

**Evaluation of
Amyl butyrate
for Use as a Cigarette Ingredient**

October 2005

INTRODUCTION

Amyl butyrate 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 amyl butyrate 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 28th 2005, unless otherwise indicated.

Overview

Amyl butyrate is found in bananas, beer, apple juice, apricots, strawberry and wine. It is used in syrup, candy, chewing gum, beverages, frozen dairy desserts, gelatin and baked goods¹.

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 recognized as safe (GRAS) under current conditions of use.

The Joint FAO/WHO Expert Committee on Food Additives has assessed Amyl butyrate as presenting no safety concerns at current levels of intake when used as a flavouring agent. The daily per capita intake is estimated at 3.3 µg/kg bw/day in the USA and at 7.5 µg/kg bw/day in Europe². 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 10 mg/kg for foods.

Amyl butyrate 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 0.15 % 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 October 28th 2005.

Health hazard data

Acute toxicity

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

Rat

LD50 - ROUTE: Oral; DOSE: 12210 mg/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (2,327,1964)]

¹ http://tobaccodocuments.org/profiles/additives/amyl_butyrate.html

² Safety evaluation of certain food additives and contaminants, WHO Food Additives Series 40, The forty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA): Esters of Aliphatic Primary Alcohols with Aliphatic Linear Saturated Carboxylic Acids, Geneva 1998. <http://www.inchem.org/documents/jecfa/jecmono/v040je14.htm>

TOXIC EFFECTS:

Behavioral - Somnolence (general depressed activity)

Skin and Appendages - Hair

Guinea Pig

LD50 - ROUTE: Oral; DOSE: 11950 mg/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (2,327,1964)]

TOXIC EFFECTS:

Behavioral - Somnolence (general depressed activity)

Behavioral - Ataxia

TOXICITY DATA ON BURNED MATERIAL

Data on the toxicity of amyl butyrate 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**

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

CONCLUSION

Cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop 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 amyl butyrate used in our cigarettes does not increase the overall toxicity of cigarette smoke.