cocoa may be subject to pyrolysis-type reactions when smoked. Cocoa may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

PM USA purge and trap studies suggest that cocoa would not distill in front of the burning cone at low temperatures.[30] At the higher temperatures used in pyrolysis studies conducted by PM USA, cocoa would be expected to pyrolyze extensively. The major peak identified in the pyrolysis study was theobromine which suggests that the theobromine would be expected to transfer to smoke intact.[31] Theobromine is a vasoactive amine[32] and the expected exposure level of theobromine from cigarette smoke is considered to be low to produce a clinically relevant blood level of theobromine.

Cocoa was part of a 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. Three pairs of test cigarettes were produced, each containing different

groups of ingredients. Cocoa was added to one pair of test cigarettes at target levels of 6470 ppm and 9705 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 cocoa) 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 cocoa) added to tobacco do not add significantly to the overall toxicity of cigarettes.[33-36]

Currently, information is only available for tests utilizing cocoa in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of cocoa as a single ingredient. Published studies show there is no meaningful difference in the composition or toxicity of smoke from cigarettes with added ingredients (including cocoa) compared to the smoke from cigarettes without added ingredients.[33-42] 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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