Evaluation Summary of Methylcyclopentenolone for Use as a Cigarette Ingredient

Methylcyclopentenolone is generally recognized as safe (GRAS) for use in food by the Flavor and Extract Manufacturers Association (FEMA No. 2700)[1] and is approved for use by the United States Food and Drug Administration (FDA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA)[2] and the Council of Europe (CoE No. 758).[3] FDA has approved methylcyclopentenolone as a flavoring agent and adjuvant with no restrictions on food categories (21 CFR § 172.515). Methylcyclopentenolone is present naturally in several foods, including cocoa, coffee, barley, filbert, almond, sukiyaki, licorice, fenugreek, dried bonito and burgundy chardonnay wines.[4-6] For addition to food, it is produced synthetically and has been added to food since at least 1930.[7-10]

Methylcyclopentenolone has a low acute toxicity.[11-15] Methylcyclopentenolone was not irritating to the skin of rabbits and humans.[11,16] It was non-sensitizing in humans.[16-18] Methylcyclopentenolone was not mutagenic in Ames test and *E. coli* assays.[19-24] Methylcyclopentenolone was found to increase the frequencies of sister chromatid exchange (SCE) in human lymphocytes.[25-27]

Methylcyclopentenolone 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). Methylcyclopentenolone may be applied directly to the tobacco as an additive, flavoring or flavoring agent, and as such, may be subject to pyrolysis-type reactions during the smoking process. Methylcyclopentenolone may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

As suggested by purge and trap[28] studies conducted by PM USA, methylcyclopentenolone would be expected to distill at 100ºC. At the higher temperatures used in the pyrolysis[29] studies conducted by PM USA, the results suggested that methylcyclopentenolone would not pyrolyze extensively during the smoking process.

Methylcyclopentenolone 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. Methylcyclopentenolone was added to two pairs at target levels of <1 ppm, 41 ppm, and 124 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 methylcyclopentenolone 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 methylcyclopentenolone) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing methylcyclopentenolone in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of methylcyclopentenolone 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 methylcyclopentenolone) compared to the smoke from cigarettes without added ingredients.[24,30-37] 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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