Evaluation Summary of Sucrose for Use as a Cigarette Ingredient

Sucrose is accepted as a generally recognized as safe (GRAS) food substance by the United States Food and Drug Administration (21 CFR § 184.1854). Sucrose is a naturally occurring carbohydrate whose consumption predates history. The carbohydrates, in general, comprise a group of nutrient substances which are readily metabolized for immediate energy utilization and/or storage. Sucrose continues to be popular foodstuff for human consumption in the United States.[1,2]

According to all conventional tests, sucrose is of low toxicity to both animals and humans.[3-9] Studies on the effects of sucrose on glucose tolerance,[10-48] diabetes,[18,20,21,49-74] cardiovascular disease (including hypertension),[75-100] blood lipids[75,77,79,101-131] and incidence of cancer[132-134] in both human and animal studies point to only transient effects seen with dosages of sucrose which far exceed the normal dietary intake in humans. Factors which weigh heavily on the results of these studies, and are considered confounding factors, are the contribution of excessive calories with resulting obesity, which itself is a contributing factor to hypertension, cardiovascular diseases and diabetes. Thus, there are no studies which have been conducted that provide scientific evidence that consumption of sucrose at concentrations which occur in the average diet directly causes diabetes,[41,135-150] hypertension, cardiovascular disease, blood lipid diseases,[36,46,47,151-167] reproductive abnormalities[67,114,168-174] or cancer.[175-180]

Currently, sucrose is used worldwide at levels below 50,000 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). Sucrose is applied directly to the tobacco as a flavor, and as such, invert sugar may be subject to pyrolysis reactions when smoked. Sucrose 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 studies conducted by PM USA, sucrose applied to tobacco would not be expected to distill at 100 °C and a significant portion of the material would be available for pyrolysis.[181] Specific smoke transfer studies with radiolabeled sucrose applied to tobacco indicate < 1% transfer of intact sucrose to the smoke, and sucrose would be expected to pyrolyze during smoking.[182,183] At the higher temperautres used in the PM USA pyrolysis studies, the major chemicals identified were furfural, 5-(hydroxymethyl)-2-furfural, levoglucosan and 1,6-anhydro-beta-d-glucofuranose.[184] Formaldehyde, acetaldehyde, furan, and carbon dioxide peaks were also identified in the pyrolysis study and these peaks are consistent with pyrolytic destruction of carbohydrate materials. An extensive review of the literature suggests little evidence that supports acetaldehyde as a major pyrolysis product of sugar.[185]

Chemical analysis of smoke from cigarettes to which sucrose was added (36,000, 72,000 or 100,000 ppm sucrose on tobacco) revealed occasional changes (decreases and increases) in some analyzed parameters. Despite the indications of statistically significant changes for some smoke chemistry parameters in test cigarettes compared to the control cigarette, the increase or decrease in yields that were noted probably reflect variability in normal cigarette construction and/or chemical analysis technique. Increased levels of acrolein and formaldehyde were identified in the smoke from cigarettes containing high levels of sucrose. However, when this chemical analysis was repeated as a part of the examination of the smoke atmosphere generated with these same

cigarettes during a 13-week smoke inhalation study, the mean acetaldehyde, acrolein, and propionaldehyde concentrations were comparable between control and test cigarette groups. However, formaldehyde concentration in the smoke atmosphere did increase with increasing levels of sucrose added to the test cigarette tobacco.[186]

The results of bacterial mutagenicity studies conducted with smoke condensate preparations and cytotoxicity assays using condensate or gas vapor phase preparations indicated no significant sucrose-related effects on these *in vitro* endpoints.[187,188]

Inhalation exposure of rats to mainstream smoke from cigarettes containing various levels of sucrose for 13 weeks did not result in any evidence of systemic toxicity. Assessment of peripheral blood or bone marrow samples for eyrthrocyte micronucleus formation during the 13-week inhalation study indicated no increased potential for clastogenic activity. Histopathologic changes were noted only in the in the respiratory tract tissues. Generally, the severity and incidence of the histopathologic changes were consistent with previous studies of cigarettes conducted at these smoke exposure levels.[189]

The smoke from the cigarette containing 100,000 ppm sucrose appeared to be slightly more irritating in that male rats exposed to the smoke from the cigarettes containing 100,000 ppm sucrose developed a more severe degree of respiratory epithelial hyperplasia in nasal section 2, and also displayed an increased number of goblet cells in the bronchial epithelium. Changes in the respiratory tissues in the female rats exposed to smoke from the cigarettes containing 100,000 ppm sucrose were comparable to control rat response. Exposure to smoke from cigarettes containing lower sucrose levels did not produce any increased incidence or severity of response over control cigarette smoke. Examination of the respiratory tract following a non-smoking recovery period indicated a reversal of the histopathologic change. While residual change was still evident in the larynx of smoke exposed animals (100,000 ppm sucrose) at the end of the 6-week recovery period, goblet cells were no longer increased.[189]

The presence of the microscopic changes seen in the upper respiratory tract of male rats exposed to smoke from cigarettes containing 100,000 ppm is consistent with the increased concentration of an irritant such as formaldehyde measured in the smoke atmosphere. The authors of the study concluded that the sucrose no-observed-effect level (NOEL) was 72,000 ppm.[189]

The results of this evaluation of sucrose, involving a review of current published information and internal studies, suggests that the addition of sucrose as a cigarette ingredient at levels below 50,000 ppm does not discernibly alter the biological effects normally associated with cigarette smoke exposure.

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