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EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Scientific Committee on Consumer Safety

SCCS

OPINION ON

THE POTENTIAL HEALTH RISKS POSED BY CHEMICAL CONSUMER PRODUCTS RESEMBLING FOOD AND/OR HAVING CHILD-APPEALING PROPERTIES

Scientific Committees
on consumer safety
on emerging and newly identified health risks
on health and environmental risks

The SCCS adopted this opinion at its 10th plenary meeting

of 22 March 2011

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.
They are: the Scientific Committee on Consumer Safety (SCCS), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Agency (EMA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCCS

The Committee shall provide opinions on questions concerning all types of health and safety risks (notably chemical, biological, mechanical and other physical risks) of non-food consumer products (for example: cosmetic products and their ingredients, toys, textiles, clothing, personal care and household products such as detergents, etc.) and services (for example: tattooing, artificial sun tanning, etc.).

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1. BACKGROUND

Chemical consumer products resembling food and/or having child-appealing properties, such as shower gels, shampoos, body lotions, soaps, liquid soaps and dish-washing liquids are common on the European market. These products resemble foodstuffs or are child-appealing due to their shape, colour, appearance, odour, consistence, packaging or other characteristics. In particular, chemical consumer products, resembling food and/or having child-appealing properties may lead consumers and especially vulnerable people, such as children or elderly people, to ingest them. Be it because of their inherent toxicity properties, be it from other characteristics (viscosity, foaming potential, vomiting induction potential) ingestion of these products may pose a risk to the health of consumers.

It is difficult to determine the level of potential health risk of such products, due to a considerable number of elements to be taken into account. These include the inherent toxic properties of the ingredients, the non-chemical attributes of the product, the amounts of product ingested, the probability that the product is confused with food or attracts children, the impact of bad taste (sometimes caused by deliberate addition of a bitter-tasting chemical), and whether bad taste can prevent ingestion to a degree that a health risk can be avoided.

The regulatory framework governing the safety of chemical consumer products includes:

* Council Directive 87/357/EEC of 25 June 1987 on the approximation of the laws of the Member States concerning products which appearing, to be other than they are, endanger the health or safety of consumers[1],
* Directive 2001/95/EC of 3 December 2001 on general products safety[2],
* Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products[3],
* Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)[4]
* Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures[5]
* Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys[6]
* Regulation (EC) No 648/2004 of the European Parliament and of the Council of 31 March 2004 on detergents[7]
* Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market[8]

Member States' authorities differ in their safety assessments of Chemical consumer products resembling food and/or having child-appealing properties. Despite several discussions with Member States' experts a common approach could not be found. As a result, on the basis of different assessment elements, Member States continue to adopt different measures to limit the marketing and use to ensure consumer health and safety of these products.

[1] OJ L 192, 11.7.1987, p. 49
[2] OJ L 11, 15.1.2002, p. 4
[3] OJ L 262, 27.9.1976, p. 169
[4] OJ L 396, 30.12.2006, p. 1
[5] OJ L 353, 31.12.2008, p. 1
[6] OJ L 170, 30.6.2009, p. 1
[7] OJ L 104, 8.4.2004, p. 1–35
[8] OJ L 123, 24.4.1998, p. 1

To move towards a harmonised solution in the EU, the Commission considers it necessary to request the Scientific Committee on Consumer Safety (SCCS) to provide guidance on the potential health risks that may result after ingestion of Chemical consumer products resembling food and/or having child-appealing properties.

2. TERMS OF REFERENCE

The SCCS is asked to assess, in the light of current scientific data and knowledge:

1. What are the elements of a product which are likely to increase the probability for confusion with foodstuffs or that make a product more child-appealing? If possible, a ranking of such elements should be given.

2. What are the inherent properties and attributes of chemical consumer products that may cause or contribute to adverse health effects upon ingestion?

3. What are the circumstances under which exposure to Chemical consumer products resembling food and/or having child-appealing properties will pose a serious risk to the health and safety of consumers, in particular to children and elderly people, taking into account e.g. volume ingested, taste of the product etc.? In which circumstances may such a risk materialise?

4. What are the most common adverse health effects observed in humans if such products are ingested?

3. EXECUTIVE SUMMARY

Consumer products on the European market such as shower gels, shampoos, body lotions, soaps, liquid soaps and dish-washing liquids may be packaged to imitate food or have other attributes that appeal to children. These products resemble foodstuffs or are child-appealing due to their shape, colour, appearance, odour, consistency, packaging or other characteristics and may therefore be ingested by mistake. The aim of this work was to assess the risk from accidental ingestion of food-resembling or child-appealing cosmetic and liquid household products by consumers. Children between 6 months and 6 years of age and elderly people over 75 years old are the most at-risk groups for accidental ingestions of these products.

Few cases of accidental ingestion of food-resembling or child-appealing products are reported. This may be due to the lack of sufficient registered information to discriminate these types of products. Data from poison centres and scientific literature on accidental ingestion of cosmetics or liquid household products suggest that the majority of such ingestions result in mild gastrointestinal effects. In some cases, more serious effects may cause cardiovascular or neurological disturbances. In the elderly, underlying health status may exacerbate these effects. Both children and the elderly are prone to aspiration, which may result in pulmonary manifestations.

Characteristics that are suspected to make cosmetics and liquid household products more food-resembling include: colour, shape, packaging, taste, smell, etc. There are no studies that have specifically tested the likelihood of increased ingestion of consumer products resembling food and/or having child-appealing properties compared to other cosmetics and liquid household products.

Regarding child-appealing products, it should be noted that the appeal of a product for children cannot be defined objectively, but only in relative terms. Unlike for consumer products resembling food, there are no general characteristics of the shape, colour, packaging, and consistency of cosmetics and liquid household products that make such a product relatively more child-appealing. Children can be attracted to nearly anything within their reach, depending on the number and type of other attractors in their environment, their situational and dispositional inclination to explore, and many other factors.

There are no studies for any of the characteristics mentioned above that tested children's preferences or the likelihood of ingestion with regard to cosmetics and liquid household products. There are no data to show directly that cosmetics with a sweet smell, strong colours or cartoon characters displayed on the packaging are more often ingested than others. Nevertheless, these characteristics can serve as proxies to evaluate whether products are more or less child-appealing, until more specific data are available.

Cosmetic formulations are not evaluated for acute oral toxicity, except for oral care products. However, the majority of cosmetic products are considered not to exhibit serious health effects following ingestion. In accidental ingestions, the most common household products were dishwashing and laundry detergents, toilet cleaners and bleaches. Generic cosmetic formulations were used to generate a list of ingredients which may be harmful. For household products, a similar list was compiled from accidental ingestion case reports.

The most harmful ingredients were:

- Corrosive substances such as acetic acid, nitric acid, sulphuric acid, hydrochloric acid, sodium bisulphate, sodium hypochlorite and sodium hydroxide.
- Surfactants, dependent on composition and concentration.

- Alcohols and glycols such as ethanol, isopropanol and butyl glycol.
- Essential oils such as pine oil, wintergreen oil and camphor.

The weight of evidence from accidental ingestion of cosmetics suggests that there is a low risk of acute poisoning in either children or the elderly. For household products, there is a slight increase of a more serious outcome. There is a lack of specific data on accidental ingestion from consumer products resembling food and/or having child-appealing properties.

4. INTRODUCTION AND SCOPE OF THIS OPINION

Consumer products resembling food (CPRF) are a sub-set of normal consumer products, such as cosmetics and household products, which in design, shape, or presentation resemble food and could mistakenly be consumed by children, the elderly or intellectually challenged. Child-appealing products (CAP) are another sub-set that includes chemical products, with an overlap that may include some CPRF, and may also be consumed by children by mistake. CPRF and CAP can be cosmetics, personal care products, fabric detergents, dish washing products, toys, candles, lamp oils (mineral oils) and other household products.

Examples of several other CPRF (also referred to as food-imitating products, FIP) and CAP can be found below in table 1 (RAPEX[9], VWA 2006), which shows cosmetic and household products that have been packed as novelty items that are considered to be food-imitating and/or child-appealing by some Member States (see annex I for pictures of consumer products resembling food). RAPEX indicates the type of FIP/CAP causing concern to the Member States.

Table 1: Examples of consumer products resembling food (CPRF)/food-imitating products (FIP) and child-appealing products (CAP) (RAPEX[9], VWA 2006).

Cosmetics	**Household cleaning products**
Soaps	Sanitary cleaning products
Shampoo	Fabric detergents (liquids)
Body cream	Fabric softeners
Perfumes, Toilet water, Cologne	Bleaching agents
Aftershave	Dish washing products (liquids)
Deodorants	
Nail polish and remover	
Dental Care	
Sun tan	

Accidental poisoning remains a major public health problem and household products are common causes of accidental poisoning, especially in children (Eldridge et al. 2007, Guyodo and Danel 2004, Villa et al. 2008, WHO 2008a)

The aim of this work was to assess the risk for consumers, especially children or the elderly, following the accidental ingestion of CPRF and/or CAP. It was anticipated that the risk assessment may not be different in terms of exposure and hazard characterisation between these two categories of products, when exposure from cosmetics and liquid household products is considered. This opinion is therefore focussed on risk assessment from oral exposure of cosmetics and liquid household products, which may look like food products or may be attractive to children because of their presentation. Health risks associated with accidental ingestion from other CPRF/CAP, for example toys and mineral oils, are not covered by this opinion.

[9] The Rapid Alert System for Non-Food Products (RAPEX): Available from: URL: http://ec.europa.eu/consumers/safety/prod_legis/index_en.htm

5. METHODOLOGY

The Health and Consumers Directorate General of the European Commission (DG SANCO) provided information on accidental ingestion of consumer products, particularly if identified as CPRF (FIP) and/or CAP. The information collected included both peer and non-peer reviewed, published and unpublished material, based on:

- Material provided as a result of a call for submission of information[10].
- A comprehensive literature search and collection of relevant information by an external contractor.
- Information on CPRF (FIP) and CAP from EU Member States collected via the RAPEX system.
- Relevant information from poison centres from both EU and non-EU countries.

In addition, the SCCS continued the collection of data throughout the preparation of the opinion. Investigators from two other parallel projects shared their expertise with the SCCS and their contribution to this opinion is acknowledged:

- Dr. Stacey Wyke, Description of the Nature of the Accidental Misuse of Chemicals and Chemical Products (DeNaMiC). Key project outputs, Health Protection Agency, UK.
- Mr. Frédéric Basso, Food-Imitating Products, Université de Rennes, FR.

A review of the available literature related to the subject was performed by the SCCS to identify the information that could be used for this opinion. The publications included:

- Poisoning following accidental ingestion.
- Toxic effects of ingredients of products involved in accidental ingestion poisoning.
- Behaviour of children and the elderly and socioeconomic parameters which may lead to possible accidental ingestion.
- Accidental ingestion related to cosmetic and household products.
- Intoxication related to corrosive ingestion.
- Influence of bittering agents on accidental ingestion.
- Influence of packaging on accidental ingestion.
- Intoxication related to flavour/fragrances/plant extracts.

A review of typical ingredients used in consumer products was performed by the SCCS. For cosmetic products, this review was based on "Frame formulations" elaborated by the Cosmetic Industry and the European Association of Poison Centres and Clinical Toxicologists (COLIPA and EAPPCT 2000). For household products, the review was based on the information available from the DeNaMic project (Wyke et al. 2009) as well as from several published case reports of intoxication by accidental ingestion of consumer products.

6. BACKGROUND INFORMATION FROM ACCIDENTAL INGESTION POISONINGS

6.1. General considerations

Poison centres in various EU and non-EU countries register cases of accidental poisoning. These cases are summarised in the poison centres' annual reports and usually include information concerning age, sex, location of exposure, acute or chronic exposure, chemical and product group classification details. Since household products are still often involved in accidental poisonings despite preventive management measures introduced by regulators or manufacturers, the European Chemical Industry Council CEFIC (Europe) funded a two and a

[10] http://ec.europa.eu/health/scientific_committees/consultations/calls/sccs_call_info_01_en.htm

half year project (Sept 2006-Feb 2009) called DeNaMic (Description of the Nature of the Accidental Misuse of Chemicals and Chemical Products) (Wyke et al. 2009). This project aimed to provide an overview of the nature and extent of injury from chemicals and chemical products in Europe and detail the circumstances of how these exposures occur. However, there were some differences in compiling data from different poison centre annual reports, as the data were not reported in a homogenous way. Specific product information, such as packaging details, concentrations of ingredients, storage details and information on the cause of exposure were not reported.

Since CPRF are a sub-set of household and personal care products, it was initially thought that information from the national poison centres or in the scientific literature would be helpful in fulfilling the mandate of this opinion. However, only a few cases following accidental intake of CPRF/CAP were reported by poison centres, mainly due to the lack of sufficient registered information to discriminate these kinds of products. There has been an "epidemic" of poisonings in the USA due to the package design and colour of a new marketed product, resembling that of a food product (Miller et al. 2006; see Annex II).

In general, it is difficult to estimate accidental ingestions of cosmetics and liquid household products because the majority of accidental ingestions are innocuous. Indeed, many incidents of accidental ingestion are not reported to physicians if they are believed to be inconsequential. In addition, physicians and hospitals will not report cases to a poison control centre if they have had experience with similar cases and do not require further information.

6.2. Characteristics of patients involved in accidental poisoning

Children are more frequently involved in accidental poisoning than any other age group. Children below three years old accounted for the majority of childhood poisoning (72% of cases reported in French poison centres in 2002) (Guyodo and Danel 2004). Between 1990 and 2006, US emergency departments treated 192,288 cases of accidental injuries involving household cleaning products in children between 1 and 3 years old (McKenzie et al. 2010). Children under the age of 6 accounted for nearly 52% of the more than 2.2 million poison exposures reported in 2004 by the American Association of Poison Control Centers (Madden 2008).

Paediatric poisonings are generally unintentional (>99% of all poisoning exposures) (McKenzie et al. 2010). Toddlers are vulnerable to accidental poisoning because they are newly mobile and curious. Moreover they may mistake a brightly coloured product for candy or a beverage. The major route of exposure was oral and involved liquids for babies (less than 3 years of age) and solid products for older children (older than 13 years). Children of the age group 4 to 12 years were exposed to both liquid and solid products (Guyodo and Danel 2004).

It is known that the home is the most common location for accidental poisoning of children. Data from UK poison centres suggest that the domestic environment is the most common location for poisoning to occur. From the total number of inquiries made to UK poison centres, the percentage of calls that concern poisoning in the home increased from 77% in 2003/2004 to 89% in 2006/2007 (National Poisons Information Service Annual Reports (UK) 2003/2004-2006/2007).

6.3. Products commonly ingested by accident

In recent decades, cleaning products have consistently been in the top five categories of paediatric poisoning exposure (McKenzie et al. 2010, WHO 2008a, Wyke et al. 2009). The toxic agents most often involved in accidental poisoning were pharmaceuticals and household products. Among children from birth to 3 years old, frequency of poisonings from pharmaceutical and non-pharmaceutical products is similar. The products most frequently involved in paediatric exposure cases were: cosmetic and personal care products; cleaning products; and analgesics, in descending order of frequency (Watson et al*.* 2005).

Exposure to cleaning products or detergents reported to the GIZ-Nord Poisons Centre in Göttingen (Germany) between 1999 and 2008 represented 10% of all exposures recorded for all age groups (Desel and Wagner 2010). Exposure to cosmetic products represented 4.8 % of all exposures recorded (Desel *et al.,* 2010).

In the DeNaMic project, the data recorded by the poison centres were analysed and the potential usefulness of these data for risk assessment purposes was evaluated. A questionnaire survey of European poison centres was carried out. Questionnaires were sent to 89 poison centres in 33 countries. In the context of this survey, 16 poison centres provided a list of products and agents which are most frequently involved in the top five categories of poisonings; this information is often available in their annual reports. The results show that household cleaning agents, such as toilet cleaners and dishwashing detergents which are commonly used in homes, are most frequently involved in accidental poisonings.

The products were often characterised by their chemical and physical properties e.g. corrosive, bleach, desiccant or solvent, and nearly all poison centres listed such products in their "top five" list. Some chemicals were specifically named due to their importance e.g. sodium hypochlorite, sodium hydroxide, alcohols and hydrogen peroxide. Corrosive chemicals and detergents/surfactants were predominant: 1) due to their toxic potential and widespread use e.g. descalers, bleach, and drain cleaners; and 2) due to the widespread use in households. Other product groups which were mentioned by poison centres were pesticides, fuels, and several alcohols, which were grouped as solvents.

Household chemical consumer products commonly ingested by children are presented in table 2. It is possible that some of these products could be ingested by children because of their child-appealing properties. However, sufficient data are not available.

Table 2: Household chemical consumer products commonly ingested by children (Wyke et al. 2009)

Bleach	**Disinfectants**
Sodium hypochlorite	Dichlorometaxylenol
Hydrogen peroxide	Phenol
Cosmetics and toiletries	Cresol
Aftershave lotions, cologne, perfume	**Petroleum Distillates**
Hair remover containing thioglycolate	Paint thinner
Nail polish	Paintbrush cleaner
Nail polish remover	Paraffin
Soap	Turpentine substitute (white spirit)
Detergents	Furniture and floor polish
Washing-up liquid	
Fabric conditioner	
Automatic washing/dishwashing liquid	

6.4. Types of adverse effects

There are no statistics available to estimate the burden of injuries caused by poisonings. Global data, in particular, on non-fatal outcomes of poisoning are not readily available (WHO 2008a). The epidemiology of poisoning can be studied from hospital admissions and discharge records, mortality data, emergency department records and surveillance systems, as well as from enquiries to poison control centres. Desel and co-workers reported that between 1999 and 2008, 2% of exposures to cleaning products and detergents and 0.8% of exposures to cosmetic products were considered moderate or severe (Desel and Wagner 2010, Desel *et al. 2010*). There were 6 lethal cases following exposure to cosmetic products, representing 0.05% of total exposure to cosmetic products and 9 cases following exposure to cleaning products and detergents, representing 0,03% of total exposure to these kind of products. Among cosmetic products, hair colouring agents were considered as the product group with the highest poisoning risks.

Concerning childhood poisoning incidents it is thought that there is substantial under-recording and under-reporting of cases. Fatalities in young children following toxic ingestions are rare (Watson et al. 2005). Most of the poisoning cases reported in children were not serious: the death rate reported by Guyodo and Danel (2004) is 0.026% of the poisoned children. In UK, less than 5% of all accidental exposures to household chemical consumer products resulted in clinical symptoms (Bateman 2003).

In two publications (Lamireau et al. 2002, Marchi et al. 2004), clinical and epidemiological features of toxic exposures observed in 14 Italian hospitals during 2001 in children under 1 year old were reported. In most cases, non–toxic exposures, or exposures without any clinical consequences, were reported and the symptoms were rarely serious. Initial symptoms reported by parents whose children were admitted to the paediatric emergency care unit were mainly gastrointestinal (vomiting, abdominal pain) or neurological (impaired consciousness, hypotonia, ataxia, seizure), although cutaneous (rash), respiratory (dyspnoea, cough) or dysphagia were also reported in some children. On arrival at the paediatric emergency care unit, most of the digestive symptoms (essentially vomiting) had stopped, whereas cardiovascular symptoms (dysrhythmia, hypotension) were noted. Nevertheless, more than half of the children remained asymptomatic. Of the children admitted to the paediatric emergency care unit, 40% received no treatment, 10.6% had symptomatic treatment and 25.5% underwent gastric emptying (Lamireau et al. 2002).

Many of the cases of accidental ingestion of cosmetic and household products brought to the poison centres are sent home untreated. However, on the basis of the available data on the adverse health effects by accidental ingestion of cosmetics and liquid household products, the following effects may be seen:

- Gastrointestinal irritation, digestion symptoms;
- Central nervous system (CNS) symptoms;
- Pneumonia due to aspiration; and
- Cardiovascular symptoms.

Only limited data are available on adverse health effects of accidental ingestion of CPRF and CAP. However, as CPRF and CAP are subsets of cosmetic and household products, similar effects are expected.

In the elderly, these effects may be exacerbated by underlying health status (Annex II). Both children and elderly persons are prone to aspiration, which may result in severe pulmonary manifestations.

Aspiration of vomited material may damage the lung tissue, particularly the alveoli because of the acidity of the stomach contents. Such material can, on its own, cause inflammation of the lung tissue, but this is usually transient. However, if the vomited material contains accidentally ingested xenobiotics, such as surfactants and emulsifiers, chemical pneumonia may develop as a result of further inflammation and damage of the lung tissue. This can also be induced by aromatic oils as their low viscosity increases the chance of inhalation rather than swallowing. Chemical pneumonia is a particular problem with children and the elderly, and has resulted in deaths.

Exposure to corrosive substances may also be of concern since minimal ingestion can cause severe oesophagogastric burns.

7. CONSUMER RELATED FACTORS FOR CPRF AND CAP INTAKE

Children and the elderly are more susceptible to the ingestion of cosmetics and liquid household products because of their behaviour and differences in some physiological parameters.

7.1. Children

There is no universally agreed age range for what constitutes childhood. Article 1 of the United Nations Convention on the Rights of the Child defines "children" as persons up to the age of 18. However, in many reports of the United Nations (UN) and the World Health Organization (WHO), the term "children" refers to persons up to the age of 14 years (e.g. UN 2010, WHO 2010b). The term "infant" refers to children between the ages of 1 month and 12 months (Berk 2009, WHO 2010c); however, other definitions vary between birth and 3 years of age. The term "toddler" refers to children who are learning to walk, so it is typically used for children aged 1 to 2 years (Berk 2009), but sometimes also up to 3 years. As children less than 6 years old are more frequently involved in accidental poisoning than older children, special attention will be paid to this category in the following section. Children less than 6 months old are not considered in this opinion because it is unlikely that they will be able to reach CPRF/CAP by themselves.

7.1.1. Child physiology

It is generally known that in organisms of different sizes, physiological functions such as basal metabolic rates correlate much better with the body surface area rather than with the body weight. This is also reflected by drug dosing; paediatric therapy usually requires higher doses (per kilogram body weight), compared to therapy of adults. In concordance, susceptibility towards xenobiotics is not generally higher in children compared to adults. However, differences in kinetics of distinct xenobiotics in children of a specific age, especially very young age groups, may well have the consequence that external exposures identical to those of adults lead to increased response due to higher ''internal'' doses (Renwick et al. 2000).

Numerous studies have been investigating the activity of xenobiotic metabolising enzymes in different age groups. There are considerable species and inter-individual differences (Schwenk et al. 2003).

In general, the most prominent differences in toxicokinetics are found in children less than 1 year old and especially in the first few days and weeks of life (Scheuplein et al. 2002). By the age of 2 years, most of the biochemical and physiological parameters that affect toxicokinetics have reached maturation, although differences still exist. Thus, it seems reasonable to be extra cautious in the risk assessment of children as an exposed group as there are differences between children and adults in toxicokinetics (especially babies in their first months) and toxicodynamics (especially at different stages of development), which may render children more susceptible to the toxic effects of a substance.

Particular attention should be paid to the effects on the nervous, reproductive, endocrine and immune systems, and also on the metabolic pathways, all of which in part develop new functional properties during childhood (Falk-Filipsson et al. 2007).

7.1.2. Children's behaviour

The present opinion focuses on children between 6 months and 6 years of age, as this is the group of children for which ingestions of cosmetics and liquid household products appear to be most likely.

- **Age**

Age has a strong association with accidental ingestion and poisoning, as with children's injuries in general (Hillier and Morrongiello 1998). Children under the age of 1 year have the highest rates of fatal poisonings, but non-fatal poisonings appear to be more common between 1 and 4 years of age. The risk of poisonings increases particularly at around 2 years of age, as young children become more mobile and have increased access to toxins (WHO 2008a). It is instructive to look at some general developmental milestones of children up to 6 years of age (see table 3, Annex III).

Young children are particularly susceptible to accidental ingestion, especially liquids, because they are very inquisitive, put most items in their mouths (e.g. hand-to-mouth activity) and are unaware of consequences. The quantities involved are often small (a mouthful/sip). The volume of a swallow is 4.5 ml for a child aged between 18 months and 3 years, and in an adult it is 15 ml (Jones and Work 1961; cited in Mofenson et al. 1984). A toddler's mouthful is approximately 9.0 ml (Ratnapalan et. al. 2003).

- **Motivation**

Children who are hungry or thirsty are more likely to accidentally ingest products within their reach than children who are not. The very fact that they want something to eat or drink increases the likelihood that they will ingest something that smells good to them (Whitford et al. 2001).

7.1.3. Children's environment and parental supervision

Reduced observation and supervision of children may increase the risk of exposure and subsequent accidental poisoning e.g. during holiday periods, festivals and other events (Amitai et al. 2000, WHO 2008a). A good example is when meals are being prepared. It is common for children to have free run of the house as adults focus their attention on preparing a meal (Whitford et al. 2001). The most significant injuries reported following ingestions of poisons by children seem to occur as a result of them drinking from opened containers within their reach. There are still many cases which are related to storing corrosive solutions in unlabelled containers or more seriously, routine drinking bottles which other adults unknowingly give to their children (Riffat and Cheng 2009, WHO 2008a).

In an American study that made in-home observations of safety hazards related to burns, poisoning and falls, maternal supervisory style, rated on dimensions of protectiveness, was an important correlate of all types of household hazards (Glik et al. 1993). In this study, risk perceptions of the mothers had little influence on home hazards. In another study, maternal perceptions of risk variables interacted with maternal safety behaviour (Dal Santo et al. 2004). A recent study on parental perceptions of injury risks shows that parents underestimated scenarios with high injury/death rates and overestimated scenarios with low injury /death rates (Morrongiello et al. 2009, Will et al. 2009).

However, direct evidence linking supervision to child injury is scarce and more research is needed to assess the independent contribution of this factor (independent, for instance, from socio-economic status) to injury risk (Morrongiello 2005).

7.1.4. Socio-economic and related factors

The variable most frequently correlated with poisonings is socio-economic status (SES). SES is a strong predictor of observed home hazards (Glik et al. 1993), unsafe childcare practices (Hapgood et al. 2000), fatal unintentional injuries, and to a lesser extent, of nonfatal injuries (Cubbin and Smith 2002). In particular, unemployment and homes needing repair appear to be risk factors for unintentional injuries at home (Dal Santo et al. 2004, Glik et al. 1993, WHO 2008a).

There are many variables related to SES, for instance, maternal social support, stress and coping (Dal Santo et al. 2004). Stress in the home in this context is defined as regular changes in lifestyle demanding social re-adjustment (Eriksson et al. 1979, Shaw 1977). More recent studies also confirmed that risk factors for accidental poisoning in children may include child behaviour but also stress at home, size, education and income of the family, absence of the parents, and the accessibility of the poisonous products (Eriksson et al. 2008, Katrivanou et al. 2004, Soori 2001).

Although SES is the best studied predictor of different injury risks, even affluent families do not undertake safety practices all the time, and most of the variation in the number of safety practices, for instance, is not explained by SES (Hapgood et al. 2000). Thus, further research is needed.

7.2. Elderly people

There is no universally agreed age range for what constitutes “elderly”. Most developed countries, however, use the chronological age of 60 or 65 years, roughly equivalent to retirement ages, as a definition of “elderly” or an “older person” (WHO 2010a). The WHO uses 60+ years to refer to older persons (e.g. WHO 2007, WHO 2008b). For the purpose of this opinion, the elderly are considered as persons aged 75 years and above.

7.2.1. Physiology of elderly people

At ages of 75 and above, a proportion of the population may show signs of aging, such as physical and mental deterioration. This is due to a combination of factors including physical and mental disease, under-/malnutrition and relative deprivation superimposed on the various physiological changes that occur with age alone. This latter group is at special risk of adverse effects of drugs, chemicals and the environment.

The elderly are exposed and respond to xenobiotic chemicals differently than younger people in a number of important aspects. These differences are wide ranging and include physiological, pathological and environmental factors (Crome 2003).

Principal differences occurring during aging are listed below (adapted from Crome 2003) (see also table 4 Annex III):

- Decline in a wide range of physiological systems characterised by a reduction of functional reserve.
- Different environmental experiences, both current and across the life-span.
- Increased prevalence of sub-clinical and clinical disease (degenerative, malignant and infectious).
- Increased use of medication and "special foods" for medical purposes.
- Increased risk of adverse response to medication.

- Different expectations (brought up before the age of consumerism).
- Frailty.
- Relative social, economic and cultural deprivation.

In adulthood, increasing age is accompanied by a progressive decline in the function of most physiological systems (Elmadfa and Meyer 2008, Young 1997). Almost all human physiological systems show evidence of deterioration in structure and/or function with age. In most cases, this is of little importance except when the body is placed under stress. For example, the same degree of chest infection is more likely to precipitate an episode of cardiac failure in an older person than in someone who is younger. Following such an event, recovery may be slower than in a younger person and there may also be permanent disability (Crome 2003).

7.2.2. Behaviour patterns of the elderly influencing safety

Poisoning is a significant problem in the elderly. However, most of the research on poisonings in elderly people is focused on the accidental intake of medication (Hahn et al. 2006, Klein-Schwartz and Oderda 1991). Research on the possible causes for accidental ingestions and poisonings in the elderly is scarce, but the following factors are likely to play a role:

- Frequently, the olfactory and gustatory perception is reduced. More than half of people between 65 and 80 years of age show major olfactory impairment. This increases to more than three-quarters in those over 80 years old (Doty et al. 1984).
- Impaired vision is also likely to decrease the ability of distinguishing between acceptable (edible, drinkable) and unacceptable products. The legibility of printed warnings therefore becomes especially important for older adults with impaired vision (Parsons et al. 1999).
- Older people are aware of hazards in the home and of safety information on products. However, they often report usability problems when using household products. In a focus group study with 45 older adults between 61 and 84 years of age, 55% of respondents reported motor difficulties in handling products, 42% reported memory difficulties, 40% perceptual difficulties, and 29% difficulties with symbol comprehension and text comprehension (Mayhorn et al. 2004).
- Older adults often have problems understanding product warning information, especially when product-specific knowledge cannot be used and memory demands are high (Hancock et al. 2005). In general, short-term memory capacity decreases as age increases, so warnings should be kept as brief and direct as possible (Parsons et al. 1999).
- Unlike young children, elderly people are often left by themselves for extended periods and they are not under constant observation, as a rule.
- Elderly people may not call for help immediately, or they may keep silent about what has happened, for reasons of shame or uncertainty.
- If elderly people are disoriented (e.g. due to illnesses or medications), they often lack the ability of distinguishing between acceptable and unacceptable products, even if their senses have been preserved (Klein-Schwartz and Oderda 1991).

8. CHARACTERISTICS OF CPRF AND CAP

8.1. Characteristics of consumer products resembling food (CPRF)

As defined in the introduction, CPRF are a sub-set of consumer products, such as cosmetics and liquid household products, which in design, shape, or presentation resemble food and could mistakenly be consumed by children or the elderly.

More specifically, products that appear to be other than they are and endanger the health and safety of consumers can be defined as in the Council directive 87 /357 /EEC (Article 1, number 2): Products "which, although not foodstuffs, possess a form, odour, colour, appearance, packaging, volume or size, so that is likely that consumers, especially children, will confuse them with foodstuffs and in consequence place them in their mouths, or suck or ingest them, which might be dangerous and cause, for example, suffocation, poisoning, or the perforation or obstruction of the digestive tract."

The scope of this opinion is limited to cosmetics and liquid household products. The present section aims to give examples of the characteristics that make cosmetics and liquid household products more food-resembling.

8.1.1. Colour

- For the category of cosmetics and liquid household products, the characteristic of a food-resembling colour can be related to the packaging, or when the packing is transparent or missing, to the product itself.
- Liquid foods can have very different colours, such as orange (orange juice, soft drinks), white (milk), black (cola), brown (coffee, cocoa), red and yellow (several fruit juices and soft drinks). The same is true for solid foods. It should also be noted that colours such as blue or green, which were previously reserved for non-food products such as cleaners, are now also used in foods. Due to new trends in food marketing, the frontier between food products and cosmetics has been blurred.

8.1.2. Shape, packaging, imagery

- For cosmetics, the characteristic of a food-resembling shape can be related to either the product shape itself (e.g. soaps that are shaped like lemons) or to the product packaging. Product packages that resemble, in their shape, real-life containers of solid foods, such as cans, bowls, plates etc. have a food-resembling shape.
- For liquid household products, the characteristic of a food-resembling shape is mainly related to the product packaging. Product packages that resemble, in their shape, real-life containers of liquid foods, such as bottles, cans, cups, glasses etc. have a food-resembling shape.
- Not only the product itself or the shape of the product package can resemble a food, but also the imagery used on the packaging can create an association with food. For instance, oranges can be pictured on an orange-coloured shower gel, or lemons on a household cleaner.
- Other aspects of food packaging that are displayed on a non-food product, such as fake nutrition tables, can also increase the extent to which a product is food-resembling.

8.1.3. Taste and odour

- For cosmetics and liquid household products, characteristics of odour or flavour are conveyed primarily either by imagery (see above), or by names and other written descriptions on the product. Product packages can also be opened to sample the odour directly.
- Odours, flavour and their descriptions can make a product more imitating when they closely resemble real food odours and flavours (e.g. fruity shower gels, honey lip balms) or when the description suggests that they do (e.g. "Sweet lime body butter").
- Bitter tastes are generally not preferred, which is why bittering agents have been used to deter ingestions and poisonings. The impact of bittering agents in poisoning prevention is discussed further in section 8.3 and Annex IV.

8.1.4. Accessibility and storage

- Placement at point of sale: products are more food-resembling when they are placed close to food products.
- Storage: food-resembling products could be consumed in error when they are stored close to food. Since the elderly often live in small spaces, this is can be a contributing factor.

The characteristics of CPRF discussed above are based on descriptions of the properties of food-resembling products that could lead to poisoning. There are no studies, for any of the characteristics mentioned, that tested experimentally the likelihood of poisoning or ingestion with regard to cosmetics and liquid household products. Although there are case reports (e.g. the ingestions of a colourful cleaning product, see Annex II), there are no experimental data available that show causally that, for instance, liquid household products with an orange colour (relatively more food-resembling) are ingested more often than the same products with a blue colour (relatively less food-resembling). Nevertheless, the above mentioned characteristics can serve as proxies to evaluate whether products are more or less food-resembling, until more specific data are available.

8.2. Characteristics of child-appealing products (CAP)

CAP can also be defined as a sub-set of normal consumer products that are appealing to children by design or presentation and may therefore be consumed by children by mistake. There is an overlap between CPRF and CAP (e.g. some food-resembling products may be particularly child-appealing), but the two categories are not identical.

The scope of this opinion is limited to cosmetics and liquid household products. The present section aims to give an overview of the characteristics that make cosmetics and liquid household products appealing to children. It should be noted, however, that the appeal of a product for children cannot be defined objectively, but only in relative terms (this is different to CPRF, where it is possible to describe the extent to which a product imitates a food by comparing it to that food). Children can be attracted to nearly anything within their reach, depending on the number and type of other attractors in their environment, their situational and dispositional inclination to explore, and many other factors. For the assessment that CAP can pose a serious risk to health and safety of children, the personal and environmental risk factors presented in section 7 will therefore be of particular importance.

Examples of characteristics of child-appealing products are given below:

8.2.1. Colour

- Attractively coloured packaging may serve to influence children's selection or persuasion in stores, and colour is also an important determinant of food liking and judgements of sweetness and other tastes (Hutchings 2003, Lavin and Lawless 1998, Léon et al. 1999).

- However, studies on colour preferences in children for different products do not show any consistent results. Examples include:

  - In an older study by Schneider (1977) with children between 3 and 5 years of age and empty product packages without any specific product relation, white containers led to the largest proportion of high attraction (48%) followed by black containers (33%), and finally, red containers (26%). Only these three colours were offered to the children.

  - In a study of colour preferences for different types of candies in children aged between 5 and 9 years, children preferred candies that were red, green, orange and yellow, in that order (Walsh et al. 1990). Only these four colours were offered.

  - Another study investigated colour preferences for three types of products (cereals, biscuits and drinks) with children aged 3 to 5 years. The colours chosen most frequently were pink (40.9%), purple (15%) and yellow (15%), and these colours were also among the favourite colours of the children in general. Nine different colours were offered in this study (Marshall et al. 2006).

- The results seem to be highly dependent on the type of product, choice set of colours and age of children. Children up to 5 years do not seem to be able to give repeatable results when asked for their favourite product colours (Léon et al. 1999).

8.2.2. Shape, packaging, imagery

- Products that are marketed for children generally use lots of vivid imagery, often in cartoon or comic style. Children are attracted to products that picture a cartoon character or other characters or objects that they are familiar with from other contexts, e.g. from TV or books (Ülger 2009). For instance, in a study with 4 to 6 year olds, children significantly preferred the taste of foods that had popular cartoon characters on the packaging, compared with the same foods without characters (Roberto et al. 2010). Food products presented in this study were graham crackers, gummy fruit snacks and carrots.

- Child-proof caps make it difficult for children less than 5 years of age to consume significant quantities of household chemical consumer products (Bateman 2003; see also WHO 2008a).

- In contrast to CPRF, there are no general characteristics of the shape or consistency of cosmetics and liquid household products that make them relatively more child-appealing.

- For young children, the presence of product labels or warnings will not have an effect because they cannot read or interpret them (WHO 2008a). Even though older children can read, the information that a product may not be suitable for a certain age group is not very likely to have an effect. The results of the study of Schneider (1977) even suggested that in children between 3 and 5 years of age the labelling of e.g. poison (skull and cross bones) may itself be attractive.

8.2.3. Taste and odour

- Children initially prefer sweet tastes and reject sour and bitter tastes; these are genetic predispositions (Berk 2009, Birch 1999, Birch and Fisher 1998b, Schwartz et al. 2009). Later on, their preferences for the majority of foods are shaped by repeated experiences (Berk 2009, Birch 1998a). A developmental study with 1,291 children aged from 4 to 16 years showed that across age and gender, children rated sugary and fatty foods most highly, although ratings for fruit were also high (Cooke and Wardle 2005). In this study, girls liked fruit and vegetables more than boys did; boys liked fatty and sugary foods, meat, processed meat products and eggs more than girls.
- Analyses of the type of foods marketed to children show correspondingly that these are predominantly high in sugar and fat (Elliott 2008, Story and French 2004).
- With growing age and perceptual-attentional skill, children seem to focus more on flavour (rather than colour) when asked to identify drinks (Oram et al. 1995; see also Liem et al. 2004).
- Bitter tastes are generally not preferred, which is why bittering agents have been used to deter ingestions and poisonings. The impact of bittering agents in poisoning prevention is discussed further in section 8.3 and Annex IV.
- Odour is an important cue for taste, so it can be expected that children will prefer sweet, fruity and candy-like odours.
- The study of Schneider (1977) showed that odour can also be an attractor in itself: packages with no fragrance, pleasant fragrance and antiseptic fragrance resulted in 30, 33 and 44% attraction, respectively, in children between 3 and 5 years of age. It is difficult to predict what sort of fragrances will attract children.

The above mentioned examples of characteristics of CAP were mainly identified in studies about children's food preferences. There are no studies, for any of the characteristics mentioned, that tested experimentally children's ingestion likelihood with regard to different characteristics of cosmetics and liquid household products. Thus, to the best of our knowledge, there are no experimental data available that show directly that, for instance, cosmetics with a sweet smell, strong colours or cartoon characters displayed on the packaging are more likely to be ingested than others. Nevertheless, the above mentioned characteristics can serve as proxies to evaluate whether products are more or less child-appealing, until more specific data are available. More systematic research, in particular, should be done on children's reactions to non-food products in order to better understand how children may react in front of a package and label design.

8.3. Food-resembling or child-appealing product characteristics and the probability for accidental ingestion

An overview of the characteristics that make a product relatively more food-resembling or child-appealing is given in sections 8.1 and 8.2. A ranking of the characteristics is not possible, given that there are no data available that allow for a direct comparison of the impact of the features on the risk of poisoning or ingesting the product.

However, in order to be able to better compare products and product designs with regard to their food-resembling or child-appealing properties, a simple summary score for each of the characteristics mentioned above could be obtained. A product that has a food-resembling shape, colour and smell, with a packaging that displays food-imagery, is probably more likely to be mistaken for a food than one that has only a food-resembling colour. Similarly, a product that displays cartoon characters on the package, tastes and smells sweet is probably more child-appealing than a product that just tastes sweet. However, given the limited data basis, and given that that the appeal of a product for children cannot be defined objectively, both CPRF and CAP scores would have to be interpreted cautiously and only have heuristic value until more systematic research is available.

The use of bittering agents as "aversives" has been advocated as a possible method of preventing toxic ingestions by children. The most commonly recommended agent denatonium benzoate (Bitrex) was found to have an unpleasant and bitter taste at concentrations as low as 50 ppb in liquid products (Berning et al. 1982, Hansen et al. 1993, Lawless et al. 1982, Payne 1988, Sibert and Frude 1991).

There are no published data on the effectiveness of aversing agents in limiting the ingestion of household products. Anecdotal information (Klein-Schwartz and Oderda, 1991) indicates that it may not prevent significant accidental ingestions. A single swallow of some products, such as caustics and hydrocarbons, may be toxic. Addition of aversive agents would not be effective on the outcomes of such ingestions.

Hydrocarbons are especially noteworthy because they produce toxicity by being aspired rather than by being ingested. Children may vomit after drinking denatonium benzoate spiked liquids. Thus the addition of denatonium benzoate to hydrocarbons might actually increase the potential for toxicity of these ingestions, because the act of vomiting increases the risk of aspiration.

There is no information available on effects of ingestion of products containing bittering agents by the elderly.

9. INHERENT PROPERTIES OF CPRF AND CAP THAT MAY BE RESPONSIBLE FOR ADVERSE HEALTH EFFECTS UPON INGESTION

9.1. Acute toxicity of cosmetics

The safety of cosmetic products is not evaluated for oral intake, except for oral care products (Directive 76/768/EEC).

The cosmetic frame formulations[11] (COLIPA and EAPCCT 2000) detail basic information about ingredient types and the maximum concentrations for most cosmetic ingredients on the European market. The frame formulations system enables rapid identification of a cosmetic product that is unlikely to result in serious effects to health, when ingested or used inappropriately. These are a voluntary initiative of the industry and have no current EU legal status, but are provided to the national competent authorities. If a product does not comply with a frame formulation, or if there is no frame formulation for a given product, then formulation details, both qualitative and quantitative, need to be declared individually. Also, some other types of cosmetic products (e.g. nail cuticle removers, nail strengtheners, nail varnish removers, permanent wave neutralisers in powder form) have always to be declared in detail to poison centres.

The majority of cosmetic products represent a relatively low risk upon ingestion. A list of ingredients that according to scientific evidence may cause serious effects to human health if ingested was established by the working group. This was based on their experience, as well as on the acute toxicity data for these substances by oral routes when available in the published literature/toxicity databases or in the dossiers evaluated by the SCCS.

[11] This initiative has support of industry and the European Association of Poison Centres and Clinical Toxicologists (EAPCCT). It is based on a simple workable system developed jointly by the UK Cosmetic, Toiletry and Perfumery Trade Association (CTPA) with the National Poisons Information Service (London).

Table 5 (Annex III) is derived from the frame formulations, indicating the categories and examples of chemicals. The selection of ingredients was based on the judgement of the SCCS experts using RAPEX listings, concentration and hazard of the substances.

9.2. Acute toxicity of household products

Currently there are no frame formulations available for household products, but they are included in the 2009 proposed Regulation that will repeal and replace the current Directive 98/8/EC concerning the placing of biocidal products on the market which is scheduled to come into force on 1 January 2013.

The current practice is to indicate the chemical types and the concentrations of the ingredients for the following ranges; <5%, 5-25%, 15-30% and >30%. The ingredient concentration of a specific chemical type varies between manufacturers for similar products.

Common household cleaning products (see table 6, Annex III), most frequently cited in poisonings, are dishwashing and laundry detergents, toilet cleaners and bleaches (Wyke et al. 2009). Sodium hypochlorite, sodium hydroxide, alcohols and hydrogen peroxide were often cited in poisonings. Individually, these chemicals have a mild to low order of acute toxicity, e.g. surfactants have low acute toxicity of >2,000 mg/kg bodyweight in oral rat studies, with the exception of linear alkylbenzene sulphonates that have a toxicity of 1,500 mg/kg bodyweight. In mixtures, the combined action of the different types of surfactants may exacerbate the toxic effects of each other and also other ingredients present in low concentrations by increasing cell membrane permeability. However, as a rule of thumb, the Material Safety Data Sheets (MSDS) of the finished household product indicate a toxicity of >2,000 mg/kg bodyweight with an emetic dose of ~500 mg/kg bodyweight. Generally, pH, contact time, physical state, amount ingested, tritrable acid and alkaline reserve of the finished product are the most critical factors. Many of the chemicals are classified irritant or corrosive, due to either high or low pH.

Considering the main ingredients used in cosmetics and household chemical products and the substances involved in poisoning reported by poison centres or published papers (Lamireau et al. 1997, Lambert et al. 2000, Madden 2008, Madsen et al. 2001), the SCCS considers that the following substances should be considered as potential harmful ingredients after accidental ingestion:

- Corrosive substances such as acetic acid, sulphuric acid, hydrochloric acid, sodium bisulphate, sodium hypochlorite, sodium hydroxide and sodium phosphate.
- Some surfactant (depending on types and/or concentration).
- Alcohols and glycols such as ethanol, isopropanol and butyl glycol.
- Essential oils such as pine oil, wintergreen oil and camphor.

The toxicity of these substances will be briefly described in the Annex IV. Discussion of all potentially toxic ingredients used in cosmetic or household products is beyond the scope of this opinion.

10. CURRENT SAFETY MEASURES

The DeNaMic report suggested that serious toxicity following exposure to household chemical consumer products is unusual, largely because of a range of risk management measures that have been instituted in the last 30 years (Wyke et al. 2009).

Such measures include modification of packaging and labelling, and substituting chemicals with a lower toxicity profile. However, certain types of products can still cause severe poisoning, such as those containing high concentrations of acid or alkaline ingredients (e.g. former household dishwasher products and oven cleaners) or alcohols and glycols, such as anti-freeze and windscreen wash (Wyke et al. 2009).

Children

Accidental ingestion and its adverse effects on children have been reduced through safer formulation, packaging and storage. This has relied on:

- Education of parents and caregivers about the risks and how to protect children.
- Legislation to prevent unsuitable containers (e.g. containers that are normally used to store food or drinks) being used to store harmful substances; and to make packaging around harmful substances resistant to tampering by children.
- Replacement of toxic substances by less toxic agents.

Most techniques proposed to control childhood poisoning involve some sort of physical restraint which prevents the child accessing the harmful substance. Child resistant packaging is one of the best documented successes in preventing the unintentional poisoning of children (WHO 2008a). In England and Wales, unintentional poisoning deaths of children aged under the age of 10 years fell steadily from 151 per 100,000 in 1968 to 23 per 100,000 in 2000 (WHO 2008a). This reduction was largely as a result of the introduction of child-resistant packaging. However, none of these techniques have proven to be totally effective or without undesirable side effects.

Another possible approach of poison prevention may be to reduce the attractiveness of the product by appropriate design of packages and labels (Schneider 1977). "Low attraction" shapes have been recommended for containers of harmful substances. Labelling containers with warning stickers showed no deterrent effect in children at risk aged less than 6 years (WHO 2008a, Wyke et al. 2009). It has even been suggested that in some cases, warning labels may attract children (Wyke et al. 2009).

Blister packs (non-reclosable packaging), used for some medicines in tablet or capsule form, may reduce the dose ingested and may be less likely to be harmful than having access to the full bottle of the comparable liquid form. The addition of bittering agents is another method of stopping children from consuming significant quantities of harmful substances. Some controlled studies have shown that this approach may be useful, but in real situations its effectiveness seems to be more questionable (see section 8.3).

Thus, Rodgers and Tenenbein (1994) recommended that the use of aversive agents must not be a substitute for other preventive measures, such as child-resistant closures. Despite limited safety data and the utter absence of data showing that denatonium benzoate or other aversive agents decreases either unintentional or suicidal poisoning severity, their use continues to be advocated.

In conclusion, the most effective way to prevent children coming into contact with a poison is to remove the poison itself. Harmful substances may be replaced by other substances with a lower toxicity having a similar intended effect.

Elderly

In its Annual Report (Cases of Poisoning Reported by Physicians in 2001), the BgVV emphasised the problem of accidental ingestion by elderly and disoriented persons. In parallel, a corresponding press release was issued (BfR 2002).

In the context of the press release, 12,000 information leaflets in the German, Turkish, Russian, Serbian/Croatian and Polish languages were distributed to hospitals and chronic care institutions.

Between 1995 and 2002, the number of cases of severe health impairment after ingestion of products containing surfactants in the age groups over 65 years increased to 15 including as many as 13 deaths. In 2003 and 2004, however, no severe cases were reported to the BfR, possibly as a consequence of appropriate instructions given to nursing and cleaning staff (BfR 2002).

11. OPINION

This opinion assesses only the risk from accidental ingestion of food-resembling or child-appealing cosmetic and liquid household products by consumers, specifically children and the elderly.

1. What are the elements of a product which are likely to increase the probability for confusion with foodstuffs or that make a product more child-appealing? If possible, a ranking of such elements should be given.

(a) Elements of CPRF

Consumer products resembling food (CPRF) are a sub-set of consumer products, such as cosmetics and liquid household products, which possess a colour, shape, packaging, imagery, taste, flavour or other characteristic that resembles food and could be accidentally ingested by children or the elderly. Although examples of food-resembling characteristics of products can be given, there are no studies that tested directly whether the likelihood of poisoning or ingestion with regard to cosmetics and liquid household products increases, given that the characteristics are present. Nevertheless, the above-mentioned characteristics can serve as proxies to evaluate whether products are more or less food-resembling, until more specific data are available.

(b) Elements of CAP

Child-appealing products (CAP) can also be defined as a sub-set of normal consumer products that are appealing to children by design or presentation and may therefore be consumed by children by mistake. There is an overlap between CPRF and CAP (e.g. some consumer products resembling food may be particularly child-appealing), but the two categories are not identical. It should be noted, however, that the appeal of a product for children cannot be defined objectively, but only in relative terms (this is different to CPRF, where it is possible to describe the extent to which a product imitates a food by comparing it to that food). Children can be attracted to nearly anything within their reach, depending on the number and type of other attractors in their environment, their situational and dispositional inclination to explore, and many other factors.

Research shows that children have a preference for sweet, fatty and fruity tastes and odours. Children also prefer product packages that display familiar cartoon or other characters from TV. There is no evidence for stable colour preferences in children up to 5 years of age, and results on product colour preferences in children generally seem to be highly dependent on the type of product and choice set of colours used. To the best of our knowledge, there is also no evidence that the shape or consistency of cosmetics and liquid household products make such a product relatively more child-appealing, or that the presence of product labels or warnings will have an effect on children up to 6 years old.

The use of bittering agents as “aversives” has been advocated as a possible method of preventing toxic ingestions by children. Some controlled studies have shown that this approach may be useful, but in real situations its effectiveness seems to be more questionable.

These characteristics of CAP were mainly identified in studies about children's food preferences. There are no studies, for any of the characteristics mentioned, that tested children's preferences or the likelihood of ingestion with regard to cosmetics and liquid household products. Thus, to the best of our knowledge, there are no data available that show directly that, for instance, cosmetics with a sweet smell, strong colours or cartoon characters displayed on the packaging are ingested more often than others. Nevertheless, the above mentioned characteristics can serve as proxies to evaluate whether products are more or less child-appealing, until more specific data are available. In particular, more systematic research should be carried out on children's reactions to non-food products to better understand how children may react in front of a package and label design.

(c) Ranking

A ranking of the characteristics is not possible, given that there are no data available that allows for a direct comparison of the impact of the features on the risk of poisoning or ingesting the product.

However, in order to be able to better compare products and product designs with regard to their food-resembling or child-appealing properties, a simple summary score for each of the characteristics mentioned above could be obtained. A product that has a food-resembling shape, colour and smell, with a packaging that displays food-imagery, is probably more likely to be mistaken for a food than one that has only a food-resembling colour. Similarly, a product that displays cartoon characters on the package, tastes and smells sweet is probably more child-appealing than a product that just tastes sweet. However, given the limited data basis, and given that the appeal of a product for children cannot be defined objectively, both CPRF and CAP scores would have to be interpreted cautiously and only have heuristic value until more systematic research is available.

2. *What are the inherent properties and attributes of chemical consumer products that may cause or contribute to adverse health effects upon ingestion?*

The common household cleaning products, most frequently cited in poisonings, are dishwashing and laundry detergents, toilet cleaners and bleaches. Sodium hypochlorite, sodium hydroxide, alcohols and hydrogen peroxide were the substances most frequently cited in poisonings.

Injury following ingestion is dependent on both the concentration and the pH of the agent. Tissue contact time, which is related to the physical corrosive properties, is also a determinant in the extent of injury. The corrosivity is primarily determined by the pH of the product formulation. In addition, physical state (liquid/solid), viscosity, and concentration are also important.

<u>The most harmful ingredients are:</u>

- Corrosive substances such as acetic acid, nitric acid, sulphuric acid, hydrochloric acid, sodium bisulphate, sodium hypochlorite and sodium hydroxide.
- Surfactant (depending on types and concentration).
- Alcohols and glycols such as ethanol, isopropanol and butyl glycol.
- Essential oils such as pine oil, wintergreen oil and camphor.

<u>The hazardous properties of the formulations are:</u>

- pH: Single acute exposure to pH >9 or <3. Liquids with a pH of less than 2 are considered to be extremely corrosive. <u>Highly alkaline products, like liquid drain cleaners</u>, also hold a high risk for injury.

- Viscosity: When the product is acidic and the viscosity low, it may cause or enhance damage to the gastro-intestinal tract. When the product is alkaline and the viscosity high, regurgitation increases the chances of lung damage by aspiration due to foaming potential.

There is uncertainty regarding the acute oral toxicity of mixtures of other ingredients (e.g. colorants, polymers, plasticizers). Many of these products, regardless of the acidity and viscosity, may cause gastric upset, feelings of nausea and vomiting effects after accidental ingestion.

3. What are the circumstances under which exposure to food-resembling or child-appealing chemical consumer products will pose a serious risk to the health and safety of consumers, in particular to children and elderly people, taking into account e.g. volume ingested, taste of the product etc.? In which circumstances may such a risk materialise?

Research on the possible causes for accidental ingestions and poisonings in children between 6 months and 6 years of age is limited, and there are no specific data on CPRF and CAP. However, the available research suggests that three main factors are likely to contribute to increased exposure:

1) Low socio-economic status: The variable most frequently correlated with poisonings is socio-economic status (SES). There are many variables related to SES, for instance family income, education, employment status, stress at home, absence of parent and social support. Low SES is a strong predictor of observed home hazards, unsafe childcare practices, fatal unintentional injuries and, to a lesser extent, of nonfatal injuries. Unemployment and homes needing repair, in particular, appear to be risk factors for unintentional injuries of children at home. However, although SES is the best studied predictor of different injury risks, even affluent families do not undertake safety practices all the time, and most of the variation in the number of safety practices, for instance, is not explained by SES. Thus, further research is needed in this area.
2) Inadequate supervision: Several studies showed that reduced supervision of children may increase the risk of exposure and subsequent accidental poisoning. However, direct evidence linking supervision to child injury is scarce and more research is needed to assess the independent contribution of this factor.
3) Low risk perception: Single studies suggest that low parental risk perception may increase exposure to poisoning hazards in the home, but evidence on the role of this factor is mixed and more research is needed.

Research on the possible causes for accidental ingestions and poisonings in the elderly is scarce. Factors such as reduced olfactory and gustatory perceptions, impaired vision, disorientation or reduced availability of supervision or help are discussed as factors that are likely to increase the risk for accidental ingestions and poisonings, but more research is needed, and there are no specific data on CPRF.

Available information from poisoning centres concerning accidental ingestion of cosmetics and liquid household products indicate that in most cases such ingestions are not serious and the effects are transient. Rare circumstances leading to serious outcomes include large amounts of a product being ingested, toxicity of the product and vulnerable members of the population (elderly and children). However, the limited data on accidental ingestion of CPRF and CAP indicate that there are only rare incidents of serious health risks.

4. What are the most common adverse health effects observed in humans if such products are ingested?

The majority of accidental ingestions reported in children were not serious (death rate reported in around 0.026% of the intoxicated children). For example, in the UK, less than 5% of all exposures to household chemical consumer products resulted in symptoms.

Only limited data are available on adverse health effects of accidental ingestion of CPRF and CAP. On the basis of the available data from poison centres on the adverse health effects by accidental ingestion of cosmetics and liquid household products, it has been observed that initial symptoms reported by parents, whose children were admitted a paediatric emergency care unit, were mainly gastrointestinal (vomiting, abdominal pain,) or neurological (impaired consciousness, hypotonia, ataxia, seizure), although cutaneous (rash), respiratory (dyspnoea, cough) or dysphagia were also reported in some children. Aspiration of vomited material may damage the lung tissue, particularly the alveoli due to the acidity of the stomach content. Such material can, on its own, cause inflammation of the lung tissue, but this is usually transient. However, if the vomited material contains accidentally ingested xenobiotics, such as surfactants and emulsifiers, chemical pneumonia may develop as a result of further inflammation and damage of the lung tissue. This can also be induced by aromatic oils as their low viscosity increases the chance of inhalation rather than swallowing. Chemical pneumonia is a particular problem with children and the elderly and has resulted in deaths. Exposure to corrosive substances may also be of concern since minimal ingestion can cause severe oesophagogastric burns.

Similar effects are seen in the elderly but sometimes these are exacerbated by underlying health status (see Annex II).

For children, no fatalities are reported for CPRF and CAP ingestions. In addition, only rare, adverse severe health effects as a result of CPRF and CAP ingestions are reported. These effects are the exacerbation of the symptoms listed above, or consequences of the treatment used. For the elderly, there are a few case histories reported as either serious adverse health effects or fatalities.

Since many accidental ingestions cause mild symptoms of gastric irritation, it is thought that there is substantial under-recording and under-reporting of these incidents.

Additional recording from poison centres, describing in a systematic way circumstances leading to accidental ingestion of household products and cosmetics, should be useful for evaluating future trends and the impact of management measures.

This opinion addresses liquid products ingested by accident, other routes of exposure such as inhalation and skin contact, or exposure to solid materials such as toys or decorative products, are not considered.

12. MINORITY OPINION

Not applicable

13. COMMENTS RECEIVED DURING THE PUBLIC CONSULTATION

A public consultation on this opinion was opened on the website of the EU non-food Scientific Committees from 20 December 2010 to 11 February 2011.

In total, 7 contributions were received from public authorities and other stakeholders.
Each submission was reviewed by the Working Group and appropriate modifications were introduced into the opinion to take account of relevant comments. The literature has been updated with relevant publications. The opinion, however, remained essentially unchanged.

Detailed explanations of the way the comments received were treated by the SCCS are provided in the explanatory notes published together with this opinion.

14. REFERENCES

Amitai Y, Bentur Y, Lifshitz M, Fainmesser P, Applebaum D, Waisman Y, et al. Poison exposure in children before Passover. Isr Med Assoc J 2000; 2:142-4.

Bateman DN. Household products. Medicine 2003; 31:52-3.

Berk LE. Developmental Psychology. [in German] (Entwicklungspsychologie). 3rd ed. Munich: Pearson Education; 2005.

Berk LE. Child Development. 8th ed. Boston: Pearson Education; 2009.

Berning CK, Griffith JF and Wild JE. Research on the effectiveness of denatonium benzoate deterrent to liquid detergent ingestion by children. Fundam Appl Toxicol 1982; 2:44-8.

Bertleff W, Baur R, Gümbel H, Welch M. Weakly foaming surfactants. [in German] (Schaumarme Tenside). SÖFW-Journal 1997; 123:222-33.

Betalli P, Falchetti D, Giuliani S, Pane A, Dall'Oglio L, de Angelis GL, et al. Caustic ingestion in children: is endoscopy always indicated? The results of an Italian multicenter observational study. Gastrointest Endosc 2008; 68:434-9.

BfR. BgVV- Pressedienst 11/2002. Ärztliche Mitteilungen bei Vergiftungen nach §16e Chemikaliengesetz; 2002. Bundesinstitut für Risikobewertung. Available from: URL: http://www.bfr.bund.de/cm/238/aerztliche_mitteilungen_bei_vergiftungen_2002.pdf (accessed 6 December 2010).

Birch LL. Development of food acceptance patterns in the first years of life. Proc Nutr Soc 1998a; 57:617-24.

Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. Pediatrics 1998b; 101 (Suppl 3):539-49.

Birch LL. Development of food preferences. Annu Rev Nutr 1999; 19:41-62.

Botma M, Colquhoun-Flannery W, Leighton S. Laryngeal oedema caused by accidental ingestion of Oil of Wintergreen. Int J Pediatr Otorhinolaryngol 2001; 58:229-32.

Brook MP, McCarron MM, Mueller JA. Pine oil cleaner ingestion. Ann Emerg Med 1989; 18:391-5.

Chan TY. Potential dangers from topical preparations containing methyl salicylate. Hum Exp Toxicol 1996a; 15:747-50.

Chan TY. The risk of severe salicylate poisoning following the ingestion of topical medicaments or aspirin. Postgrad Med J 1996b; 72:109-12.

CIRP. Final report on the safety assessment of Laureths –4 and –23. Cosmetic Ingredient Review Program; 1983, Vol. 2, No 7.

CIRP. Final report on the safety assessment of benzalkonium chloride. Cosmetic Ingredients Review Program; 1989, Vol. 8, No. 4.

CIRP. Final report on the safety assessment of cocamidopropyl betaine. Cosmetic Ingredient Review Program; 1991, Vol. 10, No. 1.

CIRP. Final report on the safety assessment of cetrimonium chloride, cetrimonium bromide, and steartrimonium chloride. Cosmetic Ingredients Review Program; 1997, Vol 16, No. 3.

COLIPA and EAPCCT. Cosmetic Frame formulations; January 2000. Available from: URL: http://colipa.eu/publications-colipa-the-european-cosmetic-cosmetics-association/guidelines.html?view=item&id=22 (accessed 18 November 2010).

Council of Europe. Plants used in cosmetics - Volume III: Potentially harmful components; 2006. Available from: URL: http://book.coe.int/EN/popupprint.php?PAGEID=36&lang=EN&produit_aliasid=1982 (accessed 6 December 2010).

Cooke LJ, Wardle J. Age and gender differences in children's food preferences. Br J Nutr 2005; 93:741-6.

Crome P. What's different about older people. Toxicology 2003; 192:49-54.

Cubbin C, Smith GS. Socioeconomic inequalities in injury: Critical issues in design and analysis. Annu Rev Public Health 2002; 23:349-75.

Dal Santo JA, Goodman RM, Glik D, Jackson K. Childhood unintentional injuries: Factors predicting injury risk among preschoolers. J Pediatr Psychol 2004; 29:273-83.

Desel H and Wagner R. Poisoning Risk Caused by Cleaning Products and Detergents. Clinical Toxicology 2010; 48:269

Desel H, Ebbecke M, Wagner R. Poisoning Risk Caused by Cosmetic Products. Clinical Toxicology 2010; 48:288Doty RL, Shaman P, Applebaum SL. Smell identification ability: changes with age. Science 1984; 226:1441-3.

Eldridge DL, Van Eyk J, Kornegay C. Pediatric Toxicology. Emerg Med Clin North Am 2007; 15:283-308.

Elmadfa I, Meyer AL. Body compositions, changing physiological functions and nutrient requirements of the elderly. Ann Nutr Metab 2008; 52(Suppl 1):2-5.

Elliott C. Assessing 'fun foods': nutritional content and analysis of supermarket foods targeted at children. Obes Rev 2008; 9:368-77.

Eriksson M, Larsson G, Windbladh B, Zetterström R. Accidental poisoning in pre-school children in the Stockholm area. Acta Pediatr Scand Suppl 1979; 275:96-101.

Eriksson M, Larsson G, Winbladh B, Zetterström R. Accidental poisoning in pre-school children in the Stockholm area. Medical, psychosocial and preventive aspects. Acta Pædiatrica 2008; 68:275.

Ervin ME, Manske MG. Petroleum distillates and turpentine. In: Haddad LM, Winchester J, editors. Clinical management of poisoning and drug overdose. 2nd ed. Philadelphia: WB Saunders; 1990. p.1177–86.

Falk-Filipsson A, Hanberg A, Victorin K, Warholm M, Wallén M. Assessment factors - applications in health risk assessment of chemicals. Environ Res 2007; 104:108-27.

Gilman AG, Rall TW, Nies AS, Taylor P, editors. Goodman and Gilman's The Pharmacology Basis of Therapeutics. 8th ed. New York: Pergamon Press; 1990. p.649-53.

Glik DC, Greaves PE, Kronenfeld JJ, Jackson KL. Safety hazards in households with young children. J Pediatr Psychol 1993; 18:115-31.

Gloxhuber C, Künstler K. Anionic surfactants: Biochemistry, Toxicology, Dermatology. 2nd ed. Vol 43. New York: Marcel Dekker Inc.; 1992.

Goldfrank LR. Hydrocarbons. In: Goldfrank LR, editor. Goldfrank's toxicologic emergencies. 5th ed. Norwalk: Appleton & Lang; 1994. p.1231-44.

Guyodo G, Danel V. Childhood poisoning data from the French Poison Control and Toxicovigilance Centres (2002). [in French] (Intoxications de l'enfant: données des centres antipoison et de toxicovigilance (CAP-TV) français (2002)). Thérapie 2004; 59:589-93.

Hahn A, Begemann K, Burger R, Hillebrand J, Meyer H, Preußner K. Cases of Poisoning Reported by Physicians in 2006. Centre for Documentation and Assessment of Poisonings at the Federal Institute for Risk Assessment (BfR) 13th Report; 2006.

Hahn A, Begemann K, Burger R, Friedemann M, Hillebrand J, Meyer H, et al. Cases of Poisoning Reported by Physicians. Centre for Documentation and Assessment of Poisonings at the Federal Institute for Risk Assessment (BfR), 15th Report; 2008.

Hancock HE, Fisk AD, Rogers WA. Comprehending product warning information: age-related effects and the roles of memory, inferencing and knowledge. Hum Factors 2005; 47:219-34.

Hansen SR, Janssen C, Beasley VR. Denatonium benzoate as a deterrent to ingestion of toxic substances: toxicity and efficacy. Vet Hum Toxicol 1993; 35:234-6.

Hapgood R, Kendrick D, Marsh P. How well do socio-demographic characteristics explain variation in childhood safety practices? J Public Health Med 2000; 22:307-11.

Hillier LM, Morrongiello BA. Age and gender differences in school-aged children's appraisals of injury risk. J Pediatr Psychol 1998; 23:229-38.

Hilmer SN. ADME-tox issues for the elderly. Expert Opin Drug Metab Toxicol 2008; 4:1321-31.

Howrie DL, Moriarty R, Breit R. Candy flavoring as a source of salicylate poisoning. Pediatrics 1985; 75:869-71.

HSDB (Hazardous Substances Data Bank). Isopropanol http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@DOCNO+116

Hutchings JB. Expectations and the food industry: the impact of colour and appearance. New York: Kluwer; 2003.

IPCS. Linear alkylbenzene sulfonates and related compounds. Environmental Health Criteria 169. World Health Organization. Geneva, Switzerland; 1996.

Isomaa B. Absorption, distribution and excretion of [^{14}C]CTAB, a quaternary ammonium surfactant in the rat. Fd Cosmet Toxicol 1975; 13:231-7.

Jones DV, Work CE. Volume of a swallow. Am J Dis Child 1961; 102:427.

Katrivanou A, Lekka NP, Beratis S. Psychopathology and behavioural trends of children with accidental poisoning. J Psychosom Res 2004; 57:95-101.

Kauffman RE, Banner W, Berlin CM. Camphor revisited: focus on toxicity. Pediatrics 1994; 94:127-8.

Kay M, Wyllie R. Caustic ingestions in children. Curr Opin Pediatr 2009; 21:651-4.

Khine H, Weiss D, Graber N, Hoffman RS, Esteban-Cruciani N, Avner JR. A cluster of children with seizures caused by camphor poisoning. Pediatrics 2009; 123:1269-72.

Klein-Schwartz W, Oderda GM. Poisoning in the elderly. Epidemiological, clinical and management considerations. Drugs Aging 1991; 1:67-89.

Lambert H, Manel J, Gabrion I. Poisoning by household products. [in French]. Rev Prat 2000; 50:365-71.

Lamireau T, Llanas B, Deprez C, el Hammar F, Vergnes P, Demarquez JL, et al. Severity of ingestion of caustic substance in children. [in French] (Gravité des ingestions de produits caustiques chez l'enfant). Arch Pediatr 1997; 4:529-34.

Lamireau T, Rebouissoux L, Denis D, Lancelin F, Vergnes P, Fayon M. Accidental caustic ingestion in children: is endoscopy always mandatory? J Pediat Gastroenterol Nutr 2001; 33:81-4.

Lamireau T, Llanas B, Kennedy A, Fayon M, Penouil F, Favarell-Garrigues J-C, et al. Epidemiology of poisoning in children: a 7-year survey in a paediatric emergency care unit. Eur J Emerg Med 2002; 9:9-14.

Lavin J, Lawless HT. Effects of colour and odor on judgements of sweetness among children and adults. Food Qual Prefer 1998; 9:283-9.

Lawless HT, Hammer LD, Corina MD. Aversions to bitterness and accidental poisonings among preschool children. J Toxicol Clin Toxicol 1982; 19:951-64.

Léon F, Couronne T, Marcuz MC, Köster EP. Measuring food liking in children: A comparison of non verbal methods. Food Qual Prefer 1999; 10:93-100.

Liebelt EL, Shannon MW. Small doses, big problems: a selected review of highly toxic common medications. Pediatr Emerg Care 1993; 9:292-7.

Liem DG, Westerbeek A, Wolterink S, Kok FJ, De Graaf C. Sour taste preferences of children relate to preference for novel and intense stimuli. Chem Senses 2004; 29:713-20.

Litovitz TL, Schmitz BF, Matyunas N, Martin TG. 1987 annual report of the American Association of Poison Control Centers National Data Collection System. Am J Emerg Med 1988; 6:479–515.

Litovitz TL, Klein-Schwartz W, Dyer KS, Shannon M, Lee S, Powers M. 1997 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 1998; 16:443-97.

Love JN, Sammon M, Smereck J. Are one or two dangerous? Camphor exposure in toddlers. J Emerg Med 2004; 27:49-54.

Madden MA. Responding to pediatric poisoning. Nursing 2008; 38:52-5.

Madsen T, Buchardt Boyd H, Nylén D, Rathmann Pedersen A, Petersen GI, Simonsen F. Environmental and Health Assessment of substances in household detergents and cosmetic detergent products, Environmental Project No. 615; 2001. Available from: URL: http://www2.mst.dk/udgiv/publications/2001/87-7944-596-9/pdf/87-7944-597-7.pdf (accessed 18 November 2010).

Marchi AG, Renier S, Valent F. Poisoning in first year of age. A multicentre study. [in Italian] (Avvelenamenti nel primo anno di vita. Studio multicentrico). Minerva Pediatr 2004; 56:541-6.

Marshall D, Stuart M, Bell R. Examining the relationship between product package colour and product selection in preschoolers. Food Qual Prefer 2006; 17:615-21.

Massey CC, Schulman JD. Acute ethanol toxicity from ingesting mouthwash in children younger than age 6, 1989-2003. Pediatr Dent 2006; 28:405-9.

Mayhorn CB, Nichols TA, Rogers WA, Fisk AD. Hazards in the home: using older adults' perceptions to inform warning design. Inj Control and Saf Promot 2004; 11:211-8.

McKenzie LB, Ahir N, Stolz U, Nelson NG. Household cleaning product-related injuries treated in US emergency departments in 1990-2006. Pediatrics 2010; 126:1-9.

Miller AM, Levsky ME, Masneri DA, Borys D. Fabuloso: a cleaning product that tastes and smells good enough to drink. Pediatrics 2006; 118:848-9.

Mofenson HC, Greensher J, Caraccio TR. Ingestions considered nontoxic. Emerg Med Clin North Am 1984; 2:159-74.

Morrongiello BA. Caregiver supervision and child-injury risk: I. issues in defining and measuring supervision; II. Findings and directions for future research. J Pediatr Psychol 2005; 30:536-52.

Morrongiello BA, Howard AW, Rothman L, Sandomierski M. Once bitten, twice shy? Medically-attended injuries can sensitise parents to children's risk of injuries on playgrounds. Inj Prev 2009; 15:50-4.

National Poisons Information Service Annual Reports (UK); 2003/2004-2006/2007. Available from: URL: http://www.hpa.org.uk/Publications/ChemicalsPoisons/NationalPoisonsInformationServiceAnnualReports/ (accessed 6 December 2010).

Oram N, Laing DG, Hutchinson I, Owen J, Rose G, Freeman M, et al. The influence of flavor and color on drink identification by children and adults. Dev Psychobiol 1995; 28:239-46.

Parsons SO, Seminara JL, Wogalter MS. A summary of warnings research. Ergonomics in Design 1999; 7:21-31.

Payne HA. A bitter solution to safety. Chemistry and Industry 1988; 22:721-3.

Ratnapalan S, Polylitsina Y, Tan LH, Roifman M, Koren G. Measuring a toddler's mouthful: toxicologic considerations. J Pediatr 2003; 142:729-30.

Renwick AG, Dorne JL, Walton K. An analysis of the need for an additional uncertainty factor for infants and children. Regul Toxicol Pharmacol 2000; 31:286-96.

Riffat F, Cheng A. Pediatric caustic ingestion: 50 consecutive cases and a review of the literature. Dis Esophagus 2009; 22:89-94.

Riordan M, Rylance G, Berry K. Poisoning in children 4: Household products, plants, and mushrooms. Arch Dis Child 2002; 87:403-6.

Roberto CA, Baik J, Harris JL, Brownell KD. Influence of licensed characters on children's taste and snack preferences. Pediatrics 2010; 126:88-93.

Rodgers GC Jr, Tenenbein M. The role of aversive bittering agents in the prevention of pediatric poisonings. Pediatrics 1994; 93: 68-9.

Salzman M, O'Malley RN. Updates on the evaluation and management of caustic exposures. Emerg Med Clin North Am 2007; 25:459-76.

Scheuplein R, Charnley G, Dourson M. Differential sensitivity of children and adults to chemical toxicity: I. Biological basis. Regul Toxicol Pharmacol 2002; 35:429-47.

Schneider KC. Prevention of accidental poisoning through package and label design. J Consumer Res 1977; 4:67-74.

Schwartz C, Issanchou S, Nicklaus S. Developmental changes in the acceptance of the five basic tastes in the first year of life. Brit J Nutr 2009; 102:1375-85.

Schwenk M, Gundert-Remy U, Heinemeyer G, Olejniczak K, Stahlmann R, Kaufmann W, et al. Children as a sensitive subgroup and their role in regulatory toxicology: DGPT workshop report. Arch Toxicol 2003; 77:2-6.

SFT. Surfactants in laundry detergents and cleaning agents - health assessment. [in Norwegian] (Tensider i vaske- og rengjøringsmidler – helsefarevurdering). Report No. 91:06B. Statens Forurensningstilsyn. Oslo, Norway; 1991.

Shaw MT. Accidental poisoning in children: A psychosocial study. N Z Med J 1977; 85:269-72.

Silbert JR, Frude N. Bittering agents in the prevention of accidental poisonings: children's reactions to denatonium benzoate (Bitrex). Arch Emerg Med 1991; 8:1-7.

Soori H. Developmental risk factors for unintentional childhood poisoning. Saudi Med J 2001; 22:227-30.

Speer F. Allergy to methyl salicylate. Ann Allergy 1979; 43:36-7.

Story M, French S. Food advertising and marketing directed at children and adolescents in the US. Int J Behav Nutr Phys Act 2004; 1:3.

Tohda G, Sugawa C, Gayer C, Chino A, McGuire TW, Lucas CE. Clinical evaluation and management of caustic injury in the upper gastrointestinal tract in 95 adult patients in an urban medical center. Surg Endosc 2008; 22:1119-25.

Ülger B. Packages with cartoon trade characters versus advertising: An empirical examination of preschoolers' food preferences. J Food Prod Market 2009; 15:104-17.

UN. Youth and the United Nations – Frequently asked questions; 2010. Available from: URL: http://www.un.org/esa/socdev/unyin/qanda.htm (accessed 18 November 2010).

USCPSC: Final Report: Study of Aversive Agents. Washington, DC: US Consumer Product Safety Commission; 2002.

Vancura EM, Clinton JE, Ruiz E, Krenzelok EP. Toxicity of alkaline solutions. Ann Emerg Med 1980; 9:118-22.

Villa A, Cochet A, Guyodo G. Poison episodes reported to French poison control centers in 2006. [in French] (Les intoxications signalées aux centre antipoison français en 2006). Rev Prat 2008; 58:825-31.

VWA. Marktverkenning en onderzoek naar reikwijdte van het warenwetbesluit imitatieproducten. Rapport nr. ND05o100-01. Voedsel en Waren Autoriteit; April 2006. Available from: URL: www.vwa.nl (accessed 18 November 2010).

Waasdorp Hurtado CE, Kramer RE. Salicylic acid ingestion leading to esophageal stricture. Pediatr Emerg Care 2010; 26:146-8.

Walsh LM, Toma RB, Tuveson RV, Sondhi L. Color preference and food choice among children. J Psychol 1990; 124:645-53.

Watson WA, Litovitz TL, Rodgers GC Jr, Klein-Schwartz W, Reid N, Youniss J, et al. 2004 Annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2005; 23:589-666.

Whitford F, Brown A, Ballentine L, Field B, Pearson K, Blessing A. Children and Poisoning. Seconds Matter. PURDUE Pesticide Programs, Coordinator, Purdue Pesticide Programs; 2001. Available from: URL: http://www.btny.purdue.edu/pubs/PPP/PPP-53.pdf (accessed 18 November 2010).

WHO. 10 facts on ageing and the life course; 2007. Available from: URL: http://www.who.int/features/factfiles/ageing/en/index.html (accessed 18 November 2010).

WHO. Chapter 6 – Poisoning. In: Peden M, Oyegbite K, Ozanne-Smith J, Hyder AA, Branche C, Fazlur Rahman AKM, et al., editors. World report on child injury prevention. Geneva, Switzerland: World Health Organization; 2008a. p.123-42. Available from: URL http://www.who.int/violence_injury_prevention/child/injury/world_report/en/ (accessed 18 November 2010).

WHO. Older persons in emergencies: An active ageing perspective. Geneva, Switzerland: World Health Organization; 2008b. Available from: URL http://www.who.int/ageing/publications/emergency/en/index.html (accessed 18 November 2010).

WHO. Definition of an older or elderly person; 2010a. Available from: URL: http://www.who.int/healthinfo/survey/ageingdefnolder/en/index.html (accessed 18 November 2010).

WHO. World Health Statistics. WHO, Geneva. Geneva, Switzerland: World Health Organization; 20010b. Available from: URL Retrievable from: http://www.who.int/whosis/whostat/EN_WHS10_Full.pdf (accessed 18 November 2010).

WHO. Newborns, infants and children; 2010c. Available from: URL: http://www.who.int/child_adolescent_health/topics/prevention_care/child/en/index.html (accessed 18 November 2010).

Will KE, Lorek EJ, Sabo CS, Kidd DG. Measuring injury risk perceptions: feasibility of a Risk Estimation Scale. Am J Health Behav 2009; 33:639-49.

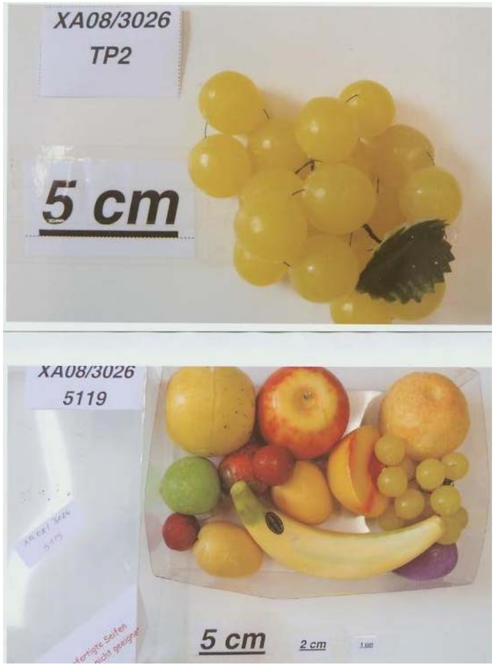
Wyke S, Duarte-Davidson R, Tempowski J, Heinemeyer G, Heiland A, Reudiger T, et al. Description of the nature of the accidental misuse of chemicals and chemical products (DENaMic). Final Project Report; 2009.

Young A. Ageing and physiological functions. Philos Trans R Soc Lond B Biol Sci 1997; 352:1837-43.

Zeiger E, Anderson B, Haworth S, Lawlor T, Mortelmans K, Speck W. Salmonella mutagenicity tests: III. Results from the testing of 255 chemicals. Environ Mutagen 1987; 9 (Suppl 9):1-109.

ANNEXES

Annex I: Pictures of consumer products resembling food and/or having child-appealing properties



Soap

Bath soap

Annex II: Case reports involving children and CPRF or CAP

From January 1 2006 to April 20 2006, the Texas Poison Centre reported 104 human exposures relating to the ingestion of "Fabuloso", a cleaning product that tastes and smells good (Miller et al. 2006). Among these 104 cases, 92 were considered accidental ingestions; 60 cases involved children <6 years old. Fabuloso is a household cleaning product that is a minor gastrointestinal irritant and unlikely to cause any major morbidity or mortality. It could be considered as a product that might easily mislead consumers into unintentionally ingesting this product.

Case reports involving the elderly and CPRF

Severe health impairment with a lethal outcome in an 82-year-old female temporally related to the ingestion of ca. 100 ml of a liquid detergent

The Rostock University Hospital reported a case of severe health impairment with a lethal outcome in a female patient aged 82 years who, at her home, had ingested ca. 100 ml of a liquid detergent containing ca. 25% surfactants. Although the course of her illness had been fairly uncomplicated, the patient died after 11 days from aspiration pneumonia associated with septicaemia. This woman suffered initial senile dementia and was in need of care. (http://www.bfr.bund.de/cm/255/cases_of_poisoning_reported_by_physicians_2006.pdf)

Accidental intake of a cleaning agent mistaken for orange juice by an elderly patient

A 69-year-old patient accidentally ingested a sip of a cleaning agent, having mistaken the product for orange juice because of its colour and the package design which resembled that of a food product. The label showed a picture of oranges and the word "Orange" appeared in the product name.

In addition to surfactants, the cleaner involved contains a relatively high share of synthetic essential oils.

The patient saw a doctor because of a burning sensation in his mouth and throat. No cough was observed. The attending physician consulted a poison control centre to assess the risk and initiate appropriate treatment. Because the cleaner contained a surfactant, the patient was administered an agent to prevent foam formation. In addition, he was recommended to drink fluid. Findings from the physical examination were non-significant, and admission to hospital was not required.

An enquiry at the Berlin poison emergency telephone service revealed that the product concerned had been involved in only one case of poisoning so far. (http://www.bfr.bund.de/cm/255/cases_of_poisoning_reported_by_physicians_2007.pdf)

Death after ingestion of surfactants: A particular risk for patients suffering from dementia

In a state of mental confusion, a 79-year-old male ingested ca. 200 ml of a detergent containing surfactants at his home. Despite cardiopulmonary resuscitation (CPR), the patient died at the hospital within 60 minutes, from lung oedema. (http://www.bfr.bund.de/cm/255/cases_of_poisoning_reported_by_physicians_2005.pdf)

Death of an elderly female due to aspiration of a dishwashing detergent and gastric contents

An 80-year-old patient accidentally ingested an unknown quantity of a manual dishwashing detergent containing surfactants. Because of its orange colour and the picture of oranges shown on the package label, the patient had in all likelihood mistaken the detergent for a food product, most probably orange juice. The following morning, she was found dead in her bed by her husband. There were no indications of a suicide risk in her history. The patient had been suffering from senile dementia. According to the forensic physicians, an aspiration of gastric contents containing the dishwashing detergent ingested had been the cause of death. The formation of foam from the surfactant ingested had presumably caused vomiting which led to the aspiration of gastric contents containing the dishwashing detergent. (http://www.bfr.bund.de/cm/255/cases_of_poisoning_reported_by_physicians_2008.pdf)

Cases of CPRF poisoning in children

The risk of mistaking consumer goods for foods as a result of their misleading appearance has recently been identified by the BfR in two cases of poisoning by another product. The product in question was an orange liquid with packaging resembling a beverage bottle, and the word "orange" in the product name. The product was accidentally ingested by an elderly person and a child. (http://www.bfr.bund.de/cm/255/cases_of_poisoning_reported_by_physicians_2008.pdf)

Annex III: Tables 3, 4, 5 and 6

Table 3: Some developmental milestones of young children up to 6 years of age (taken from a larger list of milestones in Berk 2005, see also Berk 2009)

Age	Motoric development	Cognitive development	Emotional/social development
7 – 12 months	- Can sit, crawl and walk - Uses refined pincette grip - Perception of deepness and patterns improve	- Shows intentional and goal directed behaviour - Finds objects hidden in one place - Imitates behaviour of adults with objects - Solves simple problems by analogy	- Shows clear attachment pattern with main supervising person - Uses caregiver as secure base for explorations
13 - 18 months	- Improved coordination of walking - Manipulates little objects with improved coordination	- Experiments with objects in a "trial and error" way - Finds objects hidden in more than one place - Categorizes objects - Speaks first words	- Follows simple orders - Recognizes itself in a mirror - Participates in play with parents and siblings
19 – 24 months	- Jumps, running and climbs - Manipulates little objects with good coordination	- Ability to find an object moved while out of sight - Plays as-if games - Categorizes objects more effectively - Knows about 200 words	- Self-conscious emotions emerge (1-2 years) - Self-control appears - Categorizes itself and others on the basis of age, sex, bodily features and being good or bad
2 years	- Balance and walking coordination improve - Running, jumping, throwing and catching develop - Skilful use of spoons	- As-if play is getting more complex - Recognition memory is well developed - Understands the difference between internal cognitive and external physical events	- A self-concept and self-esteem start to develop - Cooperation and instrumental aggression appear - Understands causes, effects and expressions of basic emotions
3 – 4 years	- Running, jumping, throwing and catching improve - Uses tricycle - Uses scissors	- Basic understanding of causality in familiar situations - Classifies familiar objects hierarchically - Is aware of some significant written symbols - Counts small amounts of objects	- Emotional self-regulation is improving - Play becomes more interactive - Differentiates moral rules, social conventions and personal affairs
5 – 6 years	- Jumping, throwing and catching mature - Can bind shoe strings, write names and make complex drawings	- Ability to differentiate between appearance and reality improves - Remembering and memory improves - Simple additions and subtractions - Knows about 10,000 words and uses many complex grammatical forms	- Ability to interpret and predict emotional reactions of others improves - Has taken up many morally relevant rules and behaviours

Table 4: Physiological changes in the elderly (Crome 2003, Hilmer 2008, Litovitz et al. 1998*)*

- Decrease in total body mass
- Change in body composition (decreased proportion of body water, increased proportion of body fat)
- Small reduction in serum albumin
- Decreased liver blood flow, size and hepatic clearance
- Decreased renal function
- Diminished skin mucous membrane, gastrointestinal barriers,
- Diminished organ function,
- Depressed immune function
- Reduced olfactory and gustatory perception

Table 5: Indicative categories and chemical ingredients of cosmetic products (based on frame formulations)

Category of chemicals	**Sample ingredients**
Anionic surfactants	sodium laureth sulfate, sodium/ammonium/TEA lauryl sulfates
Amphoteric surfactants	ethoxylated sorbitan esters, cocamide MIPA, ceteth-20, ethoxylated fatty alcohols
Non-ionic surfactants	fatty acid polyglycolethers, fatty alkanolamides, sodium dodecylbenzenesulfonate
Cationic surfactants and polymers	polyquaternium-7, polyquaternium-24, distearyldimonium chloride
Foam boosting agents	cocamide MIPA, linoleamide DEA
Hair conditioning agents	silicone derivatives, cysteine derivatives, cellulose derivatives, fatty acid esters
Bath salts	sodium carbonate, sodium bicarbonate, sodium sesquicarbonate, sodium chloride
Oils	vegetable and mineral e.g. liquid paraffin, waxes and fatty alcohols, including lanolin and lanolin derivatives, zea mays
Humectants	glycerin, propylene glycol, PEG
Emulsifying agents	glyceryl stearate, PEG stearate, sorbitan sequioleate & stearate, ethers of oleyl alcohol
Silicones	dimethicone, cyclomethicone
Viscosity controlling agents	carbomer, cellulose-ethers
Emollients	isopropyl myristate, fatty alcohols
Abrasives	polyethylene
Additional ingredients	vitamins, antioxidants, plant extracts
Fragrances	Essential oils
UV filters	Zinc oxide, TiO_2
Preservatives, antimicrobials	Benzyl Benzoate Methylchloroisothiazolinone, Methylisothiazolinone
Solvents	ethyl acetate, butyl acetate, toluene, diacetone, ethanol, isopropanol, PPG-2 butyl ether
Resins, polymers	nitrocellulose, acrylates copolymer, phthalic anhydride/butyl benzoic acid/propylene glycol copolymer
Plasticisers	dibutyl phthalate, triethyl citrate

Table 6: Chemicals in food- resembling/child-appealing household products (based on ingredient listing of common household products)

Category of chemicals	**Sample Ingredients**
Anionic surfactants	Alcohol ethoxysulphates, Linear Alkyl Sulphonate, Alkyl ether sulphate, sodium laurate, monoethanolamine oleate,
Amphoteric surfactants	Cocamidopropyl hydroxysultaine, Cocamidopropyl betaine, *cocamide MIPA*
Non-ionic surfactants	Alcohol ethoxylates, fatty acid polyglycolethers, fatty alkanolamides, sodium dodecylbenzenesulfonate
Cationic surfactants and polymers	Esterquat, diquaternium ethoxysulfatepolymerlaureth-9 polyquaternium-7, polyquaternium-24
Bleaching agent	Sodium hypochlorite, sodium perborate
Alcohols	Ethanol, Isoproponol
Process aids	Calcium chloride, calcium formate, sodium formate, diethylene glycol, ethanolamine, polyethylene glycol, propylene glycol, propylene glycol butyl ether, TAED (tetraacetylethylenediamine)
Dirt capturers	Borax, Citric Acid, DTPA
Polymer	Polyethyleneimine ethoxylate
Silicones	dimethicone
Anti-foam agent	Polydimethylsiloxane
Enzyme	Amylase, cellulase, mannanase, pectinase, protease
Brighteners	Disodium diaminostilbene disulfonate, disodium distyrylbiphenyl disulfonate
pH neutralizer	Sodium hydroxide
pH modifier	Formic acid, Tartrate
Chelator	diethylenetriamine pentaacetate, sodium
Preservatives, antimicrobials	Benzisothiozoline, methylthiozoline
Colorants	Numerous
Chlorine scavenger	Ammonium chloride

Annex IV: Toxicity of potential harmful ingredients

Ingestion of corrosive substances

Corrosives are the main category of agents responsible for severe accidental poisonings from household chemical consumer products (Lambert et al. 2000, Lamireau et al. 1997).

Despite limitations, the available data suggest that corrosive ingestions occur most frequently in children younger than 6 years, with the majority of cases occurring in children between 12 and 48 months old. Corrosive ingestions remain a significant cause of paediatric morbidity (Kay and Wyllie 2009) but there are only 2.3% fatalities (Watson et al. 2005).

Table 7: Alkalis and acids frequently found in household products

Alkalis	**Products**
Sodium hydroxide	sodium hydroxide products, drain cleaner, oven cleaner,
Acids	**Products**
Sulfuric acid Hydrochloric acid Sodium bisulfate Sodium hypochlorite Acetic Acid Nitric acid	Drain cleaner Toilet bowl cleaner House bleach (low concentration) Descalers

The most common symptoms following a corrosive ingestion are dysphagia, drooling, feeding refusal, retrosternal pain, abdominal pain and vomiting. The presence of three or more symptoms is an important predictor of severe oesophageal burns.

Symptoms involving the airway are less common although dyspnea is associated with a high risk of significant gastrointestinal injury (Betalli et al. 2008). Severe symptoms and complications reported following a corrosive ingestion include haemolysis, disseminated intravascular coagulation, renal failure, liver failure, perforated viscera, peritonitis, mediastinitis and death.

Most accidents were due to ingestion of caustic alkaline substances and this is clearly attributable to the widespread domestic use of alkaline products. Bleach and caustic soda were the most frequent causes of accidents some years ago, but more recently, the incidence of accidents involving dishwasher powders, detergents and drain cleaners has increased.

Injury following ingestion is dependent on both the concentration and the pH of the agent. Tissue contact time, which is related to the physical corrosive properties, is also a determinant in the extent of injury (Salzman and O'Malley 2007). The corrosivity is primarily determined by the pH of the product/chemical but titratable alkalinity/acidity reserve, physical state (liquid/solid), viscosity, and concentration are also important (Lamireau et al. 2001). The ingestion of a strong alkali results in liquefaction necrosis, which is associated with deep penetration of the lining of the bowel and may result in perforation.

Alkalis are usually odourless and tasteless. This may result in consumption of a large volume in cases of accidental ingestion. Alkalis with a pH between 9 and 11, including many household detergents, rarely cause serious injury following ingestion. Ingestion of even small quantities of an alkali with a pH above 11 may cause severe burns (Vancura et al. 1980).

Acid ingestions represent approximately 15% of ingestion in children. Ingestion of strong acidic fluids with a pH of less than 3 have the highest risk for possible injury (Salzman and O'Malley 2007) and can result in coagulation necrosis. Liquids with a pH of less than 2 are considered to be extremely corrosive and have the greatest risk of injury (Waasdorp Hurtado and Kramer 2010). Their low viscosity and specific gravity result in rapid transit to the stomach, and gastric injury is more common than oesophageal injury, especially in the pre-pyloric area. Gastric injury following ingestion may result in gastric outlet obstruction or perforation frequently in the area of the gastric antrum or pilorous. Gastric perforation in association with an acid ingestion may be life threatening as frequently there is multivisceral organ injury and rapid clinical decompensation.

Because strong acids are very bitter, large-volume ingestion is limited to suicide attempts and rarely occurs accidentally. The volume of ingested material could not be accurately determined, although estimates from patients or witnesses ranged from 10 to 500 ml. If such acid corrosive chemicals were ingested accidentally, the amounts ingested were typically much smaller than alkaline chemicals as patients would recognize the unpleasant taste and stop drinking or vomit immediately (Tohda et al. 2008).

Ingestion of Essential Oils

Essential oils have been used as a common cold remedy in medicine, as indoor air fresheners or conditioners in the household, for aromatherapy, in stain removers or other cleaning agents, in cosmetics, and also in industry, for example as a fat solvent.

The toxicity of individual essential oils varies. Lethal doses stated in the past were 50–500 mg/kg body weight. Recent toxicological data for this group is sparse, but certain oils (pine oil, wintergreen oil, camphor) have been identified in poisonings.

Pine Oil

Pine oil, a mixture of isomeric secondary and tertiary cyclic terpene alcohols, is a common component of cleaning solutions and is found in numerous household cleaning preparations. Its popularity stems from its disinfectant and deodorant properties as well as its ability to remove dirt and grease and its pleasant aroma. In addition, pine oil is reported to have a pleasant taste. Hydrocarbon ingestion (with pine oil and similar substances) accounted for 66,000 toxic exposures in 1997. Death due to pine oil ingestion was rare and was reported to be approximately 0.02% (two people). Both cases were the result of attempted suicide (Litovitz et al. 1988, Litovitz et al. 1998).

Particular concerns about ingestion of such solutions arise in the growing population of elderly and demented patients.

Pine oil has low viscosity and high volatility (Goldfrank 1994). The low viscosity of pine oil contributes to aspiration, while high volatility contributes to inhalation injury and asphyxiation. However, cleaning solutions contain additives that increase viscosity and decrease the volatility of pine oil, thus reducing its toxic risks.

Following ingestion or aspiration, pine oil is readily absorbed into the systemic circulation.

The systemic effects of pine oil primarily involve the central nervous system (CNS), gastrointestinal tract and respiratory systems (Ervin and Manske 1990). Within 90 minutes of clinically significant ingestions, most patients develop CNS depression and/or pneumonitis (Brook et al. 1989).

Wintergreen oil

Wintergreen oil is a strongly aromatic with a sweet woody odour. It is composed of methyl salicylate (approx. 98%) (Council of Europe 2006). Oil of Wintergreen may be used as a topical ointment or medicated oil for the relief of musculoskeletal pain and common colds (Botma et al. 2001, Chan 1996a). One teaspoon (5 ml) of Oil of Wintergreen is equivalent to approximately 7000 mg of salicylate or 21.7 adult aspirin tablets (Chan 1996b). Oil of Wintergreen is an important cause of salicylate poisoning in many western countries and has an appreciable morbidity and mortality (Gilman 1990).

Methyl salicylate is rapidly absorbed from the gastrointestinal tract. The onset of clinical symptoms is rapid, usually within 2 hours of ingestion, but salicylate blood levels can be detected as early as 15 minutes after ingestion (Liebelt and Shannon 1993). Clinical features are identical to those observed following poisoning with other salicylates. The major toxic effects may be grouped as gastrointestinal, neurological, haematological, metabolic and acid–base disturbances (Chan 1996a). Other systemic effects such as severe urticaria and angioedema following the use of methyl salicylate containing mints, toothpaste or liniments have been reported in patients with a past history of nasal allergy or aspirin hypersensitivity (Speer 1979). In salicylate poisoning, the dose ingested and the age of the patient are the most important factors determining the severity (Chan 1996b).

Generally, ingestion of salicylates at doses larger than 150 mg/kg body weight can produce toxic symptoms such as tinnitus, nausea, and vomiting. Salicylate sensitivity is a common adverse reaction to the methyl salicylate in oil of wintergreen; it can produce allergy-like symptoms or asthma. Ingestion of as little as 4 ml in a child can be fatal (Howrie et al. 1985).

Salicylates have also been linked with Reye’s syndrome in children and can cause retention of salt and water as well as acute reduction of renal function in patients with congestive heart failure or hypovolemia (Gilman et al. 1990).

Camphor

Camphor, originally a product from the bark of the camphor tree Cinnamommum camphora, is synthesized and is a common ingredient in many ointments. Toxicity usually results from oral ingestion, although there are reports of toxicity from dermal and inhalation exposure in a toddler. Signs and symptoms of camphor ingestion occur primarily as a result of its direct mucosal irritation and central nervous system (CNS) effects. Gastrointestinal effects include oropharyngeal irritation and burning with nausea and vomiting. Camphors’s CNS effects range from coma and apnea to agitation, anxiety, hallucinations, hyper-reflexia, myoclonic jerks, and seizures (Eldridge et al. 2007, Love et al. 2004).

Ingestion of 2g camphor generally produces dangerous effects in adults; ingestion of 0.7-2.0 g camphor has proven fatal in children (Kauffman et al. 1994, Love et al. 2004). Seizures are a known complication of camphor toxicity and are reported after ingestion, inhalation, and dermal exposure. In 1982, after the reports of several incidents of camphor toxicity in young children, often involving camphorated oil products (20% camphor), the US Food and Drug Administration (FDA) limited the camphor content of common cold preparations to 11% and restricted the sale of camphorated oil (Khine et al. 2009). The Council of Europe recommended limiting the concentration of camphor in cosmetic products and a ban of camphor in cosmetic products for children below the age of 3 years (Council of Europe 2006).

Ingestion of surfactants

Most detergents are formulated products containing surfactants which remove dirt, stains, and soil from surfaces or textiles. Surfactants consist of a hydrophobic and a hydrophilic component and have the ability to change the surface properties of water. Surfactants are grouped according to their ionic properties in water:

- Anionic surfactants have a negative charge;
- Non-ionic surfactants have no charge;
- Cationic surfactants have a positive charge; and
- Amphoteric surfactants have positive or negative charge dependent on pH.

Surfactants have low oral acute toxicity. In general, surfactants have an irritating effect on mucous membranes. Foaming is the predominant problem. Manifestations may also include vomiting, abdominal pain, flatulence and diarrhoea. In rare cases, vomiting or formation of considerable amounts of foam in the mouth involve an aspiration risk. Aspiration may have taken place if a persistent cough and respiratory complaints are observed. For healthy children and adults, ingredients containing surfactants such as shower gels, bubble baths, shampoos, all-purpose cleansers or liquid detergents do not pose a particular risk. But they may be life threatening or even fatal for elderly persons because they are more prone to foam aspiration after vomiting, which may result in severe pulmonary manifestations and a fatal outcome (Hahn et al. 2008).

The toxicity studies performed with animals show that, in general, surfactants are of low toxicity.

Anionic surfactants (AS) are readily absorbed from the gastrointestinal tract after oral administration. AS are extensively metabolized in various species resulting in the formation of several metabolites. The major site of metabolism is the liver (Gloxhuber and Künstler 1992, IPCS 1996). The acute toxicity of AS in animals is considered to be low after skin contact or oral intake.

Non-ionic surfactants are widely used in consumer products such as laundry detergents, cleaning and dishwashing agents, and personal care products. By volume, the most important non-ionic surfactants are included in the very versatile group of alcohol ethoxylates (AE) and alcohol alkoxylates (AA).

AE are used in many types of consumer and industrial products such as laundry detergents, all-purpose cleaning agents, dishwashing agents, emulsifiers, and wetting agents. AA are used as weakly foaming and foam-mitigating surfactants in household cleaning agents, dishwashing agents and cleaning agents designed for the food industry (Bertleff et al. 1997). In general, AE are readily absorbed through the gastrointestinal mucosa of rats. AE are quickly eliminated from the body through the urine, faeces, and expired air (CIRP 1983, SFT 1991). The LD_{50} values after oral administration to rats range from about 1-15 g/kg body weight indicating a low to moderate acute toxicity.

By volume, the most important **cationic surfactants** in household products are the alkyl ester ammonium salts that are used in fabric softeners. Alkyltrimethylammonium chlorides (ATMAC) and, to a minor extent, alkyltrimethylammonium bromides (ATMAB) are primarily used in cosmetic products including hair conditioners, hair dyes and colours, and other hair and personal care preparations. Studies after oral administration showed that only small amounts were found in the urine and in the blood plasma, indicating poor intestinal absorption (Isomaa 1975).

The acute oral toxicity of alkyltrimethylammonium salts is somewhat higher than the toxicity of anionic and non-ionic surfactants. This may be due to the strongly irritating effect which cationic surfactants exhibit on the mucous membrane of the gastrointestinal tract (SFT 1991). Dialkyldimethylammonium chlorides (DADMAC) are used as antistatic agents in cosmetic products including hair conditioners and hair colouring preparations and as biocides in industrial and household cleaning agents. No specific data describing the health effects of dialkyldimethylammonium salts were obtained. However, many of the properties described for alkyltrimethylammonium salts also apply to dialkyldimethylammonium salts, although these are generally less irritating than the corresponding alkyltrimethylammonium salts (CIRP 1997).

Alkyldimethylbenzylammonium chlorides (ADMBAC) and bromides (ADMBAB) are used in cosmetic products including hair conditioners and hair colouring preparations. Besides being surfactants and antistatic agents, the alkyldimethylbenzylammonium compounds function as biocides in various cosmetic and detergent products. The biocidal properties are utilized, when ADMBAC are added to all-purpose or specialized cleaning agents. No specific toxicokinetic studies were identified for ADMBAC. Different homologues of ADMBAC showed a moderate acute toxicity in experiments with rats and mice (CIRP 1989, Zeiger et al. 1987).

ADMBAC are included in Annex 1 of the list of dangerous substances of Council Directive 67/548/EEC with the following classification: C8-18 ADMBAC are classified as Harmful with the risk phrases R21/22 (Harmful in contact with skin and if swallowed) and Corrosive (C) with R34 (Causes burns).

Amphoteric surfactants are surface-active compounds with both acidic and alkaline properties and include two main groups, i.e. betaines and real amphoteric surfactants based on fatty alkyl imidazolines. Amphoteric surfactants are used in personal care products (e.g. hair shampoos and conditioners, liquid soaps, and cleansing lotions) and in all-purpose and industrial cleaning agents.

Betaines are primarily used in personal care products such as hair shampoos, liquid soaps, and cleansing lotions. Other applications include all-purpose cleaning agents, hand dishwashing agents, and special textile detergents. Amphoteric surfactants are easily absorbed in the intestine and are excreted partly unchanged via the faeces without being accumulated in the organism (SFT 1991). Betaines generally have a low acute toxicity, e.g. LD_{50} values for cocoamidopropylbetain (30% solution) by oral administration have been determined to 4,910 mg/kg body weight in rats (CIRP 1991).

Ingestion of alcohol

Alcohols are used as solvents in cosmetic and household detergents. Short chain alcohols are used in liquid laundry detergents and liquid dishwashing agents in order to ensure solubility and stability of the products.

Ethanol

Ethanol is added to mouthwash to make non-polar ingredients such as essential oils water-soluble and to kill bacteria associated with bad breath and plaque formation.

Mouthwashes have great potential to be overingested by children because they are made to look enticing, taste good, and are present in most homes. Although fatalities from ethanol-containing mouthwash are rare, ingestion by children occurs frequently, sometimes leading to nonlethal but toxic reactions (Massey and Schulman 2006). Mouthwashes contain denaturants (generally minimally toxic bittering agents) to discourage consumption. Children can ingest large amounts of mouthwash (from big containers) for their body weight and achieve high blood-ethanol levels very quickly (Massey and Schulman 2006). This is particularly true for the American market where mouthwashes may be sold in large containers, up to 2 litres.

Most serious cases of poisoning involve ingestion of large quantities of products containing a lower concentration of ethanol, for example, mouthwash, rather than the ingestion of concentrated solutions, which are more irritant (Riordan et al. 2002).

Children who have ingested the equivalent of 0.4 ml/kg pure ethanol should be observed for 4 hours. Ingestion of 1.2 ml/kg pure ethanol requires hospital admission (Riordan et al. 2002). Symptoms of ethanol toxicity vary with blood concentration, which is a function of the quantity ingested, ingestion rate, body weight and the individual's physiological tolerance to ethanol. The lethal dose of ethanol for adults is 5-8 g/kg body weight (Massey and Schulman 2006). Children exhibit many of the same symptoms as adults but irritability is often the first noticeable sign of acute ethanol toxicity (Massey and Schulman 2006). The lethal dose of ethanol for children is 3 g/kg body weight (Massey and Schulman 2006) and doses as small as 0.6 g/kg body weight have been seen to induce toxic reactions in a small child (Massey and Schulman 2006).

Isopropanol

Isopropanol is about twice as toxic as ethanol, although it generally has a low acute toxicity as measured by its oral rat LD_{50} of 5,000 mg/kg. It increases the toxicity of chlorinated solvents if exposure occurs simultaneously (HSDB 1999).

Ingestion of bittering agents

The use of bittering agents as "aversives" has been advocated as a possible method of preventing toxic ingestions by children. The most commonly recommended agent denatonium benzoate (Bitrex) was found to have an unpleasant and bitter taste at concentrations as low as 50 ppb in liquid products (Berning et al. 1982, Hansen et al 1993, Lawless et al. 1982, Payne 1988, Silbert and Frude 1991). Acute toxicity of the aversive agents does not appear to be a major issue. Many of the bittering agents, including sucrose octaacetate and denatonium benzoate, have a low toxicity at levels used for aversion. However, none of these agents have a complete toxicity profile (USCPSC 2002). Rodgers and Tenenbein (1994) reviewed the published data on efficacy and toxicity of denatonium benzoate when used in cleaning products etc. and concluded that denatonium benzoate seems to be safe when used at low concentrations.

Sucrose octaacetate (SOA) is also used as an alcohol denaturant. Although higher concentrations of SOA are needed for bitterness compared to denatonium salts (10 ppm of SOA versus 0.05 ppm for denatonium benzoate), the toxicity of SOA is very low. Acute toxicity studies conducted with rats and rabbits failed to estimate a lethal dose; an oral dose as high as 45 g/kg produced no-compound-related adverse effects.