Simultaneous determination of legacy and emerging organophosphorus flame retardants and plasticizers in indoor dust using liquid and gas chromatography–tandem mass spectrometry : method development, validation, and application

Simultaneous determination of legacy and emerging organophosphorus flame retardants and plasticizers in indoor dust using liquid and gas chromatography-tandem mass spectrometry: Method development, validation and application

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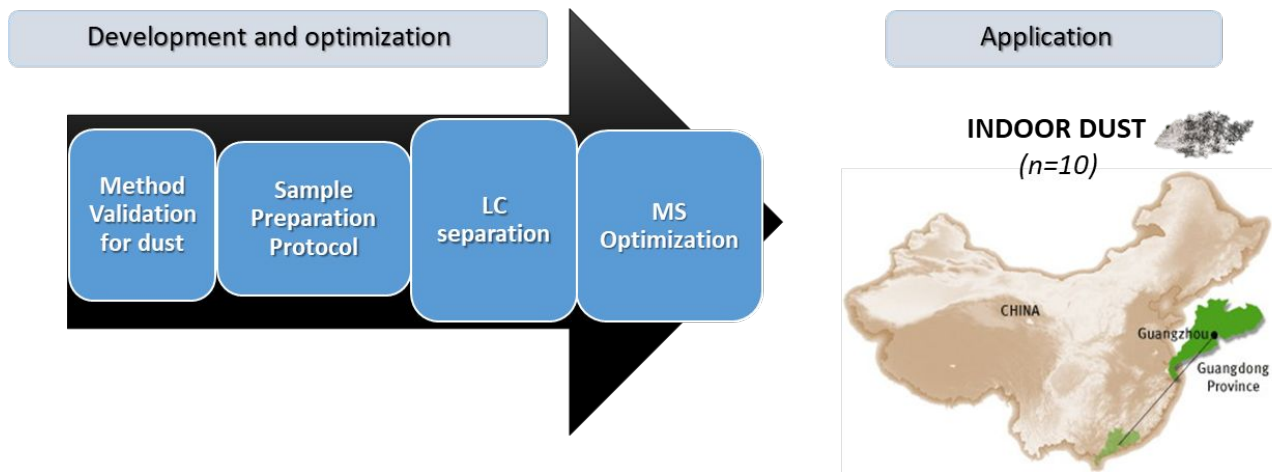a- Toxicological Center, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk Antwerp, Belgium.

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Development and optimization

| Method Validation for dust | Sample Preparation Protocol | LC separation | MS Optimization |

Application

INDOOR DUST
(n=10)

CHINA

Guangzhou

Guangdong Province

Graphical Abstract

2

21 **Abstract**

22 In the present study, an analytical method has been developed and validated for the simultaneous detection and
23 quantification of 19 PFRs (14 legacy organophosphorus flame retardants (PFRs) and 5 emerging PFRs (ePFRs)) and
24 20 plasticizers (7 legacy plasticizers (LPs) and 13 alternative plasticizers (APs)). Sample preparation was based on
25 the combination of previously validated analytical protocols including ultrasonic extraction and Florisil
26 fractionation/clean-up. The analysis was performed by using liquid chromatography tandem mass spectrometry (LC-
27 MS/MS) for all targeted compounds, except for bis (2-ethylhexyl) phthalate (DEHP) and bis (2-ethylhexyl)
28 terephthalate (DEHT), for which the separation of the isomers resulted more favorable gas chromatography electron
29 ionization mass spectrometry (GC-EI-MS). The new method was in-house validated by applying two levels of
30 fortification in dust. The achieved linearity (R^2) ranged between 0.993 and 0.999. Limits of detection and
31 quantification (LODs and LOQs) ranged between 1 and 265 ng/g and between 1 and 870 ng/g for all analytes, except
32 for DEHP and DEHT, for which relatively higher LODs (665 and 1100 ng/g, respectively) and LOQs (2100 and
33 3500 ng/g, respectively) were observed. Accuracy ranged between 75 and 125% for most of the targeted analytes
34 and repeatability was good with relative standard deviation (RSD) <15% for most compounds. Finally, the method
35 was applied for the determination and quantification of the targeted chemicals in house dust samples (n=10) from
36 the megacity of Guangzhou (China). Median values ranged from 3 to 210 ng/g for PFRs, 4 to 165 ng/g for ePFRs,
37 30 to 100,000 ng/g for LPs and 6 to 34,000 ng/g for APs. Main contributors to the total contamination were LPs 63
38 % and APs 37 % in total plasticizers, whereas PFRs and ePFRs contributed 90% and 10% in total flame retardants.

39

40 **Keywords:** simultaneous determination, organophosphorus flame retardants, plasticizers, indoor dust, liquid
41 chromatography, tandem mass spectrometry

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1. Introduction

Recently, the quality of indoor environment has been acknowledged as a hot issue due to the time humans spend indoors, leading to a fast increase to the number of research studies focused on this topic [1,2]. Indoor dust is a contributor to indoor pollution as it acts as a repository material for different groups of compounds, including semi volatile organic compounds (SVOCs) [3,4]. Humans, and especially sensitive groups such as children, are exposed to these compounds via inhalation, accidental ingestion of dust and dermal absorption [3,5]. Since there are strong indications of adverse health effects due to the human exposure to SVOCs, the importance of monitoring indoor dust contamination has been highlighted [6,7].

Major groups of SVOCs are flame retardants and plasticizers and their presence in indoor dust is constant [3,8]. Organophosphorus flame retardants (PFRs) legacy and emerging (ePFRs), are chemical compounds that have been incorporated to products such as furniture foams, textiles, construction materials, different kind of electronic devices, etc. to reduce the risk of fire [9]. They are major replacements for certain brominated flame retardants (BFRs), such as polybrominated diphenyl ethers (PBDEs), after bans and restrictions of the latter [10]. They are not chemically bonded to the materials and they can easily be released from products into the indoor environment, accumulating in dust and contributing to human exposure. Recent human bio-motoring studies linked the intake of contaminants to the adverse health effects (allergies, neuro- and reproductive toxicity, potential human carcinogenicity etc.) [11-14].

Plasticizers are a category of compounds applied as additives into polymers to provide special features of durability, elasticity and flexibility to the products [13,14]. Phthalic esters, referred in the present study as legacy phthalates (LPs), are a major group of plasticizers. Their replacements are alternative plasticizers (APs) that have been introduced lately into the market due to suspected adverse effects of LPs to human and direct links to asthma events in children [15,16]. Similarly to PFRs, plasticizers can easily be transferred from the consumer products to the indoor environment [17].

Consequently, there is a need to develop appropriate analytical methods that will allow a rapid, simultaneous, sensitive and selective determination and quantification of these compounds in dust, combined with a low cost and time consumption. Therefore, the present study aims at the simultaneous analysis of flame retardants and plasticizers, two major groups of indoor contaminants in dust. Several studies have already reported on the analysis of these compounds separately using gas chromatography (GC) coupled to MS or liquid chromatography (LC) coupled to MS/MS [18-22]. Specifically, ePFRs are suitable only to be analyzed using LC method and TBOEP showed also ambiguous analytical behavior during GC-MS analysis [21]. Recently study has reported the simultaneously analysis of PFR and ePFRs using LC-MS/MS [23-28]However, to the best of our knowledge, this is the first attempt to combine flame retardants (i.e. PFRs and ePFRs) and plasticizers (i.e. LPs and APs) in a single method, by applying a single sample treatment protocol and using LC-MS/MS for the analysis. The aims of our study were (i) to develop and validate a method for the simultaneous quantification of the targeted analytes by LC-MS/MS, and (ii) to test its applicability to the analysis of PFRs and plasticizers in household dust (n=10) sampled in Guangzhou, China.

78

2. Materials & Methods

79

80 2.1 Chemicals & Reagents

81 Labelled triphenyl phosphate (TPHP-d15), tris(1,3-dichloro-2-propyl)phosphate (TDCIPP-d15), tris(2-
82 butoxyethyl) phosphate (TBOEP-d$_6$) and tris(2-chloroethyl) phosphate (TCEP-d$_{12}$) with isotopic purity of 98%
83 (custom synthesized) were purchased from Dr. Vladimir Belov, Max Planck Institute for Biophysical Chemistry,
84 Göttingen, Germany. Labelled dibenzyl phthalate (DBzP-d$_4$) was purchased from Accustandard (New Heaven, CT,
85 USA), labelled bis (2-ethylhexyl) phthalate (DEHP-d$_4$) and labelled di-N-butyl phthalate (DNBP-d$_4$) were purchased
86 from Sigma Aldrich (St. Louis, MO, USA) and were used as ISs for LPs and APs analysis. Triamyl phosphate (TAP)
87 was used as recovery standard (RS) and was purchased from TCI Europe (Zwijndrecht, Belgium). Standards of
88 TIBP, TNBP, TDCIPP, TCIPP, TEHP, TCEP, TOTP, TPTP, TMTP, EHDPHP, TEP, TPHP, TBOEP, TBuPHP
89 were purchased from Chiron AS (Trondheim, Norway). Standards of TDBPP, V6, RDP, BDP, iDPPHP, DMP, DEP,
90 DNBP, DIBP, BBP, DEHP, DPP, DBA, ATEC, DBS, ATBC, DEHA, DCPC, BTHC, DEHT, THTM, TOTM,
91 DINCH, DINP and DIDP were purchased from Accustandard (New Heaven, CT, USA). Indoor dust standard
92 reference material SRM 2585 was purchased from the US National Institute of Standards and Technology (NIST,
93 Gaithersburg, MD, USA). Florisil® ENVI (500 mg, 3 mL) cartridges were purchased from Supelco (Bellefonte, PA,
94 USA). Centrifugal filters (modified nylon membrane) of 0.45 μm were purchased from VWR^{TM} (North America).
95 All solvents were chromatography grade. n-Hexane (n-Hex) was purchased from Acros Organics (Belgium), ethyl
96 acetate (EtAc), dichloromethane (DCM), acetone, toluene were purchased from Merck (Germany), and methanol
97 (MeOH) was purchased from Fischer Scientific (United Kingdom). Detailed information regarding the analytes is
98 provided in Table S1.

99 2.2 Sample Collection

100 Two house dust samples, one collected from USA (New England, 2015) and the other from an e-waste recycling
101 site, South China in August 2017, were chosen as representative samples for the method development and validation
102 [19]. Once validated, the method was used for the determination and quantification of 10 indoor dust samples
103 collected from the interior of 10 homes in city of Guangzhou (China) between July and September 2017. Dust
104 sampling was conducted using clean brushes onto bare floors of the living rooms, according to a protocol previously
105 described [7,21]. The brushes were thoroughly pre-cleaned with ethanol between each sampling in order to eliminate
106 the possibility of cross contamination. After collection, the samples were stored in aluminum foil, sealed in zip-lock
107 plastic bags and transported to the lab. They were stored at -20°C pending analysis and then sieved (500 μm) in
108 room temperature prior to extraction.

109 2.3 Extraction & Clean-up

110 For all targeted analytes, the applied analytical method was based on a combination of previously published
111 protocols [22,23]. Dust aliquots of 20 mg were weighted in pre-cleaned glass tubes (solvent washed and dried at 400

112 °C oven) and spiked with TCEP-d_{12}, TDCIPP-d_{15}, TPhP-d_{15}, TBOEP-d_6 (each at 100 ng), and DBzP-d_4, DEHP-d_4

113 and DNBP-d_4 (each at 500 ng). Samples were extracted using 2.5 mL of *n*-Hex/acetone mixture (3:1 *v/v*) and 0.5

114 mL toluene by a combination of vortexing (1 min) and ultrasonication (5 min) repeated for two cycles by adding

115 fresh solvents. Extracts were centrifuged for 3 minutes at 3000 rpm. Supernatants were pooled into pre-clean glass

116 tubes and evaporated to near dryness under a gentle nitrogen stream. They were redissolved in 1 mL   of *n*-

117 Hex/toluene (1:1 *v/v*) and vortexed (1 min). Florisil® ENVI cartridges (500 mg, 3 mL) were washed with 4 mL

118 acetone, 6 mL EtAc and 6 mL n-Hex. The extracts were quantitatively transferred onto the cartridges and

119 fractionation was achieved by eluting the first fraction (F1) with 12 mL *n*-hexane/DCM (4:1, *v/v*) and the second

120 fraction (F2) with 10 mL EtAc. F1 was discarded and F2, containing the targeted compounds, was evaporated till 4

121 mL under a gentle nitrogen stream. Then, elution with 8 mL acetone was followed-up for extracting V6 from the

122 Florisil cartridges. F2 was evaporated near dryness under a gentle nitrogen stream. After evaporation, the extract of

123 F2 was dissolved in 50 µL of MeOH and 50 µL of RS and vortexed (30 s). A volume of 15 µL of the final aliquot

124 was transferred to an amber injection vial with the addition of 135 µL of EtAc for the separation and quantitative

125 analysis of DEHP and DEHT by GC-EI-MS. The rest of the aliquot was filtered in 0.45 µm centrifugal filters (9000

126 rpm, 3 min), previously tested for their suitability, and transferred to a vial for LC-MS/MS analysis.

127 2.4 Instrumental analysis

128 *LC-MS/MS analysis*

129 Agilent 1200 Infinity liquid chromatography (LC) system (Agilent Technologies, Santa Clara, CA, USA) coupled

130 to an Agilent 6410 Triple Quadrupole mass spectrometer (MS) was used. The mobile phases were A; ultrapure water

131 5mM ammonium formate, B; MeOH 5 mM ammonium formate. The gradient of separation was 30%−70% B in 5

132 min, 70%−100% B in 20 min, hold for 5 min and returning to the initial conditions from 25.10 min until 35 min.

133 The total duration of each injection was 35 min and the flow rate 0.25 mL/min. Kinetex Biphenyl column (100 ×

134 2.1 mm, 2.6 µm) was used at 40 °C working temperature. Source parameters were set as; gas temperature at 350 °C,

135 gas flow at 10 mL/min, nebulizer gas at 40 psi, and capillary voltage at 4000 V. Positive electrospray ionization was

136 applied for all target analytes. The Agilent Mass Hunter software B.06.00 was used for the data analysis. Detailed

137 chromatographic information is reported in Table S1.

138 *GC-EI-MS analysis*

139 DEHP and DEHT were analyzed using Agilent GC coupled to an Agilent 5973 MS operated in electron ionization

140 mode (EI). A GC HT-8 column (25 m × 0.22 mm, 0.25 µm), electronic pressure control and a programmable-

141 temperature vaporizer (PTV) inlet were used. The injection temperature was 90 °C, hold time 0.04 min, ramped at

142 700 °C/min to 300 °C, hold time 25 min. Injection volume was 1 µL and was performed under a pressure of 14.36

143 psi until 1.25 min and purge flow to split vent of 50 mL/min after 1.25 min, ramped at 30 °C/min to 250 °C, hold

144 time 1.5 min, ramped at 10 °C/min to 310 °C, hold time 7 min. Carrier gas was Helium with a flow rate of 1.0

145 mL/min until 28 min, and then increased to 1.5 mL/min. The mass spectrometer was run in selected ion monitoring

146 (SIM) mode with 2 characteristic ions acquired for each analyte and for the IS DEHP-d$_4$ (details are reported in

147 Table S1).

148 2.5 Uncertainty

149 The uncertainty (U) of the method was calculated based the measurements during the method validation. The applied

150 equations were derived from Poma et al. [22] and were the following (Eq. (1)) :

151 $\quad$ U= $Uc\,x\,k$ $\qquad\qquad\qquad\qquad$ (1)

152 where u$_c$ is the combined standard uncertainty and k is the coverage factor equal to 2 for level of confidence 95%.

153 The combined uncertainty U$_c$, is the combination of all the contributing uncertainties and in this study were involving

154 accuracy and repeatability (Eq. (2)):

155 $\quad$ U$_c$= $\sqrt{U_r{}^2 + U_t{}^2}$ $\qquad\qquad\qquad$ (2)

156 Where u$_r$ is the uncertainty of the repeatability and expressed as the standard deviation of the measurements and ut

157 is the uncertainty of accuracy. In cases that SRM is used, the u$_t$ is calculated using (Eq. (3)) as:

158 $\sqrt{(S_t{}^2/n_t) + U_{SRM}{}^2}$ $\qquad\qquad\qquad$ (3)

159 Where S$_t$ is the standard deviation of the analyzed replicates, n$_t$ the square root of the number of the analyzed

160 replicates, and the USRM the uncertainty of SRM analysis.

161

3. Results and discussion

163 3.1 Method development

164 Standards of individual native compounds were used to set optimal values of multiple reaction monitoring (MRM)

165 , SIM m/z, quantitative and qualitative ions/transitions with the corresponding collision energy and fragmentor

166 voltage (Table S1). The source parameters of gas temperature, gas flow, nebulizer and capillary voltage were also

167 optimized pursuing the maximum response per each compound. For the optimization of the chromatographic

168 separation, different mobile phases were tested such as MeOH, acetonitrile and water with ammonium formate.

169 Various analytical columns were also tested, such as Kinetex Biphenyl (100 × 2.1 mm, 2.6 μm), Luna C18 (150 ×

170 2mm, 3 μm) and Alltima HP C18 (100 × 2.1mm, 3 μm) at temperatures of 25 °C and 40 °C. The most efficient

171 separation was obtained using MeOH 5 mM ammonium formate (B) and H$_2$O 5 mM ammonium formate (A) and

172 the best gradient in terms of separation and time duration was applied (Table S2). The optimal column was Kinetex

173 Biphenyl (100 × 2.1 mm, 2.6 μm) at 40 °C, generating a higher signal for each analyte. The separation of the isomers

174 DEHP and DEHT was not achieved by LC-MS/MS and the sample preparation protocol was adapted accordingly

175 in order to inject a sub-aliquot into GC-EI-MS for further analysis (Figure 1). Figure 2 shows chromatograms of the

176 targeted analyte standard mix in LC-MS/MS and GC-EI-MS.

177 Six various protocols were tested for sample treatment. The parameters of extraction and elution solvent were

178 optimized based on different proportions in mixes *n*-Hex/Acetone and *n*-Hex/DCM respectively. Procedural blanks

179 and dust samples were spiked with the internal standards (IS), DBzP-d_4 for LPs and APs, and a mixture of TCEP-

180 d_{12}, TDCIPP-d_{15}, TPHP-d_{15}, and TBOEP-d_6 for PFRs and ePFRs. The purpose was to test the maximum extraction

181 efficiency, combined with removal of interferences by discarding F1 (Table S3). The optimal sample protocol is

182 described in section *2.3* and the selection was based on best IS recoveries (%) and lowest RSDs of the tested

183 protocols. (Figure S1).

184 3.2 Method in-house validation

185 *Linearity*

186 Four calibration curves were prepared for the targeted analytes based on standard mixtures division; PFRs/ePFRs

187 standard mix (TCEP, TEHP, TBOEP, TPHP, EHDPHP, TCIPP, TDCIPP, TIBP, TNBP, TOTP, TPTP, TMTP, TEP,

188 TBuPHP, V6, iDDPHP, BDP, RDP, TDBPP), LPs standard mix (DMP, DEP, DNBP, DIBP, BBP, DPP) and APs

189 standard mix (DIBA, ATEC, DBS, ATBC, DEHA, DCPC, BTHC, THTM, TOTM). A separate standard mix of

190 DIDP, DINP, DINCH was created due to the special chromatographic behavior of these compounds (broader peaks)

191 (Figure S2) and a standard mix of DEHP and DEHT for use in GC-EI-MS. The ranges of the calibration curves were

192 adapted accordingly to the expected concentration in dust sample (Table 1). Calibration curves were formed by

193 plotting the area ratio analyte divided by IS against the concentration ratio of each analyte to the corresponding IS.

194 Calibration curves were best fitted to a quadratic model for all mixtures, except for PFRs/ePFRs for which the best

195 model was linear. The linearity was estimated by the R^2. All targeted analytes showed a good correlation within the

196 tested intervals with coefficients of determination higher or equal to 0.993 (Table 1).

197 *Limits of detection-quantification (LOD-LOQ)*

198 Three procedural blanks were analyzed for the LOQ estimation (Table 1). LODs were estimated from the lowest

199 calibration point, giving a signal/noise ratio of 3 (S/N=3). When the targeted analyte concentrations in the blanks

200 were negligible, LOQs were calculated by the instrument performance (S/N=10). In this case, the lowest calibration

201 point was used as LOQ. For the analytes detected in the blanks, the LOQs were based on the standard deviation of

202 the blanks, and a value equal to 3*SD of the blank concentration was used as a cut-off value. Determined LOQ range

203 was 4−98 ng/g for PFRs, 4.5−59 ng/g for ePFRs, 24−873 ng/g for LPs except for DEHP, for which it was 2,190

204 ng/g, and 15−764 ng/g for APs except for DEHT, for which it was 3,600 ng/g (Table 1). The expected relatively

205 higher LOQs for DEHP and DEHT was most probably due to the lower instrumental sensitivity for these compounds

206 (GC-EI-MS) and their ubiquitous presence in the procedural blanks.

207 *Accuracy*

208 The certified reference material SRM 2585 was analyzed in triplicate to evaluate the accuracy of our method for the

209 quantification of the targeted PFRs. This SRM has indicative values for certain PFRs, but LPs and APs have been

210 analyzed and reported by other studies in the literature [25, 20,26] (Table S5). Due to the lack of information for the

211 rest of the compounds, a real dust sample collected from an e-waste recycling site (South China) was used after

8

212 fortification (test-sample). This sample was divided in 9 aliquots; three of them were spiked with low level mass

213 (LL) with the targeted analytes, three with high level (HL) mass and three non-spiked were used as controls. Three

214 solvent blanks were included to control the laboratory background contamination. Eventually, the measured

215 concentrations in solvent blanks and controls were subtracted from the concentrations of the spiked replicates.

216 Accuracy was calculated and reported per each analyte in Table 1, ranging from 70 to 140% for all compounds

217 except for TPHP (61%), TEP (33%), iDDPHP (52%), TDBPP (48%), DMP (59%), and THTM (143%) (Figures S3

218 and S4).

219 *Intra-day repeatability*

220 The intra-day repeatability was calculated as the relative standard deviation (RSD) of three replicate analyses within

221 one day and under repeatable conditions. Three aliquots of the same dust sample (test-sample) and three solvent

222 blanks were spiked with HL and LL mass of the targeted analytes and used for the validation. RSD for LL mass was

223 <15% in 92% of the total analytes and 90% for the HL. RSD values were 21% and 24% for TEP and BDP in LL

224 mass and 23%, 22%, 49%, and 22% for TIBP, TEP, DMP, and TOTM in HL mass.

225 *Method uncertainty*

226 The expanded uncertainty, U, was calculated for all the targeted analytes and the mean expanded uncertainty (U_{mean})

227 of the two levels of fortification was reported (Table 1). The U*mean* values were range between 4 and 40% for PFRs,

228 6 and 114% for ePFRs, 6 and 14 % for LPs and 5 and 34% for APs. For the GC analyzed compounds DEHP and

229 DEHT, the U_{mean} was 16% and 28%, respectively.

230 3.3 Method applicability

231 The validated analytical method was applied for the quantification of the targeted compounds in 10 indoor household

232 dust samples collected from Guangzhou (South China). The quality assurance and quality control were performed

233 by analyzing SRM 2585 for the targeted compounds, estimating the recoveries of ISs and analyzing 3 procedural

234 blank samples in the same batch. Mean recoveries for the ISs were $86 \pm 14\%$ (TCEP-d_{12}), $86 \pm 13\%$ (TDCIPP-d_{15}),

235 $94 \pm 11\%$ (TPhP-d_{15}), $106 \pm 9\%$ (TBOEP-d_6), $98 \pm 10\%$ (DBzP-d_4), $90 \pm 31\%$ (DNBP-d_4), and $89 \pm 20\%$ (DEHP-

236 d_4). Concentration values below the LOQs were treated as LOQ*f during descriptive statistics, where f is the

237 detection frequency of the compound above the LOQ in the samples [25]. For the analyzed dust samples, 26 out of

238 39 target analytes were found in concentrations above LOQ (Table S4), while DEP, DPP, DIBA, DBS, TEP, TOTP,

239 TMTP, iDDPHP, and TDBPP were not detected in any sample.

240 Table 2 reports the descriptive statistics related to 10 dust samples from Guangzhou, and Table S4 and Figure S6

241 present the concentration levels and contribution patterns of target analytes detected in samples. DEHP (48%), DINP

242 (18%), DIDP (13%), DNBP (12%) were the main contributors in dust samples, whereas the rest of the compounds

243 much lower (5%) (Figure 3).

244 Among the 14 PFRs tested, 10 compounds were detected in the indoor dust samples from Guangzhou (Table 2),

245 and the mean concentrations of each compound was in the range between 6.4 ng/g (TNBP) and 797 ng/g (TCIPP),

246 which were lower than those recently reported in indoor home dust from other locations such as Belgium, Canada,

247 China, Japan and USA [27-31]. Among the 10 detected PFRs, TCIPP (31.9 ± 11.7%) was found as the most abundant

248 compound, followed by TCEP (17.2 ± 9.4%), and TEHP (14.1 ± 8.0%) (Figure S5). Additionally, three ePFRs (i.e.

249 V6, RDP and BDP) were also frequently detected (detection frequency = 40−80%) in the indoor dust samples from

250 Guangzhou, with mean concentrations as 31, 23 and 142 ng/g for V6, RDP and BDP, respectively (Table 2). BDP

251 dominated over the other two ePFRs in these dust samples (Figure S5), whereas its concentrations were generally

252 1−2 orders of magnitude lower than those in previously study [28].

253 DEHP (78.0 ± 13.1%) for LPs, and DINP (53.6 ± 17.6%) for APs were the dominant plasticizers found in the dust

254 samples (Figure S5); with determined mean concentrations ranged from 32 ng/g (DMP) to 100,112 ng/g (DEHP)

255 for LPs, and from 43 ng/g (CDPHP) to 36,460 ng/g (DINP) for APs, respectively (Table 2). The concentrations for

256 plasticizers (LPs and APs) found in this study were lower than those in home dust from Belgium, Netherland and

257 Ireland [22].

258 The contribution of the main groups was estimated based on means of sum i) only among plasticizers, ii) only among

259 PFRs and iii) for the total presence (Figure 3). LPs were the dominant group of plasticizers contributing   63% in

260 dust, followed by APs at 37% whereas for the flame retardants, contribution of PFRs and ePFRs was 90% and 10%

261 respectively. One possible explanation for the extremely low percentage of PFRs could be the basic level of indoor

262 equipment in the sampled homes lacking of commodities that usually contain PFRs. Figure 4 represents the

263 contribution per individual analyte in the two groups of compounds. For plasticizers, dominant compounds were

264 DEHP (49%), followed by DINP (18%) > DIDP (13%) > DNBP (12%), whereas the rest of the compounds were

265 found in percentages less than 10%. On the other hand, PFRs were more equally distributed, with main co main

266 contributors to be TCIPP (23%)> TCEP = BDP (14%) > EHDPHP (11%) > TEHP (10%) and the rest of the

267 compounds less than 10%. These results suggest that the concentrations of PFRs/ePFRs in indoor dust tend to be

268 lower than the concentrations of plasticizers. Similar results were found in previous studies where the measured

269 plasticizers were more abundant than PFRs and typically showed ten-fold higher total concentrations [13, 25].

270 Statistical correlations between concentration levels and indoor equipment (furniture and electronics), were not

271 applicable due to the low sample size and the eliminated indoor equipment, and further study is needed for a

272 comprehensive evaluation the human exposure of these chemicals in indoor environments.

273 **4. Conclusions**

274 A reliable analytical method was developed for the simultaneous analysis and quantification of 39 PFRs, ePFRs,

275 LPs and APs in indoor dust. LC-MS/MS was used for the quantification of all targeted analytes except for DEHP

276 and DEHT for which GC-EI-MS proved more suitable. The application of liquid chromatography enhanced the

277 sensitivity of the analysis and solved certain analytical problems (e.g. ambiguous analytical behavior of TBOEP

278 during GC-EI-MS analysis). Method validation proved that accuracy, repeatability, LODs and LOQs were in the

279 acceptable range for most analytes. The application of the method to indoor dust samples confirmed the feasibility

280 and robustness of the method. The results based on these 10 samples showed that DEHP, DINP, DIDP and DNBP

281 were the dominant compounds in indoor dust.

Acknowledgements

Conflict of interest

This study did not involve any financial or other relationship that could cause a conflict of interest nor human subjects.

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380

381 **Table 1.** Parameters of the *in-house* method validation.

Target analyte	Linearity R²	Calibration curve interval (ng)	LOD (ng/g)	LOQ (ng/g)	Accuracy %	LL spiking (*n=3*)			HL spiking (*n=3*)			U_mean
						spiked mass (ng)	SD (ng)	RSD %	spiked mass (ng)	SD (ng)	RSD %	%
PFRs[1]												
TCEP	0.999		2.4	8	95*	20	1	4	75	1	2	28
TEHP	0.993		1.2	4	127	20	0.4	1	75	2	3	40
TBOEP	0.999		9.7	32	93	20	0.2	1	75	1	2	4
TPHP	0.999		30	98	61*	20	2	2	75	2	1	26
EHDPHP	0.999		15	50	71	20	0.3	2	75	1	2	11
TCIPP	0.999		16	54	112*	20	2	5	75	3	4	34
TDCIPP	0.999	0.05-80	14	45	97	20			75	2	2	5
TIBP	0.999		8.8	29	76	20	0.2	1	75	12	23	39
TNBP	0.997		6.7	22	124*	20	1	5	75	4	5	13
TOTP	0.999		1.5	5	131	20	0.3	1	75	4	4	12
TPTP	0.999		1.5	5	131	20	1	3	75	4	4	12
TMTP	0.999		1.5	5	131	20	1	3	75	4	4	12
TEP	0.999		22	71	33	20	3	21	75	3	22	39
TBuPHP	0.995		1.4	4.5	140	20	1	3	75	2	2	4
ePFRs												
V6	0.999		1.4	4.5	91	20	0.4	2	75	3	4	15
iDDPHP	0.998		18	59	52	20	1	6	75	2	6	27
RDP	0.998	0.05-80	3.9	13	108	20	2	7	75	3	4	6
BDP	0.999		10	32	137	20	10	24	75	5	5	20
TDBPP	0.998		1.4	4.5	48	20	0.4	3	75	1	2	114
LPs												
DMP	0.999		7.3	24	59	375	25	9	1000	199	49	14
DEP	0.999		123	407	73	375	14	4	1000	95	15	8
DNBP	0.999	2-1500	265	873	118	375	19	3	1000	24	2	6
DIBP	0.999		171	565	118	375	19	3	1000	24	2	6
BBP	0.998		19	63	74	375	12	4	1000	49	7	9
DPP	0.999		0.3	1	97	375	24	7	1000	91	10	9
APs												
DIBA	0.996		4.2	14	107	375	18	5	1000	99	9	29
ATEC	0.997		1.2	4	116	375	18	4	1000	46	4	22
DBS	0.996		118	388	109	375	12	3	1000	88	7	9
ATBC	0.997		73	241	140	375	26	5	1000	23	1	20
DEHA	0.997	2-1500	122	403	115	375	12	3	1000	32	3	5
DCPC	0.997		4.5	15	103	375	40	11	1000	21	2	34
BTHC	0.998		10	34	119	375	19	4	1000	38	3	13
THTM	0.998		3.9	13	143	375	27	5	1000	47	3	26
TOTM	0.998		52	170	118	375	91	16	1000	324	22	17
DINCH[1]	0.998		149	493	112	975	37	3	2600	299	8	28
DINP[1]	0.998	25-3900	232	764	90	975	35	2	2600	48	1	7
DIDP[1]	0.999		101	334	114	975	67	4	2600	95	3	34
DEHP[2]	0.998	2-1500	664	2190	118	375	97	8	1000	50	3	16
DEHT[2]	0.998		1108	3657	84	375	5	2	1000	49	5	28

382 LL; low level of spiking, HL; high level of spiking; *Values estimated using SRM 2585
383 [1]compounds with particular chromatographic behavior (wider peaks) were treated separately
384 [2]compounds analyzed in GC-EI-MS.

385

386   **Table 2.** Descriptive statistics for 10 household dust samples from Guangzhou, China (ng/g).

| Targeted Analyte	Mean	Median	Min	Max	SD	Detection Frequency %
PFRs						
TCEP	493	96	22	3809	1168	100
TEHP	181	86	41	850	243	100
TBOEP	19	10	10	47	15	30
TPHP	75	29	29	187	73	30
EHDPHP	204	104	45	953	272	90
TCIPP	797	211	124	6137	1877	100
TDCIPP	67	56	27	165	52	60
TIBP	9.0	2.9	2.9	64	19	10
TNBP	6.4	4.4	4.4	25	6	20
TPTP	62	61	12	119	29	100
ePFRs						
V6	31	4.4	2.5	160	55	40
RDP	24	22	10	52	12	80
BDP	142	164	56	210	53	100
LPs						
DMP	32	28	12	65	22	50
DNBP	24594	23818	7621	44960	11239	100
DIBP	4200	4067	1498	6861	1912	100
BBP	132	82	50	617	171	80
DEHP	100112	99944	42117	167125	40487	100
APs						
ATBC	3291	2696	1460	9315	2352	100
DEHA	380	161	161	794	285	40
CDPHP	43	6	6	288	88	40
DEHT	4282	105	105	30352	9484	30
TOTM	2360	2230	607	4044	1277	100
DINCH	2824	2941	1149	6024	1370	100
DINP	36460	33893	10934	83881	20978	100
DIDP	26727	23526	1440	60932	23857	100

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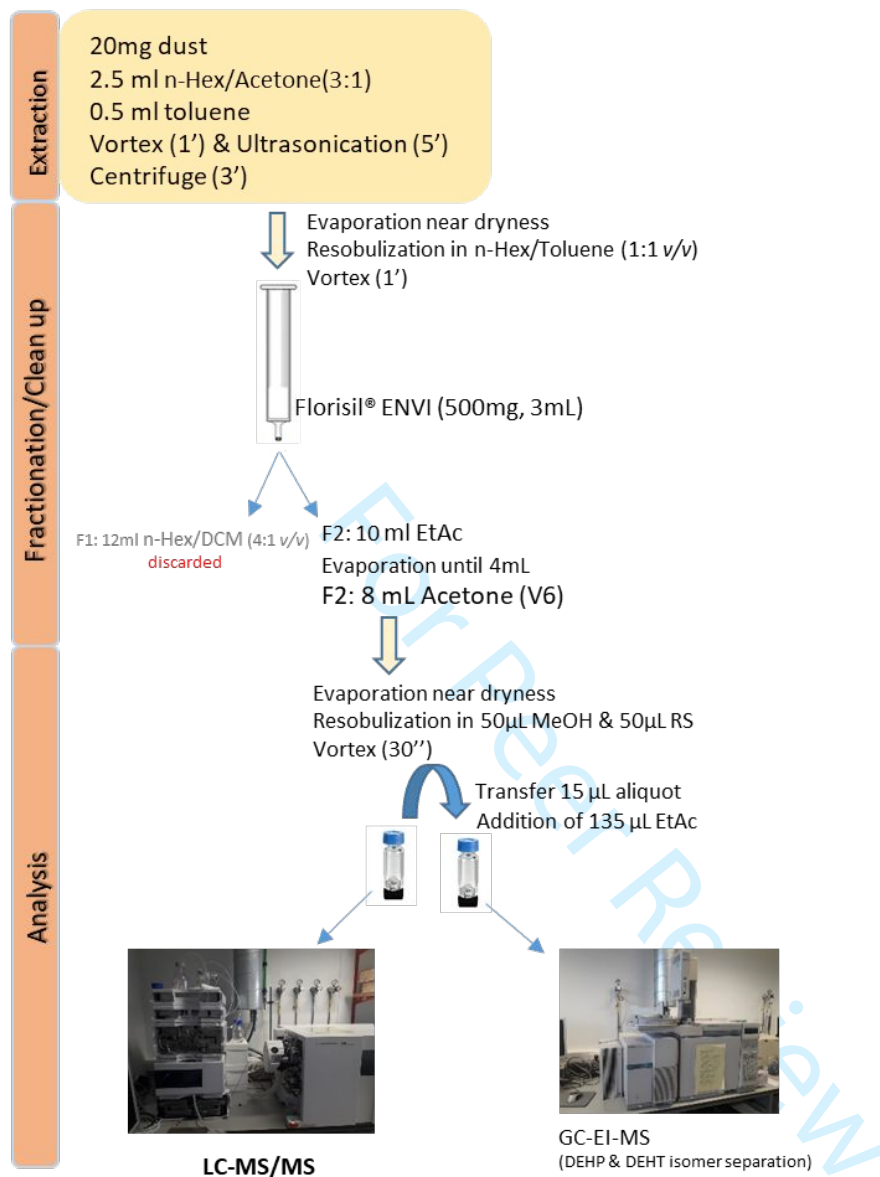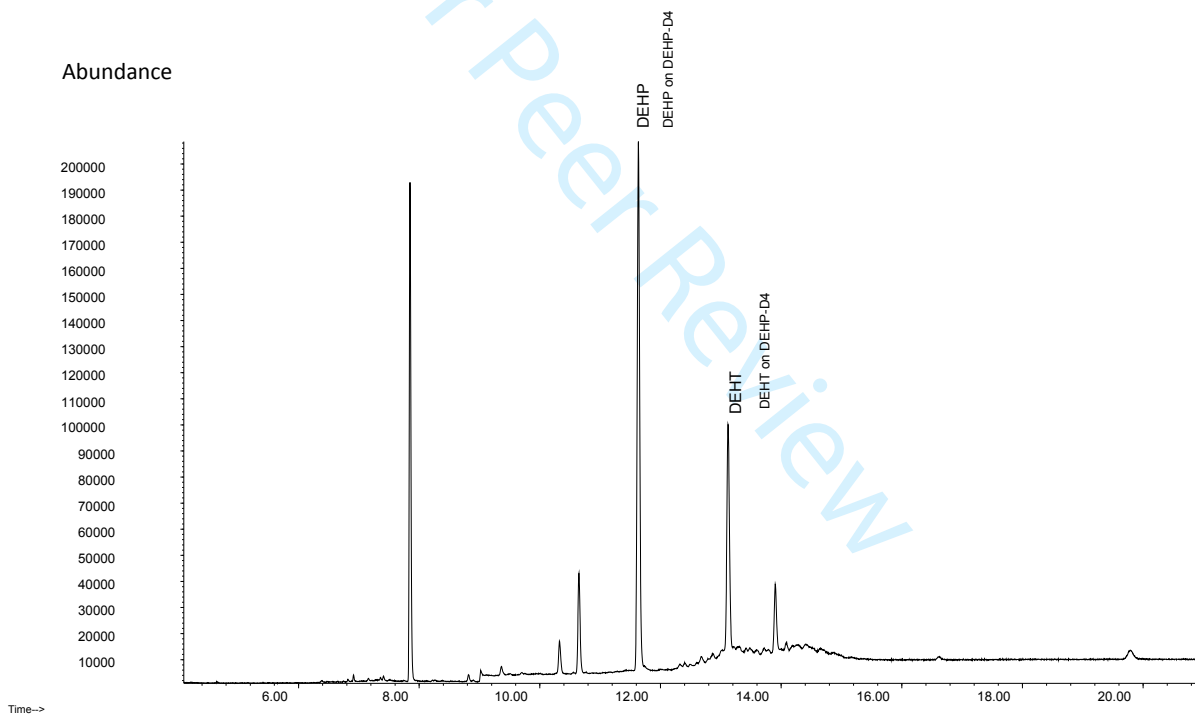
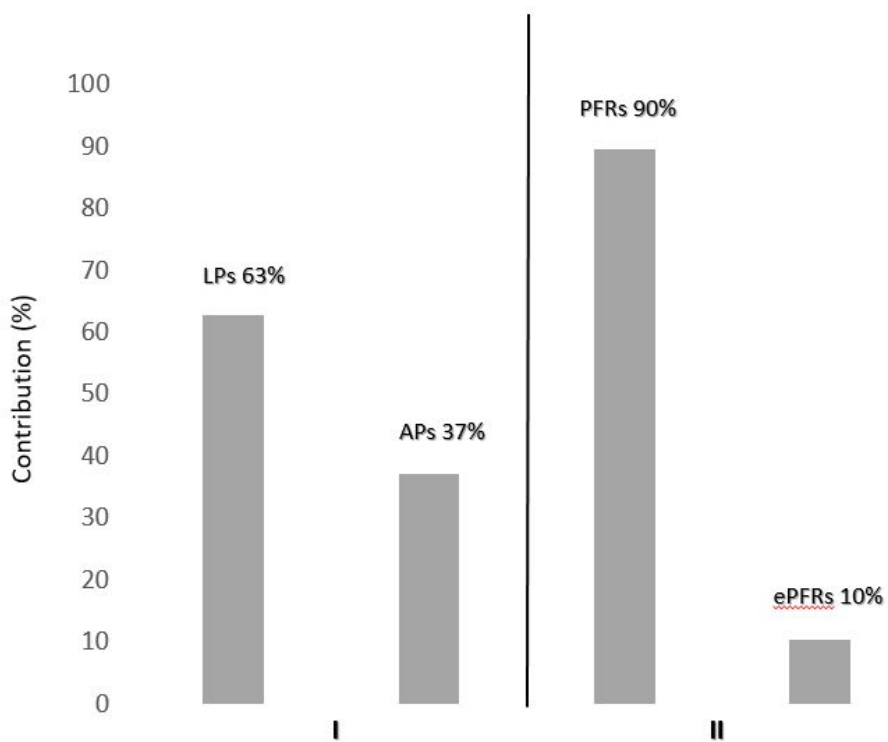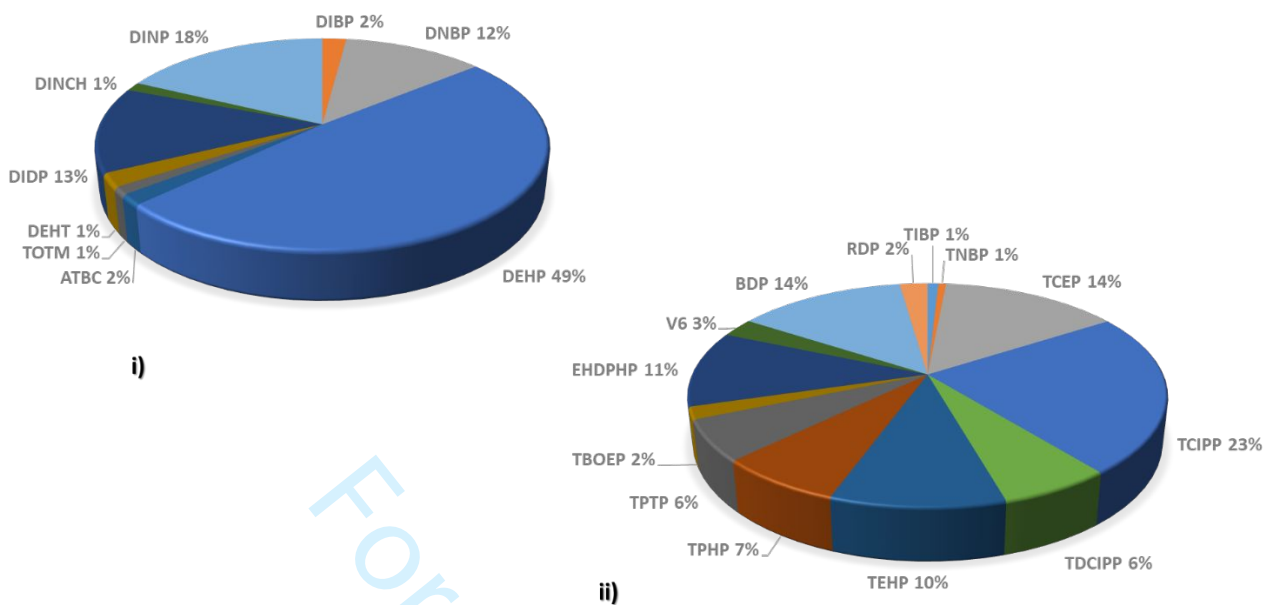**Figure 1** Workflow of the sample treatment and analysis

(i)
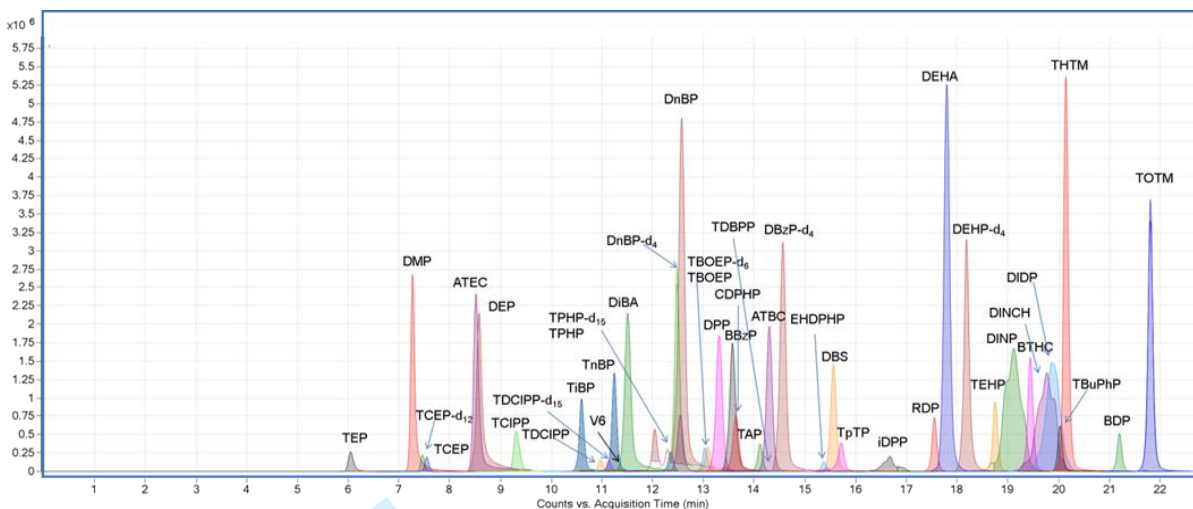
393

394 **(ii)**

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396 **Figure 2.** Chromatograms of the targeted analytes in standards mix (i) LC-MS/MS and (ii) GC-EI-MS.

397

Figure 3 Contribution (%) per compound group in 10 dust samples I) estimation between LPs and APs group, II) estimation for PFRs and ePFRs group. The calculated average standard error is 44%

Figure 4 Contribution (%) per analyte in 10 dust samples i)LPs and APs, ii) PFRs and ePFRs

Simultaneous determination of legacy and emerging organophosphorus flame retardants and plasticizers in indoor dust using liquid and gas chromatography-tandem mass spectrometry: Method development, validation and application

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Table S1. General and chromatographic information for the targeted analytes.

Target analyte	Acronym	Molecular formula	Molecular weight	CAS Number	Vapor pressure **	Log K_{OW}**	Retention time (min)	Precursor (m/z)	Fragmentor Voltage (V)	Quantitative Ions (m/z)	Collision Energy (eV)	Qualitative Ions (m/z)	Collision Energy (eV)
ISs													
Bis(2-ethylhexyl) phthalate-d4	DEHP-d$_4$	C$_{24}$D$_4$H$_{34}$O$_4$	394.6	93951-87-2			18.3	395.3	95.0	153.0	20	71.1	10
Di-N-butyl phthalate-d4	DNBP-d$_4$	C$_{16}$D$_4$H$_{18}$O$_4$	282.4	93952-11-5			12.7	283.2	35.0	153.1	10	125.1	40
Tris(2-chloroethyl) phosphate-d12	TCEP-d$_{12}$	C$_9$H$_4$D$_{12}$ClO$_6$P	297.6	n.a			7.5	297.1	95.0	67.0	25	102.0	25
Triphenyl phosphate-d15	TPHP-d$_{15}$	C$_{18}$D$_{15}$O$_4$P	341.4	n.a			12.4	342.3	103.0	82.0	45	160.0	50
Tris(1,3-dichloro-2-propyl) phosphate-d15	TDCIPP-d$_{15}$	C$_9$D$_{15}$Cl$_6$O$_4$P	443.0	13674-87-8			11.2	446.9	95.0	102.0	25	332.0	10
Tris(2-butoxyethyl) phosphate-d6	TBOEP-d$_6$	C$_{18}$H$_{33}$D$_6$O$_7$P	404.2	n.a			13.1	405.3	110.0	57.2	30	202.0	12
RS													
Triamyl phosphate	TAP	C$_{15}$H$_{33}$O$_4$P	308.3	2528-38-3			14.2	332.0	80.0	191.0	5	135.0	13
PFRs													
Tris(2-chloroethyl) phosphate	TCEP	C$_6$H$_{12}$Cl$_3$O$_4$P	285.4	115-96-8	1.1×10^{-4} [a]	1.44	7.5	285	88	93	27	99	23
Tris(2-ethylhexyl) phosphate	TEHP	C$_{24}$H$_{51}$O$_4$P	434.6	78-42-2	2.0×10^{-6} [a]	4.22	18.8	435.4	95	99	12	71	13
Tris(2-butoxyethyl) phosphate	TBOEP	C$_{18}$H$_{39}$O$_7$P	398.4	78-51-3	2.1×10^{-7} [a]	3.65	13.2	399.3	110	299.2	10	199	10
Triphenyl phosphate	TPHP	C$_{18}$H$_{15}$O$_4$P	326.2	115-86-6	1.2×10^{-6} [a]	4.59	12.4	327	148	77	45	152	50
2-ethylhexyl diphenyl phosphate	EHDPHP	C$_{20}$H$_{27}$O$_4$P	362.4	1241-94-7	6.5×10^{-7} [a]	5.73	15.1	363.2	50	251	30	77	50
Tris(chloro-2-propyl) phosphate	TCIPP	C$_9$H$_{18}$Cl$_3$O$_4$P	327.5	13674-84-5	1.9×10^{-6} [a]	2.59	9.5	327.1	65	99	20	175	5
Tris(1,3-dichloro-2-propyl) phosphate	TDCIPP	C$_9$H$_{15}$Cl$_6$O$_4$P	430.8	13674-87-8	7.4×10^{-8} [a]	3.8	11.2	432.9	95	99	27	211	10
Tri-iso-butyl phosphate	TIBP	C$_{12}$H$_{27}$O$_4$P	266.3	126-71-6	1.3×10^{-2} [a]	3.6	10.8	267.2	65	99	10	81	50
Tri-N-butyl phosphate	TNBP	C$_{12}$H$_{27}$O$_4$P	266.3	126-73-8	1.1×10^{-3} [a]	4.0	11.3	267.2	65	99	15	81	50
Tri-O-cresyl phosphate	TOTP	C$_{21}$H$_{21}$O$_4$P	368.3	78-30-8	1.8×10^{-7} [a]	5.48	15.8	369.2	170	91	40	165	45
Tri-P-cresyl phosphate	TPTP	C$_{21}$H$_{21}$O$_4$P	368.3	78-32-0	1.8×10^{-7} [a]	5.48	15.8	369.2	185	165	50	91	45
Tri-M-cresyl phosphate	TMTP	C$_{21}$H$_{21}$O$_4$P	368.3	563-04-2	1.4×10^{-7} [a]	6.34	15.8	369.2	178	165	48	91	43
Triethyl phosphate	TEP	C$_6$H$_{15}$O$_4$P	182.1	78-40-0	0.29 [a]	0.8	6	183.1	65	99	18	81	45
Tris(4-tert-butylphenyl) phosphate	TBuPHP	C$_{30}$H$_{39}$O$_4$P	494.6	78-33-1	/	/	20.2	495.2	200	327	35	383	28
ePFRs													
2,2-bis(chloromethyl)-propane-1,3-diyltetrakis(2-chloroethyl) biphosphate	V6	C$_{13}$H$_{24}$Cl$_6$O$_8$P$_2$	582.9	38051-10-4	1.2×10^{-14} [a]	1.9	11.4	582.9	140	360.9	15	235	35
Isodecyl diphenyl phosphate	iDDPHP	C$_{22}$H$_{31}$O$_4$P	390.4	29761-21-5	8.3×10^{-8} [a]	5.44	16.7	391.2	80	251	7	77	50
Resorcinol bis(diphenylphosphate)	RDP	C$_{30}$H$_{24}$O$_8$P$_2$	574.4	57583-54-7	2.1×10^{-8} [a]	7.41	17.5	592.1	110	575	15	481	45
Bisphenol A - bis(diphenyl phosphate)	BDP	C$_{39}$H$_{34}$O$_8$P$_2$	692.6	5945-33-5	9.0×10^{-6} [a]	4.5	21.17	710.1	150	367	40	693	17
Tris (2,3-dibromopropyl) phosphate	TDBPP	C$_9$H$_{15}$Br$_6$O$_4$P	697.6	126-72-7	1.9×10^{-4} [a]	4.29	14.4	698.5	95	99	28	299	10
LPs													
Dimethyl phthalate	DMP	C$_{10}$H$_{10}$O$_4$	194.1	131-11-3	0.263 [b]	1.66	7.29	195.1	57	163	5	77	40
Diethyl phthalate	DEP	C$_{12}$H$_{14}$O$_4$	222.2	84-66-2	6.48×10^{-2} [b]	2.65	8.63	223.1	72	148.9	13	177	1
Di-N-butyl phthalate	DNBP	C$_{16}$H$_{22}$O$_4$	278.3	84-74-2	4.73×10^{-3} [b]	4.61	12.6	279.2	72	149	9	77	45
Di-iso-butyl phthalate	DIBP	C$_{16}$H$_{22}$O$_4$	278.3	84-69-5	4.73×10^{-3} [b]	4.46	12.4	279.2	72	149	10	77	40
Benzyl butyl phthalate	BBP	C$_{19}$H$_{20}$O$_4$	312.3	85-68-7	2.49×10^{-3} [b]	4.84	13.8	313.2	72	149	5	91	1
Bis(2-ethylhexyl) phthalate (*in GC-EI-MS*)	DEHP*	C$_{24}$H$_{38}$O$_4$	390.5	117-81-7	2.52×10^{-5} [b]	8.39	12.1	-	-	279	-	167	-
Diphenyl phthalate	DPP	C$_{20}$H$_{14}$O$_4$	318.3	84-62-8	/	/	13.6	319.2	50	225	7	77	7
APs													
Di-iso-butyl adipate	DIBA	C$_{14}$H$_{26}$O$_4$	258.3	141-04-8	0.751 [b]	4.19	11.5	259.2	80	129	5	111	13
Acetyltriethyl citrate	ATEC	C$_{14}$H$_{22}$O$_8$	318.3	77-89-4	/	/	8.6	319	65	157	15	139	22
Dibutyl sebacate	DBS	C$_{18}$H$_{34}$O$_4$	314.4	109-43-3	6.3×10^{-4} [b]	6.3	15.5	315.2	110	185	10	241.2	5
Acetyltributyl citrate	ATBC	C$_{20}$H$_{34}$O$_8$	402.4	77-90-7	6.07×10^{-4} [b]	4.29	14.4	403.3	80	129	33	139	23
Diethylhexyl adipate	DEHA	C$_{22}$H$_{42}$O$_4$	370.5	103-23-1	4.27×10^{-4} [b]	8.12	17.9	371.3	110	129.1	10	111	20
Cresyl diphenyl phosphate	DCPC	C$_{19}$H$_{17}$O$_4$P	340.3	26444-49-5	4.7×10^{-6} [a b]	4.51	13.9	341.1	170	91.1	40	152.1	42
Butyryl trihexyl citrate	BTHC	C$_{28}$H$_{50}$O$_8$	514.7	82469-79-2	/	/	19.6	515.3	95	129	27	213	15
Bis (2-ethylhexyl) Terephthalate (*in GC-EI-MS*)	DEHT*	C$_{24}$H$_{38}$O$_4$	390.5	6422-86-2	2.86×10^{-3} [b]	8.39	13.5	-	-	261	-	167	-
Tri-n-hexyl trimellitate	THTM	C$_{27}$H$_{42}$O$_6$	546.7	1528-49-0	/	/	20.35	463.3	95	277	10	193	40
Tris(2-ethylhexyl) trimellitate	TOTM	C$_{33}$H$_{54}$O$_6$	546.392	3319-31-1	6.80×10^{-8} [b]	8.0	21.82	547.5	110	305.2	17	139.1	47
1,2- Cyclohexane dicarboxylic acid diisononyl ester	DINCH	C$_{26}$H$_{48}$O$_4$	424.6	166412-78-8	1.28×10^{-4} [b]	10	19.8	425.3	95	155	10	71	15

| Di iso nonyl phthalate | DINP | $C_{26}H_{42}O_4$ | 418.6 | 28553-12-0 | 5.17×10^{-6} [b] | 9.52 | 19.3 | 419.3 | 110 | 71.2 | 13 | 57.3 | 25 |
| Di iso decyl phthalate | DIDP | $C_{28}H_{46}O_4$ | 446.6 | 19269-67-1 | 1.84×10^{-6} [b] | 9.46 | 20.15 | 447.5 | 125 | 85 | 10 | 71 | 15 |

*analyzed in GC-EI-MS; **(Bui et al., 2016; Subedi et al., 2017; van der Veen and de Boer, 2012); [a] mm Hg; [b] Pascal.

Table S2. Gradient applied in LC-MS/MS analysis.

t (min)	B (%)
0	30
5	70
20	100
25	100
25.1	30
35	30

Flow: 0.25 ml/min

B: organic phase; MeOH 5mM ammonium formate

Table S3. Tested protocols.

Protocol trial version	Extraction solvents	Elution Solvents (F1)
3:1 I	*n*-Hex/Acetone (3:1) & toluene	*n*-Hex/DCM (1:1)
3:1 II	**n-Hex/Acetone (3:1) & toluene**	**n-Hex/DCM (4:1)**
3:1 III	*n*-Hex/Acetone (3:1) & toluene	*n-Hex*
1:1 I	*n*-Hex/Acetone (1:1) & toluene	*n*-Hex/DCM (1:1)
1:1 II	*n*-Hex/Acetone (1:1) & toluene	*n*-Hex/DCM (4:1)
1:1 III	*n*-Hex/Acetone (1:1) & toluene	*n*-Hex

in green the final selection.

Table S4. Concentration levels of individual targeted analytes in 10 indoor dust samples from Guangzhou, China (ng/g).

Target Analytes	Indoor dust samples									
	GZ-L-01	GZ-L-02	GZ-L-03	GZ-L-04	GZ-L-05	GZ-L-06	GZ-L-07	GZ-L-08	GZ-L-09	GZ-L-10
PFRs										
TCEP	95	22	126	3809	263	303	96	60	65	92
TEHP	77	41	60	850	127	79	87	113	260	115
TBOEP	10	10	10	32	39	47	10	10	10	10
TPHP	177	29	29	187	29	29	29	29	29	180
EHDPHP	119	45	89	953	168	89	65	160	127	227
TCIPP	256	151	211	6137	215	192	271	124	199	212
TDCIPP	27	55	27	155	165	66	27	27	61	57
TIBP	2.9	2.9	64	2.9	2.9	2.9	2.9	2.9	2.9	2.9
TNBP	4.4	4.4	4.4	25	4.4	4.4	4.4	4.4	4.4	4.4
TPTP	60	12	56	34	88	62	62	119	48	78
ePFRs										
V6	2.5	<LOQ	2.6	8.8	83	160	4.4	2.7	14	4.4
RDP	15	10	52	26	16	13	33	20	25	26
BDP	82	56	96	169	168	210	184	160	101	190
LPs										
DMP	51	12	44	65	54	12	47	12	12	12
DNBP	24562	7621	34796	23074	32675	30437	44960	16951	14464	16402
DIBP	5416	2545	6035	6861	6297	3452	4682	1498	2036	3176
BBP	79	93	50	617	83	86	82	77	50	107
DEHP	90791	42117	73407	107092	113034	45428	92797	119645	149684	167125
APs										
ATBC	1877	1460	1554	4367	3752	1767	3425	9315	2100	3293
DEHA	161	161	161	658	161	161	648	731	794	161
CDPC	6.0	6.0	15	288	63	6.0	6.0	25	6.0	6.0
DEHT	105	105	105	30352	105	105	7035	4694	105	105
TOTM	1807	607	2611	3869	2916	616	1554	1849	4044	3722
DINCH	1149	1569	1529	2513	2999	2895	6024	3247	2988	3329
DINP	35036	10934	32749	22208	83881	12923	32259	39911	50578	44124
DIDP	1440	3683	12606	46194	60932	1647	6539	45767	34446	54018

Table S5. Concentrations of targeted analytes in SRM 2585 replicates (n=4) analyzed in the present study (ng/g)

	SRM1	SRM2	SRM3	SRM4	mean	SD	RSD	Values reported in Literature* Mean	Range	Trueness%
PFRs										
TCEP	748	795	647	612	700	86	12	925	776-1074	76
TEHP	252	321	314	316	301	33	11	155		194
TBOEP	75210	54388	58349	58298	61561	9286	15	63930		96
TPHP	585	594	513	557	562	36	6	1190	1060-1320	47
EHDPHP	989	1080	1161	1159	1097	81	7	1027		107
TCIPP	1488	1577	1277	1239	1395	163	12	1220	870-1570	114
TDCIPP	1398	1165	1245	1343	1288	103	8	1762		73
TIBP	0	0	0	0	0	0		276	262-290	-
TNBP	152	80	240	246	179	79	44	276	262-290	65
TPTP	642	326	330	308	402	160	40	n.a		-
TEP	0	0	0	0	0	0		n.a		-
TBuPHP	78	64	54	64	65	10	15	39		166
ePFRs										
V6	137	109	117	168	133	26	20	n.a	n.a	-
iDDPHP	353	209	263	263	272	60	22	n.a	n.a	-
TDBPP	10	22	19	12	16	5	35	n.a	n.a	-
LPs										
DMP	2289	1844	1782	1861	1944	233	12	1700	600-2600	114
DEP	18324	15104	11965	15275	15167	2597	17	7800	5200-11100	194
DNBP	74359	62107	62541	70043	67263	5971	9	33700	31000-38000	200
DIBP	11958	5717	5718	7501	7723	2946	38	6700	6000-7900	115
BBP	46669	97686	95358	107646	86840	27306	31	97300	85000-112000	89
DEHP	392178	350161	428423	471475	410559	51690	13	567300	538000-609000	72
APs										
ATEC	319	190	147	669	331	237	71	n.a	n.a	-
ATBC	619	549	434	430	508	92	18	700	n.a	73
DEHA	0	0	0	0	0	0		200	n.a	-
DCPC	160	166	87	101	129	41	32	100	n.a	129
BTHC	0	0	0	0	0	0		400	n.a	-
DEHT	27874	25264	32063	38846	31012	5926	19	n.a	n.a	-
THTM	345	245	233	262	271	51	19	n.a	n.a	-
TOTM	12132	12971	11625	14141	12717	1100	9	20000	n.a	64
DINP	421402	328446	280529	351232	345402	58612	17	195300	182000-205000	177
DIDP	230608	250839	228234	308297	254495	37275	15	103300	98000-109000	246

SRM1-3; analyzed for trueness, SRM4;analyzed in the batch of real samples

*(NIST, 2018; Larsson et al., 2017; Luongo & Ostman, 2016; Bradsma et al., 2013; Bergh et al., 2012)
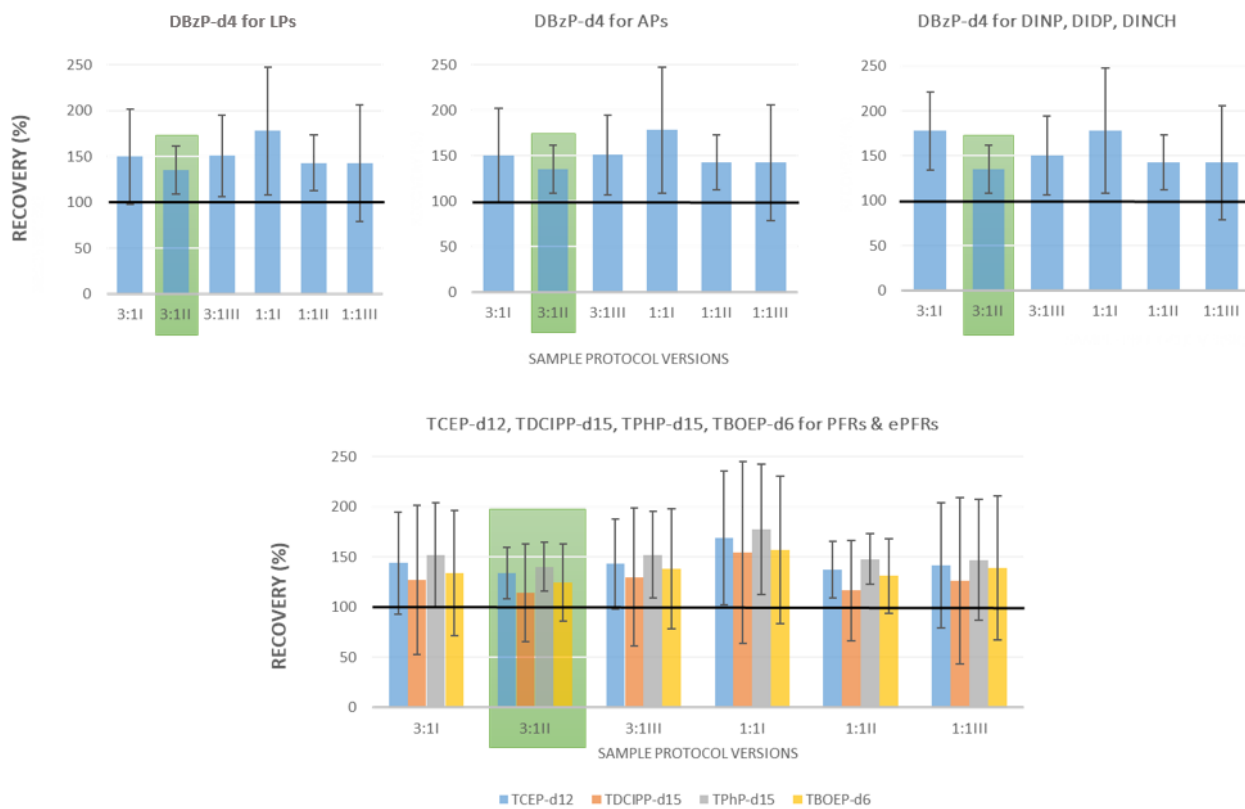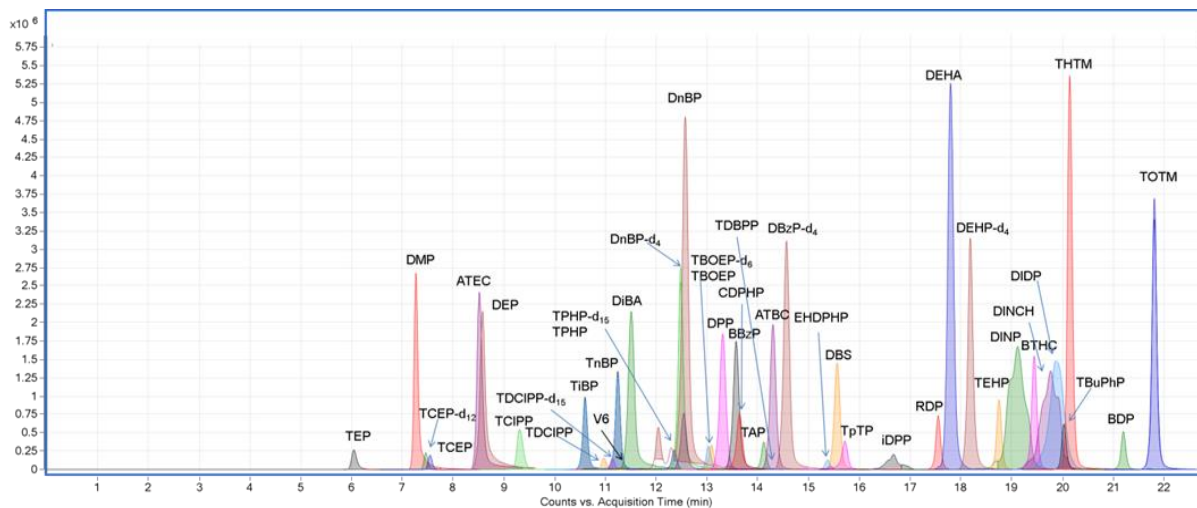
Figure S1. Calculated recoveries (%) of ISs for the tested protocols.
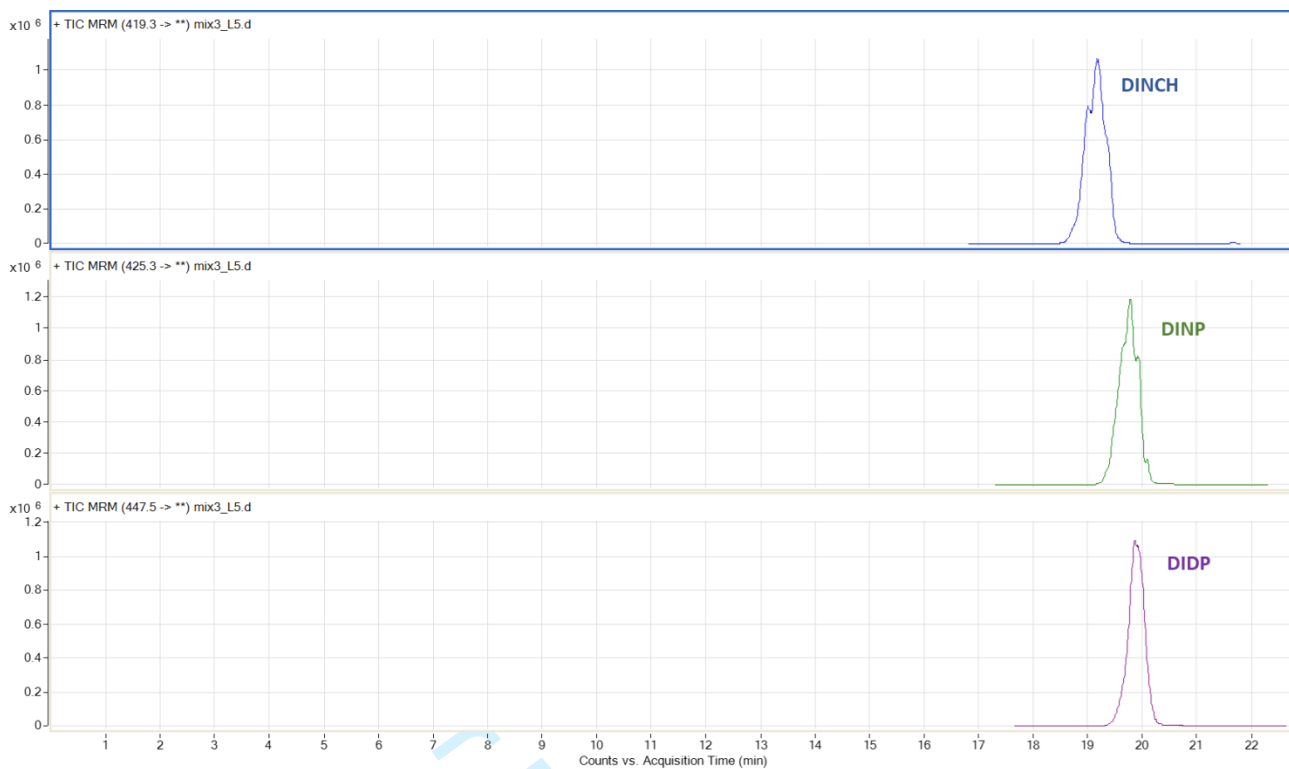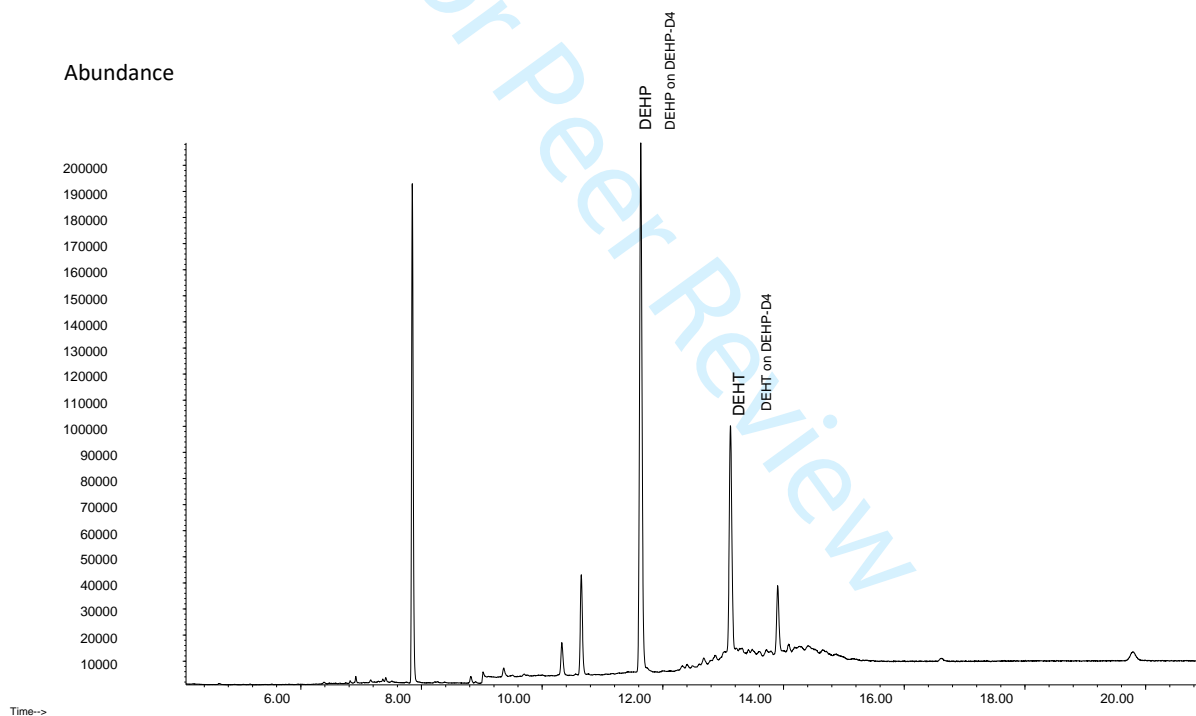
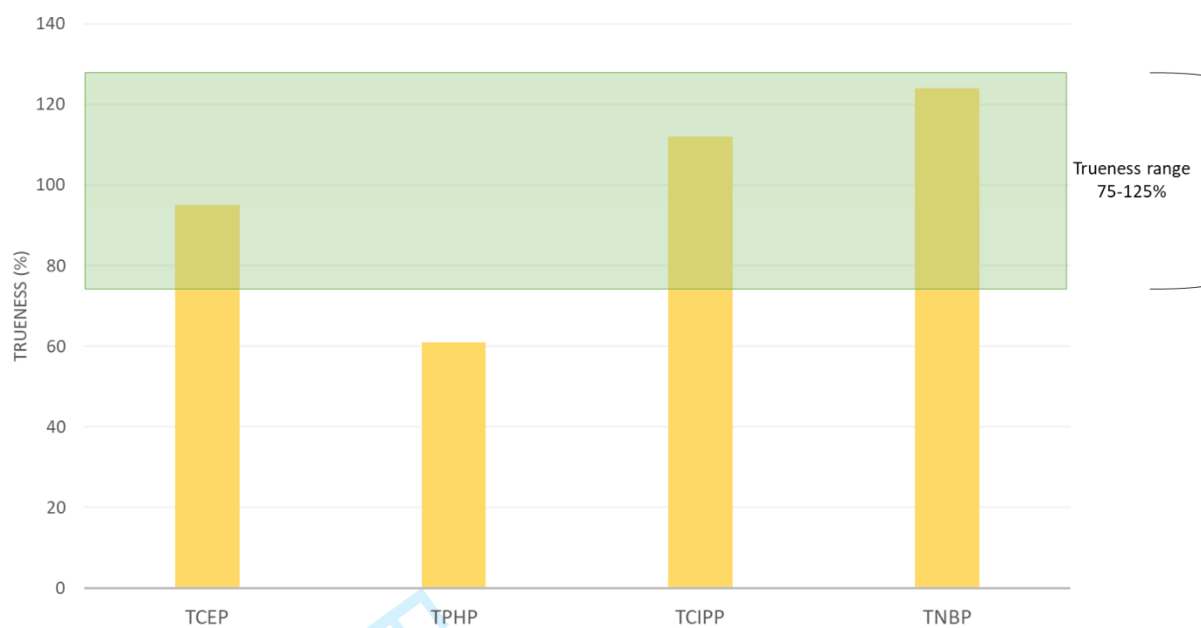**Figure S2.** Chromatographic peaks of DINCH, DINP and DIDP in LC-MS/MS.

(i)

(ii)

Figure S3. Chromatograms of the targeted analytes in standards mix (i) LC-MS/MS and (ii) GC-EI-MS.

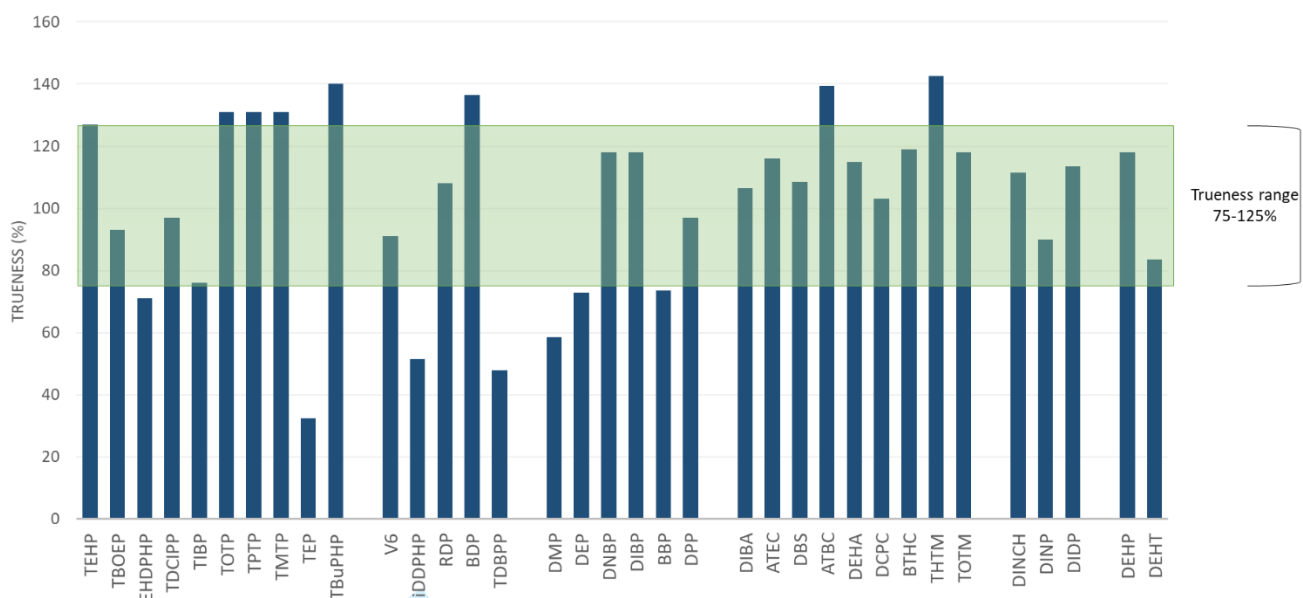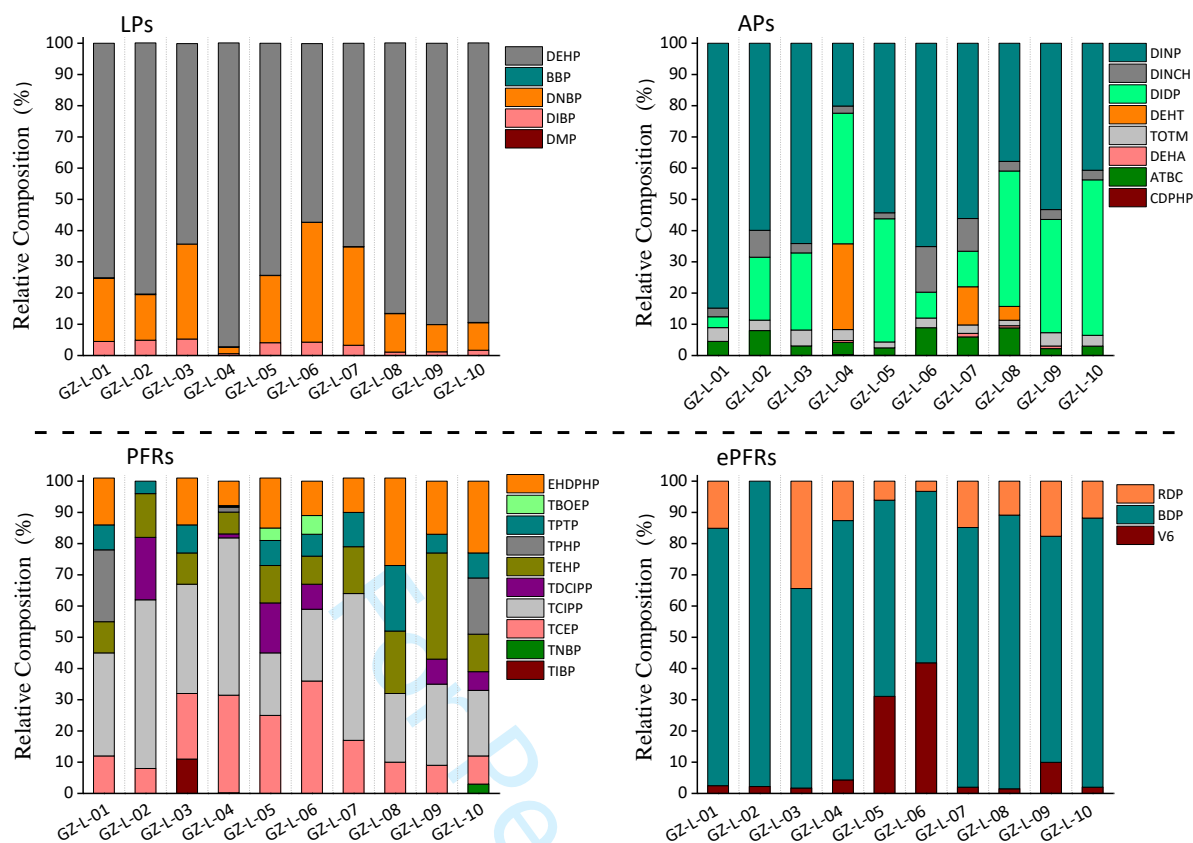**Figure S4.** Trueness (%) for 4 PFRs certified in SRM 2585.

Figure S5. Mean trueness (%) for target analytes not certified in SRM 2585.

Figure S6. Contribution of the targeted analytes in each compound group in 10 indoor dust samples from Guangzhou, China

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