

**Evaluation of
cis-3-Hexen-1-yl acetate
for Use as a Cigarette Ingredient**

December 2005

INTRODUCTION

Cis-3-hexen-1-yl acetate (CAS # 3681-71-8) 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 cis-3-hexen-1-yl acetate 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 December 7th 2005, unless otherwise indicated.

Overview

Cis-3-hexen-1-yl acetate is an ester of the aliphatic acyclic primary alcohol 3-hexen-1-ol which occurs naturally in leaves of odoriferous plants (including trees and shrubs). It has the typical odour of “green leaves”¹.

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 cis-3-hexen-1-yl acetate as presenting no safety concerns at current levels of intake when used as a flavouring agent. The daily per capita intake is estimated at 0.95 µg/kg bw/day in the USA and 11 µg/kg bw/day in Europe².

Cis-3-hexen-1-yl acetate is a common cosmetic ingredient.

This material appears on the list of “Permitted Additives to Tobacco Products in the United Kingdom” (Department of Health, 2003) at a maximum level permitted for inclusion in cigarettes of 0.001 % w/w tobacco.

The following information was generated from the RTECS – Registry of Toxic Effects of Chemical Substances, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on December 7th 2005.

Health hazard data

Acute toxicity

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

¹ The Merck index, an encyclopedia of chemicals, drugs and biologicals; 11th edition; Merck & Co., Inc, 1989

² Safety evaluations of certain food additives and contaminants, WHO Food Additive Series 40: Esters of aliphatic acyclic primary alcohols with aliphatic linear saturated carboxylic acids
<http://www.inchem.org/documents/jecfa/jecmono/v040je14.htm>

Rat

LD50 - ROUTE: Oral; DOSE: >5 gm/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (13,454,1975)]

Rabbit

LD50 - ROUTE: Skin; DOSE: >5 gm/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (13,454,1975)]

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. 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 judgement, based on the best available data, that cis-3-hexen-1-yl acetate used in our cigarettes does not increase the overall toxicity of cigarette smoke.