

**Evaluation of**  
***alpha*-Terpineol**  
**For Use as an Ingredient in**  
**Tobacco Products**

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## **INTRODUCTION**

*alpha*-Terpineol (CAS # 98-55-5) is currently used worldwide at levels below **5 ppm** in selected brands of tobacco products manufactured and/or distributed by Philip Morris International, including cigarettes and fine-cut tobacco. This document is a review of the published toxicology information on *alpha*-terpineol abstracted from online toxicity databases.

### ***Overview<sup>a</sup>***

The following information was generated from the MICROMEDEX database system <http://csi.micromedex.com> on December 22<sup>nd</sup> 2008, unless otherwise indicated.

*alpha*-Terpineol is a terpene alcohol possessing a lilac odour<sup>[1]</sup>. It is found in numerous plants and foods, but is produced in commercial quantities by a synthetic process<sup>[1],[2],[3]</sup>. *alpha*-Terpineol is commonly used in perfumes, soaps, and cosmetics<sup>[1],[2]</sup>, and is a major constituent in pine oil, a common cleaner and cleaner ingredient<sup>[4]</sup>. In the food industry, *alpha*-terpineol is used as a flavouring agent, especially in citrus flavours (lemon, lime, orange), and as an adjuvant<sup>[3]</sup>. Other flavours where *alpha*-terpineol is used include berry, nutmeg, ginger, anise, and peach. It is also used in spice flavours for Frankfurter sausages<sup>[5]</sup>.

As a food flavouring additive, the material has been assessed under the provisions of the *Federal Food, Drug and Cosmetic Act, section 201 (s)*, by the Expert Committee of the USA Flavour and Extract Manufacturers Association (FEMA), to be generally recognised as safe (GRAS) under current conditions of use.

The Joint FAO/WHO Expert Committee on Food Additives has assessed *alpha*-terpineol as presenting no safety concerns at current levels of intake when used as a flavouring agent. The daily intake is estimated at 1100 µg/day in the USA and 3000 µg/day in Europe<sup>[6]</sup>.

The use of this ingredient on tobacco products is regulated in several countries worldwide. It is approved for use in tobacco products as an additive or flavouring in several countries with Tobacco Product Regulations, including e.g., Belgium, Croatia, Czech Republic, Egypt, Finland, France, Germany, Great Britain, Hungary, Lithuania, Macedonia, Romania, Slovak Republic, Spain, Switzerland. Apart from countries that approve its use, there is no country, regardless of the extent to which tobacco products are regulated therein, that affirmatively prohibits the use of this ingredient on tobacco products.

## **TOXICITY DATA ON UNBURNT MATERIAL**

### ***Health Hazard Data***

Toxicity studies have shown that  $\alpha$ -terpineol is slightly toxic with lethal oral doses in rats of approximately 4.3 g/kg<sup>[7]</sup>. Similarly, the lethal oral dose for the mouse is approximately 2.8 g/kg<sup>[8]</sup>.

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<sup>a</sup> **Note:** Philip Morris International shares the concerns of regulators and the public health community about the proliferation of certain cigarette brands that have a predominantly candy-like or fruity flavour and are particularly appealing to minors, and we support legislation that would ban such cigarettes. However, there is currently no consistent terminology used by regulators and the public health community to describe such cigarettes. This can lead to confusion and potential for misinterpretation. In this document, any references to flavours or "smoke aroma" or flavour perceptions such as "sweet", "fruity", etc. are not meant to describe a flavour, taste or aroma that would dominate the taste of the final product, let alone dominate it in a way that is appealing to minors. Rather, such references are only used to explain the differences and nuances between the various flavours described in this and related documents.

One subchronic study in mice treated by i.p. injection with *alpha*-terpineol indicated that *alpha*-terpineol is not a carcinogen and with a no observed adverse effect level (NOAEL) of 250 mg/kg/day<sup>[9]</sup>. Genotoxicity studies in bacterial and mammalian cell systems, with and without metabolic activation, proved negative for mutagenicity up to 10 mg/plate<sup>[10],[11]</sup>, with one study reporting a weak positive for mutagenicity in strain TA102 at concentrations  $\geq 750$   $\mu\text{g}/\text{plate}$ <sup>[11]</sup>. *alpha*-Terpineol is a skin irritant in animal models<sup>[7],[12],[13],[14]</sup> and may be a human skin sensitiser<sup>[15],[16]</sup>. In humans, pine oil can cause numerous adverse effects<sup>[17],[18]</sup>, but pine oil is a complex mixture of several terpine alcohols and, therefore, the significance to *alpha*-terpineol toxicity cannot be determined.

## **TOXICITY DATA ON BURNT MATERIAL**

Data on the toxicity of *alpha*-terpineol as a cigarette ingredient has been evaluated in a series of studies. The results of these studies may be found in the following references:

Baker R.R. *et al.* 2004, "An overview of the effects of tobacco ingredients on smoke chemistry and toxicity", Food and Chemical Toxicology, 42S:53-83. \*\*PEER REVIEWED\*\*

Carmines E.L., 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes. Part I: Cigarette Design, Testing Approach and Review of Results," Food and Chemical Toxicology, 40:77-91. \*\*PEER REVIEWED\*\*

Rustemeier K. *et al.* 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes Part II. Chemical Smoke Composition," Food and Chemical Toxicology, 40:93-104. \*\*PEER REVIEWED\*\*

Roemer E. *et al.* 2002, "Evaluation of the Potential Effects of Flavor Ingredients Added to Cigarettes. Part 3. In Vitro Genotoxicity and Cytotoxicity," Food and Chemical Toxicology, 40:105-111. \*\*PEER REVIEWED\*\*

Vanscheeuwijck P.M. *et al.* 2002, "Toxicological Evaluation of Cigarettes without and with the Addition of Flavor Ingredients to the Tobacco. Part 4. Subchronic Inhalation Toxicity," Food and Chemical Toxicology, 40:113-131. \*\*PEER REVIEWED\*\*

Renne R.A. *et al.* 2006, "Effects of Flavoring and Casing Ingredients on the Toxicity of Mainstream Cigarette Smoke in Rats," Inhalation Toxicology, 18:685-706. \*\*PEER REVIEWED\*\*

## **CONCLUSION**

Smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop serious diseases, like lung cancer, than non-smokers. There is no "safe" cigarette. Government health warnings about smoking apply to all cigarettes, regardless of the ingredients added, including those containing only tobacco and paper.

While Philip Morris International has not conducted human studies on the health effects of ingredients used in cigarette manufacture, studies have been conducted by Philip Morris International and/or others using scientifically accepted *in vitro* and *in vivo* toxicity assays with various ingredient mixtures. These studies show there is no meaningful difference in the composition or toxicity of smoke when the smoke from cigarettes with the added ingredient is compared to the smoke from cigarettes without this added ingredient. Based on a review of current published toxicological information, it is our scientific judgement that the addition of *alpha*-terpineol as an ingredient, at the levels used in our brands, does not increase the overall toxicity of tobacco smoke.

## References

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