# Organophosphates and phthalates in air and dust from indoor environments

– Method development and applied measurements

Caroline Bergh


Stockholm University

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Stockholm University
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# Abstract

Organophosphate and phthalate esters are polymer additives that are frequently found in air and dust in indoor environments. This thesis describes the development and application of air sampling and selective mass spectrometric (MS) determination of these two compound groups. (**Paper I**). MS ionization efficiency and overall method performance was evaluated using different reagent gases in positive chemical ionization mode (PICI) (**Papers I and IV**). It also describes the sampling and screening of these compounds in indoor air and dust from different environments **(Papers II and III)** and the development and evaluation of a method for the extraction and determination of these compounds in indoor dust **(Paper IV)**. Throughout this work, the separation technique of choice was gas chromatography (GC) and sampling, clean-up and analysis of the two target groups of compounds were performed simultaneously.

An air sampling method previously used for air sampling of only organophosphate esters, is here demonstrated to be applicable for simultaneous sampling of both phthalate and organophosphate esters (**Paper I)**. Isobutane reagent gas was shown to be superior to methane (**Paper I**) and further results presented in **Paper IV** showed ammonia to be even better. Selective detection using tandem mass spectrometry (MS/MS) showed good results for simultaneous determination of organophosphate and phthalate esters in air (**Paper I and IV**). The high selectivity of this technique was especially advantageous when analyzing the comparably more complicated indoor dust matrix.

Comparison of chemical profiles of organophosphate esters between indoor environments including daycare centers, offices and private

homes differed between the types of locations while the phthalate profiles were rather similar (**Paper I**). Comparison of concentration levels of these compounds in multi-storey apartment buildings classified as either high or low risk "sick" buildings could not differentiate the two classes of buildings. The differences in levels between apartments indicated apartment specific sources of these compounds (**Paper III**). In general the levels of phthalate esters were consistently higher than the levels of organophosphate esters both in air and in dust (**Paper II–III**). Further, the studies include correlation of air and dust profiles of the two compounds groups and also points out some potential sources of organophosphate and phthalate esters in these indoor environments (**Paper II–III**).

In **Paper I**, a pilot study of the standard reference material SRM 2585 "Organic Contaminants in House Dust", showed that several organophosphate and phthalate esters was present in this complex matrix. In **Paper IV** seventeen phthalate and organophosphate esters were determined in SRM 2585, out of which ten had not previously been reported for this reference material.

# Populärvetenskaplig sammanfattning

Avhandlingen beskriver utveckling och tillämpning av metoder för provtagning, provupparbetning och kemisk analys av inomhusluft och damm. Fokus ligger på analys av två grupper av föreningar: ftalater och organofosfatestrar. Dessa föreningar används framför allt som mjukgörare och flamskyddsmedel i polymera material, d.v.s. olika typer av plaster, gummi, ytbehandlingsmaterial och mycket mera. Den omfattande användningen av dessa produkter medför att organofosfater och ftalater är vanligt förekommande i både luft och damm i vår inomhusmiljö.

Arbetet i denna avhandling innefattar utveckling och tillämpning av en metod där båda dessa föreningsgrupper provtogs respektive upparbetades simultant. Detta underlättar inte bara under själva provtagningen, utan det reducerar även antalet analyssteg och minskar mängden lösningsmedel. Under arbetets gång har en masspektrometrisk* detektionsmetod utvecklats där man genom att välja ur specifika joner i två separata led (s.k. ”tandemmasspektrometri”) sorterar bort föreningar som kan störa analysen och får en metod som har hög selektivitet för de utvalda föreningarna. Metoden visade sig extra fördelaktig för analys av damm som ur ett analytisk kemiskt perspektiv är en mer komplicerad matris** än luft då den inte bara innehåller en mängd kemiska ämnen utan också t.ex. fett och hudavlagringar som kan störa analysen.

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* Masspektrometer: Ett analysistrument som joniserar och därefter sorterar föreningar med avseende på massa och laddning för att sedan registrerar dem med hjälp av elektroniska sensorer, används både för identifiering och haltbestämmning av kemiska föreningar i en mängd olika prover.

** Matris: Det material som avses att analyseras så som luft, damm, vatten, förbränningsavgaser m.m.

Flera ftalater misstänks ha hormonstörande effekter. Båda föreningsgrupperna har även påvisats kunna ha allergena effekter och organofosfaterna har indikerats vara både cancerogena och neurotoxiska. Detta föranleder större studier för att få en så god bild av alla källor till exponering och i detta steg är bra analysmetoder mycket viktiga. I samarbete med två större projekt, ”Nya gifter – nya verktyg” och ”Hälsomässigt hållbara hus” (3H)*, utfördes provtagning av damm och luft i olika typer av inomhusmiljöer (kontor, daghem, villor och lägenheter) i Stockholmsområdet. Den dagliga dosen som kunde beräknas ur halterna av de föreningar som bestämdes i luft och damm i inomhusmiljöerna uppnår inte en dos som kan klassas som hälsovådlig ur ett toxiskt perspektiv. Men, då den dagliga exponeringen inte bara sker från luft och damm utan dessutom också sker genom konsumtion av mat som har förpackats och förvarats i material som innehåller dessa föreningar, genom hygienprodukter, för barn genom leksaker som innehåller dessa föreningar, för att nämna några, så kan den totala exponeringen utgöra ett potentiellt problem.

För att kunna bestämma riktigheten i sina analyser och även för att kunna jämföra resultat mellan olika laboratorier kan man använda sig av s.k. standardreferensmaterial. En mängd sådana referensmaterial finns tillgängliga genom National Institute of Standards and Technology (NIST) i USA. Idealt har ett sådant referensmaterial certifierade halter, d.v.s. analys kemiskt säkerställda halter, av de föreningar man vill analysera. Det finns tre referensdamm tillgängliga via NIST dock har

* Mer information om projekten ”Nya gifter – Nya Verktyg” och ”Hälsomässigt Hållbara Hus (3H)” finns på Sockholms Miljöförvaltnings hemsida: http://www.stockholm.se/miljoforvaltningen

inget av dessa certifierade halter av organofosfater och ftalater. Ett av de tre referensmaterialen (SRM 2585) har i dessa studier undersökts och föreningarna haltbestämts, vilket öppnar för andra att jämföra halterna i sin analysmetod och kan så småningom leda till certifiering av halterna av organofosfater och ftalater i detta damm.

# List of papers

This thesis is based upon the following publications which are referred to in the text by corresponding Roman numerals I–IV. Papers I and II are reproduced with the kind permission of the publishers. Some unpublished results are also included in this thesis.

**I** **Simultaneous selective detection of organophosphate and phthalate esters using gas chromatography with positive ion chemical ionization tandem mass spectrometry and its application to indoor air and dust**

*Caroline Bergh, Ralf Torgrip, Conny Östman,*

Rapid communications in Mass spectrometry 2010;24(19):2859-2867

The author was responsible for most of the experimental work, all the data evaluation and the major part of writing the paper.

**II** **Organophosphate and phthalate esters in air and settled dust – a multi location indoor study**

*Caroline Bergh, Ralf Torgrip, Gunnel Emenius, Conny Östman,*

Indoor Air 2011;21(1):67-76

The author was responsible for a large part of the experimental work, for a major part of the data evaluation and writing the paper.

**III Organophosphate and phthalate esters in indoor air: a comparison between multi-storey buildings with high and low prevalence of sick building symptoms**

*Caroline Bergh, K. Magnus Åberg, Magnus Svartengren, Gunnel Emenius, Conny Östman*

Accepted for publication in Journal of Environmental Monitoring (2011-04-27)

The author was responsible for a major part of the experimental work, for a large part of the data evaluation and writing the paper.

**IV Organophosphate and phthalate esters in Standard Reference Material 2585 "Organic Contaminants in House Dust"**

*Caroline Bergh, Giovanna Luongo, Stephen Wise, Conny Östman*

Manuscript

The author was responsible for a major part of the experimental work, for all the data evaluation and the major part of writing the paper.

# Abbreviations

| | |
|---|---|
| ANOVA | Analysis of variance |
| AGD | Anogenital distance |
| CI | Chemical ionization |
| CID | Collision induced dissociation |
| CSTEE | Scientific Committee for Toxicity, Ecotoxicity and the Environment |
| DC | Direct current |
| ECHA | European Chemicals Agency |
| ECNI | Electron capture negative ionization |
| EI | Electron ionization |
| EU | European Union |
| FID | Flame ionization detector |
| GC | Gas chromatography |
| $K_{OA}$ | Octanol-air partition coefficient |
| LOQ | Limit of quantification |
| MS | Mass spectrometry |
| MS/MS | Tandem mass spectrometry |
| NIST | National Institute of Standards and Technology |
| NPD | Nitrogen phosphorous detector |
| OPE | Organophosphate esters |
| PBDE | Polybrominated diphenyl ethers |
| PBT | Persistence, bioaccumulation and toxicity |
| PCA | Principal component analysis |
| PICI | Positive-ion chemical ionization |
| POM | Particulate organic matter |
| PVC | Poly vinyl chloride |
| Q, q | Quadrupole |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| RF | Radio frequency |
| RfD | Reference dose |
| RIC | Reconstructed ion chromatogram |
| SBS | Sick building symptoms |
| SIM | Selected ion monitoring |
| SPE | Solid phase extraction |
| SRM (1) | Selected reaction monitoring |
| SRM (2) | Standard reference material |
| SVOC | Semi-volatile organic compounds |

| | |
|---|---|
| TDI | Tolerable daily intake |
| TDS | Testicular dysgenesis |
| USEPA | U.S. Environmental Protection Agency |
| WHO | World Health Organization |
| VOC | Volatile organic compounds |
| VVOC | Very volatile organic compounds |
| 3H | Helthy sustainable houses<br>(SWE: Hälsomässigt hållbara hus) |

Table of contents

# 1. Introduction

The workflow in analytical chemistry is often referred to as the "*analytical chain"*. It consists of a series of steps - sampling, work-up, analysis, and data evaluation (**Figure 1.1**). The work described in this thesis centred on the determination of two groups of polymer additives— organophosphate and phthalate esters — and involved several of these steps. Specifically, the studies conducted involved the s*ampling* of indoor air and dust, the *extraction* and *clean-up* of the samples, chromatographic *separation* using gas chromatography, *detection* using tandem mass spectrometry, and finally *data evaluation*. With the data evaluation focused primarily on comparing the chemical profiles of air and dust sampled in different locations (day-care centres, work environments, and home environments, including both single- and multi-family houses).

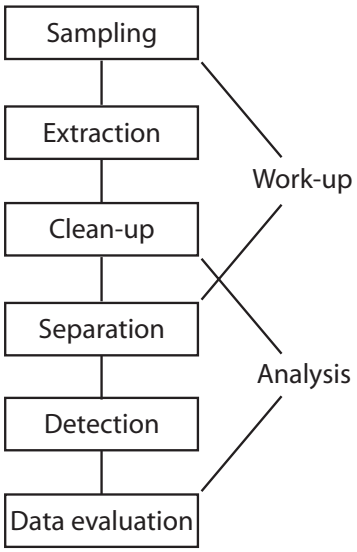



**Figure 1.1:** The "analytical chain"

Indoor pollutants are suspected to be a contributing factor to the increasing problems related to human health. The widespread use of consumer products that contain and may emit harmful substances in conjunction with energy saving methods that reduce the indoor air exchange the number and concentration of (harmful) compounds is likely to increase in the indoor environment [1]. The prevalence of organophosphate and phthalate esters indoors originates mainly from their use as additives in polymeric materials [2]. The organophosphorous

and phthalate ester additives are not covalently bonded to the polymer and can therefore migrate and escape from the polymer matrix into the surrounding air [3]. Consequently, these have become ubiquitous pollutants in the indoor environment [4-10], and are generally more abundant indoors than outdoors [3, 5, 10, 11]. These compounds are typically present in indoor air, but can also readily partition to materials in contact with air (*e.g.* furniture and surfaces) and they will also be distributed to airborne particles and dust, both which are important sources of chemical exposure [3].

## 1.1. Polymeric materials and additives

Polymeric materials are produced in large quantities and comprise a large number of materials such as plastics, rubbers, surface coatings, etc. Polymeric materials are made by forming bonds between a large number of small molecules (monomers) to produce long chains — a polymer; this process is referred to as polymerization. Additives are frequently added to polymers to alter their processing and final properties [12, 13]. Two important groups of additives are plasticizers and flame retardants [14, 15].

### 1.1.1. Plasticizers

Plasticizers are incorporated to improve polymers' processability, flexibility, elasticity, and durability. Phthalic acid esters (phthalates) and organophosphate triesters (also known as organophosphate esters or OPEs) are two groups of compounds that are used for this purpose. However, OPEs are primarily used to improve polymers' fire resistance [12].

### 1.1.2. Flame retardants

Most polymeric materials are organic materials and are thus combustible. As such, they have to satisfy fire resistance requirements when used in various applications. Unlike most additives, flame retardants can impair the properties of polymeric material. Because they have both flame-retarding and plasticizing properties, OPEs are an important group of polymer flame retardants on the market [2, 12].

## 1.2. Phthalates

Phthalates are the most common plasticizing agents, and are used to increase the desirable flexibility and durability of hard polymeric materials such as PVC. Phthalate additives are typically used as plasticizers in polymers such as cellulose esters, PVC and other vinyl chloride copolymers [16]. The general structure of the phthalates is shown in **Figure 1.2**.

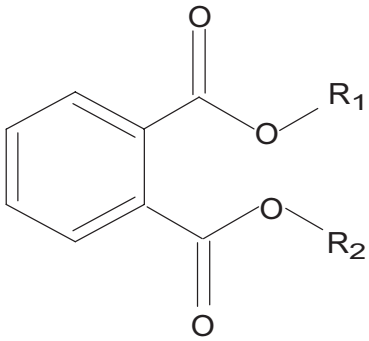



**Figure 1.2:** General structure of the phthalate esters.

The phthalates that were examined in this work are listed in **Table 1.1**. PVC is used in production of furniture, flooring, wall coating, cables, building and construction materials, and also in other consumer products such as shower curtains, footwear, plastic bags, food packing material, toys, etc. [2].

Phthalates are such ubiquitous indoor pollutants that contamination of blanks is a common problem associated with their determination. This problem must be considered and accounted for during sampling, sample work-up, and the subsequent analysis.

**Table 1.1:** Names, abbreviations CAS numbers, vapour pressures ($V_p$) and boiling points of the reference compounds.

| Name | Abbreviation | CAS No. | $V_p$ [Torr][4] | $B_p$ (°C)[4] |
|---|---|---|---|---|
| **Phthalates** | | | | |
| Dimethyl[1] | DMP | 131-11-3 | $3.31 \cdot 10^{-3}$ | 283 |
| Diethyl[1] | DEP | 84-66-2 | $1.67 \cdot 10^{-3}$ | 294 |
| Dibutyl[1] | DBP | 84-74-2 | $1.08 \cdot 10^{-4}$ | 295 |
| Diisobutyl[1] | DiBP | 84-69-5 | $1.54 \cdot 10^{-3}$ | 337 |
| Benzylbutyl[1] | BzBP | 85-68-7 | $7.09 \cdot 10^{-7}$ | 408 |
| Di(2-ethylhexyl)[1] | DEHP | 117-81-7 | $3.95 \cdot 10^{-6}$ | 385 |
| Di(*n*-octyl)[1] | DnOP | 3115-39-7 | $1.38 \cdot 10^{-7}$ | 402 |
| Diisononyl[2] | DiNP | 28553-12-0 | - | - |
| Diisodecyl[2] | DiDP | 26761-40-0 | - | - |
| $d_4$ -Diethy [3] | $d_4$ -DEP (IS) | - | - | - |
| $d_4$ -Benzylbutyl [3] | $d_4$ -BzBP (IS) | - | - | - |
| $d_4$ -Di(2ethylhexyl)[3] | $d_4$ -DEHP (IS) | - | - | - |

[1]Sigma Aldrich, Marbor, USA, [2]Fluka Chemie GmbH, Sigma-Aldrich Company, Japan. [3]Cambridge Isotope Laboratories Inc, Andover, USA. [4]Obtained through SciFinder©; Calculated using Advanced Chemistry Development (ACD/Labs) Software V9.04 (© 1994-2010 ACD/Labs). Temp 25°C, Pressure. 760Torr

## 1.3. Organophosphate esters

Organophosphate triesters (OPEs) are derivates of phosphoric acid; their general structure is shown in **Figure 1.3**. The three substituents can be either aryl, alkyl, haloalkyl or a combination of these.

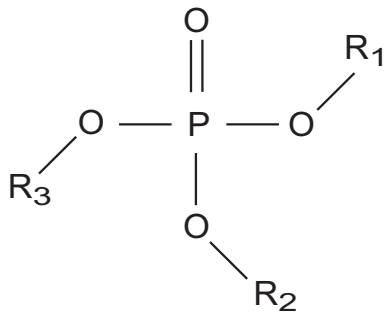



**Figure 1.3:** General structure of the organophosphate esters.

The OPEs examined in this work are listed in **Table 1.2**. OPEs can have a wide range of physical and chemical properties depending on the nature of their substituents. This makes OPEs a challenging group of compounds to analyze; frequently-encountered problems include minimizing chromatographic column tailing, the identification of suitable internal standards, and difficulties associated with blanks, among other. OPEs are used as flame retardants, stabilizers, and plasticizers in numerous products, including building materials, flooring and wall coatings, electronic goods, furnishing material and textiles. They are also used in paper coatings, adhesives, latex paints, lacquers, printed circuit boards, synthetic leather, etc. [17, 18].

OPEs can be divided into three subclasses, depending on the nature of their substituents: triaryl-, trialkyl- and tris(haloalkyl). These different subclasses have slightly different properties and uses. The triaryl phosphates are mainly used as flame retardants, but are also somewhat

effective plasticizers. Alkyl substituents make OPEs more flammable, and flammability increases with the length of the alkyl chain. As such, trialkyl phosphates are more flammable, and are primarily used as plasticizers. Haloalkanes are effective flame retardants; trihaloalkyl phosphates combine the flame-retarding properties of the haloalkane substituents and the phosphorous group, and are mainly used in rigid and flexible polyurethane foam products.[18-20].

**Table 1.2:** Names, abbreviations CAS numbers, vapour pressures ($V_p$) and boiling point ($B_p$) of the reference compounds.

| Name | Abbreviation | CAS No. | $V_p$ [Torr][5] | $B_p$ (°C)[5] |
|---|---|---|---|---|
| **Phosphates** | | | | |
| Triethyl[1] | TEP | 78-40-0 | $1.77 \cdot 10^{-1}$ | 219 |
| Triisopropyl [1] | TiPrP | 513-02-0 | $1{,}53 \cdot 10^{-1}$ | 222 |
| Tripropyl [1] | TPrP | 513-08-6 | $2{,}88 \cdot 10^{-2}$ | 254 |
| Triisobutyl[1] | TiBP | 126-71-6 | $1.91 \cdot 10^{-2}$ | 261 |
| Tributyl[1] | TBP | 126-73-8 | $4.09 \cdot 10^{-3}$ | 288 |
| Tris(2-chloroethyl) [1] | TCEP | 115-96-8 | $1.08 \cdot 10^{-4}$ | 347 |
| Tris(2-chloroisopropyl)[2] | TCiPP | 13674-84-5 | $5.25 \cdot 10^{-5}$ | 359 |
| Tripentyl [3] | TPeP | 2528-38-3 | $5.45 \cdot 10^{-4}$ | 322 |
| Trihexyl [1] | THP | 2528-39-4 | $6{,}99 \cdot 10^{-5}$ | 354 |
| Tris(1,3-dichloroisopropyl) [3] | TDCPP | 13674-87-8 | $4.07 \cdot 10^{-8}$ | 457 |
| Tris(2-butoxyethyl)[1] | TBEP | 78-51-3 | $1.11 \cdot 10^{-6}$ | 414 |
| Triphenyl[1] | TPP | 115-86-6 | $1.24 \cdot 10^{-6}$ | 412 |
| Diphenyl-ethylhexyl [3] | DPEHP | 1241-94-7 | $6.49 \cdot 10^{-7}$ | 421 |
| Tris(2-ethylhexyl)[1] | TEHP | 78-42-2 | $2.04 \cdot 10^{-6}$ | 406 |
| Tritolyl [1] | TToP | 1330-78-5 | - | 420 |
| $d_{27}$-Tributyl[4] | $d_{27}$-TBP (IS) | - | - | - |

[1]Aldrich Chemicals, Milwaukee, USA, [2]Akzo Nobel, The Netherlands, [3]TCI, Tokyo, Japan, [4]Cambridge Isotope Laboratories Inc, Andover, USA. [5]Obtained through SciFinder©; Calculated using Advanced Chemistry Development (ACD/Labs) Software V9.04 (© 1994-2010 ACD/Labs). Temp 25°C, Pressure. 760 Torr, except TToP $V_p$: "Hazardous Substances Data Bank" data are provided by the National Library of Medicine (US).

## 1.4. Occurrence and health effects

It has been estimated that one million metric tonnes of phthalates were produced in Western Europe in 2010 [21]. Western European production of organophosphorous flame-retardants in 2001 was estimated at 83,000 metric tonnes, and has since increased [5, 17, 22]; in 2006, approximately 91,000 metric tonnes of OPEs were produced for use as flame retardants, corresponding to an increase of approximately 9 % [5, 22]

DBP, DiBP, DEHP, BzBP and TCEP have all been placed on the "*Candidate List of Substances of Very High Concern for authorization*" [23], and DBP, DiBP, BzBP, TCEP and DEHP had been recommended for inclusion in Annex XIV (List of substances subject to authorization) of the EU's REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulations as of the 1st of June 2009 and the 30th of march 2010. [24]. Specific risk assessments for several phthalates and OPEs have been published by the European Union (EU). These assessments can be obtained via ORATS (the Online EUropean Risk Assessment Tracking System), which contains risk assessment reports on DBP (which is on the 1st priority list), DEHP, TCEP, DiNP, and DiDP (which are all on the 2nd priority list), BzBP (3rd priority list), and TCiPP and TDCPP (4th priority list) [25-30].

In general, the risk profiles of the phthalates DBP, DEHP and BzBP indicate that there is little concern about exposure to these species from the air in the indoor environment [26, 29, 30]. However, it is recognized that exposure to DEHP from multiple sources (*e.g.* from baby food, indoor air, indoor dust, toys, and other soft PVC products) is as a possible cause for concern, especially in infants [26]. The phthalates are strongly suspected to exhibit reproductive toxicity. Several animal

studies have shown that fetal exposure to DBP, DEHP and BzBP correlates with a reduction in fetal testosterone levels, resulting in male reproductive organ abnormality syndromes including anogenital distance (AGD) and testicular dysgenesis (TDS)-like disorders, which are also referred to as "phthalate syndrome" [31-34]. Recent research indicates that in humans there is a possible relationship between the presence of phthalate metabolites in maternal urine and AGD in boys [34-36]. In humans, TDS is among the most common congenital disorders. The TDS-like disorders (*e.g*. cryptorchidism and hypospadias) have been shown to be related to phthalates (mainly DBP, DEHP and BzBP) in several animal studies, indicating that increased exposure to these compounds, individually or in combination, may cause similar effects in humans [36, 37]. There are also a number of epidemiological studies that suggest a possible correlation between exposure to phthalates and asthma and airway diseases in children [1, 38].

In 1998, the chlorinated organophosphorous flame retardant TCEP was classified as a hazardous compound by the world health organization (WHO). It has subsequently been replaced by TCiPP [20, 39]. However, an EU risk assessment report published in July 2009 concluded that there is little or no need for further studies on the effects of TCEP or for measures aimed at reducing human exposure to this species. The risk assessment report also recommends that the trend towards decreased use of TCEP be monitored and encouraged. The report also recognized the potential carcinogenicity, high toxicity, and environmental persistence of TCEP, even though it does not satisfy the PBT (persistence, bioaccumulation and toxicity) criteria [25]. Both TCiPP and TDCP are suspected carcinogens; the (*in vitro*) evidence for the carcinogenicity of

TDCP is somewhat stronger than that for TCiPP [27, 28]. OPEs have also been reported to have other biological effects: TPP may cause contact dermatitis in humans and has been shown to significantly reduce cholinesterase activity in red blood cells [40, 41], both TBEP and TBP have shown possible neurotoxicity *in vitro*, and TBP and TEHP may cause skin irritation [42, 43].

# 2. Gas phase, suspended particles and dust

With respect to their volatility, compounds can be divided into four classes; very volatile organic compounds (VVOC), volatile organic compounds (VOC), semi-volatile organic compounds (SVOC) and particle-associated organic matter (POM). The WHO criteria used for this classification are detailed in **Table 2.1**.

**Table 2.1:** Classification of indoor organic pollutants [44]

| Description | Abbrev. | Boiling-point range* (°C) |
|---|---|---|
| Very volatile (gaseous) organic compounds | *VVOC* | < 0 to 50-100 |
| Volatile organic compounds | *VOC* | 50-100 to 240-260 |
| Semi-volatile organic compounds | *SVOC* | 240-260 to 380-400 |
| Organic compounds associated with particulate matter or particulate organic matter | *POM* | >380 |

* Polar compounds appear at the higher end of the range

Most phthalate and phosphate esters are classified as semi-volatile organic compounds (SVOC) [6]. SVOC substances are known to adsorb to solids such as airborne particles and settled dust, and are therefore partitioned between the gaseous and particulate phases [45, 46]. The dynamic distribution of these species between the air, suspended particles and dust means that it is important to evaluate SVOC levels in dust as well as in air in order to assess overall human exposure. Exposure occurs by inhalation of SVOC in the gas phase and airborne particles and also via dermal and oral uptake of settled dust [6].

# 3. Sampling

## 3.1. Air Sampling

Active air sampling is performed by pumping air through a filter and/or adsorbent [47]. In this work**,** commercially available SPE-cartridges (IST, Hengoed, UK) equipped with an aminopropyl silica adsorbent (**Figure 3.1**) were used for active air sampling of the two investigated compound groups (**Paper I-III**).

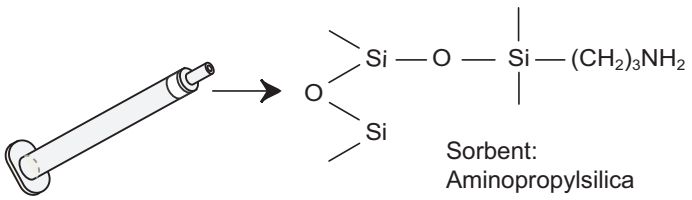



**Figure 3.1:** SPE-cartridge used for air sampling (IST, Hengoed, UK).

Solid phase extraction (SPE) is a common and general sample extraction technique used for the clean-up and concentration of samples prior to analysis. The first report of successful air sampling using SPE cartridges was published in 1995 [48]; many other papers have since been published on the same topic [49-52]. The SPE technique captures both gaseous compounds by adsorption and suspended particles. Using the SPE-cartridge as an adsorptive air sampler has the advantage that the same cartridge is used for both the active air sampling and the subsequent extraction and clean-up, **Paper I**.

The method works well for OPEs [8, 50] and in **Paper I** its applicability to the sampling of phthalates was assessed with good results. There were no sampler breakthrough of any of the phthalates and the desorbtion efficiency recoveries of the SPE sampler were more than 98 % for all phthalates, with the exception of DMP that had slightly lower recovery (90%) attributed to evaporative losses during work-up, **Paper I**

## 3.2. Dust Characterization and Sampling

Dust simply means "*solid particles formed by crushing or other mechanical breakage of parent material, larger than about 0.5 µm"* [53]. The dust that is usually compared to indoor air samples is called **house dust**. According to the US Environmental Protection Agency (US EPA, 1997), house dust is "*a complex mixture of biologically derived material (animal dander, fungal spores etc.), particulate matter deposited from the indoor aerosol, and soil particles brought in by foot"* [54]. Another frequently used term is *indoor settled dust*, which is defined by the US EPA (2008) as *"particles in building interiors that have settled onto objects, surfaces, floors, and carpeting. These particles may include soil particles that have been tracked into the indoor environment from outdoors as well as organic matter"* [55].

Dust can be sampled in a number of different ways, including dust wipes of surfaces, analysis of the contents of vacuum cleaner bags, using open dishes to collect settling dust, and a technique used in recent publications involving a filter mounted in a nozzle (**Figure 3.2**) adapted to a vacuum cleaner that is used to collect settled dust usually from selected surfaces above the floor [53, 56, 57]. This sampling technique was used in **Paper II.** The analyzed dust was sampled from surfaces at least 0.8 m above the floor. This dust could be described as *surface-settled indoor dust* or possibly just as *surface dust*.

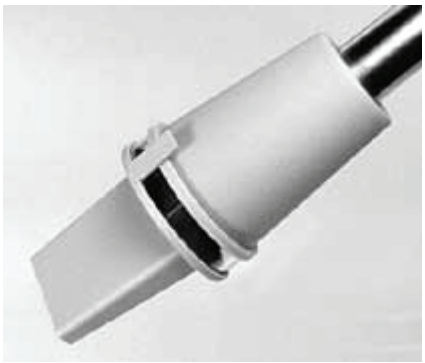


**Figure 3.2:** Polypropylene nozzle with a filter mounted in styrene-acrylonitrile holder (Kriminalteknisk Materiel AB, Bålsta, Sweden).

There is a need for common guidelines regarding the sampling methodology of dust [53, 58]. Furthermore, certified reference materials would be useful for the development and evaluation of the sample pre-treatment methods and the overall analytical method performance [58, 59].

**Paper II** describes the evaluation of OPE and phthalate levels in dust samples from different indoor environments and presents a comparison of the concentrations of these compounds observed in the dust samples to those observed in air, sampled in parallel with the sampling of the dust.

The partitioning of compounds between the gas phase, airborne particles and dust is complex. In some recent publications, the octanol-air partitioning coefficient ($K_{OA}$) has been suggested to be a useful parameter for describing the partitioning and kinetic behavior of semivolatile compounds in terms of their distribution between the gas phase, airborne particles, and dust [3, 60].

In **paper II,** a weak correlation between air and dust concentrations was found for five analytes: TBP, TCEP TCiPP DBP and BzBP. It has previously been shown that there is a correlation between SVOC levels in settled dust, in airborne particles, and in the gas phase [3, 60]. The weak correlation found in **Paper II** is consistent with these results; the weakness of this study was that the sampled dust was of unknown age and that the amount of each analyte that originated solely from airborne particles was unknown.

From an analytical perspective, dust is a complicated matrix. The utility of highly-selective methods when analyzing such an intricate sample such as dust is shown in **Paper I and IV**.

### 3.2.1. Dust Standard Reference Materials

**Paper IV** focuses on the analysis of the Standard Reference Material (SRM) 2585 "Organic Contaminants in Indoor Dust," which is produced by the National Institute of Standards and Technology (NIST), Gaithersburg, MD, USA. It originates from material collected from vacuum cleaner bags from homes, motels, hotels and cleaning services in Maryland, Montana, New Jersey, North Carolina, Ohio and Wisconsin during the years 1993 and 1994. After collection, the material was processed and sieved so as to exclude particles with a diameter in excess of 100μm [61-64].

A wide range of environmental-matrix SRMs are available from the NIST, including SRMs originating from air and diesel particulate matter, mussel tissue, fish oil/tissue, and human serum [59]. Notably, three different indoor dust SRMs can be obtained from the NIST (SRM 2583, 2584 and 2585). SRMs 2583 and 2584 (both of which are named "Trace Elements in Indoor Dust") were originally designed for use when analyzing inorganic constituents (*e.g.* lead), while SRM 2585 is used for organic contaminants in indoor dust (*e.g.* polycyclic aromatic hydrocarbons, pesticides, polychlorinated biphenyls and polybrominated biphenyl ethers); certified values of the levels of these constituents in the reference material are available [63-66].

However, all three materials have been used for the determination of organic constituents such as polybrominated biphenyl ethers (PBDE) and some OPEs (TBP, TCEP, TCiPP, TDCPP, TBEP, TPP and TToP) [63, 67]. In **Paper IV,** the levels of the targeted OPEs and phthalates in SRM 2585 were quantified. However, none of the values measured for SRM

2583 and 2584 have been certified by NIST, and neither have the concentrations of OPEs and phthalates in SRM 2585 [64-66].

# 4. Analytical Methods

## 4.1. Gas chromatography

In gas chromatography (GC), compounds are separated on the basis of their partitioning between a stationary solid phase and a mobile gas phase. Nowadays, the most widely-used GC column type is the open tubular column. The inner surface of the column is coated with a thin film of the stationary phase; in the studies described herein, the stationary phase was made of the non-polar polymer polydimethylsiloxane in which 5% of the methyl groups had been replaced by phenyl groups.

The main criterion for separation with GC is that the compounds must be volatile; it is thus suitable for use with substances ranging from very volatile organic compounds (VVOC) to organic compounds associated with organic matter (POM), as outlined in **Table 2.1**. The retention of a compound on the chromatographic column is mainly dependant on its vapour pressure and thus on its boiling point (the boiling point is strongly associated with the vapour pressure of the compound). GC is the most widely-used separation technique for the analysis of OPEs and phthalates [58, 68]; it is used in conjunction with various detection techniques. Some of the most important detection techniques used in the analysis of phthalates and OPEs are described below.

## 4.2. Flame ionization detection

Flame ionization detection (FID) is a general and non-selective detection technique. It is based on the combustion of the sample; this generates organic ions, resulting in a measurable electric current whose magnitude is approximately proportional to the compound's carbon content [69]. Because of their simplicity and ability to detect almost all carbon-

containing organic compounds, FID detectors can be found in most laboratories that use GC.

FID is very useful for method development and it is also good for monitoring background levels in more complicated sample matrices such as dust, since the background matrix may affect the response of selective detection techniques and also increase degradation of the GC column. However, for quantitative analysis, more selective detectors are preferred, since FID cannot be used to unambiguously identify the detected compound.

## 4.3. Nitrogen phosphorous detection

The nitrogen phosphorus detector (NPD) is a modified FID in which a ceramic bead containing an alkali metal (usually rubidium or caesium) is placed into the eluent gas stream. NPD has a specific response for nitrogen and phosphorus; together with its relatively high sensitivity, this makes it especially useful for the analysis of many pharmaceuticals and environmental samples containing nitrogen- or phosphorus containing compounds.[69, 70]

The main disadvantage of NPD is that the performance of the detector deteriorates with time and that the rubidium- or caesium-containing bead needs to be changed regularly [69, 70]. NPD is the most widely-used detection technique in quantitative OPE analysis[71], but it is not suitable for combined analyses of OPEs and phthalates. These disadvantages, together with the need for more secure simultaneous identification of both compound groups prompted our use of a mass spectrometric detection system, as described in **Papers I -IV**.

## 4.4. Mass spectrometric detection

For most GC detectors, compounds are identified solely on the basis of their retention times – this holds for the FID and the NPD detectors discussed above. Mass spectrometry (MS) can be used to obtain structural information on the desired analyte; depending on the ionization mode used and the monitoring of specific ions, high specificity can be achieved and information on the chemical structure of the compound can be obtained.

A mass spectrometer has three primary functional units: the ionization source, the analyzer, and the detector. In GC/MS the ionization source converts the gaseous neutral eluted analyte molecules into ions. The analyzer selects specific ions or allows the passage of a range of ions within a mass to charge (*m/z*) window defined by the operator. The last unit is the detector, which monitors the number of ions that have passed through the analyzer.

Commonly-used ionization techniques in GC/MS are Electron Ionization (EI) and Chemical Ionization (CI). The latter can be operated in both positive (Positive ion chemical ionization, PICI) and negative (mainly electron capture negative ionization, ECNI) ionization mode. Two ionization techniques were used in this work, EI and PICI and the performance of the two methods is compared in **Paper I.**

### 4.4.1. Electron ionization

In Electron ionization (EI), the molecules eluting from the GC are exposed to a beam of 70 eV electrons emitted from a heated filament. The interaction of these electrons with the molecule results in the ejection of one of the molecule's own electrons, turning it into a cation with an odd number of electrons (*i.e.* the molecular ion). EI is a "hard" ionization

technique; the relatively high energy of the electrons not only ionizes the molecule but also causes it to fragment. At the standard 70 eV, this fragmentation generates a characteristic "fingerprint" spectrum for the molecule in question, making it possible to identify specific analytes by comparing experimental spectra to spectral libraries. The presence of specific fragmentation patterns also allows experienced interpreters of EI mass spectra to obtain useful insights into the structural features and potential identity of unknown analytes. In many cases, GC/MS in EI mode is used as a complement to other detection techniques when confirmation of the identity of a specific analyte is needed.

The limitation of EI is that since it is a hard ionization technique, the molecular ion seldom survives and so information on the molecular weight of the compound is lost. To obtain the molecular ion, a "softer" ionization technique is often required. One such "softer" ionization technique that is often used to complement EI is Chemical Ionization.

### 4.4.2. Chemical ionization

Chemical ionization (CI) is achieved by introducing a reagent gas into the ion source. Upon electron ionization, the reagent gas is ionized and form positively charged ions, gaseous Brønstedt acids, by $H^-$ abstraction.[72] The most common reagent gas used in CI is methane, which forms the reactant ions $CH_5^+$, $C_2H_5^+$ and $C_3H_5^+$ [72, 73]. These gaseous ionic acids primarily react by proton transfer with analyte molecules that have a higher proton affinity than they do; the proton affinity of methane is 131.6 kcal/mol [72].

The ionization efficiency for phthalates and OPEs when using methane as reagent gas was evaluated in **Paper I**. This paper includes a comparison of methane and isobutane as reagent gases. Isobutane has a

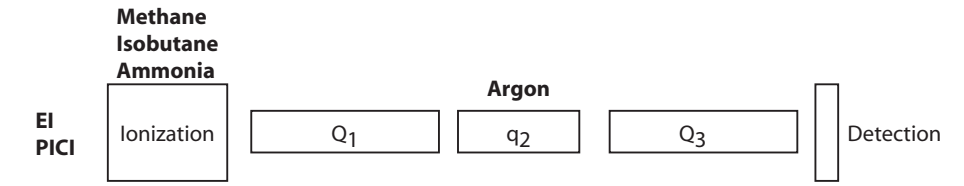
proton affinity of 195.9 kcal/mol; its main reagent gas ion is $C_4H_9^+$ [72, 73]. The higher proton affinity of isobutane means that ionization with this gas is "softer" than ionization with methane. As a result, the molecular $[M+H]^+$ ion was observed almost exclusively for all of the targeted compounds (**Paper I**). The softer ionization results in more of the molecular ions reaching the detector which not only facilitates identification of a compound but also opens the possibility of using tandem mass spectrometry (MS/MS).

An alternative to isobutane is ammonia (**Paper IV**), which has a proton affinity of 204.5 kcal/mol. In this case the main reagent gas ions are $NH_4^+$ and $[NH_4+NH_3]^+$. In addition to proton transfer, electrophilic addition $[M+NH_4]^+$ often occurs when ammonia is used as reagent gas [72, 73]. Some electrophilic addition occurred for the OPEs, notably TCEP, TCiPP, TDCPP, TPP and TToP. In the case of the phthalates, electrophilic addition could be minimized by increasing the temperature in the ion source (**Paper IV**).

### 4.4.3. Quadrupole analyzer scan modes

An MS quadrupole analyzer system may be equipped with one or three quadrupoles; such instruments are referred to as single quadrupole and triple quadrupole instruments, respectively. The quadrupole transmits ions of a specific *m/z* (mass to charge ratio) by applying a fixed direct current (DC) and a radio frequency (RF) voltage to four steel rods arranged in parallel. The DC polarity of the rods shifts and thus guides the resonant ion through the analyzer in a tumbling rotating manner. The ions outside the selected *m/z* ratio region will not be resonant and will therefore hit the rods and discharge.

The instrument can be set to scan a range of *m/z* ratios (full scan mode, FS), or to scan discrete *m/z* ratios in selected ion monitoring mode (SIM). When analysing small molecules in GC/MS, the full scan range is usually limited to 35–600 *m/z*. A triple quadrupole instrument consists of three sequential quadrupoles ($Q_1q_2Q_3$). The first and third quadrupole are used as analyzers, while $q_2$ is operated in RF-only mode and serves to guide the ions from the first to the third quadrupole. By introducing a collision gas (*e.g.* nitrogen, helium or argon) into the second quadrupole ($q_2$), it can be used as a collision cell, where ions are further fragmented — a technique called collision induced dissociation (CID). As shown in **Figure 4.1,** the triple quadrupole instrument can be operated in four different tandem mass spectrometry scan modes: precursor ion scan, product ion scan, neutral loss, and selected reaction monitoring (SRM).




| Scan modes | | | | | |
|---|---|---|---|---|---|
| **FS** | **scan range** | → | **RF-only** | → | **RF-only** |
| **SIM** | **discrete scan** | → | **RF-only** | → | **RF-only** |
| Precursor ion scan | scan range | → | CID | → | discrete scan |
| **Product ion scan** | **discrete scan** | → | **CID** | → | **scan range** |
| Neutral loss | scan range | → | CID | → | scan range - X |
| **SRM** | **discrete scan** | → | **CID** | → | **discrete scan** |

**Figure 4.1:** An overview of the scan modes that can be utilized on a triple quadrupole instrument; FS, SIM, precursor ion scan, product ion scan, neutral loss and SRM. The ionization modes, reagent gases, scan modes and collision gas used in this work are marked in bold.

Full scan mode (FS) is useful for identifying compounds using spectral library searches and also for identification on the basis of fragmentation patterns. Data treatment of the chromatogram that originates from FS, such as reconstructed ion chromatogram (RIC), where a chromatogram are reconstructed by viewing the signal of a specific ion or ions, can be used when the compound is known and decomposed into a specific fragment (*m/z*). When operated in SIM mode, the mass spectrometer only allows the passage of ions falling within an operator-defined *m/z* window through the analyzer (**Figure 4.1**). This has the advantage of increasing the signal for the selected ions due to the higher duty cycle of those ions. SIM detection also results in noise reduction and thus increased selectivity of the analysis. The technique is often sufficient for identification and generally achieves adequate quantification limits in quantitative analysis.

Three of the tandem mass spectrometry scan modes (precursor ion scan, product ion scan, neutral loss) are predominantly used for identification, for obtaining structural information, and for mass analysis evaluation purposes. Precursor ion scan (**Figure 4.1**) can be used when identifying a compound group with a common specific fragment (*e.g.* phthalates) and to obtain structural information by relating primary ions to fragment formation. Neutral loss (**Figure 4.1**) scanning provides a means of identifying, *e.g.* a group of compounds in a complex mixture that all lose a common neutral fragment during fragmentation. Product ion scan, which detects all of the secondary ions formed from a single primary precursor ion (**Figure 4.1**) provides structural information and facilitates the selection of suitable product ions for SRM mode, *e.g. m/z* 149 for most phthalates and *m/z* 99 for most OPEs, as described in **Paper I**. As

for SIM, the duty cycle is almost 100% when using a triple quadrupole instrument in SRM mode and the noise reduction is even higher.

With the exception of dimethyl phthalate, all of the phthalates examined yielded a characteristic ion with *m/z* 149 in EI. This ion arises from the sequential loss of both the substituent groups by cleavage of the ester bonds and subsequent formation of a phthalic anhydride ion.[74] The occurrence of the stable *m/z* 149 ion in conjunction with suitable additional confirmation ions makes SIM mode a favourable choice for phthalates [68, 74].

Analogously to the phthalates, most OPEs in EI undergo a characteristic fragmentation that generates an ion with *m/z* 99. This ion is formed by three consecutive hydrogen rearrangements ("Mcafferty+1") of the molecular ions, yielding a protonated phosphoric acid ion [74]. However, the relatively low mass of the *m/z* 99 ion hampers both qualitative and quantitative analysis, because matrix constituents introduce significant noise into the low mass region of the spectrum [58, 75] and less-abundant fragment ions such as those arising from the loss of one substituent are used in EI-SIM analysis [67, 76]. In **Paper I,** PICI-SRM was demonstrated to be a highly specific scan mode whose high selectivity makes it possible to analyze specific compounds in complex mixtures without having to completely purify the samples.

## 4.5. Discussion — analytical determination

The determination and analysis of OPEs and phthalates presents a number of analytical challenges. In particular, blank contamination problems are common when working with phthalates [77].

The quantity of phthalates in the blanks was reduced in all studies described in **papers I-IV** by minimizing surface contact during sample handing, by cleaning all glassware and by avoiding the use of plastic materials where possible; the only plastics used were those in the SPE cartridges, which were used for air sampling in **papers I-III** and for clean-up in **paper IV**. The possibility that the SPE cartridges might be a source of blank contamination was investigated in detail by analysis of blank samples and by extraction. Neither provided any evidence that the SPE cartridges were a significant source of either phthalates or OPEs.

Additional measures were taken to minimize contamination, such as changing the septa on the sample vials after each injection and always performing at least three solvent injections prior to the analysis by GC-MS when the instrument had been idle for a period of time.

In **papers I-IV**, the analyte concentrations reported for each experimental sample were corrected by subtracting the amount of the corresponding compound observed in the blank samples. Furthermore, a given compound was only considered to have been detected if its concentration was more than three times the standard deviation of the concentration observed in the procedural blanks (**Paper I-IV**).

Blank problems are also encountered when working with OPEs, to at least some extent, and so for compounds with detectable blank levels the same approach as with the phthalates was used. The OPEs are a relatively heterogeneous group of compounds because of the varied properties of

their substituents. This presents some analytical problems: their relatively high polarity and their tendency to interact with glass surfaces make them very susceptible to decreased instrumental performance and column degradation that necessitates regular maintenance. Increased tailing with time is common for the alkyl chain OPEs especially the short chain OPEs; TCEP, TDCPP and TBEP are particularly strongly affected by column/injector liner degradation, and exhibit a noticeable decrease in response with time.

A particular advantage of using mass spectrometry for determination and detection rather than NPD detection is that one can use deuterated standards for determination. However, the commercial availability of such compounds is sparse. The only presently available standard is deuterated tributyl phosphate ($d_{27}$-TBP) (used as an internal standard in **papers I-IV**) and deuterated triphenyl phosphate ($d_{15}$-TPP). The availability of an analogous deuterated reference for TBEP would be particularly beneficial, as described in **Paper IV.** Determination with CG/PICI-SRM was found to yield a clean chromatographic profile with high selectivity and low limits of detection and quantification (LOD and LOQ, respectively), as described in **Papers I and IV**. The high selectivity of this method is illustrated in **Figure 4.2**.

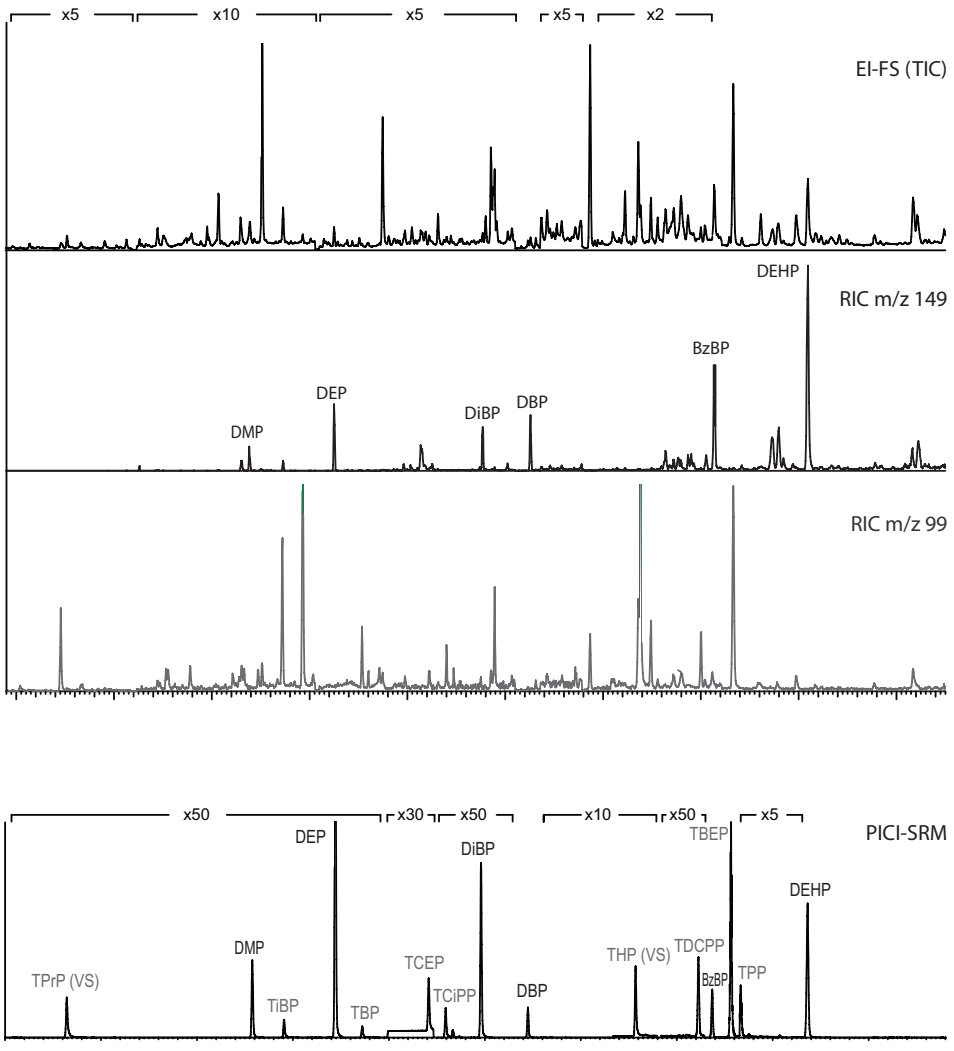



**Figure 4.2:** Comparison of chromatograms of Indoor Dust (SRM 2585) acquired using different MS modes. EI-FS = full scan MS analysis, RIC *m/z* 149 for phthalate detection, RIC *m/z* 99 for OPE detection, PICI-SRM (isobutane) selective detection of OPEs and phthalates, **Paper I**.

Three different reagent gases were examined in the course of this work: methane and isobutane in **Papers I-III**, and ammonia in **Paper IV**. All three gases gave similar results in terms of selectivity and LOQ (defined as the quantity for which the signal to noise ratio, S/N, was >10) with isobutane yielding superior performance to methane, as discerned in **Paper I.** In the study described in **Paper IV**, ammonia was shown to perform better than the other two reagent gases, as shown in **Table 4.1** (**Papers I and IV**).

**Table 4.1:** LOQs of determinations of the indicated compounds observed using CI-MS/MS with methane, isobutane, or ammonia as the reagent gas.

| | CI-MS/MS methane* | CI MS/MS isobutane* | CI MS/MS ammonia* |
|---|---|---|---|
| **Phosphates** | | | |
| TEP | 30 | 8 | 0.5 |
| TiPrP | 10 | 10 | 0.1 |
| TPrP | 7 | 7 | 0.1 |
| TiBP | 6 | 9 | 4 |
| TBP | 4 | 7 | 7 |
| TCEP | 10 | 10 | 6 |
| TCiPP | 10 | 10 | 10 |
| TPeP | 4 | 4 | 5 |
| THP | 6 | 7 | 2 |
| TDCPP | 200 | 200 | 50 |
| TBEP | 100 | 100 | 20 |
| TPP | 20 | 8 | 4 |
| DPEHP | 30 | 30 | 2 |
| TEHP | 20 | 20 | 8 |
| TToP | 7 | 5 | 20 |
| **Phthalates** | | | |
| DMP | 10 | 3 | 1 |
| DEP | 20 | 10 | 2 |
| DiBP | 10 | 10 | 1 |
| DBP | 10 | 10 | 20 |
| BzBP | 30 | 20 | 1 |
| DEHP | 20 | 20 | 6 |
| DnOP | 20 | 20 | 4 |

*All values are in pg

When using ammonia as the reagent gas, a reduced LOQ was achieved for all but a few compounds. Notably, the LOQs for TiPrP and TPrP were reduced 100- and 70-fold, respectively, while those of TEP, DPEP, DiBP and BzBP were reduced by factors of 10-20 and those of eleven other analytes were reduced by at least a factor of two compared to those achieved when using isobutane as reagent gas.

An exception was TToP, which exhibited a *higher* LOQ when using ammonia as reagent gas. This compound undergoes electrophilic addition, forming two precursor ions, $[M+H]^+$ and $[M+NH_4]^+$; of the two, the latter has a somewhat higher response, which contributes to the increased LOQ. However, using the $[M+NH_4]^+$ as precursor ion did present an advantage in terms of selectivity for TToP. The quasi-molecular ions of TToP are not susceptible to collision-induced dissociation and do not form any suitable fragment regardless of collision energy (**Paper I and IV**). However**,** the $[M+NH_4]^+$ ion loses ammonia and yield the $[M+H]^+$ as a product ion (**Paper IV**). Thus, by using the ammonia adduct ion as precursor ion, the selectivity can be increased by introducing a double criterion: co-eluting compounds must be susceptible to electrophilic addition and be stable.

The comparison between ammonia and isobutane was performed using two different GC/MS systems, a TSQ 7000 MS system (**Paper I**) and a Varian 320 triple quadrupole MS system (**Paper IV**), and this may be the cause of some of the observed differences; in particular, the lower quantification limits of the phthalates is mainly due to a reduced instrumental background. There were also indications that isobutane is more prone to contaminate the ion source and analyzer assembly, whereas ammonia, due to its corrosive nature, makes the instrument

"self-cleaning"— modern MS instruments with stainless steel tubing and connectors are in general designed to withstand chemical ionization using ammonia as reagent gas.

In both **Papers I and IV** the standard calibration curves exhibit a slight curvature. This is a potential problem if the concentrations of the compounds in the sample span over a wide range, since it would necessitate a tedious series of dilutions to bring their concentrations into a suitable range. In **Paper I,** it was shown that this curvature can largely be compensated for by using internal standards, which extended the linear range from ~2000 pg to 4000 pg. The air samples in **Paper III** were quantified by using relative response factors from multiple calibration levels covering the entire range of concentrations observed in the samples. As discussed in **Paper IV,** both polynomial quantification and linear regression quantification with two adjacent calibration points gave equivalent results even for compounds present in high concentrations (e.g. DEHP ~10 ng).

The methods of quantification used in **Paper II** differed slightly from those used in **Paper I**. In **Paper II,** TPeP and $^{13}C_2$-DPeP ($^{13}C_2$-dipentyl phthalate) were used as internal standards, and quantification was performed using relative response factors using single point calibration against a standard with a concentration of ~600 pg for the OPEs and ~1300 pg for the phthalates. This could potentially decrease the accuracy of the determination, but most of the analytes were well within the linear range.

The only analytes in **Paper II** that were above ~2000 pg in the analysed sample were DEP and DBP in the air samples and also DEHP and TBEP in the dust samples. There is a possibility that these compounds might be

slightly overestimated when present at concentrations above ~1000 ng/m$^3$ in air or 600 μg/g in dust. However, the determined median concentrations of these three phthalates in **Paper II** are consistent with current literature, as shown in **Table 5.1** and **Table 5.4**

# 5. Organophosphates and phthalates in indoor air and dust

## 5.1. Air samples

The median concentrations of selected OPEs and phthalates examined in **Papers II and III** are listed in **Tables 5.1 and 5.2,** facilitating a comparison between the studies. In general, the phthalate concentrations in the air were higher than the corresponding OPE concentrations.

### 5.1.1. Phthalates in air

**Table 5.1** also summarizes the phthalate air concentrations reported in previous studies. The list is not comprehensive; instead, it focuses on results from selected studies performed after the year 2000 that analyzed samples from a large number of dwellings and looked at a large number of compounds. Preference was given to studies in which concentrations were determined in both air and dust, and studies were selected so as to include data from Europe, Asia, and the U.S.

**Table 5.1:** Concentrations of phthalates (ng/m$^3$) in the air in residences, as reported in selected relevant studies. All values are medians

| Country | Location type | *n* | DMP | DEP | DiBP | DBP | BzBP | DEHP |
|---|---|---|---|---|---|---|---|---|
| Germany[7] | Day care centers | 74 | 331 | 353 | 505 | 1188 | – | 458 |
| Germany [7, 46][a] | Apartments | 30 | 403 | 648 | 563 | 1070 | 19 | 120 |
| USA;MA [78] | Homes | 120 | – | 590 | 61 | 220 | – | 77 |
| USA;CA [11] | Homes | 40 | – | 330 | 130 | 140 | 6.8 | 68 |
| Japan [79] | Houses | 40 | 48 | 61 | 75 | 200 | – | 147 |
| **Paper II** | Houses | 10 | 15 | 1300 | 270 | 850 | 21 | 200 |
| **Paper II** | Daycare centers | 10 | 4.7 | 870 | 190 | 600 | 21 | 240 |
| **Paper II** | Work places | 10 | 4.4 | 620 | 230 | 550 | 15 | 100 |
| **Paper III** | Apartments | 169 | 16 | 210 | 230 | 190 | 8.9 | 220 |

[a]as reported by Weschler et.al (2008)
– Values not reported or below reported determination limit

These studies show that the most abundant compounds are DEP, DiBP and DBP. This is probably due to with their relatively high volatility and widespread and large-scale use in a variety of products, (**Paper II–III**).

### 5.1.2. Organophosphates in air

**Table 5.2** summarizes the OPE concentrations in air reported in previous studies and the studies in **Papers II and III.** Again, the list is not comprehensive and only includes data from larger studies in which sampling were conducted at multiple locations. Data from screening studies with only single or double measurements at various locations were excluded. Several such screening studies have been performed in Sweden [8-10, 17, 80, 81]; their results and those of similar studies have been summarized by Reemtsma et al. [5].

**Table 5.2:** Air concentrations of OPEs (ng/m$^3$) in residences as reported in selected relevant studies. All values are medians

| Country | Location type | *n* | TEP | TiBP | TBP | TCEP | TCiPP | TBEP |
|---|---|---|---|---|---|---|---|---|
| Japan [82] | Houses | 18 | 2.4 | – | 4.0 | 1.3 | 1.9 | 1.8 |
| Japan [82] | Office building | 14 | 3.2 | – | 6.6 | 3.3 | 6.0 | 1.0 |
| Japan [79] | Houses | 41 | 62 | – | 27 | 15 | 89 | 23 |
| **Paper II** | Houses | 10 | 7.3 | 13 | 9.1 | 4.8 | 5.6 | – |
| **Paper II** | Day care centers | 10 | 1.7 | 7.2 | 18 | 25 | 8.4 | 84 |
| **Paper II** | Work places | 10 | 6.5 | 7.3 | 2.3 | 10 | 100 | 5.8 |
| **Paper III** | Apartments | 169 | 4.4 | 8.6 | 11 | 3.7 | 14 | – |

– Values not reported or below reported determination limit

**Table 5.2** does not contain any data on TiPrP, TPrP, DPEHP, TEHP, TPP and TToP as none of these compounds were frequently detected in the air samples collected in the studies described in **Papers II and III** or in any of the other studies presented. That is to say, these compounds are not often found in indoor air samples. TDCPP is also excluded although this compound was detected in workplaces with a median concentration of 28 ng/m$^3$ in **Paper II**. The compounds with the highest concentrations

in air in the study described in **Paper II** were TCiPP, with a median concentration in workplaces of 100 ng/m$^3$, and TBEP, with a median concentration in daycare centers of 84 ng/m$^3$. The air concentration of OPEs differs a lot between studies and locations, as shown in **Table 5.2**.

**Paper II** describes a screening study in which sampling was conducted at various types of locations: private homes ($n$ = 10), work places ($n$ = 10), and daycare centers ($n$ = 10). The selected locations were prone to natural variation, *i.e.* the home environments were furnished and designed by the owners, and the buildings differed in both age and construction. The work environments ranged from small single-office rooms to landscape-designed offices and workshop-like environments. The daycare centers were similar in terms of indoor design and furniture but exhibited a degree of variation in terms of age and construction that is representative of day care centers in Stockholm.

The results showed that there were similarities in the OPE concentration-profiles observed within individual environment types (intra-environment) but significant differences between environment types (inter-environment), as can be seen in the principal component analysis (PCA) plots in **Figure 5.1.**

No significant differences were found between the environment types with respect to phthalate concentration. The inter-environment differences in the OPE profiles were due to the high concentrations of TCiPP in work places and TBEP in day-care centers (**Paper II**).

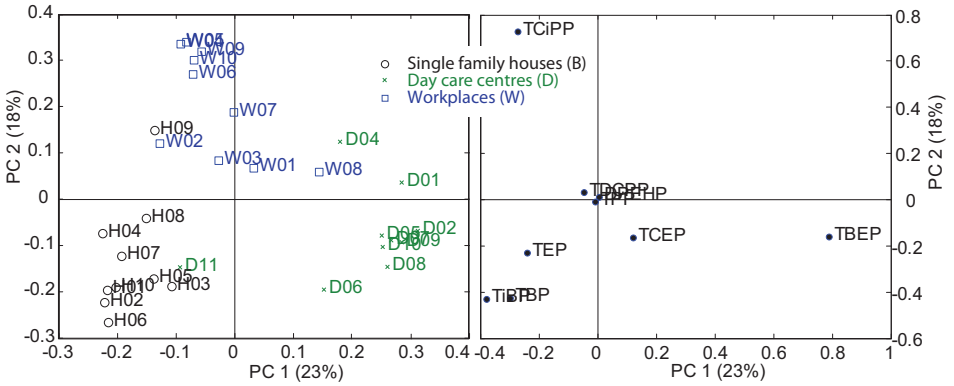



**Figure 5.1:** PCA scores and loadings of OPEs in air samples from workplace (W), day-care (D) and private home environments (H). Left panel – scores. Right panel – loadings. The data from each location (sample) were normalized against the highest measured concentration of each analyte to facilitate comparison of the relative amounts of the analytes (profiles) in the samples.

**Paper III** describes a study conducted in collaboration with the "Healthy sustainable houses" (3H) project conducted in Stockholm [83, 84]. Air sampling was performed in a large selection of multi-story apartment buildings ($n$ = 45). The apartment buildings selected for sampling had previously been classified as high or low risk with respect to "sick building" symptoms (SBS) in the course of the 3H project [85]. The term "sick building syndrome" is commonly used to describe situations where the occupants of a building experience acute health and comfort problems that appear to be linked to time spent in a building, but where no specific illness or cause can be identified [86, 87]. For comparative purposes, the concentrations of airborne OPEs measured in **Paper III** have been projected onto the PCA scores plot for the corresponding data presented in **Paper II** (**Figure 5.2**). The scores plot could be interpreted to mean that the apartment buildings exhibit characteristics similar to those of both single family houses and workplaces and/or that the variation in TCiPP concentration in the apartments is comparatively

large. No significant correlation was found between the classification of the buildings (in terms of the incidence of sick building symptoms) and the measured concentrations of phthalates or OPEs in the air.

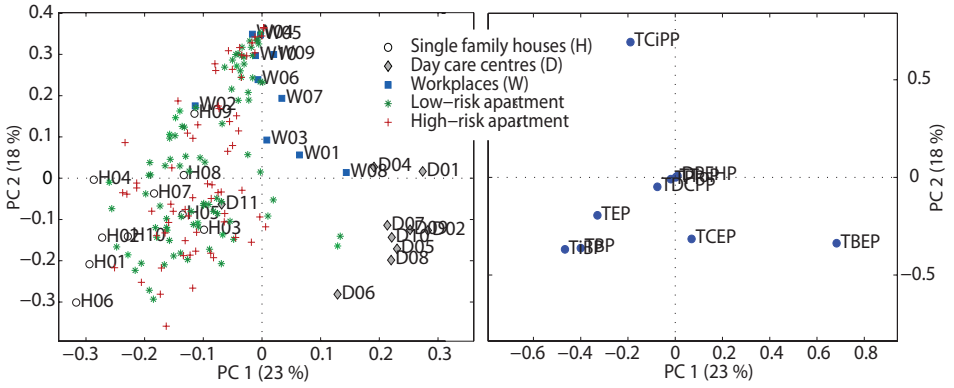



**Figure 5.2:** Concentrations of OPEs measured in apartment buildings, projected onto the PCA scores of OPEs in air samples reported in **Paper II**. Left panel – scores. Right panel – loadings. The data from each location (sample) were normalized against the highest measured concentration, as before.

Within each of the 45 buildings, sampling was conducted in 4 apartments, making it possible to compare inter- and intra-building differences. The previous risk classification had been made on a per-building basis. Consequently, the identification of significant, significant differences in airborne compound concentrations between buildings relative to those observed *within* the buildings is probably a necessary prerequisite for identifying correlations between the risk classifications and the measured airborne compound concentrations. Most of the variance was associated with differences between apartments, indicating that a correlation with the risk classification of the buildings is unlikely, **Paper III.**

The distribution of the variance was investigated using nested analysis of variance (ANOVA), five compounds whose concentrations might show significant differences between buildings were identified: TCiPP, DEP, DBP BzBP and DEHP. For these five compounds, the distribution of the variance (between buildings, between apartment and between the duplicate samples) is displayed in **Table 5.3** illustrating the high apartment variance, **Paper III**.

**Table 5.3:** Distribution of variance between buildings, apartments and duplicate analyses.

| | Between buildings (%) | Between apartments (%) | Duplicates (%) |
|---|---|---|---|
| **TCiPP** | 11.3 | 84.6 | 4.1 |
| **DEP** | 17.2 | 82.4 | 0.4 |
| **DBP** | 27.5 | 70.6 | 1.9 |
| **BzBP** | 25.3 | 73.1 | 1.6 |
| **DEHP** | 43.7 | 44.8 | 11.5 |

TBP has previously been found be associated with mucosal sick building symptoms [79], and epidemiology studies have found correlations between phthalate concentrations and asthma in children [1, 38]. The study described in **Paper III** does not support these results, although the analysis was limited in that the incidence of symptoms was reported in terms of single frequencies for occupants in the building as a whole, and SBS data was not available on a per-apartment basis.

## 5.2. Dust samples

The dust concentrations of selected OPEs and phthalates examined in **Papers II and IV** are listed in **Tables 5.4 and 5.5.** In general, the phthalate concentrations in the dust were higher than the corresponding OPE concentrations. One organophosphorus compound, TBEP, can be found in levels in the same order of magnitude as the phthalates.

### 5.2.1. Phthalates in dust

**Table 5.4** shows the phthalate concentrations measured in previously-reported studies conducted at various locations around the world, those determined in indoor dust from the locations described in **Paper II**, and those measured in SRM 2585 as reported in **Paper IV**. The previous studies whose results are presented in this table were selected using the same criteria as were used when compiling data on airborne phthalate concentrations. The samples were taken from vacuum cleaner bags unless otherwise stated (in some cases, samples were acquired by filter sampling or with a nylon sock). In general, samples were collected from the floor with the exception of those labeled "surf," which were taken from selected surfaces above the floor. Data on DMP and DnOP concentrations were excluded from the summary. Because of its high volatility, the concentrations of DMP in dust were typically below 2 μg/g [7, 46] (**Papers II and IV**), and the concentration of DnOP was generally not reported in the selected studies; the only determination of this compound in the studies examined is that reported for SRM 2585 in **Paper IV (**17μg/g).

In general, DEHP is the most abundant of the phthalates examined in the selected studies (**Table 5.4)**. Interestingly, the concentration of DBP in the Swedish study was noticeably higher than those measured in studies conducted elsewhere (including its neighbor, Denmark). Furthermore, the concentration of DiBP in home environments is around ten times higher in Western Europe than in Japan and the US; the only exceptions to this finding were single family detached/terrace houses and the daycare centers, which had DiBP concentrations similar to those observed in Japan and the US, **Table 5.4 (Paper II).**

**Table 5.4:** Dust concentrations of phthalates (µg/g) in residences as reported in selected relevant studies. All values are medians unless otherwise stated

| Country | Dust description | *n* | DEP | DiBP | DBP | BzBP | DEHP |
|---|---|---|---|---|---|---|---|
| Germany [6, 88] | (H) < 63µm[c] | 286 | – | 34 | 49 | 49 | 740 |
| Germany [6, 89] [a] | (H) < 2mm[c] | 199 | – | 22 | 42 | 15 | 416 |
| Germany [7, 46] [b] | (H) | 30 | 6 | 36 | 47 | 29 | 659 |
| USA:MA [78] | (H) < 150µm[c] | 120 | 5.0 | 1.9 | 20 | 45 | 340 |
| Japan[79] | (H) Surf. | 41 | 0.4 | 2.4 | 22 | 2.4 | 1200 |
| Japan[79] | (H) | 41 | 0.3 | 2.9 | 20 | 4.2 | 880 |
| Denmark; [90] | (H) FS | 497 | 1.7 | 27 | 15 | 3.7 | 210 |
| Denmark; [90] | (D) FS | 151 | 2.2 | 23 | 38 | 17 | 500 |
| Sweden[56] | (H) Surf., FS | 346 | – | 45 | 150 | 135 | 770 |
| **Paper II:** | (H), Surf., FS | 10 | 3.7 | 4.0 | 130 | 17 | 680 |
| **Paper II:** | (D) Surf., FS | 10 | 4.2 | 2.6 | 150 | 31 | 1600 |
| **Paper II:** | (W) Surf., FS | 10 | 20 | 37 | 100 | 8.8 | 1100 |
| **Paper IV** | SRM 2585[c, d] | 7 | 6.7 | 6.0 | 31 | 93 | 570 |

– Values not reported or below reported determination limit
[a]as reported by Wensing et. al (2005)
[b]as reported by Weschler et.al (2008)
[c]Samples are sieved, (SRM 2585 <100µm)
[d]Mean value of 7 replicates
H: home environment; D: daycare centers; W: Workplaces; Surf.: Sampling performed only on surfaces above the floor; FS; A nozzle sampler similar to that shown in **Figure 3.2** was used.

### 5.2.2. Organophosphates in dust

The concentrations of OPEs in dust are summarized in **Table 5.5**. There are no obvious similarities or differences in terms of concentrations between the different studies. In general, the analyte with the highest concentration in dust is TBEP. The levels of TBEP in dust collected from daycare centers was particularly high, see Table 5.5. In the Japanese study by Kanazawa *et al.*, the concentration of TBEP in dust samples collected directly from floors was ten orders of magnitude higher than that in dust sampled from surfaces above the floor in the same apartments [79]. This is consistent with the conclusion drawn in **Paper II** that TBEP levels are related to flooring, and may originate from floor polishes [42].

**Table 5.5:** Dust concentrations of OPEs (µg/g) in residences as reported in selected relevant studies. All values are medians unless otherwise stated

| Country | Dust description | *n* | TBP | TCEP | TCiPP | TDCPP | TBEP | TPP |
|---|---|---|---|---|---|---|---|---|
| Japan[79] | (H) Surf. | 41 | 1.1 | 9.8 | 51 | 22 | 164 | 14 |
| Japan[79] | (H) | 41 | 1.4 | 7.5 | 19 | 4.0 | 1570 | 5.4 |
| Belgium[67] | (H) nylon sock | 33 | 0.1 | 0.2 | 1.4 | 0.4 | 2.0 | 0.5 |
| **Paper II** | (H) Surf., FS | 10 | 0.3 | 2.1 | 1.6 | 10 | 4.0 | 1.2 |
| **Paper II** | (D) Surf., FS | 10 | 1.2 | 30 | 3.1 | 9.1 | 1600 | 1.9 |
| **Paper II** | (W) Surf., FS | 10 | 0.2 | 6.7 | 19 | 17 | 87 | 5.3 |
| SRM 2585 | **Paper IV** [a] | 7 | 0.2 | 0.8 | 0.9 | 2.3 | 82[b] | 1.1 |
| SRM 2585 | Belgium study [a] | 11 | 0.2 | 0.7 | 0.8 | 2.0 | 49 | 1.0 |

– Values not reported or below reported determination limit
[a] Mean values of 7 and 11 replicates, respectively
[b] Concentration also determined by standard addition in which case the measured value was 73±13µg/g
H: home environment; D: daycare centers; W: Workplaces; Surf.: Sampling preformed only on surfaces above the floor; FS; A nozzle sampler similar to that shown in **Figure 3.2** was used.

**Paper IV** presents an analysis of the house dust Standard Reference Material (SRM) 2585 "Organic Contaminants in House Dust". This work further validates the extraction method used in **Paper I** and its use for the

quantification of OPEs and phthalates. The availability of certified reference materials is very important for estimating the accuracy of the data obtained using different sample preparation methods. The concentrations of phthalates in SRM 2585 had not been determined prior to the work described in **Paper IV**. Further work on the standardization of these compounds in this reference material would be beneficial and would make it possible to use this standard for quality control purposes in future studies. In **Figure 5.3**, the concentrations of six OPEs in SRM 2585 determined in **Paper IV** (TBEP, TBP, TCEP, TCiPP, TDCPP, TPP and TToP) are compared to the corresponding values measured by Van den Eede *et al.* in the same material in a recent study [67]. With the exceptions of TBEP and TToP, the two studies' results are in good agreement.

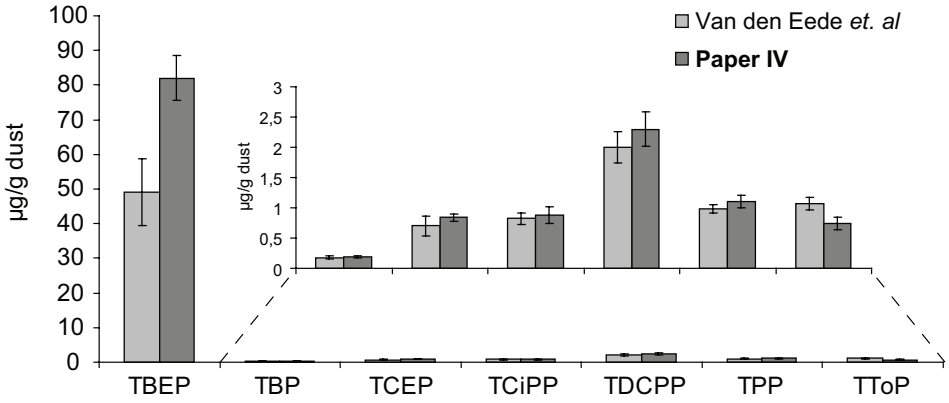



**Figure 5.3:** Comparison between quantified amounts in SRM 2585. Bars in light gray denote data obtained by Van den Eede *et. al*. Bars in dark grey denote data reported in **Paper IV**.

The determined concentrations of phthalates and OPEs in SRM 2585 "Organic Contaminants in House Dust" are summarized in **Tables 5.4** and **5.5**. Some compounds do not feature in these tables because they

were not detected or were detected at concentrations below their limit of determination; TEP, TiPrP, TPrP, TiBP and TPeP also excluded are the compounds had the quantified levels of; THP 0.25 µg/g, DPEHP 1.3 µg/g, TEHP 0.37 µg/g, TToP 0.74 µg/g, and DOP 17 µg/g, **Paper IV**. The most abundant phthalate was DEHP, with a measured concentration of 570 µg/g, followed by BzBP (93 µg/g) and TBEP (around 80 µg/g). TBEP was determined using both external standard calibration and standard addition the concentrations measured using these methods were; 82 ± 6.5 and 73 ± 13 µg/g, respectively. The differences in the determined concentrations of TBEP indicate that analytical determination of this compound is more unreliable. As mentioned earlier, the use of deuterated reference compounds would enhance the accuracy of the determinations. In the initial analysis of SRM 2585 in **Paper II,** the two high molecular weight phthalates DiNP and DiDP were detected. However, the determination method was never finalized for these two compounds. By reviewing the data from **Paper I,** a rough estimate of the number of dust samples that contained DiNP and DiDP was obtained; 93% of the 30 samples were observed DiNP and 73% contained DiDP. **Figure 5.4** shows PICI-SRM chromatograms for DiNP and DiDP. Neither of these analytes was observed in the air samples, which is consistent with their low volatility.

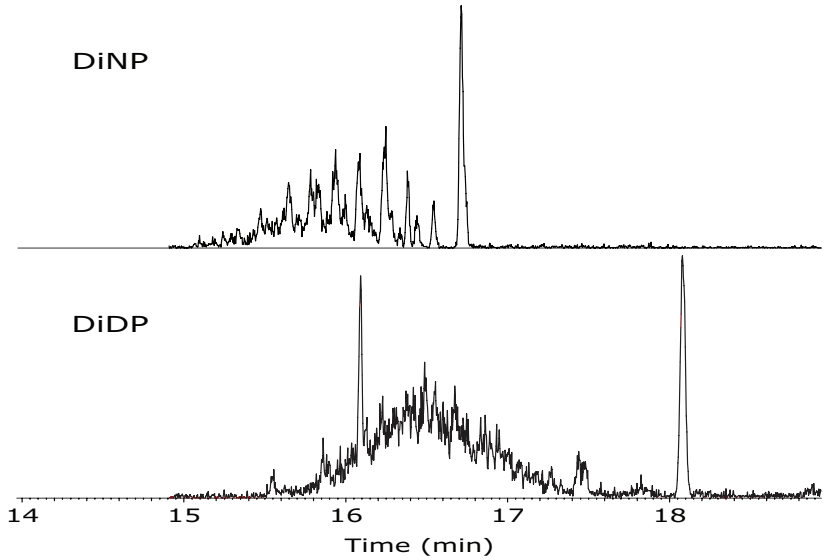



**Figure 5.4:** Chromatogram of a dust sample acquired in a workplace location (**Paper II**) and analysed by PICI SRM. Top chromatogram: DiNP; bottom chromatogram: DiDP

## 5.3. Potential sources

Potential sources of the detected phthalates and OPEs were discussed in **Papers II and III:**

- TBEP is generally associated with flooring and probably derives from floor polish [42, 91] (**Paper II)**.
- The chlorinated OPEs (TCiPP, TCEP and TDCPP) were mainly associated with work environments (**Paper II)**. This is slightly contradicted by the data on multi-storey apartments where concentrations up to 1200ng/m$^3$ was determined, **Paper III**
- TBEP were mainly associated with day care centers in the location study in **Paper II**
- The air concentration of BzBP increases significantly ($p< 1 \cdot 10^{-10}$) with the number of PVC floors within an apartment (**Paper III),** and indications of correlations between PVC flooring and airborne

concentrations were found for DEHP and DBP. This is consistent with previously-published results of phthalates in dust [56].

- In **Paper III,** TBP and DBP correlated negatively ($p < 1 \cdot 10^{-4}$ and $1 \cdot 10^{-6}$, respectively) with the age of the multi-storey apartment buildings, indicating that these compounds are associated with building materials. The data suggest that either the use of building materials containing these compounds has declined or that their emission from building materials decreases over time.
- There were indications that leather furniture might be a possible source of TBP (**Paper III)**.
- DiBP was detected in very high concentrations (11,000 ng/m$^3$) in an apartment whose inhabitant was manufacturing pillows containing synthetic fiber material. (**Paper III)**.
- The high variance between apartments within a building indicate that building materials are not a major source of phthalates and OPEs

For more information and for further discussion of potential sources, the interested reader is directed to the current literature [6, 17, 56, 82, 92-94].

## 5.4. Exposure

In **Papers II** and **III,** the primary objective was to determine the general levels of the different compounds and to identify differences and similarities in the concentrations of phthalates and organophosphates in the different environments. The most abundant phthalates in the air and dust samples (**Paper II**) were DEP, DBP, DiBP and DEHP; the most abundant OPEs were TCiPP, TCEP, TDCPP and TBEP. The median concentrations determined in **paper II,** can be used to estimate the daily

human exposure to OPEs and phthalates. The USEPA estimates human inhalation exposure on the basis of the daily mean air inhalation volume [55, 95]. For adults, this inhalation volume is 16 $m^3$/day, while for children between the ages of 2 and 6, it is 9.5 $m^3$/day. The latter age range is typical for children attending daycare centers in Sweden. The USEPA has also estimated that children ingest 60 mg of indoor settled dust/day. There is as yet no data on the ingestion of indoor settled dust by adults, and so a value of 50 mg/day (corresponding to the general tendency of soil ingestion), was used. In an English study by Harrad *et al.*, the percentage of time spent per day at home, at the office, in public indoor environments, in the car and outdoors was estimated at 63.8, 22.3, 5.1, 4.1, and 4.5%, respectively [96]. Estimates were made on the basis of two assumptions: that children spend the same amount of time at the day-care centre as adults do at the office, and the uptake is 100%. The estimated exposures are shown in **Tables 5.6 and 5.7**.

**Table 5.6:** Estimated exposure of adults from median concentrations in **Paper II** (µg/day)

| **Adult** | **Home (63.8%)** | | **Work (22.3%)** | | **Exposure** | | |
|---|---|---|---|---|---|---|---|
| [µg/day] | $I_h$ ($D_h$)* | | $I_W$($D_W$)* | | $I_{tot}$ ($D_{tot}$)* | | ∑ **Exposure** |
| **Phosphates** | | | | | | | |
| TCEP | 0.05 | (0.07) | 0.07 | (0.07) | 0.08 | (0.14) | **0.23** |
| TCiPP | 0.06 | (0.05) | 0.21 | (0.21) | 0.41 | (0.26) | **0.68** |
| TDCPP | - | (0.32) | 0.19 | (0.19) | 0.10 | (0.51) | **0.61** |
| TBEP | 0.01 | (0.13) | 0.97 | (0.97) | 0.03 | (1.1) | **1.1** |
| **Phthalates** | | | | | | | |
| DEP | 13 | (0.12) | 0.22 | (0.22) | 15 | (0.34) | **16** |
| DiBP | 2.8 | (0.13) | 0.41 | (0.41) | 3.6 | (0.54) | **4.1** |
| DBP | 8.7 | (4.2) | 1.1 | (1.1) | 11 | (5.3) | **16** |
| BzBP | 0.21 | (0.54) | 0.1 | (0.10) | 0.27 | (0.64) | **0.91** |
| DEHP | 2.0 | (22) | 12 | (12) | 2.4 | (34) | **36** |

*I= inhalation exposure; D=dust ingestion

**Table 5.7:** Estimated exposure of children from median concentrations in **Paper II** (µg/day)

| Child | Home (63.8%) | | Day-care 22.3% | | Exposure | | |
|---|---|---|---|---|---|---|---|
| [µg/day] | $I_h$ ( $D_h$)* | | $I_h$ ( $D_{DCC}$)* | | $I_{tot}$ ($D_{tot}$)* | | ∑ Exposure |
| **Phosphates** | | | | | | | |
| TCEP | 0.03 | (0.08) | 0.10 | (0.40) | 0.08 | **(0.48)** | **0.61** |
| TCiPP | 0.03 | (0.06) | 0.04 | (0.04) | 0.41 | **(0.10)** | **0.18** |
| TDCPP | - | (0.38) | - | (0.12) | 0.10 | **(0.50)** | **0.50** |
| TBEP | 0.003 | (0.15) | 0.28 | (21) | 0.03 | **(22)** | **22** |
| **Phthalates** | | | | | | | |
| DEP | 8.5 | (0.14) | 1.8 | (0.06) | 15 | **(0.20)** | **11** |
| DiBP | 1.8 | (0.15) | 0.40 | (0.03) | 3.6 | **(0.19)** | **2.4** |
| DBP | 5.6 | (5.0) | 1.3 | (2.0) | 11 | **(7.0)** | **14** |
| BzBP | 0.14 | (0.54) | 0.04 | (0.10) | 0.27 | **(0.64)** | **0.82** |
| DEHP | 1.3 | (26) | 0.51 | (21) | 2.4 | **(47)** | **50** |

*I= inhalation exposure; D=dust ingestion

For some of these compounds, 70–99% of the exposure originates from dust ingestion. Especially for children the exposure of TBEP and DEHP through dust is relatively high and the high levels of TBEP in daycare centers are of potential concern, **Paper II**. DEHP is known to have several biological effects and was found to be one of the predominant compounds in dust. The calculated daily exposure for an adult was around 36 µg DEHP/day; that for a toddler was 50 µg DEHP/day. Thus, an adult with a weight of 70 kg will have a daily exposure of 0.5 µg DEHP/kg bodyweight, while the daily exposure for a toddler of 12 kg will be around 4.2 µg DEHP/kg bodyweight. These levels should be compared to the tolerable daily intake (TDI) of 37 µg per kg body weight per day stated in 1998 by the EU Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE) and the reference dose (RfD) of 20 µg/kg body weight and day set by USEPA in 1999 [97, 98]. These

values are estimated for adults and do not, for example, take into account dermal exposure from dust.

There are also interesting indications that exposure can occur via direct air to skin transport [3]. Exposure to SVOC compounds in the indoor environment is thus a complex phenomenon. Compounds in the gaseous phase ($C_a$) are partitioned between airborne particles and dust, but are also found on surfaces, furniture, in humans, and elsewhere. An adequate exposure model cannot be obtained simply by considering partitioning and assuming that equilibrium obtains. Instead, it is necessary to consider the material balance (*i.e.* source and sink processes) and mass transport kinetics in order to properly understand the prevalence and potential health risks associated with SVOCs [3]. When discussing the biological effects associated with daily exposure to compounds in our immediate environment the topic of combination effects, also known as the "cocktail effect", is of great interest. This means that the biological effects of combinations of toxic or potentially toxic chemicals have to be considered as well as examining the effects of each compound separately. Of the two compound groups studied in this work, the phthalates in particular are suspected to give rise to combination effects [31, 99, 100].

# 6. Conclusions and future perspectives

This work provides further support for the position that OPEs and phthalates are ubiquitous indoor environment pollutants in both air and dust. **Papers I-IV** clearly demonstrates the scope for simultaneous sampling and analysis of both OPEs and phthalates. Phthalates concentrations are consistently higher than the OPEs in both air and dust, with the exception of TBEP that occurs in similar concentrations as phthalates in dust.

The selective detection method using GC/PICI-SRM/MS for the determination of phthalates and OPEs in air and dust presents a good alternative to the conventional detection techniques GC/EI-SIM/MS and NPD. It was demonstrated that both isobutane and ammonia are suitable reagent gases for analysis of OPEs and phthalates, and that the latter generates the lowest LOQs. (**Papers I** and **IV**).

The approach of sampling in different environments adopted in **Paper II** generated interesting results in terms of the differences in the OPE concentration profiles in the air samples from offices, day-care centers and home environments. Consequently, the OPEs and phthalates present in consumer products or building materials used in these different sampled environments are similar even though the environments are rather diverse in terms of design, building type and age. Further analysis of the types of consumer products used in the different locations would provide valuable context for these findings. The relatively high concentrations of TBEP observed in day-care centers in **Paper II** is of great interest, because they imply that small children in Sweden are likely to be highly exposed to this compound through ingestion and dermal uptake of dust.

In **Paper III**, no correlation was found between the measured concentrations of phthalates and OPEs and the incidence of sick building symptoms (SBS) in the inhabitants of specific buildings. Some of the data implied interesting things about the sources of OPEs and phthalates, among other things the levels of BzBP in air was correlated to the number of PVC floors within an apartment.

The concentrations of twelve OPEs and seven phthalates in SRM 2585 "Organic Contaminants in House Dust" were determined in **Paper IV**. SRMs are useful for validating and comparing the analytical method. The results obtained in **Paper IV** were compared to those reported by van den Eede *et al.* [67] for seven of the OPEs in the same reference material; the results for five were in good agreement. The compounds that are in good agreement can be used as a non-certified reference value of these compounds in SRM 2585. The concentration of TBEP in SRM 2585 needs to be verified and the concentrations of the OPEs and phthalates whose concentration in this reference material has not previously been analysed would benefit from further work by another lab to assess the accuracy of the determined values.

The study reported in **Paper I** revealed that two high molecular weight phthalates, DiNP and DiDP, are present in SRM 2585. As such, further studies on the incidence and abundance of these compounds would be of great interest. DiNP and DiDP were not observed in the air samples analyzed in **Paper I** but were prevalent in the dust samples; this difference is probably attributed to their low vapour pressure.

Many of these compounds are potentially harmful for the health and that some are adopted as candidates for restrictions by ECHA In future studies alternative compounds for replacement to those included in this

thesis are of great interest. Some “non-phthalate” compounds are entering the market to replace the potentially harmful “old” phthalates. Two such compounds are diisononyl 1,2-cyclohexanedicarboxylic acid (DINCH) and di(2-ethylhexyl) terephthalate (DEHT) [101]; levels of these compounds in air and dust samples should be considered in future studies.

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# 8. References


1 Mendell, M.J. (2007). Indoor residential chemical emissions as risk factors for respiratory and allergic effects in children: a review. *Indoor Air,* 17: 259-277.

2 Werner, B. (2004). Plasicizers in the Indoor Environment, In *Handbook of Plasticizers,* Wypych, G., Ed.; ChemTec Publishing: Toronto, Canada, pp. 568-589.

3 Weschler, C.J. and Nazaroff, W.W. (2008). Semivolatile organic compounds in indoor environments. *Atmos. Environ.,* 42: 9018-9040.

4 Garcia-Jares, C.; Regueiro, J.; Barro, R.; Dagnac, T.; Llompart, M. (2009). Analysis of industrial contaminants in indoor air. Part 2. Emergent contaminants and pesticides. *J. Chromatogr. , A,* 1216: 567-597.

5 Reemtsma, T.; Garcia-Lopez, M.; Rodriguez, I.; Quintana, J.B.; Rodil, R. (2008). Organophosphorus flame retardants and plasticizers in water and air I. Occurrence and fate. *TrAC, Trends Anal. Chem,* 27: 727-737.

6 Wensing, M.; Uhde, E.; Salthammer, T. (2005). Plastics additives in the indoor environment - flame retardants and plasticizers. *Sci. Total Environ.,* 339: 19-40.

7 Fromme, H.; Lahrz, T.; Piloty, M.; Gebhart, H.; Oddoy, A.; Rueden, H. (2004). Occurrence of phthalates and musk fragrances in indoor air and dust from apartments and kindergartens in Berlin (Germany). *Indoor Air,* 14: 188-195.

8 Staaf, T. and Östman, C. (2005). Organophosphate triesters in indoor environments. *J. Environ. Monit.,* 7: 883-887.

9 Marklund, A.; Andersson, B.; Haglund, P. (2003). Screening of organophosphorus compounds and their distribution in various indoor environments. *Chemosphere,* 53: 1137-1146.

10 Carlsson, H.; Nilsson, U.; Becker, G.; Östman, C. (1997). Organophosphate Ester Flame Retardants and Plasticizers in the Indoor Environment: Analytical Methodology and Occurrence. *Environ. Sci. Technol.,* 31: 2931-2936.

11 Rudel, R.A.; Dodson, R.E.; Perovich, L.J.; Morello-Frosch, R.; Camann, D.E.; Zuniga, M.M.; Yau, A.Y.; Just, A.C.; Brody, J.G. (2010). Semivolatile Endocrine-Disrupting Compounds in Paired Indoor and Outdoor Air in Two Northern California Communities. *Environ. Sci. Technol.,* 44: 6583-6590.

12 Gächter, R. and Müller, H. (1993). *Plastic Additives.* 4th, Hanser/Gardner Publications Inc.: Cincinatti.

13 Brydson, J.A. (1995). *Plastic Materials.* 6th ed., Butterworth-Heinemann Ltd: Jordan Hill, Oxford.

14 WHO (1997). Flame retardants: A General Introduction. Environmental Health Criteria 192, World Health Organization, Geneva

15 Wypych, G. (2004). *Handbook of Plasicizers.* ChemTec Publishing: Toronto, Canada.

16 Meier, L. (1993). Phthalates, In *Plastics Additives,* 4th ed.; Gächter, R. and Müller, H., Eds.; Hanser/Gardner Publications Inc.: Cincinatti, pp. 369-380.

17 Marklund, A.; Andersson, B.; Haglund, P. (2005). Organophosphorus flame retardants and plasticizers in air from various indoor environments. *J. Environ. Monit.,* 7: 814-819.

18 Wypych, G. (2004). Plasicizers Types, In *Handbook of Plasticizers,* Wypych, G., Ed.; ChemTec Publishing: Toronto, Canada, pp. 2-71.

19 Green, J. (1996). A review of phosphorus-containing flame retardants. *J. Fire Sci.,* 14: 353-366.

20 WHO (1998). Flame retardants: Tris(chloropropyl) Phosphate and Tris(2-chlorethyl) Phosphate. Environmental Health Criteria 209, World Health Organization, Geneva

21 European Council for Plasticisers and Intermediates (ECPI), A sector group of Cefic, European Chemical Industry Council. (2010). Plasticisers, (Accessed 2010/08/16) http://www.ecpi.org

22 European Flame Retardants Association (EFRA), A sector group of Cefic, European Chemical Industry Council:. (2007). (Accessed 2010/08/11) http://www.cefic-efra.com

23 European Chemicals Agency (ECHA). (2010). Candidate List of Substances of Very High Concern for authorisation, (Accessed 2010/05/28) http://echa.europa.eu/chem_data/authorisation_process/candidate_list_table_en.asp

24 European Chemicals Agency (ECHA). (2009). Annex XIV recommendations, (Accessed 2010/05/28) European Chemicals Agency http://echa.europa.eu/chem_data/authorisation_process/annex_xiv_rec_en.asp

25 European Commission (2009). European Union Risk Assessment Report, Tris (2-chloroethyl) phosphate, TCEP. Final report, European Chemicals Bureau (ECB), Avaliable through ORATS (Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

26 European Commission (2008). European Union Risk Assessment Report, bis(2-ethylhexyl)phthalate (DEHP). EUR 23384 EN, European Chemicals Bureau (ECB), Avaliable through ORATS (Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

27 European Commission (2008). European Union Risk Assessment Report, tris(2-chloro-1-methylethyl) phosphate (TCPP). Final report, European Chemicals Bureau (ECB), Avaliable through ORATS

(Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

28 European Commission (2008). European Union Risk Assessment Report, tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP). Final report, European Chemicals Bureau (ECB), Avaliable through ORATS (Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

29 European Commission (2007). European Union Risk Assessment Report, benzyl butyl phthalate (BBP). EUR 22773 EN, European Chemicals Bureau (ECB), Avaliable through ORATS (Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

30 European Commission (2003). European Union Risk Assessment Report, Dibutyl phthalate (with addendum 2004). EUR 19840 EN, European Chemicals Bureau (ECB), Avaliable through ORATS (Online EUropean Risk Assessment Tracking System): http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

31 Sharpe, R.M. (2008). "Additional" Effects of Phthalate Mixtures on Fetal Testosterone Production. *Toxicol. Sci.,* 105: 1-4.

32 Welsh, M.; Saunders, P.T.K.; Fisken, M.; Scott, H.M.; Hutchison, G.R.; Smith, L.B.; Sharpe, R.M. (2008). Identification in rats of a programming window for reproductive tract masculinization, disruption of which leads to hypospadias and cryptorchidism. *J. Clin. Invest.,* 118: 1479-1490.

33 Foster, P.M.D. (2006). Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. *Int. J. Androl.,* 29: 140-147.

34 Swan, S.H. (2008). Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. *Environ. Res.,* 108: 177-184.

35 Swan, S.H.; Main, K.M.; Liu, F.; Stewart, S.L.; Kruse, R.L.; Calafat, A.M.; Mao, C.S.; Redmon, J.B.; Ternard, C.L.; Sullivan, S.; Teague,

J.L.; Drobnis, E.Z.; Carter, B.S.; Kelly, D.; Simmons, T.M.; Wang, C.; Lumbreras, L.; Villanueva, S.; Diaz-Romero, M.; Lomeli, M.B.; Otero-Salazar, E.; Hobel, C.; Brock, B.; Kwong, C.; Muehlen, A.; Sparks, A.; Wolf, A.; Whitham, J.; Hatterman-Zogg, M.; Maifield, M. (2005). Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environ. Health Perspect.,* 113: 1056-1061.

36 Sharpe, R.M. (2005). Phthalate exposure during pregnancy and lower anogenital index in boys: wider implications for the general population? *Environ. Health Perspect.,* 113: A504-5.

37 Fisher, J.S. (2004). Environmental anti-androgens and male reproductive health: focus on phthalates and testicular dysgenesis syndrome. *Reproduction (Bristol, U. K. ),* 127: 305-315.

38 Bornehag, C.G. and Nanberg, E. (2010). Phthalate exposure and asthma in children. *Int. J. Androl.,* 33: 333-345.

39 Salthammer, T.; Fuhrmann, F.; Uhde, E. (2003). Flame retardants in the indoor environment - Part II: Release of VOCs (triethylphosphate and halogenated degradation products) from polyurethane. *Indoor Air,* 13: 49-52.

40 Saboori, A.M.; Lang, D.M.; Newcombe, D.S. (1991). Structural requirements for the inhibition of human monocyte carboxylesterase by organophosphorus compounds. *Chem. -Biol. Interact.,* 80: 327-338.

41 WHO (1991). Triphenyl Phosphate. Environmental Health Criteria 111, World Health Organization, Geneva

42 WHO (2000). Flame Retardants: Tris (2-butoxyethyl) phosphate, Tris (2-ethylhexyl) phosphate and Tetrakis (hydroxymethyl) phosphonium salts. Environmental Health Criteria 218, World Health Organization, Geneva

43 WHO (1991). Tri-*n*-butyl Phosphate. Environmental Health Criteria 112, World Health Organization, Geneva

44 WHO (1989). Indoor Air Quality: Organic pollutants. Euro Report and Studies 111, World Health Oranization, Regional Office for Europe, Copenhagen

45 Ayoko, G.A. and Uhde, E. (2003). Organic Compounds Adsorbed on Particles and Settled House Dust, In *Indoor Environment: Airborn Particles and Settled Dust,* Morawska, L. and Salthammer, T., Eds.; WILEY-VCH GmbH & Co. KGaA: Weinheim, pp. 143-166.

46 Weschler, C.J.; Salthammer, T.; Fromme, H. (2008). Partitioning of phthalates among the gas phase, airborne particles and settled dust in indoor environments. *Atmos. Environ.,* 42: 1449-1460.

47 Vogel, M. (2005). Sampling of airborne pollutants: strategies and developments. *Anal. Bioanal. Chem.,* 381: 84-86.

48 Kootstra, P.R. and Herbold, H.A. (1995). Automated solid-phase extraction and coupled-column reversed-phase liquid chromatography for the trace-level determination of low-molecular-mass carbonyl compounds in air. *J. Chromatogr. , A,* 697: 203-211.

49 Jahnke, A.; Huber, S.; Temme, C.; Kylin, H.; Berger, U. (2007). Development and application of a simplified sampling method for volatile polyfluorinated alkyl substances in indoor and environmental air. *J. Chromatogr. , A,* 1164: 1-9.

50 Staaf, T. and Östman, C. (2005). Indoor air sampling of organophosphate triesters using solid phase extraction (SPE) adsorbents. *J. Environ. Monit.,* 7: 344-348.

51 Chafer-Pericas, C.; Herraez-Hernandez, R.; Campins-Falco, P. (2004). Selective determination of trimethylamine in air by liquid chromatography using solid phase extraction cartridges for sampling. *J. Chromatogr. , A,* 1042: 219-223.

52 Ramil Criado, M.; Rodriguez Pereiro, I.; Cela Torrijos, R. (2002). Determination of polychlorinated biphenyl compounds in indoor air samples. *J. Chromatogr. , A,* 963: 65-71.

53 Morawska, L. and Salthammer, T. (2003). *Indoor Environment: Airborn Particles and Settled Dust.* WILEY-VCH GmbH & Co. KGaA: Weinheim.

54 U.S. EPA. (1997). Exposure Factors Handbook (Final Report) 1997. EPA/600/P-95/002F a-c, U.S. Environmental Protection Agency, Washington D.C.

55 U.S. EPA. (2008). Child-Specific Exposure Factors Handbook (Final Report) 2008. EPA/600/R-06/096F, U.S. Environmental protection Agency, Washington D.C.

56 Bornehag, C.; Lundgren, B.; Weschler, C.J.; Sigsgaard, T.; Hagerhed-Engman, L.; Sundell, J. (2005). Phthalates in indoor dust and their association with building characteristics. *Environ. Health Perspect.,* 113: 1399-1404.

57 Schnelle-Kreis, J.; Scherb, H.; Gebefugi, I.; Kettrup, A.; Weigelt, E. (2000). Pentachlorophenol in indoor environments. Correlation of PCP concentrations in air and settled dust from floors. *Sci. Total Environ.,* 256: 125-132.

58 Quintana, J.B.; Rodil, R.; Reemtsma, T.; Garcia-Lopez, M.; Rodriguez, I. (2008). Organophosphorus flame retardants and plasticizers in water and air II. Analytical methodology. *TrAC, Trends Anal. Chem,* 27: 904-915.

59 Wise, S.A.; Poster, D.L.; Kucklick, J.R.; Keller, J.M.; VanderPol, S.S.; Sander, L.C.; Schantz, M.M. (2006). Standard reference materials (SRMs) for determination of organic contaminants in environmental samples. *Anal. Bioanal. Chem.,* 386: 1153-1190.

60 Weschler, C.J. and Nazaroff, W.W. (2010). SVOC partitioning between the gas phase and settled dust indoors. *Atmos. Environ.,* 44: 3609-3620.

61 Schantz, M.M.; Keller, J.M.; Kucklick, J.R.; Poster, D.L.; Stapleton, H.M.; Vander Pol, S.S.; Wise, S.A. (2007). New standard reference material (SRM) 2585: Organic contaminants in house dust to support exposure assessment measurements. *Am. Lab.,* 39: 22-+.

62 Poster, D.L.; Kucklick, J.R.; Schantz, M.M.; Vander Pol, S.S.; Leigh, S.D.; Wise, S.A. (2007). Development of a house dust standard reference material for the determination of organic contaminants. *Environ. Sci. Technol.,* 41: 2861-2867.

63 Stapleton, H.M.; Harner, T.; Shoeib, M.; Keller, J.M.; Schantz, M.M.; Leigh, S.D.; Wise, S.A. (2006). Determination of polybrominated diphenyl ethers in indoor dust standard reference materials. *Anal. Bioanal Chem.,* 384: 791-800.

64 NIST (2010). Certificate of Analysis for SRM 2585 Organic Contaminants in House Dust. Last certificate revision: 06 January 2010; Original certificate date: 20 December 2005, National Institute of Standards & Technology, Gaithersburg, USA,

65 NIST (2010). Certificate of Analysis for SRM 2583 Trace Elements in Indoor Dust. Last certificate revision: 30 November 2010; (Original certification date: 30 December 1996), National Institute of Standards & Technology, Gaithersburg, USA,

66 NIST (2010). Certificate of Analysis for SRM 2584 Trace Elements in Indoor Dust. Last certificate revision: 07 November 2010 ; (Original certification date: 15 December 1999 ), National Institute of Standards & Technology, Gaithersburg, USA,

67 Van den Eede, N.; Dirtu, A.C.; Neels, H.; Covaci, A. (2011). Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. *Environ. Int.,* 37: 454-461.

68 David, F.; Sandra, P.; Tienpont, B.; Vanwalleghem, F.; Ikonomou, M. (2003). Analytical methods review - Part 2: Analysis of phthalates, In *The Handbook of Environmental Chemistry: Phthalate Esters,* Vol. 3, Part Q Staples, C.A., Ed.; Springer: Berlin, Heidelberg, pp. 12-26.

69 Robards, K.; Haddad, P.R.; Jackson, P.E. (2004). *Principles and Practice of Modern Chromatographic Methods.* Elsevier Ldt.: London.

70 Scott, R.P.W. (2003). *Gas Chromatography Detectors.* Libraryforsience, LLC: World Wide Web: http:/www.library4science.com.

71 Quintana, J.B.; Rodil, R.; Lopez-Mahia, P.; Muniategui-Lorenzo, S.; Prada-Rodriguez, D. (2007). Optimization of a selective method for the determination of organophosphorous triesters in outdoor particulate samples by pressurized liquid extraction and large-volume injection gas chromatography-positive chemical ionization-tandem mass spectrometry. *Anal. Bioanal. Chem.,* 388: 1283-1293.

72 Harrison, A.G. (1992). *Chemical Ionization Mass Spectrometry.* 2:nd Edition, CRC press LLC: Boca Raton, Florida.

73 de Hoffman, E. and Stroobant, V. (2001). *Mass Spectrometry - Prniciples and Application.* 2:nd edition, John Wiley & Sons, Ldt: Chicester.

74 McLafferty, F.W. and Tureček, F. (1993). *Interpretation of Mass Spectra.* 4th, University Science Books: Sausalito, CA.

75 Björklund, J.; Isetun, S.; Nilsson, U. (2004). Selective determination of organophosphate flame retardants and plasticizers in indoor air by gas chromatography, positive-ion chemical ionization and collision-induced dissociation mass spectrometry. *Rapid Commun. Mass Spec.,* 18: 3079-3083.

76 Toda, H.; Sako, K.; Yagome, Y.; Nakamura, T. (2004). Simultaneous determination of phosphate esters and phthalate esters in clean room air and indoor air by gas chromatography-mass spectrometry. *Anal. Chim. Acta,* 519: 213-218.

77 Fankhauser-Noti, A. and Grob, K. (2007). Blank problems in trace analysis of diethylhexyl and dibutyl phthalate: Investigation of the sources, tips and tricks. *Anal. Chim. Acta,* 582: 353-360.

78 Rudel, R.A.; Camann, D.E.; Spengler, J.D.; Korn, L.R.; Brody, J.G. (2003). Phthalates, Alkylphenols, Pesticides, Polybrominated Diphenyl Ethers, and Other Endocrine-Disrupting Compounds in Indoor Air and Dust. *Environ. Sci. Technol.,* 37: 4543-4553.

79 Kanazawa, A.; Saito, I.; Araki, A.; Takeda, M.; Ma, M.; Saijo, Y.; Kishi, R. (2010). Association between indoor exposure to semi-volatile organic compounds and building-related symptoms among the occupants of residential dwellings. *Indoor Air,* 20: 72-84.

80 Sjödin, A.; Carlsson, H.; Thuresson, K.; Sjölin, S.; Bergman, Å.; Östman, C. (2001). Flame Retardants in Indoor Air at an Electronics Recycling Plant and at Other Work Environments. *Environ. Sci. Technol.,* 35: 448-454.

81 Sanchez, C.; Ericsson, M.; Carlsson, H.; Colmsjö, A. (2003). Determination of organophosphate esters in air samples by dynamic sonication-assisted solvent extraction coupled on-line with large-volume injection gas chromatography utilizing a programmed-temperature vaporizer. *J. Chromatogr. A,* 993: 103-110.

82 Saito, I.; Onuki, A.; Seto, H. (2007). Indoor organophosphate and polybrominated flame retardants in Tokyo. *Indoor Air,* 17: 28-36.

83 Corner, R. (2009).
Stockholms väg mot Hälsomässigt hållbara hus - 3H. 3H-projektet, http://www.stockholm.se/ByggBo/Inomhusmiljo/Projektet-Halsomassigt-hallbara-hus/

84 Engvall, K.; Corner, R.; Emenius, G.; Hult, M. (2009).
"Upplevd inomhusmiljö och hälsa i Stockholms flerbostadshus".
Rapport 1, 3H-projektet,
http://www.stockholm.se/ByggBo/Inomhusmiljo/Projektet-Halsomassigt-hallbara-hus/

85 Engvall, K.; Norrby, C.; Bandel, J.; Hult, M.; Norback, D. (2000). Development of a multiple regression model to identify multi-family residential buildings with a high prevalence of sick building syndrome (SBS). *Indoor Air,* 10: 101-110.

86 Burge, P.S. (2004). Sick building syndrome. *Occup Environ Med,* 61: 185-190.

87 Redlich, C.A.; Sparer, J.; Cullen, M.R. (1997). Sick-building syndrome. *Lancet,* 349: 1013-1016.

88 Butte, W.; Hoffmann, W.; Hostrup, O.; Schmidt, A.; Walker, G. (2001). Endocrine disrupting chemicals in house dust: results of a representative monitoring. *Gefahrstoffe - Reinhalt. Luft,* 61: 19-23.

89 Becker, K.; Seiwert, M.; Kaus, S.; Krause, C.; Schultz, C.; Seifert, B. **(2002).** German Environmental Survey 1998 (GerES III): pestecides and other pollutants in house dust. H. Levin. (Ed.), Proceedings of the 9th International Conferens on Indoor Air Quality and Climate, *Indoor Air,* Montrey, Carlifornia, Santa Cruz, CA, *Vol.4,* 883-887.

90 Langer, S.; Weschler, C.J.; Fischer, A.; Bekoe, G.; Toftum, J.; Clausen, G. (2010). Phthalate and PAH concentrations in dust collected from Danish homes and daycare centers. *Atmos. Environ.,* 44: 2294-2301.

91 Weschler, C.J. (1980). Characterization of Selected Organics in Size-Fractionated Indoor Aerosols. *Environ. Sci. Technol.,* 14: 428-431.

92 Marklund, A.; Andersson, B.; Haglund, P. (2003). The distribution of organophosphorus compounds in various indoor environments. *Organohalogen Compd.,* 62: 367-370.

93 Wormuth, M.; Scheringer, M.; Vollenweider, M.; Hungerbuhler, K. (2006). What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? *Risk Anal,* 26: 803-824.

94 Ingerowski, G.; Friedle, A.; Thumulla, J. (2001). Chlorinated ethyl and isopropyl phosphoric acid triesters in the indoor environment - an inter-laboratory exposure study. *Indoor Air,* 11: 145-149.

95 U.S. EPA. (2009). Exposure Factors Handbook 2009 Update (External review draft). EPA/600/R-09/052A, U.S. Environmental Protection Agency, Washington D.C.

96 Harrad, S.; Hazrati, S.; Ibarra, C. (2006). Concentrations of Polychlorinated Biphenyls in Indoor Air and Polybrominated Diphenyl Ethers in Indoor Air and Dust in Birmingham, United

Kingdom: Implications for Human Exposure. *Environ. Sci. Technol.,* 40: 4633-4638.

97 U.S. EPA. (1999). Integrateted Risk Information System (IRIS) on Di(2-ethylhexyl)phthalate. U.S. Environmental Protection Agency, National Center for Environmental Assessment, Office of Research and Development, Washington D.C.

98 CSTEE (1998). Opinion on phthalate migration from soft PVC toys and child care articles - opinion expressed at the 6th CSTEE plenary meeting, Brussels 26/27 November 1998. Scientific Comittee for Toxicity, Ecotoxicity, and the Environment, http://ec.europa.eu/health/scientific_committees/environmental_risks/opinions/sctee/sct_out19_en.htm

99 Kortenkamp, A. (2008). Low dose mixture effects of endocrine disrupters: implications for risk assessment and epidemiology. *Int. J. Androl.,* 31: 233-240.

100 Kortenkamp, A.; Backhaus, T.; Faust, M. (2009). State of the Art Report on Mixture Toxicity. Study contract No. 070307/2007/485103/ETU/D.1, Project on mixture toxicology and ecotoxicology commissioned by the European Commission, http://ec.europa.eu/environment/chemicals/pdf/report_Mixture%20toxicity.pdf

101 Nagorka, R.; Conrad, A.; Scheller, C.; Suessenbach, B.; Moriske, H. (2011). Diisononyl 1,2-cyclohexanedicarboxylic acid (DINCH) and Di(2-ethylhexyl) terephthalate (DEHT) in indoor dust samples: Concentration and analytical problems. *Int. J. Hyg. Environ. Health,* 214: 26-35.