Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on a request from the Commission related to the use of

Epoxidised soybean oil in food contact materials

(Question N° EFSA-Q-2003-073)

adopted on 26 May 2004 by written procedure

SUMMARY

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) has been asked to evaluate the results of the studies available on the migration of epoxidised soybean oil (ESBO) and ESBO-derivatives from containers of baby foods and to give an opinion on the risk for infants and, as regards the ESBO-derivatives, for the consumer in general. ESBO is used as a plasticiser and stabiliser in polyvinyl chloride (PVC) gaskets of metal lids used to seal glass jars and bottles. The gasket forms an airtight seal preventing microbiological and other contaminations. This type of packaging is common for baby foods packed in glass jars and bottles.

The evaluation was conducted in the context of the current uses of ESBO in food packaging, with an emphasis on assessment of migration into baby foods that might result in intakes of ESBO close to or exceeding the Tolerable Daily Intake (TDI) of 1 mg/kg body weight. In addition, the evaluation considered the formation of derivatives of ESBO such as chlorohydrins, which may occur as the PVC is heated to high temperatures.

The TDI of 1 mg/kg body weight is based on a no-effect level of 140 mg/kg body weight/day for organ weight changes observed in a 2-year rat study. The estimated exposure of infants aged 6-12 months to ESBO migrating into baby foods packaged in glass jars and bottles with metal lids sealed with PVC gaskets can sometimes exceed the TDI by up to 4- to 5-fold. Since there is an inbuilt safety factor of more than 100 in the derivation of the TDI, exceeding the TDI by 4- to 5-fold does not imply that there will be adverse health effects in infants. Moreover, the Panel notes that ESBO is neither carcinogenic nor genotoxic. However, such a situation is undesirable because it could reduce on a regular basis the safety margin between exposure and adverse effects.

It is therefore recommended to develop a specific migration limit for ESBO in baby foods, derived from the TDI of 1 mg/kg body weight and taking into consideration the amounts which might be eaten on a daily basis by an infant of 6 months of age, weighing 7.5 kg, fed mainly or exclusively on processed baby foods.

In the absence of adequate toxicological data on ESBO derivatives, no advice can yet be given on the significance for health of such derivatives in foods. The Panel notes that up to

5% of the fatty acids in ESBO in gaskets is converted into derivatives. These derivatives are expected to migrate at the same rate as ESBO and so their concentration in food could achieve about 5% that observed for ESBO itself.

Further analytical and toxicological data on ESBO derivatives are needed and a programme should be established to that end.

KEY WORDS
Epoxidised soybean oil, ESBO, PVC, baby foods, gaskets, chloro derivatives

BACKGROUND

Epoxidised soybean oil (ESBO) is used as a plasticiser as well as a stabiliser for plastics polymers such as polyvinyl chloride (PVC). It is used in particular in closure gaskets for the metal lids used to seal glass jars and bottles, forming the airtight seal needed to prevent microbiological contamination of baby foods, where it can be employed at up to 40% of the formulation weight of the gasket. There is thus a potential for migration into the food both during sterilisation and storage. Previous national and EU surveys have shown fairly high levels of ESBO in foods, in which about 4% were above the current overall migration limit for plastics of 60 mg/kg and about 15% of the samples were above 30 mg ESBO/kg food. The highest level found was 135 mg/kg. High migration levels might lead to an intake that exceeds the existing Tolerable Daily Intake of 1mg/kg bw/day.

In addition, the main pathway of PVC degradation involves the elimination of HCl which can react with ESBO, leading to the formation of chlorohydrins. Thus such compounds may be present in quantifiable amounts in baby foods and other foods and may be of toxicological concern. Finally, it has been noticed that, confirming previous work, cyclic compounds are also formed and that mass balance of disappearing substances versus appearing substances is not preserved, suggesting that some reaction products are not currently known and accounted for.

TERMS OF REFERENCE

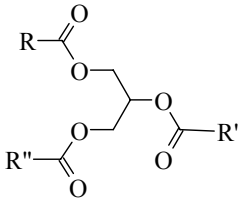
The Commission asks the European Food Safety Authority (EFSA) to evaluate the results of the studies available on the migration of ESBO and ESBO-derivatives from food containers into foods and to issue an opinion on the risk of dietary exposure to ESBO and ESBO-derivatives for the consumer with particular attention to infants.

ASSESSMENT

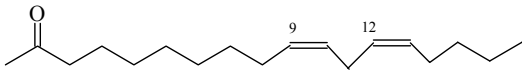
Chemistry

ESBO is a modified oil resulting from an epoxidation reaction of soybean oil. Soybean oil consists of a mixture of triglycerides whose average composition in predominant fatty acids is about 11% palmitic (16:0), 4% stearic (18:0), 23% oleic (18:1), 55% linoleic (18:2), and 8% linolenic (18:3).

ESBO is a clear pale yellow viscous liquid of low odour, with a melting point of circa –4°C. Its CAS Registry Number is CAS 8013-07-8 EINECS/ELINCS 232-391-0 (Ash and Ash, 1999). The plastics Directive (72/2002/EC) imposes for ESBO a specification for oxirane <8% and iodine number <6 for food contact use in plastics. Its structural formula can be represented as shown in figure 1:



Soybean oil:
R and/or R' and/or R" (represented with linoleic acid, 18:2) =



ESBO:
R and/or R' and/or R" (represented with epoxidised linoleic acid, 18:2) =

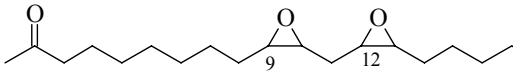


Figure 1: general structure of ESBO

ESBO is one of the most used additives for PVC, especially food-contact PVC where it can be present up to 40%, and particularly for sealing closures. It is also used in the range of 10% in PVC stretch films. It can also be mixed with PVC based lacquers that coat metal cans. There is only limited information on the presence of naturally-occurring epoxy-triglycerides in foods or edible oils. Monoepoxy fatty acids do seem to be rather widespread in foods, up to around 200 mg/kg in some foods and higher in edible oils. For this reason, the migration of ESBO is monitored and measured using the diepoxy fatty acid component depicted in Figure 1 (Castle et al., 1988a).

The formation of reaction products such as chlorohydrins from ESBO in PVC comes from the release of HCl from the PVC at high temperature and the reactions of this HCl with an epoxy group of ESBO. The major chlorohydrins formed are a function of the nature of the unsaturated triglycerides present in soybean oil which have been epoxidised (i.e. mainly from 18:1, 18:2 and 18:3), and are thus of three main types, as shown in Figure 2 (shown as fatty acid methyl esters, isomers not considered).

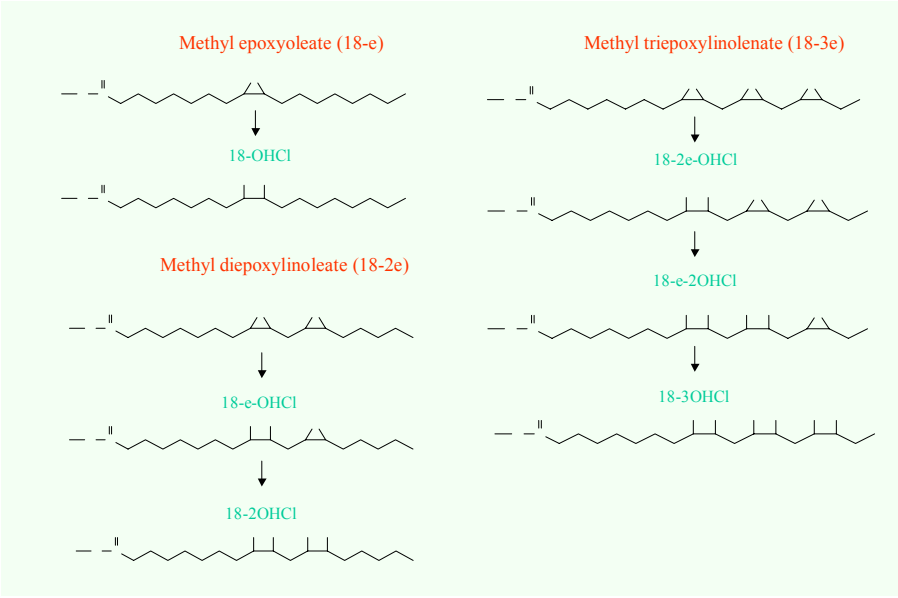


Figure 2: Potential chlorohydrins formed (isomers not shown, for the main unsaturated triglycerides)

Manufacturing process

Preparation of ESBO

The preparation of ESBO is performed by epoxidation, i.e. the reaction of a compound containing a -C=C- (carbon-carbon double bond) with an active oxygen compound, usually a peroxide or a peracid, to add an atom of oxygen and convert the -C=C- bond to the three-membered epoxide or oxirane ring group (Figure 3).

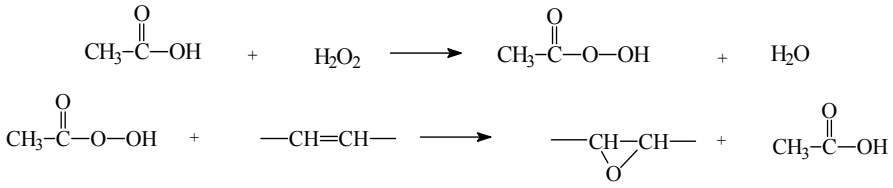


Figure 3: generic reaction of epoxidation

Preparation of food contact materials

Metal closures (e.g. Push-on Twist-off) incorporate a ring-shaped gasket formed from a bead of liquid plastisol containing up to 40% ESBO which is moulded into the correct profile in the closure shell using a hot punch, then fused (gelled) by passing through an oven at 200 °C for 90 seconds. At these temperatures, PVC starts to break down and releases hydrogen chloride (HCl). ESBO is added as a stabiliser to scavenge this HCl to prevent the autocatalytic breakdown of the polymer. It also functions as a plasticiser.

PVC stretch film formulations typically contain up to 30% plasticisers of which about 10% may be ESBO. The formulation is blended together in a dry blend mixer at about 120 °C and extruded at 200 °C to form a fully gelled PVC bubble that can be collapsed and further processed into rolls of film.

Some coatings such as those for some types of deep drawn cans and easy open lids contain PVC plastisols which are processed at high curing temperature (200°C or above).

Methods of analysis in foods

The methodology used for the determination of ESBO has been reported (Castle et al., 1988a; Castle et al, 1988b) and extensively used in previous studies (Castle et al., 1990; Castle et al., 1994; Hammarling et al., 1998; Anon., 1999, Fantoni and Simoneau, 2003). It consists of a gas-chromatographic mass spectrometric (GC-MS) method after derivatisation to provide stability of the compounds, and optimise shift in characteristic MS fragmentation ions. The limit of detection (LOD) is ca. 1-2 mg/kg and the limit of quantification (LOQ) typically 7 mg/kg (with LOD = three times baseline noise and LOQ = 3 times the LOD). The variability remains around 5%.

The quantitative analysis of ESBO derivatives in foods presents great difficulties owing to matrices that are complex, varied in composition and contain fat, leading to interferences. It is also complex due to low levels of chlorohydrins that can be at the detection limit. Most work studying the occurrence of such compounds has focused on model systems or PVC (Gilbert and Startin, 1980a; 1980b; Sheperd and Gilbert, 1981; Biedermann-Brem et al., 2001; Biedermann-Brem et al., 2003) rather than analysis in foods, which has been considered a too complex matrix. Analyses in foods require an extraction of the fat from the matrix, a transesterification step to form fatty acid methyl esters (FAME) and a further derivatisation (acetylation or silylation) to allow adequate GC analysis. An internal standard is required, the conditions of transesterification and derivatisation must be specifically optimised to ensure complete methylation of the triglycerides without significant loss of chlorohydrins, and a clean up step is necessary to increase the sensitivity of the method by removing the fatty acids originating from the fat present in food (Valzacchi et al., 2003). The analysis can then be carried out by GC-MS (e.g. with positive chemical ionisation and single ion monitoring). The quantification considers the sum of peaks in the region of the mixture of C18-2OHCl[1] and

[1] C18-2OHCl: dichlorohydrin from diepoxylinoleate, as shown in figure 2

cyclic compounds originating from the diepoxide (C18-2E)[2] and assuming a similar response factor for C18-E-OHCl[3]. The method in foods was tested for matrix interference on a number of baby foods (e.g. fruit, vegetables, cheese and meat) (Piccinini et al., 2004).

Reaction and fate in foods, stability

The presence of chlorohydrins from ESBO has been extensively reported and shown to occur in model systems and foods (Gilbert and Startin, 1980a, 1980b; Sheperd and Gilbert 1981; Biedermann-Brem et al., 2001, 2003, Piccinini et al., 2004). The presence of cyclic compounds formed from ESBO due to a specific reactivity of α-diepoxides leading to formation of 5 or 6 membered rings, most likely facilitated by acid catalysis, is illustrated in Figure 4. These have also been reported in foodstuffs (Biedermann et al., 2001) and likely structures are shown in Table 1 in their trimethylsilyl [TMS] derivatised form (Valzacchi et al., 2003). A number of studies have also noted that the extent of loss of epoxide is not all accounted for in conversion products including cyclics that can be identified /quantified. The substances detected as transformation products only account for about half of the lost epoxides in PVC (Gilbert and Startin, 1980a, 1980b; Sheperd and Gilbert 1981; Biedermann-Brem et al., 2001). In addition, it is relatively unknown to what extent other products could be formed from reaction of ESBO and food components (Juangvanich and Stoffer, 2002).

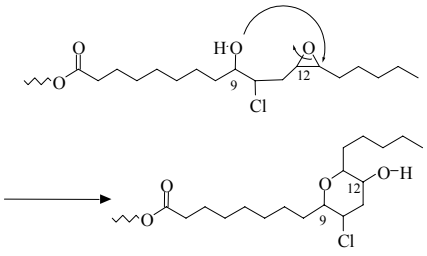


Figure 4: formation of cyclic structures due to specific reactivity of α-diepoxides

Type of chlorohydrin	Likely cyclic compound elucidated

[2] C18-2E: diepoxylinoleate, as shown in figure 2
[3] C18-E-OHCl: epoxymonochlorohyrin from diepoxylinoleate, as shown in figure 2

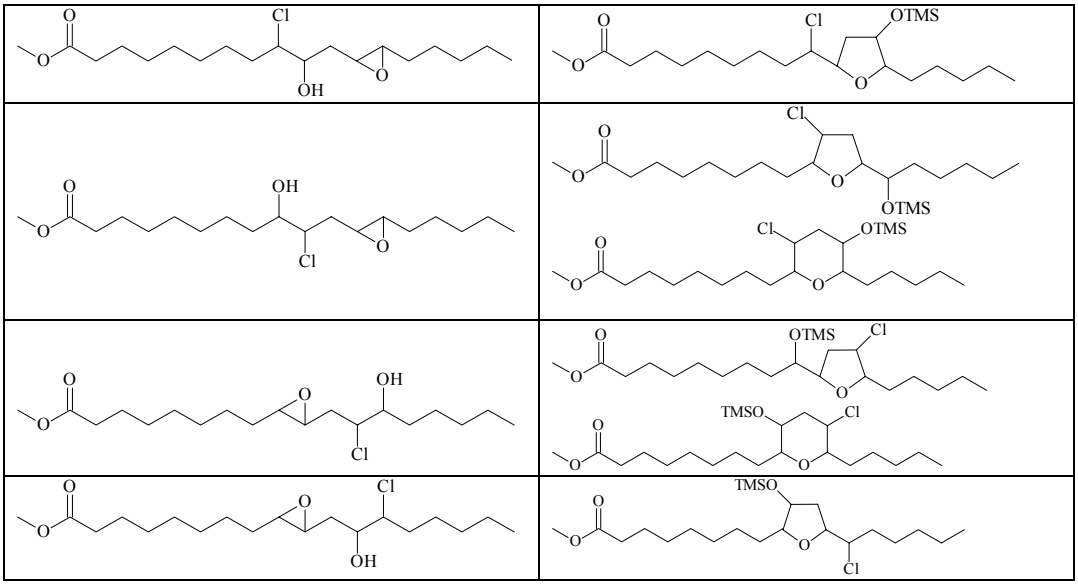


Table 1: structures of cyclic compounds potentially present (shown as TMS derivatives)

Exposure

The emphasis is placed in this part on exposure of infants to ESBO and derivatives from baby foods, which is justified considering the higher levels found in such foods, the potential frequency of intake of such foods, and the smaller bodyweights of infants.

Migration/contamination values – emphasis on commercial infant foods

ESBO in the diet

Three large surveys have been conducted on the presence of ESBO in baby foods between 1997 and 2002 (Hammarling et al., 1998; Anon. MAFF, 1999; Fantoni and Simoneau, 2003). Their results, based on analysis of derivatised diepoxy derivative in commercial infant food matrices, are summarised in Table 2.

Parameters	JRC study	MAFF survey	Swedish survey
Year purchase of samples	2000-2001	1998-99	1996
Number of samples in survey	248	137	81
Maximum concentration found (mg/kg)	135	105	51
Percentage of samples above 60 mg/kg (%)	4	6	0
Percentage of samples 30- 60 mg/kg (%)	11	8	7.5
Percentage of samples above 30 mg/kg (%)	15	14	7.5
Upper bound average overall contamination (mg/kg)[4]	15.3	13.8	12.8
Lower bound average overall contamination (mg/kg)[5]	13.1	12.0	10.6

Table 2: summary of all tabulated data from the various surveys

Although the studies were conducted at different time periods, geographical locations, sample types and sampling sizes, the results are remarkably similar especially between the MAFF and JRC studies, which allows a refined exposure assessment. The overall results suggest that the level of contamination is significant and indicate a lack of improvement over time. Thus the presence of ESBO in samples in amounts exceeding the overall migration limit for plastics, and the possibility of intakes exceeding the TDI by a significant margin in infants, is of concern.

ESBO derivatives in the diet

There is still a lack of data and correspondingly large uncertainty on concentrations of ESBO derivatives in foodstuffs, both for averages and extremes. Estimations have been approached by migration experiments, extrapolations from model systems and direct measurements in foods.

Migration experiments from early work based on PVC material containing 3% of a model compound (epoxidised glyceryl trioleate, figure 1, R=R'=R"=18:1) for 10 days at 40°C on a number of simulants and foodstuffs showed detectable epoxy and chlorohydrins (Sheperd and Gilbert, 1981).

Recent studies extrapolated the amounts to be expected in foods starting from an estimated 5 % ESBO derivatives in the gasket, based on measurements in model systems using 1,2-

[4] upper bound average: results that are less than the LOQ are taken as being equal to the LOQ, and 'not detected' results are treated as being equal to the LOD

[5] lower bound average: results that are less than the LOQ are taken as being equal to the LOD, and 'not detected' results are treated as being equal to zero.

epoxy-octane and 1,2-3,4-diepoxy-pentane –simulating linoleic acid- as models (Biedermann-Brem et al., 2003). It was assumed that reacted ESBO (i.e. chloro-derivatives) would migrate to a similar extent as ESBO itself since the derivatised epoxy fatty acids are attached to the same glycerol moiety as the underivatised ones. If, for example, 50 mg/kg ESBO migrates into food, then 2.5 mg/kg of ESBO chloro-derivatives (measured as derivatised fatty acids) would be expected.

There are only a few results of direct measurements of ESBO derivatives in foodstuffs due to the difficulties in developing an analytical method for complex matrices. The limited results and low levels found so far (Piccinini et al., 2004) are thus only indicative. Results have shown levels in the range of 0.02-0.1mg/kg (all measurable reaction products from ESBO).

Results from recent studies have suggested that the epoxy oleic acid was largely converted to chlorohydrins whereas diepoxy linoleic acid was primarily converted to chlorinated cyclic compounds. In addition, it is generally accepted that up to 50% of the lost epoxides do not appear as detectable transformation products.

Food intake[6]

Human exposure is likely to occur over a lifetime, resulting from the consumption of a wide range of food products in jars/bottles, cans and PVC films, including for jars: baby foods, fruit juices, sauces, mustard, mayonnaise, ketchup, cheese, meat and others. A significant variation in exposure is expected according to life stage, with the highest intakes on a body weight basis likely to occur within the first year of life, due to the progressive introduction of dietary solids from 4 months on, including commercial infant foods. Intake data for relevant manufactured baby food products were reviewed from data available in literature. Data from Germany (Kersting et al., 1998), France (Even et al., 2001) and UK (Mills and Tyler, MAFF, 1992) are presented (table 3). In the EFSA assessment of semicarbazide intake (EFSA, 2003), a conservative value of 700 g of processed baby foods was assumed for a 6-month baby weighing 7.5 kg.

[6] In this evaluation, infants and young children are defined according to Directive 96/5/EC: “infants shall mean children under the age of twelve months [and] young children shall mean children aged between 1 and 3 years”.

Study reference and country of origin	MAFF (UK)		DONALD (D)			AFSSA (F)	
Age group (months)	6-9	9-12	6	9	12	4-6	7-12
Average intake (g/infant/day)	148 [a]	134 [a]	195	234	208	186	212
95th percentile (g/infant/day)	375 [b]		407	464	424	-	-
Body weight (kg)	8.8		7.8	8.8	9.8	6.56	8.77
Ratio (average/bw)	17	15	25	27	21	28	24
Ratio (95th /bw)	43		52	53	43	-	-

Table 3: summary of food intake data and weight evaluations.
[a: mean for "consumers"; b: 97,5th percentile, for "consumers"]

Beyond the first year, studies in France and UK have indicated that the contribution of baby foods in jars and bottles to the total diet decreases significantly. Regarding adults, the quantity of available data on target foods is very limited, but it is expected that the contribution of food in jars and bottles to the total diet of adults is likely to be much smaller than in the diet of infants.

Exposure estimates

In terms of exposure of infants to ESBO itself from commercial infant foods, contamination values are extensively known from data of the two most recent surveys and food intakes are available from a number of food consumption studies. As the highest ESBO residue levels have been found in baby foods in jars and infants consume significantly more food than adults on a body-weight basis, this exposure is the most critical. If a concentration of 50 mg of ESBO/kg baby foods is assumed, the TDI of 1 mg/kg bw is exceeded in all cases, even considering an average food intake value (table 4). In addition, if the worst case food intake scenario is taken (exclusive commercial infant food feeding), then the TDI is also exceeded even for average ESBO concentrations (both upper and lower bound).

Adult exposures to ESBO are likely to be much lower than infant exposures, both due to the lower contribution of target foods particularly in jars to the total diet of adults and the generally lower levels of ESBO in closures used in packaging of adult food. Their main intake is likely to result from PVC cling films. Considering a scenario of a 60 kg adult consuming 1 kg/day of foods contaminated with ESBO at a level of 12 mg/kg, the exposure remains well below the TDI. Even if contaminated with ESBO at a level of 60 mg/kg, the intake of ESBO does not exceed the TDI for a 60 kg adult.

In terms of derivatives from ESBO (e.g. chlorohydrins, cyclic compounds), it is difficult to provide an adequate exposure assessment from baby foods due to the uncertainties in measurements (data points insufficient) or in estimation (number of assumptions). Assuming 2.5 mg of derivatives /kg food, as extrapolated from the model system studies, and assuming an exclusive intake of commercial infant foods corresponding to 680 g food (i.e. 2 meals, each with a main dish of 220 g and a dessert of 120 g of commercial infant food) and an average 8.5 kg circa 9-month infant, would lead to an exposure of 0.2 mg ESBO derivatives/kg bodyweight. Similarly, this exposure value can also be reached considering a 6-month old infant of about 7.5 kg with a 600 g commercial infant food intake.

The overall summary of estimations are reported in table 4, where the food intake factor is based on estimates for 95th or 97.5th percentile food intake, and for infant bodyweights.
The exposure is calculated as:

$$\text{Exposure}\frac{[\text{mg ESBO}]}{[\text{kg bw/day}]} = \text{food intake (g food/kg bw/day) x concentration (mg ESBO/kg food) x } \frac{1}{1000}\ \frac{[\text{kg food}]}{[\text{g food}]}$$

Note: bw = bodyweight; 1/1000: conversion of food weight unit, g to kg

Food intake/kg body weight (g food/kg bw/day)	ESBO concentrations (mg ESBO/kg food)	ESBO exposure (mg ESBO/kg bw/day)	ESBO derivatives concentrations (mg derivatives/kg food)	ESBO derivatives exposure (mg/kg bw/day)
A	B	= A*B*1/1000 *(see above)*	D	=A*D*1/1000 *(see above)*
93[a]	50.0[e]	**4.65**	2.50[h]	0.233
53[b]	50.0[e]	**2.65**	2.50[h]	0.133
43[c]	50.0[e]	**2.15**	2.50[h]	0.108
28[d]	50.0[e]	**1.40**	2.50[h]	0.070
93[a]	15.3[f]	**1.42**	0.50[i]	0.047
53[b]	15.3[f]	0.81	0.50[i]	0.027
43[c]	15.3[f]	0.66	0.50[i]	0.022
28[d]	15.3[f]	0.43	0.50[i]	0.014
93[a]	12.0[g]	**1.12**	0.10[j]	0.009
53[b]	12.0[g]	0.64	0.10[j]	0.005
43[c]	12.0[g]	0.52	0.10[j]	0.004
28[d]	12.0[g]	0.34	0.10[j]	0.003

a: worst case intake estimate from EFSA statement on semicarbazide (EFSA, 2003); b: 95th percentile from consumers in German study; c: 95th and 97.5th percentile from German and UK studies; d: highest average from French study; e: assumed value for ESBO migration; f: ESBO upper bound average; g: ESBO lower bound average; h: estimates from theoretical calculations; i: estimates from measurements in gaskets; j: estimated upper bound average from measurements in food.

Table 4: infant exposures for various scenarios

Existing authorisations and evaluations

The EC Scientific Committee for Food (SCF) established a TDI of 1 mg/kg body weight (SCF, 1999), resulting in a maximum tolerated migration corresponding to the overall migration limit of 60 mg/kg of food, based on a 60 kg adult. On this basis, the use of ESBO as

an additive is currently authorised without a specific migration limit (SML) in foods. For plastics, they are on the positive list (Directive 90/128/EEC) and for coatings in the resolution AP96/5 of the Council of Europe.

Biological and toxicological data

The toxicity data on ESBO are as follows[7]:

- ESBO samples with different specifications (oxygen content and iodine number) show mild skin and eye irritating properties in rabbits, and do not induce sensitization in guinea pigs.
- ESBO has very low acute toxicity in rats (LD_{50}>5 g/kg bw).
- Repeated exposure studies show slight changes in uterus, liver and kidney weight, and no alteration of blood parameters, in rats fed with diet containing up to 5% ESBO (approx 2.5 g/kg bw/day) for 2 years. The No Observed Adverse Effect Level (NOAEL) was approximately 140 mg/kg bw/day and the Lowest Observed Adverse Effect Level (LOAEL) was approximately 1400 mg/kg bw/day. This figure was used by the UK Committee on Toxicity to derive, using an uncertainty factor of 100, a TDI of 1 mg/kg bw (DoH, 1995). The same TDI was adopted by the SCF in 1995-96.
- No effect on fertility or offspring development was observed in rats treated with up to 1 g ESBO/kg bw/day by gavage before and after mating. No statistically significant increase in skeletal abnormalities was observed when treatments were given on days 6-15 of pregnancy.
- No evidence of carcinogenicity was seen in rats fed with 2.5 % ESBO in the diet for two years.
- No evidence of genotoxicity was obtained in the Ames/Salmonella test, in the forward mutation assay in mouse lymphoma L5178Y cells, or in a chromosomal aberration assay in human lymphocytes, all carried out with and without exogenous metabolic activation.

Toxicity data on chloro derivatives of ESBO are scanty. Mutagenicity tests in bacteria and in cultured mammalian cells with the reaction product of ESBO and HCl were mainly negative (Monsanto, 1986; 1987). However, it is unclear how representative were the reaction conditions applied in these studies (excess HCl at room temperature), compared to the chlorination conditions during PVC curing (lower HCl content and high temperature).

[7] Sources: BIBRA, 1997; SCF, 1999

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The TDI of 1 mg/kg bw previously established by the SCF for ESBO (SCF, 1999) remains valid in view of the negative results provided by genotoxicity assays, not available to SCF at the time of its evaluation (1995-1996). It is noted that ESBO is neither carcinogenic nor genotoxic.

Measurements of ESBO in foods in the EU have focused on baby foods. In recent surveys, analyses of ESBO, on the basis of diepoxy fatty acids, revealed a small percentage of baby food samples with ESBO concentrations above the overall migration limit of 60 mg/kg of food. The highest concentration of ESBO found in baby food was 135 mg/kg of food.

Human exposure to ESBO via the diet varies significantly according to life-stage. The highest exposures occur in infants consuming baby foods packaged in glass jars and bottles, with a peak between 6 and 12 months of age. From 12 months of age onwards, exposure to ESBO is expected to decrease significantly.
Exposure to ESBO can be estimated as follows:

- Infants (6-12 months of age): using reasonable worst case scenarios of food contamination (i.e. 50 mg ESBO/kg food), and a range of food intake estimates from average to 97.5th percentile, the TDI can be exceeded by up to 4- to 5-fold
- Adults: the contribution of food in jars and bottles to the total diet is likely to be small and exposure to ESBO on a bodyweight basis will be lower than for infants. The main intake for adults is likely to originate from PVC cling films. Estimates indicate that intakes are unlikely to exceed the TDI.

ESBO has been found to generate chlorohydrins and chlorinated cyclic derivatives during processing of PVC-containing materials. Not all the derivatives of ESBO are yet fully identified. All these compounds may migrate into foods. However, a quantitative analysis of the ESBO derivatives is still severely hampered by lack of good data. Furthermore the available data do not allow an evaluation of the toxicity of ESBO derivatives.

Human exposure to ESBO derivatives is expected to follow the same pattern as exposure to ESBO, peaking at between 6 and 12 months of age and decreasing significantly afterwards.
There are large uncertainties in the assessment of exposure to ESBO derivatives but indicative estimates are as follows:

- Infants (6-12 months of age): using the same reasonable worst case scenarios as for ESBO and assuming 2.5 mg of derivatives/kg food are formed, highest exposures are expected to be in the range 0.02-0.2 mg/kg bw.
- Adults: exposures to ESBO derivatives will be lower than those of infants on a bodyweight basis.

Recommendations

In some scenarios, the estimated exposure of infants aged 6-12 months to ESBO migrating into baby foods packaged in glass jars and bottles with metal lids sealed with PVC gaskets may exceed the TDI by up to 4- to 5-fold. Since there is an inbuilt safety factor of more than 100 in the derivation of the TDI (and noting that the numerical value of the TDI is more than 1000-fold lower than that causing effects in rats), exceeding the TDI 4- to 5-fold does not imply that there will be adverse health effects in infants. However, such a situation does reduce the safety margin between exposure and adverse effects on a regular basis.

It is therefore recommended that a specific migration limit for ESBO in baby foods be developed, derived from the TDI of 1 mg/kg body weight and taking into consideration the amounts which might be eaten on a daily basis by an infant of 6 months of age, weighing 7.5 kg, fed mainly or exclusively on processed baby foods.

In the absence of adequate analytical and toxicological data on ESBO derivatives, no advice can yet be given on the significance for health of such derivatives in foods. The Panel notes that experimental data on fatty acid model systems indicated that an estimated 5% of ESBO fatty acids in gaskets is converted into chloro-derivatives. These chloro-derivatives are expected to migrate at the same rate as the non-reacted ESBO itself, also measured as derivatised fatty acids.

Further analytical and toxicological data on derivatives are needed and a programme should be established to that end.

DOCUMENTATION PROVIDED TO EFSA

1. Informative note on the contamination of baby food from ESBO and ESBO derivatives (attached to the terms of reference)
2. Analysis of reaction products of ESBO in PVC and coatings (EMB/751) (electronic format)
3. Letter from SCF Secretariat (Granero) to CEFIC (31.10.2000) (EMB/777) (electronic format)
4. Letter from SANCO (Rossi) to CEFIC (17.08.2001) (EMB/777add1) (electronic format)
5. Comments of industry on ESBO and ESBO chlorohydrins (19.12.2001) (EMB/847) (electronic format)
6. Determination of chlorohydrins formed from ESBO in PVC gaskets etc. (Valzacchi et al) (EMB/932) electronic format)
7. European survey of contamination of homogenised baby food by ESBO migration from plasticized PVC gaskets) (EMB/989) (electronic format)

REFERENCES

Anon., 1999, Survey of epoxidised soya bean oil (ESBO) migration from plasticised gaskets. Joint Food Safety and Standard Group, Ministry of Agriculture, Fisheries and Food, *Food Surveillance,* sep 1999, Information sheet No. 186. http://archive.food.gov.uk/maff/archive/food/infsheet/1999/no186/186esbo.htm#ref8

Ash, M. and Ash, I., 1999, Epoxidized soyabean oil, In: *Handbook of food packaging chemicals and materials*, Synapse Information Resources, (430)

Baltacioğlu, H and Balköse, D, 1999, Effect of zinc stearate and/or epoxidized soybean oil on gelation and thermal stability of PVC-DOP plastigels., *J. of applied polymer science*, **74**, 2488-2498.

BIBRA, 1997. The British Industrial Biological Research Association (BIBRA): Toxicity profile: epoxidised soy bean oil. Carlshalton, Surrey, UK.

Biedermann, M. and Grob, K, 1998, Food contamination from epoxy resins and organosols used as can coatings; analysis by gradient NPLC. *Food Add. Cont.* **15**, 609-618.

Biedermann-Brem, S, Grob, K. and Biedermann, M., 2001, Analysis of reaction products (e.g. chlorohydrins) of ESBO in poly(vinyl chloride) type polymers and coatings. *Mitt. Lebensm. Hyg.* **92**, 515-534 (2001).

Biedermann-Brem, S., Biedermann, M. and Grob, K., 2003, Reaction of Epoxidized Soya Bean Oil (ESBO) with Hydrogen Chloride formed in PVC: Investigation on Model Systems, *Mitt. Lebensm. Hyg, in print*

Bush, J., Gilbert, J. and Goenaga, X., 1993, In: Spectra for identification of monomers in food packaging, *Kluwer Academic Publishers*, 375-376.

Castle, L., Jickells, S.M, Nichol, J., Johns, S.M. and Gramshaw, J.W., 1994, Determination of high- and low-molecular-mass plasticisers in stretch-type packaging films. *J. of chromatography A*, **675,** 261-266

Castle, L., Mayo, A. and Gilbert, G., 1990, Migration of epoxidised soya bean oil into foods from retail packaging materials and from plasticised PVC film used in the home. *Food Add. Cont.*, **7**, 29-36.

Castle, L., Sharman, M., and Gilbert, J., 1988a , Analysis of the epoxidised soybean oil in plastics by gas chromatography. *J. of chromatography*, **437**, 274-280.

Castle, L., Sharman, M., and Gilbert, J., 1988b Gas chromatographic mass-spectrometric determination of epoxidized soybean oil contamination of foods by migration from plastic packaging. *J.A.O.A.C.*, **71**, 1183-1186.

Demertzis, P.G., Riganakos, K.A. and Akrida-Demertzi, K., 1991, Gas chromatographic studies on polymer-plasticizer compatibility: interactions between food-grade PVC and epoxidized soybean oil. *European Polymer Journal,* **27**, 231-235.

DoH (1995) 1994 Annual Report. Committees of Toxicity, Mutagenicity Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO, London.

EFSA (2003) Statement of the scientific panel on additives, flavourings, food processing aids and food contact materials updating the advice available on semicarbazide in packaged foods. 1 October 2003, http://www.efsa.eu.int/press_room/press_release/30/15-10-2003_en1.pdf

EU Commission Directive 90/128/EEC of 23 February 1990 relating to plastic materials and articles intended to come into contact with foodstuffs, Official Journal L 075 , 21/03/1990 P. 0019 – 0040.

EU Commission Directive 2002/72/EC of 6 August 2002 relating to plastic materials and articles intended to come into contact with foodstuffs, Official Journal 13.02.2003, L 39, P. 1 – 42.

EU Commission, Synoptic Document: provisional lists of monomers and additives notified to European Commission as substances which may be used in the manufacture of plastics intended to come into contact with foodstuffs. Update 07/ 2003. http://europa.eu.int/comm/food/fs/sfp/food_contact/synoptic_doc_en.pdf

Even, I, Berta, J.L., and Volatier, J.L. (2002). Evaluation de l'exposition théorique des nourrissons et enfants en bas âge aux résidus de pesticides apportés par les aliments courants et infantiles, AFFSA, Janvier 2002

Fantoni, L. and Simoneau C., 2003, European survey on the contamination of homogenised baby food by epoxidised soybean oil from plasticised PVC gaskets", *Food Add. Cont.*, **20**, 1087-1096

Gilbert, J., and Startin, J.R., 1980a, The determination of the transformation products of epoxides used in the heat stabilization of poly(vinyl chloride). *European Polymer J.* **16**, 73-77.

Gilbert, J., and Startin, J.R., 1980b, GC-MS of the flophemesyl derivatives of a series of fatty acid methyl ester chlorohydrins. *J. Chromatogr*. **189**, 86-88.

Hammarling, L., Gustavsson, H., Svensson, K., Karlsson, S, and Oskarsson, A., 1998, Migration of epoxidized soya bean oil from plasticized PVC gaskets into baby food. *Food Add. Cont.*, **15**, 203-208.

Han, L.-M.T. and Szajer, G., 1994, Analysis of epoxidized soybean oil by gas chromatography. *J.A.O.C.S*, **71**, 669-670.

Han, S.Y., Lee, D.H., Kim, C.K., Shin, J.H., Moon, H.J., Kim, H.S., Kim, S.H., OH, S.D., Lee, R.D., Kim, T.S.,Won, E.H., and Park, K.L., 2000, Embryotoxicity and teratogenicity studies of epoxidized soy bean oil (ESBO) using in vitro battery test system, *Teratology*, **61**, 485

Heath, J.L. and Reilly, M., 1982, Mutagenesis testing of acetyl-tributylcitrate and epoxidized soybean oil, *Poultry Science*, **61**, 2517-2519

Howell, B.A., Betso, S.R., Metzer, J.A., Smith, P.B., and Debney, M.F., 1990, Thermal degradation of epoxidized soybean oil in the presence of chlorine-containing polymers. *Termochimica ACTA*, **166**, 207-218.

Juangvanich, N. Stoffer, J. (2002) Reactions of Amines with epoxidized soybean oil, In: Polymer Preprints -America-, Division of Polymer Chemistry, American Chemical Society; 224th ACS National meeting Vol. 43 Part 2, 922-923

Kersting M., Alexy U., Sichert-Hellert W., Manz F. and Schöch G. (1998). Measured consumption of commercial infant food products in German infants: Results from the DONALD study. *J. of Pediatric Gastroenterology and Nutrition* 27: 547-552.

MAFF (1992). Food and nutrient intakes of British infants aged 6-12 months.

MAFF (1995). National diet and nutrition survey: children aged $1^1/_2$-$4^1/_2$ years.

Monsanto, Ames/Salmonella mutagenicity assays of epoxidized soybean oil (ESO) and chlorinated ESO, 1986, study n. MSL-5707. EPA/OTS doc #86870000311

Monsanto, CHO/HGPRT gene mutation assay with epoxidized soybean oil (ESO) and chlorinated ESO, 1987, study n. MSL-6395. EPA/OTS doc #86870000312

Pauli, G, Bessot, J.C, Kopferschmitt, M.C., Lingot, G, Wendline, R, Ducos, P, Limasset, J.C., 1980, Meat Wrapper's Asthma: Identification of the Causal Agent, *Clinical Allergy*, **10**, 263-269

Piccinini, P., Valzacchi, S. and Simoneau, C. Optimisation of an analytical method for the quantification of chlorohydrins from epoxidised soybean oil in various food matrices using gas chromatography mass spectrometry. Hyphenated Techniques in Chromatography, Bruges, 04-06 February 2004.

SCF, 1999, Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastic materials intended to come into contact with foodstuffs until 21 March 1997. Reports of the Scientific Committee for Food (42nd series). European Commission, Luxembourg.

Sheperd, M.J. and Gilbert, J., 1981, Studies on the stabilization of poly(vynil chloride) with epoxides - transformation products and their migration from packaging to foods. *European Polymer J.*, **17**, 285-289.

Startin, J.R., Gilbert, J. and McWeeney, D.J., 1978, Gas chromatography-mass spectrometry of series of fatty acid methyl ester chlorohydrins and their tri-methyl silyl derivatives. *J. of Gas Chromatography* **152**, 495-499

Valzacchi, S., Fantoni, L., Piccinini, P. and Simoneau, C., 2003, Determination of chlrohydrins formed from ESBO in PVC gaskets and baby food by gas chromatography-mass spectrometry, EMB 932.

SCIENTIFIC PANEL/COMMITTEE MEMBERS

Robert Anton, Sue Barlow, Dimitrios Boskou, Laurence Castle, Riccardo Crebelli, Wolfgang Dekant, Karl-Heinz Engel, Stephen Forsythe, Werner Grunow, John Chr. Larsen, Catherine Leclercq, Wim Mennes, Maria Rosaria Milana, Ivonne Rietjens, Kettil Svensson, Paul Tobback, Fidel Toldrá,

ACKNOWLEDGEMENTS

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food wishes to thank Catherine Simoneau for the preparation of the draft opinion.