# Evaluation Summary of Valerian Root Extract for Use as a Cigarette Ingredient

Valerian root extract is used in the food industry as a flavor ingredient. It is an United States Food and Drug Administration (FDA) approved food additive (21 CFR § 172.510), is generally recognized as safe (GRAS) for use in food by the Flavor Extract Manufacturers Association (FEMA No. 3099)[1] and is approved for use by the Council of Europe (CoE No. 473).[2] A primary source in the diet is through addition to food (0.0016-0.0029 mg/kg/day).[3-5] However, this is a relatively low amount when compared with intake by individuals consuming the recommended dose of valerian root extract herbal supplements (17 mg/kg/day).[6,7]

Acute i.p. toxicity studies in mice indicate that valerian ethanol extract is slightly to practically non-toxic with an $LD_{50}$ of 3.3 g/kg.[8] There were no genotoxicity or carcinogenicity studies identified using valerian root extract, but studies using various valerian root extract constituents were equivocal with some mutagenicity reported in bacterial mutagenicity assays, especially for the epoxide containing constituents, such as the valpotriates.[9-12] Some *in vitro* cytotoxicity in mammalian cells was also reported for the valpotriates.[12-17] Valerian root extract exhibited sedative activity in animals and humans with the majority of studies showing no long-term adverse effects directly attributable to valerian root extract or its constituents noted in animals or humans.[6,8,18-50] However, in some instances valerian has been reported to cause acute and chronic adverse effects.[48-58] There were no reported reproductive or teratogenic effects directly attributable to valerian root extract or its constituents in animals or humans.[59-62] Clinical studies have identified positive therapeutic effects for the treatment of nervous disorders and insomnia and there were no adverse effects from valerian consumption reported in these clinical studies.[63-73]

Valerian root extract 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). Valerian root extract 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. Valerian root extract 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, valerian root extract would be expected to distill at 100ºC.[74] At the higher temperatures used in the pyrolysis studies conducted by PM USA, valerian root extract produced a number of individual chemical entities, including some pyrolysis products such as phenol.[75] The formation of small amounts of these materials is not unexpected, since pyrolysis of organic materials may lead to formation of these compounds. Therefore, the results of these analyses suggest that valerian root extract applied to cigarette tobacco would distill in front of the burning cone, but would be pyrolyzed and would not be delivered in the smoke intact. Neither study identified valpotriates in the purge and trap or pyrolysis studies.

Valerian root extract 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.[76-79] Three pairs of test cigarettes were produced, each containing different groups of ingredients. Valerian root extract was added to one pair at target levels of 7 ppm, and 21 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 valerian root extract 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 valerian root extract) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing valerian root extract in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of valerian root extract 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 valerian root extract up to a target level of 812 ppm)[81] compared to the smoke from cigarettes without added ingredients.[76-84] 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.

## References


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