

**Evaluation of  
beta-Ionone  
for Use as a Cigarette Ingredient**

**October 2005**

## **INTRODUCTION**

Beta-ionone (CAS # 14901-07-6) is currently used worldwide at levels below **5 ppm** in selected cigarette brands manufactured and/or distributed by Philip Morris International. This document is a review of current published toxicology information on beta-ionone 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 31<sup>st</sup> 2005, unless otherwise indicated.

### ***Overview***

Beta-ionone is present in the diet via beer, orange juice and carrots<sup>1</sup>. It has been found to inhibit rat mammary carcinogenesis<sup>2</sup> and to induce apoptosis of human gastric adenocarcinoma cells<sup>3</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 beta-ionone as presenting no safety concerns at current levels of intake when used as a flavouring agent. The daily per capita intake is estimated at 2 µg/kg bw/day in the USA and at 3 µg/kg bw/day in Europe<sup>4</sup>.

Beta-ionone 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>) October 31<sup>st</sup> 2005.

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<sup>1</sup> <http://www.thegoodscentscompany.com>, viewed on October 31<sup>st</sup> 2005.

<sup>2</sup> Liu J and Liu RH. Beta-ionone inhibits rat mammary carcinogenesis. 2005 IFT Annual Meeting – New Orleans, Louisiana.  
[http://ift.confex.com/ift/2005/techprogram/paper\\_31143.htm](http://ift.confex.com/ift/2005/techprogram/paper_31143.htm), viewed on October 31, 2005.

<sup>3</sup> Liu JR, Chen BQ, Yang BF, Dong HW, Sun CH, Wang Q, Song G and Song YQ. Apoptosis of human gastric adenocarcinoma cells induced by beta-ionone. *World J Gastroenterol*, 10(3):348-351, 2004.

<sup>4</sup> Safety Evaluation of Certain Food Additives. WHO Food additives series 42, The fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA): Ionones and structurally related substances, Geneva 1999.  
<http://www.inchem.org/documents/jecfa/jecmono/v042je19.htm>

**Health hazard data**

*Acute toxicity*

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

**Rat**

LD50 - ROUTE: Oral; DOSE: 4590 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* - Tremor

**Mouse**

LD50 - ROUTE: Intraperitoneal; DOSE: 2277 mg/kg [FAO Nutrition Meetings Report Series. (Rome, Italy) No.?-57, 1948-77. Discontinued. (44A,48,1967)]

*Other multiple dose toxicity data*

**Rat**

TDLo - ROUTE: Intraperitoneal; DOSE: 4 gm/kg/4D intermittent [Brazilian Journal of Medical and Biological Research. (Associacao Brasileira de Divulgacao Cientifica, Faculdade de Medicina de Ribeirao Preto, USP, 141000 Ribeirao Preto, SP, Brazil) V.14-1981- (36,839,2003)]

TOXIC EFFECTS:

*Lung, Thorax, or Respiration* - Other changes

*Biochemical* - Cytochrome oxidases (including oxidative phosphorylation)

*Biochemical* - Effect on cyclic nucleotides

**TOXICITY DATA ON BURNT MATERIAL**

Data on the toxicity of beta-ionone as a cigarette ingredient 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 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 judgement, based on the best available data, that beta-ionone used in our cigarettes does not increase the overall toxicity of cigarette smoke.