

TOXICOLOGY LABORATORY  
GASTHUISBERG CAMPUS, O&N2  
P8 922, HERESTRAAT 49  
D-3000 LEUVEN

CATHOLIC UNIVERSITY  
LEUVEN

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**“SUPER SMOKER” EXPERT REPORT  
FINAL REPORT**

On 28 February 2007 the following were forwarded to us by Dr. H. LERUT:

- a liquid labelled “TOBACCO AROMA TYPE”, “FS” Flavour, BSt 1/163-1, 02-2007, 50 g
- 2 plastic “SUPER SMOKER” cigarettes,
- 1 plastic “SUPER SMOKER” cigar;
- some accessories, including a battery, transformer, mouthpieces.

On 30 May 2007 the following were also forwarded to us by Dr. H. LERUT:

- 4 x 4 cartridges with different nicotine concentrations;
- 1 “SUPER SMOKER” cigarette (new model);
- a battery charger.

**EXPERT APPRAISAL AND ANALYSIS REQUESTED**

- To determine which substances are present in the liquid with the above-mentioned label?
- To determine which substances are present in the smoke produced by the “SUPER SMOKER” cigarettes?
- To determine which substances are present in the smoke produced by the “SUPER SMOKER” cigar?
- To give a risk evaluation of the type of substances found.

PROF. DR. J. TYTGAT – *head of department*

- In addition to the above qualitative analyses, if necessary a quantitative approximation to be carried out of these qualitative data.
- To carry out a concentration determination of nicotine in the 4 cartridges.

### **TEST ARRANGEMENT AND METHODOLOGY**

2 types of test arrangements or simulation tests were carried out.

- a “SUPER SMOKER” cigarette is connected to an Erlenmeyer flash under low pressure for the purpose of simulating a sucking effect, whereupon the air can be dissolved in an organic solvent for gas chromatographic analysis. The purpose of this arrangement is to examine the visible smoke without the smoke coming into contact with the mouth.
- gas chromatographic analysis of (partially) inhaled smoke from a “SUPER SMOKER” cigarette or cigar. The purpose of this simulation is to examine the smoke effectively inhaled (i.e. after contact with the mouth).

The following methodology was applied:

- sampling: “headspace solid-phase microextraction” (HSPME) with the aid of a polydimethyl siloxane (PDMS) fibre at room temperature (Supelco, US);
- analysis: gas chromatography together with mass selective detection (Series 6890N – 5974R) (Agilent, US).

## QUALITATIVE RESULTS

Liquid labelled "TOBACCO AROMA TYPE", Flavour "FS", BSI I/163-1, 02-2007, 50 G

- presence of the following substances: ethanol, acetone ethyl acetate, propylene glycol, acetals (2 types: 2-(1-methyl ethyl)-4-methyl-1,3-dioxolane and 2-(1 methyl propyl)-4-methyl-1,3-dioxolane), 2-methylpropanal (also called isobutyraldehyde), 2-methyl butanal (also called 2-methylbutyraldehyde), 1,2,3-propane triol (= glycerol), nicotine and liquid substances characteristic of essential oils.

The 1<sup>st</sup> test arrangement or simulation relating to the smoke study was temporarily placed 'on hold' because of the appearance of a brown, viscous liquid when the vacuum was applied in the Erlenmeyer flask (an example is shown to the persons concerned). In consultation with the applicant it will be decided whether the appropriate conditions are to be further examined.

The 2<sup>nd</sup> test arrangement or simulation relating to the smoke study produced the following results:

Smoke from "SUPER SMOKER" cigarettes

- presence of the following substances: propylene glycol, acetals (2 types), 1,2,3-propane triol (= glycerine) and nicotine.

Smoke from "SUPER SMOKER" cigar

- presence of the following substances: propylene glycol, acetals (2 types), phenol and nicotine

## QUANTITATIVE RESULTS

Deuterated 2-methyl propanal and 2-methyl butanal were synthesised ((for an explanation of these substances see also the discussion) with the aid of deuterated methyl iodide because these substances are not commercial available. The yield from the synthesis and the purification of these 2 substances is now (i.e. after 1 ½ months' work) not yet ideal for carrying out an accurate concentration determination of the non-deuterated 2-methyl propanal and 2-methyl butanal present in the samples. It was therefore decided to follow a different *modus operandi* for the time being for determining the concentration of these substances, in particular by organising calibration lines using non-deuterated 2-methyl propanal and 2-methyl butanal, as well as anethol (internal standard).

On the basis of the above the following results were obtained:

- presence of 2-methyl propanal: approx. 0.42 nanolitre per millilitre of liquid; converted to the corresponding weight this means approx. 420 nanograms per millilitre.
- presence of 2-methyl butanal: approx. 0.46 nanolitre per millilitre of liquid, converted to the corresponding weight this means approx.. 460 nanograms per millilitre
- presence of 2-(1-methyl ethyl)-4-methyl-1,3-dioxolane: approx. 27 nanolitres per millilitre of liquid; converted to the corresponding weight, this means approx. 27 micrograms per millilitre.
- presence of 2 (1 methyl propyl)-4-methyl-1,3-dioxolane: approx. 35 nanolitres per millilitres of liquid; converted to the corresponding weight this means approx. 35 micrograms per millilitre.

Taking into account the volume (i.e. the suction volume in classic smoking) that is inhaled during smoking, 50 millilitres per puff of the cigarette can be taken as an average. For example,

if it is assumed that 20 x 50 millilitres are sucked in per cigarette, a total suction volume of 1000 millilitres (~ 1 L) is absorbed via the mouth. The following estimate may also be made taking account of the fact that this is *i)* a vapour or aerosol, i.e. liquid droplets in contrast to classic smoke, and *ii)* that during atomisation the acetals are hydrolysed to the corresponding aldehydes:

- maximum presence of 2-methyl propanal: *approx.* 420 nanograms x 1000 = *approx.* 0.420 milligrams in total.
- maximum presence of 2-methyl butanal: *approx.* 460 nanograms x 1000 = *approx.* 0.460 milligrams in total.

It is evident that the above-mentioned suction volume cannot be considered, in its entirety for determining absorption (through inhalation or orally), for it may be assumed that most of it is removed again by “blowing out” the smoke, possibly together with the 2-methyl propanal and 2-methyl butanal (if this does not react away in the mouth). The calculated values may therefore be regarded as the clear upper limit. We also note that the suction volume may variably quite considerably (as a function of normal use), as can the number of cigarettes per day.

## DISCUSSION

Nicotine is present in all the samples examined. The nicotine concentration determination, using deuterated nicotine, will be carried out as soon as this standard is available (it has been ordered).

An interesting, correlated presence of the following substances was found::

propylene glycol, acetals (2 types), 2-methyl propanal and 2-methyl butanal

- the presence of the acetals was clearly greater in the liquid and smaller in the smoke;
- on the other hand the presence of propylene glycol was clearly smaller in the liquid compared to that in the smoke;
- this observation may indicate the (reaction) mechanism that takes place during atomisation (or thereafter): acetals which can hydrolyse, under the influence of water (e.g. moisture in the mouth) and acidity (pH), to propylene glycol and the corresponding aldehydes, namely 2-methyl propanal and 2 methyl butanal;
- the fact that no aldehydes could be demonstrated in the “smoke samples” may be due to their high reactivity (e.g. they can react away immediately in the mouth with basic groups such as amides).

The essential oils may derive from the tobacco plant (i.e. to create a similar aroma).

The presence of the essential oils, ethanol (= consumption alcohol) and acetone amounts to trace amounts.

We would stress that the term “smoke” used in this report cannot be compared with the classic “smoke” caused by the consumption of “classic smoking products”. For this is not classic

pyrolysis (complete or incomplete combustion)( of vegetable substances, but rather atomisation of the constituents of a liquid. In fact an aerosol or vapour results from this atomisation.

**Toxicity data** (summary):

- propylene glycol: proposal of the “Joint FAO/WHO Expert Committee on Food Additives” ADI (“Acceptable Daily Intake”) in humans = 0 to 25 mg/kg of body weight, by the “Food and Drug Administration”, generally assumed to be safe (“GRAS” Statute = Generally Recognised as Safe”)  
[See also the appendix to INCHEM – WHO FOOD ADDITIVES SERIES No. 5]
- 2-methyl propanal: no exposure limits established, i.e. no MAC (“Maximal Allowable Concentration”) or TLV (“Threshold Limited Value”) values, inhalation may give rise to a sore throat, coughing, a burning sensation, shortness of breath and difficulty in breathing,; contact with the skin and eyes may give rise to pain, redness and burns. The following standards have been published:
  - Acute oral toxicity LD-50 (rat) = 960 mg/kg, other study = 3700 mg/kg;
  - Acute dermal toxicity LD-50 (rabbit) = 7130 mg/kg;
  - Acute toxicity after inhalation LC-50 (mouse, 2 u) = 39.5 mg/L

*Note: a LD-50 value is a statistically derived value, in particular a total dose which 50% deaths in the experimental animals used: a LC-50 value is comparable but does not express the lethal concentration.*

[See also the appendix to INCHEM – SUMMARY JOINT FAO/WHO COMMITTEE]

[See also the appendix to MSDS – isobutyraldehyde – 2-methyl propanal]

Taking account of the calculated upper limit of 0.420 milligram of 2-methyl propanal per cigarette, i.e. expressed per litre and per use of one cigarette, this value is *approx.* 100 x lower than the LC-50 value.

If we assume that 2-methyl propanal is considered for oral absorption, we see, for a person weighing 60 kg, that we must have  $60 \times 960 = 57.6$  grams of 2-methyl propanal to expect 50% deaths (when extrapolating from rat to human, in fact). The value found, 0.420 milligram of 2-methyl propanal, is *approx.* 100,000 x lower than the reported LD-50 value.

We should mention that this substance is known as a “flavouring agent”.

- 2-methyl butanal: assumed to be “slightly” toxic after inhalation; despite the fact that no MAC value is established there are the following standards.
  - Acute oral toxicity LD-50 (rat) = 6920 mg/kg;
  - Acute dermal toxicity LD-50 (rabbit) – 5440 mg/kg;
  - Acute toxicity after inhalation LC-50 (rat, 4 u) = 50 mg/L.

Absorption via the skin, eyes and after oral intake can give rise to sore throat, coughing, a burning sensation, shortness of breath, difficulty in breathing, redness and burns.

[See also the appendix to INCHEM – SUMMARY JOINT FAO/WHO COMMITTEE]

[See also the appendix to MSDS – 2-methyl butyraldehyde = 2-methylbutanal]

Taking account of the calculated upper limit of 0.460 milligram of 2-methyl butanal per cigarette, i.e. expressed per litre and per use of one cigarette, this value is *approx.* 100 x lower than the LC-50 value.

If we assume that 2-methyl butanal is considered for oral absorption, we see, for a person weighing 60 kg, that we must have  $60 \times 6920 = 415.2$  grams of 2-methyl butanal to expect 50% deaths (when extrapolating from rat to human). The value found, 0.40 milligram of 2-methyl butanal, is *approx.* 1,000,000 x lower than the reported LD-50 value.

We should mention that this substance is known as a “flavouring agent”.

- Acetals: this relates here to 2-(1-methyl ethyl)-4-methyl-1,3-dioxolane and 2-(1-methyl propyl)-4-methyl-1,3-dioxolane; although 1,3-dioxolane is itself classified as toxic (probably because formaldehyde is formed), this does not mean that substituted dioxolanes are also toxic; it may generally be stated that it is assumed that 4-methyl-1,3-dioxolanes are permitted as a “flavouring agent” in food and present no safety risk in normal use.



[See also the appendix to INCHEM – SUMMARY JOINT FAO/WHO COMMITTEE]

Regarding the quantity of 2-(1-methyl ethyl)-4-methyl-1,3-dioxolane and 2-(1-methyl propyl)-4-methyl-1,3-dioxolane, it may be stated that this will be very low in the “smoke” because of the hydrolysis (in other words their presence was observed mainly in the liquid).

- phenol: 5 pm (“parts per million”) permitted as “TWA” (- time-weighted average); since this substance was only detected in the cigar analysis, and in a very low concentration, we consider that this substance is not relevant in the analysis and discussion.
- 1,2,3-propane triol: assumed to be a very slightly toxic substance, mainly because it is not a xenobiotic (in the conversion from fat to energy glycerine is released in the circulation and finally converted to glucose).
- Data reported: the liquid in which nicotine and the above-mentioned “flavouring agents” are present would also contain a number of classic amino acids together with one or more sugars. This information is not insignificant from the toxicological viewpoint since so-called heterocyclic amines can be formed at high temperatures (such substances were demonstrated, among other things, in meat broths after pyrolysis of proteins and amino acids). Different heterocyclic amines are highly mutagenic and are considered to be pro-carcinogenic. For the formation of this type of substance we would mention the presence of tryptophane and glutamic acid, among other things, in addition to a reducing sugar such as glucose or lactose, among other things. The mechanism for the formation of heterocyclic amines is known as the Milan reaction (“browning reaction”).

Based on the one hand on a declaration by Dr. Th. Golz, *dated* 19 June 2007, according to which tryptophane and glutamic acid are not present in the formulation of “Borgwaldt Flavour” products, and on the other hand on a certificate forwarded to us from the same company, *dated* 30 May 2007, according to which *i*) all “tobacco flavours” are produced according to the German tobacco legislation, *ii*) all “flavouring ingredients” conform to the food and tobacco legislation (such as the German TVO), *iii*) these substances are also regarded as “Generally Recognised as Safe” (the so-called “GRAS” Statute, according to the “Food and Drug Administration”, FDA), and *iv*) the products made by the e ..... conform to the quality guarantee and ISO 9001:2000 standards, there are no scientific reasons for assuming the presence or formation of heterocyclic amines. Moreover, it may be added that the short-term temperature at which evaporation takes place in the products of “SUPER SMOKERS”, namely *approx.* 100 to 130°C, is much lower than in the case of pyrolysis in a

classic cigarette (where temperatures of several hundred degrees Celsius are reached), so that here there are no elements leading to the assumption of heterocyclic amines. Taking account of the elements summarised above, it may also be concluded that there is no reason to assume the presence of metals (such as nickel, cadmium, arsenic, etc.).