Evaluation Summary of Mate Absolute for Use as a Cigarette Ingredient

Mate absolute is used in the food industry as a flavor ingredient and adjuvant. As a result of its aromatic, refreshing and restorative effects, mate beverage or tea is the most popular drink in South American countries and has been consumed for many centuries.[1] Green as well as roasted mate is reported to contain over 250 volatile components and approximately 150 are also found in tea.[2,3] The important constituents of mate are caffeine, other purines, tannins or tannoid substances.[3-8] It has been recognized as generally recognized as safe (GRAS) for use in food by U.S. Food and Drug Administration (21 CFR § 182.20).

Because mate has been in use as a beverage for centuries and is approved for food uses, few animal studies evaluating its toxic effects were found in the scientific literature.[9] However, several studies in humans describing effects of mate drinking have appeared. In acute and subchronic toxicity studies, mate prepared from *I. dumosa* did not produce toxicity in rats.[10] In genotoxicity studies with *S. typhimurium,* mate extract was mutagenic in strains TA100 and TA102, but not in TA97 and TA98.[11] In *in vivo* studies, mate was not clastogenic to bone marrow cells of rats.[11]

Several case-control studies in South America have investigated the association between mate drinking and upper aerodigestive tract cancer. In two studies, even after adjustment of confounding factors including alcohol consumption and smoking, an increased risk of esophageal cancers among mate drinkers and a dose-response was noted.[12,13] However, in another similar study in Brazil, no significant increase in risk between mate drinking and esophageal cancer was observed.[14] In the study from Brazil, mate intake was lower and no attempt was made to estimate a possible dose-response relationship. In yet another study from Brazil, mate drinking was not significantly related to the oral cancer.[15] In a two separate studies from Uruguay, a dose-response association between mate drinking and oropharyngeal and laryngeal cancer was noted.[16,17] In other studies, mate drinking was not associated with bladder[18] or tongue cancer.[19]

Overall, human studies on mate drinking and cancer of upper aerodigestive tract suggest an association.[20,21] In all these studies, hot mate is consumed and the role of temperature in the causation is not clear. Experimental data suggest that ingestion of liquid at high temperature is associated with carcinogenesis.[22] Results from human studies also suggest the temperature of mate at which it was consumed was significantly associated with risk.[23-25] The International Agency for Research on Cancer (IARC) has stated that mate is “not classifiable as to its carcinogenicity to humans” (Group 3); hot mate drinking is “probably carcinogenic to humans” (Group 2A).[8]

Currently, mate absolute 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). Mate absolue is primarily used in cigarettes as an additive, flavoring or flavoring agent where it may be subject to distillation and/or pyrolysis. Mate absolute may also be added to the filter where it would not be subjected to pyrolysis temperatures.

As suggested by purge and trap studies conducted by PM USA, a small portion of mate absolute applied to cigarette tobacco would be expected to distill at 100ºC in front of the burning cone.[26] Pyrolysis studies conducted by PM USA on mate absolute suggest that mate absolute would be pyrolyzed extensively and would not be delivered in the smoke intact.[27] Although the pyrolysis technique is not quantitative, it is apparent that caffeine, hexadecanoic acid and squalene were the must abundant materials formed. Isoprene was identified and has been identified as possibly carcinogenic to humans by IARC.[28] Isoprene has been identified in tobacco smoke and is considered the most important building block of lipids, steroids, and terpenoids in addition to a wide variety of other natural products.[29] Formation of materials such as isoprene is not unexpected, since pyrolysis of organic materials may lead of formation of these compounds.

Mate absolute 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.[30-33] Three pairs of test cigarettes were produced, each containing different groups of ingredients. Mate absolute was added to two pairs at target levels of <1 ppm, 5 ppm, and 14 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 mate absolute 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 mate absolute) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing mate absolute in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of mate absolute 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 mate absolute) compared to the smoke from cigarettes without added ingredients.[30-38] 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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