Survey of chemical substances in consumer products

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Survey of chemical substances in toothbrushes

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Preface

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The project *Survey and migration of chemical substances in toothbrushes* **is a part of the Danish Environmental Protection Agency's (E P A) joint efforts in connection with survey of chemical substances in a number of consumer products. The project is divided into four phases.**

Phase 1 "Survey of the market for toothbrushes, incl. which materials the toothbrushes consist of, together with an assessment showing how often toothbrushes are being replaced, in average". Phase 1 has been carried out by Danish Technological Institute, Centre for Plastics Technology, by M.Sc. Nanna Svendsen in the period May - June 2003.

Phase 2 "Qualitative analysis showing which substances are being released to artificial saliva from selected toothbrushes, together with an examination of the substances released when scratching the hard part of the toothbrush". Phase 2 has been carried out by Danish Technological Institute, Centre for Plastics Technology, by M.Sc. Søren F. Pedersen, Chemical Technology by Cand. Scient. Jakob Toft Mossing and Chemical Technology by Cand. Scient. Nils Bernth in the period June - July 2003.

Phase 3 "Screening for possible harmful effects from substances, which are migrated/released from toothbrushes". Phase 3 has been carried out by Danish Technological Institute by Cand. Scient. Ole Chr. Hansen in the period June - July 2003.

Phase 4 "Quantitative analysis of selected substances released during normal use of toothbrushes, together with an assessment of health effects of the released substances and the health risk at daily use of toothbrushes". Phase 4 has been carried out by Danish Technological Institute, Chemical Technology by Cand. Scient. Jakob Toft Mossing and Cand. Scient. Nils Bernth and Cand. Scient. Ole Chr. Hansen in the period August - September 2003.

The project was followed by a steering committee consisting of:

Shima Dobel, Danish Environmental Protection Agency
Annette Orloff, Danish Environmental Protection Agency
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Summary and conclusions

As a part of the Danish Environmental Protection Agency's survey of chemical substances in a number of consumer products, knowledge of which substances are contained in and migrates from the toothbrushes is requested. The project *Survey and migration of chemical substances in toothbrushes* **is carried out in four phases. The examination includes survey of the market, qualitative and quantitative analyses and health evaluation of possible harmful effects from substances, which migrate from the toothbrushes.**

Phase 1 concerns examination of the toothbrush market in Denmark. This information has been procured from four sources:

- **Search via the Internet**
- **Purchase of toothbrushes in groceries and specialist shops**
- **Through contact to suppliers and producers, whose identity appeared from the packaging**
- **Through contact to a range of relevant shops and organisations**

Approx. 8 million toothbrushes are sold in Denmark yearly, of these approx. 80% are one of the following three brands:

- **Aquafresh**
- **Jordan**
- **Colgate**

They are primarily sold in groceries throughout the country.

According to the producers' information most of the common toothbrushes are made of thermoplastic, e.g. polypropylene, SAN (Styrene-Acrylic Nitrile-copolymer) or other styrene copolymers. The bristles are made of polyamide. Furthermore, they inform that the dye used when manufacturing the toothbrushes is approved for foodstuff use, and they all have a policy not to use materials or packaging containing phthalates.

Phase two deals with qualitative analyses of constituents in toothbrushes. The following analyses have been carried out:

- **Screening by means of FT-IR for identification of antioxidants, types of polymer, phthalates and - to a certain extent - inorganic pigments of all 26 types of purchased toothbrushes**
- **GC-MS and ICP-MS for analysis and identification of antioxidants and organic pigments in order to evaluate the migration of substances from the toothbrush to artificial saliva on 10 types of toothbrushes chosen on the basis of information gained in Phase 1 and in the screening by means of FT-IR**
- **Determination of calcined residue followed by an ICP-screening for identification of the possible inorganic pigments on the same 10 chosen types of toothbrushes, on which GC-MS analyses have been carried out**

The results of the FT-IR-screening showed that the majority of the toothbrush

handles are made from polypropylene, homopolymer or copolymer. At some of the handles smaller amounts of additives are identified in the polypropylene material. The brushes of all the examined toothbrushes are made of polyamide, which are evaluated to be identical - according to the FT-IR analysis.

At a subsequent GC-MS screening of 10 chosen toothbrushes almost 80 different compounds are identified. Of special interest for further quantification were 1-methyl-2-pyrrolidinone (toothbrush M-005), carvone (B-004 and B-005), 2-methyl-benzene sulphonamide (B-004 and B-006), 4-methyl-benzene sulphonamide (B-004 and B-006) and benzyl butyl phthalate (M-005). The selection is based on the classification of the substances and description of effects that potentially may cause concern to the consumer, if the concentration of the migrated substances from the toothbrushes is found to be too high.

Compared with the results from the FT-IR screenings, at which a high amount of chalk has been identified, a high amount of calcium has been found at the ICP-MS-screenings. In most cases also a high amount of magnesium has been identified. The deposit of calcium and/or magnesium in the toothbrushes probably derives from the use of chalk or dolomite as fillers. Titanium has been found in most cases and derives from titanium dioxide used as a white pigment. A high amount of aluminium derived from aluminium oxide could serve the same purpose or may have an opal effect.

In some cases a high amount of copper, nickel and zinc and traces of manganese has been found. These elements presumably derive from metal thread or otherwise for fastening the brushes on the toothbrush or from the mechanical parts in electrical toothbrush heads.

Phase 3 deals with screening for possible harmful effects from substances, which migrate from the toothbrushes. A screening has been made of the substances, which have been identified by the GC-MS-analyses. The screening is based on a literature survey in order to secure that the substances focused on at the quantitative analyses are the most relevant.

It was suggested to select 5 toothbrushes for a quantitative analysis. The suggested selection was based on the identified substances and the found descriptions of effects, which might be important for the consumer's use of the toothbrushes.

Phase 4 deals with the quantitative analysis of substances migrated from the toothbrush during use under normal conditions (these substances are selected based on the results found in the first 3 phases of this project), and the evaluation of health effects of migrated substances and health risks from daily use of toothbrushes.

The health assessment was based on a specific quantitative analysis of the amount of the following migrated (released) substances from the 5 selected toothbrushes:
2-Butoxy-ethanol
2-Butoxyethyl acetate
1-Butoxy-2-propanol
Benzyl butyl phthalate
Carvone
N,N-dimethylacetamide
2-Methyl-benzene sulphonamide

4-Methyl-benzene sulphonamide
1-Methyl-2-pyrrolidinone
Naphthalene
1,1,2,2-Tetrachlorethane
3,5,5-Trimethyl-1-hexanol
Nickel

Based on the measured concentrations of the 13 substances found migrated from the 5 toothbrushes and by the use of the suggested exposure scenario, it was concluded that none of the substances were found in concentrations exceeding the used values for tolerable daily intake. These reference values were based on established or suggested ADI, TDI or RfD values.

The evaluation does not comprise sensitive consumers (allergic or the like), who might experience problems using some of the toothbrushes.

Overall it was concluded that the evaluated migrated substances do not constitute a health risk for the consumer of toothbrushes.

Sammenfatning og konklusioner

Som et led i Miljøstyrelsens kortlægning af kemiske stoffer i en række forbrugerprodukter ønskes viden om, hvilke stoffer der indgår i og afgives fra tandbørster. Projektet *Kortlægning og afgivelse af kemiske stoffer i tandbørster* **er udført i fire faser. Undersøgelsen omfatter kortlægning af markedet, kvalitative og kvantitative analyser samt sundhedsmæssig vurdering af eventuelle sundhedsskadelige effekter fra stoffer, som afgives fra tandbørster.**

Fase 1 omhandler undersøgelse af tandbørstemarkedet i Danmark. Disse oplysninger er fremskaffet ad fire veje:

- **Søgning via Internettet**
- **Indkøb af tandbørster i dagligvare- og specialbutikker**
- **Ved kontakt til leverandører og producenter, hvis identitet fremgik af emballagen**
- **Ved kontakt til et udvalg af relevante foreninger og organisationer**

Der sælges ca. 8 mio. tandbørster i Danmark om året, ca. 80% af dem er et af følgende tre mærker:

- **Aquafresh**
- **Jordan**
- **Colgate**

De forhandles primært i dagligvarebutikker landet over.

Producenterne oplyser, at de fleste almindelige tandbørster er lavet af termoplast, f.eks. polypropylen, SAN (Styren-acrylnitril-copolymer) eller andre styrencopolymerer. Børstehårene er af polyamid. De oplyser endvidere, at de farvestoffer, der er brugt ved fremstilling af tandbørster, er godkendt til fødevarebrug, og de har alle en politik om ikke at anvende materialer eller emballage indeholdende phthalater.

Fase 2 omhandler kvalitative analyser af indholdsstoffer i tandbørster. Der er foretaget følgende analyser:

- **Screening vha. FT-IR for identifikation af antioxidanter, polymertyper, phthalater og i nogen udstrækning uorganiske farvestoffer på alle 26 indkøbte tandbørstetyper.**
- **GC-MS for analyse og identifikation af antioxidanter og organiske farvestoffer til vurdering af afgivelse af stoffer fra tandbørsten til kunstigt spyt på 10 tandbørstetyper udvalgt på baggrund af oplysninger fundet i fase 1 og i screeningen vha. FT-IR.**
- **Bestemmelse af gløderest efterfulgt af en ICP-MS-screening til identifikation af de mulige uorganiske pigmenter fra de 10 udvalgte tandbørstetyper.**

Resultatet af FT-IR screeningen viste, at hovedparten af tandbørsteskafterne er fremstillet af polypropylen, homopolymer eller copolymer. Ved enkelte af skafterne er der fundet mindre mængder additiver i polypropylen materialet.

Ved alle de undersøgte tandbørster er børsterne fremstillet af polyamid, der ud fra FT-IR analysen vurderes at være ens.

Ved en efterfølgende GC-MS screening af 10 udvalgte tandbørster findes næsten 80 forskellige forbindelser. Af disse 80 forbindelser fremhæves bl.a. fundet af 1-methyl-2-pyrrolidinon (tandbørste M-005), carvon (B-004 og B-005), 2-methyl- benzene sulphonamide (B-004 og B-006), 4-methyl-benzene sulphonamide (B-004 og B-006) og benzylbutyl-phthalate (M-005) som værende af interesse for yderligere kvantificering. Udvælgelsen er baseret på stoffernes klassifikation og be-
skrivelse af effekter, som kan være potentielt problematiske for forbrugeren, hvis afgivelsen (migrationen) af stofferne fra tandbørsterne er for stor.

Sammenholdt med resultaterne fra FT-IR screeningerne, hvor der er identificeret et højt indhold af kridt, måles tilsvarende et højt indhold af calcium ved ICP-MS screeningen foruden i mange tilfælde også et højt indhold af magnesium. Forekomsten af calcium og/eller magnesium i tandbørsterne hidrører antageligt fra anvendelsen af kridt eller dolomit som fyldstoffer. Titan er målt i hovedparten af tandbørsterne og indgår som et hvidt pigment i form af titandioxid. En tilsvarende funktion kan et højt indhold af aluminium i form af aluminiumoxid formodes at have, foruden i visse tilfælde at være anvendt med det formål at frembringe en opaliserende effekt.
I enkelte tilfælde er der påvist et højt indhold af kobber, nikkel og zink foruden spor af mangan. Disse grundstoffer må formodes at stamme fra metaltråd eller tilsvarende til fastgørelse af børsterne på tandbørsten eller fra mekaniske dele i tilfælde af mundstykker til elektriske tandbørster.

Fase 3 omhandler screening af eventuelle sundhedsskadelige effekter fra stoffer, som afgives fra tandbørster. Der er foretaget screening af de stoffer, der er identificeret ved GC-MS-analyserne. Screeningen er baseret på litteraturoplysninger og har til formål at sikre, at de stoffer, som der fokuseres på ved de kvantitative analyser, er de mest relevante.

Det blev foreslået, at der udtages 5 tandbørster til en kvantitativ analyse. Forslaget til udvælgelsen var baseret på de fundne stoffer og de fundne beskrivelser af effekter, der kan have betydning for brugerens sundhed, når tandbørsterne anvendes.

Fase 4 omhandler kvantitative analyser af stoffer, der afgives under normal brug af tandbørster (disse stoffer er udvalgt på baggrund af resultaterne i de tre første faser af projektet), samt vurdering af sundhedseffekter ved de afgivne stoffer og sundhedsrisikoen ved daglig brug af tandbørster.

Sundhedsvurderingen er baseret på en specifik kvantitativ analyse af migrerede (udvaskede) mængder af følgende stoffer fra de 5 udvalgte tandbørster:

2-Butoxy-ethanol
2-Butoxyethyl acetat
1-Butoxy-2-propanol
Benzylbutylpthahlat
Carvon
N,N-dimethylacetamid
2-Methyl-benzene sulphonamide
4-Methyl-benzene sulphonamide
1-Methyl-2-pyrrolidinon

Naphthalen
1,1,2,2-tetrachlorethan
3,5,5-Trimethyl-1-hexanol
Nikkel

Baseret på de målte koncentrationer af 13 enkeltstoffer, der er fundet udvasket af 5 hele tandbørster, og med anvendelsen af det foreslåede eksponeringsscenarie, kunne det samlet konkluderes, at ingen af enkeltstofferne optrådte i koncentrationer, der overskred de anvendte værdier for tolerabel daglig indtag. Disse referenceværdier var baseret på etablerede eller foreslåede ADI, TDI eller RfD værdier.

Der er i vurderingerne ikke taget hensyn til, at der kan være specielt følsomme forbrugere (allergikere eller lignende), der alligevel vil kunne få problemer med visse tandbørster.
Det konkluderes derfor samlet, at de vurderede stofafgivelser af tandbørster ikke medfører sundhedsrisiko for forbrugeren.

Abbreviations

ADI	Acceptable Daily Intake. Estimated intake, which is assumed not to have any adverse effects. Can be acute or chronic. Is usually based on additives in food
bw	Body weight
CAS	Chemical Abstract Service
DL	Detection level
DVN	The Danish Institute for Informative Labelling
EC	Effect concentration
EC_{50}	Median effect concentration, i.e. the concentration where effects are observed in 50% of the test animals
h	Hour(s)
LC_{50}	Median lethal concentration, i.e. the concentration where 50% of the test animals are dead
LD_{50}	Median lethal dose, i.e. the dose where 50% of the test animals are dead
LOAEL	Lowest Observed Adverse Effect Level
MAK	Maksimaler Arbeitsplatz Konzentration. Limit value for working environment defined by German working environment authorities
MOS	Margin of Safety, which is the distance between the estimated exposure and the concentration which is considered not to constitute a health risk (e.g. NOAEL)
Ni	Nickel
NOAEL	No Observed Adverse Effect Level
PBT	Polybutylterephthalate
PET	Polyethylenterephthalate
POM	Polyoxymethylene
PP	Polypropylene
PVC	Polyvinyl chloride
RD_{50}	The air concentration of a chemical substance necessary to evoke a 50% decrease in respiratory rate (Alarie 1980).
Repr.	Repro-toxic
RfC	Inhalation reference concentration. A concentration in air (e.g. $\mu g/m^3$) which is an estimate of a daily exposure by inhalation that is assumed to be without adverse effects by inhalation during a human lifetime. It is presumed that a threshold limit value exists for the toxic effect used to derive the value

RfD	Oral reference Dose, which is an estimate of a daily exposure by intake (e.g. µg/kg bw/day) that is assumed to be without adverse effects by intake during a human lifetime. It is presumed that a threshold limit value exists for the toxic effect used to derive the value
SAN	Styrene acrylonitril
SBS	Styrene-butadiene-styrene
TDI	Tolerable daily intake. Estimated as intake that is assumed not to have any adverse effects. Can be acute or chronic. Is usually based on pollutants.
TGD	Technical Guidance Document: EU guidance in risk assessment of chemicals
TLV	Threshold Limit Value relevant for the working environment. Typically a time weighted average value over 8 hours is used
TWA	Time Weighted Average

1 Introduction

1.1 Introduction

Toothbrushes are products, which are used approx. two times daily by almost all people in Denmark. Consequently, chemical substances in toothbrushes are substances, to which the consumers might be exposed, in case the substances are released. Toothbrushes are put in the mouth, and many times small children also put the wrong end of the toothbrush in the mouth and bite into and suck the toothbrush for a rather long time. The expose for chemical substances from toothbrushes takes place by ingestion through the mouth and at skin contact. The exposure can happen to all people at all ages.

It is possible to buy toothbrushes in many different designs, particularly to children. Toothbrushes for children are often designed like various small figures, and sometimes they remind of toys. Toys are defined as products, which are clearly designed and intended for playing purpose for children under 14 years. However, toothbrushes designed with figures are not immediately evaluated to be toys, as the primary purpose of the brush is to brush the teeth.

Today, it is prohibited to produce, import or sell toys and some infants' articles to children at the age of 0-3 years, if the products contain more than 0.05 weight% phthalates. In some toothbrushes plasticised PVC or printing ink containing phthalates might also occur. Consequently, in phase 2 of the examination screening for phthalates, among other things, has been carried out.

Nickel is another immediately problematic substance, which might be found in toothbrushes. Nickel constitutes a problem for the patients in the form of nickel allergy, for which reason the Ministry of Health has dictated an upper threshold limit value for nickel content of max. 0.05% Ni for dental materials for e.g. crowns of teeth and bridges. In some toothbrushes nickel is used for fixation of the bristles, and therefore a screening for Ni has also been carried out.

1.2 Purpose

The purpose of this project is to evaluate the exposure of chemical substances from toothbrushes. It has been examined, which chemical substances are used in toothbrushes, and, - in case these substances gave rise to concern – whether they were released when being used. The examination comprised children's toothbrushes, designed with figures, electrical toothbrushes and other toothbrushes. In the project the primary focus has been on toothbrushes for children.
Subsequently, a quantitative analysis of selected substances was carried out together with an assessment of health effects at the released substances and the health risk at daily use of toothbrushes.

1.3 Procedure

In Phase 1 of the project it has been examined, which toothbrushes are on the market in Denmark. Furthermore, an evaluation of the percentage distribution of the market between the producers has been made. Furthermore, it has been examined which materials they consist of, or which materials are constituents, and how often they in average are being replaced. This information has been procured from four sources:

- **Search via the Internet**
- **Purchase of toothbrushes in groceries and specialist shops**
- **Through contact to suppliers and producers, whose identity appeared from the packaging**
- **Through contact to a range of relevant shops and organisations**

In total, 26 toothbrush types have been purchased from four different dealers and from 10 different producers.

In Phase 2 of the project a screening by means of FT-IR has been carried out on all 26 purchased toothbrush types for identification of antioxidants, polymer types, phthalates and – to some extent – inorganic colouring substances. This analysis has been carried out on a scrape from the hard part of the toothbrush, partly in order to identify which substances can be released, when the teeth wear the hard part of the toothbrush, and partly in order to get information about the substances being contained in the toothbrushes, in general.

Subsequently, antioxidants and organic colouring substances have been analysed and identified by means of GC-MS on 10 toothbrushes selected on the basis of the FT-IR analyses and the results from Phase 1. An analysis method has been drawn up in order to evaluate the release of substances from the toothbrush to artificial saliva produced according to Amtliche Sammlung von Untersuchungsverfahren nach § 35 LMBG No. 82.10 1, the saliva recipe has been copied from DIN std, no. 53 160.

In order to get a complete identification of the possible inorganic pigments the calcined residue is determined followed by an ICP-MS-screening of 10 selected toothbrush types.

In Phase 3 a screening for possible harmful effects from substances, which are migrated/released from toothbrushes at the qualitative analyses has been carried out.

The purpose of the screening is to give a first impression whether harmful substances are present, in the next place to contribute to the selection of the toothbrushes to be passed on to a quantitative analysis of the chemical substances selected on the basis of the screening.

The evaluation of possible health effects has been made from classification of the chemical substances. If the substances are not or have not been classified, data from handbook-literature or Internet search have been used.

The most essential documentation used in the screening phase is: The List of Dangerous Substances (Miljøministeriet 2002), The list of undesirable substances (Miljøministeriet 2000) and WHO (IPCS). The substances, which

could not be found here, have subsequently been evaluated based on information found in recognised databases (HSDB, IUCLID). Finally, Internet search for substance names and/or CAS numbers has been used.

In Phase 4 quantification has been carried out by means of GC-MS and ICP-MS of substances, which migrated from toothbrushes selected on the basis of Phase 2 and 3. In addition to this, an evaluation of the health risk at daily use of toothbrushes has been made. This evaluation, which comprises 13 selected substances, is based on the amount of the relevant substances, the duration of the exposure and their effects.

2 Market Analysis

2.1 Market surveys

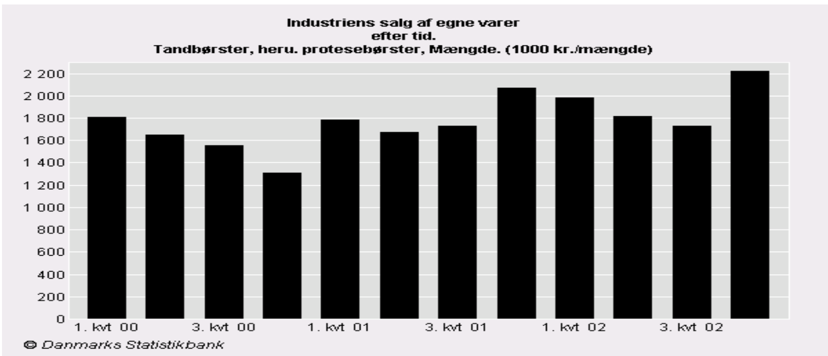
2.1.1 The Internet

In connection with this project the Internet has been used partly to form a general view of the toothbrush market and partly to form the basis of further contact to relevant companies.

2.1.2 Statistics

According to Danmarks Statistik the Industry has stated a sale of own articles of 7 Mio. toothbrushes per year in 2002 shown in Figure 2.2.1

Figure 2.2.1 The Industry's sale of own articles, toothbrushes year 2000-



The opinion-research institute ACNielsen AIM, ScanTrack informs that the market for toothbrushes in 2002 was distributed as follows:

Toothbrushes are primarily sold in groceries (Coop Danmark and Dansk Supermarked Gruppen (DSG)). A smaller amount is sold through Matas and other specialist shops.

The top 3 brands among manual toothbrushes in the grocery stores in 2002 were:

1 Aquafresh
2 Jordan
3 Colgate

Total value share 81,7%
The rest of the market is covered by Oral-B, Zendium and Tandex, among others.

The top 3 suppliers/manufacturers among manual toothbrushes in the grocery stores in 2002 were

1 GlaxoSmithKline

2 Cederroth A/S
3 Colgate-Palmolive A/S
Total value share 85,4%

The picture appears to be similar regarding the market for electrical toothbrushes.

2.1.3 The retail trade

Today, there are two big chains of groceries at the Danish market: Coop Danmark
(among others the chains of shops Kvickly, Irma, Fakta, SuperBrugsen, Dagli'Brugsen and LokalBrugsen) and DSG (among others the chains of shops Bilka, Føtex, Netto and A-Z).

Coop Danmark is Denmark's greatest member- and consumer organisation with 1.5 Mio. members, who "*work according to ethical considerations and in an ethically justifiable way. The ethics policy describes the ethical directions, which apply to Coop Danmark and affiliated companies".* This means that not only does Coop Danmark make ethical demands on their own products and employees, they also make demands to their suppliers to live up to the ethical objectives of Coop Danmark.
With regard to choice of materials and choice of packaging Coop Danmark is not in possession of any written material, but they choose their products in accordance with existing legislation. They inform that they have an internal policy not to use products and packaging containing PVC. There are only a few exceptions to this rule, and these exceptions do not concern toothbrushes.

DSG does not have a written drawn up environment- or ethics policy, but act according to the motto "common sense". This means that they follow the scientifically well-documented directions, which exist today. This makes it possible for them to make their purchases of various products according to the present directions, and it makes these directions and the product line flexible. DSG has an internal policy regarding materials and packaging. For toothbrushes their demands are among others:

- No PVC in product or packaging
- Toothbrushes must be able to withstand dipping in hot water without melting
- Toothbrushes must not break during load corresponding to normal use
- The toothbrush bristles must not fall out

DSG's own toothbrushes are subject to tests, which are designed to take into account the above-mentioned demands, and the purchased toothbrushes are subject to the same demands.

2.1.4 Producers

The various toothbrush producers have a varying amount of information on their homepages. One of the most extensive is *Oral-B,* who - besides general information regarding their assortment - also states a range of clinical examinations of their toothbrushes. There are comparative tests and clinical tests, but only little information on constituents in their toothbrushes.

There is only one producer, whose homepage gives information about constituents in their toothbrush, MAM. They inform the following concerning

their children's toothbrush: handle of polypropylene and thermoplastic elastomer, bristles of polyamide and safety ring of polyoxymethylene.

At our request the producers gave the following information about constituents in selected toothbrush types stated in Table 2.1.

Table 2.1. Index list showing acquired toothbrushes

ID no.	Material information
N-001	PP handle with thermoplastic elastomer. Polyamide bristles
N-002	PP handle with thermoplastic elastomer. Polyamide bristles
N-003	No PVC
M-001	No information
M-002	PP handle with thermoplastic elastomer. Polyamide bristles
M-003	No information
M-004	SAN handle, polyamide bristles. Fulfils DVN's demands for strength and fixation of bristles
M-005	No information
M-006	No information
M-007	PP handle
M-008	PP handle with thermoplastic elastomer
M-009	No information
K-001	PP handle
K-002	PP handle with Maxithen blue transp. colour and thermoplastic elastomer, polyamide bristles, polyoxymethylene safety ring. PET based colour
K-003	PP handle with thermoplastic elastomer. Polyamide bristles
K-004	PP handle
B-001	PP handle
B-002	PP handle
B-003	No information
B-004	PP handle with thermoplastic elastomer
B-005	PP handle with thermoplastic elastomer
B-006	PP handle with thermoplastic elastomer. Polyamide bristles
B-007	PP handle with thermoplastic elastomer
B-008	PP handle with thermoplastic elastomer. Polyamide bristles
B-009	PP handle with thermoplastic elastomer
B-010	No PVC

PP: Polypropylene, SAN: Styrene - Acryl - Nitril. PET: Polyethylene terephthalate

Generally, it is stated that all the used colouring agents are on the list of colouring agents approved for use in food, and that PVC with phthalates has not been used neither in the product nor in the packaging. Colgate also informs that there are no heavy metals in the used colouring agents.

2.1.5 Suppliers

Both Plastindustrien and the producers inform that only one brand of toothbrushes is manufactured in Denmark, Tandex. All other toothbrushes are manufactured all over the world, among others in Norway, England, Germany and USA.

2.1.6 Trade organisations

The producers inform that in the field of toothbrushes they are not affiliated to a trade organisation.

2.1.7 Organisations

Renewal of the toothbrush
Contacting the School of Dentistry and various dentist associations has not lead to procurement of any scientific documentation regarding renewal of the toothbrush at a certain time interval. Dentists inform that this is individually dependent on various parameters such as tooth position, age, time of brushing etc.

At Oral-B's homepage there is a reference to a comparative test from USA between a new toothbrush and same type of toothbrush used in a normal way for three months. This investigation partly shows that renewal of toothbrushes in USA is made after 2.5 to 6 months, partly that no statistically significant difference could be demonstrated regarding the ability of the two toothbrushes to remove plaque.

Broken toothbrushes
Some practising dentists have experienced a problem with toothbrushes, which break the handle while being used. According to the Danish Dental Association there has previously been a problem with toothbrushes from one producer, but it was one batch, which was subsequently recalled.

Previous investigations
It has not been possible to procure material regarding previous examinations concerning chemical substances in toothbrushes. None of the respondent producers or organisations is acquainted with similar examinations, just as search via the Internet was unsuccessful.

2.1.8 Legislation

One of the chemical substances, which might be problematic, and which might be found in soft PVC or printing inks in some toothbrushes, is phthalates.

The Danish Ministry of Environment and Energy has issued Statutory Order no. 151 of 15 March 1999 banning phthalates in toys for children at the age of 0-3 years and in some articles for small children due to the suspicion health effects of the substances.

In this connection the Danish EPA has worked out a list of products which must not contain phthalates. Under the point *tooth-mug and toothbrushes for small children* is stated "As a starting point these will be affected by the prohibition against phthalates, as children under 3 years might be expected to suck at these objects". Today, it is forbidden to produce, import or sell toys and articles for small children to children at the age 0-3 years, if the products contain more than 0.05 weight% phthalates.

Consequently, screening for phthalates, among others, was a part of the examination.

3 RESULTS

3.1 FT-IR screening

3.1.1 Equipment and methods

For the FTIR analyses a Nicolet Magna 550 FTIR equipment with installed optical bench has been used. The bench gathers the IR pencil of rays to approx. 2 mm in diameter.
The specimens have been cut out from brushes by means of a scalpel, from the edge of the handle and from soft material on the handle, if any.
In the case of thermoplastic materials the sample preparation has consisted of hot-pressing of approx. 2 to 5 mg of material for film with a thickness of 10 to 20 µm.
This has been analysed by screening.
In the case of non-thermoplastic materials, in this case materials from printing, the sample preparation has consisted in abrasion of a representative area, grinding with potassium bromide and finally pressing of a tablet, on which the analysis has been done. A sample amount of approx. 1 mg is used.
Interpretation of the FTIR spectra has been done partly based on experience and partly according to our reference library, among others "Hummel Polymer and Additives."
In addition to the actual material analyses, we have looked for phthalates and larger amounts of additives, e.g. antioxidants.

Mixing phthalates into plastic and polymer materials is usually done in order to achieve a softening effect, and consequently the amounts are normally relatively large, 5 to 30 weight%.
At the used preparation methods such amounts are normally easy to observe, as the detection limit is estimated to be below 1%.

In connection with antioxidants, which are added in far smaller amounts than softening components, only in the cases where over approx. 0.1 weight% is added and that the antioxidants or other additives have strong absorption bands outside the absorptions from the polymer, it will be detectable.

All types of material found on each purchased toothbrush have been analysed by FT-IR. This means that in case of toothbrushes with more colours and brush types, analyses have been made on all variants. The same procedure was used at the handle materials and possible prints of the handles.

3.1.2 Results from the FT-IR screening

Results are shown in Table 3.1 and in Encl. B.

Table 3.1 Results from the FT-IR screening

No.	Bristles	Handle	Print
N-001	Grey bristles: polyamide Black bristles: polyamide	Grey handle: polypropylene Black parts: "SBS" elastomer with a high content of chalk	No print
N-002	White bristles: polyamide Green bristles: polyamide	Purple handle: polypropylene Yellow part: Acrylic-based elastomer	Print: acrylic-based binder
N-003	White bristles: polyamide Purple bristles: polyamide	Grey handle: polypropylene homopolymer Purple parts: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder
M-001	Clear bristles: polyamide Light blue bristles: polyamide	Yellow handle: polypropylene copolymer Blue and green insert: "SBS" elastomer with a high content of chalk	Print: acrylic-based binder
M-002	Clear bristles: polyamide Light blue bristles: polyamide	Yellow handle: polypropylene copolymer	Print: acrylic-based binder
M-003	Blue bristles: polyamide Pink bristles: polyamide Purple bristles: polyamide Orange bristles: polyamide	Light handle with mica: polypropylene Purple part: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder
M-004	Bristles: polyamide	Handle: styrene acrylonitril, SAN	Print: acrylic-based binder
M-005	White bristles: polyamide Blue bristles: polyamide	Blue house: polyester	Print: acrylic-based binder
M-006	White bristles: polyamide Blue bristles: polyamide	Blue handle: polypropylene copolymer Yellow insert: "SBS" elastomer with a high content of chalk	Print: acrylic-based binder
M-007	Print: Acrylic-based binder	White handle: polypropylene copolymer Green insert: "SBS" elastomer with a high content of chalk	Not identified
M-008	White bristles: polyamide Grey bristles: polyamide Black bristles: polyamide	White handle: polypropylene homopolymer Black insert: "SBS" elastomer with a high content of chalk	
M-009	Green bristles: polyamide Blue bristles: polyamide Red bristles: polyamide Yellow bristles: polyamide	Red handle: polypropylene modified with isoprene (rubber) Orange part: styrene ethylene elastomer with a high content of chalk	Print: might be acrylic-based binder
K-001	White bristles: polyamide	Handle: polypropylene homopolymer	Print: presumably polyester-based binder
K-002	White bristles: polyamide Pink bristles: polyamide Blue bristles: polyamide	Blue handle: polypropylene copolymer Pink parts: "SBS" elastomer with a high content of chalk. Safety ring: polyoxymethylene, POM	No print
K-003	White bristles: polyamide Green bristles: polyamide	Green handle: polypropylene Clear part: styrene acrylonitrile, SAN	No print
K-004	White bristles: polyamide Green bristles: polyamide	Blue handle: polypropylene homopolymer Light blue part: SBS/polypropylene elastomer	
B-001	White bristles: polyamide	Purple handle: polypropylene homopolymer Yellow part: styrene ethylene elastomer with a high content of chalk	No print
B-002	Clear bristles: polyamide	Clear handle: Acrylic Holder: PVC with (phthalate) plasticiser	
B-003	White bristles: polyamide Orange bristles: polyamide	Yellow handle: polypropylene with unknown additives Orange part: ethylene-propylene-styrene elastomer	Print: polyester- based binder
B-004	White bristles: polyamide Black bristles: polyamide	Clear handle: polyester Black part: styrene-ethylene elastomer	Print: polyester-based binder
B-005	White bristles: polyamide Blue rubber bristles: styrene ethylene elastomer with a high content of chalk	White handle: polypropylene with a small amount of unknown material Dark blue part: styrene ethylene with a high content of chalk	No print
B-006	White bristles: polyamide Yellow bristles: polyamide	Handle parts: polyoxymethylene, POM	No print

B-007	Pink bristles: polyamide	Dark blue handle: polypropylene copolymer Pink part: styrene ethylene elastomer with a high content of chalk	No print
B-008	White bristles: polyamide Green bristles: polyamide Green “rubber” bristles SBS/polypropylene elastomer	White handle: polypropylene Green part: SBS/polypropylene elastomer	No print
B-009	Green bristles: polyamide	Yellow handle: polypropylene copolymer Green part: styrene ethylene elastomer with a high content of chalk	No print
B-010	White bristles: polyamide Orange bristles: polyamide	Grey handle: polypropylene homopolymer Orange part: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder

SBS: Styrene-butadiene-styrene, SAN: Styrene acrylonitrilel, PBT: Polybutylterephthalate, POM: Polyoxymethylene

General conclusions:

Brushes:

At all the examined toothbrushes the bristles are made of polyamide. Based on the FT-IR analysis it is our evaluation that these are identical.
On the basis of the analysis it is not possible to show which type of colour has been used for the coloured brushes.
Some toothbrushes have “massage brushes” of another material, which has also been used in connection with the handle.

Handle:

The majority of the handles is made of polypropylene, homopolymer or copolymer.
At some of the handles smaller amounts of additives can be observed in the polypropylene material.
As decoration or another function at the handles different “styrene ethylene elastomers” are used, which in most cases contain a large amount of chalk.

Styrene acrylonitrile, SAN, acrylpolymer and polyester have also been used as handle material.

At the toothbrush with polyester handle an elastomer has been used, which - based on the FT-IR analysis - might contain phthalate.

The two examined parts for electrical toothbrushes are made of polyozymethylene, POM and polyester, (PBT).

Printing ink:

The printing ink has been evaluated based on the used binder system. In most cases the binders are based on acrylic polymers.

The FT-IR screening did not show any sign that phthalates have been used as softening components in the printing ink.

3.2 GC-MS Analysis (screening) migration to saliva

3.2.1 Analysis method

The migration analysis was carried out on 10 selected toothbrushes. Artificial saliva (DIN 53160-1) was added to an entire toothbrush, or 2 heads for electrical toothbrushes, and placed at 37°C for 10 hours. Subsequently, the liquid

was divided into two, and the analyts were concentrated through evaporation and "solid phase extraction" (SPE) respectively. The resulting extracts were analysed using gas chromatography with mass spectrometer detector (GC-MS).

Detailed analysis method is described in Encl. C.

For the GC-MS analyses we have used a Perkin Elmer AutoSystem XL GC gaschromatograph with a Turbomass GC mass spectrometer as detector. The detection limit will be approx. 0.5 μg/g. The uncertainty at screening is 100%.

3.2.2 Result of GC-MS screening

Based on the results from the GC-MS screening the substances identified at the screening are mentioned in table 3.2. It should be noted that substance names put in " " are uncertain, starts with " are more certain.

The unidentified substances, which are stated with ion-numbers in Encl. C, have been left out in table 3.2. It is assumed that these are mostly residues from the plastic. As it would be possible to identify monomers at the screening, it is consequently assumed to be oligomer residues from the used polymers.

As a part of the detected substances are solvents and substances, which are considered to be absolutely extraneous in the plastic production, it is assumed that a great part of the detected compounds derive from surface treatment, impression of film, colours etc.

Table 3.2 Substances found at GC-MS screening according to DEHP standard (µg total per toothbrush)

	Toothbrush ID			M003	M005	M009	K001	K002	B003	B004	B005	B006	B007
	Anal. ID (30642-)			-11	-12	-13	-14	-15	-16	-17	-18	-19	-20
ID	Compound	CAS no.	Classification *										
4	N,N-dimethyl-acetamide	127-19-5	Rep.2;R61 Xn;R20/21								0.3		
9	1,1,2,2 tetrachlorethane	79-34-5, 25322-20-7	Tx;R26/27 N;R51/53: Xn;R22 R43 R52/53									0.4	
6	2-butoxy-ethanol	111-76-2	Xn;R20/21/22 Xi;R36/38	1.0		1.2			0.5	1.8	0.1	1.0	
11	1-butoxy-2-propanol	5131-66-8 15821-83-7	Xi;R36/38									0.3	
3	"methylpropoxy-propanole"	23436-19-3			17.9			1.4	3.9				
8	"methylpropoxy-propanole"	53907-96-2					19.6						
14	"2-propyl-1-pentanol" chained alkane	104-76-7, 58175-57-8				1.6		3.3	0.5	0.9	0.5	1.1	0.7
16	3,5,5-trimethyl-1-hexanol	3452-97-9							1.1				
31	2-phenoxy ethanol	122-99-6	Xn;R22 Xi;R36			0.5							
2	"4-hydroxy-4-methyl-2-propanone	123-42-2	Xi;R36						0.6				
5	Cyclohexanone	108-94-1	R10 Xn;R20	2.0	13.3	1.0	7.3	2.1	0.5				
12	"methoxy-butanol acetate"	4435-53-4						1.0					
21	2-butoxyethyl acetate	112-07-2	Xn;R20/21	3.0	2.2	2.5			1.6				
13	4-hydroxy-benzene sulphonic acid	98-67-9			20.1								
18	1-methyl-2-pyrrolidinone	872-50-4	Xi;R36/38		127.6	2.1				1.2	0.4		
24	Benzo acid methyl ester	93-58-3					3.5						
26	Pentandiacid dimethyl ester	1119-40-0				1.0		0.3					
25	"Tetramethylbenzene"	488-23-3	N;R51/53		6.2								
27	"Tetramethylbenzene"	25619-60-7			3.5								
28	Naphthalene	91-20-3	Xn;R22 N;R50-53		3.7								
29	Naphthalene (against own Internal Standard)	91-20-3	Xn;R22 N;R50-53		5.3								
33	Carvone	99-49-0								0.6	0.5		
37	?? 31-61	fx. 110-88-3	Xn;R22		2.0								
38	"butoxyethoxy ethanol acetate"	124-17-4			3.1	2.5							
46	Alken/alcohol C16-C18			6.1				2.8					
50, 53	"N,4-dimethyl-benzene sulphonamide"	640-61-9								3.8		2.5	
51	2-methyl benzene sulphonamide	88-19-7								6.1		300.0	1.8
54	4-methyl benzene sulphonamide [or. Tolbutamid]	70-55-3 el. 64-77-7								5.4		387.3	3.0
57	4-(dimethylamino)-benzo acid ethyl ester	10287-53-3					9.5						
61	"dimethoxy-diphenyl-ethanone"	24650-42-8					14.2						
62	"BHT"	128-37-0				1.0		0.7					
67	4-benzoyl-benzo acid methyl ester	6158-54-9					2.0						
70	Phthalate								5.1				
48	Diethylphthalate	84-66-2			3.1								
71	Benzyl butyl phthalate	85-68-7			17.5								
72	"Phosphoric acid, tris(2-ethylhexyl) ester"	78-42-2							0.6				
69	Alcohol C15 +			1.1									
59	Alken/alcohol C16-C18	629-73-2, 6765-39-5		4.9		4.5		2.2		1.2	2.7		3.2

	Toothbrush ID			M003	M005	M009	K001	K002	B003	B004	B005	B006	B007
	Anal. ID (30642-)			-11	-12	-13	-14	-15	-16	-17	-18	-19	-20
ID	Compound	CAS no.	Classification *										
65	Alken/alcohol C16-C18			3.5				1.7					
66	Alken/alcohol C20+	6971-40-0		1.1				0.5	0.6				
45	Alkan/alken-amide C6-C12	fx. 628-02-4 1120-07-6									1.0		
73	Alkan/alken-amide C18+										1.6		

*: Classification according to the List of Dangerous Substances (Miljøministeriet 2002)

In the light of previous knowledge regarding possible health risk the following compounds out of 80 are pointed out as being of interest for further quantification:
1-methyl-2-pyrrolidinone (toothbrush M-005), carvone (B-004 and B-005), 2-methyl-benzene sulphonamide (B-004 and B-006), 4-methyl-benzene sulphonamide (B-004 and B-006) and benzyl butyl phthalate (M-005). These substances are assumed to derive from surface application of printing ink, finishing material like varnish etc.

3.3 Calcined residue and elemental substance screening through ICP-MS

3.3.1 Analysis method: Calcined residue, preparation and screening

Calcined residue:
The toothbrushes were divided into appropriate pieces and incinerated in a porcelain crucible at heating in a muffle furnace under programmed heating to 625°C over a period of 6 hours. After cooling in a desiccator the calcined residue was determined. Identifiable metal parts in the ash were isolated and weighed. The mass of the ash was adjusted for the metal part.

Preparation of the ash:
5 ml concentrated nitric acid (sub-boiling quality) was added to 50 mg ash and placed in an ultrasonic bath for 60 min. Subsequently, 1 drop of concentrated hydrochloric acid and 2 drops of 40% (m/m) hydrofluorid acid were added, after which the mixture was left overnight. Further 2 drops of concentrated hydrochloric acid were added, and the solution was treated in an ultrasonic bath for 30 min. Finally, 25 ml demineralised water was added to the solution and diluted to 50 ml with 2.8 M nitric acid.

Elemental substance screening:
Dilutions of the prepared samples, added "on-line" germanium, rhodium and rhenium as internal standards, were screened for the content of trace elements through inductive-coupled-plasma mass spectrometry (ICP-MS) using the expert programme TotalQuantII, which - on the basis of an instrument response curve for the elemental substances from mass 6 (Li) to mass 238 (U) - quantifies the content. The instrument response curve was updated by means of a multi-element standard containing Li, Be, B, Na, Mg, Al, K, Ca, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Rb, Sr, Mo, Ag, Cd, Te, Ba, Tl, Pb, Bi and U, which covers all of the mass area. Elemental substances like Br, C, Cl, F, N, O, P, S and Si are not quantified because of interferences.

The screenings were carried out on a Perkin Elmer Sciex Elan 6100 DRC Plus ICP Mass Spectrometer attached to a FIAS 400 system with AS93 Plus autosampler.

3.3.2 Summary of the ICP-MS screening

The result of the ICP-MS screening is shown in Table 3.3 and in detail in Encl. D.

Table 3.3 Results from the ICP-MS screening

Reg no:	M-003	M-005	M-009	K-001	K-002	B-003	B-004	B-005	B-006	B-007	
Analyt	**µg/g tooth-brush**	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	DL ug/g ash
Na	121	266	102	7	100	0	0	864	107	413	100
Mg	1768	143	2090	265	2687	535	301	1358	294	1154	100
Al	1616	348	1025	5294	134	134	20	802	1003	654	100
Ca	50505	389	45082	275	79602	181	9694	50000	2406	36538	500
Ti	707	192	1680	69	80	299	61	10494	455	596	100
Cr	11	0	18	4	0	2	2	0	7	0	50
Mn	12	53	0	8	0	20	0	0	0	0	50
Ni	0	2863	0	0	0	1024	5	0	0	0	100
Cu	0	15337	34	5	0	5669	10	235	40	15	50
Zn	0	5521	0	0	0	2126	45	0	74	0	100
Se	0	0	0	0	0	10	0	105	0	0	500
Sr	49	0	35	0	50	0	10	46	13	27	50
Ba	0	25	0	0	104	0	0	0	19	0	50
Pb	0	0	9	0	0	0	0	0	0	0	50
g ash per											
toothbrush	2.94	0.17	3.41	0.07	4.15	0.19	0.59	2.38	0.5	1.22	
metal piece		0,53							1,07		
g toothbrush	19.8	4.89	24.4	10.2	20.1	12.7	19.6	16.2	7.48	10.4	

DL states the detection limit in µg/g ash. In order to get the detection limit for a parameter in µg totally for a given sample, DL must be multiplied by g ash per toothbrush

Compared with the results from the FT-IR screenings, where a big amount of chalk has been identified, a proportionately big amount of calcium is measured at the ICP-MS screenings, and - in many cases - also a big amount of magnesium.
The existence of calcium and/or magnesium in the toothbrushes presumably derives from the use of chalk or dolomite as filling materials. At the same time, smaller amounts of strontium and barium are observed in the same samples. This is due to the fact that when you detect calcium as a natural impurity, traces of strontium and barium are often detected, too. The impurity originates from the use of naturally occurring minerals.

Titanium has been measured in the majority of the toothbrushes and is a constituent part of a white pigment in the form of titanium dioxide. A big amount of aluminium in the form of aluminium oxide is assumed to have a corresponding function, and - in some cases - it is used with the purpose of achieving an opalescent effect.
In some cases, a big amount of copper, nickel and zinc together with traces of manganese have been detected. These elemental substances are assumed to originate from metal wire or something similar for fixing the bristles to the toothbrush or from mechanical parts in the case of mouthpieces for electrical toothbrushes.

3.4 Summary of qualitative analyses

The qualitative analyses carried out in Phase 2 served the purpose of stating which chemical substances are used in toothbrushes, and - if these substances give cause for concern - whether they are released when using the toothbrushes.

A wide range of the toothbrush types being on the market today has been analysed; the main emphasis has been laid on children's toothbrushes. The analyses primarily showed the following:

- **Toothbrush handles are mainly made of polypropylene, homopolymer or copolymer**
- **Toothbrush bristles are made of polyamide**
- **Chalk has - to a great extent - been used as filling material in the handles**
- **Metal wire has been used for fixation of the bristles to the toothbrush, mainly consisting of alloys of copper, nickel and zinc**
- **Titanium was measured in the majority of the toothbrushes and is a constituent part of a white pigment in the form of titanium dioxide**
- **Several organic compounds were found after extraction in artificial saliva; the following are pointed out as being of interest for further quantification: 1-methyl-2-pyrrolidinone (toothbrush M-005), carvone (B-004 and B-005), 2-methyl-benzene sulphonamide (B-004 and B-006), 4-methyl-benzene sulphonamide (B-004 and B-006) and benzyl butyl phthalate (M-005). These substances are supposed to originate from surface applications of printing ink, finishing materials like varnish etc. The selection is based on the classification of the substances and description of effects that potentially may cause concern to the consumer, if the migration of the substances from the toothbrushes is too high.**

1-methyl-2-pyrrolidinone is a solvent often used by synthesis of plastic and varnishes.

Carvone is a terpene. Terpenes are found in essential oils. The terpenes might derive from the use of vegetable oils and resins in the printing and printing ink as a solvent.

Toluene sulphonamides are often residual products from syntheses of preservatives to e.g. varnishes.

Phthalate is a plasticiser, which is used in both plastic and varnishes.

The mentioned substances are of special interest based on their classification and description of effects that potentially may cause concern to the consumer, if the migration of the substances from the toothbrushes is too high.

4 Screening for possible harmful effects

4.1 Screening for harmful substances

In phase 2, the substances, which are extracted from 10 toothbrushes with artificial saliva, were identified by means of GC-MS screening according to DEHP internal standard. This means that the detected amounts of released substances (µg per toothbrush) must be taken with some reservations. However, the numerical values give the impression of relative amounts.

Based on the identified chemical compounds a screening for possible harmful substances has been made. The screening is based on the classifications in the List of Dangerous Substances and available information on effects that potentially may cause concern to the consumer, if the migration of the chemical substance is too high in relation to the concentrations where effects are observed.

Five chemical substances (carvone, 2-methyl-benzene sulphonamide, 4-methyl- benzene sulphonamide, benzyl butyl phthalate and 1-methyl-2-pyrrolidinone) were detected, which might be considered to be problematic substances, and some, which may be of concern. These substances are shortly reviewed below as well as other classified substances. The substances are presented in order based on an evaluation presenting the most concerning substances first.

N,N-Dimethylacetamide

N,N-Dimethylacetamide (CAS no. 127-19-5) is classified "Rep.2;R61 Xn;R20/21". This means that the substance is toxic to reproduction in category 2, Harmful to embryos in animal experiments. R61 states that the substance may cause harm to the unborn child. Xn states that the substance is harmful to health. R20/21 states that the substance is harmful by inhalation and in contact with skin**. Chronic effects have been mentioned as "may cause chronic liver- and kidney damages" (Clayton and Clayton, 1981). The substances may cause systemic damages when inhaled and absorbed via the skin in sufficient amounts over a prolonged period of time. The substance was detected in one toothbrush (B-005). However, although the amount is relatively low in the screening analysis, the detection is confirmed in a quantitative analysis.**

1,1,2,2-Tetrachloroethane

1,1,2,2-Tetrachloroethane, CAS no. 79-34-5, is classified "Tx;R26/27 N;R51/53". This means that the substance is very toxic by inhalation and in contact with skin. 1,1,2,2-Tetrachloroethane is known as a toxic substance with the liver as its prime target. The substance is observed in one toothbrush (B-006) but even if the relative amount is low in the screening the detection is confirmed in a quantitative analysis.

3,5,5-Trimethyl-1-hexanol

3,5,5-Trimethyl-1-hexanol, CAS no. 1331-39-1, is not classified but mentioned in the IPCS safety data sheet. It is stated that the effects at short time exposure are absorption through skin, irritation of the eyes, skin and respiratory system. Prolonged exposure from the substance may affect liver and kidneys and may affect embryos (IPCS 1993). The substance is observed in one toothbrush (B-003) but even if the relative amount is low in the screening the detection is confirmed in a quantitative analysis.

Carvone

Carvone, CAS no. 99-49-0, is not classified, but carvone is a terpene. The terpenes are generally mucous membrane irritating. The terpenes are found in essential oils. The terpenes might originate from the use of vegetable oils and resins in the printing and the printing ink as a solvent. Furthermore, carvone with the chemical name p-mentha-6,8-dien-2-one is closely related to limonene (p-mentha-6,8-dien), which is known to be skin irritating and classified ”Xi;R38 R43. This means that the substance is irritating; and classified as Irritating to skin. Besides the substance may cause sensitization by skin contact.

Carvone is generally considered to have a low sensitising potential, but sometimes carvone has been found to be the cause of contact allergy in users of spearmint toothpaste and -chewing gum (HSDB 2003). The substance is observed in two toothbrushes (B-004 and B-005) but even if the relative amounts are low in the screening the detections are confirmed in quantitative analyses.

Methyl-benzene sulphonamides

2-Methyl-benzene sulphonamide, CAS no. 88-19-7, is not classified, but according to the Advisory list for self-classification of dangerous substances by the Danish-EPA (2001) a classification could be: R43, i.e. the substance may cause sensitization by skin contact. The substance is observed in three toothbrushes (B-003, B-006 and B-007). The detection in B-006 indicates a high migration and, therefore, the detection is confirmed in a quantitative analysis.

4-Methyl-benzene sulphonamide, CAS no. 70-55-3, is not classified, but according to the Advisory list for self-classification of dangerous substances by the Danish-EPA (2001) a classification could be: R43, i.e. the substance may cause sensitization by skin contact. The screening identification might also indicate that it could be tolbutamide, CAS no. 64-77-7, which is classified Xn;R43, i.e. harmful and may cause sensitization by skin contact. The substance was observed together with 2-methyl-benzene sulphonamide in three toothbrushes (B-003, B-006 and B-007). The detection in B-006 indicates a high migration and, therefore, the detection is confirmed in a quantitative analysis.

Phthalates

An unidentified phthalate and diethyl-phthalate and benzyl butyl-phthalate have been detected. The phthalates have been entered on the List of undesirable substances. The inclusion in the list is based on a political objective and the health and environmental impact from the phthalates in connection with waste such as slag, compost and sludge (Danish EPA 2000).

Benzyl butyl phthalate is being risk assessed in EU but the assessment is not yet finalised. Benzyl butyl phthalate is not classified but new classification has been suggested based on repro-toxic characteristics. The substance is observed in one toothbrush (B-005) but even if the relative amount is low in the screening the detection is confirmed in a quantitative analysis.

2-Butoxy-ethanol

2-Butoxy-ethanol, CAS no. 111-76-2 is classified "Xn;R20/21/22 Xi;R36/38".

This means that the substance is harmful by inhalation, in contact with skin and if swallowed. Furthermore, it has been classified as an Irritant: irritating to eyes and skin. 2-butoxy-ethanol is easily absorbed after inhalation or through oral or dermal contact (IPCS 1998, CICAD 10). 2-Butoxy-ethanol is a glycolether commonly used as a solvent in surface treatments as for instance varnish and colour. The substance is detected in several of the toothbrushes (6 out of 10). Even if the relative amounts are low in the screening the detections are confirmed in quantitative analyses.

1-Butoxy-2-propanol

1-Butoxy-2-propanol (maybe better known under the synonym propylene glycol butyl ether), CAS no. 5131-66-8 (a-isomer) and 15821-83-7 (b-isomer) are classified "Xi;R36/38", i.e. Irritatant: irritating to eyes and skin. The substance is observed in one toothbrush (B-006) but even if the relative amount is low in the screening the detection is confirmed in a quantitative analysis.

2-Butoxyethyl acetate

2-Butoxyethyl acetate, CAS no. 112-07-2 is classified Xn;R20/21, i.e. harmful by inhalation and in contact with skin. A great deal of information has been found. However, none seems to be conclusive with regard to effect level. The substance is detected in four of the toothbrushes (M-003, M-005, M-009 and B-003). Even if the relative amounts are low in the screening the detections are confirmed in quantitative analyses.

1-Methyl-2-pyrrolidinone

1-Methyl-2-pyrrolidinone, CAS no. 872-50-4 is classified Xi;R36/38, i.e. Irritant, irritating to eyes and skin. The substance is suspected to give contact dermatitis by repeated use. The substance is detected in four of the toothbrushes (M-005, M-009, B-004 and B-005). The relative amounts were high in M-005 and low in the remaining toothbrushes in the screening. The detection is confirmed in a quantitative analysis.

Naphthalene

Naphthalene, CAS no. 91-20-3, is classified Xn;R22, i.e. Harmful if swallowed.

It should be noted that a further classification of Carc3;R40, has been suggested at 29 ATP (29th Adaptation to Technical Progress in Dir. 67/548). This means that the substance is considered to be possibly carcinogenic. Studies of animals indicate that naphthalene is easily absorbed through oral exposure or inhalation (IARC 2002). Naphthalene is used as an intermediate in the production of phthalate ("phthalic anhydride") and in the production of dyes. The detected amount is partly stated as an analysis result against DEHP as internal standard (3.7 µg), but also against its own standard with the correct result of 5.3 µg for the relevant toothbrush. The substance is observed in one toothbrush (M-005) but even if the relative amount is low in the screening the detection is confirmed in a quantitative analysis.

2-Phenoxyethanol

2-Phenoxyethanol, CAS no. 122-99-6, is classified Xn;R22 Xi;R36, i.e. harmful if swallowed and irritating to the eye. The substance is observed in one toothbrush (M-009). The relative amount is low in the screening and the detection is not confirmed in a quantitative analysis.

Other substances
The following other classified substances have been found:

*Cyclohexanone***, CAS no. 108-94-1, is classified Xn;R20, Harmful by inhalation.**
The substance is classified as harmful by inhalation, but inhalation is hardly an actual route of exposure for toothbrushes. However, in the screening the substance was detected in six out of ten toothbrushes.

*4-Hydroxy-4-methyl-2-propanon***, CAS no. 123-42-2, is classified Xi;R36, i.e. irritating to eyes. The substance is thus an irritant. The substance is observed in one toothbrush (M-005).**

Furthermore, a large number of chemical compounds have been detected. These are considered to be less problematic: long-chained alkanes, alkenes and alcohols with chain length C_{16} and higher.

4.2 Selection of chemical substances and toothbrushes for quantitative analysis

At the screening 73 more or less identified chemical compounds were identified. Twelve of the identified substances were classified in the List of Dangerous Substances.

It is our assessment that many of the unidentified substances are oligomer residues from the plastic material or the coating material.

Many of the substances are solvents, which presumably originate from the surface applications (coatings) of printing ink, finishing material like varnish etc.

It should be emphasised that the question whether the detected substances constitute a real problem cannot be assessed until a quantitative analysis is carried out, and the results used at the assessment of the exposure. A risk assessment cannot be carried out until the exposure is known and can be compared with the effect of the substances.
Consequently, in co-operation with the Danish Environmental Protection Agency, 5 toothbrushes were selected for quantitative analyses. The selection is based on the detected substances and the available descriptions of effects, which might influence the consumer's use of the toothbrushes.

In co-operation with the Danish Environmental Protection Agency, a specific quantitative analysis of migrated amounts was selected for the following substances to perform a more detailed health and exposure assessment:

N,N-Dimethyl acetamide
1,1,2,2-Tetrachlorethane
3,5,5-Trimethyl-1-hexanol
Carvone
2-Methyl-benzene sulphonamide

4-Methyl-benzene sulphonamide
Benzyl-butyl-phthalate
2-Butoxy-ethanol
1-Butoxy-2-propanol
Naphthalene
2-Butoxyethyl acetate
1-Methyl-2-pyrrolidinone
Nickel

As these substances are considered to be the most problematic, an assessment of possible health problems at exposure of migrated chemical compounds with known harmful effects from the selected toothbrushes should be covered.

Based on the detected substances a quantitative analysis of 5 toothbrushes has been carried out:

M-005
Based on the detection of undesirable phthalates. Naphthalene has only been detected in this toothbrush. Methylpyrrolidinone has been detected in the largest amount released from the screened toothbrushes. Seventeen more or less identified substances have been detected; which is the second largest number among the 10 screened toothbrushes.

B-003
Based on the detection of trimethylhexanol, 2-butoxyethanol and an unknown phthalate.

B-004
Based on the detection of methyl-benzene sulphonamides, 2-butoxyethanol (highest value in the screening), and methylpyrrolidinone.

B-005
Based on the detection of N,N-dimethylacetamide, which was the most harmful of the examined substances, and the presence of carvone.

B-006
Based on the detection of tetrachlorethene, 2-butoxyethanol, butoxypropanol and methyl-benzene sulphonamide (which was detected in large amounts). Furthermore, this toothbrush had the greatest number of “hits”; a total of 24 more or less identified chemical compounds.

5 Quantitative analyses

Based on the obtained information, and having consulted the Danish Environmental Protection Agency, 12 substances have been selected for a quantitative determination in 5 toothbrushes by means of GC-MS. Furthermore, a quantitative determination of Nickel by means of ICP-MS has been carried out.

5.1 GC-MS Analysis (quantitative determination) migration

5.1.1 GC-MS Analysis method

The migration was carried out in simulated saliva (DIN 53160-1) at 37°C for 10 hours. After this, the analyts in the migration liquid were evaporated on SPE tubes and eluted in an organic solvent. After evaporation the eluate was analysed by means of GC-MS. All of the 10 toothbrushes were analysed. With the help of purchased standards the detection of the selected compounds was confirmed, and the amount of the compounds was quantified.

5.1.2 GC-MS Analysis results

The analysis results are shown in Table 5.1 below for the 5 selected toothbrushes. A detailed survey of all 10 toothbrushes is shown in Encl. E.

Table 5.1 GC-MS analysis results, quantitative determination on 5 selected toothbrushes

ID no.	M- 005 *	B– 003	B– 004	B– 005	B– 006 *	Recom-mended detection limit
Component	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush	µg/g tooth-brush
N,N-dimethyl acetamide	-	-	-	0.05	-	0.25
2-butoxy-ethanol	0.04	0.05	0.11	0.03	0.04	0.15
1,1,2,2-tetrachloroethane	-	-	-	-	0.05	0.25
1-butoxy-2-propanol	0.02	-	0.01	-	0.02	0.15
3,5,5-trimethylhexanol	-	0.06	-	-	-	0.25
1-methyl-2-pyrrolidinon	40.90	-	0.22	0.09	0.03	0.15
2-butoxyethyl acetate	0.14	0.30	-	-	-	0.15
Naphthalene	0.53	-	-	-	0.04	0.25
Carvone	-	-	0.03	0.03	-	0.15
o-toluen sulphonamide	-	-	0.97	-	52.14	0.25
p-toluen sulphonamide	-	-	1.33	-	108.29	0.25
Benzyl butyl phthalate	4.29	-	-	-	-	0.15

5.2 ICP-MS Analysis (quantitative determination)

5.2.1 ICP-MS Analysis method

A quantitative determination of Nickel in 5 selected toothbrushes has been carried out. The migration analysis was performed in simulated saliva (DIN st, no. 53 160-1) at 37°C for 10 hours. After this nickel was determined in the extract, which was made acid by means of nitric acid (sub boiling), prior to analysis by means of FI-ICP-MS with internal standardisation. One of the

samples was "spiked" with nickel at the same level as found in the sample; the recovery was 103%, and the detection limit of the analysis corresponds to approx. 0.005 µg Ni per toothbrush.

5.2.2 ICP-MS Analysis results

The result of the analysis is stated in below Table 5.2. The amounts are stated in µg per toothbrush.

Table 5.2 Result of the FI-ICP-MS analysis

Sample name	M-005	B-003	B-004	B-005	B-006
Ni (µg /toothbrush)	1.06	0.84	0.34	0.032	0.20

6 Health assessment

6.1 Assessment of the health risk when using toothbrushes

In order to assess the health risk at daily use of toothbrushes the effect values of the detected chemical substances are assessed and compared with the relevant time of exposure and exposure pathway.

The time of exposure for toothbrushing might vary a lot, but the most usual practice for adults are toothbrushing in the morning and in the evening. If it is assumed that the average time for each toothbrushing is 2 minutes, this corresponds to a time of exposure of 4 minutes daily. For children, it is not unusual to brush their teeth in the middle of the day. With the same time of exposure at each event, this corresponds to a daily exposure of 6 minutes.

In consideration of realistic "worst case", oral absorption is used for children with an assumed body weight of 10 kg. The absorption through the oral cavity will be specific to each substance and thus dependent on the detected substance released from the toothbrushes. If no information was found about the specific absorption through oral cavity/ mucous membranes of the individual substance, it is assumed that the absorption is 100%. As smaller children might swallow the "toothbrushing product" (i.e. foam from toothpaste, water, saliva and thus including potential substances released from the toothbrush), it is not considered to be unrealistic.

In this examination, 12 specific substances were selected in co-operation with the Danish EPA for evaluation. The selection was based on the classification of the substances, etc.

6.1.1 General procedure

Each of the selected substances has been identified by its common name and CAS no. for unambiguously identification. Besides, the most common synonyms are stated.

Furthermore is mentioned:

- **The origin and purpose of the substance in order to evaluate where in or on the toothbrush the potential source of the substance might be.**

- **The physical-chemical data of the substances, which may be relevant to the assessment.**

- **The classification of the substance with possible specification of the concentration levels which might result in classification of the product.**

- **The effects of the substances on human health have been summarised, partly acute effect levels, but also long-term studies, if available.**

- **The threshold limiting values (TLV) of the substance, valid for the working environment (they cover the concentration in air in the working environment). The available values for tolerable daily intake (TDI), acceptable daily intake (ADI) or reference dose (RfD) are mentioned (for explanation cf. the abbreviation list).**

- **Finally, an assessment of the amount of detected released substances has been carried out. This has been done by calculating/estimating the absorbed amount based on the time of exposure and the body weight of the person (amount/kg body weight/day). If possible, one of the established values for tolerable daily intake (TDI, ADI or RfD) is used for evaluation of the exposure by comparing the values with the obtained analysis results used to estimate the exposure. The basis is the maximum found value, if they appear in several toothbrushes. The used uncertainty factors are mentioned in the text. In case more TDI, ADI or RfD values exist, the lowest value is preferred. If there is no TDI, ADI, RfD value, a tolerable concentration based on one or more published studies is suggested. The procedure is mentioned at the individual substances.**

6.1.2 Exposure

At oral exposure absorption takes place after release (migration) of the substances from the toothbrush, after which they are mixed with toothpaste, saliva, water etc. Absorption is assumed to take place over the oral cavity mucous membrane or the gastrointestinal tract.

A further exposure may possibly take place via the skin of the palm being in contact with the toothbrush. Since the release is measured for the entire surface of the toothbrush, this is presumed to be included in the assessment.

As a basis for assessment of the oral intake, a general equation has been set up for the ingestion of substances (OECD 1993, EC 2003):

$$I_{oral} = \frac{V_{oral} \times C_{oral} \times F_{orl} \times N_{event}}{BW}$$

where

I_{oral}	Intake of the substance	µg/kg BW/day
V_{prod}	Weight of product put in the mouth	g or mg
C_{oral}	Concentration of the substance released from the product per hour	µg/hour
N_{event}	Times per day	default assumed 1 time/day
BW	Body weight	kg
F_{oral}	Fraction which is absorbed (bioavailable part)	

After this the equation has been adjusted according to the present scenario

$$I_{oral} = \frac{C_{oral} \times F_{orl} \times t \times N_{event}}{BW}$$

where

I_{oral}	Intake of the substance	µg/kg BW/day
C_{oral}	Concentration of the substance released from the product per hour	µg/ toothbrush/10 (as extracted for 10 hours)
t	Time of exposure	minutes per hour (60 minutes)
N_{event}	Times per day	here assumed 3 times/day
F_{oral}	Fraction which is absorbed (bioavailable part)	
BW	Body weight	kg

This means that the calculations are carried out as follows:

Extracted substance (based on analysis extraction during 10 hours) × the time of exposure/day compared with the time for extraction × absorption/body weight:

Oral intake = µg released/10 hours ´ 6/60 (minutes) ´ % absorption/100%)/10 (kg) = µg/kg body weight per day

The analysis results state the migrated amount detected in the saliva extractions after 10 hours of extraction. The amount is converted into release per hour.

The time of exposure is converted into a temporal fraction per hour (6/60 minutes).
As a basis it is assumed that a child brushes its teeth 3 times daily. Each toothbrushing event lasts 2 minutes, i.e. a total time of exposure of 6 minutes daily.

The result using the above equation would be the same as if one had calculated release per day (i.e. emission from the toothbrush/day = measured release in 10 hours/10 × 24 hours) and the time of exposure in minutes per day (i.e. 6/(60 × 24) minutes). This would result in a factor of 24/10 × 6/(60 × 24) = 0.01.

The body weight has been set at 10 kg, which corresponds to a child at the age of 2-3 years.

Absorption
After exposure of the oral cavity the chemical substance must pass the mucous membranes, before being defined as a true absorption. Only few data have been found for dermal absorption of the examined substances. Consequently, the dermal absorption has been estimated for many of the substances.

The dermal penetration can be estimated from the substance octanol/water partition coefficient (log Kow) and the size of the molecule. Kow, which is an expression of the substance partitioning between octanol and water, also indicates whether the substance is lipophilic (high Kow i.e. prefers lipid phase) or hydrophilic (low Kow i.e. prefers the water phase). Dermal penetration is considered to be very low for substances with a log Kow less than –1, i.e. very hydrophilic (Vermeire *et al.* 1993). The potential for dermal penetration increases with Kow up to an upper limit above, which the potential is decreasing. The upper limit for Kow above which the dermal penetration decreases again to insignificant levels, is approximately at log Kow 5 (OECD 1993, EC 2003).

The molecular weight influences the dermal penetration as larger molecules have more difficulties in penetrating the skin than smaller molecules. Dermal penetration is considered insignificant for substances having a molecular weight above 700 g/mol (Vermeire *et al.* 1993).

At standard evaluations or in case no information is available, a dermal absorption of 100% (EC 2003) is typically used. This has been done in all cases of organic substances, unless information about the absorption was found. If so, these have been used as a refinement of the estimates.

No batch to batch variation has been evaluated; partly because the purpose has not been to evaluate each separate toothbrush, partly because the number is too small. The purpose of the survey has been to evaluate which substances were released from toothbrushes and in how large quantities. Finally – at these short times of exposure - such an evaluation would be of limited value at a normal consumer pattern, because the detected concentrations are so low.

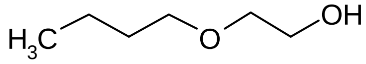
6.2 Evaluation of single substances

6.2.1 2-Butoxy-ethanol

2-Butoxy-ethanol is used as a solvent for surface coatings, adhesives in vinyl and acrylic paint (Kirk-Othmer 1991).

2-Butoxy-ethanol is used as a solvent in surface coatings such as spray lacquers, quick dry lacquers, enamels and latex paint (CICAD 1998).

Identification

Name	2-Butoxy-ethanol
CAS no.	111-76-2
EINECS no.	203-905-0
Molecular formula	$C_6H_{14}O_2$
Molecular structure	
Molecular weight	118.20 g/mol
Synonyms	ethylene glycol n-butyl ether EGBE butylglycol

The melting point of the substance is –74.8°C. The boiling point is 168.4°C (DOW 1990). The vapour pressure is 117 Pa at 25°C (0.88 mmHg) (DOW 1990). The water solubility is 1 kg/l at 25°C (miscible, DOW 1990). The partitioning coefficient log Kow has been experimentally determined to 0.83 (Hansch *et al.* 1995).

Classification

2-butoxy-ethanol is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Xn;R20/21/22	Harmful. Harmful by inhalation, in contact with skin and if swallowed
Xi;R36/38	Irritant. Irritating to eyes and skin

6.2.1.1 Effects on health

2-Butoxy-ethanol is moderately acute toxic, irritating to eyes and skin (but not a skin sensitizer) (CICAD 1998).

The effects have mostly been registered as a haematolytic activity of butoxy-ethanol. The effect was dependent on age with elder rats as the most sensitive (CICAD 1998).

Eye irritation examinations showed that 30 and 70% concentrations of the substances were irritating to the eyes with increasing irritation with corresponding increasing time of exposure. The skin irritation was mild at 4 hours of exposure of rabbit skin, but the irritation increased with increased time of exposure (CICAD 1998).

Acute toxicity:

Acute oral, rat	LD_{50}	1480 mg/kg	Budavari 1989
Acute oral, mouse	LD_{50}	1400 mg/kg	CICAD 1998
Acute oral, rabbit	LD_{50}	320 mg/kg	CICAD 1998

In a subchronic 90 days inhalation study, rats were exposed to 2-butoxy-ethanol at 0, 5, 25, or 77 ppm for 6 hours/day, 5 days a week for 13 weeks. Based on haematotoxic effects, the NOAEL and LOAEL were 25 ppm (121 mg/m^3) and 77 ppm (372 mg/m^3), respectively (Dodd *et al*. 1983).

In a study on developmental effects, pregnant rats were exposed to 2-butoxyethanol at 0, 25, 50, 100 or 200 ppm (35 per group) for 6 hours/day on days 6-15 on gestation. Based on haematotoxic effects the NOAEL and LOAEL were 50 ppm (242 mg/m^3) and 100 ppm (483 mg/m^3), respectively (Tyl *et al.* 1984).

In a 13 weeks study with rats groups of 10 of each sex were exposed through the drinking water. Based on the water consumption, the male rats were exposed to 0, 69, 129, 281, 367 or 452 mg/kg/day and female rats to 0, 82, 151, 304, 363 or 470 mg/kg/day. Based on effects of the blood parameter and liver, which were observed at even the smallest concentration, LOAEL was 69 mg/kg/day for males and 82 mg/kg/day for females. When water consumption and body weight from the last week of the exposure is used, LOAEL is converted into 55 mg/kg/day for males and 59 mg/kg/day for females. NOAEL could not be determined in the examination (NTP 1993, IRIS 1999).

2-Butoxy ethanol has been evaluated as potential human carcinogen, Group C (IRIS 2003).

6.2.1.2 Threshold limit values

The threshold limit value for the working environment is 20 ppm corresponding to 98 mg/m^3 with skin notation, i.e. the substance is skin penetrable (AT 2002).

Inhalation RfC: 13 mg/m^3 based on sub-chronic rat inhalation study (Tyl *et al.* 1984, cf. above). The value is based on NOAEL 242 mg/m^3 and calculated with an uncertainty factor 10, 6/24 in order to convert 6 hours' exposure to 24 hours per day, a conversion from rat to human (inhalation rate for rat 0.16 m^3/day and for human 22 m^3/day, the body weight of rat 0.215 kg and for human 64 kg) (CICAD 1998). The RfC calculated using the mentioned variables is then:

$RfC = (242/10) \times (6/24) \times [(0.16/0.215)/(22/64)] = 13.1 \ mg/m^3$.

Oral RfD: 0.5 mg/kg/day.

The value is based on a 13-week of subchronic study, where haematological effects were found as the most sensitive endpoint with a LOAEL of 55 to 59 mg/kg/day for rats (NTP 1993, see above). US-EPA converted the value into 5.1 mg/kg bw/day for humans and used a safety factor of 10 for intraspecies sensitivity (US-EPA 1999).

6.2.1.3 Bioavailability

2-Butoxy-ethanol is easily absorbed after inhalation, or by oral or dermal exposure (CICAD 1998). Consequently, an absorption of 100% has been used.

6.2.1.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. From this the amount of absorbed substance has been calculated below.

Example of calculation based on the highest measured migration of 2.20 µg/toothbrush:

Oral, child **= 2.20/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.0022 µg/kg bw/day**

Table 6.1 Analysis results and estimated absorption of 2-butoxy-ethanol

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	0.18	0.00018
B-003	0.66	0.00066
B-004	2.20	0.00220
B-005	0.46	0.00046
B-006	0.30	0.00030
Maximum	2.20	0.0022

-: Below the detection limit of 0.15 µg/toothbrush

2-Butoxy-ethanol has thus been detected in all the selected products in amounts above the detection limit of 0.15 µg/toothbrush.

From the above it is seen that none of the amounts ingested or absorbed at toothbrushing will result in a dose above the RfD value 0.5 mg/kg/day, for which reason it is assessed not to involve any health risk.

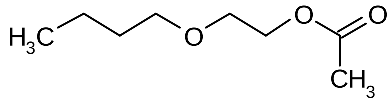
6.2.1.5 Overall evaluation

2-Butoxy-ethanol implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.2 2-Butoxyethyl acetate

2-Butoxy-ethyl acetate is used as a solvent for printing inks, paint and resins.

Identification

Name	2-Butoxyethyl acetate
CAS no.	112-07-2c
EINECS no.	203-933-3
Molecular formula	$C_8H_{16}O_3$
Molecular structure	
Molecular weight	160.21 g/mol
Synonyms	2-butoxy-ethanol acetate ethylene glycol butyl ether acetate (EGBEA) glycol monobutyl ether acetate butylglycolacetate

The melting point of the substance is –63.5°C. The boiling point is 192.3°C (Lewis 1996). The vapour pressure is 50 Pa at 20°C (0.375 mmHg) (Weber *et al.* 1981). The water solubility is 15000 mg/l at 25°C (Ashford 1992, HSDB). The partitioning coefficient log Kow has been measured to 1.51 (Verschueren 1983).

Classification

2-Butoxyethyl acetate is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Xn;R20/21	Harmful. Harmful by inhalation and in contact with skin
Classification in mixtures:	
Xn;R20/21	conc.>=25%

6.2.2.1 Effects on health

Acute toxicity to rats by ingestion has been determined to at least 2400 mg/kg (LD_{50}).

Acute toxicity:

Acute oral rat, female	LD_{50}	2400 mg/kg	Truhaut *et al.* 1979
Acute oral rat, male	LD_{50}	3000 mg/kg	Truhaut *et al.* 1979
Acute dermal, rabbit	LD_{50}	1500 mg/kg	Truhaut *et al.* 1979

When examining repeated dose exposure studies, only results from an oral rat study has been found, where LOAEL was 4060 mg/kg/14 days with continuous exposure based on harmful effects in the blood parameter (Arch. Toxicol.73 (1999): 229- in RTECS 2002).

Based on experiences with glycol ethers NIOSH recommends reducing exposure to lowest feasible concentration and preventing contact with the skin (NIOSH 1988, HSDB)

6.2.2.2 Threshold limit values

The threshold limit value for the working environment is 20 ppm corresponding to 130 mg/m^3 with skin notation, i.e. the substance is skin penetrable (AT 2002).

6.2.2.3 Bioavailability

No data have been found regarding skin absorption of the substance itself. However, for the analogue diethylene glycol butyl ether acetate ingested in doses of 200 and 2000 mg/kg, 82% was retrieved in urine and 2-3% in faeces (HSDB 2003).

Absorption and elimination of dermal applied doses of ^{14}C-diethylene glycol butyl ether and ^{14}C-diethylene glycol butyl ether acetate derivative were determined in rats. The materials were applied the skin under occlusion for 24 hours at dose levels of 0.2 and 2.0 g/kg (undiluted) and as a 10% aqueous solution (0.2 g/kg diethylene glycol butyl ether). The dermal absorption rates were estimated to be 1.58 (diethylene glycol butyl acetate derivative, male), 1.28 (diethylene glycol butyl acetate derivative, female), 0.73 (diethylene glycol butyl ether, male), and 1.46 (diethyl glycol butyl ether, female), expressed as mg/cm^3/hour (Boatman RJ *et al*. 1993).

6.2.2.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. The data on a lower absorption observed in an analogous substance was not found adequate to be used in this context. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest measured migration of 3.80 µg/toothbrush:

Oral, child **= 3.8/10 (µg/hour) ×6/60 (minutes) × 1 (100%) / 10 (kg) = 0.0038 µg/kg bw/day**

Table 6.2 Analysis results and estimated ingestion of 2-Butoxy-ethyl acetate

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	0.69	0.00069
B-003	3.80	0.0038
B-004	-	
B-005	-	
B-006	-	
Maximum	3.8	0.0038

-: Below the detection limit of 0.15 µg/toothbrush

2-Butoxy-ethyl acetate has thus been detected in 2 of the products in amounts above the detection limit of 0.15 µg/toothbrush.

From the above it is seen that none of the amounts ingested or absorbed at toothbrushing will result in a dose above 0.029 mg/kg/day. This value is based on 14 days oral rat study: LOAEL 4060 mg/kg/14 days (RTECS, cf. above). The study contained the only available value for oral intake at repeated dose. If a safety factor of 10000 is used (a factor 10 for interspecies and 10 for intraspecies variation, 10 for subchronic to chronic and 10 for LOAEL to NOAEL), this gives a tolerable dose of (4060/(14 × 10000)) = 0.029 mg/kg/day.

Glycol ether acetates have the same systematic toxicological effects as their corresponding glycol ethers. It is therefore reasonably to assume that their toxicity is equivalent on molar basis according to Jensen *et al.* (1999). If this calculation is used on e.g. the RfD value 0.5 mg/kg/day from 2-butoxy-ethanol (cf. section 4.2.1), an indicative value should be $0.5 \times 118.2/160.2$ = 0.37 mg/kg bw/day. The calculation uses the molar ratio between the two glycol ethers: 118.2 is the molecular weight of 2-butoxyethyl acetate and 160.2 is the molecular weight of 2-butoxy ethanol. This would support that the used effect level used in the evaluation above is not too high.

Another suggestion would be to use the acute toxicity LD_{50}-value 2400 mg/kg. Using a safety factor of 10000 as above this would result in an indicative tolerable dose value of 0.24 mg/kg.

Based on the few available data, the used value for tolerable dose is considered sufficiently supported for this purpose. With a safety margin of almost (29/0.0038=) 8000 the margin of safety should be sufficient to assess the substance not to be a health risk.

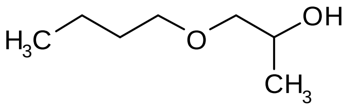
6.2.2.5 Overall evaluation

2-Butoxy-ethyl acetate implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.3 1-Butoxy-2-propanol

1-Butoxy-2-propanol is used as a solvent for printing inks, paint and resins.

Identification

Name	1-Butoxy-2-propanol
CAS no.	5131-66-8 (a-isomer) 15821-83-7 (b-isomer) 63716-40-5 (Mixture) 29387-86-8 (Mixture)
EINECS no.	225-878-4 (a)
Molecular formula	$C_7H_{16}O_2$
Molecular structure	
Molecular weight	132.20 g/mol
Synonyms	propylene- glycol butyl ether propylene- glycol n-butyl ether (PGnBE) 3-butoxy-2-propanol (a-isomer, CAS no. 5131-66-8) 1,2propyleneglycol, 1-monobutyl ether

The melting point of the substances is estimated at -22°C. The boiling point is 171.5°C (Kirk- Othmer 1982). The vapour pressure is estimated at 50 Pa at 20°C (0.4 mmHg). The water solubility is estimated at 42 g/l at 25°C. The partitioning coefficient log Kow is estimated at 0.98 (BIOWIN).

Classification

1-Butoxy-2-propanol, CAS 5131-66-8, is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Xi;R36/38	**Irritant, Irritating to eyes and skin**
Classification in mixtures:	
Xi;R36/38	**conc.>=20%**

It should be noted that the b-isomer, CAS no. 15821-83-7, is not classified.

6.2.3.1 Effects on health

The acute toxicity of 1-butoxy-2-propanol (PGBE) is low. The LD_{50} values for oral rat are between 1900 and 5200 mg/kg (Jensen *et al.* **1999).**

1-Butoxy-2-propanol is eye irritating and somewhat injurious to the eyes, but only mildly irritating to the skin. No sensitisation in guinea pigs has been found (Jensen *et al* **1999).**

A 31 days inhalation study showed no effects in rats at 541 mg/m^3. Chronic toxicity NOEL by oral administration (13 weeks) to rats was 350 mg/kg/day.

In reproduction studies (oral, dermal or injection studies) on mice, rats and rabbits there has been found no effects on maternal toxicity or on foetuses (Jensen *et al.* **1999).**

In Ames test, 1-butoxy-2-propanol was not mutagenic. It did not produce chromosomal aberrations in hamster ovary cells. No carcinogenic data available (Jensen *et al.* **1999).**

6.2.3.2 Threshold limit values

Tentative threshold limit value for the working environment is found of 100 ppm, corresponding to 540 mg/m^3 (AT 2002).

6.2.3.3 Bioavailability

No skin absorption data available, but the low fat-solubility indicates that dermal adsorption might be low. However, in the absence of data, 100% absorption has been used.

6.2.3.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest measured migration of 0.24 µg/toothbrush:
Oral, child **= 0.24/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.00024 µg/kg bw/day**

Table 6.3 Analysis results and estimated ingestion of 1-Butoxy-2-propanol

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	0.11	0.00011
B-003		
B-004	0.24	0.00024
B-005		
B-006	0.15	0.00015
Maximum	0.24	0.00024

-: Below the detection limit of 0.15 µg/toothbrush

1-Butoxy-2-propanol has thus been detected in 2 of the products in amounts above the detection limit of 0.15 µg/toothbrush.

Based on chronic NOEL of 350 mg/kg bw/day and an uncertain factor of 1000, the tolerable effect level is calculated at 0.35 mg/kg bw/day.

From the above it is seen that none of the amounts ingested or absorbed at toothbrushing will result in a dose above 0.35 mg/kg bw/day. The ratio between the estimated exposure is (350/0.00024=) >1×10^6. Therefore, the exposure to 1-butoxy-2-propanol is assessed not to involve any health risk.

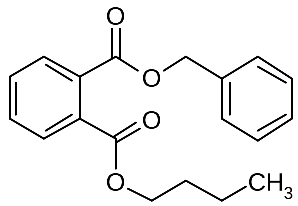
6.2.3.5 Overall evaluation

1-Butoxy-2-propanol implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.4 Benzyl butyl phthalate

Benzyl butyl phthalate is used as a plasticiser for polyvinyl chloride, polyvinyl acetate, rubbers, cellulose plastics and polyurethane. End applications include PVC floorings and wall coverings, PVC foams, films, sealing and adhesive systems based on polyurethane or polysulphide, PVA based adhesives and paint binders.

Identification

Name	**Benzyl butyl phthalate**
CAS no.	**85-68-7**
EINECS no.	**201-622-7**
Molecular formula	$C_{19}H_{20}O_4$
Molecular structure	
Molecular weight	**312.39 g/mol**
Synonyms	**Benzyl butyl phthalate** **Benzyl-n-butyl phthalate** **1,2-Benzene dicarboxylic acid, butyl phenylmethyl ester** **Phthalic acid, benzyl butyl ester** **BBP**

The melting point of the substance is -35°C. The boiling point is 370°C at 1.01 kPa (Kirk-Othmer 1982). The vapour pressure is found to be between 0.04 to 8.0 mPa in various handbooks. In this case 1.15 mPa at 20°C ($8.6x10^{-6}$ mmHg) has been used. The water solubility has been found in various references to be between 0.71 mg/l at 25°C (Yalkowsky and Dannenfelser 1992), and 82.2 mg/l. A used value has been found to be 2.69 mg/l (IUCLID). The partitioning coefficient log Kow has been found in literature to vary between 3.5 and 5.8. The experimental values are found between approx. 4.7 to 4.9 (e.g. 4.91 (Hansch *et al.* 1995)).

Classification

Benzyl butyl phthalate is not classified (Miljøministeriet 2002).

However, benzyl butyl phthalate is included on 29th Adaptation to Technical Progress of July 2003 (ATP 2004). This means that though the substance is not yet included in the Danish regulatory order for dangerous substances, the classification may be included in the next revision of the List of Dangerous Substances. In the ATP list, the classification is:

T;R61 (Rep. cat.2)	**Toxic. May cause harm to the unborn child**
Xn;R 62 (Rep.cat.3)	**Harmful. Possible risk of impaired fertility**
N;R50/53	**Dangerous to the environment. Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment**

T;R61 (Rep, cat. 2) is based on a new 2-generation study in rats (Tyl *et al.,* **2001).**

Xn;R62 (Rep.cat.3) is based on signs of testicular toxicity (atrophy of the testes and decrease in epididymal spermatozoa concentration), and decreased testosterone and follicle stimulating hormone (FSH) levels are reported in the absence of effects in other organs. It is therefore concluded that benzyl butyl phthalate may affect fertility (ECB 2002).

6.2.4.1 Effect on health

Benzyl butyl phthalate is being evaluated under EU's risk assessment programme for existing substances. The evaluation is not yet finalised but an almost final draft from February 2002 is available (ECB 2002). Most information is recovered from the draft.

Benzyl butyl phthalate possesses a relatively low degree of acute toxicity:

Acute oral rat	**LD_{50}**	**2330 mg/kg**	**NCM 1999**
Acute oral mouse (female-male)	**LD_{50}**	**4170-6160 mg/kg**	**NCM 1999**
Acute dermal rat	**LD_{50}**	**6700 mg/kg**	**NCM 1999**

Benzyl butyl phthalate does not irritate the skin since no promaty irritation or sensitisation reactions were observed in 200 human volunteers after 15 daily applications of a subsequent challenge with benzyl butyl phthalate. Following oral or inhalatory administration of benzyl butyl phthalate to rodents, peroxisome proliferation appeared to be the most sensitive effect (Hammond *et al.* **1987).**

In an oral 90-day study in rats, at dose levels of 0, 171, 422 or 1069 mg/kg bw/day for females and 0, 151, 381 or 960 mg/kg bw/day for males, increased liver weights were seen at all dose levels in females and at 381 mg/kg bw/day and at 960 mg/kg bw/day in males. The increased liver weight in females was only slight at the two lower doses. The LOAEL for increased liver and cecal weights in females was 171 mg/kg bw/day. The NOAEL for increased liver weight in males was 151 mg/kg bw/day (Hammond et al., 1987).

In an oral 6 month study on rats, food concentrations of 0, 0.03, 0.09, 0.28, 0.83 and 2.5% benzyl butyl phthalate were applied, corresponding to 0, 17, 51, 159, 470 and 1417 mg/kg bw/day, respectively. A relative increase in weight of liver and brain was observed. The study showed a LOAEL of 8300 ppm (470 mg/kg bw/day) and a NOAEL of 2800 ppm in the food (corresponding to 159 mg/kg bw/day) (NTP study referred in IRIS 2003).

In a 2-generation study of rats where rats were administered 0, 750, 3750 or 11250 ppm in the diet corresponding to 0, 50, 250 or 750 mg/kg bw/day. The NOAEL for effects on the development of the young was 50 mg/kg bw/day based on a dose-dependent effect on the reproductive organs (decrease in absolute and adjusted anogenital distance (AGD)) from 250 mg/kg bw/day in both the F1 and the F2 generation (Tyl *et al.* **2001).**

An effect on the development of reproductive organs (AGD) was also found in a study by Nagao *et al.* **(2000 cit. in ECB 2002) at 500 mg/kg bw/day together with deformities in the reproduction organs after 10 and 18 weeks. In the Nagao study using the dose levels 0, 20, 100 or 500 mg/kg bw/day, a sig-**

nificant decrease in body weight was also seen in offspring at birth in both the 100 and the 500 mg/kg bw/day dose groups. NOAEL for developmental effects was 20 mg/kg bw/day (ECB 2002).

Effects on male reproductive organs and/or fertility are reported after oral administration of benzyl butyl phthalate in doses equal to or higher than those which induce minimal systemic toxicity such as relative organ weight changes, and in some studies histopathological changes in the liver and pancreas. Furthermore, since signs of testicular toxicity, evident as a dose-dependent decrease in epididymal spermatozoa concentration and atrophy of the testis, and decreased testosterone and FSH levels, are reported in the absence of effects in other organs, benzyl butyl phthalate may affect fertility (ECB 2002).

With regard to cancer-causing effect no unambiguous conclusions can be drawn from the available animal experiments. IARC has put the substance in category 3, i.e. not classifiable as to its carcinogenicity to humans.

Oestrogenic effects

For benzyl butyl phthalate oestrogenic effects have been found in test tube experiments (NCM 1996).

Benzyl butyl phthalate has been entered on EU's list of 118 substances, which are considered to be endocrine disrupting or suspected endocrine disrupting substances. Benzyl butyl phthalate is one of 66 substances, which have been documented to be an endocrine disruptor in at least one animal experiment (COM 1999).

Toys and certain articles for small children

In a recommendation of 1 July 1998, the EU Commission has recommended the Member States – in the necessary extent – to "agree on the necessary measures in order to guarantee an extensive protection of children under 3 years against toys and articles for small children, which is designed to be put into the mouth, and which is produced of soft PVC containing phthalates, especially the substances DINP, DEHP, DBP, DIDP, DNOP and BBP, and particularly with the focus on the substances DINP and DEHP". A proposal for common regulation has been discussed in the EU (MEM 1999).

On 1 April 1999, the Danish Statutory Order regarding banning of phthalates in toys and certain articles for small children at the age of 0-3 years became effective (Statutory Order no. 151 of 15 March 1999).

6.2.4.2 Threshold limit values

TDI: a temporary TDI of 0.1 mg/kg bw/day is found (EC 1997 in Baars *et al*. 2001). However, the value is based on an evaluation by the EU Scientific Committee on Foods (SCF). The EU-SCF evaluated benzyl butyl phthalate in 1988 and established a temporary TDI of 0.1 mg/kg bw/day, based on a NOAEL of 140 mg/kg bw/day for changes in liver weight in a 26 week dietary study on rats. The SCF applied an uncertainty factor of 1000 since no adequate studies for teratogenicity or the like were available (CSTEE/97/1-Add 8). Since then several studies have been performed with BBP.

The EU scientific committee CSTEE recommends that guideline values for extractable amounts of individual phthalates in toys be produced, incorporating a margin of safety of at least 100 from their respective NOAEL values. In the table below, TDI (tolerable daily intake) values have been calculated by dividing the NOAEL values by 100. In the table below (table 6.4) is presented

the TDI values calculated as NOAEL/100. The scientific committee CSTEE has several times evaluated the risk from the different phthalates. The table includes a summary of the critical effects, no-effect levels (NOAEL) and the tolerable daily intake for the most frequently used phthalates (CSTEE 1998 a and b).

Table 6.4 NOAEL and TDI values for phthalates in toys (CSTEE 1998b)

Phthalate		Critical effect	NOAEL mg/kg bw/day	Tolerable daily intake mg/kg bw/day
DINP	Di-iso-nonylphthalate	Increased liver and kidney weight	15	150
DNOP	Di-n-octylphthalate	Microscopic cell changes in liver and thyroid gland	37	370
DEHP	Di-ethyl-hexylphthalate	Adverse effects on testis	3,7	37
DIDP	Di-iso-decylphthalate	Increased liver weight	25	250
BBP	Benzylbutylpthahlate	Decreased spermatozoa production	20	200
DBP	Dibutylphthalate	Reduced weight of progeny	52 a	100 b

a LOAEL value
b An additional uncertainty factor of 5 has been used as no NOAEL was found

In an action plan for phthalates by the Danish Ministry of the Environment, based on decreased spermatozoa production, a NOAEL of 20 mg/kg/day and a TDI-value of 0.2 mg/kg bw/day has been stated (MEM 1999).

A reference dose (RfD) of 0.2 mg/kg bw/day has been determined by US-EPA based on an oral 6 month study, which gave a relative increase in weight of liver and brain. The study showed a NOAEL of 2800 ppm in the food (corresponding to 159 mg/kg bw/day). RfD was found using an uncertainty factor of 1000 (10 × 10 for intra- and interspecies variation and 10 in order to extrapolate from sub-chronic to chronic (NTP study referred in IRIS 2003).

6.2.4.3 Bioavailability

In an *in vivo* **study of rats it was found that approx. 5% BBP was absorbed per day via the skin (Elsisi** *et al***. 1989).**

In male rats, orally dosed with ring labelled ^{14}C-benzyl butyl phthalate in 2, 20, 200 or 2000 mg/kg to determine routes and rates of excretion it was found that in the course of 24 hours 61 to 74% was excreted with the urine, and 13 to 19% in faeces (Eigenberger 1986).

The absorption via the skin was thus low (5%/day), while it was up to 74% by oral administration. Oral absorption has been used because it probably simulates the mucous membrane absorption most accurately.

6.2.4.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 74%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest measured migration of 21 µg/toothbrush:
Oral, child **= 21/10 (µg/hour) × 6/60 (minutes) × 0.74 (74%) / 10 (kg) = 0.016 µg/kg bw/day**

Table 6.5 Analysis results and estimated ingestion of benzyl butyl phthalate

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	21.0	0.016
B-003	-	
B-004	-	
B-005	-	
B-006	-	

-: Below the detection limit of 0.15 µg/toothbrush

Benzyl butyl phthalate has thus been detected in 1 of the products in amounts above the detection limit of 0.15 µg/toothbrush.

As the Danish EPA, CSTEE and the US-EPA agree upon a tolerable value (TDI) of 200 µg/kg bw/day, this has been used in the evaluation.

From the above it is observed that none of the amounts of benzyl butyl phthalate ingested or absorbed at toothbrushing will result in a dose above the TDI (or RfD)-value of 0.2 mg/kg bw/day, for which reason it is assessed not to involve any health risk.

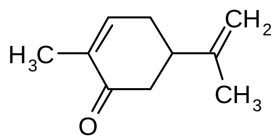
6.2.4.5 Overall evaluation

Benzyl butyl phthalate implies no health risks to the consumer by oral intake or inhalation at the concentrations measured in the selected toothbrushes.

6.2.5 Carvone

Carvone is a natural plant substance. Carvone can be produced from distillation of spearmint oil, which contains 50-70% L-carvone (Kirk-Othmer 1983), or synthesised from D-limonene or *alfa*-pinene (Budavari 1989). Carvone is mostly used as fragrant in perfumes and soaps and as flavouring in order to emphasise the peppermint taste in e.g. toothpaste.

Identification

Name	**Carvone**
CAS no.	**99-49-0**
EINECS no.	**202-759-5**
Molecular formula	**$C_{10}H_{14}O$**
Molecular structure	
Molecular weight	**150.22 g/mol**
Synonyms	**2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-one, p-mentha-6,8-dien-2-on L-carvone carvol**

The melting point of the substance is -15°C. The boiling point is 228.5°C (Budavari 1989). The vapour pressure is 13.7 Pa at 25°C (0.03 mmHg) (Daubert and Danner 1989). The water solubility is 1300 mg/l at 25°C

(Yalkowsky and Dannenfelser 1992). The partitioning coefficient log Kow is estimated at 3.07 (QSAR, EC 2003).

Classification

L-carvone is not classified under its own name, but the substance is a monoterpene. Terpenes are found in essential oils. The terpenes might derive from the use of plant oils and resins as a solvent in the printing ink. The terpenes are generally irritating to the mucous membrane. Turpentine from coniferous trees is skin sensitising. However, the sensitising has not been confirmed for the individual terpenes, except for 3-carene, CAS no. 13466-78-9 (ASS 2000).
If carvone is considered as either mineral or vegetable turpentine (Miljøministeriet 2002), the classification is:

Turpentine, mineral		
CAS no.:	**8052-41-3**	
EF no.:	**232-489-3**	
Classification:	**Carc2;R45 R10 Xn;R48/20-65**	**May cause cancer. Inflammable Harmful: Danger of serious damage to health by prolonged exposure through inhalation. – May cause lung damage if swallowed**
Classification in mixtures:		
Carc2;R45 Xn;R48/20-65	**conc.>=10%**	
Carc2;R45	**0,1%<=conc.<10%**	

Turpentine, vegetable		
CAS no.:	**8006-64-2**	
EF no.:	**232-350-7**	
Classification:	**R10**	**Inflammable**
	Xn;R20/21/22-65	**Harmful by inhalation, in contact with skin and if swallowed – May cause lung damage if swallowed**
	Xi;R36/38 R43	**Irritant, Irritating to eyes and skin. May cause sensitization by skin contact**
	N;R51/53	**Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment**

6.2.5.1 Effects on health

Carvone is a monoterpene (terpenoid ketone).

The sensitising potential of L-carvone is normally considered low, but it has occasionally caused contact allergy in users of spearmint toothpaste and chewing gum. In a "patch-test" examination of 541 patients, 15 (2.8%) had positive and 12 had doubtful positive reactions towards L-carvone. In a repeated test with L-carvone in the same or lower concentrations only 2 out of 8 patients had positive reactions (Paulsen 1993: HSDB).

L-carvone is also an oxidation product of d-limonene, whose oxidation products are known as skin sensitising (AT 2002).

Acute toxicity:

Acute oral rat	**LD_{50}**	**1640 mg/kg**	**Budavari 1989**

Acute oral guinea pig	**LD_{50}**	**766 mg/kg**	**Jenner 1964**

A one-year study was performed on groups of 5 male and 5 female rats fed a diet containing 0, 0.1 or 0.25% carvone. No adverse effects were noted on body-weight gain or main organs and tissues, including testes (Hagan *et al.* **1967).**
Level causing no toxicological effect was thus 0.25% (= 2500 ppm) in the diet, equivalent to 125 mg/kg bw/day. Based on the rat experiment a temporary ADI (acceptable daily intake) for man of 0-1.25 mg/kg bw was defined by the Joint FAO/WHO Expert Committee on food additives (JECFA 1967). The daily intake of carvone (both isomers) per capita is estimated at 2.8 mg/person (JECFA 1999).

I a later discussion whether L and D-carvone could be evaluated identically, it has been confirmed that the study was carried out with L-carvone (p-mentha-6,8-dien-2-one). However, this has not caused a change in the temporary ADI (JECFA 1999).

In a two-year study, where groups of 50 male- and 50 female mice were orally administered 0, 375 or 750 ppm d-carvone, 5 days per week for 103 weeks, no signs of carcinogenic activity were found (NTP 1990).

From the data it was not possible to define a limit for effects (NOAEL).

6.2.5.2 Threshold limit values

Threshold limit value (TLV) for the working environment is 25 ppm corresponding to 140 mg/m^3, equivalent to high-boiling aromatic hydrocarbons (terpenes, turpentine) (AT 2002).

A temporary ADI of 0-1.25 mg/kg bw has been set by JECFA (1967, 1999).

6.2.5.3 Bioavailability

No data have been found regarding skin absorption, but the high fat-solubility of carvone indicates that dermal adsorption is a probable route of exposure and therefore 100% absorption has been used in the evaluation.

6.2.5.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 0.65 µg/toothbrush:
Oral, child **= 0.65/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.00065 µg/kg bw/day**

Table 6.6 Analysis results and estimated ingestion of L-carvone

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw
M-005	-	-
B-003	-	-
B-004	0.65	0.00065
B-005	0.46	0.00046
B-006	-	-
Maximum	0.65	0.00065

-: Below the detection limit of 0.15 µg/toothbrush

L-carvone has thus been detected in 2 of the products in amounts above the detection limit of 0.15 µg/toothbrush.

From the above it is seen that none of the amounts ingested or absorbed at toothbrushing will result in a dose above the temporary ADI of 1.25 mg/kg bw/day, for which reason it is assessed not to involve any health risk.

6.2.5.5 Overall evaluation

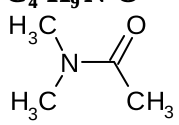
Carvone implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.6 N,N-Dimethylacetamide

N,N-Dimethylacetamide is mostly used as a solvent in industrial applications. N,N-Dimethylacetamid is e.g. used as a solvent for plastics, resins and gums, as catalyst in chemical processes, and paint remover. Polyacrylonitrile, polyvinylchloride, polyamide and polyimide can be dissolved by N,N-dimethylacetamide.

N,N-Dimethylacetamide is furthermore used in the production of films and fibres. For instance, BASF informs that N,N-dimethylacetamide is used in the production of polyacrylonitril fibres, films and coatings and for special lacquers (BASF 2001).

Identification

IUPAC name	**N,N-Dimethylacetamide**
CAS no.	**127-19-5**
EINECS no.	**204-826-4**
Molecular formula	$C_4 H_9 N O$
Molecular structure	
Molecular weight	**87.12 g/mol**
Synonyms	**dimethylacetamide** **acetdimethylamide** **dimethylamide acetate**

The melting point of the substance is –18.59°C. The boiling point is 164°C. The vapour pressure is 267 Pa at 25°C (2 mmHg) The water solubility is high, the substance is stated as miscible with water at 25°C (Budavari 1989). The partitioning coefficient n-octanol/water log Kow has experimentally been determined to –0.77 (Hansch *et al.* 1995).

Classification
N,N-Dimethylacetamide is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Rep.2;R61	**Repro-toxic. May cause harm to the unborn child**
Xn;R20/21	**Harmful. Harmful by inhalation and in contact with skin**
Classification in mixtures:	
conc.>=25%	**Rep2;R61 Xn;R20/21**
5%<=conc.<25%	**Rep2;R61**

6.2.6.1 Effects on health
N,N-Dimethylacetamide is readily absorbed through the skin. Animal studies show that dimethylacetamide may be embryotoxic at high doses (concentration levels not presented) by various routes of exposure, including inhalation (BASF).

N,N-Dimethylacetamide is capable of producing systemic injury when inhaled or absorbed through the skin in sufficient quantities over a prolonged period of time (Kirk-Othmer 1978).

N,N-Dimethylacetamide has a low order of acute toxicity when swallowed or upon brief contact of the liquid or vapour with the eyes or skin (Kirk-Othmer 1978).

Acute toxicity:

Acute oral rat	**LD_{50}**	**4300 mg/kg**
Acute dermal rabbit	**LD_{50}**	**2240 mg/kg**
Acute inhalation rat	**LC_{50}, 1 hour**	**2475 ppm**

The NOEL (no effect level) in rats fed N,N-dimethylacetamide for 90 days was 200 ppm. In the overall toxicological profiles of N,N-dimethylacetamide, the target organ was the liver (Kennedy *et al.* 1986).

N,N-Dimethylacetamide has shown some evidence of reproductive effects in laboratory animals (BASF). The reference presents no concentration levels.

By oral administration of N,N-dimethylacetamide to rats over 22 days during gestation in 5 doses (0, 20, 65, 150 and 400 mg/kg bw/day) in groups of 25 animals per dose with exposure in day 7-21 during gestation significant effects were found at 400 mg/kg. NOEL for maternal toxicity was 65 mg/kg bw/day and for teratogenic effect a NOEL of 65 mg/kg bw/day was found (OECD 2002a).

6.2.6.2 Threshold limit values
The threshold limit value for the working environment is 10 ppm corresponding to 35 mg/m^3 with skin notation i.e. skin penetrable (AT 2002).

6.2.6.3 Bioavailability
N,N-Dimethylacetamide can be absorbed by all exposure routes (inhalation, absorption via skin and by oral intake).

In a study with two rats were intubated with 33 and 93 mg radiolabelled dimethylacetamide in corn oil. After 72 hours, 93% of the radiocarbon was re-

covered from the urine, 5% in the faeces, 2% in the tissue and <1% as CO_2 (OECD 2002a). An absorption of 100% is therefore used in the evaluation.

6.2.6.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest measured migration:
Oral, child **= 0.87/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.00087 µg/kg bw/day**

Table 6.7 Ingestion of N,N-dimethylacetamid calculated from the measured releases

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	-	
B-003	-	
B-004	-	
B-005	0.87	0.00087
B-006	-	
Maximum	0.87	0.00087

-: Below the detection limit of 0.25 µg/toothbrush

N,N-Dimethylacetamid has thus been detected in 1 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

Based on NOEL 200 ppm in 90 days diet toxicity studies. If it is assumed that a 200 g rat eats 20 g food, 200 ppm corresponds to 200 × (20/1000) × (1000/200) =20 mg/kg bw/day. Using a safety factor of 1000 (a factor 10 for interspecies variation, 10 for intraspecies variation and 10 for going from sub-chronic to chronic) a tolerable dose of 20 µg/kg bw/day is derived. The distance between the suggested tolerable dose value and the exposure is still above 20000. Thus even using a safety factor of 1000 the exposure can not be assumed to cause a problem.

Alternatively, the NOEL for maternal toxicity and for teratogenic effect of 65 mg/kg bw/day could be used. With an uncertainty factor of 1000 a value of 0.06 mg/kg bw/day can be used in the evaluation. However, as the value is >60000, this will not result in any changes in the conclusion.

From the above it is seen that none of the amounts being ingested or absorbed by toothbrushing, will result in a dose above 20 µg/kg bw/day, for which reason it is assessed not to involve any health risk.

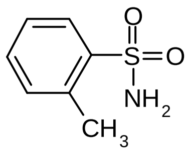
6.2.6.5 Overall evaluation

N,N-Dimethylacetamid implies no health risks to the consumer by oral intake or inhalation at the concentrations measured in the selected toothbrushes.

6.2.7 2-Methyl-benzene sulphonamide

2-Methyl-benzene sulphonamide is mainly used as an additive in the chemical industry. Minor amounts are used as a chemical intermediate for the production of Saccharin. A mixture of 2-methyl-benzene sulphonamide and 4-methyl-benzene sulphonamide is used as a plasticiser for hot-melt adhesives, a chemical intermediate for fluorescent pigments and a chemical intermediate for plasticiser resins (OECD 2002).

Identification

Name	2-Methyl-benzene sulphonamide
CAS no.	88-19-7
EINECS no.	201-808-8
Molecular formula	$C_7H_9NO_2S$
Molecular structure	
Molecular weight	171.23 g/mol
Synonyms	o-methyl-benzene sulphonamide o-toluene sulphonamide toluene-2-sulphonamide

The melting point of the substance is 156.3°C. The boiling point is 214°C (Budavari 1989). The vapour pressure is 6.6×10^{-5} Pa at 25°C (OECD 2002b). The water solubility is 1620 mg/l at 25°C (Yalkowsky and Dannenfelser 1992). The partitioning coefficient log Kow has experimentally been determined to 0.84 (Hansch *et al.* 1995).

Classification

2-Methyl-benzene sulphonamide is not classified (Miljøministeriet 2002). However, in the Danish EPA's Advisory list to Self-classification of Dangerous Substances (MST 2003), the substance (named as o-toluene sulphonamide) is suggested classified:

R43	May cause sensitization by skin contact

6.2.7.1 Effects on health

The acute toxicity for rats is low with LD_{50}- values above 1000 mg/kg bw.

Acute toxicity:

Acute oral rat, males	LD_{50}	>2000 mg/kg	OECD 2002
Acute oral rat, females	LD_{50}	>1000 mg/kg	OECD 2002

The substance is moderately eye irritating for rabbits. No information has been found about skin irritation or skin sensitization (OECD 2002b).

Skin irritation is often described and it is assumed to be a result of the sulphonamide moiety of the chemical substance, as the sensitization increases with increasing amount of sulphonamide, also in other chemical compounds (HSDB).

In an OECD combined repeated dose and reproductive/developmental toxicity screening test (OECD TG 422), o-toluene sulphonamide (2-methyl-benzene sulphonamide) was administered by oral gavage to rats in doses 0, 20, 100, 500 mg/kg bw/day for at least 38 days. At 100 and 500 mg/kg effects on behaviour, reduced increase in weight and histopathological changes in both sexes in a dose-dependent manner. Based on clinical signs and hepathological effects NOAEL for repeated dose toxicity was set to 20 mg/kg bw/day (OECD 2002b).

In the same study, significant reduction in body weights of pups was observed at birth and on day 4 in both sexes at 500 mg/kg bw. There was no change in reproductive parameters at up to 500 mg/kg bw. On the other hand, in a two generation lifetime feeding study, decrease of litter size and pup body weight was observed at 250 mg/kg bw/day. Based on overall evaluation of both results, 100 mg/kg bw/day for reproductive toxicity is considered to be the appropriate NOAEL (OECD 2002b).

Genotoxicity tests in bacteria and mammalian cells *in vitro* **were negative.**

In the two generation lifetime rat study, no tumour incidence up to 250 mg/kg bw/day was observed. Another lifetime rat study indicated slight increase of urinary bladder tumours at 20 mg/kg bw/day and more (OECD 2002b).

6.2.7.2 Threshold limit values

None found.

6.2.7.3 Bioavailability

In a human experiment, 0.2 mg/kg 2-Methyl-benzene sulphonamide (named as o-toluene sulphonamide) was administered orally. Almost all was recovered from urine, and only <1% from faeces within 4 days. In rat experiments, 94% was recovered from urine and 5-7% in faeces (OECD 2002b). An absorption of 100% is therefore used in the evaluation.

6.2.7.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 390 µg/toothbrush:

Oral, child **= 390/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.39 µg/kg bw/day.**

Table 6.8 Analysis results and estimated ingestion of 2-methyl-benzene sulphonamide

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	-	
B-003	-	
B-004	19.0	0.019
B-005	-	
B-006	390	0.390
Maximum	390	0.390

-: Below the detection limit of 0.25 µg/toothbrush

2-Methyl-benzene sulphonamide has thus been detected in 2 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

Based on a NOAEL 20 mg/mg bw and a safety factor of 1000 a tolerable concentration of 20/1000 = 20 µg/kg bw/day has been used.

From the above it is seen that none of the amounts being ingested or absorbed by toothbrushing, will result in a dose of more than 20 µg/kg, for which reason it is assessed not to involve any health risk.

6.2.7.5 Overall evaluation

2-Methyl-benzene sulphonamide implies no health risks to the consumer by oral intake at the concentrations measured migrating from the selected toothbrushes.

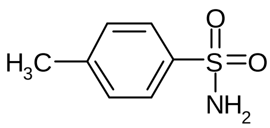
6.2.8 4-Methyl-benzene sulphonamide

6.2.8.1 Origin

Mixtures of 2- and 4-methyl-benzene sulphonamide (= o- and p-toluene sulphonamides) are used as a reactive plasticiser in hot-melt adhesives and to increase the flexibility of surface finishing coat based on resins (OECD 2002b).

UNEP (1995) mentions that 4-methyl-benzene sulphonamide is used as raw material for the synthesis of pesticides, fluorescent colorants and drugs and that it is also used as plasticiser for thermosetting resins below 1%.

Identification

Name	**4-Methyl-benzene sulphonamide**
CAS no.	**70-55-3**
EINECS no.	**200-741-1**
Molecular formula	$C_7H_9NO_2S$
Molecular structure	
Molecular weight	**171.23 g/mol**
Synonyms	**p-methyl-benzene sulphonamide p-toluene sulphonamide toluene-4-sulphonamide tolyl sulphonamide**

The melting point is 138.5°C. The boiling point is 214°C at 1.33 kPa (10 mmHg) (Kirk-Othmer 1982). The vapour pressure is 100 Pa at 170°C (0.75 mmHg) (SIAR). The water solubility is 3160 mg/l at 25°C (Yalkowsky and Dannenfelser 1992). The partitioning coefficient log Kow has experimentally been determined to 0.82 (Hansch *et al.* 1995).

Classification

4-Methyl-benzene sulphonamide is not classified (Miljøministeriet 2002). However, in the Danish EPA's Advisory list to Self-classification of Dangerous Substances (MST 2003), the substance (named as p-toluene sulphonamide) is suggested classified:

R43	May cause sensitization by skin contact

6.2.8.2 Effects on health

Since many of the adverse effects appear to be hypersensitivity reactions there is no specific toxic dose. The incidence of the adverse effects appears to increase with increased sulphonamide dosage (HSDB).

There has not been found much literature about acute lethal effects after skin contact or oral intake. Most of the data have been found in an OECD/SIDS report (UNEP 1995).

Acute toxicity:

Acute oral, rat	LD_{50}	>2000 mg/kg	UNEP 1995
Acute oral, mouse	LD_{50}	400 mg/kg	UNEP 1995

A combined repeat dose and reproductive/developmental toxicity screening test was performed according to OECD TG 422. Doses of: 0, 120, 300 and 750 mg/kg/day were administered by oral gavage for 42 days to male rats and from day 14 before mating through day 3 of lactation to female rats. 4-Methyl-benzene sulphonamide did not show any genotoxic effects, and LOAEL (lowest adverse effect level) for repeated dose toxicity was established as 120 mg/kg bw/day (UNEP 1995).

NOAEL on reproductive toxicity was 300 mg/kg bw/day and resulted in a lowest acceptable concentration of 0.60 mg/kg bw/day (UNEP 1995).

6.2.8.3 Threshold limit values

TDI: 0.024 mg/kg bw/day. Based on the study on repeated toxicity (UNEP 1995), an estimated dose of tolerable daily intake was calculated using a safety factor of 5000 (a factor 10 for interspecies variation, 10 for intraspecies variation, 10 for extrapolating from LOAEL to NOAEL and 5 because it is not a chronic study but performed at a sensitive lifestage), i.e. 120/5000 = 0.024 mg/kg bw/day.

6.2.8.4 Bioavailability

No data have been found regarding skin absorption. As there are no data for the absorption, 100% ingestion has been used.

6.2.8.5 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 810 µg/toothbrush:
Oral, child **= 810/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.81 µg/kg bw/day**

Table 6.9 Analysis results and estimated ingestion of 4-methyl-benzene sulphonamide

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005		
B-003		
B-004	26.0	0.026
B-005		
B-006	810	0.810
Maximum	810	0.810

-: Below the detection limit of 0.25 µg/toothbrush

4-Methyl-benzene sulphonamide has thus been detected in 2 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

Based on the study of repeated oral exposure, a tolerable dose of 0.024 mg/kg bw/day was established.

From the table above it is seen that none of the amounts being ingested or absorbed by toothbrushing, will result in a dose of more than 24 µg/kg, for which reason it is assessed not to involve any health risk.

6.2.8.6 Overall evaluation

4-Methyl-benzene sulphonamide implies no health risks to the consumer by oral intake at the concentrations measured in the analyses of the selected toothbrushes.

6.2.9 1-Methyl-2-pyrrolidinone

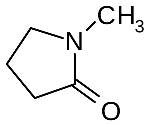
1-Methyl-2-pyrrolidinone is used as solvent for resins, pigment dispersant and as constituent in the PVC production.

1-Methyl-2-pyrrolidinone is mainly used as a solvent for extraction in the petrochemical industry, as a reactive medium in polymeric and non-polymeric chemical reactions, as a remover of graffiti and paint. 1-Methyl-2-pyrrolidinone is also used as a formulating agent in pigments, dyes, and inks and in the production of pesticides. 1-Methyl-2-pyrrolidinone is further used as an intermediate in the pharmaceutical industry, as a penetration enhancer for topically applied drugs, and as a vehicle in the cosmetics industry.

Identification

Name	**1-Methyl-2-pyrrolidinone**
CAS no.	**872-50-4**
EINECS no.	**212-828-1**
Molecular formula	C_5H_9NO

Molecular structure



Molecular weight **99.13 g/mol**
Synonyms **N-methylpyrrolidinone**
Methylpyrrolidone
***N*-methyl-2-pyrrolidon**

The melting point of the substance is -25°C. The boiling point is 202°C at kPa (760 mmHg) (Budavari 1989). The vapour pressure is 46 Pa at 25°C (0.345 mmHg) (Daubert and Danner 1989). The water solubility is high (miscible) mg/l at 25°C (Lewis 1993). The partitioning coefficient log Kow has experimentally been determined to –0.54 (Hansch *et al.* **1995).**

Classification
1-Methyl-2-pyrrolidinone is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Xi;R36/38	**Irritant. Irritating to eyes and skin**
Classification in mixtures:	
Xi;R36/38	**conc.>=10%**

6.2.9.1 Effects on health
1-Methyl-2-pyrrolidinone may effect the skin. It can cause dermatitis with blistering, oedema and erythrema with prolonged or repeated skin contact (Sullivan and Krieger 1992).

Workers have experienced irritant reactions of the skin after a few days of working with the solvent. After two days of work with 1-methyl-2-pyrrolidone, 10 of 12 workers displayed acute irritant contact dermatitis (Leira *et al.* **1992).**

1-Methyl-2-pyrrolidinon is eye irritating (Kirk Othmer 1982).

The acute toxicity of the substance is low:

Acute oral rat	**LD_{50}**	**7000 mg/kg**	**NIOSH 2003**
Acute oral mouse	**LD_{50}**	**7725 mg/kg**	**NIOSH 2003**
Acute dermal rabbit	**LD_{50}**	**8000 mg/kg**	**Snyder 1990**

In a 28-day diet toxicity study with repeated dose 0, 2000, 6000, 18000 or 30000 ppm 1-Methyl-2-pyrrolidinone were administered to the rats. *In vivo* **parameters, haemathological and clinical-chemical parameters, together with a complete pathological evaluation were carried out after 28 days. NOAEL was 6000 ppm (429 mg/kg bw) in males and 18000 ppm (1548 mg/kg bw) in females (Malek** *et al***. 1997).**

In a 28-day intubation study in rats, a dose-dependent increase in relative liver and kidney weights and a decrease in lymphocyte count in both sexes were observed at 1028 mg/kg bw. The NOAEL in this study was 514 mg/kg bw (CICAD 2001).

Rats (10 per sex) were administered 0, 3000, 7500, or 18 000 ppm 1-Methyl-2-pyrrolidinone in the diet for 90 days. The mean daily 1-Methyl-2-

pyrrolidinone dose was 0, 169, 433 and 1057 mg/kg body weight in males and 0, 217, 565 and 1344 mg/kg bw in females. A dose-related decrease in body weight was observed from 7500 ppm. Together with other observations of clinical and behavioural kind, the NOAEL for this study was 3000 ppm equivalent to 169 mg/kg bw in males and 217 mg/kg bw in females (CICAD 2001).

6.2.9.2 Threshold limit values

At the moment, there is no Danish threshold limit value. Based on acute data a German maximum value for the working environment (MAK) of 20 ppm has been suggested; this corresponds to 80 mg/m^3; with skin notation (DF 2001).

An American threshold limit value for the working environment (TWA, 8 hour) is 10 ppm with skin notation (AIHA 1999).

6.2.9.3 Bioavailability

When applied on the skin 61 to 70% of the dose was recovered in urine over 5 days, of which most of it within 24 hours. 6 to 7% was released with the expiration air and 1 to 2% with faeces. By oral ingestion 85 to 88% was recovered in the urine within the first 5 days (Midgley *et al*. 1992). The absorption was so high that is considered reasonable to use 100% adsorption in the evaluation.

6.2.9.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 200 µg/toothbrush:
Oral, child **= 200/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.20 µg/kg bw/day.**

Table 6.10 Analysis results and estimated ingestion of 1-methyl-2-pyrrolidinone

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	200.0	0.20
B-003	-	
B-004	4.30	0.0043
B-005	1.40	0.0014
B-006	0.19	0.00019
Maximum	200.0	0.20

-: Below the detection limit of 0.15 µg/toothbrush

1-Methyl-2-pyrrolidinone has thus been detected in 4 of the products in amounts above the detection limit of 0.15 µg/toothbrush.

For the evaluation of oral exposure, NOAEL of 169 mg/kg bw/day from the 90-days study is used. Subsequently, a tolerable concentration (TDI) has been calculated as:

TDI = 169 mg/kg bw/day / 300

= 0.6 mg/kg bw/day

The uncertainty factor of 300 was combined from several factors, i.e. 10 for interspecies variation, 10 for interindividual variation at humans and 3 for an adjustment from the 90-days study to a chronic exposure (IPCS 1994).

From the above it is seen that none of the amounts being exposed to the consumer by toothbrushing, will result in a dose of more than 0.6 mg/kg bw/day (600 µg/kg bw/day), for which reason it is assessed not to involve any health risk.

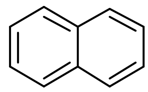
6.2.9.5 Overall evaluation

1-Methyl-2-pyrrolidinone implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.10 Naphthalene

Naphthalene is used mostly in the production of other chemical substances. The major part is used in the manufacture of phthalic acid anhydride. Naphthalene is also used in the production of colorants via the intermediates naphthol and naphthalene sulphonic acid.

Identification

IUPAC name	Naphthalene
CAS no.	91-20-3
EINECS no.	202-049-5
Molecular formula	$C_{10}H_8$
Molecular structure	
Molecular weight	128.18 g/mol
Synonyms	Naphthalin Naphthene

The melting point is 80.2°C. The boiling point is 218°C. The vapour pressure is 10.5 Pa at 25°C. The water solubility is 31 mg/l at 25°C (Budavari 1989). The partitioning coefficient n-octanol/water log Kow is 3.4 (ECB 2003).

Classification

Naphthalene is classified in the List of Dangerous Substances (Miljøministeriet 2002):

Carc3;R40*	Carcinogenic. Possible risk of irreversible effects
Xn;R22	Harmful. Harmful if swallowed
N;R50/53	Dangerous for the environment. Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

*: Added at 29th ATP (2004) (29^{th} Adaptation to Technical Progress. Dir 67/548/EEC) and therefore not yet included in the List of Dangerous Substances (Miljøministeriet 2002). Same classification is stated in the risk assessment report (EC B 2003).

6.2.10.1 Effects on health

Naphthalene can be taken up via all exposure routes (inhalation, percutaneous and by ingestion).

Based on several reported incidences of acute poisoning with acute systemic effects after oral intake of naphthalene, e.g. as mothballs, haemolytic anaemia is considered the major problem to humans (Gosselin *et al.* 1984).

Acute oral toxicity to rats is determined to 2300 mg/kg (LD_{50}). The lowest oral dose with lethal effects was 1500 mg/kg for female and 2000 mg/kg for male rats (Gaines 1969).

For mouse the acute oral toxicity LD_{50} was 533 mg/kg for males and 710 mg/kg for females (Shopp *et al.* 1984).

At repeated oral exposure the highest dose where no adverse effects were observed (NOAEL) was 133 mg/kg for systemic toxicity in a 90 days mouse study (ACGIH 1991).

In an unpublished study, 500 mg naphthalene was applied to the skin of rabbits for 4 hours. In half the animals (3/6) erythremes were visible after 30 minutes to 6 days of exposure (IUCLID).

Another study on dermal contact included repeated applications for 6 hours per day, 5 days a week for 13 weeks (90 days) at up to 1000 mg/kg bw/day. The highest level without adverse effects (NOAEL) was 1000 mg/kg for systemic effects even though mild skin irritation could be observed (Bushy Run 1986).

In a study on short-time oral intake on mice, a LOAEL of 250 mg/kg/day for mortality and reproduction toxicity was found (Hassauer *et al*. 1993).

In a study on long-time oral intake on rats, a NOAEL of 30 mg/kg/day for nephro- and haematotoxicity was found (Hassauer *et al*. 1993).

In a subchronic oral rat study, a NOAEL of 71 mg/kg bw/day was found (IPCS 1998, IRIS 1999).

Referring to the carcinogenic effect no conclusions from the limited data on man can be made. However, the carcinogenic potential of naphthalene is well examined in animal studies. In a 2-year inhalation study on rats an increased incidence of respiratory epithelial adenomas and olfactory epithelial neuroblastomas were observed even at the lowest exposure of 10 ppm (50 mg/m^3) which is considered the result of chronic tissue irritation (ECB 2003).

A rat study that indicates that naphthalene may be carcinogenic has caused an amendment to the classification ”Carc. cat. 3” (29 ATP 2003), i.e. possible carcinogenic.

6.2.10.2 Threshold limit values

The threshold limit value for the working environment is 10 ppm corresponding to 50 mg/m^3 (AT 2002).

TDI short-time oral intake: 250 µg/kg bw/day based on LOAEL 250 mg/kg/day for mice, an assumed absorption of 85% and a safety factor of 1000 (Hassauer *et al*. 1993).

TDI long-time oral intake: 30 µg/kg bw/day based on NOAEL 30 mg/kg/day for rats, an assumed absorption of 85% and a safety factor of 1000 (Hassauer *et al*. 1993).

TDI: 40 µg/kg bw/day has been found in a Dutch evaluation (Baars *et al.* **2001).**

RfD (roughly corresponding to chronic TDI) is 20 µg/kg bw/day. The value is based on sub-chronic oral rat study, which gave a NOAEL of 71 mg/kg bw/day. An uncertainty factor of 3000 has been used (10 for interspecies, 10 for intraspecies variation, 10 for sub-chronic study and 3 for lacking data of other species (IPCS 1998, IRIS 1999).

6.2.10.3 Bioavailability

The absorbed naphthalene is excreted quickly in the urine. Rats administered single dosages of ^{14}C-labelled naphthalene excreted 75.6% of the radioactivity within 24 hours and after 72 hours, 83% was recovered from urine, 6% from faeces, and 4% remained in the body. The remaining part was unaccounted for (Bakke *et al.* **1985).**

An absorption of 100% has been used in the evaluation even if the absorption may be between 85% and 94%.

6.2.10.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 2.6 µg/toothbrush:
Oral, child **= 2.60/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.0026µg/kg bw/day.**

Table 6.11 Analysis results and estimated ingestion of naphthalene

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	2.60	0.0026
B-003	-	-
B-004	-	-
B-005	-	-
B-006	0.29	0.00029
Maximum	2.60	0.0026

-: Below the detection limit of 0.25 µg/toothbrush

Naphthalene has thus been detected in 2 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

In agreement with the worst case principle the lowest available tolerable dose, the RfD value of 20 µg/kg bw/day has been used in the evaluation.

From the above it is seen that none of the amounts being ingested or absorbed will result in a dose of more than 20 µg/kg bw/day, for which reason it is assessed not to involve any health risk.

6.2.10.5 Overall evaluation

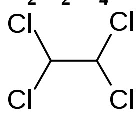
Naphthalene implies no health risks to the consumer by oral intake or inhalation at the concentrations measured in the selected toothbrushes.

6.2.11 1,1,2,2-Tetrachloroethane

1,1,2,2-Tetrachloroethane is being produced by chlorination of ethylene, ethane or 1,2-dichlorethane. 1,1,2,2-Tetrachloroethane is used as solvent for a wide range of substances, but the use is decreasing due to the high toxicity of the substance and the emergence of suitable alternatives.

The source of the recoveries might be the use in the production of polymers or the use as solvent in adhesives. Thus, 1,1,2,2-tetrachloroethane can be a residue from the use in the production process, but it can also be an accidental by-product from the production of another substance, which is used in the production.

Identification

Name	**1,1,2,2-Tetrachloroethane**
CAS no.	**79-34-5,** **25322-20-7 (tetrachloro-ethane)**
EINECS no.	**201-197-8**
Molecular formula	$C_2H_2Cl_4$
Molecular structure	
Molecular weight	**167.85 g/mol**
Synonyms	**Sym-tetrachloroethane** **acetylene tetrachloride**

The melting point of the substance is –43.8°C. The boiling point is 146°C (Budavari 1989). The vapour pressure is 800 Pa at 25°C (Howard 1990), 1200 Pa at 30°C (9 mmHg) (Flick 1985: HSDB). The water solubility is 2860 mg/l at 25°C (1 g/350 ml, Budavari 1989). The partitioning coefficient log Kow has experimentally been determined to 2.39 (Hansch *et al*. 1995).

Classification

1,1,2,2-Tetrachlorethane, CAS no. 79-34-5, is classified (Miljøministeriet 2002):

Tx;R26/27	**Toxic. Very toxic by inhalation and in contact with skin**
N;R51/53	**Dangerous for the environment. Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment**
Classification in mixtures:	
Tx;R26/27	**conc.>=7%**
T;R23/24	**1%<=conc.<7%**
Xn;R20/21	**0,1%<=conc.<1**

6.2.11.1 Effects on health

The acute toxicity of 1,1,2,2-tetrachloroethane is slight to moderate.

Acute toxicity:

Acute oral rat	**LD_{50}**	**800 mg/kg**	**NIOSH 1997**
Acute oral rat	**LD_{50}**	**200 mg/kg**	**HSDB 2003**
Acute oral human	**TD_{LO}***	**30 mg/kg**	**NIOSH**

***: Lowest observed dose with toxic effect**

In a rat inhalation study, based on immunotoxicity a NOAEL of 2 mg/m^3 was observed. The reference has recalculated the exposure to a NOAEL of 60 µg/kg/day assuming an absorption from inhalation of 50% (Hassauer *et al*. 1993).

Based on the results of principally limited short term and subchronic studies, the liver appears to be the most sensitive target organ.

1,1,2,2-Tetrachloroethane is found to be hepathotoxic and nephrotoxic. In a rat study with short-time oral exposure of 1,1,2,2-tetrachloroethane, hepathotoxicity, nephrotoxicity, effects on testes etc. were observed at the lowest dose level. Thus, LOAEL was 8 mg/kg bw/day (Hassauer *et al.* 1993).

In a long-term oral exposure of 1,1,2,2-tetrachloroethane to rats, hepathotoxicity, nephrotoxicity, effects on testes etc. were observed. NOAEL was 3.2 mg/kg bw/day (Hassauer *et al.* 1993).

Long-time oral intake of tetrachloroetane resulted in an increased number of liver-tumours in mice. It has not been possible to repeat the results in other species of animal. The exposure for 78 weeks for 0, 142 or 284 mg/kg bw/day is used in an American model (Multistage model) for the evaluation of its carcinogenic potency. The potency, which resulted in 5% increase of liver-tumours, was between 5.8 and 28 mg/kg bw/day (CICAD 1998).

6.2.11.2 Threshold limit values

An American threshold limit value for the working environment, TWA (8 hours Time Weighted Average) was 1 ppm corresponding to 7 mg/m^3 (ACGIH 2000).

ADI for short-time oral absorption of 8 µg/kg bw/day (based on a LOAEL for rats of 8 mg/kg bw/day and a safety factor of 1000 (Hassauer *et al.* 1993).

ADI: 0.6 µg/kg bw/day based on absorption via inhalation (NOAEL 60 µg/kg/day from 2 mg/m^3, and a safety factor of 100) (Hassauer *et al*. 1993)

ADI for long-time oral absorption of 0.3 µg/kg bw/day (based on a NOAEL for rats of 3.2 mg/kg bw/day and a safety factor of 10000) (Hassauer *et al.* 1993).

6.2.11.3 Bioavailability

1,1,2,2-Tetrachloroethane is readily absorbed via the skin (MSDS, HSDB).

References suggest an absorption between 70 and 100% after oral exposure. In an experiment with 1.5 mg/kg for rats and mice, 41% was recovered in the exhaled air, 23% in urine and 4% in faeces for rats, for mice the figures were

51%, 22% and 6%, respectively (ATSDS 1996). An absorption of 100% is used in the evaluation.

6.2.11.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured of 0.41 µg/toothbrush:
Oral, child **= 0.41/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.00041 µg/kg bw/day.**

Table 6.12 Analysis results and estimated ingestion of 1,1,2,2-tetrachloroethane

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw
M-005	-	
B-003	-	
B-004	-	
B-005	-	
B-006	0.41	0.00041

-: Below the detection limit of 0.25 µg/toothbrush

1,1,2,2-tetrachlorethane has thus been detected in 1 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

For the evaluation, the lowest found ADI value of 0.3 µg/kg bw/day has been used (se the section for threshold limit values).

From the above it is seen that none of the amounts being ingested or absorbed by toothbrushing will result in a dose above the ADI value of 0.3 µg/kg bw/day, for which reason it is assessed not to involve any health risk.

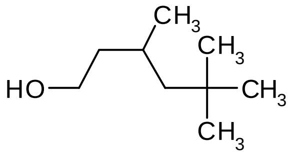
6.2.11.5 Overall evaluation

1,1,2,2-Tetrachloroethane implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.12 3,5,5-Trimethyl-1-hexanol

3,5,5-Trimethyl-1-hexanol is used in the production of plasticisers, i.e. phthalates and esters.

Identification

Name	**3,5,5-Trimethyl-1-hexanol**
CAS no.	**3452-97-9**
EINECS no.	**222-376-7**
Molecular formula	$C_9H_{20}O$
Molecular structure	
Molecular weight	**144.26 g/mol**
Synonyms	**Isononylalcohol** **Nonylol**

The melting point of the substance is -70°C. The boiling point is 193°C (Kirk-Othmer 1982). The vapour pressure is 40 Pa at 20°C (0.3 mmHg) (Flick 1991). 9.01 Pa at 25°C (OECD 2002c). The water solubility is 450 mg/l at 25°C (OECD 2002c). The partitioning coefficient log Kow has experimentally been determined to 3.42 (OECD 2002c).

Classification

3,5,5-Trimethyl-1-hexanol is not classified (Miljøministeriet 2002)

6.2.12.1 Effects on health

In a study for oral toxicity in rats, a single dose toxicity test at 500, 1000 and 2000 mg/kg was performed. No deaths occurred and the LD_{50} was estimated to be more than 2000 mg/kg. A decrease in spontaneous motor activity was observed on the day of administration, and body weight gains were reduced during the first 14 days of administration. No changes were detected on autopsy or histopathological examination (OECD 2002b).

Acute toxicity:			
Acute oral rat	LD_{50}	**>2000 mg/kg**	**OECD 2002c**

In a combined study (OECD TG 422: Combined repeated dose and reproductive/ developmental toxicity screening test), 3,5,5-trimethyl-1-hexanol was administered by oral gavage to rats at the dose levels 0, 12, 60 and 300 mg/kg/day. The doses were administered to male rats for 46 days and to female rats from 14 days before mating until day 3 in the period of lactation. A slight to moderate effect was observed in the kidneys at 60 and 300 mg/kg/day for males and females, respectively. Based on these observations NOAEL for repeated dose toxicity was set at 12 mg/kg/day (OECD 2002c).

Dermal and inhalation studies on 3,5,5-trimethyl-1-hexanol are not available.

There is no available information on humans.

6.2.12.2 Threshold limit values

None found.

6.2.12.3 Bioavailability

No data found regarding adsorption.

6.2.12.4 Evaluation

By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured to 0.77 µg/toothbrush:
Oral, child **= 0.77/10 (µg/hour) × 6/60 (minutes) × 1 (100%) / 10 (kg) = 0.00077 µg/kg bw/day.**

Table 6.13 Analysis results and estimated ingestion of 3,5,5-trimethyl-1-hexanol

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	-	
B-003	0.77	0.00077
B-004	-	
B-005	-	
B-006	-	

-: Below the detection limit of 0.25 µg/toothbrush

3,5,5-Trimethyl-1-hexanol has thus been detected in 1 of the products in amounts above the detection limit of 0.25 µg/toothbrush.

The accepted exposure is based on NOAEL 12 mg/kg bw/day and an uncertainty factor of 1000 (a factor 10 for interspecies variation, 10 for intraspecies variation and 10 for extrapolating from subchronic to chronic exposure). The tolerable exposure would thus be 12/1000 = 0.012 mg/kg bw/day equal to 12 µg/kg bw/day.

From the table above it is seen that none of the amounts being ingested or absorbed by toothbrushing will result in a dose above 12 µg/kg, for which reason it is assessed not to involve any health risk. The margin of safety between the NOAEL value and the exposure level is approx. 12000/0.00077 = 15600, which is considered sufficient.

6.2.12.5 Overall evaluation

3,5,5-Trimethyl-1-hexanol implies no health risks to the consumer by oral intake at the concentrations measured in the selected toothbrushes.

6.2.13 Nickel

Identification

Name	**Nickel**
IUPAC name	**Nickel**
CAS no.	**7440-02-0**
EINECS no.	**231-111-4**
Molecular formula	**Ni**
Atomic weight	**58.69**

The melting point of nickel is 1455°C.

Classification
Nickel is classified: Carc3;R40 R43

Most nickel compounds are classified for sensitisation potentials as R43, May cause sensitization by skin contact.

A range of nickel compounds is either known as carcinogenic or suspected to be carcinogenic, as e.g. nickel carbonate and nickel sulphate.

Furthermore, most nickel compounds are classified as dangerous for the environment at R50/53, Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

6.2.13.1 Effect on health
Skin contact with nickel is very essential, as most nickel compounds may cause allergic reactions at sensitised persons. An assessment of skin contact would therefore be relevant. However, it has not been possible to find relevant data for such an assessment. EU has included nickel in the risk evaluation programme for existing substances, but this has not yet been completed (ECB 2002).

6.2.13.2 Threshold limit values
The tolerable daily dose at ingestion (TDI) has been calculated to 5 µg/kg bw/day (WHO 1996). However, a Dutch assessment on nickel suggests 0.05 mg/kg bw/day (Baars *et al.* **2001).**

6.2.13.3 Bioavailability
The bioavailability by oral intake has been estimated at 5% (Baars *et al.* **2001).**

6.2.13.4 Evaluation
By ingestion, it is assumed that a child uses the toothbrush 3 times/day for 2 minutes, totally 6 minutes/day. The weight of the child has been set at 10 kg, and the absorption (bioavailability) at 100%. Based on this, the amount of absorbed substance has been calculated below.

Example of calculation based on the highest migration measured of 1.06 µg/toothbrush:
Oral, child **= 1.06/10 (µg/hour) × 6/60 (minutes) × 0.05 (5%) / 10 (kg) = 0.000053 µg/kg bw/day.**

Table 6.14 Analysis results and estimated injection of nickel

Toothbrush	Measured migration	Oral, child
	µg/toothbrush	µg/kg bw/day
M-005	1.06	0.000053
B-003	0.84	0.000042
B-004	0.34	0.000017
B-005	0.032	0.0000016
B-006	0.20	0.000010
Maximum	1.06	0.000053

-: Below the detection limit of 0.005 µg/toothbrush

Nickel has thus been detected to migrate from all the products in amounts above the detection limit of 0.005 µg/toothbrush.

The tolerable daily intake calculated by WHO was at 5 µg/kg bw as the lowest of the two available TDI-values.

From the above calculations in the table it is seen that none of the amounts being ingested or absorbed by toothbrushing will result in a dose of more than 5 µg/kg bw/day, for which reason it is assessed not to involve any health risk.

6.2.13.5 Overall evaluation

Nickel implies no health risks to the consumer by oral intake at the concentrations measured in the migration analyses of the selected toothbrushes.

Nickel is a well-known allergen. There is no information as to how high the values should be in order to exclude the possibility of allergic reactions, as it is individual and dependent on the sensitivity of the person concerned. Consequently, reservations are made regarding particularly sensitive persons.

6.3 Conclusion

Based on the measured concentrations of 13 single substances, which have been detected migrating to artificial saliva from the 5 complete toothbrushes, and using the suggested exposure scenario, the overall conclusion was that none of the single substances were found in concentrations exceeding the used values for tolerable daily intake. These reference values were based on established or suggested ADI, TDI or RfD values.

Further refinement of the health evaluation by reducing the exposure for parts of the toothbrush or reducing the exposure time (or increasing, in certain cases) is considered only to result in unimportant changes. The safety distance between the estimated intakes and the used tolerable values was as a rule more than 1000, for which reason such an examination has not been carried out. The fact that the evaluation is furthermore based on a child with a body weight of 10 kg, and an assumption of a rather high absorption, has - of course - been a contributory factor increasing the safety margin.

In the evaluations it has not been taken into consideration that particularly sensitive consumers (allergic or the like) might experience problems using some of the toothbrushes. The analysis indicates that most of the problematic substances were solvents or substances used in the surface treatment or coatings of toothbrushes. Therefore, it is suggested that sensitive consumers use less colourful toothbrushes, where a potential presence of these substances will be further reduced.

Overall it was concluded that the evaluated migrated substances do not constitute a health risk for the consumer when using the toothbrushes.

At the same time, the producers could be urged to be more aware of the fact that the use of some substances should/could be further reduced when they are classified as possible carcinogenic (e.g. naphthalene) or repro-toxic (e.g. dimethylacetamide). Especially, if their presence in the product is not necessary or less significant. It should be considered whether they could be removed by substitute substances, even though the exposure to the consumer is considered insignificant.

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Encl. A: List of toothbrushes purchased

No.	Colours	Information stated on the packaging
N-001	Plain grey	Rubber handle
N-002	Purple with yellow handle with purple snake	Extra soft bristles
N-003	Grey with white and purple bristles	
M-001		Extra soft bristles
M-002	Plain yellow	Extra soft bristles
M-003	Purple with princess picture	Brush head with soft rubber edge. Cup-shaped bristles
M-004	White with print	Extra soft rounded bristles. SAN handle, polyamide bristles. Fulfils DVN's demands for strength and fixation of bristles
M-005	Blue with Buzz Lightyear print	Blue indicator bristles
M-006	Blue/yellow with Donald Duck	Brush head with soft rubber edge. Power Tip bristles
M-007	White/green handle with white/blue bristles	Produced in Denmark
M-008	Black/white handle, black/white/grey bristles	
M-009	Orange/red, multi-coloured bristles	Brush head with soft rubber edge. Varying structure of bristles
K-001	Plain blue with white bristles and print	Soft bristles
K-002	Pink rubber on blue handle, multi-coloured bristles	Massage part to chew on. PP handle thermoplastic elastomer, polyamide bristles, polyoxymethylene safety ring
K-003	Green with figures	Soft bristles
K-004	Plain blue/purple	
B-001	Purple with yellow stripes and white bristles	Rubber-coated handle. Recommended replacement each 3 months
B-002	Transparent handle and bristles. T&J holder	Soft bristles
B-003	Yellow with white/orange bristles and orange suction disc. Bee print	Soft bristles
B-004	Black/transparent handle, white/black bristles	Soft bristles, rubber handle
B-005	Dark blue/white handle, blue/white bristles	Rubber bristles and handle
B-006	Green with white/green bristles	
B-007	Blue/purple handle, pink bristles	Soft bristles, rubber handle
B-008	White/green handle with white/green bristles	Soft rubber bristles
B-009	Green/yellow handle, green bristles	Soft bristles, rubber handle
B-010	Grey/orange handle, grey/orange bristles	

Encl. B: FT-IR Analysis results from screening

No.	Bristles	Handle	Print
N-001	Grey bristles: polyamide Black bristles: polyamide	Grey handle: polypropylene Purple parts: "SBS" elastomer with a high content of chalk	
N-002	White bristles: polyamide Green bristles: polyamide	Purple handle: polypropylene Yellow part: Acrylic-based elastomer	Print: acrylic-based binder
N-003	White bristles: polyamide Purple bristles: polyamide	Grey handle: polypropylene homopolymer Purple parts: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder
M-001	Clear bristles: polyamide Light blue bristles: polyamide	Yellow handle: polypropylene copolymer Blue and green insert: "SBS" elastomer with a high content of chalk	Print: acrylic-based binder
M-002	Clear bristles: polyamide Light blue bristles: polyamide	Yellow handle: polypropylene copolymer	Print: acrylic-based binder
M-003	Blue bristles: polyamide Pink bristles: polyamide Purple bristles: polyamide Orange bristles: polyamide	Light handle with mica: polypropylene Purple part: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder
M-004	Bristles: polyamide	Handle: styrene acrylonitril, SAN	Print: acrylic-based binder
M-005	White bristles: polyamide Blue bristles: polyamide	Blue house: polyester	Print: acrylic-based binder
M-006	White bristles: polyamide Blue bristles: polyamide	Blue handle: polypropylene copolymer Yellow insert: "SBS" elastomer with a high content of chalk	Print: acrylic-based binder
M-007	Print: Acrylic-based binder	White handle: polypropylene copolymer Green insert: "SBS" elastomer with a high content of chalk	Not identified
M-008	White bristles: polyamide Grey bristles: polyamide Black bristles: polyamide	White handle: polypropylene homopolymer Black insert: "SBS" elastomer with a high content of chalk	
M-009	Green bristles: polyamide Blue bristles: polyamide Red bristles: polyamide Yellow bristles: polyamide	Red handle: polypropylene modified with isoprene (rubber) Orange part: styrene ethylene elastomer with a high content of chalk	Print: might be acrylic-based binder
K-001	White bristles: polyamide	Handle: polypropylene homopolymer	Print: presumably polyester-based binder
K-002	White bristles: polyamide Pink bristles: polyamide Blue bristles: polyamide	Blue handle: polypropylene copolymer Pink parts: "SBS" elastomer with a high content of chalk. Safety ring: polyoxymethylene, POM	No print
K-003	White bristles: polyamide Green bristles: polyamide	Green handle: polypropylene Clear part: styrene acrylonitrile, SAN	No print
K-004	White bristles: polyamide Green bristles: polyamide	Blue handle: polypropylene homopolymer Light blue part: SBS/polypropylene elastomer	
B-001	White bristles: polyamide	Purple handle: polypropylene homopolymer Yellow part: styrene ethylene elastomer with a high content of chalk	No print
B-002	Clear bristles: polyamide	Clear handle: Acrylic Holder: PVC with (phthalate) plasticiser	
B-003	White bristles: polyamide Orange bristles: polyamide	Yellow handle: polypropylene with unknown additives Orange part: ethylene-propylene-styrene elastomer	Print: polyester- based binder
B-004	White bristles: polyamide Black bristles: polyamide	Clear handle: polyester Black part: styrene-ethylene elastomer	Print: polyester-based binder
B-005	White bristles: polyamide Blue rubber bristles: styrene ethylene elastomer with a high content of chalk	White handle: polypropylene with a small amount of un-known material Dark blue part: styrene ethylene with a high content of chalk	No print
B-006	White bristles: polyamide Yellow bristles: polyamide	Handle parts: polyoxymethylene, POM	No print
B-007	Pink bristles: polyamide	Dark blue handle: polypropylene copolymer Pink part: styrene ethylene elastomer with a high content of chalk	No print
B-008	White bristles: polyamide Green bristles: polyamide Green “rubber” bristles SBS/polypropylene elastomer	White handle: polypropylene Green part: SBS/polypropylene elastomer	No print

B-009	Green bristles: polyamide	Yellow handle: polypropylene copolymer Green part: styrene ethylene elastomer with a high content of chalk	No print
B-010	White bristles: polyamide Orange bristles: polyamide	Grey handle: polypropylene homopolymer Orange part: styrene ethylene elastomer with a high content of chalk	Print: acrylic-based binder

Encl. C: GC-MS analysis results from screening

Migration:

The entire toothbrush is used at the migration analysis. Of practical reasons the toothbrushes are divided into 2 (possibly more) parts, in order to get the entire toothbrush into the used glass tube. The migration liquid simulating saliva is produced according to DIN 53160-1. The liquid is added so that the toothbrush is exactly covered. Subsequently, a known amount of deuterium-marked internal standards is added. The containers are closed and put in an incubator for 10 hours at 37°C. At the same time, a 50 ml blank determination is carried out, which is subject to the same migration and preparation.

Preparation:

After the migration the migration liquid from each toothbrush is divided into two equal parts. One portion is evaporated down to dryness by using a rotary evaporator (Buchi Rotavapor-RE) at 80ºC. The residue is washed more times with dechlormethane. The dichlormethane extract is evaporated to 0.25 ml.
The other portion of the migration liquid is prepared by means of ”solid phase extraction” (SPE). For this purpose, SPE filters with a sorbent of C18/ENV+ (IST - Isolute) are chosen. The filters are conditioned, and the migration liquid from each toothbrush is sucked through an SPE filter. Blowing through with nitrogen dries the filters, and subsequently they are eluted with 10 ml dichlormethane. The dichlormethane extract is evaporated to 0.25 ml.

Description of method and data processing

For the GC-MS analyses a Perkin Elmer AutoSystem XL GC gas chromatograph with a Turbomass GC mass spectrometer as detector has been used. Each extract is analysed in SCAN mode. The chromatogram of each extract is added to the chromatogram of the corresponding blank determination. It has been tried to identify and quantify peaks, which are not concurrently found in the blank determination, according to the most stabile internal standard (semi-quantitative determination). The detection limit will be approx. 0.5 µg/g.
The most informative chromatograms appeared to derive from the preparation with SPE, and the preparation through evaporation was consequently used for verification.

Selected compounds found at the screening

In the table (see Encl. C) all the compounds found at the concentration on SPE filters have been stated. If the substance has quotation marks, it means that the mass spectre was not quite in agreement with the reference spectre of the stated compound. On the other hand, great similarities are found, and consequently the found compound is the same type as the one stated in the table.
In case the compound could not be identified by means of the Nist library, the compound is stated with two question marks followed by the main ions in the mass spectre. Thus it is stated whether the same unknown compound is found in more samples. In addition, the retention time (RT) has been stated. RT is put in brackets in cases, where the concentration after evaporation of the compound is so high that the peak has been displaced.

The results are shown in µg totally per toothbrush. It applies for all the compounds that this amount is calculated according to the same internal standard (DEHP-d_4).
At the top of the table the known added amount of internal standard together with the response for this are shown. It is assumed that all the compounds have the same extraction efficiency and response factor as the internal standard (semi-quantitative determination). Therefore, based on each compound, the measured response has been stated and subsequently converted into µg.

Concentration through evaporation confirms the previously identified compounds. However, it does not contribute to further interesting compounds.

			IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response
			5	103977	5	117336	5	148313	5	225245	5	266978
IS = DEHP d4 RT 17.84									30642-14		30642-15	
	Compound	RT*	response	µg tot	response	µg tot	response	µg tot	response	µg tot	response	µg tot
			M-003		M-005		M-009		K-001		K-002	
1	"1-ethoxy-2-propanole"	3.27										
2	"4-hydroxy-4-methyl-2-propanone"	4.29										
3	"methylpropoxy-propanole"	4.51			420203	18					73328	1
4	N,N-dimethyl-acetamide	4.60										
5	Cyclohexanon	4.98	40626.7	2	313013	13	29974	1	327945	7	110641	2
6	2-butoxy-ethanole	4.99	20313.3	1			36324	1				
7	?? 31-61	5.16										
8	"methylpropoxy-propanole"	5.21							881871	20		
9	1,1,2,2 tetrachlorethane	5.23										
10	?? 43-45-75	5.24							87062	2		
11	1-butoxy-2-propanole	5.39										
12	"methoxy-butanole acetate"	5.79									52773	1
13	4-hydroxy-benzene sulphonic acid	6.07			472510	20						
14	"2-propyl-1-pentanol" branched alkane	6.39					47387	2			175188	3
15	?? 41-54-68-69	6.42			52461	2						
16	3,5,5-trimethyl-1-hexanol	6.61										
17	?? 77-79-107-108 co-eluates with 18	6.56										
18	1-methyl-2-pyrrolidinone	6.56 (6.62)			2994936	128	60927	2				
19	?? 43-73-103	6.69										
20	?? 55-59	6.86										
21	2-butoxyethyle acetate	6.99	62582	3	52461	2	104673	4				
22	?? 43-121	7.10					45118.7	2				
23	?? 43-71-93	7.18										
24	Benzoic acid methyl ester	7.21							157663	3		
25	"Tetramethylbenzene"	7.48			74520	3						
26	Pentandioic acid dimethyl ester	7.52					30812	1			18187	0
27	"Tetramethylbenzene"	7.83			81808	3						
28	Naphthalene	8.28			86969	4						
29	Naphthalene (here according to own IS)	8.28			86969	5						
30	?? 43-73-103	8.52										
31	2-phenoxy ethanol	8.53					15183	1				
32	?? 43-45-73-75-101-103	8.65										
33	Carvone (99-49-0)	8.78										
34	?? 59-77-105	9.14							54291	1		
35	?? 43-55-73-103-137	9.36										
36	?? 43-55	9.45										
37	?? 31-61	9.68			47031	2						
38	"butoxyethoxy ethanol acetate"	9.70			72015	3	77134	3				
39	?? 43-73-103	10.21										
40	?? 43-45-73-75-103-105	10.33										

*: RT: retention time in the analysis

			IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response
			5	103977	5	117336	5	148313	5	225245	5	266978
IS = DEHP d4 RT 17.84									30642-14		30642-15	
	Compound	RT	response	µg tot	response	µg tot	response	µg tot	response	µg tot	response	µg tot
			M-003		M-005		M-009		K-001		K-002	
41	?? 141-161-197-199	10.77										
42	?? 77-95-123-151	10.85							95902	2		
43	?? 43-103-145	10.98										
44	?? 31-61	11.37			57207	2						
45	Alkan/alken-amide C6-C12	11.47										
46	alken/alcohol C16-C18	11.69	126777	6					148506	3		
47	?? 43-73-103-133	11.72										
48	diethylphthalat	11.78			71841	3						
49	?? 43-45-73-75-103-105	11.83										
50	"N,4-dimethyl-benzene sulphona-mide (640-61-9)" AGAIN later	12.15										
51	2-methyl-benzene sulphonamide	12.21 (12.36)										
52	?? 82-83-105-153-156	12.25			17105	1						
53	"substituted benzene sulphonamide (ex.:640-61-9)"	12.42										
54	4-methyl-benzene sulphonamide [or Tolbutamide (64-77-7)]	12.54										
55	?? 134-179	12.57					84739	2				
56	?? 61-81-99-121	12.77			48707	2						
57	4-(dimethylamino)-benzoic acid ethyl ester	12.81					428560	10				
58	?? 43-73-103-133	13.12										
59	alken/alcohol C16-C18	13.21	101900	5					117761	2	132900	4
60	?? 43--98-127	13.36										
61	"dimethoxy-diphenyl-ethanone"	14.03					659818	15				
62	"BHT"	14.17							37795	1	30000	1
63	?? 104-149-193	14.22					42954	1				
64	?? 43-73-103	14.39										
65	alken/alcohol C16-C18	14.60	71917	3					90668	2		
66	alken/alcohol C20+	14.97	23061	1					27831	1		
67	4-benzoyl-benzoic acid methyl ester	15.31					88806	2				
68	?? 57-147-251	16.17									36863	1
69	alcohol c15 +	16.25	23569	1								
70	phthalate	16.29										
71	Benzyl butyl phthalate	16.95			409706	17						
72	"phosphoric acid, tris(2ethylhexyl) ester"	17.32										
73	Alkan/alken-amid C18+	19.13										

***: RT: retention time in the analysis**

			IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response
			5	301737	5	221217	5	278968	5	155093	5	159837
IS = DEHP d4 RT 17.84			30642-16								30642-20	
	Compound	RT	response	µg tot	response	µg tot	response	µg tot	response	µg tot	response	µg tot
			B-003		B-004		B-005		B-006		B-007	
1	"1-ethoxy-2-propanol"	3.27										
2	"4-hydroxy-4-methyl-2-propanone"	4.29	37147	1								
3	"methylpropoxy-propanol"	4.51	232817	4								
4	N,N-dimethyl-acetamide	4.60					14234	0				
5	Cyclohexanon	4.98	31265	1								
6	2-butoxy-ethanol	4.99	30000	0	80069	2	7336	0	30000	1		
7	?? 31-61	5.16							10327	0		
8	"methylpropoxy-propanol"	5.21										
9	1,1,2,2 tetrachlorethan	5.23							10917	0		
10	?? 43-45-75	5.24							10917	0		
11	1-butoxy-2-propanol	5.39							9281	0		
12	"methoxy-butanol acetate"	5.79										
13	4-hydroxy-benzene sulphonic acid	6.07										
14	"2-propyl-1-pentanol" branched alkane	6.39	28788	0	37716	1	29059	1	35000	1	23913	1
15	?? 41-54-68-69	6.42							35000	1		
16	3,5,5-trimethyl-1-hexanol	6.61	63551	1								
17	?? 77-79-107-108 co-eluates with 18	6.56									17085	1
18	1-methyl-2-pyrrolidinone	6.56 (6.62)					25013	0				
19	?? 43-73-103	6.69							256450	8		
20	?? 55-59	6.86							42914	1		
21	2-butoxyethyl acetate	6.99	97101	2								
22	?? 43-121	7.10										
23	?? 43-71-93	7.18							27440	1		
24	Benzoic acid methyl ester	7.21										
25	"Tetramethyl benzene"	7.48										
26	Pentandioic acid dimethyl ester	7.52										
27	"Tetramethyl benzene"	7.83										
28	Naphthalene	8.28										
29	Naphthalene (here according to own IS)	8.28										
30	?? 43-73-103	8.52							1104960	36	**13660**	**0**
31	2-phenoxy ethanol	8.53										
32	?? 43-45-73-75-101-103	8.65							211108	7		
33	Carvone (99-49-0)	8.78			26054	1	27807	0				
34	?? 59-77-105	9.14										
35	?? 43-55-73-103-137	9.36							16468	1		
36	?? 43-55	9.45							51875	2		
37	?? 31-61	9.68										
38	"butoxyethoxy ethanol acetate"	9.70										
39	?? 43-73-103	10.21							1337567	43		

40	?? 43-45-73-75-103-105	10.33							376187	12			

***: RT: retention time in the analysis**

			IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response	IS (µg)	response
			5	301737	5	221217	5	278968	5	155093	5	159837
IS = DEHP d4 RT 17,84			30642-16								30642-20	
	Compound	RT	response	µg tot	response	µg tot	response	µg tot	response	µg tot	response	µg tot
			B-003		B-004		B-005		B-006		B-007	
41	?? 141-161-197-199	10.77	21714	0								
42	?? 77-95-123-151	10.85					50119	1			25003	1
43	?? 43-103-145	10.98							66303	2		
44	?? 31-61	11.37										
45	Alkan/alken-amide C6-C12	11.47					53298	1				
46	alken/alcohol C16-C18	11.69										
47	?? 43-73-103-133	11.72							1072563	35		
48	diethylphthalate	11.78										
49	?? 43-45-73-75-103-105	11.83							139170	4		
50	"N,4-dimethyl-benzene sulphona-mide (640-61-9)" AGAIN later	12.15							78254	3		
51	2-methyl-benzene sulphonamide	12.21 (12.36)										
52	?? 82-83-105-153-156	12.25										
53	"substituted benzene sulphonamide (ex.:640-61-9)"	12.42			167013	4						
54	4-methyl benzene sulphonamide [el. Tolbutamide (64-77-7)]	12.54			237900	5			12012877	387	94765	3
55	?? 134-179	12.57										
56	?? 61-81-99-121	12.77										
57	4-(dimethylamino)-benzoic acid ethyl ester	12.81										
58	?? 43-73-103-133	13.12							565236	18		
59	alken/alcohol C16-C18	13.21			52653	1	148741	3			101287	3
60	?? 43--98-127	13.36							41465	1		
61	"dimethoxy-diphenyl-ethanone"	14.03										
62	"BHT"	14.17										
63	?? 104-149-193	14.22										
64	?? 43-73-103	14.39							87028	3		
65	alken/alcohol C16-C18	14.60										
66	alken/alcohol C20+	14.97	35891	1								
67	4-benzoyl-benzoic acid methyl ester	15.31										
68	?? 57-147-251	16.17										
69	alcohol c15 +	16.25										
70	phthalate	16.29	308851	5								
71	Benzyl butyl phthalate	16.95										
72	"phosphoric acid, tris(2ethylhexyl) ester"	17.32	37744	1								
73	Alkan/alken-amide C18+	19.13					90747	2				

*: RT: retention time in the analysis

Encl. D: Calcined residue and ICP analysis results from screening

Reg. no:	M-003		M-005		M-009		K-001		K-002	
Element	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total
Na	810	2400	7700	1300	740	2500	980	69	490	2000
Mg	12000	35000	4100	700	15000	51000	39000	2700	13000	54000
Al	11000	32000	10000	1700	7200	25000	770000	54000	650	2700
Ca	340000	1000000	11000	1900	330000	1100000	40000	2800	390000	1600000
Ti	4900	14000	5500	940	12000	41000	10000	700	380	1600
Cr	70	210	< 50		130	440	630	44	< 50	
Mn	77	230	1500	260	< 50		1100	77	< 50	
Ni	< 100		82000	14000	< 100		< 100		< 100	
Cu	< 50		440000	75000	240	820	800	56	< 50	
Zn	< 100		160000	27000	< 100		< 100		< 100	
Se	< 500		< 500		< 500		< 500		< 500	
Sr	330	970	< 50		250	850	< 50		240	1000
Ba	< 50		690	120	< 50		< 50		510	2100
Pb	< 50		< 50		68	230	< 50		< 50	
g ash per										
toothbrush		2.94		0.17		3.41		0.07		4.15
metal piece	-			0.53	-		-		-	
g toothbrush		19.8		4.89		24.4		10.2		20.1

Reg. no:	B-003		B-004		B-005		B-006		B-007	
Element	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total	µg/g ash	µg total
Na	< 100		< 100		5900	14000	1600	800	3500	4300
Mg	36000	6800	10000	5900	9300	22000	4300	2200	9500	12000
Al	9100	1700	650	383	5300	13000	15000	7500	5600	6800
Ca	12000	2300	320000	190000	340000	810000	36000	18000	310000	380000
Ti	20000	3800	2000	1200	72000	170000	6700	3400	5100	6200
Cr	120	23	75	44	< 50		100	50	< 50	
Mn	1300	250	< 50		< 50		< 50		< 50	
Ni	71000	13000	150	89	< 100		< 100		< 100	
Cu	380000	72000	320	190	1600	3800	590	300	130	160
Zn	140000	27000	1500	880	< 100		1100	550	< 100	
Se	700	130	< 500		720	1700	< 500		< 500	
Sr	< 50		340	200	310	740	190	95	230	280
Ba	< 50		< 50		< 50		270	140	< 50	
Pb	< 50		< 50		< 50		< 50		< 50	
g ash per										
toothbrush		0.19		0.59		2.38		0.5		1.22
metal piece	-		-		-			1.07	-	
g toothbrush		12.7		19.6		16.2		7.48		10.4

Encl. E: GC-MS Analysis results from quantitative determination

ID no.	M- 003	M- 005 *	M- 009	K– 001	K– 002	B– 003	B– 004	B– 005	B– 006 *	B– 007	Recommended detection limit
Component	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush	µg / tooth-brush
N,N-dimethyl acetamide	-	-	-	-	-	-	-	0.87	-	-	0.25
2-butoxy-ethanol	1.7	0.18	1.0	0.23	0.53	0.66	2.2	0.46	0.30	0.26	0.15
1,1,2,2-tetrachloroethan	-	-	-	-	-	-	-	-	0.41	-	0.25
1-butoxy-2-propanol	0.38	0.11	0.37	-	-	-	0.24	-	0.15	-	0.15
3,5,5-trimethylhexanol	-	-	-	-	-	0.77	-	-	-	-	0.25
1-methyl-2-pyrrolidinon	-	200	2.8	0.86	-	-	4.3	1.4	0.19	0.72	0.15
2-butoxyethyl acetate	8.6	0.69	4.8	0.26	0.26	3.8	-	-	-	-	0.15
Naphthalene	-	2.6	-	-	-	-	-	-	0.29	-	0.25
Carvone	-	-	-	-	-	-	0.65	0.46	-	-	0.15
o-toluene sulphonamide	-	-	-	-	-	-	19	-	390	2.6	0.25
p-Toulon sulphonamide	-	-	-	-	-	-	26	-	810	4.7	0.25
Benzyl butyl phthalate	-	21	-	-	-	-		-	-	-	0.15

”*”: As two toothbrush heads have been used at the migration, it is assumed, that the migrated amount is twice as big compared with one single toothbrush head. The stated number is for one toothbrush head, and the detection limit for this sample is consequently half the limit stated in the table.
”-”: Below the detection limit