

Please note that this report, published on 7 November 2005, replaces the earlier version which contained an error in table 1, page 6.



Brussels, 22 December 2004

#### NOTE TO THE

#### INITIAL REPORT OF THE SCIENTIFIC PANEL ON CONTAMINANTS IN THE FOOD CHAIN ON PROVISIONAL FINDINGS ON FURAN IN FOOD

1. In August 2004 EFSA welcomed the proposal of the Panel on contaminants in the food chain (CONTAM) to establish an *ad hoc* working group to start collecting information on the chemical furan regarding: (i) methods of analysis, (ii) its occurrence and formation in food and food products in Europe, (iii) exposure through consumption, and (iv) its toxicity. The initiative followed the U.S. Food and Drug Administration (FDA) survey published in May 2004 that revealed the occurrence of furan in a number of foods that undergo heat treatment such as canned and jarred foods.

2. The Panel was requested by a self-tasking procedure to provide at a relatively short notice an initial report on the state-of-the-art on exposure and adverse effects of furan and, in particular, on gaps in our knowledge and possible research needs essential for a future comprehensive risk assessment. This pro-active approach has resulted in the attached report on initial findings.

3. The CONTAM Panel adopted the initial report on furan in food by written procedure on 7<sup>th</sup> December 2004. The Panel concluded that the toxicity data base is incomplete and strongly emphasised that the presented occurrence data are only of an exploratory nature. The number of samples and the variety of food products were far too limited and considerably more data on a full range of food items are needed to draw any conclusion. Therefore the reported data are not a reflection of the actual <u>distribution</u> of furan in foods. Equally, the furan levels reported in food are not an indicator of actual furan <u>intake</u> via food nor should these be interpreted as suggesting possible risk associated with eating certain foods. As an example, initial data have shown that 10 minutes after brewing coffee a strong reduction of the furan levels are observed in this beverage as a result of its high volatility. It should also be kept in mind that the presence of furan in food is not new.

4. Therefore the reported range of estimated exposure and intake data are merely an overview of the sparsely available data which are made available at this early stage for reasons of transparency and to provide a basis for recommendations for further work. The data presented in the report are insufficient to draw conclusion with respect to human health risks and no specific recommendations can be made other than that on the basis of the information available today there is no justification to recommend any changes in dietary habits.

- 5. From the initial study it appears that there is a strong need for further research with respect to:
  - occurrence and formation of furan in a wide variety of food and food products;
  - fate of furan in food and food products as a result of food processing;
  - regional food consumption patterns in Europe;
  - the toxicity of furan and in particular its mode of action.

6. EFSA will continue to stimulate and coordinate the collection of data which are essential for a full risk assessment of furan. EFSA will need however again the assistance of and support from Member States and stakeholders for the collection and analyses of the required data. Cooperation is also sought with the European Commission and in particular its Community Reference Laboratories. Furthermore, EFSA is in close contact with the Canadian authorities of Health Canada, the US FDA and other national food safety authorities outside Europe as well as with international organisations in the field of food safety to ensure that any new data and assessments will be shared immediately and duplication of work is avoided.

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## Report of the Scientific Panel on Contaminants in the Food Chain on provisional findings on furan in food (Question N° EFSA-Q-2004-109)

## Adopted on 7 December 2004

### **SUMMARY**

In May 2004, US Food and Drug Administration (FDA) published the results of a survey of furan in canned and jarred foods that undergo heat treatment (U.S. FDA, 2004). The CONTAM Panel was of the opinion that the available data indicate that this is an emerging issue in food safety and therefore decided to compile a scientific report comprising currently available data on methods of analysis, occurrence, formation, exposure, and toxicity.

Furan is a volatile molecule and headspace gas chromatography and the use of an internal standard is currently the analytical method of choice to quantify furan in foods. Furan occurs in a variety of foods such as coffee, canned and jarred foods including baby food containing meat, and various vegetables, which suggests that there are probably multiple routes of formation rather than a single mechanism which was postulated for flavour volatiles. Fresh vegetables do not contain furan. Only a limited set of data on occurrence of furan in various food categories as well as consumption data are available. In the view of this, the Panel decided to present in the report the range of estimated exposure rather than average exposure. For baby food 273 analyses show furan concentrations ranging from non detectable to 112  $\mu$ g/kg. Assuming an exclusive intake of commercial baby food in glass jars, corresponding to 234 g food per day, this would lead to exposures ranging from <0.2 - 26  $\mu$ g furan per day.

Furan can easily pass through biological membranes and is readily absorbed from the lung or intestine. It is rapidly metabolised by P-450 enzymes and cis-2-butene-1,4-dial has been identified as a key metabolite. The amounts of furan reaching body tissues are limited by the high capacity of the liver to eliminate furan from the blood stream.

The toxicity database of furan in is incomplete as no data are available on reproductive and developmental toxicity. There are also no human studies. Furan is cytotoxic and the liver is the primary target organ of furan toxicity after oral application.

Furan is clearly carcinogenic to rats and mice, showing a dose-dependent increase in hepatocellular adenomas and carcinomas in both sexes. In rats, also a dose-dependent increase in mononuclear leukaemia was seen in both sexes. A very high incidence of cholangiocarcinomas of the liver was present in both sexes, even at the lowest dose tested.



Taking into account all the presently available data on the mode of action of furan, the Panel concluded that the weight of evidence indicates that furan-induced carcinogenicity is probably attributable to a genotoxic mechanism. However, chronic toxicity with secondary cell proliferation may indirectly amplify the tumour response.

From the presently available data it appears that there is a relative small difference between possible human exposures and the doses in experimental animals that produce carcinogenic effects, probably by a genotoxic mechanism. However, a reliable risk assessment would need further data on both toxicity and exposure.

### **KEY WORDS**

Furan, occurrence, carcinogenicity, cytotoxicity

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## BACKGROUND

In May 2004 the U.S. Food and Drug Administration (FDA) published the results of a survey of furan in food<sup>1</sup>. Furan was identified in a number of foods that undergo heat treatment such as canned and jarred foods (levels ranging from non detectable to 125  $\mu$ g/kg). Previously, levels up to 4000  $\mu$ g/kg were detected under experimental conditions in canned meat (Maga, 1979). Furan is carcinogenic in rodents (NTP, 1993). The CONTAM panel was of the opinion that the available data indicate that this is an emerging issue in food safety and therefore proposed to establish an ad hoc working group to address this issue.

### **TERMS OF REFERENCE**

Recognising the importance and urgency of this issue, the Panel on Contaminants in the food chain (CONTAM) has decided to task itself to deliver a scientific report using the data available on:

- Information for furan on methods of analysis, occurrence, formation, exposure, and toxicity.
- Identifying gaps and research needs.
- Providing scientific arguments with respect to the need for consumer advice, if any.

### ASSESSMENT

#### 1. Introduction

Furan (C<sub>4</sub>H<sub>4</sub>O) (CAS-Nr. 110-00-9) (Figure 1) serves as an intermediate in the synthesis and preparation of numerous linear polymers used to prepare temperature-resistant structural laminates and to prepare copolymers used in machine dishwashing products as alternatives to phosphorous- and nitrogen-containing detergents (NTP, 1993). Previously, levels up to 4000  $\mu$ g/kg were detected in canned meat (Maga 1979). On 7 May 2004, FDA reported the occurrence of furan levels in foods up to 125  $\mu$ g/kg<sup>2</sup>. Furan is classified by IARC as possibly carcinogenic to humans (group 2B; IARC, 1995).



Figure 1. Chemical structure of furan

<sup>&</sup>lt;sup>1</sup> http://www.fda.gov/OHRMS/DOCKETS/98fr/04n-0205-nrd0001.pdf

<sup>&</sup>lt;sup>2</sup> http://www.fda.gov/bbs/topics/news/2004/NEW01065.html



### 2. Analytical methodology

Furan is a small volatile molecule which can be determined by headspace gas chromatography (GC). This is a relatively simple and well-proven methodology in which a food sample in liquid or slurry form is heated in a sealed vial to achieve equilibrium partition between the liquid phase and the gaseous headspace. The headspace gas is sampled and the vapour injected into a GC. Detection can be by non-selective means such as FID or by mass spectrometry. A headspace method of analysis is available on the FDA web-site which involves heating the sample at  $80^{\circ}$ C for a minimum of 30 min. followed by sampling the headspace gas and GC/MS monitoring m/z 39 and 68. Quantification is by internal standardisation using isotopically labelled furan (monitoring m/z 72 for d4-furan).

This approach has the advantage that there is no need for a sample clean-up and it can be automated for high sample throughput. The disadvantages are that the foodstuff is heated, meaning that furan might be formed during analysis, although this is unlikely at the low temperatures used; that sample sizes are small (typically 5 g), meaning good homogenisation is required; and that because furan has a low molecular weight and even with MS detection there may not be adequate specificity. For good quantification, the labelled internal standard is essential but there seem to be problems of availability of the standard, meaning that laboratories may be undertaking this analysis with less ideal internal standards or using external standardisation.

Both the FDA method and a similar one used by the Swiss Federal Office of Public Health, claim a limit of quantification (LOQ) of 2.0 - 5.0 ng/g and a limit of detection (LOD) of 1.0 to 4.0 ng/g depending on the food type. There are no precision data given in terms of repeatability, and neither of the methods which have been validated, so there is no available insight into the robustness of the method. There has been no proficiency testing undertaken to date, so comparability of data between laboratories has not yet been established.

### **3.** Formation of furan

The presence of furan in foods as a flavour volatile has been known for many years and a basic formation pathway through carbohydrate thermal decomposition has been postulated. However, in view of the occurrence in widely differing foods such as roasted coffee, canned meat and various vegetables, it is probable that there are multiple routes of formation rather than a single mechanism. It should be noted that the occurrence in canned and jarred foods is a probable consequence of volatiles being trapped in the food container. There is little information on levels of furan in foods prepared in the home, where volatiles might be expected to be released during cooking. This also raises the issue of whether there might be inhalation exposure in the domestic or in catering environment where foods are being cooked.



#### 4. Substituted Furans

A number of alkyl furans, dihydrofurans, furanones and tetrahydrofurans can occur in food (WHO, 2004), which raises the question as to whether these could show similar toxicological properties as the parent molecule furan. In principle, mono-alkyl furans, such as 2methylfuran, could undergo epoxidation of the unsubstituted double bond and rearrangement to an alkyl substituted dialdehyde, which could show similar properties to cis-2-butene-1,4dial (see section 6.3). However, mono-alkyl substituted furans have an additional site of oxidation, and it is predicted that side-chain oxidation would be a major route of metabolism, rather than epoxidation of a double bond, which is the only option for furan. Dialkyl furans could yield a reactive metabolite containing both an aldehyde and ketone group, but only if both alkyl substituents are on the same double bond, and again side-chain oxidation is predicted to be a major route of metabolism. Dialkyl substituted furans with one group on each double bond would undergo side chain oxidation to inactive metabolites, rather than epoxidation. Dihydrofurans and furanones would not undergo epoxidation of the double bond and ring opening to form a dialdehyde-like compound, while tetrahydrofurans do not contain a double bond. The tetrahydrofuran and furanone derivatives that were evaluated at the recent JECFA in relation to their use as flavouring agents did not contain unsubstituted ring double bonds and therefore would not form epoxide intermediates (WHO, 2004). Although a number of the tetrahydrofuran and furanone derivates were positive in tests for genotoxicity, this was considered to be a high-dose phenomenon due to DNA damage caused by the generation of free radicals. This is supported by the absence of carcinogenicity in a recent 2-year rodent bioassay on 4-hydroxy-2,5-dimethyl-3(2H)-furanone (Kelly and Bolte, 2003).

#### 5. Occurrence data

Table 1 summarises occurrence data aggregated in 11 categories and expressed as a range. Such a presentation was chosen because only 1 to 45 samples were available for each food category (except for baby food) and therefore no calculations were made of mean, median or standard deviation. Also consumption data for the same food categories extracted from the GEMS food regional diet were included. It is obvious that canned food which contains furan represent only a fraction of those food categories. Nevertheless, they can allow ranking the food categories as a function of their contribution to the overall exposure via food.

The resulting range of estimated exposures is not intended to be a representation of the current situation but rather to compile the available data in a transparent way.

For baby food 273 analyses showed a range of furan concentrations from non detectable to 112  $\mu$ g/kg. Considering a consumption of 234 g/day of canned baby food (Kersting *et al.*, 1998), this would result in an exposure of <0.03 to 3.5  $\mu$ g/kg b.w./day (assuming a body weight of 7.5 kg of a 6 month baby, EC, 1993).



Table 1. Furan in food. Data derived from the U.S. FDA Laboratory as published on CFSAN website, the Swiss Federal Office of Public Health, the Kantonales Laboratorium Basel-Stadt Switzerland, the Confederation of the Food and Drink Industries of the EU, and the chemische und Veterinäruntersuchungsamt Stuttgart Germany.

Food category	of positiv	Maximum ve samples /kg)	Number of samples (n <loq<sup>4))</loq<sup>	Average consumption (GEMS Food) (g/day)	Range of intake <sup>3)</sup> (µg/person)
Coffee <sup>5</sup>	3	146	45 (4)	791 <sup>9)</sup>	2.4 - 115.5
Baby food (including porridge, juices for babies and young children) <sup>6)</sup>	1	112	273 (11)	234 <sup>7)</sup>	0.2 - 26.2
Infant formula	2	13	19 (8)	870 <sup>8)</sup>	1.7 – 11.3
Vegetables (canned or jarred)	3	61	35 (7)	372	1.1 – 22.7
Fish	5	7	6 (3)	47	0.2 – 0.3
Fruit juices	1	6	18 (11)	69 <sup>9)</sup>	0.07 - 0.4
Cereals/products (only bread)	2	30	13 (8)	176	0.4 - 5.3
Food non classified <sup>10)</sup>	3	125	84 (11)	-	-
Meat products	4	39	11 (6)	217	0.9 - 8.5
Milk products (milk)	<0.5		1 (1)	336	<0.2
Beer	5	13	6 (0)	258 <sup>9)</sup>	1.3 – 3.4
Honey	3	10	5 (0)	1	0.003 - 0.01

<sup>&</sup>lt;sup>3)</sup> Calculated from the minimum and maximum of the positive samples

<sup>&</sup>lt;sup>4)</sup> Number of samples below the limit of quantification (LOQ)

<sup>&</sup>lt;sup>5)</sup> Both concentration and consumption figures are related to liquid coffee ready to drink. The consumption figure is for filter coffee.

<sup>&</sup>lt;sup>6)</sup> Out of 273 samples 33 Swiss samples were baby food in small glass jars containing mainly fruits with a range of furan levels from 1 (minimum) to 16 (maximum) μg/kg.

<sup>&</sup>lt;sup>7)</sup> Figure taken from DONALD study (Kersting *et al.*, 1998).

<sup>&</sup>lt;sup>8)</sup> Figure in mL per day taken from SCF report (EC, 2003).

<sup>&</sup>lt;sup>9)</sup> Figure taken from SCOOP report task 4.1 (EC, 1996).

<sup>&</sup>lt;sup>10)</sup> Food non classified consist of soups, broths, sauces, tomato and chilli sauces, soy sauce.



#### 6. Kinetics and Metabolism

#### 6.1 Absorption

Experiments in male F344 rats with  $[2,5^{-14}C]$  furan (8 mg/kg body weight (b.w.), purity > 99 %), administered by gavage for up to 8 days in corn oil show that furan is rapidly and extensively absorbed (Burka *et al.*, 1991). After inhalation furan is readily adsorbed, (about 90 %) in dogs. The amount of retained furan was proportional to the concentration in inhaled air (Egle and Gochberg, 1979).

#### 6.2 Distribution

Due to its low polarity, furan can pass biological membranes and enter various organs. The rapid hepatic metabolism seems to limit, however, its systemic delivery. The capacity to bio-activate furan is also of relevance for the distribution, since it can result in an irreversible binding to the respective tissue.

24 hours after oral gavage of <sup>14</sup>C-labeled furan to rats at a dose level of 8 mg/kg b.w. the recovery of radioactivity (expressed as furan equivalent) in nmol per g tissue was: liver 307, kidney 60, large intestine 25, small intestine 13, stomach 6, blood 6, lung 4 (Burka *et al.*, 1991) . In total, 15 % of the dose was recovered in these tissues. The radioactivity was associated with protein and not with the DNA fraction (see also genotoxicity section 7.2). Seven days after treatment, the radioactivity had almost returned to the limit of detection. After repeated dosing, accumulation of radioactivity was found particularly in liver and kidney.

### 6.3 Metabolism

The fate of [<sup>14</sup>C]-labelled furan in rats was investigated by Burka *et al.* (1991) after oral dosing of 8 mg/kg b.w. The major metabolite found was carbon dioxide, probably resulting from oxidative metabolism involving opening of the furan ring. Similar to methylfuran derivatives (Ravindranath *et al.*, 1984), an  $\alpha$ ,  $\beta$ -unsaturated dialdehyde is formed (Kedderis *et al.*, 1993).

In the case of furan, cis-2-butene-1,4-dial has been identified as a key reactive and cytotoxic metabolite of furan, which has been found to bind to protein (Burka *et al.*, 1991) and nucleosides (Byrns *et al.*, 2002). This metabolite would be formed by oxidation of one of the double bonds of furan, possibly with the formation of an epoxide intermediate, followed by spontaneous rearrangement and ring opening. Both in vitro and in vivo studies show that metabolic activation by cytochrome P450 (CYP) enzymes is involved in furan-induced toxicity. Glutathione inhibited the covalent binding of reactive furan metabolites to microsomal protein in vitro (Parmar and Burka, 1993), presumably by forming less reactive,



water-soluble conjugates with the activated furan. Inter-individual differences in glutathione conjugation would be predicted to influence the consequences of bioactivation.

In a two compartment-PBPK model, Kedderis *et al.* (1993) predicted 84 % metabolism and 16 % exhalation of a single dose of 8 mg furan/kg b.w. in rats within 24 hours after oral treatment. These estimates were in good agreement with actual measurements by Burka *et al.* (1991). Inhibition and induction experiments revealed that CYP2E1 is the major enzyme involved in furan biotransformation indicating that furan metabolism can be enhanced by pre-treatment of rats with acetone (induction of CYP2E1) but not with phenobarbital (induction of CYP2B isozymes). Furthermore, the model of Kedderis *et al.* (1993), which was based on data from isolated hepatocytes, predicts that the rate-limiting step in metabolic clearance is the delivery of furan to the liver rather than metabolic turnover.

Similar conclusions were drawn from experiments with human hepatocytes in primary culture (Kedderis and Held, 1996). The authors concluded that even the induction of hepatic CYP2E1 would not affect the rate of hepatic metabolism because the metabolic capacity of CYP2E1 for furan is so high that hepatic blood flow is the rate-limiting step in elimination of the parent compound. Inter-individual differences in CYP2E1 activity could be of greater importance in determining the extent of first-pass metabolism and bioactivation of furan in the liver following ingestion.

Isolated hepatocytes from mice, rats and humans (3 samples) humans, rats and mice rapidly metabolised furan with  $V_{max}$  values of 48, 18 and 19 - 44 nmol/hour/10<sup>6</sup> human hepatocytes, for mice, rats and humans (3 samples) respectively, and with K<sub>M</sub> values of 1.0, 0.4 and 2.1 - 3.3  $\mu$ M, in mice, rats and humans (3 samples) respectively (Kedderis and Held, 1996).

### 6.4 Elimination

Within the first 24 hours after a single oral application of furan (8 mg/kg b.w.) to male rats, 80 % of the total radioactivity was eliminated via the lung, urine and faeces (Burka *et al.* (1991). About 14 % of the applied furan dose was eliminated in the exhaled air as the parent compound and 26 % as carbon dioxide. In urine, 20 % was found as the sum of  $\geq$  10 different compounds. About 22 % was found in the faeces. Repeated dosing over eight days resulted in an increased percentage of urinary elimination.

In conclusion, furan is an organic compound with high volatility and low polarity. Hence it can pass through biological membranes and it is readily absorbed from the lung or intestine (probably also from the skin). Its systemic availability is limited by the high capacity of the liver to eliminate furan from the blood stream by CYP2E1-catalysed metabolism and furan is predicted to undergo extensive first-pass metabolism. The major primary metabolite, a reactive dialdehyde, was shown to bind in an irreversible manner to nucleophiles such as proteins and nucleotides *in vitro* and to proteins *in vivo*. The liver has a high metabolic



capacity for furan, and furan is predicted to undergo extensive first-pass metabolism which limits the concentrations of the parent compound in the systemic circulation.

#### 7. Toxicology

The toxicity database of furan is incomplete and qualitative data only are available on the acute toxicity. According to the U.S. National Research Council (NAS, 2000), furan vapours are narcotic (anaesthetic and convulsant). No data are available on reproductive and developmental toxicity of furan and there are no data from human studies.

#### 7.1 Oral toxicity and carcinogenicity

Toxicology and carcinogenesis studies were conducted by the National Toxicology Program (NTP) by administering furan (purity > 99 %) in corn oil by gavage to groups of F344/N rats and B6C3F1 mice of each sex for 16 days, 13 weeks, and 2 years (NTP, 1993). These studies are summarized below.

In the 16-day studies, male rats (n=5) received furan doses of 0, 5, 10, 20, 40, or 80 mg/kg b.w. and female rats and mice of each sex (n=5) received doses of 0, 10, 20, 40, 80, and 160 mg/kg b.w. Mortality was increased in both species and both sexes at 80 mg/kg b.w. and higher, in male mice already at 40 mg/kg b.w. Final mean body weights of male rats that received 20 mg/kg and of male and female rats that received 40 mg/kg were significantly lower than controls. Final mean body weights of male mice that received 10 or 20 mg/kg were significantly greater than controls. Mottled and enlarged livers were observed at necropsy in male rats that received 20, 40, or 80 mg/kg and in females that received 40, 80, or 160 mg/kg. At necropsy no lesions were observed that were considered to be related to furan administration to mice.

In the 13-week studies, rats of each sex and female mice (n=10) received furan doses of 0, 4, 8, 15, 30, or 60 mg/kg b.w., and male mice (n=10) received doses of 0, 2, 4, 8, 15, or 30 mg/kg b.w.

Nine male and four female rats that received 60 mg/kg died before the end of the studies. Final mean body weights of male rats that received 15 mg/kg b.w. or more and female rats that received 60 mg/kg were significantly lower than controls. A dose-dependent increase in relative liver- and kidney weights was found in both sexes of rats that received 15 mg/kg b.w. or more. Thymus weights were decreased in male rats that received 30 or 60 mg/kg b.w. and females that received 60 mg/kg b.w. Toxic lesions of the liver (bile duct hyperplasia, cholangiofibrosis, cytomegaly and degeneration of hepatocytes, and nodular hyperplasia of hepatocytes) were associated with furan administration in all dose groups of rats; the severity of the lesions increased with dose. Kidney lesions (tubule dilatation and necrosis of tubule

epithelium) were present in rats that received 30 or 60 mg/kg. Thymic atrophy and testicular or ovarian atrophy were also observed in rats exposed to 60 mg/kg furan.

There were no chemical-related deaths in mice. Final mean body weights of male mice that received 30 mg/kg were significantly lower than controls. Relative and absolute liver weights in mice of both sexes were dose-dependently increased in male mice that received 15 or 30 mg/kg b.w. and in females that received 30 or 60 mg/kg b.w. Toxic liver lesions (cytomegaly, degeneration necrosis) were present in all groups of furan-exposed mice. Bile duct hyperplasia and cholangiofibrosis were observed in groups of mice receiving 30 or 60 mg/kg.

In the 2-year rat study, animals of each sex (n=70) were administered furan at 2, 4, or 8 mg/kg b.w. 5 days per week for 2 years with interim kills of 10 rats per group after 9 and 15 months. Mean body weights of male rats that received 8 mg/kg furan were lower than controls from approximately week 73 to the end of the study. Survival of male and female rats that received 8 mg/kg was lower than controls from approximately week 85 to the end of the studies as a result of moribund condition associated with liver and biliary tract neoplasms and mononuclear cell leukemia (see below). Increased incidences of numerous non-neoplastic liver lesions were present in treated rats. These lesions included biliary tract fibrosis, hyperplasia, chronic inflammation, and proliferation and hepatocyte cytomegaly, cytoplasmic vacuolization, degeneration, nodular hyperplasia, and necrosis. Furthermore, the severity of nephropathy increased with dose and the incidence was significantly increased in all groups of dosed rats; this increased severity was accompanied by an associated increased incidence of parathyroid hyperplasia (renal secondary hyperparathyroidism). The incidence of forestomach hyperplasia was also increased in male and female rats (males: 1/50, 4/49, 7/50, 6/50; females: 0/50, 2/50, 5/50, 5/50) and the incidence of sub-acute inflammation of the forestomach was increased in female rats (0/50, 1/50, 5/50, 6/50). No forestomach neoplasms were observed in males; a squamous papilloma was present in one low-dose female. Cholangiocarcinoma of the liver occurred in all groups of dosed rats (males: 0/50; 43/50; 48/50; 49/50; females: 0/50; 49/50; 50/50; 48/50) and was present in many rats of each sex at the 9- and 15-month interim evaluations (9-month: males - 0/10, 5/10, 7/10, 10/10; females females - 0/10, 4/10, 9/10, 10/10; 15-month: males - 0/10, 7/10, 9/10, 6/10; females -0/10, 9/10, 9/10, 7/10). Hepatocellular adenomas or carcinomas (combined) were significantly increased in male rats after 2 years of administration (1/50, 5/50, 22/50, 35/50) and hepatocellular adenomas were significantly increased in female rats (0/50, 2/50, 4/50, 7/50); hepatocellular neoplasms were not observed at the 9- or 15-month interim evaluations. The incidence of mononuclear cell leukaemia was increased in male and female rats that received 4 or 8 8 mg/kg furan (males: 8/50, 11/50, 17/50, 25/50; females: 8/50, 9/50, 17/50, 21/50); the incidence in the 8 8 mg/kg groups of each sex exceeded the historical control ranges for corn oil gavage studies.

In the 2-year mice study, animals of each sex (n=50) received doses of furan of 8 or 15 mg/kg b.w. 5 days per week for 2 years. Mean body weights of male and female mice that received 15 mg/kg furan were lower than controls during the studies. Survival of low- and high-dose



male and high-dose female mice was lower than controls from approximately week 80 to the end of the study as a result of moribund condition associated with liver neoplasms (see below). The incidences of squamous papilloma, focal inflammation, and papillary hyperplasia of the forestomach were increased in male mice (squamous papilloma: 0/49, 1/50, 3/50; focal inflammation: 9/49, 13/50, 21/50; papillary hyperplasia: 7/49, 14/50, 22/50). The incidences of benign pheochromocytoma and focal hyperplasia of the adrenal medulla were increased in low- and high-dose male and in high-dose female mice (benign pheochromocytoma: males - 1/49, 6/50, 10/50; females - 2/50, 1/50, 6/50). The-neoplastic hepatocellular lesions were increased in dosed mice. These lesions included hepatocyte cytomegaly, degeneration, necrosis, multifocal hyperplasia, and cytoplasmic vacuolization and biliary tract dilatation, fibrosis, hyperplasia, and inflammation.

The incidences of hepatocellular adenomas and carcinomas were significantly increased (males: adenoma - 20/50, 33/50, 42/50; carcinoma - 7/50, 32/50, 34/50; females: adenoma - 5/50, 31/50, 48/50; carcinoma - 2/50, 7/50, 27/50).

A separate 2-year study was conducted in which 50 male rats were administered 30 mg/kg furan in corn oil by gavage 5 days per week for 13 weeks and then maintained for the remainder of the 2 years without additional furan administration (NTP, 1993). Groups of 10 animals were evaluated for the presence of treatment-related lesions at the end of the 13-week period of furan administration and at 9 and 15 months. Cholangiocarcinoma of the liver occurred with an overall incidence of 100 % (40/40) and hepatocellular carcinoma occurred with an overall incidence of 15 % (6/40) in stop-exposure male rats that survived at least 9 months. Cholangiocarcinoma was observed in all 10 males at both the 9-month and 15-month interim evaluations. Hepatocellular carcinoma was first observed in 2 males at the 15-month interim evaluation.

According to FDA (2004), a preliminary report from a second 2-year bioassay in female mice found an increased incidence and multiplicity of hepatic tumours and a decreased tumour latency in mice dosed with 4 or 8 mg/kg b.w. furan, but not in mice dosed with 0.5, 1.0, or 2.0 mg/kg b.w. furan (Goldsworthy *et al.*, 2001).

Preweaning male B6C3F1 mice were treated by intraperitoneal administration of furan in tricaprylin either as a single dose of 400 mg/kg b.w.  $(LD_{10})$  or six doses of 200 mg/kg b.w. The mice were sacrificed between 28 and 95 weeks after dosing (Johansson *et al.*, 1997). The total number of mice was 215 in the 400 mg/kg furan group, 52 in the single-dose vehicle group, 78 in the 6 x 200 mg/kg furan group, and 79 in the 6 x vehicle group. In the single-dose group the furan-treated mice showed a statistically non-significant increase of the overall frequency of hepatocytic neoplasia and of the overall liver tumour multiplicity, compared with the vehicle control group. No treatment-related histopathological lesions other than development of liver tumours were found. In mice given six doses of 200 mg/kg furan, there was a statistically significant increased incidence of hepatocellular neoplasms (adenomas and carcinomas) and tumour multiplicity compared with the vehicle control group. The relative



frequency of *Hras1* activation was 82 % in the 28 tumours analysed from the single-dose group and 32 % in the 28 tumours analysed from the multiple-dose group. The development of liver tumours after short-term exposure to chemicals is a characteristic response observed in this infant mouse liver tumour model after treatment with a variety of genotoxic hepatocarcinogens (Vesselinovitch and Mihailovich, 1983; Wiseman *et al.*, 1986).

In male F344 rats, furan (30 mg/kg b.w. by gavage, 5 days/week) for 9, 12, and 13 weeks induced primary hepatic adenocarcinomas exhibiting small intestine mucosal cell differentiation at 70 to 90 % incidences by 16 months (Elmore and Sirica, 1993). The incidences of primary hepatocellular carcinomas ranged from 0 to 20 % (two hepatocellular carcinomas). The authors concluded that the small intestinal metaplasia and subsequent cholangiofibrosis developing early in furan-treated rats do not simply reflect reactive changes, but strongly correlate with the high incidences of intestinal-type of primary hepatic adenocarcinoma that occurs in rats after long-term exposures to furan.

Metaplastic small intestinal-like glands were selectively derived from putative hyperplastic bile ductule-like progenitor structures of young adult F344 male rats given furan by gavage at a daily dose of 30-45 mg/kg b.w. 5 times/week for 2-6-weeks (Sirica, 1996). Administration of furan at 30 mg/kg/day for 9-19 wk resulted in the preferential development of primary hepatic adenocarcinomas, which were characterized by small intestine mucosal cell differentiation.

## 7.2 Genotoxicity

### <u>In vitro</u>

Furan was not mutagenic in the *Salmonella typhimurium* strains TA100, TA1535, TA1537 and TA98 with and without S9 metabolic activation (NTP, 1993). In another study (Lee *et al.*, 1994) furan was weakly mutagenic in strain TA100 with and without S9 activation. Furan was negative in the sex-linked recessive lethal mutation test in *Drosophila melanogaster* (Foureman *et al.*, 1994) but was mutagenic in the thymidine kinase locus of L5178Y mouse lymphoma cells in the absence of S9 activation (McGregor *et al.*, 1988 and, in another study, with and without S9 activation (NTP, 1993). Furan induced chromosomal aberrations and sister chromatid exchanges (SCE) in Chinese hamster ovary cells (CHO) both with and without S9 activation (NTP, 1993). In another study on CHO cells (Stich *et al.*, 1981) furan caused chromosome aberrations only in the presence of S9 metabolic activation. Furan produced DNA double-strand breaks in isolated rat hepatocytes (Mugford and Kedderis, 1996).

The furan metabolite cis-2-butene-1,4-dial was directly mutagenic at non-toxic concentrations in the *S. typhimurium* strain TA104, a strain sensitive to aldehydes (Peterson *et al.*, 2000). Compared with that of other reactive aldehydes, its mutagenic activity in TA104 is similar to that of crotonaldehyde, acrolein and glyoxal. It was negative in strains TA97, TA98, TA100



and TA102; furthermore, its mutagenic activity was inhibited by glutathione. Cis-2-butene-1,4-dial caused DNA single-strand breaks and DNA cross-links in CHO cells (Marinari *et al.*, 1984) and produced DNA adducts *in vitro* (Byrns *et al.*, 2002). The adducts resulted from the addition of cis-2-butene-1,4-dial to the exo- and endo-cyclic nitrogens of 2'-deoxyguanosine and 2'-deoxyadenosine. Cis-2-butene-1,4-dial is structurally related to a variety of  $\alpha$ , $\beta$ unsaturated compounds that react with DNA and to known mutagens such as carbonyl compounds. In particular, the structurally-related agent cis-4-oxo-2-pentenal reacts with 2'deoxyguanosine to form a 1,N2-ethenodeoxy-guanosine adduct.

### <u>In vivo</u>

Furan (250 mg/kg b.w. by i.p. injection) induced structural chromosome aberrations in mice bone marrow cells, but not sister chromatid exchage (SCE) up to the dose of 350 mg/kg b.w. i.p. (NTP, 1993). Furan did not induce unscheduled DNA synthesis (UDS) in mouse or rat hepatocytes *in vivo* after a single oral dose of 200 or 100 mg/kg b.w, respectively (NTP, 1993).

In the study with [2,5-<sup>14</sup>C]-furan by Burka et al. (1991) which was discussed earlier (see metabolism section 6) the liver contained more radioactivity than other tissues and 80 % was associated with proteins, while no radioactivity was associated with DNA. Repeated daily administration of the radiolabelled furan at four dose levels resulted in an approximately linear increase in covalent protein binding. There was either no binding to DNA or the furan-DNA adduct was not stable to the isolation procedure. The results of this study were considered inconclusive by the CONTAM panel, for the following reasons: i) the specific activity of [2,5-<sup>14</sup>C] furan was probably too low to detect DNA adducts (75 µCi/nmol, limit of detection of about 3 nmol); ii) the labelled carbon atoms at position 2 and 5 are the labile carbons giving rise to CO<sub>2</sub>, further reducing the sensitivity of the radioactivity determinations on DNA; iii) furan-derived DNA adducts may be unstable to the isolation method used (with phenol), as also suggested by the findings by Byrns et al. (2002), showing that the DNA adducts formed "in vitro" by the furan dialdehyde metabolite are unstable. A study performed with <sup>14</sup>C-furan labelled on carbons 3 and/or 4, using a DNA extraction method different from that based on phenol and possibly the Accelerator Mass Spectrometry as analytical technique would allow for a more conclusive evaluation on the potential DNA binding of furan metabolites.

#### Mutation of proto-oncogenes in liver tumours induced in mice by furan

*Ras* proto-oncogene activation was studied in hepatocellular tumours (both adenomas and carcinomas) induced in mice by furan (Reynolds *et al.*, 1987). The frequencies of activated *H*-*ras* and *K*-*ras* oncogenes were similar in liver tumours from 12/29 treated mice and 15/27 vehicle controls, but the spectrum of mutations in the *H*-*ras* gene differed significantly. In addition to finding five tumours with commonly occurring point mutations in codon 61 of



*Hras1*, Reynolds *et al.* found novel mutations in eight liver tumours, including G-T and G-C transversions in codon 117 of *Hras1* in four tumours and activation of *Ki-ras*. The unique *ras* oncogene mutational profile was interpreted by the authors as a suggestion that the novel mutations could have been due to a genotoxic effect of furan.

### 8. Mode of Action

The mechanism of carcinogenic activity of furan in rodents has not yet been fully elucidated. Hypotheses of both direct (genotoxic) and indirect mechanisms have been formulated.

Several pieces of evidence now available suggest that furan or its proximate metabolite cis-2butene-1,4-dial can react directly with DNA in target cells and can play a role in furaninduced tumours:

- furan was able to induce gene mutations, chromosome aberrations and sister chromatid exchanges (SCE) in cultured mammalian cells and chromosomal aberrations in mice bone marrow cells; the furan metabolite cis-2-butene-1,4-dial induced gene mutations in bacterial cells, DNA single-strand breaks and DNA cross-links in cultured mammalian cells; it was also able to react with deoxyribonucleotides in vitro to form unstable DNA adducts;
- ii) hepatocellular tumours, obtained from furan-exposed mice from the 2-year bioassay, have different patterns of point mutations leading to *ras* oncogen activation, suggesting that furan, or a reactive metabolite, can directly activate protooncogenes (Reynolds *et al.*, 1987); consistent with these findings were the observations by Johansson *et al.* (1997) of *ras* activation in liver tumours induced in mice by short-term pre-weaning exposure to furans;
- iii) the findings by Johansson *et al.* (1997) in infant male mice demonstrate a liver tumour response after short-term pre-weaning exposure to furan in the absence of histomorphologic liver damage and argue against a major role from chronic hepatic cytotoxicity in the genesis of tumours;
- iv) in the NTP rat study, at 2 mg/kg b.w., furan induced cholangiocarcinomas in the males (86 % versus 0 % in the control group) and in the females (98 % versus 0 % in the control group) with only modest signs of hepatic toxicity. At the same dose, monocytic cell leukemias were induced with minimal hyperplasia of bone marrow.

Wilson *et al.* (1992) found no evidence of unscheduled DNA synthesis (UDS) after shortterm exposure of male mice to furan by gavage (up to 200 mg/kg), but did find evidence of cytotoxicity and secondary enhanced cell proliferation after exposure to 15 mg/kg b.w. furan for up to 6 weeks. These authors postulated that furan-induced hepatocellular proliferation secondary to cytotoxicity (necrosis/apoptosis), rather than *in vivo* genotoxicity, was primarily responsible for the production of liver tumours. Supporting evidence available at that time for an indirect mechanism was the observation that radiolabelled furan given orally to rats produced metabolites that covalently bound to proteins but not to DNA (Burka *et al.*, 1991). However, the results of Burka *et al.* were considered to be inconclusive by the Panel because



of limitations in the experimental protocol (see chapter 7.2 on Genotoxicity). Furthermore, the Panel noted that negative results of the liver UDS cannot be taken as a proof of absence of genotoxicity of furan, because this assay detects only bulky DNA adducts and is unable to detect mutagenicity resulting from misrepair and non-repair.

Furan has been shown to induce apoptosis in mice at doses of 8 and 15 mg/kg b.w., possibly in response to an increase in DNA damage (Fransson-Steen *et al.*, 1997). In addition, cytotoxic doses of furan were shown *in vivo* and *in vitro* to cause irreversible uncoupling of hepatic mitochondrial oxidative phosphorylation, leading to ATP depletion (Mugford *et al.*, 1997).

Kedderis and Ploch (1999) found that furan-treated rat hepatocytes show 95 % loss of ATP, due to uncoupling mitochondrial oxidative phosphorylation. This depletes the energy stores, with activation of cytotoxic enzymes, including endonucleases that produce DNA double-strand breaks prior to cell death (necrosis or apoptosis). The endonuclease inhibitor aurinotricarboxylic acid reduced the formation of DNA double-strand breaks. These authors postulated that erroneous repair of the DNA double-strand breaks may lead to mutations that are involved in tumour development and supported an indirect mechanism for the formation of DNA double-strand breaks.

Taking into account all the presently available data on the mode of action of furan, the Panel concluded that the weight of evidence indicates that furan-induced carcinogenicity is probably attributable to a genotoxic mechanism. However, chronic toxicity with secondary cell proliferation may indirectly amplify the tumour response.

### 9. Open questions and gaps

The CONTAM Panel noted the following open questions and gaps and recommends research to be performed related to:

- Performance of analytical methods through inter-laboratory trials
- Mechanism of formation and stability in food
- Significance of furan in the context of other substituted furans in food
- Occurrence data: The presently available data do not allow a sound dietary exposure assessment and additional information in following areas would be required:
  - broader coverage of different food categories including beverages
  - data on the variability within and between brands
  - information on freshly prepared foods (home cooking)
  - release of furan from food due to volatilisation in food



- Other sources of furan exposure (indoor air e.g. during cooking)
- Identification of suitable biomarkers to clarify internal exposure
- Dose-response data at lower dose-levels combined with mechanistic studies
- Clarification of the formation and significance of the cholangiocarcinomas in rats
- Role of species differences in metabolism in the generation of toxic effects
- Further data on the toxicity of furan such as data on reproductive and developmental toxicity

### CONCLUSIONS

Furan has been identified in a number of foods that undergo heat treatment such as canned and jarred foods. Furan is an organic compound with high volatility and lipophilicity. It can pass through biological membranes and is readily absorbed from the lung or intestine (probably also from the skin). The amounts of furan reaching body tissues are limited by the high capacity of the liver to eliminate furan from the blood stream by CYP2E1-catalysed bioactivation. The major primary metabolite, a reactive dialdehyde, binds to nucelophiles including proteins in an irreversible manner. The liver has a high metabolic capacity for furan, and furan undergoes first-pass metabolism which limits the concentrations in the systemic circulation as the parent compound.

Furan is clearly carcinogenic to rats and mice, showing a dose-dependent increase in hepatocellular adenomas and carcinomas in both sexes. In rats, also a dose-dependent increase in mononuclear leukaemia was seen in both sexes and a very high incidence of cholangiocarcinomas of the liver was present in both sexes, even at the lowest dose tested (2 mg/kg b.w.). Taking into account all of the presently available data on the mode of action of furan, the Panel concluded that the weight of evidence indicates that furan-induced carcinogenicity is probably attributable to a genotoxic mechanism. However, chronic toxicity with secondary cell proliferation may indirectly amplify the tumour response.

From the presently available data it appears that there is a relative small difference between possible human exposures and doses in experimental animals that produce carcinogenic effects, probably by a genotoxic mechanism. However, a reliable risk assessment would need further data on both toxicity and exposure.



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### ANNEX

Individual data on furan values in food samples from organisations who have agreed to publish their data.



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CFSAN/Office of Plant and Dairy Foods May 7, 2004; updated June 7, 2004

#### Exploratory Data on Furan in Food Data through May 27, 2004

Most Recent Data Data through April 28, 2004

#### Background

During investigations relating to review of a petition for the use of irradiation in certain foods, FDA scientists identified the substance furan in a number of foods that undergo heat treatment, such as canned and jarred foods. The presence of furan is a potential concern because, based on high-dose animal tests, furan is considered possibly carcinogenic to humans. FDA has developed a gas chromatography/mass spectrometry method to measure furan levels in food, which is posted on FDA's website at

http://www.cfsan.fda.gov/~Ird/pestadd.html#furan. FDA is also issuing a Federal Register Notice (May 10, 2004), requesting data and information from the public on furan in food and furan toxicology, and is bringing the topic of furan to its Food Advisory Committee on June 8, 2004.

#### The data

FDA is now posting furan data that were collected through May 27, 2004. Data are presented in chronological order with data collected between April 29, 2004 and May 27, 2004 presented in Table 2. FDA previously posted exploratory furan data collected through April 28, 2004, which are found in Table 1. We are presenting these data to inform the public of FDA's progress and to help stimulate research into the formation of furan in food. The results reflect furan levels detected in samples of individual food products.

#### Limits of the data

These data are exploratory and should not be understood to be a reflection of the distribution of furan in foods in the U.S. food supply. The data cover a limited number of food categories, a limited number of products in those categories, and a limited number of brands. Also, the data do not fully address the variation from one unit of a food product to another unit of the same product, or from one production lot of a food product to another lot. Also, the choice of products for testing in this exploratory survey should not be taken as an indicator of food product choices by consumers.

#### What consumers should understand

Consumers should not view the furan levels in Table 1 as an indicator of furan exposure, or

as the "risk" of eating certain foods. First, furan levels alone do not equate to furan exposure; calculating exposure requires consideration of both furan levels, and the amounts of food that consumers eat. Second, estimates of furan exposure take into account not single food items, but the wide variety of foods found in a range of diets. Third, the scope of data in Table 1 is too limited to properly consider potential sources of variation in measured furan levels, such as variability between different units or lots of food and the effect of consumer cooking practices on furan levels.

#### Notes:

- 1. ND = nondetect
- 2. The estimated limit of quantitation (LOQ) is 2.0 ppb for coffee, applesauce and juices and 5.0 ppb for all other foods. Values below the LOQ but above the estimated limit of detection (0.7 ppb for coffee, applesauce and juices and 1.5 ppb for all other foods) are reported as <2.0 ppb and <5.0 ppb respectively.</p>
- Concentrates (infant formulas and broth) were mixed with water (1:1) for analysis. Results are reported as table ready.
- 4. All ground coffee was brewed using automatic drip coffee makers. Instant coffees were reconstituted per manufacturer directions.
- 5. Foods with multiple results were from different cans or jars within the same lot.

#### FDA/CFSAN - Exploratory Data on Furan in Food

# Table 1: Furan values in food product samples throughApril 28, 2004

	Product	Furan (ppb)
Baby Foods	Gerber 100% Apple Juice, Lot 1	3.2
	Gerber 100% Apple Juice, Lot 2	3.4
	Gerber 100% Apple Juice, Lot 2Beechnut Naturals Apple JuiceBeechnut Naturals Apple JuiceEarth's Best Apple JuiceGerber 1st Foods Applesauce, Lot 1Gerber 1st Foods Applesauce, Lot 1Gerber 1st Foods Applesauce, Lot 2Gerber 1st Foods Applesauce, Lot 2Berber 1st Foods Applesauce, Lot 2Berber 1st Foods Applesauce, Lot 2Beechnut Naturals Stage 1 Applesauce, Lot	
	Earth's Best Apple Juice	8.2
	Gerber 1 <sup>st</sup> Foods Applesauce, Lot 1	4.4
	Gerber 1st Foods Applesauce, Lot 1	5.2
	Gerber Tender Harvest Organic Apples	4.7
	Gerber 1st Foods Applesauce, Lot 2	3.2
	Gerber 1 <sup>st</sup> Foods Applesauce, Lot 2	3.6
	Beechnut Naturals Stage 1 Applesauce, Lot 1	4.7
	Beechnut Naturals Stage 1 Applesauce, Lot 1	3.7
	Beechnut Naturals Stage 1 Applesauce, Lot 2	4
	Earth's Best First Apples	5.3
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	74.9
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	90.2
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	93.1
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	91
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	64.7
	Gerber 1 <sup>st</sup> Foods Sweet Potatoes	58
	Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 1	74.4
	Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 2	75.7
	Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 2	81.1
	Beechnut Naturals Stage 1 Tender Golden	

Sweet Potatoes, Lot 2	84.2
Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 2	79.7
Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 2	87.1
Beechnut Naturals Stage 1 Tender Golden Sweet Potatoes, Lot 2	87.5
Earth's Best First Sweet Potatoes	88.1
Earth's Best First Sweet Potatoes	82.9
Earth's Best First Sweet Potatoes	73.8
Organic Baby Sweet Potatoes	108
Organic Baby Sweet Potatoes	72.7
Gerber 1 <sup>st</sup> Foods Carrots	38.2
Gerber 1 <sup>st</sup> Foods Carrots	39.6
Beechnut Naturals Stage 1 Tender Sweet Carrots	50.6
Earth's Best First Carrots, Lot 1	20.2
Earth's Best First Carrots, Lot 2	26
Organic Baby Carrots	47.6
Organic Baby Carrots	40.8
Gerber 1 <sup>st</sup> Foods Green Beans	39.6
Gerber 1 <sup>st</sup> Foods Green Beans	42.6
Beechnut Naturals Stage 2 Tender Young Green Beans	34
Beechnut Naturals Stage 2 Tender Young Green Beans	34.2
Organic Baby Green Beans & Rice	72
Organic Baby Green Beans & Rice	66.5
Gerber 1 <sup>st</sup> Foods Squash	38
Gerber 1 <sup>st</sup> Foods Squash	39.4
Gerber 1 <sup>st</sup> Foods Squash	51.3
Beechnut Naturals Stage 1 Butternut	57

.

	Squash, Lot 1	52.2
	Beechnut Naturals Stage 1 Butternut Squash, Lot 2	41.9
	Earth's Best Winter Squash	55.1
	Beechnut Naturals Stage 2 Chicken Dinner	29.4
	Earth's Best Chicken and Stars	15.9
	Gerber 3 <sup>rd</sup> Foods Pears	5.2
	Beechnut Naturals Stage 1 Bartlett Pears, Lot 1	5.8
	Beechnut Naturals Stage 1 Bartlett Pears, Lot 2	<5.0
	Earth's Best First Pears	5.8
	Gerber 1 <sup>st</sup> Foods Bananas (in plastic containers)	13
	Gerber Tender Harvest Organic Bananas	17.6
	Beechnut Naturals Stage 1 Chiquita Bananas, Lot 1	31.7
	Beechnut Naturals Stage 1 Chiquita Bananas, Lot 2	26.1
	Earth's Best First Bananas	17.7
	Gerber 2 <sup>nd</sup> Foods Garden Vegetables, Lot 1	76
	Gerber 2 <sup>nd</sup> Foods Garden Vegetables, Lot 1	73.4
	Gerber 2 <sup>nd</sup> Foods Garden Vegetables, Lot 2	112
	Gerber 2 <sup>nd</sup> Foods Garden Vegetables, Lot 3	79.4
	Beechnut Naturals Stage 2 Mixed Vegetables, Lot 1	61.5
	Beechnut Naturals Stage 2 Mixed Vegetables, Lot 2	
<u>.</u>	Earth's Best Garden Vegetables	51
Infant Formulas	Enfamil with Iron Concentrate	16.8
	Enfamil with Iron Concentrate	18.8
	Enfamil with Iron Concentrate	12.7
	Enfamil ProSobee Concentrate	8.5
	Enfamil ProSobee Concentrate	8.3

	Good Start Supreme Concentrate	ND
	Good Start Supreme Ready to Feed	ND
	Good Start Supreme DHA & ARA Concentrate	ND
	Good Start Supreme DHA & ARA Ready to Feed	ND
	Good Start Essentials Soy Concentrate	ND
	Good Start Essentials Soy Ready to Feed	ND
	Similac with Iron Concentrate, Lot 1	8.6
	Similac with Iron Concentrate, Lot 1	8.5
	Similac with Iron Concentrate, Lot 2	11.6
	Similac Advance Concentrate, Lot 1	7.5
	Similac Advance Concentrate, Lot 2	8.4
Coffee	Maxwell House Coffee (brewed)	37.4
	Maxwell House Coffee (brewed)	40.4
	Folgers Classic Roast Coffee Crystals	<2.0
	Folgers French Roast Coffee (brewed)	44.7
	Nescafe Classic Instant Coffee	<2.0
	Nescafe Classic Instant Coffee	<2.0
	Starbucks Yukon Blend whole bean (brewed)	84.2
	Maxwell House Sanka Decaffeinated Coffee (brewed)	33.6
	Maxwell House Sanka Decaffeinated Instant Coffee	<2.0
	Folgers Classic Decaf (brewed)	42.5
	Folgers Classic Decaf (brewed)	38.3
	Folgers Classic Decaf (brewed)	52.6
	Nescafe Taster's Choice Decaffeinated Instant Coffee	4.8
	Nescafe Taster's Choice Decaffeinated Instant Coffee	7.2
Mixtures (e.g. soups,	Ragu Old World Style Traditional Pasta Sauce	11
sauces, broths, chili)	Ragu Old World Style Traditional Pasta	26.1

Sauce	<u> </u>
Francesco Rinaldi Traditional Spaghetti Sauce	<5.0
Francesco Rinaldi Traditional Spaghetti Sauce	<5.0
Prego Traditional Spaghetti Sauce, Lot 1	5.9
Prego Traditional Spaghetti Sauce, Lot 1	6.1
Prego Traditional Spaghetti Sauce, Lot 2	<5.0
College Inn Chicken Broth, Lot 1	8.2
College Inn Chicken Broth, Lot 2	6.7
Swanson Chicken Broth, Lot 1	12.7
Swanson Chicken Broth, Lot 2	9.7
Campbell's Chicken Broth, Lot 1	15.2
Campbell's Chicken Broth, Lot 1	18.2
Campbell's Chicken Broth, Lot 2	13.3
Campbell's Chunky Old Fashioned Vegetable Beef Soup	52
Campbell's Chunky Beef with Country Vegetables	49.7
Progresso Rich & Hearty Slow Cooked Vegetable Beef Soup	81.4
Progresso Traditional Beef & Vegetables Soup	110
Safeway Hearty Beef and Country Vegetables Soup, Lot 1	125
Safeway Hearty Beef and Country Vegetables Soup, Lot 2	110
Hormel Chili with Beans	77
Giant Chili with Beans, Lot 1	66.3
Giant Chili with Beans, Lot 2	
Castleberry's Hot Dog Chili Sauce, Lot 1	46
Castleberry's Hot Dog Chili Sauce, Lot 2	35
Franco-American Spaghetti, Lot 1	39.2
Franco-American Spaghetti, Lot 1	42.9
Franco-American Spaghetti, Lot 2	36.7

	Food Lion Mini Beef Ravioli, Lot 1	42.2
	Food Lion Mini Beef Ravioli, Lot 2	42.7
	Chef Boyardee Beefaroni, Lot 1	29.8
	Chef Boyardee Beefaroni, Lot 2	42.3
Fish	StarKist Solid White Albacore Tuna in water	<5.0
	Chicken of the Sea Chunk White Tuna in water	6.4
	Bumble Bee Solid White Albacore in water, Lot 1	<5.0
	Bumble Bee Solid White Albacore in water, Lot 2	<5.0
	Chicken of the Sea Solid White Albacore Tuna in water, Lot 1	6.3
	Chicken of the Sea Solid White Albacore Tuna in water, Lot 2	7.1
Canned Fruit,	Bush's Original Baked Beans, Lot 1	56.3
Fruit Juices and Vegetables	Bush's Original Baked Beans, Lot 2	61
	Hanover Baked Beans Brown Sugar & Bacon, Lot 1	89.7
	Hanover Baked Beans Brown Sugar & Bacon, Lot 2	117
	Hanover Baked Beans Brown Sugar & Bacon, Lot 2	
	Campbell's Pork & Beans, Lot 1	
	Campbell's Pork & Beans, Lot 2	78.7
	Campbell's Pork & Beans, Lot 2	85.6
	Del Monte Sweet Corn Cream Style	39.1
	Giant Home Sliced Green Beans	6.3
	Green Giant Cut Green Beans	5.9
	Musselman's Premium Natural Apple Juice, Lot 1	2.5
Musselman's Premium Natural Appl Lot 2		3.4
	Giant Orchard Harvest Apple Juice, Lot 1	<2.0
Giant Orchard Harvest Apple Juice, Lot 2		<2.0

Motts 100% Apple Juice	<2.0
White House 100% Apple Juice	<2.0
Minute Maid 100% Apple Juice (juice box)	<2.0
Giant Concord Grape Juice	3.2
Giant White Grape Juice	<2.0
Welch's White Grape Juice	ND
Welch's Concord Grape Juice	<2.0
Libby's Juicy Juice white grape flavored	2.3
Libby's Juicy Juice grape flavored	2.8
Northland Cranberry Juice	3.4
Ocean Spray Light Cranberry Juice Cocktail	ND
Ocean Spray Cranberry Juice Cocktail	<2.0
Giant Cranberry Flavored Juice Blend	<2.0

# Table 2: Furan values in food product samples from April29, 2004 to May 27, 2004

	Product	Furan (ppb)
Infant Formulas	Enfamil ProSobee Powder	ND
	Enfamil with Iron Powder	ND
	Enfamil with Iron Ready to Use	13.1
	Enfamil AR Lipil Ready to Use	8
	Enfamil ProSobee Lipil Ready to Use	
	Good Start Supreme DHA and ARA Powder	ND
	Good Start Soy Essentials Powder	ND
	Similac NeoSure Advance Powder	ND
	Isomil Advance Powder	ND
	Similac with Iron Ready to Feed	<5.0
	Similac Isomil Advance Ready to Feed	6.8
Canned Fruit,	Del Monte Whole Kernel Corn	ND
Fruit Juices and Vegetables	Green Giant Whole Kernel Corn	<5.0
_	Giant Cream Style Corn	6.8
	Libby's Sweet Peas	7.3
	Del Monte Sweet Peas	5.8
	Giant Tomato Juice	4.1
	Giant 100% Vegetable Juice	3.2
	Campbell's Tomato Juice	5.6
	Campbell's Tomato Juice	5.4
	V8 100% Vegetable Juice	7.6
	V8 100% Vegetable Juice	5.6
	V8 Low Sodium 100% Vegetable Juice	5.6
Bread	Wonder Buttermilk Calcium Fortified Enriched Bread	
	Giant 100% Stone Ground Whole Wheat Bread	<2.0
	Pepperidge Farm Jewish Rye Bread, Seeded	ND

Meats	Armour Treet luncheon loaf	<5.0
	Armour Treet luncheon loaf	<5.0
× .	Spam classic	ND
	Hormel Vienna Sausage	39.2
	Armour Vienna Sausage	<5.0
	Armour Potted Meat Food Product	11.7
	Libby's Potted Meat Food Product	31.6
	Super G Bologna	ND
	Oscar Mayer Bologna	ND
Nuts and Nut	Jif Creamy Peanut Butter	6.1
Butters	Peter Pan Creamy Peanut Butter	7.5
	Peter Pan Creamy Peanut Butter	7.1
Miscellaneous	Smucker's Caramel Topping	2.1
	Hershey's Classic Caramel Topping	4.3

Furan in Food, Thermal Treatment; Request for Data and Information; Federal Register, May 10, 2004 (available in PDF)

Pesticides, Metals, Chemical Contaminants & Natural Toxins

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FDA/Center for Food Safety & Applied Nutrilion Hypertext updated by <u>dav/cjm</u> June 7, 2004



#### Swiss Federal Office of Public Health; 2004-06-22

#### List for experts

#### overview furan determinations

specifications of the method used: limit of quantitation: about 1-10 ppb, usually 1-2 ppb 1 ppb = 1  $\mu$ g/kg n\_d. = not detected v = visible

The variation within the same product may be relative high.

No.	sample description	concen- tration [ppb]	ingredients in more detail; but usually not complete, minor ingredients not always listed
	Baby Food in small glass jars	T	1
	containing meat		
2037	veal and broccoli (organic)	42	potato flakes, broccoli 14%, veal 10%
2109	Swiss veal and broccoli (organic), may be similar to 2037	45	potato flakes, broccoli 14%, veal 10%
2040	(organic) "Aelpler Maccaroni"	25	skim milk, potato flakes, ham (pork) 8%, pasta 5%, cheese 4%
2073	Pasta Bolognese (organic)	34	vegetable 45%: tomatoes (from concentrate), carrots, onions; beef 10%, rice flour, pasta 4.5%
2106	vegetable with ham (organic)	31	carrots 28%, potato flakes 8%, sweet fennel 5%, spinach 2%, ham (pork)
2107	veal potatoes (organic)	21	veal 30%, potato flakes 25%
2108	Swiss beef (organic)	5	beef 40%, rice flour
2110	poultry with vegetable and rice (organic)	16	carrots 12%, sweet fennel 3%, celeriac 3%, turkey 10%, rice flour
2111	vegetable meat "polenta" (corn) (organic)	31	tomatoes from concentrate 9%, carrots 7%, broccoli 7%, onions 1%, semolina of maize 6%, turkey 5%, veal 5%
2115	carrots-potatoes-chicken (organic)	42	carrots 36%, potatoes 16,5%, chicken 8%
2117 2118	vegetable-veal (organic) carrots-spaghetti-veal (organic)	<u>51</u> 45	potatoes, carrots, tomato puree, parsnips, peas, onions, leek, veal 8,5% carrots 35%, parsnips, tomato puree, maize, leek, spaghetti boiled 11%,
2119	carrots-rice-turkey (organic)	26	veal 8% carrots 47%, semolina of rice boiled 24%, turkey 8%
2119	vegetable-pasta-ham (organic)	42	carrots, tomato puree, peas, pasta boiled 10,5%, ham 8%
	Baby Food in small glass jars vegetable (mainly)	-	
2038	"pumpkin-magic" (organic)	80	carrots 31%, potato flakes 30%, pumpkin 13%
2071	"pumpkin-magic" (organic); similar to 2038	64	carrots 31%, potato flakes 30%, pumpkin 13%
2039	vegetarian meal (organic)	53	vegetable 52%: carrots, potato flakes, sweet fennel, celeriac, spinach; tofu 8%
2072	vegetarian meal (organic); similar to 2039	35	vegetable 52%: carrots, potato flakes, sweet fennel, celeriac, spinach; tofu 8%
2080	vegetable dish (organic)	35	carrots, potatoes, Blumenkohl, peas (vegetable 73%)
2081	cream vegetable (organic)	17	parsnips, skimmed milk, potatoes, cauliflower, semi-cream 4%, parsley, (vegetable 60,5%)
2082	carrots	25	carrots 76%
2103	carrots potatoes (organic)	31	carrots, potato flakes
2104	carrots, sweet fennel, potatoes (organic)	44	carrots, potato flakes, sweet fennel carrots 30%, potato flakes 20%, celeriac 6%, spinach 3%
2105	vegetable dish (organic)	49	zucchini 30%, potatoes 30%, peas, parsnips
2116 2121	zucchini purée (organic)	68	vegetable 81%: carrots, potatoes, maize, sweet fennel, parsnips
2121	tender garden vegetables (organic) garden carrots (organic)	16	carrots 75%
2122	cauliflower with potatoes and broccoli (demeter)	27	potatoes 30%, cauliflower 10%, broccoli 10%, rice flour
2143	spinach with rice (demeter)	32	spinach 20%, potatoes, rice 10%
2143		42	carrots 65%, potatoes 20%
2144	carrots with potatoes (demeter) zucchini and pumpkin with potatoes (demeter)	25	potatoes 18%, zucchini 12%, pumpkin 12%, rice flour
2146	carrots with apple (demeter)	25	carrots 70%, apples 20%
2147	pumpkin with potatoes (demeter)	34	potatoes 30%, pumpkin 22%, rice flour
2148	carrots (demeter)	34	carrots 80%
2149	vegetable mixture (demeter)	51	vegetable 85% (carrots, potatoes, spinach, tomatoes, leek)
2150	vegetable risotto (demeter)	45	vegetable 59% (carrots, potatoes, tomatoes, spinach), rice 3%

	Baby Food in small glass jars		
	fruit (mainly)		
2067	apple-apricot (organic)	4	apples (75%), apricots 15%, cane sugar, rice flour
2068	fruit puree exotic (organic)	2	fruit 50%: banana puree, peach, pineapple, cane sugar 8%, rice flour
2069	semolina (organic)	1	berries 18% (strawberries, blueberries), cane sugar 10%, semolina of durum wheat 6.5%
2070	fruit snack (organic)	16	fruit 67%: apples, pears; potato flakes 21%
2074	fruit cocktail	2	fruit puree 91.2%: apples, apricots, pineapples, pears, bananas; orange juice from concentrate, sugar
2133	fruit cocktail, similar to 2074	2	fruit puree 91.2%: apples, apricots, pineapples, pears, bananas; orange juice from concentrate, sugar
2075	apple-banana	2	apples 83.8%, banana puree 16%
2076	apples and pears (organic)	2	apples 70%, apple juice 19,8%, pears 6%
2077	apricot apple dessert	2	low acid apple juice, apricots 25%, apples 23%
2078	bananas (organic)	3	bananas 70%, apple juice
2079	apples and blueberries (organic)	2	apples 42%, blueberries 17%, low acid apple juice
2083	fruit - wholemeal - muesli	8	61% fruit: apples, bananas, apricots; wheat flour, cane sugar, oat flour
2098	granny's apple puree (organic)	3	apples 78%
2099	rusk with fruits (organic)	9	bananas 27%, apples 13%, rusk (zwieback) 5%
2100	semolina with apricots (organic)	13	apricots 8%, cane sugar, semolina of durum wheat, skim milk powder, bananas
2101	bananas apricots (organic)	6	84% fruit: bananas, apricots
2102	Birchermusli (organic)	5	skim milk, apples 20%, bananas 15%, raspberry 10%, sultanas 5%, oat flakes 4,3%
2112	cereals apple with rice (organic)	1	apples 60%, rice 21%, (flour partially converted to starch sugar, semolina), apple juice from concentrate 18%
2113	cereals peach banana (organic)	2	banana 25%, peach 25%, rice 20%
2114	cereals fruit cocktail (organic)	6	fruit puree 46%: apple, mango, banana; oat flour partially converted to starch sugar 24,5%, fruit concentrate 4,5% (orange, pineapple)
2128	baby fruit fruit basket with straw berries	1	apple puree 62%, banana puree 19%, strawberry puree 15%, concentrated apple juice
2129	Baby Fruit fruit cocktail with apricots	4	fruit cocktail 92% (apple, apricot, pear, peach), cereals 4% wholemeal wheat flour partially converted to starch sugar apple puree 76%, peach puree 18%, honey 4%, concentrated apple
2130 2131	Baby Fruit fruit magic with honey	1	apricot puree 46,5%, apples 45,5%, sugar
2131	apricot apple	2	apples 83,8%, banana puree 16%
2132	apple banana	3	pears 95%, sugar
2134	pear Birchermusli (organic)	7	fruit 30% (apples, apricots, bananas), pear juice concentrate, oat flakes, sultanas 5%
2136	apple and pear with wholemeal flakes (organic)	7	apples 22%, pears 13%, pear juice concentrate, wholemeal wheat flour, wholemeal wheat flakes, lemon juice 4%
2137	apple and blueberry with wholemeal flakes (organic)	12	apples 30%, pear juice concentrate, blueberries 5%, wholemeal wheat flakes 4%
2138	apple and banana with wholemeal flakes (organic)	8	apples 20%, bananas 15%, pear juice concentrate, wholemeal wheat flakes 4%
2139	apple-banana with apricots (organic)	2	apples 26%, bananas 16%, pear juice concentrate, rice starch, apricots 4%, lemon juice 4%
2140	delicious apple (organic)	2	apples 45%, pear juice concentrate, rice flour, lemon juice
2141	delicious banana with semolina (organic)	5	banana 21%, pear juice concentrate, semolina of durum wheat 6%, lemon juice
	fruit and vegetable juices for babies and		
	young children		
2124	carrot juice (organic)	40	carrot juice 99,9%, vitamin C
2123	orange juice + vitamin C	2	orange juice from concentrate, vitamin C
2125	apple-grape juice (organic)	4	fruit juices from concentrates 85% (grapes, apples, pears, redcurrants)
2126	apple-pear juice (organic)	1	fruit juices from concentrates 100% (apples, pears), vitamin C
	canned or jarred vegetables		
2041	lentils with bacon	5	lentils 87%, smoked bacon 7 %
2042	lentils	3	lentils 95%, vegetable oils, bouillon
2043	fine bean (grean)	11	beans, salt
2044	chickpeas boiled	7	chickpeas, produced from dried chickpeas, salt
2045	"Russian salad"	6	carrots, potatoes, peas, Bohnen, Kochsalz, Zucker
2046	vegetable dish (type huntsman)	3	peas, carrots, black salsify 8,5%, egg-mushroom 4,5%, salt, sugar
2047	peas with carrots extra fine	3	peas, carrots, salt, sugar
2048	haricot beans boiled	8	beans, produced from dried beans, salt
2049	haricot beans (ready to eat)	12	haricot beans 40%, tomato puree (concentrate), vegetable oil, salt, wheat flour, sugar, vegetable concentrate, (carrots, celeriac, head lettuce, beetroot, parsley, water cress, spinach)

2057	sweet corn	< 3, v	sweet corn, sugar, salt
2156	baby carrots	6	baby carrots, sugar, salt
2159	Mixed Pickles	< 2, v	gherkins, baby corn, cauliflower, onions, sweet pepper, carrots, celeriac, sweet fennel, alcohol and grape vinegar, sugar, salt
2160	asparagus (white)	< 2, v	asparagus, salt
2161	green asparagus	< 2, v	green asparagus, salt
2178	small potatoes	< 3, v	potatoes, salt
	canned fruits		
2157	plum	< 1, v	plum, sugar
2158	fruit cocktail	6	fruits (peaches, pears, pineapples, grapes, cherries), sugar
	canned soup		1
2050	"Minestrone" (vegetable soup with pasta)	19	tomato puree, carrots, potatoes, celeriac, borlotti beans, leek, cabbage, pasta, vegetable oil, processed cheese, salt, onions
2051	goulash soup	43	potatoes 16%, beef 15%, onions, animal fats and oils partially hydrogenated, sweet pepper, wheat flour, spices, tomato puree (concentrate), soy sauce
	tins containing meat		1
2052	corned beef	4	beef, nitrite brining salt, sugar
2056	"egg-ravioli" (pasta with pork filling)	14	
	"sugo", tomato and chili sauces (with or		
2053	without meat (canned or jarred) "sugo" tomato sauce with mincemeat	39	tomato puree 23%, meat 13% (turkey, beef), carrots, salt, sugar,
2053	"sugo" tomato sauce with mincemeat,	17	modified corn starch, dried onions tomato purce 23%, meat 13% (turkey, beef), carrots, salt, sugar,
	similar to 2053		modified corn starch, dried onions
2054	sweet chili sauce	6	sugar, rice vinegar with chili (6%), garlic, salt
2055	hat chili sauce	6	rice vinegar, chilies (40%), salt, modified starch
2084	tomato sauce "Napoletana"	4	tomato puree (38,5%), tomato puree (concentrate), carrots (8,3%), onions (5%), sunflower oil, salt, basil (1%)
2085	tomato sauce with tuna	6	tomato puree (23%), tuna in olive oil (14%), tomato puree (concentrate), sunflower oil (6,6%), onions, modified starch
2086	tomato sauce with bacon "Amatriciana"	19	tomatoes 60%, bacon 15%, onions 6%, tomato puree (concentrate), olive oil, sugar, rice starch
2087	Italian peeled tomatoes	8	tomatoes, tomato juice
2092	tomato sauce with basil	5	tomato flesh 76%, tomato puree 12,1%, olive oil, onions, basil 1,5%, sugar
2093	tomato sauce "Napoletana"	7	tomato flesh 66,8%, tomato puree 10,1%, onions 7%, carrots, olive oil 3,5%, salt, sugar
2094	tomatosauce "Arrabbiata"	5	tomato flesh 83%, tomato puree 7,9%, olive oil, paprika 2%, salt
2096	peeled tomatoes "Pelati"	5	peeled tomatoes, tomato juice
2179	tomato puree (doppio concentrato di pomodoro)	< 4, v	tomatoes, salt
	soy sauce, hydrolysed vegetable protein		
2058	soy sauce, hydrolysed vegetable protein liquid hydrolysed vegetable protein (soy	18	
	liquid hydrolysed vegetable protein (soy sauce)		
2059	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed	91	
	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy		
2059 2088 2089	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce)	91 29 18	
2059 2088 2089 2090	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce	91 29 18 50	
2059 2088 2089 2090 2091	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce	91 29 18 50 78	
2059 2088 2089 2090	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce	91 29 18 50	
2059 2088 2089 2090 2091 2097	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b>	91 29 18 50 78 58	
2059 2088 2089 2090 2091 2097 2097	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b> head lettuce	91 29 18 50 78 58	
2059 2088 2089 2090 2091 2097 2097 2062 2062-	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b>	91 29 18 50 78 58	
2059 2088 2089 2090 2091 2097 2097 2062 2062- 2	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b> head lettuce head lettuce	91 29 18 50 78 58 <1, n.d.	
2059 2088 2089 2090 2091 2097 2097 2062 2062- 2 2063 2063-	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b> head lettuce	91 29 18 50 78 58	
2059 2088 2089 2090 2091 2097 2062 2062- 2 2063 2063- 2	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce dark soy sauce dark soy sauce <b>vegetable, fresh</b> head lettuce head lettuce lollo lettuce (red) lollo lettuce (red)	91 29 18 50 78 58 58 <1, n.d. <1, n.d. <1, n.d. <1, n.d.	
2059 2088 2089 2090 2091 2097 2097 2062 2062- 2 2063 2063-	liquid hydrolysed vegetable protein (soy sauce) soy sauce naturally brewed high quality soy sauce liquid hydrolysed vegetable protein (soy sauce) spicy soy sauce sweet soy sauce dark soy sauce <b>vegetable, fresh</b> head lettuce head lettuce lollo lettuce (red)	91 29 18 50 78 58 < < 1, n.d. < 1, n.d. < 1, n.d.	

	coffee		
c01	ground coffee (powder)	959	
c01	ground coffee (powder)	1022	
c101	coffee (brewed, filtered coffee of c01, a few hours in thermos)	13	
c102	coffee (brewed, vending machine)	58	
c103	coffee (espresso, brewed, vending machine, same coffee beans as c102)	78	
c104	coffee (brewed, professional machine)	105	
c105	coffee (espresso, brewed, professional machine)	146	
c106	coffee (brewed, professional machine)	46	
c107	coffee (espresso, brewed, professional machine)	109	
c02	ground coffee (powder)	2740	
c108	coffee (espresso, brewed of c02, simple piston machine)	74	
c01-1	ground coffee (powder)	1438	
c109	coffee (brewed, filtered coffee of c01-1)	40	
	hot chocolate and malt beverage		
2202	Ovomaltine (beverage from vending machine)	<2, v	
2203	hot chocolate (beverage from vending machine)	<2, v	
	bread, toast	1	
2151	butter toast (out of the packet)	<2, n.d.	wheat flour, butter fat 8%, yeast, salt, sugar, skim milk powder, malt extract, milk sugar, malt flour, flour improver: ascorbic acid
2151-ht	butter toast, light toasted	<2, n.d.	
2151-dt	butter toast, dark toasted	18	
2154	"Rustico" toast (out of the packet)	< 2, n.d.	wholemeal wheat flour, wheat flour, canola oil, malt vinegar, skim milk powder, yeast, sait, sugar, milk sugar, flour improver: ascorbic acid
2154-ht	"Rustico" toast, light toasted	<2, n.d.	
2154-dt	"Rustico" toast, dark toasted	< 8, v	wheat flour, wholemeal flour (wheat, rye, oat, barley), salt, yeast, dried
2177	bread	30	sour dough, malt flour from barley
	other samples		
2061	whole milk UHT	< 0.5, n.d.	
2152	plum beverage	6	extract of dried plums (800 g plums gives 0.75L beverage), 30% apple juice from concentrate, 2% lemon juice from concentrate
2153	beetroot juice with fruit juices (organic)	1	beetroot juice 89%, pear juice, lemon juice concentrate
2155	potato flakes for mashed potatoes (flakes, not prepared)	<5, n.d.	potatoes 99%



# Sanitätsdepartement des Kantons Basel-Stadt Kantonales Laboratorium

Abteilung Lebensmittel Kannenfeldstrasse 2, Postfach, CH-4012 Basel

Internal Standard: Furan-d-4; LOQ: 1 mg/kg except for corn and peanuts 4 mg/kg

#### Furan in Lebensmitteln

Resultate bis 2.11.2004

Lebensmittelkategorie	Minimum	Maximum	Median	n	
Beikost für Säuglinge und Kleinkinder (in Gläschen)	12	69	29	20	details see next page
Beikost für Säuglinge und Kleinkinder (Pulver für Breizubereitung)	1	38	13	4	details see next page
Honig (Herkunft Schweiz)	3	10	4	5	
Kaffee (Extrakt)	73	125	98	4	
Kaffee (Bohnen, gemahlen)	2650	5050	4400	4	
Süssmaiskonserve	4	4		1	~
Erdnüsse, in Honig geröstet	4	4		1	
Aprikosen-Konfitüre	1	1		1	

Angaben in μg/kg bzw. μg/l n = Anzahl untersuchte Proben Single data for "Beikost für Säuglinge und Kleinkinder (in Gläschen) -Food for babies and young children in jars

Probennummer Proben	Furan [µg/kg]
Erhobene Proben - Bezeichnung	Ergebnis - Wert
1 Karotten-Kartoffeln-Poulet	25
2 Karotten-Reis-Truthahn	21
3 Tomatennudeln mit Kalbfleisch	12
4 Gemüseplatte	24
5 Spaghetti mit Tomaten und Mozarella	29
6 Ruebli-Kartoffeln	53
7 Kürbiszauber	69
8 Karotten, Fenchel, Kartoffeln	48
9 Gemüseteller	55
10 Gemüse m. Schinken	20
11 Geflügel mit Mais	16
12 Pasta Bolognese	19
13 Gemüse, Fleisch-Polenta	21
14 Gemüseallerlei	45
15 Karotten	24
16 Spinat mit Reis	37
17 Karotten mit Apfel	30
18 Zucchini + Kürbis mit Kartoffeln	28
19 Blumenkohl mit Kartoffeln + Brokkoli	46
20 Kürbis mit Kartoffeln	43

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Single data for "Beikost für Säuglinge und Kleinkinder (Pulver für Breizubereitung) -Food for babies and young children (powder for porridge preparation)

Probennummer	Proben Erhobene Proben - Bezeichnung	Furan [µg/kg] Ergebnis - Wert
	1 Milchbrei mit Gemüse	14
2	2 Gemüsebrei	38
3	3 Folgenahrung mit Karotten	1
2	4 Getreide- und Gemüsebrei	12

## Furan in Lebensmitteln,

Please note that this list, published on 8 June 2005, replaces the earlier version which contained an error for the food group "Bier und Malz" entry number 7-12, page 2.

Chemische und Veterinäruntersuchungsamt Stuttgart

Note Secretariat:. Internal Standard:tetrahydrofuran; analytical method: FDA method (<u>http://www.cfsan.fda.gov/~dms/furan.html</u>). LOD: 0.3-0.5 µg/kg LOQ: 1 µg/kg except for soups and sauces: LOD: 1 µg/kg; LOQ: 3 µg/kg

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
1	Kaffee entkoffeiniert	Deutschland	04.07.05	1970
1 Aufguss	Kaffee entkoffeiniert			13 µg/l
2	Kaffee koffeinhaltig	Deutschland	unbekannt	2180
2 Aufguss	Kaffee koffeinhaltig	,		15 µg/l
3	Kaffee entkoffeiniert, löslich	Deutschland	Ende 04/06	529
3 Aufguss	Kaffee entkoffeiniert, löslich			7 μg/l
4	Schonkaffee entkoffeiniert, löslich	Deutschland	Ende 04/06	239
4 Aufguss	Schonkaffee entkoffeiniert, löslich			3 µg/l
5	Kaffee entkoffeiniert, löslich	Deutschland	Ende 02/05	2200
5 Aufguss	Kaffee entkoffeiniert, löslich			14 µg/l
6	Kaffee, löslich	Deutschland	Ende 03/06	1991
6 Aufguss	Kaffee, löslich			25 µg/l
7	Kaffee, löslich	Deutschland	Ende 06/06	279
7 Aufguss	Kaffee, löslich			5 µg/l
8	Cappuccino löslich, entkoffeiniert	Deutschland	Ende 04/05	663
8 Aufguss	Cappuccino löslich, entkoffeiniert			15 µg/l
9	Kaffee, löslich	Deutschland	Ende 03/06	461

#### Kaffee

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
9 Aufguss	Kaffee, löslich			11 µg/l
10	Röstkaffee, Bohnen, entkoffeiniert	Deutschland	unbekannt	1039
10 Aufguss	Röstkaffee, Bohnen, entkoffeiniert			11 µg/l
11	Kaffee, Bohnen	Deutschland	unbekannt	2307
11 Aufguss	Kaffee, Bohnen			24 µg/l

## **Bier und Malz**

1	Doppel-Bock, dunkel	Deutschland	25.03.05	6
2	Pilsner	Deutschland	Ende 09.04	5
3	Dark Bier	Deutschland	15.05.04	13
4	Dunkles Bier	Deutschland	Ende 08.04	12
5	Schwarzbier	Deutschland	unbekannt	11
6	Schwarzbier	Deutschland	Ende 08.03	7
7	Röstmalzbier, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	173
8	Röstmalzbier, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	34
9	Röstmalzbier, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	36
10	Röstmalzbier, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	195
11	Röstmalzbier, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	16
12	Röstmalz, Rohstoff z. Bierherstellung	Deutschland	keine Angabe	n.n.

## Babynahrung

1	Baby Früchtetrank	Deutschland	Ende 10.05	2 µg/l
2	Apfel-Schorle	Deutschland	19.05.06	2 µg/l
3	Fencheltee mit Apfel-Saft	Deutschland	18.05.06	1 µg/l
4	Trink Brei, Multi-Frucht	Deutschland	21.01.06	6 µg/l
5	Fencheltee mit Apfel-Saft	Deutschland	Ende 11.06	1 µg/l
6	Kohlrabi fein	Deutschland	01.03.06	22
7	Pastinake fein	Deutschland	21.06.06	18

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
8	Blumenkohl mit Kartoffeln	Deutschland	03.05.06	27
9	Trinkbrei Apfel-Banane	Deutschland	Ende 11.05	11 µg/l
10	Spinat mit Kartoffeln	Deutschland	22.01.06	47
11	Karotten mit Kartoffeln	Deutschland	21.04.06	29
12	Gemüseallerlei	Deutschland	02.04.06	18
13	Karotten mit Kartoffeln	Deutschland	22.06.06	10
14	Kürbis mit Reis und Huhn	Deutschland	14.06.06	30
15	Karotten mit Kartoffeln und Huhn	Deutschland	07.05.06	24
16	Karotten-Kartoffeln mit Rindfleisch	Deutschland	29.04.06	20
17	Karotten mit Kartoffeln und Rindfleisch	Deutschland	17.06.06	27
18	Gemüsereis mit Putenfleisch	Deutschland	25.06.06	7
19	Kartoffelpüree mit Gemüse und Schweinefleisch	Deutschland	18.06.06	14
20	Feiner Obstbrei	Deutschland	31.05.05	8
21	Heidelbeeren in Apfel	Deutschland	30.06.05	3
22	Banane & Pfirsich in Apfel	Deutschland	28.02.06	3
23	Äpfel mit Bananen	Deutschland	30.11.05	5
24	Frucht & Joghurt Banane	Deutschland	31.05.05	2
25	Pfirsich mit Maracuja	Deutschland	31.10.05	4
26	Williams-Christ-Birnen	Deutschland	30.11.05	3
27	Früchte mit Reisbrei Banane & Pfirsich	Deutschland	31.10.05	2
28	Feines Früchte-Allerlei	Deutschland	31.01.06	n.n.
29	Erdbeere mit Heidelbeere in Apfel	Deutschland	31.03.05	n.n.
30	Feines Gemüse-Allerlei	Deutschland	31.03.06	22
31	Gemüsecreme mit Geflügel	Deutschland	31.07.05	9
32	Gemüse-Allerlei	Deutschland	30.09.05	32
33	Zucchini mit Kartoffeln	Deutschland	31.10.05	3
34	Kürbis mit Reis	Deutschland	31.10.05	9
35	Karotten	Deutschland	31.12.05	21

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
36	Karotten	Deutschland	30.09.05	26
37	Karotten und Kartoffeln	Deutschland	31.10.05	12
38	Banane u. Pfirsich in Apfel	Deutschland	30.11.2005	1
39	Bio Banane	Deutschland	30.11.2005	2
40	Heidelbeeren Apfel	Deutschland	31.03.2005	5
41	Pasta Bambini, Komplettmahlzeit	Deutschland	30.09.2005	13
42	Früchte Duett, Beikost	Deutschland	31.12.2004	4
43	Zucchini mit Kartoffeln	Deutschland	31.10.2005	17
44	Gemüse-Risotto	Deutschland	30.11.2005	25
45	Apfel mit Mango	Deutschland	30.04.2006	25
46	Apfel mit Banane	Deutschland	26.02.2006	3
47	Fruchtallerlei	Deutschland	22.03.2006	3
48	Feines Gemüse-Allerlei	Deutschland	31.01.2006	21
49	Brokkoli-Rahmgemüse mit Karotten und Reis	Deutschland	30.04.2005	11
50	Grünes Gemüse	Deutschland	31.05.2005	22
51	Baby-Birne	Deutschland	30.09.2005	2
52	Gemüse-Allerlei	Deutschland	18.02.2006	20
53	Vollkorn-Früchtebrei Banane in Apfel	Deutschland	31.10.2004	8
54	Baby-Birne	Deutschland	31.08.2005	3
55	Fruchtmus	Deutschland	04.02.2005	<1
56	Zartes Gartengemüse	Deutschland	31.10.2005	17
57	Karottengemüse	Deutschland	31.12.2004	11
58	Gemüsereis mit Schweinefleisch	Deutschland	31.01.2005	42

## Suppen-/Soßenpulver

1	Fleischsuppe	Deutschland	06/2005	n.n.
2	Fleischsuppe	Deutschland	8/2005	n.n.
3	Klare Fleischsuppe	Deutschland	10.2004	n.n.
4	Braune Soße	Deutschland	01.2005	<3

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
5	Helle Soße	Deutschland	02.2005	n.n.
6	Bratenfond	Deutschland	08.2005	43
7	Nudel-Schinken-Gratin	Deutschland	11.2004	n.n.
8	Zwiebel-Suppe, Französische Art	Deutschland	07.2005	n.n.
9	Jägersoße	Deutschland	10/05	23
10	Soße zu Schweinebraten	Deutschland	15.12.2005	3
11	Soße zu Braten (pflanzlich)	Deutschland	01.03.05	14
12	Soße zu Braten	Deutschland	06.2005	4
13	Soßenpulver, braun	Deutschland	unbekannt	8
14	Bratensoße extra	Deutschland	11/05	29
15	Soße zum Braten	Deutschland	12/05	12
16	Bratensoße extra	Deutschland	06/05	14
17	Instant Bratensoße	Deutschland	unbekannt	32
18	Fix für Gulasch	Deutschland	10.08.2005	11
19	Delikateß-Soße zum Braten	Deutschland	10/2005	15
20	Klarer Bratensaft	Deutschland	09/05	46

## Fertiggerichte

1	Rinderroulade	Deutschland	12.01.2005	3
2	Gulaschsuppe, würzig-pikant	Deutschland	12.05.07	35
3	Schwäbische Kutteln	Deutschland	05.2006	9
4	Feuertopf	Deutschland	2008	71
5	Ochsenschwanzsuppe, konzentriert	Deutschland	20.01.07	47
6	Gulaschsuppe	Deutschland	18.03.07	27
7	Braune Sauce, servierfertig zubereitet	Deutschland	keine Angabe	9
8	Feuriger Texastopf	Deutschland	19.05.07	30
9	Kohlrouladen	Deutschland	2008	74
10	Gulasch	Deutschland	29.03.07	6
11	Eier-Ravioli in Sauce Bolognese	Deutschland	31.12.2005	38

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
12	Schweinegulasch in Sauce mit Nudeln und Erbsen-Möhren-Gemüse	Deutschland	03.2005	34
13	Mexikanischer Bohnentopf	Deutschland	06.05.07	31
14	Schaschlik, pikant	Deutschland	31.12.2007	15
15	Feuertopf	Deutschland	2008	40
16	Linseneintopf mit durchwachsenem Rauchspeck	Deutschland	2008	20
17	Sauerbraten in pikanter Sauce	Deutschland	03.02.2008	20
18	Jägertopf	Deutschland	15.03.06	39
19	Linseneintopf mit Würstchen	Deutschland	2008	15
	Apfelsaft	•		
1	Apfelsaft trüb, Direktsaft	Deutschland	24.01.06	<b>n.</b> n.
2	Apfelsaft klar, Direktsaft	Deutschland	24.01.06	n.n

2	Apfelsaft klar, Direktsaft	Deutschland	24.01.06	n.n.
3	Apfelsaft klar, Direktsaft	Deutschland	06.10.05	n.n.
4	Apfelsaft trüb, Direktsaft	Deutschland	20.10.05	n.n.
5	Apfelsaft klar, aus Konzentrat	Deutschland	23.09.05	n.n.
6	Apfelsaft klar, Direktsaft	Deutschland	30.09.05	n.n.
7	Apfelsaft trüb, aus Konzentrat	Deutschland	15.04.05	n.n.
8	Apfelsaft trüb, Direktsaft	Deutschland	05.04.05	n.n.
9	Apfelsaft trüb, Direktsaft	Deutschland	31.05.05	<1,1 µg/l
10	Apfelsaft klar, Direktsaft	Deutschland	22.11.05	<1,1 µg/l
11	Apfelsaft klar, Direktsaft	Deutschland	01.04.05	n.n.
12	Apfelsaft trüb, Direktsaft	Deutschland	15.09.05	n.n.
13	Apfelsaft klar, aus Konzentrat	Deutschland	27.07.05	n.n.

#### **Diverses**

1	Pflaumenmus, fein gewürzt	Deutschland	22.10.05	8
2	Pflaumenmus, fein gewürzt	Deutschland	10.08.05	7
3	Pflaumenmus	Deutschland	11.12.05	2
4	Pflaumenmus	Deutschland	02.10.05	7

Ordnungs zahl	Verkehrsbezeichnung	Herkunftsland der Ware	MHD	Ergebnis µg/kg
5	Pflaumenmus, gewürzt	Deutschland	10.05.06	16
6	Birnenkraut aus Birnen und Äpfeln	Deutschland	15.10. 2006	16
7	Birnen-Apfel-Kraut	Deutschland	16.06. 2005	27
8	Caramel, sprühgetrocknet	Deutschland	Herstelldatum: 06.07.2004	192
9	Zuckerkulör	Deutschland	24.11.2005	420
10	Schoko-Kuchen-Backmischung	Deutschland	21.02.05	n.n.