

**Evaluation of
alpha-Phellandrene
for Use as a Cigarette Ingredient**

October 2005

INTRODUCTION

Alpha-phellandrene (CAS # 99-83-2) is currently used worldwide at levels below **1 ppm** in selected cigarette brands manufactured and/or distributed by Philip Morris International. This document is a review of current published toxicology information on alpha-phellandrene abstracted from online toxicity databases.

TOXICITY DATA ON UN-BURNED MATERIAL

The following information was generated from the MICROMEDEX database tool <http://csi.micromedex.com> on October 27th 2005, unless otherwise indicated.

Overview

Alpha-phellandrene is an alicyclic hydrocarbon that naturally occurs in Eucalyptus and bitter fennel¹.

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 manufacturer's Association (FEMA), to be generally recognized as safe (GRAS) under current conditions of use.

The Joint FAO/WHO Expert Committee on Food Additives has assessed alpha-phellandrene as presenting no safety concerns at current levels of intake when used as a flavouring agent². It has also been defined as a flavouring substance which may be used as foodstuffs by the *Council of Europe Committee of Experts on Flavouring Substances* at an upper level of 130 mg/kg in foods.

Alpha-phellandrene is a common cosmetic ingredient.

The following information was generated from the HSDB – Hazardous Substances Data Bank, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on October 27th 2005.

Non-Human Toxicity Excerpts

Alpha-phellandrene applied full strength to intact or abraded rabbit skin for 24 hr under occlusion was moderately irritating. [**PEER REVIEWED**] [Opdyke DLJ; Food Cosmet Toxicol 16 (suppl 1) 843-4 (1978)]

The following information was generated from the RTECS – Registry of Toxic Effects of Chemical Substances, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) October 27th 2005.

Health hazard data

Acute toxicity

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

Rat

¹ The Merck Index, Eleventh edition, 1989.

² Joint FAO/WHO Expert committee on food additives, sixty-third meeting: Summary and conclusions, Geneva 2004 http://www.who.int/ipcs/publications/jecfa/en/summary_final.pdf

LD50 - ROUTE: Oral; DOSE: 5700 mg/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (16,843,1978)]

LD50 - ROUTE: Unreported; DOSE: 5700 mg/kg [Handbook of pesticide toxicology. Robert Krieger ed, Academic press, 2001 (1,827,2001)]

TOXICITY DATA ON BURNT MATERIAL

Data on the toxicity of alpha-phellandrene after combustion has been evaluated in a series of studies. The results of these studies may be found in the following references:

R.R. Baker 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**

E.L. Carmines, 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**

K. Rustemeier 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 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**

P.M. Vanscheeuwijck 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**

Gaworski et al, 1998, "Toxicological evaluation of flavor ingredients added to cigarette tobacco: 13-week inhalation exposure in rats" Inhalation Toxicology, 10:357-381. **PEER REVIEWED**

Gaworski et al, 1999, "Toxicological evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice" Toxicology, 139 1-17. **PEER REVIEWED**

These studies indicate that chemicals used in the production of cigarettes do not increase the overall toxicity of cigarette smoke.

DATA ON THE EFFECTS ON HUMAN HEALTH

The following information was generated from the HSDB – Hazardous Substances Data Bank, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on October 27th 2005.

Human Toxicity Excerpts

1. ...Can be irritating to, & absorbed through, skin. Ingestion can cause vomiting, diarrhea. [**PEER REVIEWED**] [The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 932]
2. Hypersensitivity found due to sensitizing properties of 3 ingredients: alpha-pinene, limonene, & phellandrene in dental prepn. [**PEER REVIEWED**] [Dooms-Goossens A et al; Turpentine-induced hypersensitivity to peppermint oil; contact dermatitis 3 (6): 304-8 (1977)]

The following information was generated from the RTECS – Registry of Toxic Effects of Chemical Substances, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) October 27th 2005.

Health hazard data

Irritation

SKIN - STANDARD DRAIZE TEST

Man

ROUTE: Skin; DOSE: 100%; REACTION: Severe [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (16,843,1978)]

CONCLUSION

Cigarette 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 using scientifically accepted in vitro and in vivo toxicity assays with various ingredient mixtures (see Toxicity Data on Burnt Material above). These studies show there is no meaningful difference in the composition or toxicity of smoke when the smoke from cigarettes with added ingredients is compared to the smoke from cigarettes without added ingredients. These findings are supported by similar studies from the published literature. It is our scientific judgment, based on the best available data, that alpha-phellandrene used in our cigarettes does not increase the overall toxicity of cigarette smoke.