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Harmful compounds might be formed when foods containing the sweetener Sucralose are heated

BfR opinion No 012/2019 of 9 April 2019

Sucralose is a sweetener authorised in the European Union as E 955. The German Federal Institute for Risk Assessment (BfR) has assessed the current data situation on the stability of Sucralose and the formation of possibly harmful chlorinated compounds at high temperatures.

The available data show that harmful compounds, some with carcinogenic potential, might occur when Sucralose and especially Sucralose-containing foods such as canned vegetables or baked goods are heated. When Sucralose (E 955) is heated to temperatures higher than 120 °C a gradual – and with further increasing temperature continuous – decomposition and dechlorination of the sweetener occurs. Temperatures of between 120 °C and 150 °C are possible during industrial manufacturing and processing of foods and are also reached in private households during cooking and baking of foods containing Sucralose. This may lead to the formation of chlorinated organic compounds with a health-damaging potential, such as polychlorinated dibenzo-p-dioxins (PCDD), dibenzofurans (PCDF) and chloropropanols.

However, there are currently insufficient data to draw final conclusions. It is unclear on the one hand which toxic reaction products are generated in detail and in which quantities they are formed when Sucralose-containing foods are heated to temperatures above 120 °C on the other. Moreover, representative data on the levels in thus manufactured foods are required for exposure estimation within the scope of a risk assessment.

The European Food Safety Authority (EFSA) is also currently dealing with Sucralose in the context of the re-assessment of authorised food additives in line with Regulation (EC) No. 1333/2008 and Regulation (EU) No. 257/2010. The result of the assessment is still pending. Until a conclusive risk assessment is available, the BfR recommends not to heat foods containing Sucralose to temperatures that occur during baking, deep-frying and roasting, or to add Sucralose only after heating. This applies to consumers as well as to commercial food manufacturers.

	BfR Risk Profile [Harmful compounds might be formed when foods containing the sweetener Sucralose are heated] (Stellungnahme Nr. 012/2019)			
A	**Affected groups**	**General Population**		
B	**Probability of a health impairment through heating of food containing Sucralose (> 120 °C) [1]**	**The data currently available are not sufficient to permit a definitive assessment of the probability of a health impairment.**		
C	**Severity of the health impairment through heating food containing Sucralose (> 120 °C) [2]**	**The data currently available are not sufficient to permit a definitive assessment of the potential health risks.**		
D	**Reliability of available data [3]**	High: The most important data are available and free of contradiction.	Moderate: Some important data are missing or contradictory	**Low: Numerous important data are missing**
E	**Controllability by the consumer [4]**	Control not necessary	**Controllable through precautionary measures**	Controllable through avoidance	Not controllable

Squares highlighted in dark blue indicate the properties of the risk assessed in this Opinion (more detailed information on this is contained in BfR Opinion No. 012/2019 of 9 April 2019)

Explanations

The risk profile is intended to visualise the risk outlined in the BfR Opinion. It is not intended for the purpose of comparing risks. The risk profile should only be read in conjunction with the corresponding opinion.

Line B – Probability of a health impairment
[1] – Heating of foods containing Sucralose (> 120 °C) can result in the formation of chlorinated compounds that may be harmful.

Line C – Severity of the health impairment:
[2] – The data currently available are not sufficient to permit the final assessment of the potential health risks.

Line D – Reliability of the currently available data
[3] – There are data gaps with regard to the identification of reaction products and the extent to which they are formed during heating of foods containing Sucralose (> 120 °C).

Line E – Controllability by the consumer
[4] – Until a final risk assessment is possible, the BfR advises consumers and food producers not to heat foods containing Sucralose to temperatures reached during baking, deep frying and roasting or only to add Sucralose after the foods have been heated.

GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT (BfR)

1 Subject of the assessment

The German Federal Institute for Risk Assessment (BfR) has assessed the currently data on the stability of Sucralose when foods containing Sucralose as additive E 955 are heated. In this assessment, the BfR investigated whether industrial processes for the production and processing of foods containing Sucralose and the use of Sucralose by consumers during the cooking or baking of foods can result in the formation of chlorinated compounds that may be damaging to health.

2 Findings

In order to address this question, the BfR conducted comprehensive literature research and assessed the identified publications in line with the criteria of Klimisch *et al.* to determine the reliability of the data collected and the methods used.

Based on the currently available data, the BfR comes to the conclusion that, when heated to temperatures of approx. 120 °C – 250 °C, reached

- during the industrial production and processing of foods for which the use of Sucralose is approved, or

- during the use of Sucralose by consumers during cooking or baking of foods,

Sucralose (E 955) is dechlorinated, possibly leading to the generation of chlorinated organic compounds exhibiting potential health risk (e.g. polychlorinated dibenzo-p-dioxins (PCDDs), dibenzofurans (PCDFs) or chloropropanols).

The currently available data are not sufficient to permit a definitive assessment of the potential health risks, as there is still a lack of data on the identity of toxic reaction products and on the extent to which these products are formed during the heating of foods containing Sucralose to the temperatures that occur during baking, deep-frying and roasting. It is therefore not possible to estimate exposure levels.

Recommendations

In consideration of the systematically evaluated data on this topic and the outcome of a discussion of the data situation by an expert panel, the BfR recommends the following measures:

(1) In the opinion of the BfR, higher priority should be attached to the re-assessment of Sucralose (within the framework of the re-evaluation of approved food additives by the European Food Safety Authority (EFSA) pursuant to Regulation (EC) No. 1333/2008 and Regulation (EU) No. 257/2010) than to the reassessment of other sweeteners.

(2) The BfR recommends that existing data gaps should be closed.

There are data gaps with regard to the identification of reaction products and the extent to which they are formed during relevant production and processing stages. The necessary information should be requested from Sucralose producers during the re-evaluation process, as they are required to prove the safety of the food additive Sucralose as the entities that distribute it in the market.

In order to permit an exposure assessment within the context of a risk assessment, it is necessary to collect representative data on levels in foods containing Sucralose produced in the various ways.

(3) Until a conclusive risk assessment is possible, the BfR advises consumers and food producers not to heat foods containing Sucralose to temperatures reached during baking, deep frying and roasting or only to add Sucralose after the foods have been heated.

3 Reasons

3.1 Potential source of risk (agent)

The following section outlines the toxicological profile of the most important compounds that currently data suggests may be formed when Sucralose is heated in combination with other foods. This information is based above all on assessments of international expert bodies, reviews and earlier publications of the BfR in which the relevant studies are described in more detail and the more in-depth literature listed.

3.1.1 Chloropropanols

These include 3-monochloro-1,2-propandiol (3-MCPD), 1,3-dichloro-2-propanol (1,3-DCP) and 1,2-dichloropropanol (1,2-DCP). The characteristic feature of this group of substances is that they possess a basic structure in which at least one hydroxyl group is replaced by a chlorine atom.

3-monochloro-1,2-propandiol (3-MCPD)

In the case of 3-MCPD, the chlorine atom is in position 3. The substance can occur in unbound form or in the form of fatty acid esters from chloropropanol and one or two fatty acid esters (monoester and diester). A study on bioavailability in rats commissioned by the BfR showed that 3-MCPD fatty acid esters are almost totally hydrolysed and release 3-MCPD during resorption in the intestine (BfR 2012a). The International Agency for Research on Cancer (IARC) has classified 3-MCPD as “possibly carcinogenic to humans (Group 2B)” (IARC 2012a). EFSA assessed 3-MCPD in 2016 and 2017 (EFSA 2016, 2018) and, based on the available toxicological data – in particular from long-term studies following administration of 3-MCPD to laboratory animals – considered the increase in the number of cells (hyperplasia) in the renal tubules as most sensitive endpoint. High doses of 3-MCPD (100 and 400 mg/L drinking water) resulted in benign tumours in the treated animals. There was no evidence of a genotoxic effect, which means it can be assumed that the tumours observed in the animal study only occur above a certain threshold value. These data were used to determine a benchmark dose lower confidence limit 10% ($BMDL_{10}$) of 0.20 mg/kg bodyweight (BW) and day for male rats. Based on this value and using a safety factor of 100, a tolerable daily intake (TDI) of 2 µg/kg BW was derived for 3-MCPD. This derived value confirms the TDI derived by the BfR in 2012 via benchmark dose modelling using a $BMDL_{10}$ of 0.27 mg/kg BW (BfR 2012a; EFSA 2018).

Glycidol

This substance has the same basic glycerol structure as chloropropanols but possesses an epoxide structure. The formation of glycidol is associated with the generation and degradation of 3-MCPD (EFSA 2016). In contrast to 3-MCPD, however, analytical determination of glycidol presents problems, as no suitable methods are currently available to detect this unstable compound (EFSA 2016). It is therefore possible that generation of glycidol is associated with the formation or degradation of 3-MCPD but has not been analytically recorded (EFSA 2016). Glycidol is genotoxic and carcinogenic (BfR 2009; EFSA 2016). IARC has classified glycidol as “probably carcinogenic to humans (Group 2A)” (IARC 2000). The MAK Commission has classified glycidol in Category 3 A (“germ cell mutagenic effect”) (DFG 2015).

1,3-dichloro-2-propanol (1,3-DCP)

1,3-DCP is considered to be non-genotoxic but potentially carcinogenic (NTP 2005; Andres *et al.* 2013). IARC, for example, has classified 1,3-DCP as “possibly carcinogenic to humans (Group 2B)” (IARC 2013). In addition, various toxic effects have been described for this substance *in vitro* and *in vivo*, in particular with regard to its toxicity in the liver as well as the kidneys (JECFA 2002; NTP 2005; BfR 2012a; Andres *et al.* 2013). The liver was identified as target organ for the toxicity of 1,3-DCP. Cytochrome P450 enzymes play a role in the toxification of this substance. In the few available studies with test persons exposed to this substance due to their occupations, liver toxicity effects were seen similar to those observed in animal studies (BfR 2012a). With regard to carcinogenicity, long-term studies on rats showed that moderate and high doses of 1,3-DCP led to increased mortality as well as increased

tumour formation (e.g. in liver, thyroid and tongue) in rats of both sexes, as outlined in the BfR Opinion issued in 2012 (BfR 2012a).

1,2-dichloropropanol (1,2-DCP)

A lack of data means that it is not yet possible to define the risk potential of 1,2-DCP. The only option would be to form assumptions based on structural similarities with other chloropropanols.

3.1.2 PCDD and PCDF congeners and dioxin-like polychlorinated biphenyls (dl-PCBs)

The substance group of dioxins comprises chlorinated dioxins and furans, substances that are similar in chemical terms. All told, the group of dioxins consists of around 200 compounds with varying levels of toxicity. They include 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,3,7,8-tetrachlorodibenzofuran (TCDF) and 2,3,4,7,8-pentachlorodibenzofuran (PeCDF).

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

TCDD has been comprehensively assessed by international expert bodies and institutions (JECFA 2002; Van den Berg *et al.* 2006; EFSA 2010). In 2012, IARC classified this substance as non-genotoxic but a “known human carcinogen (Group 1)” (IARC 2012b). EFSA emphasised that TCDD is one of the most toxic representatives of the substance class of polychlorinated dibenzodioxins (PCDDs) (EFSA 2008, 2010, 2015). The observed effects include, in particular, dermal toxicity, immune, reproduction and developmental toxicity as well carcinogenic effects (EFSA 2008). The Joint FAO/WHO Expert Committee on Food Additives arrived at the conclusion that TCDD and other PCDD congeners have a carcinogenic effect (JECFA 2002). It was found that TCDD promotes the growth and development of tumours *in vitro* and *in vivo* and results in the development of tumours primarily in the liver. Moreover, various effects were described following acute exposure, such as a reduction in body weight (JECFA 2002). The BfR also described the adverse effects of dioxins like TCDD on health in its Opinion of 10 April 2012 (BfR 2012b). It is not yet clear whether effects such as disruption of reproductive functions, immune system, nervous system and hormone levels of the kind observed in animal studies are also relevant to humans. Moreover, it was not possible to conclusively determine whether there is any carcinogenic potential for humans. Persisting inflammatory skin changes (“chloracne”) are a proven effect in humans (with the intake of high concentrations). In addition, there are also indications of liver damage and changes in fat metabolism as outlined in a BfR Opinion published in 2012 (BfR 2012b).

The World Health Organisation (WHO) has used the system of toxicity equivalents (Van den Berg *et al.* 2006) to describe the toxicity of PCDD congeners and that of various PCDF compounds and dioxin-like polychlorinated biphenyls (dl-PCBs). In this process, the toxicity of individual substances is compared with the toxicity of TCDD. In this context, all PCDD, PCDF and dl-PCB congeners were assigned a toxicity equivalency factor (TEF) corresponding to their toxicity relative to the toxicity of TCDD (Van den Berg *et al.* 2006). The concentrations of individual congeners were multiplied by the relevant TEF derived by the WHO and then added, thereby supplying the total dioxin toxicity equivalent concentration (WHO-PCDD/F-TEQ) (Van den Berg *et al.* 2006; BfR 2012b).

2,3,7,8-tetrachlorodibenzofuran (TCDF)

TCDF has a toxicity equivalency factor (TEF) of 0.1 (Van den Berg *et al.* 2006; EFSA 2010) relative to the toxicity of TCDD. No adequate information is currently available on the risk

potential of this substance. However, there are indications that the risk potential of TCDF is comparable to that of TCDD (McNulty 1985).

2,3,4,7,8-pentachlorodibenzofuran (PeCDF)

PeCDF has a TEF of 0.3 (Van den Berg *et al.* 2006; EFSA 2010). In addition, IARC classified PeCDF as non-genotoxic but as a “known human carcinogen (Group 1)” (IARC 2012b). However, no adequate information on the risk potential of PeCDF is currently available.

Dioxin-like polychlorinated biphenyl (dl-PCB) congeners

The substance group of polychlorinated biphenyls (PCBs) comprises 209 substances that differ in terms of the number and position of the chlorine atoms on the biphenyl and that possess different properties (EFSA 2008). Some of the substances in this group are particularly toxic and long-lived, and they accumulate in the body. Twelve substances in this PCB group are similar to TCDD in terms of structural properties and toxicity (EFSA 2010). These substances are called “dioxin-like” PCBs (dl-PCBs) and include 3,3′,4,4′-tetrachlorobiphenyl (PCB 77), 3,4,4′,5-tetrachlorobiphenyl (PCB 81), 3,3′,4,4′,5-pentachlorobiphenyl (PCB 126) and 3,3′,4,4′,5,5′-hexachlorobiphenyl (PCB 169) (EFSA 2010). The toxicity of dl-PCB compounds is also specified using their respective TEF values (JECFA 2002; Van den Berg *et al.* 2006). The TEF of PCB 77 is 0.0001, while the TEFs of PCB 81, PCB 126 and PCB 169 are 0.0003, 0.1 and 0.03, respectively (Van den Berg *et al.* 2006; EFSA 2010).

In its Opinion No. 104/2014 dated 11 March 2014 (BfR 2014), the BfR outlines that the WHO specified a tolerable daily intake (TDI) in the range from 1 - 4 pg WHO-PCDD/F-PCB-TEQ/kg BW and day (WHO 2000). The upper limit (TDI of 4 pg WHO-PCDD/F-PCB-TEQ/kg BW) was understood as being the provisional basis for the maximum tolerable intake. The lower value documented the aim of the WHO to reduce the intake of WHO-PCDD/F-PCB-TEQ in humans to below 1 pg/kg BW. The WHO used the lowest observed adverse effect level (LOAEL) described by various authors for different species and for different endpoints as basis for the TDI range (WHO 2000). In 2001, the former Scientific Committee on Food (SCF) of the European Commission defined a tolerable weekly intake (TWI) of 14 pg WHO-PCDD/F-PCBTEQ/kg BW (SCF 2001). As the basis for derivation of the TWI, the SCF used the LOAEL for reduced sperm production and the changed sexual behaviour of male Wistar rats as described by Faqi and colleagues (Faqi *et al.* 1998). EFSA also referred to this TWI value in its opinions (EFSA 2008, 2012).

3.1.3 Polychlorinated naphthalene (PCN) congeners

This group includes compounds, such as tetrachloronaphthalene (TeCN) and pentachloronaphthalene (PeCN). To date, no sufficient information is available on the risk potential of this class of chlorinated compounds. In terms of "dioxin-like toxicity”, they are considered to be comparable to the most potent PCB congeners (van de Plassche & Schwegler 2002; Fernandes *et al.* 2017). In initial animal studies, medium and long-term exposure led to liver damage (van de Plassche & Schwegler 2002). Human exposure to PCN compounds is possibly associated with the occurrence of chloracne. These substances have not yet been tested for genotoxic and/or carcinogenic potential (van de Plassche & Schwegler 2002).

3.2 Data on the stability of Sucralose

3.2.1 Assessments by national and international expert bodies and institutions

Sucralose has been assessed by various national and international institutions such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the Scientific Committee on Food (SCF) of the EU Commission, the US Food and Drug Administration (FDA), the Hong Kong Special Administrative Region (HKSAR) Food and Environmental Hygiene Department, the Norwegian Scientific Committee for Food Safety (VKM), the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) and the Federal Institute for Consumer Health Protection and Veterinary Medicine (BgVV) (JECFA 1990; BgVV 1994; FDA 1999; SCF 2000; HKSAR 2003; VKM 2014; ANSES 2015). Individual aspects have also already been assessed by the European Food Safety Authority (EFSA) (EFSA 2016; EFSA 2017), but the assessment within the context of the re-evaluation of approved food additives pursuant to Regulation (EC) No. 1333/2008 and Regulation (EU) No. 257/2010 is still outstanding.

Sucralose has been approved as food additive E 955 in the EU since 2004. This approval was based on the assessment by the SCF of the EU Commission in the year 2000. In its Opinion on Sucralose dated 7 September 2000, the SCF followed the arguments of the applicants regarding the high stability of Sucralose – also at high temperatures (SCF 2000).

The studies by Barndt and Jackson and by Miller (Barndt & Jackson 1990; Miller 1991) available to the BgVV up to the year 1994 indicated that Sucralose is stable at higher temperatures (BgVV 1994).

3.2.2 Publications on the chemical stability of Sucralose at high temperatures

Experimental work of Barndt und Jackson (1990)

Barndt and Jackson conducted a study on the stability of Sucralose in baked goods manufactured at high temperatures (Barndt & Jackson 1990). During this study, radioactively ^{14}C-marked Sucralose was produced and then used in the preparation of different baked goods (yellow cake, cookies, graham crackers*)* under the same conditions found in industrial production processes (yellow cake: 180 °C, 25 min; cookies: 210 °C, 8 min; graham crackers: 230 °C, 4 min). The recovery of radioactivity from the product samples was determined by means of liquid scintillation. ^{14}C-marked Sucralose and the hydrolysis products 4-chlorogalactose (4-CG) and 1,6-dichlorofructose (1,6-DCF) were then analysed via thin-layer chromatography (TLC). Analytical standards for 4-CG and 1,6-DCF were produced by the manufacturer in his own analytical department.

The findings of this study showed that ^{14}C-marked Sucralose was still almost completely retained in the samples of the products – yellow cake, cookies and graham crackers – after they had been prepared. The recovery of radioactivity was at a level of between 98.2 and 101.2%. The authors interpreted this as an indication that the ^{14}C-marked Sucralose did not react with any other ingredients in the baked goods (Barndt & Jackson 1990). To confirm this finding, further tests were performed on the samples using TLC. The chromatograms for the yellow cake and graham cracker samples showed the same peaks as the ^{14}C-marked Sucralose. One of the exceptions, however, was the chromatogram for the cookie sample, in which multiple different but closely eluting peaks were detected (Barndt & Jackson 1990). This was interpreted as a result of possible overloading of the TLC plate. The authors concluded that Sucralose is "heat-stable" (Barndt & Jackson 1990).

Experimental work of Miller (1991)

Miller *et al*. studied the stability of Sucralose at a temperature of 100 °C over a period of 1 to 2 hours (h) and at different pH levels (pH 3, 5 and 7) (Miller 1991). "HPLC" technology was named as the employed analytical method (Miller 1991). The outlined findings of this study showed that there was only a 2% loss of Sucralose in aqueous solution after 1 h at 100 °C and with a pH of 3, 5 and 7. Subsequent losses after 2 h were 2% (pH of 5), 3% (pH of 7) and 4% (pH of 3). The authors concluded from these results that Sucralose is stable at high temperatures in conditions that are typical for food processing (Miller 1991).

Reviews of Binns (2003) and Grotz & Munro (2009)

These reviews briefly refer to the studies by Barndt and Jackson (1990) and Miller (1991) (Binns 2003; Grotz & Munro 2009). In the articles, the authors described Sucralose as highly stable, especially at high temperatures of the kind occurring in the manufacturing process for various foods and beverages as well as during the production of medications. However, these findings were determined exclusively in relation to the preservation of the sweetening power of Sucralose under the influence of manufacturing processes such as cooking, baking or pasteurisation

Studies by Hutchinson (1996, 1999)

Analyses conducted by Hutchinson in 1996 indicate that the stability of Sucralose is reduced at higher temperatures between 100 °C and 180 °C , leading to dechlorination and therefore decomposition of the substance and the release of reactive hydrogen chlorides (Hutchinson 1996). In her dissertation, the author described in detail the methods used as well as the properties and composition of the substances and buffer solutions. High performance liquid chromatography (HPLC) was performed to determine Sucralose in the heated samples (Hutchinson 1996). The first step was the characterization of the influence of increased temperatures of 100 °C, 140 °C and 180 °C at different pH levels (3, 7 and 11) on the stability of Sucralose in buffered aqueous solutions during heating for 1 h.

The findings of this study showed that, after 1 h at 100 °C, approximately 77% (at pH 11), 86% (at pH 7) and 96% (at pH 3) of stable Sucralose was still present. Using HPLC for analyses at all pH levels (3 – 11), the amount of remaining Sucralose continued to fall at temperatures above 140 °C, and no Sucralose at all was detectable after 1 h at 180 °C . Hutchinson concluded that the stability of Sucralose falls with rising temperature and rising pH (Hutchinson 1996). Subsequent studies on the stability of Sucralose in the presence of glycine led to similar results. In addition to investigating the stability of Sucralose, the release of chlorides from Sucralose in buffered aqueous solutions when heated for 1 h was also determined this study. Chloride release was assessed using a chloride electrode (Hutchinson 1996). Results of these measurements also showed that release of chlorides from Sucralose in buffered aqueous solutions was increased with rising temperature from 100 °C – 180 °C and rising pH (3 – 11). At about 120 °C, there was a clear increase in chloride release under all tested pH conditions, followed by a further increase between the temperatures of 140 °C and 180 °C (Hutchinson 1996). The determination of chloride release from Sucralose in the presence or absence of glycine, respectively, supplied similar results. All in all, this led to the conclusion that Sucralose is destabilised when heated in buffered aqueous solutions in dependence on pH and an increase in temperature from 100 °C to 180 °C. This is accompanied by the release of chlorides from Sucralose at temperatures from 120 °C to 180 °C (Hutchinson 1996). One reservation noted by the author is that the ions used to buffer the aqueous solutions may have possibly influenced the stability of Sucralose in terms of its hydrolysis.

Building on these results, Hutchinson published a review in 1999 focusing on a comparison of the statements on the stability and/or thermal degradation of Sucralose at high temperatures (Hutchinson *et al*. 1999). In this article the findings of the 1996 study were further discussed in the context of the data situation available at that time. In this work, the author emphasised that Sucralose is unstable and is dechlorinated at high temperatures (100 °C – 180 °C). This effect is reinforced by the rising pH levels (pH 3 – 11) (Hutchinson *et al.* 1999).
In the following years, the findings of Hutchinson on the instability of Sucralose at high temperatures were confirmed in various studies of other research groups (Table 1) (Bannach *et al.* 2009; Rahn & Yaylayan 2010; de Oliveira *et al.* 2015).

Experimental studies by Bannach et al. (2009)

In 2009, Bannach *et al*. used simultaneous thermogravimetry and differential thermoanalysis (TG-DTA) to show that both >98% pure Sucralose and freely available Sucralose were stable up to a temperature of 119 °C (Bannach *et al.* 2009). In contrast, higher temperatures (>119 °C to 550 °C) resulted in thermal decomposition of Sucralose. A first thermal decomposition reaction was observed in both Sucralose samples at around
119 °C – 137 °C. This was accompanied by the release of hydrogen and hydrogen chloride molecules (Bannach *et al.* 2009). Further thermal decomposition events were detected at around 160 °C to 370 °C and at 370 °C to 500 °C. Based on these data, the authors stated that Sucralose is thermally degraded at temperatures >119 °C to 550 °C. In contrast to Barndt and Jackson (Barndt & Jackson 1990), they concluded that Sucralose might be unsuitable for the production of cookies at 210 °C or graham crackers at 230 °C, as thermal degradation of Sucralose takes place at temperature above 119 °C accompanied by the release of hydrogen chloride (Bannach *et al.* 2009).

Experimental studies by de Oliveira et al. (2015)

De Oliveira *et al*. confirmed the findings of Bannach *et al*. (de Oliveira *et al.* 2015). Using various methods that are described in detail in the article, such as differential scanning calorimetry and thermogravimetric analysis coupled with Fourier transform infrared spectroscopy (DSC/TGA-FTIR), hot-stage microscopy (HSM) and high-resolution mass spectrometry (HRMS), the authors showed that Sucralose was thermally decomposed at 125 °C. This was confirmed by subsequent software-supported analysis of the FTIR results on the samples treated at 125 °C. Characteristic profiles were identified for both water and hydrogen chloride. Moreover, the authors used HRMS to detect various chlorinated aromatic by-products in the released gas phase, such as chlorinated furan derivatives. The authors concluded from their data that Sucralose is thermally decomposed under "relatively mild conditions" (125 °C), and this may contribute to the formation of polychlorinated aromatic hydrocarbons (PCAHs) (de Oliveira *et al.* 2015).

3.2.3 Publications on the identification of thermal decomposition products of Sucralose

Experimental work of Rahn and Yaylayan (2010)

The study of Rahn and Yaylayan characterised the degradation of Sucralose during heating (Rahn & Yaylayan 2010). The authors used pyrolysis gas chromatography and mass spectrometric analysis (Py-GC/MS) to show that Sucralose was thermally decomposed and dechlorinated by pyrolysis at 250 °C for 20 s (Rahn & Yaylayan 2010). In their study, they used commercially available Sucralose that can be purchased by the consumer. Glycerine, which is contained – amongst others – in some baking ingredients, and moisture play an important role in baking processes (Rahn & Yaylayan 2010). Therefore, Rahn and Yaylayan

also investigated the influence of the pyrolysis of Sucralose at 250 °C for 20 s in the presence of glycerine and moisture. They used mass spectroscopic analysis to prove the formation of the three chloropropanol compounds 3-MCPD, 1,3-DCP and 1,2-DCP in the released gas phase (Rahn & Yaylayan 2010). These compounds constitute approximately 15% of the total area of all detected peaks and therefore represent the majority of all the generated products. The authors concluded that pyrolysis of Sucralose at 250 °C led to the release of reactive chlorides that can contribute to the formation of chloropropanols in presence of glycerine and moisture. Moreover, they stated that Sucralose should be used with caution as a sweetening agent during baking of foods containing glycerine and/or lipids due to the potential formation of toxic chloropropanols (Rahn & Yaylayan 2010).

Experimental work of Wu et al. (2011)

The findings of Wu *et al*. led to conclusions similar to those of Rahn und Yaylayan (Wu *et al.* 2011). This study investigated the formation of different toxic PCDF and PCDD congeners such as TCDF, PeCDF and TCDD during the heating (roasting) of Sucralose in presence of soybean oil and beef. Temperatures reached 250 °C in the oil and <200 °C in the beef. Each test mixture was heated for 15 min, and the samples were taken for a further 10 min (Wu *et al.* 2011). The authors described that the methods used for analysis of the aforementioned PCDD and PCDF congeners (high-resolution gas chromatography and high-resolution mass spectrometry; HRGC-HRMS) complied with national or international testing guidelines, that recognised standards were used, and that the necessary controls (*US EPA Method 1613, European Method 1948*) were performed. The results of mass spectroscopic analysis showed that various PCDF and PCDD congeners such as TCDF, PeCDF and TCDD were found in the occurring solid/liquid phase and in the gas phase. Under the tested laboratory conditions, they observed an increase in the concentrations of the PCDF and PCDD congeners by a factor of roughly 5 (PCDF congeners) and a factor of 2 (PCDD congeners) in the solid and liquid phase (meat, soybean oil) compared to control mixtures without Sucralose. Furthermore, they observed increases by a factor of 6 to 15 (PCDF congeners) and 4 to 10 (PCDD congeners) in the released gas phase (Wu *et al.* 2011). The authors concluded that the heating (roasting) of Sucralose in the presence of soybean oil and beef at 250 °C led to the formation of various toxic PCDF and PCDD congeners which were transferred from the solid to the gas phase. Moreover, they emphasised that it is important to ensure effective ventilation when cooking with Sucralose in order to reduce the exposure risk of consumers to the occurring volatile PCDFs and PCDDs via inhalation (Wu *et al.* 2011).

Experimental work of Dong et al. (2011)

In a further study of this group in the same year, Dong *et al*. used a similar test set-up to detect the generation of various dl-PCB compounds in the oil vapours released during roasting of beef and soybean oil together with Sucralose at about 160 °C after 25 min (Dong *et al.* 2011). Analysis and detection of the occurring dl-PCB compounds was performed in line with national guidelines and standards by means of gas chromatography and high-resolution mass spectrometry (*US EPA Method 1668 A*) (Dong *et al.* 2011). Mixtures without Sucralose containing beef alone or meat and soybean oil, respectively, were used as controls. Results of these analyses show that twelve dl-PCB congeners were formed under the conditions described above. This was accompanied by an increase in the values for toxicity equivalents (TEQs; calculated using the WHO toxicity equivalency factors (TEFs)) (Dong *et al.* 2011). The authors concluded that, due to thermal decomposition during heating (roasting) to 160 °C in the presence of soybean oil and beef, Sucralose became a source of chloride, which in turn promoted the formation of dl-PCB compounds, which were finally found in the oil vapours. They also hypothesised that an “appropriate” use of chloride-containing additives dur-

ing cooking could therefore help to reduce exposure of consumers to dl-PCBs (Dong *et al.* 2011).

Experimental work of Dong et al. (2013a,b)

In 2013, further experiment studies of this group showed that heating of Sucralose with different vegetable oils led to the formation of different PCN, dl-PCB, PCDD and PCDF congeners (Dong *et al.* 2013b). The formation of these compounds was investigated in the presence of Sucralose and peanut oil or olive oil. For this purpose, 5 g Sucralose and 50 g peanut oil or olive oil were heated for 15 min (and a further 10 min for sample taking) to 245° C in a stainless steel pan. This led to the formation of dl-PCBs and 2,3,7,8-substituted PCDD and PCDF compounds as well as PCN congeners, such as TeCN or PeCN. Methods used for the analysis of the generated chlorinated compounds were performed in line with national guidelines and standards (*US EPA Method 1668 A*) (Dong *et al.* 2013b). Based on their findings, Dong *et al*. concluded that the heating of Sucralose with vegetable oil can potentially lead to the formation of harmful chlorinated aromatic compounds, such as PCN, dl-PCB, PCDF and PCDD congeners. The authors were of the opinion that the use of Sucralose in the preparation of foods at high temperatures (e.g. deep frying) should be avoided in order to reduce potential exposure to toxic compounds (Dong *et al.* 2013b).

In an additional publication by the same research group, the authors describe how the heating of Sucralose on its own in the presence of stainless steel and/or various metal oxides that typically occur in other cooking utensils can also lead to the formation of undesirable, potentially toxic chlorinated compounds (Dong *et al.* 2013a). In this study, 5 g Sucralose (>98% HPLC grade) was heated to 400° C on its own or in the presence of aluminium oxide (Al_2O_3), iron(III) oxide (Fe_2O_3) or copper oxide (CuO). The cooking utensils used in the study were made of stainless steel and other materials (the authors list the materials as quartz, aluminium and copper*)*. In order to investigate the formation of chlorinated compounds in the absence of metal oxides, the authors stated that the metal cooking utensils were polished ("metal utensils were polished and rust was removed before use…"). Samples from the gas phase were then analysed for the formation of polycyclic aromatic hydrocarbon compounds (PAHs) in line with national testing guidelines (based on *Californian Environmental Protection Agency method 429*) by means of gas chromatography and high-resolution mass spectrometry. Characterisation of the PCDD and PCDF congeners that were also formed was based on the *U.S. Environmental Protection Agency method 1613 (US EPA Method 1613)* (Dong *et al.* 2013a). This study showed that heating of 5 g Sucralose to 400 °C in polished cooking utensils ("quartz", "aluminium", "copper") and in the absence of metal oxide, did not lead to the generation of detectable amounts of PCDF or PCDD congeners. The use of stainless steel cooking utensils led to another result: various PCDF and PCDD compounds like TCDF, PeCDF and TCDD were formed (3,1 x 10^4 pg/g) in the presence of Sucralose at 350 °C and 400 °C. Even higher amounts of these PCDF and PCDD congeners were formed (CuO: 4.2 x 10^6 pg/g; Fe_2O_3: 1.2 x 10^6 pg/g; Al_2O_3: 9.7 x 10^4 pg/g) when cooking utensils containing oxidised metals were used (Al_2O_3, Fe_2O_3 or CuO) compared to the use of stainless steel cooking utensils (Dong *et al.* 2013a). Comparative tests showed that the proportion of PCDF congeners formed was higher than the proportion of PCDD compounds in all test mixtures. The authors concluded that heating of Sucralose using cooking utensils made of stainless steel or in the presence of metal oxides in the utensils, respectively, can lead to the formation of significant amounts of PCDF and PCDD compounds at high temperatures. Therefore, the authors suggested that the "inappropriate use" of Sucralose at high temperatures may result in increased exposure to potentially harmful PCDF and PCDD compounds (Dong *et al.* 2013a).

Overview article of Fernandes (2017)

The potential formation of harmful substances during the heating of foods containing Sucralose was addressed in a review by Fernandes and colleagues (Fernandes *et al.* 2017) and interpreted in the same way as by Dong *et al*. (Dong *et al.* 2013b). First, the authors also discuss the fact that Sucralose is degraded at high temperatures and acted as a source of chloride in the context of PCN formation (Fernandes *et al.* 2017). Moreover, they also conclude that heating of Sucralose together with peanut or olive oil free of PCN, can lead to the formation of various PCN congeners as well as PCDD, PCDF and PCB compounds , which were released with the vapours generated during the further course of the process (Fernandes *et al.* 2017).

Overview article of Schiffman et al. (2012-2013)

Three reviews by Schiffman and colleagues focussed on the influence of high temperatures on the stability of Sucralose and the formation of potentially harmful chlorinated compounds (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013). Once again, these articles outlined the discrepancy with regard to the thermal stability of Sucralose, as described in the work of Miller *et al.* and by Barndt and Jackson (Barndt & Jackson 1990; Miller 1991), and addressed and critically discussed this issue with reference to more recent studies by other groups (Hutchinson 1996; Rahn & Yaylayan 2010; de Oliveira *et al.* 2015). First, they discussed the possible misinterpretation of the data on the stability of Sucralose during the preparation of cookies at 210 °C by Barndt und Jackson (Barndt & Jackson 1990). The “closely eluting peaks” in chromatograms of the cookie samples detected by Barndt and Jackson were interpreted by Schiffman and colleagues as thermal decomposition products and therefore as an indication for the instability of Sucralose at high temperatures (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013). The authors also pointed out that the tests showing thermal decomposition of Sucralose were performed in independent laboratories in the USA (Hutchinson 1996), Canada (Rahn & Yaylayan 2010) and Brazil (Bannach *et al.* 2009). Independently of each other, all three studies showed that Sucralose was unstable at high temperatures. Moreover, work has been conducted to investigate the thermal decomposition of Sucralose and the associated release of chlorides as well as their effect on the formation of possibly harmful compounds such as chloropropanols (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013). The articles of Schiffman and colleagues were published as secondary literature (reviews and commentaries). Nevertheless, the findings and interpretations of the authors confirm the findings of the aforementioned original studies on thermal instability of Sucralose and the associated formation of possibly harmful chlorinated compounds (Hutchinson 1996; Bannach *et al.* 2009; Rahn & Yaylayan 2010).

Overview articles of Berry et al. (2016) and Magnuson et al. (2017)

This contrasts with two recently published overview articles on “carcinogenicity” and the “safety of Sucralose” (Table 1) (Berry *et al.* 2016; Magnuson *et al.* 2017). The 2016 publication by Berry emphasised thermal stability (e.g. during baking) with reference to the study by Barndt and Jackson (Barndt & Jackson 1990) as well as the chemical stability of Sucralose (Berry *et al.* 2016). Magnusson and colleagues (Magnuson *et al.* 2017) also underlined the stability of Sucralose. In both articles data or critical literature on the thermal instability and decomposition of Sucralose (Hutchinson *et al.* 1999; Bannach *et al.* 2009; Rahn & Yaylayan 2010) as well as on the formation of possibly harmful compounds (Rahn & Yaylayan 2010; Dong *et al.* 2011; Dong *et al.* 2013a; Dong *et al.* 2013b; de Oliveira *et al.* 2015) were only briefly touched.

3.3 Comparative assessment of the considered literature

3.3.1 Methodology

Comprehensive research was conducted and the relevant literature evaluated to answer the question of whether chlorinated compounds with potential health risks may be formed in the context of industrial processes for the production and processing of foods containing Sucralose and with the use of Sucralose by the consumer when heating foods to temperatures that occur during cooking, baking, deep frying and roasting.

The publications summarised in section 3.2 were comparatively assessed to determine the reliability of the collected data and methods used based on the criteria of Klimisch *et al.* and allocated to one of the four categories explained below (Klimisch *et al*. 1997).

Category 1) “reliable without restriction”; criteria: studies conducted in line with nationally or internationally accepted guidelines (preferably in line with “Good Laboratory Practice” (GLP)) or that were conducted closely in line with these guidelines (in terms of the parameters of the experiments).

Category 2) “reliable with restriction”; criteria: studies that were not fully conducted in line with specific testing guidelines (generally not according to GLP) or that are not fully covered by these guidelines but that are described and documented in “sufficient detail” so that they are transparent and can be accepted from a scientific point of view.

Category 3) “not reliable”; criteria: studies in which there is interference between the measuring apparatus and the test substance or in which unsuitable test systems or methods were used that are inadequately documented or that are not convincing from the point of view of expert assessment.

Category 4) “not assignable”; criteria: studies that do not contain sufficient experimental details and that were only published in the form of abstracts or in secondary literature, such as book contributions or overview articles.

3.3.2 Result of the comparative assessment of the considered literature

The findings of the assessment of the quality and robustness of the considered publications are summarised in Table 1.

Table 1. Publications considered in the Opinion and allocation to one of the four categories based on the criteria of Klimisch et al. (Klimisch et al. 1997).

Publication	Type of publication	Category
A. To prove the chemical stability of Sucralose at high temperatures		
Barndt und Jackson, 1990	Experimental work	3
Miller *et al*., 1991	Experimental work	4
Binns, 2003	Overview article	4
Grotz und Munroe, 2009	Overview article	4
Berry *et al*., 2016	Overview article	4
Magnuson *et al*., 2017	Overview article	4
B. To prove the thermal decomposition of Sucralose		
Hutchinson, 1996	Experimental work	2
Hutchinson, 1999	Overview article	4
Bannach *et al*., 2009	Experimental work	2
Rahn und Yaylayan, 2010	Experimental work	2
Wu *et al*., 2011	Experimental work	2
Dong *et al*., 2011	Experimental work	2
Dong *et al*., 2013	Experimental work	2
Dong *et al*., 2013	Experimental work	2
Schiffman, 2012	Overview article	4
Schiffman und Abou-Donia, 2012	Overview article	4
Schiffman und Rother, 2013	Overview article	4
de Oliveira *et al*., 2015	Experimental work	2
Fernandes *et al*., 2017	Overview article	4

The results outlined in ***Table 1*** show that:

(1) There is no publication in Category 1 (“reliable without restriction”)

(2) The studies designed to confirm the stability of Sucralose are allocated to the categories 3 (“not reliable”) and 4 (“not assignable”)

(3) All studies allocated to Category 2 (“reliable with restriction”) indicate the thermal instability of Sucralose. This can promote the formation of chlorinated toxic compounds, such as chloropropanols and PCDD, PCDF or dl-PCB congeners in the foods that contain Sucralose.

All in all, the available information shows that there are data gaps. One thing that is currently missing for assessment of the potential health risks is representative and robust data on the identity and extent of the creation of reaction products during relevant production and processing routines for foods containing Sucralose.

3.3.2.1 Explanation of the assessment of the considered studies as evidence for the chemical stability of Sucralose

The studies by Barndt and Jackson as well as Miller *et al*. (Barndt & Jackson 1990; Miller 1991)) attempt, in the opinion of the authors, to confirm the thermal stability of Sucralose.

In the opinion of the BfR, however, the study by Barndt and Jackson (1990) is not reliable, in particular as the thin-layer chromatography method used does not possess the same sensitivity as modern analytical methods. Rahn and Yaylayan also consider the findings of Barndt and Jackson to be not reliable (Rahn & Yaylayan 2010). Moreover, Schiffman and colleagues point out in various publications that Barndt and Jackson interpreted their data incorrectly, in particular in relation to the chromatograms of the cookie samples (Schiffman 2012;

Schiffman & Abou-Donia 2012; Schiffman & Rother 2013). They interpret the “closely eluting peaks” detected by Barndt and Jackson as the occurrence of thermal decomposition products in the cookie samples, something that in turn points to the instability of Sucralose in the production of baked goods (such as cookies) (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013).

Some of the data on which the work of Barndt and Jackson is based (such as the chromatograms) is not available to the BfR, and therefore this work cannot be verified. This is a further limitation of the study of Barndt und Jackson (Barndt & Jackson 1990). Beside this the lack of information on methodology and on the substances used (e.g. details of purity) as well as the on experimental conditions are additional critical factors, which makes it difficult to assess the reliability of the findings. Based on the criteria of Klimisch *et al*. (see 3.3.1), the work by Barndt and Jackson was classified as “not reliable” (Category 3; Table 1).

The study by Miller *et al*. was classified in Category 4 (“not assignable, see 3.3.1), as it was published as a book contribution (secondary literature) and because it provides only inadequate methodological information, which cannot be verified regarding their reliability.

Based on the findings of Barndt and Jackson (1990) as well as Miller *et al*. (1991), two review articles by Binns (2003) and Grotz *et al*. (2009) determined the thermal stability of Sucralose (e.g. during baking or in industrial processing routines) with regard to the maintenance of its sweetening power (Binns 2003; Grotz & Munro 2009), but they do not make any reference to possible thermal decomposition.

Two other reviews by Berry in 2016 and Magnuson *et al*. in 2017 emphasised the thermal stability of Sucralose (Berry *et al.* 2016; Magnuson *et al.* 2017). The authors briefly discussed the experimentally validated formation of possibly harmful chlorinated compounds during the heating of Sucralose. However, Berry and Magnuson *et al*. concluded that these experimental results were obtained from quite “artificial” systems that are not of relevance for the “typical use” of Sucralose (e.g. baking) (Berry *et al.* 2016; Magnuson *et al.* 2017). However, neither of the reviews provides any information on an experimental system that would be suitable for investigating the formation of chlorinated compounds in association with the heating of foods containing Sucralose under “relevant” conditions.

The BfR would like to point out that various sources provide recipe ideas that suggest the roasting of meat with Sucralose as one of the ways in which the consumer can use this additive. This closely resembles the experimental conditions employed by, among others, Dong and colleagues (Dong *et al.* 2011; Wu *et al.* 2011; Dong *et al.* 2013b).

The reviews by Binns, Grotz & Munroe, Berry *et al*. and Magnuson *et al*. (Binns 2003; Grotz & Munro 2009; Berry *et al.* 2016; Magnuson *et al.* 2017) emphasising the stability of Sucralose are exclusively published as secondary literature containing to little or no transparent data or methodological information to allow scientific verification of their reliability. Based on the criteria of Klimisch *et al*. (see 3.3.1), this resulted in the classification of these studies in Category 4 as “not assignable”.

3.3.2.2 Explanation of the assessment of the considered studies as evidence that Sucralose is not stable and is dechlorinated at high temperatures

The findings of different, independently conducted studies by different working groups confirm that Sucralose is not stable and is dechlorinated at high temperatures (Hutchinson 1996; Hutchinson *et al.* 1999; Bannach *et al.* 2009; de Oliveira *et al.* 2015). The results obtained from the work of Hutchinson (1996) are based on good evidence and are logically derived through detailed descriptions of the analytical procedures used and the methodological information (e.g. employed substance concentration, purity of substances etc.). One reserva-

tion mentioned by the author herself is that the ions used to buffer the aqueous solutions may possibly have influenced the stability of Sucralose regarding the hydrolysis. Overall, this study was classified as “reliable with restriction” (Category 2) based on the criteria of Klimisch *et al*. (see 3.3.1). In the same way, the experimental investigations of Bannach and colleagues as well as de Oliveira *et al*. (Bannach *et al.* 2009; de Oliveira *et al.* 2015) are also classified in Category 2 “reliable with restriction”. One limitation of the work of de Oliveira and colleagues was the lack of information on the procurement source, as well as on the concentration and purity of the Sucralose used. Moreover, the classification of the studies of Bannach *et al*. and de Oliveira *et al*. in Category 2 was based on the fact that the methods and results of these studies were well documented and outlined in sufficient detail to permit logical comprehension of the relevant processes from a scientific point of view (see 3.3.1).

In contrast to these experimental studies, the overview article of Hutchinson (secondary literature) from 1999 based on her work in 1996 does not contain any transparent methodological information (Hutchinson *et al.* 1999) and was therefore classified as “not assignable” (Category 4) (see 3.3.1).

Building on these studies on the decomposition of Sucralose at high temperatures, multiple independently conducted studies showed that the thermal decomposition of Sucralose (e.g. during cooking) leads to the formation of possibly harmful and, in some cases, carcinogenic chlorinated compounds, such as 3-MCPD, TCDD and TCDF (Rahn & Yaylayan 2010; Dong *et al.* 2011; Wu *et al.* 2011; Dong *et al.* 2013a; Dong *et al.* 2013b; de Oliveira *et al.* 2015). These findings are further supported by publications of Schiffman and colleagues as well as Fernandes *et al*. (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013; Fernandes *et al.* 2017). Studies by Wu *et al*. and Dong and colleagues (Dong *et al.* 2011; Wu *et al.* 2011; Dong *et al.* 2013a; Dong *et al.* 2013b) were classified as “reliable with restriction” (Category 2), as the analytical methods were performed in line with national or international guidelines and standards, and as the methods and results are presented in a largely comprehensible way. However, there were individual limitations in association with the description of the methodological set-up (e.g. in terms of the amounts of the individual ingredients that were used). The work of Rahn & Yaylayan was also classified as “reliable with restriction” (Category 2), as, although the experiments were not performed in line with international testing guidelines, the findings were well documented and presented in a transparent manner from a scientific point of view. A further criticism of this study was that there were no details on purity and concentration of the Sucralose used, and this led to classification in Category 2. As already outlined in the above section, the studies by de Oliveira *et al.* and Bannach *et al*. were also assessed as being “reliable with restriction”

The aforementioned publications (Schiffman 2012; Schiffman & Abou-Donia 2012; Schiffman & Rother 2013; Fernandes *et al.* 2017) were classified in Category 4 (“not assignable”) with regard to their reliability due to the fact that these studies were published as secondary literature and do not contain comprehensible methodological information or data.

3.4 Conclusion

Based on the data currently available, the BfR concludes that, when heated to temperatures encountered in:

- industrial processing of foods containing Sucralose such as baked goods and tinned vegetables

- the use of Sucralose (E 955) by the consumer when baking, deep frying and roasting foods (approx. 120 °C – 250 °C),

Sucralose is dechlorinated and this may lead to the formation of chlorinated organic compounds with possibly harmful potential (e.g. polychlorinated dibenzo-p-dioxins (PCDDs) or dibenzofurans (PCDFs) or chlorpropanols).

However, based on the data currently available, it is not possible to conclusively assess the potential health risks, as there is a lack of data on the identity of toxic reaction products and on the extent to which they are formed during the heating of foods containing Sucralose to temperatures occurring during baking, deep frying and roasting, and it is therefore also not possible to estimate exposure levels.

From the point of view of the respective authors, there are only two experimental studies that support the hypothesis that Sucralose is “thermostable” (Barndt & Jackson 1990; Miller 1991). All the other literature supporting this claim comes in the form of review articles (Binns 2003; Grotz & Munro 2009; Berry *et al.* 2016; Magnuson *et al.* 2017). As a result, these publications cannot be considered in the scientific assessment.

On the other hand, various experimental studies by different and independent research groups showed that Sucralose is not stable at high temperatures (Hutchinson 1996; Bannach *et al.* 2009; de Oliveira *et al.* 2015). This may promote the formation of chlorinated compounds such as chloropropanols and PCDD, PCDF or dl-PCB congeners (Rahn & Yaylayan 2010; Dong *et al.* 2011; Wu *et al.* 2011; Dong *et al.* 2013a; Dong *et al.* 2013b; de Oliveira *et al.* 2015). These findings have been confirmed based on adequate methodological information and mostly robust data, and the corresponding studies were classified as “reliable with restriction” (Table 1).

The questions as to the methodological reliability and validity of the publications on the stability of Sucralose and the creation of potentially harmful chlorinated compounds at high temperatures were also discussed at an expert meeting attended by experts from the European Union Reference Laboratory for halogenated persistent organic pollutants (POPs) in Feed and Food (Freiburg), the National Reference Laboratory for Dioxins and PCBs in Food and Feed (Berlin) and the food monitoring authorities (Sigmaringen Chemical and Veterinary Investigation Office).

All the participants agreed that the currently data prove the instability and potential dechlorination of Sucralose at high temperatures (>120 °C). In addition, the available studies by Rahn and Yaylayan as well as from the working group of Dong *et al*. (Rahn & Yaylayan 2010; Dong *et al.* 2011; Wu *et al.* 2011; Dong *et al.* 2013b) indicate that, during this process, there is the possibility that toxic compounds such as dioxin congeners or chloropropanols may be formed, particularly in the presence of other foods.

However, the experts also concluded that the available studies do not logically and reliably show which compounds are formed in detail. Based on the data currently available, it is in particular not possible to judge the extent to which toxicologically relevant congeners like 2,3,7,8-TCDD are generated. Moreover, it may also be possible that the occurring Maillard reactions not only result in the formation of dioxins but also in the generation of various other potentially toxic compounds such as polychlorinated naphthalenes (PCNs) and other chlorinated hydrocarbon compounds. The experts recommended that the formation of these substances should also be investigated quantitatively and qualitatively in transparent studies. The participants of the expert meeting unanimously concluded that further studies are needed to address these questions. These studies should be performed in line with valid specifications with regard to suitable analytical procedures and methodological approaches (see Regulation (EU) No. 2017/644) in qualified and accredited laboratories.

4 Framework for action, recommendation of measures

Based on the systematically evaluated data on this topic and in consideration of the results of the expert meeting, the BfR recommends the following measures:

(1) Sucralose has been approved as food additive E 955 in the EU since 2004. This approval was based on the assessment by the Scientific Committee on Food (SCF) of the EU Commission in the year 2000. According to Regulation (EC) No. 1333/2008, all food additives approved for use in the EU before 20 January 2009 must be re-evaluated. In the case of sweetening agents, this process should be completed by 31 December 2020 in line with Regulation (EU) No. 257/2010. This time frame may be adjusted, however, if safety concerns are raised with regard to certain additives.

In the opinion of the BfR, the data currently available indicate that heating of Sucralose may lead to the formation of compounds that are harmful to health and in some cases carcinogenic, particularly in interaction with other foods.

The BfR advocates bringing to the attention of the EU Commission the insights into the possible creation of chlorinated compounds in industrially produced foods (e.g. baked goods) as well as during the use of Sucralose by consumers when cooking and baking – so that this aspect in particular can be taken into consideration in the re-evaluation of this sweetener as a food additive. In the opinion of the BfR, higher priority should be attached to the reassessment of Sucralose than to the reassessment of the other sweeteners.

(2) The BfR suggests that the existing data gaps should be closed.

There are data gaps regarding the identification of reaction products and the extent to which they are formed during relevant production and processing stages. The necessary information should be requested from the Sucralose producers during the re-evaluation process, as they are required to prove the safety of the food additive Sucralose as the entities that distribute it in the market.

In order to permit an exposure assessment within the context of a risk assessment, it is necessary to collect representative data on levels of chlorinated compounds in foods containing Sucralose produced in the various ways.

(3) Until a conclusive risk assessment is possible, the BfR advises consumers and food not to heat foods containing Sucralose to temperatures reached during baking, deep frying and roasting or only to add Sucralose after the foods have been heated.

More information on the BfR website

Initial evaluation of the assessment of levels of glycidol fatty acid esters detected in refined vegetable fats. **BfR Opinion Nr. 007/2009 of 10 March 2009:** https://www.bfr.bund.de/cm/349/initial_evaluation_of_the_assessment_of_levels_of_glycidol_fatty_acid_esters.pdf .

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