

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

**November 2005**

## **INTRODUCTION**

Butyl butyrate (CAS# 109-21-7) 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 butyl 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 November 1<sup>st</sup> 2005, unless otherwise indicated.

### ***Overview***

Butyl butyrate is present in the diet via various fruits such as apples, berries, strawberries and passion fruits, but also via mushrooms, cheese and honey<sup>1</sup>. It is used in the flavouring and fragrance industry<sup>2</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 recognized as safe (GRAS) under current conditions of use.

The Joint FAO/WHO Expert Committee on Food Additives has assessed butyl 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 1.1 µg/kg bw/day in the USA and at 6.5 µg/kg bw/day in Europe<sup>3</sup>. 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 50 mg/kg for foods.

Butyl 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.

Butyl butyrate and isobutyl isobutyrate are moderate eye, mucous membrane, and respiratory irritants. An exposure of 5000 ppm for 6 hours killed two out of three rats exposed, but there were no exposure symptoms when rats were exposed to 500 ppm for 6 hours<sup>2</sup>.

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 November 1<sup>st</sup> 2005.

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<sup>1</sup> <http://www.thegoodscentscompany.com/data/rw1014091.html>, viewed on November 1, 2005.

<sup>2</sup> <http://www.osha-slc.gov/dts/sltc/methods/partial/t-pv2090-01-9303-ch/t-pv2090-01-9303-ch.html>

<sup>3</sup> 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 acyclic primary alcohols with aliphatic linear saturated carboxylic acids, Geneva, 1998.  
<http://www.inchem.org/documents/jecfa/jecmono/v040je14.htm>

## ***Health hazard data***

### *Acute toxicity*

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

#### ***Rat***

LD50 - ROUTE: Intraperitoneal; DOSE: 2300 mg/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (17,521,1979)]

#### ***Mouse***

LD50 - ROUTE: Intraperitoneal; DOSE: 8900 mg/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (17,521,1979)]

#### ***Rabbit***

LD50 - ROUTE: Oral; DOSE: 9520 mg/kg [Industrial Medicine and Surgery. (Northbrook, IL) V.18-42, 1949-73. For publisher information, see IOHSA5. (41,31,1972)]

LD50 - ROUTE: Skin; DOSE: >5 gm/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (17,521,1979)]

### *Irritation*

SKIN - STANDARD DRAIZE TEST

#### ***Rabbit***

ROUTE: Skin; DOSE: 500 mg/24H; REACTION: Moderate [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (17,521,1979)]

## **TOXICITY DATA ON BURNT MATERIAL**

Data on the toxicity of butyl 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 chemicals 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 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 butyl butyrate used in our cigarettes does not increase the overall toxicity of cigarette smoke.