Evaluation Summary of Glycerol for Use as a Cigarette Ingredient

Glycerol is generally recognized as safe (GRAS) by United States Food and Drug Administration (FDA), and is an approved food additive (21 CFR § 182.1320). Glycerol is also listed as GRAS by the Flavor Extract Manufacturers Association (FEMA No. 2525)[1] and is approved for use in food by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).[2]

Glycerol is a trihydric alcohol, which may be obtained from natural sources or synthesized.[3] It is present naturally in foods, predominantly as the tri-acyl backbone of fats.[4] Glycerol because of its numerous desirable physical characteristics (and that of its derivatives) make it a popular ingredient for addition to foods as a humectant, plasticizer, anticaking agent, texturizer, solvent, nutritive sweetener, and emulsifier and as such, it is added to candy, chewing gum, meats, cheese, margarine, marshmallows and many other foods.[5-7]

It is estimated that humans consume 58.3 mg/kg of glycerol from food containing glycerol as a food ingredient.[8-10] The consumption of the "food ingredient" glycerol is approximately one-fourth of the total amount (approximately 216 mg/kg) of glycerol from all sources.[8-11]

In laboratory animals, the toxic effects of glycerol have been extensively investigated.[3,12-87] Acute lethality studies have reported glycerol's oral LD_{50} values to be about 25 g/kg in rats.[3,13,14,20,88] Glycerol is reported in the literature to be neither carcinogenic nor produce adverse effects to offspring.[13,23,42,55-58,60-65] In humans, glycerol has been used therapeutically to reduce intraocular and intracranial pressure.[3,89-91] The therapeutic dose of glycerol for these effects is 0.5 to 1.5 g/kg.[3,89-91] There are reported side effects at these doses, including headache, nausea, dizziness, drowsiness and diuresis.[92-107] Similar effects have been observed in laboratory animals given 1 to 2 g/kg glycerol.[13,22,23,26,35-37,40,52,108] Although there are cases of people receiving large doses (>30 g/kg) of glycerol and resulting in an adverse effect, such as hemolysis, the precise dose required to elicit these effects has not been established in a well-characterized human population.[23,80,107-126]

Glycerol is currently used worldwide at levels below 3.5% (35,000 ppm) in selected conventional cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). Glycerol may be applied directly to the tobacco as an additive, humectant or solvent, and as such, may be subject to pyrolysis-type reactions during the smoking process. Glycerol may also be applied to the filter where it would not be subjected to pyrolysis temperatures.

As suggested by purge and trap studies conducted by PM USA, glycerol would not be expected to distill extensively at 100ºC.[129] At the higher temperatures used in the pyrolysis studies conducted by PM USA, the results suggested that glycerol would not be pyrolyzed extensively during the smoking process and would be delivered to the smoke intact.[130] The results also suggested that very small amounts of acrolein and glycolaldehyde may be formed as a result of glycerol pyrolysis.[131-133]

In a specific study conducted to determine the role of glycerol as a precursor of acrolein and formaldehyde in mainstream and sidestream smoke, non-filtered radiolabeled cigarettes were

prepared from 2R1 filler by spraying with ^{14}C-glycerol.[134] In this study, about 30-40% of the radioactivity was transferred to the sidestream gas phase of all cigarettes tested, whereas only 5% of the radioactivity was transferred to mainstream gas phase. The sidestream smoke fractions (TPM and gas) were analyzed; ^{14}C-glycerol was the primary compound in both fractions. Less than 10% ^{14}C-formaldehyde was recovered in each fraction. Similar analyses were conducted on the mainstream fraction. Thirteen to 16% of the total activity was found in the mainstream TPM. Further analysis showed that while non-radiolabeled acrolein was detected as a normal smoke component, there was little or no radioactivity associated with acrolein. Radiochromatography of sidestream TPM, mainstream TPM and butt derivitized with DNPH showed essentially all radioactivity to be associated with ^{14}C-glycerol. Radiolabeled carbon dioxide, carbon monoxide, and methane were also detected. The results of this study indicated that glycerol is a precursor of formaldehyde and acetaldehyde, and to a lesser extent acrolein.

In another study of glycerol containing cigarettes, aldehyde concentration decreased with increasing glycerol concentration.[135,136] However, the formaldehyde concentration of sidestream smoke increased with increasing glycerol. Acrolein appeared to be the least affected aldehyde measured.

Glycerol 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.[137-140] Three pairs of test cigarettes were produced, each containing different groups of ingredients. Glycerol was added to two pairs at target levels of 61 ppm, 126 ppm, 28031 ppm and 42048 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 glycerol 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 glycerol) added to tobacco do not add significantly to the overall toxicity of cigarettes.

A National Cancer Institute mouse skin painting study with cigarette smoke condensate prepared from cigarettes containing glycerol alone (2.8%) indicated little or no effect on tumorigenicity.[127] The results of the study suggested that the combination of invert sugar (5.3%) and glycerol (2.8%) at a condensate application amount of 12.5 mg/application had little effect on tumorigenicity, but at a higher condensate application rate the combination "may contribute to condensate tumorigenicity."[127] In another ingredient mixture mouse skin painting study conducted with 2.4% glycerol on tobacco, there was no discernible difference between control and test cigarettes containing ingredients.[128]

The results of this evaluation of glycerol involving a review of published information and internal studies show there is no meaningful difference in the composition or toxicity of smoke from cigarettes with added ingredients (including glycerol) compared to the smoke from cigarettes without added ingredients.[128,137-144] 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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