Formaldehyde in cultivated mushrooms: a negligible risk for the consumer

Wendie Liliane Claeys, Christiane Vleminckx, Alain Dubois, André Huyghebaert, Monica Höfte, Paul Daenens, Bruno Schiffers

► To cite this version:

Wendie Liliane Claeys, Christiane Vleminckx, Alain Dubois, André Huyghebaert, Monica Höfte, et al.. Formaldehyde in cultivated mushrooms: a negligible risk for the consumer. Food Additives and Contaminants, 2009, 26 (09), pp.1265-1272. 10.1080/02652030903081929 . hal-00573893

HAL Id: hal-00573893

<https://hal.science/hal-00573893>

Submitted on 5 Mar 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Formaldehyde in cultivated mushrooms: a negligible risk for the consumer

Journal:	<i>Food Additives and Contaminants</i>
Manuscript ID:	TFAC-2008-431.R1
Manuscript Type:	Review
Date Submitted by the Author:	12-May-2009
Complete List of Authors:	Claeys, Wendie; FASFC, Policy Control Vleminckx, Christiane; Scientific Institute of Public Health Dubois, Alain; Federal Agency for the Safety of the Food Chain Huyghebaert, André; Ghent University Höfte, Monica; Ghent University Daenens, Paul; Catholic University Leuven Schiffers, Bruno; Gembloux Agricultural University
Methods/Techniques:	HPLC
Additives/Contaminants:	Natural toxicants, Pesticide residues
Food Types:	Mushrooms

SCHOLARONE™
Manuscripts

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1 FORMALDEHYDE IN CULTIVATED MUSHROOMS: A NEGLIGIBLE RISK FOR THE
2 CONSUMER

5 Wendie Claeys ¹, Christiane Vleminckx ², Alain Dubois ¹, André Huyghebaert ³, Monica Höfte ³,
6 Paul Daenens ⁴ and Bruno Schiffers ⁵

- 9 ¹ Federal Agency for the Safety of the Food Chain, Brussels, Belgium
10 ² Scientific Institute of Public Health, Brussels, Belgium
11 ³ Ghent University, Ghent, Belgium
12 ⁴ Catholic University Leuven, Leuven, Belgium
13 ⁵ Gembloux Agricultural University, Gembloux, Belgium

Abstract

Following the detection of formaldehyde in cultivated mushrooms, an evaluation was carried out to assess whether its presence in food poses a risk to public health. Formaldehyde, a carcinogenic chemical, has a broad range of industrial applications and hence, exposure to formaldehyde is ubiquitous through diverse consumer goods, food, the air, etc. The observed levels of formaldehyde in mushrooms are lower than the levels that are reported for vegetables, fruit, meat, fish and dairy products. On the basis of available data, a rough estimate of the dietary exposure to formaldehyde was performed. The exposure through the consumption of cultivated mushrooms ($\sim 0.19 \mu\text{g/kg bw}$ per day on average, consumers only) appeared to be small compared to the total dietary intake of formaldehyde ($\sim 99.0 \mu\text{g/kg bw}$ per day, total population). Based on comparison with toxicological safety limits for chronic exposure and given that formaldehyde is carcinogenic only through inhalation and not by ingestion, it can be concluded that the dietary exposure to formaldehyde is not a cause for concern.

Keywords: *formaldehyde, food, mushrooms, exposure*

Introduction

Formaldehyde (CH₂O, CAS 50-0-0) is a colourless, flammable gas that is commercially available as a 35-40% aqueous solution (formalin), as formol (a mixture of formaldehyde, formic acid and methanol in water) or as the precursor hexamethylenetetramine (a complex of formaldehyde with ammonium). In the solid form formaldehyde is available as the trimer trioxane (1,3,5-trioxane or s-trioxane) or as the polymer paraformaldehyde ((CH₂O)_n with n ≥ 8) (IPCS 1989, 2002).

Formaldehyde is classified by the “International Agency on Cancer” (IARC) into Group 1, carcinogenic to humans (IARC 2006). Within the EU formaldehyde is currently classified as a category 3 carcinogen with the risk phrase 'R40, limited evidence of a carcinogenic effect' (Directive 2001/59/EC), but discussions are currently taking place to change this classification to category 1 - 'R49, may cause cancer by inhalation'. Most studies regarding the toxicity of formaldehyde relate to the inhalation of formaldehyde, which is probably the most important route of exposure. The available data on the effects of ingestion or of skin contact with formaldehyde are limited. Since formaldehyde is water soluble, highly reactive with biological macromolecules (formaldehyde induces DNA-protein and protein-protein cross-links) and rapidly metabolized, the effects of exposure are mainly observed in those tissues or organs which come into first contact with formaldehyde, namely the respiratory and gastrointestinal tract, oral and gastro-intestinal mucosa included (erosion, ulceration, inflammation and hyperplasia of stomach and fore-stomach were observed in rats) (IPCS 1989, 2002; BfR 2006 a & b; IARC 2006). There is no evidence that formaldehyde is carcinogenic by the oral route (EFSA 2006). Formaldehyde causes toxicity to the nasal epithelium of rats and mice upon inhalation and induces above certain concentrations dose-related increases in nasal tumours. Epidemiological data have shown that formaldehyde is carcinogenic in human by the inhalation route (nasopharyngeal cancers and sinonasal cancers). While a genotoxic mode of action (MOA) can never be ruled out for a compound that is clearly genotoxic, at least *in vitro* and locally *in vivo*, the MOA would be based on the induction at the site of contact of sustained cytotoxicity and cell proliferation upon long-term exposure (McGregor *et al.* 2006).

Formaldehyde is produced industrially for a large number of applications such as the production of resins that act as adhesives and binders for wood products, pulp, paper, glass wool and rock wool, and the production of some plastics, coatings, paints and varnishes, industrial chemicals and textile finishing. It is also used in packaging, cosmetics and as a disinfectant and preservative. For example, formaldehyde is currently allowed as a preservative under the form of hexamethylene tetramine (E 239) in Provolone cheese at a residual concentration of 25 mg/kg expressed as formaldehyde (Directive 95/2/EC). For materials and articles made of plastic that come into contact with food, a specific migration limit (SML) of 15 mg/kg is set for formaldehyde (Directive 2002/72/EC).

In the context of its monitoring programme, the Belgian Federal Agency for the Safety of the Food Chain (FASFC) analysed formaldehyde in cultivated mushrooms. In Belgium the use of formaldehyde as a disinfectant in the cultivation of mushrooms is not allowed. However, there are biocides admitted that contain formaldehyde and the regulation provides the possibility of exemptions for mushroom substrates and fertilisers (Royal Decree of January 7th, 1998 on the trade in fertilizers, soil improvers and growing substrates). Currently, there are no European nor Belgian standards for formaldehyde in mushrooms. The main objective of this paper is to evaluate if the presence of formaldehyde in cultivated mushrooms poses a risk to consumers and if regular control of formaldehyde in cultivated mushrooms is necessary. To place the potential risk into perspective, the total dietary exposure to formaldehyde is considered as well.

Materials & Methods

Samples

A first batch of mushrooms (*Agaricus*, *Pleurotus*) was sampled in the context of the monitoring programme of the FASFC. Mainly mushrooms of Belgian origin were sampled, but also imported mushrooms were considered (Table 1). Next, an inquiry was performed at corresponding Belgian production sites, where a second mushroom sample (ready for harvesting), a sample of the compost bed and a sample of the casing soil were taken. Samples were stored frozen until analysis.

90

91 *Analysis of formaldehyde*

92 Formaldehyde levels in mushrooms and substrates were analysed after extraction with
93 acetonitrile and derivatization with dinitrophenylhydrazine (DNPH) by HPLC with ultra violet -
94 diode array detection (HPLC-UV-DAD, Varian, USA), according to the method described by
95 Tomkins *et al.* (1998).

96 For the extraction, fresh mushroom (100 g) was mixed with 1acetonitrile (100 ml) and
97 placed for 30 min in an ultrasonic bath and for 30 min on an orbital shaker. After filtration, 5 ml
98 DNPH derivatization reagent was added (i.e. 300 mg DNPH dissolved in 50 ml acetonitrile with
99 0.5 ml H₃PO₄ (85%)). The mixture was further diluted to 200 ml with acetonitrile and placed for 3
100 h in a thermostatic oven at 40 °C. After filtration on a membrane filter (0.45 µm), 20 µl of sample
101 was injected on a Luna C18 column (250 x 4.6 mm, 5 µm, Phenomenex). Mobile phase A was
102 acetonitrile, mobile phase B was a 0.02M NaH₂PO₄ solution in acetonitrile at pH 4 (50:50 v/v).
103 Gradient elution started at 0% A, rising after 12 min linearly to 60% A over 2 min, held at 60% A
104 for a further 6 min before returning to the initial conditions. The total injection cycle time was 24
105 min and the flow rate was 1.0 ml/min. The presence of formaldehyde was confirmed by
106 comparison of the samples' retention time (~9.6 min) and characteristic spectrum with a
107 standard sample (formaldehyde solution, > 36.5%, Sigma-Aldrich) at 353 nm. The limit of
108 quantification (LOQ) for 100 g of sample was determined as 0.02 mg/kg.

109

110 *Consumption data*

111 Consumption data were obtained from the Belgian Food Consumption Survey (BFCS)
112 performed in 2004 and coordinated by the Scientific Institute of Public Health (Devriese *et al.*
113 2005). The survey involved 3,214 participants older than 15 years, which were interviewed twice
114 about their consumption during the last 24 hours (non-consecutive 24h recall). Participants were
115 selected by a multistage procedure from the National Register and the fieldwork was spread
116 over one year to anticipate seasonal effects. The usual food intake was estimated by the Nusser
117 method using C-side software (Dodd 1996).

119

120 Results & Discussion

121 Occurrence of formaldehyde

122 Formaldehyde is ubiquitous. Possible anthropogenic sources of formaldehyde are
123 combustion (vehicular exhaust, waste, cigarettes, etc.), industrial applications (resins, paints,
124 etc.) and consumer goods (cosmetics, pesticides, contact materials, etc.).

125 In the atmosphere, formaldehyde is both directly emitted and formed as a result of
126 photochemical oxidation of reactive organic gases. The concentration of formaldehyde in the air
127 is generally below 0.001 mg/m³ in rural areas and below 0.020 mg/m³ in urban areas (IARC
128 2006). The indoor air may contain higher levels of formaldehyde compared to the outdoor air
129 due to evaporation from furniture, paints and construction materials. Reported levels for indoor
130 air range between 0.02 and 0.06 mg/m³ (IARC 2006). The formaldehyde level due to
131 occupational exposure (e.g. during the varnishing of furniture and wooden floors, in the finishing
132 of textiles, in the garment industry, in the treatment of fur and in certain jobs within
133 manufactured board mills and foundries, ...) is on average 2 mg/kg (Heck & Casanova 2004;
134 IARC 2006). In rainwater, formaldehyde concentrations of 0.1-0.2 mg/l are measured (IPCS
135 1998). In drinking water, formaldehyde is mainly formed by natural oxidation of humic
136 substances during the ozonation and chlorination of the water or is released into the water from
137 plastic plumbing. Water treated with ozone likely contains less than 50 µg formaldehyde / l
138 (WHO 2005; Owen *et al.* 1990).

139 Formaldehyde is also naturally present in the majority of living organisms. As an
140 intermediary metabolic product formaldehyde is essential for the biosynthesis of certain amino
141 acids. *In vivo* most formaldehyde is probably (reversibly) bound to macromolecules (IPCS
142 2002). The content of endogenously metabolically formed formaldehyde can range between 3
143 and 12 ng/g tissue (Owen *et al.* 1990). The endogenous concentration of formaldehyde
144 measured in blood is 2-3 mg/l (IARC 2006). A similar concentration was found in the blood of
145 rats and monkeys (Heck *et al.* 1985; Casanova *et al.* 1988) and a 2 to 4 times higher
146 concentration was observed in the liver and the nasal mucosa of rats (Heck *et al.* 1982).

1
2 147 Additionally, formaldehyde is a natural component of a variety of foodstuffs. Monitoring the
3
4 148 formaldehyde level of food however, has generally been performed sporadically and source-
5
6 149 directed and only few data are available to characterize the range and distribution of
7
8 150 formaldehyde concentrations in food (IPCS 2002). In the context of the monitoring programme,
9
10 151 the FASFC analysed the formaldehyde level of cultivated mushroom samples. The
11
12 152 concentration ranged between 0.08 and 0.65 mg/kg ($n = 29$) (Table I). It seems that the
13
14 153 formaldehyde concentration of organically cultivated mushrooms (on average 0.34 ± 0.19 mg/kg
15
16 154 ($n=5$)), is similar to the concentration measured in conventionally cultivated mushrooms (on
17
18 155 average 0.29 ± 0.15 mg/kg ($n = 24$)). (The production of organic food within the EU, as well as
19
20 156 the importation of organic food from outside the EU is controlled by EU Regulation 2092/91). No
21
22 157 correlation is observed between mushrooms and compost bed or casing soil with respect to the
23
24 158 formaldehyde concentration. Moreover, there seems to be no transfer of formaldehyde between
25
26 159 substrate treated with formaldehyde and mushrooms (internal communication, data not given).
27
28 160 At the production site no indications were found of unauthorized treatment of substrates
29
30 161 (compost bed and casing soil) with formaldehyde. Data given in Table I thus concerns
31
32 162 endogenously formed formaldehyde.

33
34
35
36 163 In literature studies considering the presence of formaldehyde in mushrooms are scarce.
37
38 164 Existing data concern Shiitake mushrooms, which have a relatively high formaldehyde level. In
39
40 165 a study of the British 'Food Safety Agency' (FSA) formaldehyde concentrations in the order of
41
42 166 100 to 300 mg/kg were observed in both fresh and partially dried Shiitake mushrooms due to
43
44 167 natural production. These formaldehyde concentrations refer however, to a combination of free
45
46 168 and 'bound' formaldehyde (i.e. formaldehyde derived from the breakdown of larger molecules by
47
48 169 thermal degradation, by acidic and enzymatic hydrolyses, e.g. during analysis). After 6 minutes
49
50 170 of cooking, the formaldehyde level was significantly decreased. Preservation for 10 days had no
51
52 171 effect on the formaldehyde content of the mushrooms (Mason *et al.* 2004). In an opinion of the
53
54 172 French 'Agence Française de Sécurité Sanitaire des Aliments' (AFSSA), it was concluded that
55
56 173 a maximum formaldehyde level of 63 mg/kg in fresh Shiitake mushrooms can be considered
57
58 174 safe for the consumer (AFSSA 2001). Formaldehyde levels observed in the present study are
59
60 175 well below these values.

176

177 [Table I]

178

179 For comparison, literature data regarding the formaldehyde concentration of different

180 foodstuffs are presented in Table II. Formaldehyde levels range between 3 and 60 mg/kg for

181 vegetables and fruits, between < 1 and 34 mg/kg for fish and meat (for crustaceans between 1

182 and 98 mg/kg), and around 1 mg/kg for milk and milk products. For alcoholic beverages, soft

183 drinks and coffee, formaldehyde levels between 0.02 and 16.3 mg/L are reported. It should be

184 noted however, that literature data are scarce and that data presented in Table II could be

185 biased (e.g. because they are based on a limited number of samples). Most of the levels

186 reported in Table II are due to the natural occurrence of formaldehyde, but it can not be

187 excluded that some values are a result of processing (e.g. fumigation, the use of formaldehyde-

188 containing food additives, migration from melamine-, phenol- and urea-formaldehyde plastics,

189 addition to feed to improve handling characteristics or as a preservative, etc.). Moreover, the

190 analytical method used to quantify formaldehyde may affect the formaldehyde level measured

191 since there are many potential precursors that can form formaldehyde under certain extraction

192 and derivatization conditions used during analysis (Mason *et al.* 2004).

193

194 [Table II]

195

196 *Formaldehyde intake*

197 Table III presents the intake of formaldehyde through the consumption of cultivated mushrooms

198 based on monitoring data of the FASFC (Table I) and consumption data of the BFCS (IPH

199 2006). The intake was calculated by a deterministic approach multiplying a fixed value for

200 consumption with a fixed value for the formaldehyde level (such as the mean or P97.5), and

201 concerns only consumers of mushrooms and not the whole population. One of the main

202 criticisms of the deterministic approach is its inherent conservatism. Nevertheless, due to its

203 simplicity and its worldwide use and acceptance, this point estimate approach may be used as a

204 screening tool.

On average, the formaldehyde intake due to the consumption of cultivated mushrooms was 0.2 µg/kg bw per day. In the (upper) worst case scenario, the intake could amount to 4.0 µg/kg bw per day. In the FSA study cited above, the formaldehyde intake due to consumption of Shiitake mushrooms was estimated to be 0.15-0.16 mg/kg bw. It was concluded that such an intake level poses probably no appreciable risk to public health (Mason *et al.* 2004). The intake determined in the FSA study is two orders of magnitude higher than estimated in the present study. Not only different types of mushrooms were considered in both studies, but also different analytical methods were applied. As mentioned above, the analytical conditions used can affect the formaldehyde level measured due to the breakdown by thermal degradation, acidic and enzymatic hydrolyses of larger molecules. In the FSA study, formaldehyde levels were determined after extraction by acid hydrolysis and steam distillation using a spectrophotometric method and LC-MS. Formaldehyde formation and potential routes for its generation in mushrooms by steam distillation under acidic conditions have been described in literature (Tyihak *et al.* 1996 and Yamazaki *et al.* 1980, cited by Mason *et al.* 2004).

[Table III]

Additionally the total dietary exposure of formaldehyde was estimated deterministically for the whole population (Table IV). Based on the formaldehyde data available in literature, an average formaldehyde intake of approximately 7.5 mg/day (0.10 mg/kg bw per day) was obtained (beverages not included). This is a rough estimate of the actual intake, for one because it was assumed that each person consumes each day average amounts of fruit, vegetables, meat or fish, milk and dairy products. Also, formaldehyde levels used for calculations were taken arbitrary as the average between the minimum and maximum concentration found in literature and are as such biased (see *supra*). In addition, the effect of e.g. cooking before consumption on the formaldehyde content, which can lower the formaldehyde content of the food by evaporation, was not accounted for. Moreover, the proportion of formaldehyde in foods that is bioavailable and the amount that is in a bound and unavailable form, is unknown (IPCS 1989, 2002; Health Canada 2001).

A similar exercise was performed by Owen *et al.* (1990), who calculated an annual dietary formaldehyde intake of about 4000 mg/year, equivalent to approximately 11 mg/day. The intake through drinking water was calculated to be on average less than 40 µg/day. The rough estimate given by the 'International Programme on Chemical Safety' (IPCS 1989) for formaldehyde exposure through food is of the same range, namely between 1.5 to 14 mg/day for an average adult.

It is clear that the intake through the consumption of mushrooms is negligible compared to the intake of formaldehyde via the consumption of different food products (only 0.2%).

[Table IV]

When considering the 'total' exposure to formaldehyde, also other routes of exposure should be considered such as inhalation and skin absorption by dermal contact (e.g. by use of cosmetics). The latter route of exposure can be considered negligible (except in certain workplaces) whereas the first route is probably the most important one. Probabilistic simulations of Health Canada indicate that through air one of every two persons would be exposed to 24-h average formaldehyde concentrations of $\geq 20\text{--}24\text{ }\mu\text{g/l}$ ($24\text{--}29\text{ }\mu\text{g/m}^3$) and that 1 in 20 persons (i.e. the 95th percentile) would be exposed to 24-h average formaldehyde concentrations in air $\geq 67\text{--}78\text{ }\mu\text{g/l}$ ($80\text{--}94\text{ }\mu\text{g/m}^3$) (Health Canada 2001). The German 'Bundesinstitut für Risikobewertung' (BfR) established in a recent toxicological evaluation a tolerable air concentration of 0.1 mg/l formaldehyde, which is in line with the MAC value or 'Maximum Allowable Concentration' of 0.3 mg/l determined to protect workers in the workplace (BfR 2006b).

Risk Characterization

The WHO guideline for drinking water sets a maximum limit of 900 µg formaldehyde/l water (WHO 2006). The limit was determined on the basis of a TDI ('tolerable daily intake') of 0.15 mg/kg bw per day and assuming that drinking water accounts for 20% of the intake. This TDI was established on the basis of a NOAEL ('no observed adverse effect level') of 15 mg/kg bw

per day from a 2-year study in rats where irritations of the stomach and papillary hyperplasia were observed at a formaldehyde dose of 82 mg/kg bw per day. Based on the same NOAEL the U.S. Environmental Protection Agency (EPA) determined a chronic reference dose (RfD) of 0.2 mg/kg bw per day for oral exposure (U.S. EPA 1990). The formaldehyde intake through consumption of mushrooms estimated in this study is 0.10% of the chronic U.S. EPA RfD and 0.13% of the TDI determined by the WHO. As to the total dietary intake, it amounts to more or less 50% and 66% of the U.S. EPA and WHO safety limits respectively.

The risk associated with the formaldehyde levels measured in food appears thus to be acceptable. Moreover, in an opinion regarding the use of formaldehyde as a preservative in food manufacturing the EFSA AFC Panel ('Panel on food additives, flavourings, processing aids and materials in contact with food') concluded on the basis of recent and past toxicological evaluations that there is no evidence indicating that formaldehyde is carcinogenic by the oral route (EFSA 2006).

Conclusion

The levels of formaldehyde detected in cultivated mushrooms are generally lower than the levels reported to occur naturally in vegetables, fruit, meat, fish and dairy products. The consumption of mushrooms results in a formaldehyde intake 1000 times lower than the toxicological safety limits given by the WHO and the U.S. EPA and contributes only little to the total formaldehyde intake. Regular control of formaldehyde in cultivated mushrooms is thus not a priority.

Due to a lack of data, it is difficult to assess precisely the total dietary intake. Nevertheless, the rough estimate presented in this paper is in line with values reported elsewhere and is 66% of the WHO TDI of 0.15 mg/kg bw per day. Since probably not all formaldehyde is bioavailable and since there are no indications that formaldehyde is carcinogenic via the oral route, it can be concluded that the natural occurrence of formaldehyde in food presents no immediate cause for concern.

290

291 **Acknowledgement**

292 The authors like to acknowledge the Scientific Committee of the Belgian Federal Agency for

293 the Safety of the Food Chain for their guidance of this study.

For Peer Review Only

References

- AFSSA. 2004. Evaluation des risques liés à l'utilisation du formaldéhyde en alimentation animale [internet]. January 2004. France: Agence française de la Sécurité Sanitaire des Aliments; [cited: 2008 Oct 6]. Available from: <http://www.afssa.fr/Documents/ALAN-Ra-formaldehyde.pdf>
- AFSSA. 2001. Avis de l'Agence française de sécurité sanitaire des aliments relatif à un projet d'arrêté relatif à la teneur maximale en formaldéhyde que doivent présenter les champignons de l'espèce shiitaké (*Lentinus edodes*) [internet]. September 24, 2001. France: Agence française de la Sécurité Sanitaire des Aliments; [cited: 2008 Oct 6]. Available from: <http://www.afssa.fr/Documents/AAAT2001sa0228.pdf>
- BfR. 2006a. Schulte A, Bernauer U, Madle S, Mielke H, Herbst U, Richter-Reichhelm H-B, Appel K-E & Gundert-Remy U. Assessment of the carcinogenicity of formaldehyde [CAS No. 50-00-0] [internet]. February 2006. Germany: Bundesinstitut für Risikobewertung; [cited: 2008 Oct 6]. Available from: http://www.bfr.bund.de/cm/238/assessment_of_the_carcinogenicity_of_formaldehyde.pdf
- BfR. 2006b. Toxicological assessment of formaldehyde. Opinion of BfR No. 023/2006 [internet]. March 30, 2006. Germany: Bundesinstitut für Risikobewertung; [cited: 2008 Oct 6]. Available from: http://www.bfr.bund.de/cm/290/toxicological_assessment_of_formaldehyde.pdf
- Casanova M, Heck H d'A, Everitt J, Harrington Jr W, Popp J. 1988. Formaldehyde concentrations in the blood of rhesus monkeys after inhalation exposure. Food Chem Toxicol. 26: 715-716.
- CFS. 2008. Yau A. - Formaldehyde in food [internet]. April 2008. Hong Kong: Centre for Food Safety – The Government of the Hong Kong Special Administrative Region; [cited: 2008 Oct 6]. Available from: http://www.cfs.gov.hk/english/multimedia/multimedia_pub/multimedia_pub_fsf_06_01.html
- Commission Directive 2002/72/EC of 6 August 2002 relating to plastic materials and articles intended to come into contact with foodstuffs. Off J. L 220, 15/8/2002, p.18.
- Commission Directive 2001/59/EC of 6 August 2001 adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. Off J. L 225, 21/08/2001, p.1.
- Commission Directive 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. Off J. L 61, 18/3/1995, p.1.
- Council Regulation (EEC) No 2092/91 of 24 June 1991 on organic production of agricultural products

and indications referring thereto on agricultural products and foodstuffs. Devriese S, De Backer G, De Henauw S, Huybrechts I, Kornitzer K, Leveque A, Moreau M, Van Oyen H. 2005. The Belgian food consumption survey: Aims, design and methods. Arch Public Health 63: 1-16.

Dodd K. 1996. A technical guide to C-SIDE. Software for Intake Distribution Estimation. Technical Report 96-TR 32, 1-68. Department of Statistics and Center for Agricultural and Rural Development; Iowa State University.

EFSA. 2006. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to the use of formaldehyde as a preservative during the manufacture and preparation of food additives (Question N° EFSA Q-2005-032). The EFSA Journal 415: 1-10. [cited: 2008 Oct 6]. Available from: http://www.efsa.europa.eu/EFSA/Scientific_Opinion/afc_op_ej415_formaldehyde_op_en,2.pdf

FSA. 1998. MAFF UK – Survey of chemical migration from can coatings into food and beverages – 1, Formaldehyde [internet]. September 1998. UK: Food Safety Agency; [cited: 2008 Oct 6]. Available from: <http://archive.food.gov.uk/maff/archive/food/infosheet/1998/no157/157form.htm#ref2>

Hayashi T, Reece CA, Shibamoto T. 1986. Gas Chromatographic determination of formaldehyde in coffee via thiazolidine derivative. J Assoc Off Anal Chem. 69: 101-105.

Health Canada. 2008. Environmental and Workplace Health. Health-based guidance values for substances on the second priority substances list. 3.3 Estimates of exposure to PSL2 substances [internet]. February 2008. Canada: Health Canada; [cited: 2008 Oct 6]. Available from: <http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/value-valeur/table-tableau-3-eng.php>

Health Canada. 2001. Canadian environmental protection act, 1999. Priority substances list assessment report. Formaldehyde [internet]. February 2001. Canada: Health Canada; [cited: 2008 Oct 6]. Available from: http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/psl2-lsp2/formaldehyde/formaldehyde-eng.pdf

Heck H d'A, Casanova-Schmitz M, Dodd P, Schachter E, Witek T, Tosun T. 1985. Formaldehyde (CH₂O) concentrations in the blood of humans and Fischer-344 rats exposed to CH₂O under controlled conditions. Am Ind Hyg Assoc J. 46: 1-3.

Heck H d'A, Casanova M. 2004. The implausibility of leukemia induction by formaldehyde: A critical review of the biological evidence on distant-site toxicity. Regul Toxicol Pharmacol. 40: 92-106.

Heck H d'A, White E, Casanova-Schmitz M. 1982. Determination of formaldehyde in biological tissues by gas chromatography/mass spectrometry. Biomed Mass Spectrom. 9: 347-353.

- IARC. 2006. Formaldehyde, 2-butoxyethanol and 1-*tert*-Butox-2-propanol. IARC Monographs on the evaluation of carcinogenic risks to humans. 88: 2-9 [internet]. 2006. Franc: IARC; [cited: 2008 Oct 6]. Available from: <http://monographs.iarc.fr/ENG/Monographs/vol88/mono88.pdf>
- IPCS. 2002. International Programme on Chemical Safety. Formaldehyde. Concise international chemical assessment document [internet]. 2002. Stuttgart, Germany: WHO; [cited: 2008 Oct 6]. Available from: <http://www.inchem.org/documents/cicads/cicads/cicad40.htm>
- IPCS. 1989. International Programme on Chemical Safety, Formaldehyde. Environmental Health Criteria, Geneva, 219 p [internet]. 1989. Geneva, Switzerland: WHO; [cited: 2008 Oct 6]. Available from: <http://www.inchem.org/documents/ehc/ehc/ehc89.htm>
- Larsen P. 1998 Toxicological evaluation and limit values for methyl-*tertiary*-butyl ether (MTBE), formaldehyde, glutaraldehyde, furfural. pp. 31-39 [internet]. February 1998. Denmark: Danish Veterinary and Food Administration - The Institute of Food Safety and Toxicology; [cited: 2008 Oct 6]. Available from: <http://www2.mst.dk/udgiv/Publications/1999/87-7909-563-1/pdf/87-7909-562-3.PDF>
- Lawrence J, Iyengar J. 1983 The determination of formaldehyde in beer and soft drinks by HPLC of the 2,4-dinitrophenylhydrazone derivative. Intern J Environ Anal Chem. 15 : 47-52.
- Mason DJ, Sykes MD, Panton SW, Rippon EH. 2004. Determination of naturally-occurring formaldehyde in raw and cooked Shiitaki mushrooms by spectrophotometry and liquid chromatography-mass spectrometry. Food Add Cont. 21: 1071-1082.
- McGregor D, Bolt H, Cogliano V, Richter-Reichhelm HB. 2006. Formaldehyde and glutaraldehyde and nasal cytotoxicity: Case study within the context of the 2006 IPCS human framework for the analysis of a cancer mode of action for humans. Crit Rev Toxicol. 36: 821-835.
- Owen BA, Dudney CS, Tan EL, Easterly CE. 1990. Formaldehyde in drinking water: Comparative hazard evaluation and an approach to regulation. Regul Toxicol Pharmacol. 11: 20-236.
- Soffritti M, Maltoni C, Maffei F, Biagi R. 1989. Formaldehyde: an experimental multipotential carcinogen. Toxicol Ind Health. 5: 699-730.
- Soffritti M, Belpoggi F, Lambertin L, Lauriola M, Padovani M, Maltoni C. 2002. Results of long-term experimental studies on the carcinogenicity of formaldehyde and acetaldehyde in rats. Ann NY Acad Sci. 982: 87-105.
- Tomkins BA, McMahon JM, Caldwell WM, Wilson DL. 1989 Liquid chromatographic determination of total formaldehyde in drinking water. J Assoc Off Anal Chem. 72: 835-839.
- US EPA. 1990. Integrated Risk Information System (IRIS) – Formaldehyde [internet]. January 1990. US: Environmental Protection Agency; [cited: 2008 Oct 6]. Available from:

<http://www.epa.gov/iris/subst/0419.htm>

WHO. 2006. Guidelines for drinking-water quality. Third Edition. p. 194 [internet]. Geneva, Switzerland: World Health Organisation; [cited: 2008 Oct 6]. Available from: http://www.who.int/water_sanitation_health/dwg/gdwq3/en/

WHO. 2005. Formaldehyde in drinking-water. Background document for development of WHO Guidelines for drinking-water quality. Geneva, World Health Organization (WHO/SDE/WSH/05.08/48) [internet]. Geneva, Switzerland: World Health Organisation; [cited: 2008 Oct 6]. Available from: http://www.who.int/water_sanitation_health/dwg/chemicals/formaldehyde130605.pdf

Table I. Formaldehyde concentration (mg/kg) measured in cultivated mushrooms, compost bed and casing soil.

Mushroom sample 1	Mushroom sample 2	Compost bed	Casing soil	Remarks
0.35	0.40	0.23	0.02	Belgian origin, Conventional farming
0.27	0.08	0.10	< LOQ (0.02)	Belgian origin, Conventional farming
0.31	0.13	0.36	0.02	Belgian origin, Conventional farming
0.30	0.21	0.12	0.05	Belgian origin, Conventional farming
0.21	0.53	0.49	0.06	Belgian origin, Organic farming
	0.56	0.49	0.06	Belgian origin, Organic farming
	0.16	0.28		Belgian origin, Organic farming
0.39	0.38	0.44	0.04	Belgian origin, Conventional farming
0.42				Belgian origin, Conventional farming
0.53	0.18	0.05	0.02	Belgian origin, Conventional farming
0.21				Belgian origin, Conventional farming
	0.18	0.27	0.03	Belgian origin, Conventional farming
	0.30	0.20	0.03	Belgian origin, Conventional farming
0.16	0.07	0.34		Belgian origin, Conventional farming; 5.1 mg formaldehyde / kg was measured in supplementary feeding
0.18	0.09	0.30		Belgian origin, Conventional farming
0.65				Belgian origin, Conventional farming
0.24				Dutch origin, Organic farming
0.28				Polish origin, Conventional farming
0.34				Polish origin, Conventional farming
0.45				Polish origin, Conventional farming

Table II. Formaldehyde level of different foodstuffs reported in literature .

Food	Concentration mg/kg (litre)	Remarks	Ref.
<i>Fruit & vegetables</i>			
Apples	17.3 (38.7) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
	6.3-22.3		(2)
Banana	16.3		(2)
Pears	60 (38.7) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Cauliflower	4.7 (5.3) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
	26.9		(2)
Carrots	6.7 (10) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Onion	13.3 (26.3) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Spinach	3.3 (7.3) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Tomatoes	5.7 (7.3) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Radish	3.7 (4.4) ^a	Colorimetric determination using chromotropic acid (Schiff 's reagent)	(1)
Shiitake mushrooms	100 - 406 / 6 - 54.4		(2)
	100-320	Colorimetric determination using chromotropic acid and dimedone/ammonium acetate derivative measured by LC-MS/MS	(3)
<i>Meat products</i>			
Beef	0.094 ± 0.044	France	(4)
	0.079 ± 0.051 and 0.161 ± 0.071	European Member States	(4)
Poultry	5.7	Colorimetric analysis	(1)
	2.3 - 5.7		(4)
Pork	20	Colorimetric determination using chromotropic acid	(1)
Sheep	8		(1)
Beef, pork, sheep and chicken	2.5 - 20		(2)
<i>Fish products</i>			
Freshwater fish	8.8	Fumigated, colorimetric analysis	(1)
Sea fish	20	Fumigated, colorimetric analysis	(1)
Cod	20	Frozen	(1)
	4.6 – 34		(2)
Crustaceans	1-60	Mediterranean	(1)
	3-98	Ocean	(1)
Shrimp	1	Live, HPLC	(1)
<i>Milk & dairy products</i>			
Milk	0.041 ± 0.045	France	(4)
Goat's milk	1		(1)
Cow's milk	Up to 3.3	Colorimetric analysis	(1)
Fresh milk	0.013-0.057	(mean = 0,027 mg/l)	(5)
Treated milk	0.075-0.255	(mean = 0,164 mg/l)	(5)
Cheese	up to 3.3	Colorimetric analysis	(1)
Dairy products	0.02		(4)
<i>Beverages</i>			
Alcoholic beverages	0.04-1.7	Fluorescence detection after on-line condensation with 4-amino-3-penten-2-one (Japan)	(5)
	0.02-3.8	Spectrofluorimetric determination (Brazil)	(5)

Soft drink	7.4-8.7	4 samples of canned and bottled cola (Canada); HPLC-MS of DNPH-derivative	(6)
	< 2 (LOD) ^a	5 samples of canned soft drink (UK); HPLC of DNPH derivative	(7)
Beer	0.1-1.5	9 samples of canned and bottled beer (Canada); HPLC-MS of DNPH-derivative	(6)
	< 1 (LOD)	5 samples of canned beer (UK); HPLC of DNPH derivative	(7)
Coffee	3.4-4.5	Higher levels of formaldehyde were found in instant coffees than in brewed coffees, perhaps	(8)
Instant coffee	10-16.3	because formaldehyde escapes from coffee during brewing (USA)	(8)

(1) IPCS (1989); (2) CFS (2008); (3) Mason *et al.* (2004); (4) Afssa (2004); (5) IPCS (2002); (6) Lawrence & Iyengar (1983); (7) FSA (1998) (8) Hayashi *et al.* (1986)

^(a) limit of detection

Table III. Intake of formaldehyde by the consumption of mushrooms.

	[Formaldehyde] ¹ Consumption ²		Intake ³	
	mg/kg	g/day	mg/day	µg/kg bw per day
Mean	0.288	49	0.01	0.19
P50	0.275	34	0.01	0.12
P95	0.547	160	0.09	1.15
P97,5	0.585	200	0.12	1.54
P99	0.624	233	0.15	1.91
P100	0.650	465	0.30	3.98

¹ 29 samples, see Table I

² usual consumption of the Belgian population ('consumers only') – 460 consumption days (Devriese *et al.* 2005)

³ calculated deterministically; the body weight was assumed to be 76 kg

Table IV. Formaldehyde intake by the consumption of different foodstuffs.

	[Formaldehyde] ¹	Average consumption ²	Intake ³	
	mg/kg	g/day	mg/day	µg/kg bw per day
Vegetables ⁴	15.1	138.3	2.1	27.48
Fruit	33.2	118.2	3.9	51.56
Meat	10.0	120.7	1.2	15.92
Fish and seafood	49.5	23.9	1.2	15.57
Milk and dairy beverages	1.7	90.6	0.2	1.97
Cheese	1.7	30.2	0.1	0.66
Yoghurt and pudding	1.7	63.1	0.1	1.38

¹ concentration = average of minimum and maximum concentration reported (Table II); it was assumed that preparation of food (e.g. cooking) did not reduce the formaldehyde concentration

² usual average consumption of the Belgian population (Devriese *et al.* 2005)

³ calculated deterministically; the body weight was assumed to be 76 kg

⁴ Shiitake mushrooms excluded