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1 **Occurrence and Risk Assessment of Organophosphate Esters in**
2 **Drinking Water from Eastern China**

3
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17 **ABSTRACT**

18 Organophosphate esters (OPEs) are ubiquitous in the environment and may pose
19 potential health risks to humans. Drinking water is suspected as one possible exposure
20 pathway of OPEs to humans. In this study, we investigated the residues of 9 OPEs in
21 five types of drinking water in Eastern China. The median concentrations of Σ_9 OPEs
22 were determined to be 3.99, 4.50, 27.6, 59.2 and 192 ng/L in the bottled, well,
23 barreled, direct drinking and tap waters, respectively. Triethyl phosphate (TEP) was
24 the most abundant OPE in the tap water and direct drinking water with median
25 concentrations of 50.2 and 30.2 ng/L, respectively. Tri(chloropropyl) phosphate
26 (TCPP, including tri(chloroisopropyl) phosphate, TCIPP) dominated in the barreled
27 and well water with median concentrations of 8.04 and 2.49 ng/L, respectively. The
28 calculated average daily doses of OPEs ranged from 0.14 to 7.07 ng/kg bw/day for
29 people consuming the five different types of drinking water. Among the drinking
30 water, the tap water exhibited the highest exposure doses of OPEs. The calculated
31 non-cancer hazard quotients (10^{-4} - 10^{-7}) from OPEs were much lower than the
32 theoretical threshold of risk. The carcinogenic risks posed by TCEP were very low
33 ($<10^{-7}$) for all types of drinking water. The results revealed that there was currently
34 low risk to human health from exposure to OPEs through drinking water in Eastern
35 China.

36 **Keywords:** Organophosphate esters, drinking water, exposure assessment,
37 non-cancer risk, carcinogenic risk

38 **Highlights**

- 39 • Residuals of OPEs in drinking water were investigated in eastern China
- 40 • Uptake of OPEs from tap water is higher than from other drinking waters
- 41 • The ADD of OPEs via drinking water are not less than airborne exposure for
- 42 adults
- 43 • Non-cancer and carcinogenic risks of OPEs for people via drinking water are low

44 **1. Introduction**

45 Organophosphate esters (OPEs), also known as organophosphate flame retardants
46 and plasticizers, have become increasingly prosperous since the restriction and
47 phase-out of brominated flame retardants (BFRs), such as polybrominated diphenyl
48 ethers (PBDEs) (USEPA, 2005). The market demand for OPEs in Europe was 93,000
49 tons in 2006, accounting for 20% of the total annual flame retardants (FR)
50 consumption (van der Veen and de Boer, 2012). In China, the OPE production was
51 more than 70,000 tons in 2007 and was estimated to increase 15% annually (Ou,
52 2011).

53 However, a growing number of toxicological studies have revealed that several
54 OPEs may cause adverse effects in organisms. Chlorinated alkyl phosphates, such as
55 tri(2-chloroethyl) phosphate (TCEP) and tri(1,3-dichloroisopropyl) phosphate
56 (TDCIPP), were observed to cause tumor growth in different organs in rodents after
57 long-term exposure and thus are suspect carcinogens (WHO, 1998). TCEP has been
58 classified as a “potential human carcinogen” (carcinogen category 3) by the EU in
59 2008 (EU, 2008). TDCIPP was added to California’s Proposition 65 List of Potential
60 Carcinogens in 2011 (Stapleton et al., 2012). Moreover, TDCIPP was also identified
61 to have neurotoxic properties in PC12 cells (Dishaw et al., 2011), and caused
62 reproductive and developmental toxicity in zebrafish (Fu et al., 2013; Liu et al., 2013).
63 In addition, several studies have suggested that OPEs may be associated with certain
64 effects on human health, such as mucosal irritation and hormone level alteration
65 (Kanazawa et al., 2010; Meeker and Stapleton, 2009). Even so, the current

66 information is still limited regarding the toxicological effects of OPEs. To better
67 understand their adverse effects, the U.S. Environmental Protection Agency (USEPA)
68 is currently conducting full risk assessments on some OPEs (USEPA, 2013a).

69 In most cases, OPEs are used as additives and are not chemically bonded to
70 materials, being thus able to diffuse easily into the environment (Marklund et al.,
71 2003; Wensing et al., 2005). The occurrence of OPEs has been proven in various
72 environmental matrices, including air (Saito et al., 2007; Salamova et al., 2014), dust
73 (Van den Eede et al., 2011), water (Cristale et al., 2013b; Schaidler et al., 2014; Wang
74 et al., 2014), sediment (Cristale et al., 2013a), and soil (Fries and Mihajlović, 2011).
75 Furthermore, organisms may be exposed to OPEs through various pathways such as
76 inhalation, ingestion and dermal contact (Wei et al., 2015). OPEs and their
77 metabolites have been detected in wildlife (Greaves and Letcher, 2014) and human
78 tissues (Sundkvist et al., 2010; Van den Eede et al., 2013).

79 Given the relatively high water-solubility of most OPEs, their occurrence in various
80 water bodies, especially in drinking water, is an increasing issue of concern
81 worldwide. The technologies currently employed in the production of drinking water
82 are believed to have limited OPE removal capacity, since these substances have been
83 detected in drinking water from the United States (Benotti et al., 2009), Spain (Rodil
84 et al., 2012), South Korea (Kim et al., 2007), and China (Li et al., 2014). The
85 consumption of drinking water may be an important pathway of OPE exposure for
86 humans. However, the risk has not been well investigated to date.

87 In China, tap water is available in most urban areas. However, in some cases,

88 people drink tap water after boiling to reduce the risk of microbiological
89 contamination and improve the taste and smell of water. Additional devices with
90 activated carbon filtration and/or membrane processes are often used to produce direct
91 drinking water from tap water in some households. In addition, commodity water
92 (packed in bottles or barrels) is also popular, especially in the work environment. In
93 rural areas, untreated well water (groundwater) is the main drinking water source. A
94 description of the various drinking waters is detailed in the Supporting Information.

95 In the study, we have collected five types of drinking water samples including tap
96 water, direct drinking water, bottled water, barreled water, and well water from both
97 urban and rural areas in Eastern China. The residues and profiles of OPEs were
98 analyzed in these water samples. A preliminary exposure risk was also estimated for
99 the local residents by consumption of drinking water based on the measured
100 concentrations of OPEs.

101

102 **2. Materials and methods**

103 **2.1. Chemicals and reagents**

104 Triethyl phosphate (TEP, 99.9%), tri-n-butyl phosphate (TnBP, 99.5%), tri-n-propyl
105 phosphate (TnPP, 99.5%), TCEP (98.5%), tributoxyethyl phosphate (TBEP, 93.0%)
106 were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). Triphenyl
107 phosphate (TPhP, 100%), TCPP, 99.9%, TDCIPP (97.8%) were obtained from
108 Accustandard Inc. (New Haven, CT, USA). Tricresyl phosphate (TCrP, 99%, mixture
109 of isomers) was obtained from J & K Scientific (Beijing, China). Isotope-labeled

110 standards tributyl phosphate (TBP-d27, 98-99%) and TPhP-d15 were purchased from
111 Cambridge Isotope Laboratories Inc. (Andover, MA, USA) and Sigma-Aldrich (St.
112 Louis, MO, USA), respectively.

113 Acetonitrile and methanol were LC/MS grade from J.T. Baker, Inc. (Phillipsburg,
114 NJ, USA) and Fisher Scientific Co. LLC (Fair Lawn, NJ, USA), respectively.
115 Ultra-pure water (UPW, 18.2 MΩ) was produced with a Milli-Q Gradient system
116 (Millipore, Bedford, USA).

117 Individual stock solutions of analytes and isotope-labeled standards were prepared
118 in acetonitrile and kept at 4 °C. Working standard solutions were prepared by mixing
119 the stock solutions and diluting with methanol.

120 **2.2. Sample collection**

121 All water samples were collected in Hangzhou and Quzhou, Eastern China during
122 April to July 2014. Tap water (n=21) was sampled in kitchens from 21 households in
123 urban communities. In the same households or communities, direct drinking water
124 (n=17) which was produced from tap water by household filtering apparatuses (seven
125 samples, H1-H7) or public purifying machines (ten samples, P1-P10) were also
126 collected when available. Well water (n=19) was sampled from rural areas. Bottled
127 water (n=23) and barreled water (n=19) was purchased from local markets. The
128 bottled water was packaged in 550-1000 mL polyethylene terephthalate bottles. The
129 barreled water was packaged in 18.9 L polycarbonate plastic barrels. Detailed
130 description of the drinking waters is given in the Supporting Information. All samples
131 were stored at 4 °C until analysis. The analysis was conducted within 48 h after

132 sampling.

133 **2.3. Analytical methods**

134 One L of water sample was spiked with 10 ng TBP-d27 as internal standard and
135 extracted using solid phase extraction with cartridge (Oasis[®] HLB, 60 mg, 3cc:
136 Waters, USA) which was conditioned sequentially with 3 mL acetonitrile and 3 mL
137 water prior to loading. The water sample was loaded on the cartridge at a flow rate of
138 4-5 mL/min. After loading, the cartridge was washed with 3 mL UPW and then dried
139 under vacuum. Analytes were then eluted with 2 × 2 mL acetonitrile at a flow rate of
140 approximately 1 mL/min. The eluent was concentrated to near dryness under a gentle
141 stream of nitrogen. After adding 10 ng TPhP-d15, the analytes were reconstituted to
142 0.5 mL with methanol. Finally, the sample was filtered (0.2 µm, Waters, USA) before
143 UPLC-MS/MS analysis.

144 The quantification of OPEs was performed on an ultra-performance liquid
145 chromatography tandem mass spectrometry system (Xevo TQ-S, Waters, USA). The
146 operation conditions of the instrument were described in our previous study (Yang et
147 al., 2014). In brief, a 2 µL sample was injected into a Waters BEH C18 column (2.1
148 mm × 50 mm, 1.7 µm) coupled with a VanGuard precolumn (C18, 2.1 mm × 5 mm,
149 1.7 µm). A binary gradient of water (A) and acetonitrile (B), both containing 0.1%
150 formic acid, was used for the separation of analytes at a flow rate of 0.4 mL/min. The
151 gradient was as follows (with reference to B): 0 min 10% B, 4 min 50% B, 6 min 50%
152 B, 7 min 100% B, 9 min 100% B, and 10 min 10% B. The mass spectrometry was run
153 in positive electrospray ionization mode with multiple reaction monitoring. The

154 capillary voltage was 3.5 kV. Nitrogen and argon served as desolvation gas with a
155 flow of 800 L/h at 400 °C and collision gas, respectively. The detection parameters of
156 each OPE compound are shown in Table S1 and Figure S1 of the Supporting
157 Information.

158 **2.4. QA/QC**

159 The limit of detection (LOD) of OPEs was defined as three times of signal to noise
160 (S/N=3) and ranged from 2 to 25 pg/L in water sample (Table S1 in Supporting
161 Information). Instead of any substitution for the data below the LODs, the so-called
162 nondetects were included in statistical analysis without modification (Helsel, 2006) to
163 reduce or avoid the bias of data analysis in the study. Data with nondetects were
164 analyzed with R (2014) using a software library called NADA which was developed
165 by Lee (2014).

166 The background was checked by procedural blank (n=6). Only TEP, TnBP and
167 TPhP were detected to be higher than their LODs, averagely at 0.02, 0.08, 0.26 ng/mL,
168 respectively, in the final extraction. The recoveries of OPEs were determined in UPW
169 spiked with OPE standards (n=5) and ranged from 58.1 (TCrP) to 101.8% (TCEP)
170 (Table S1 in Supporting Information).

171 All water samples were spiked with TBP-d27 and TPhP-d15 as recovery standard
172 and internal standard, respectively, to monitor test performance for chemical analysis.
173 The recovery of TBP-d27 was $87.3 \pm 6.5\%$ (mean \pm SD) during sample analysis.

174 TCP and TCIP co-eluted and shared the same quantification ion transitions in
175 LC-MS/MS in the present study. Therefore, the concentration of TCP is the sum of

176 TCP and TCIP. TCP was used to indicate TCP and TCIP for simplification
177 unless specification. In addition, TCrP determined in the study is the sum of isomers
178 because the standard of TCrP is the mixture of isomers.

179 **2.5. Exposure and risk assessment methods**

180 The average daily doses (ADD) of each OPE through drinking water was calculated
181 using the following equation:

$$182 \quad \text{ADD}=(C \times \text{IR} \times \text{AP}) / \text{BW}$$

183 where C is concentration of OPE in drinking water (ng/L), IR is ingestion rate of
184 water (L/day), AP is absorption percent of intake which is assumed to be 100% for
185 drinking water (Li et al., 2014), BW is body weight (kg). In the exposure assessment,
186 mean concentration and 95th percentile of concentration range were employed to
187 assess average exposure scenarios and high exposure scenarios, respectively. Age and
188 gender-specific intake of drinking water were also included.

189 Non-cancer and carcinogenic risks of OPEs were estimated according to the
190 methods recommended by the U.S. EPA (USEPA, 2013b). Non-cancer risks from
191 OPE exposure via drinking water were appraised using hazard quotient (HQ), which
192 was calculated by the following equation:

$$193 \quad \text{HQ}=\text{ADD} / \text{RfD}$$

194 where RfD is reference dose value of each OPE (ng/kg bw/day). The local residents
195 are considered to be exposed to a non-cancer risk if the value of HQ is greater than 1.

196 The carcinogenic risk was assessed according to the equation:

$$197 \quad \text{Risk}=\text{ADD} \times \text{SFO}$$

198 where SFO is an oral slope factor $((\text{ng/kg bw/day})^{-1})$, representing the theoretical
199 upper-bound cancer potency. In our study, only TCEP's carcinogenic risk was
200 estimated since only its SFO is available. People are considered to be exposed to a
201 carcinogenic risk if $\text{Risk} > 10^{-6}$. The values of parameters for exposure and risk
202 assessments are listed in Table S2 of the Supporting Information (Ali et al., 2012;
203 MEPC, 2013; Shi et al., 2011; USEPA, 2013b).

204

205 **3. Results and discussion**

206 **3.1. Concentrations of OPEs in drinking water**

207 OPE compounds were detected in all samples, but the detection frequency of each
208 OPE compound varied among the types of drinking water (Table 1). TEP, TCEP and
209 TPhP were found with a detection frequency of 100% in each type of drinking water.
210 TnPP had the lowest detection frequency, ranging from 4.4% in bottle water to 33.3%
211 in tap water.

212 The sum concentration of nine detected OPE compounds were highest in the tap
213 water ranged from 123 to 339 ng/L, with a median of 192 ng/L, followed by direct
214 drinking water and barreled water with medians of 59.2 and 27.6 ng/L, respectively
215 (Table 1). Lower concentrations of OPEs were found in the well water and bottled
216 water, which were about two orders of magnitude lower than in the tap water.

217 **3.1.1. Concentrations of OPEs in tap water**

218 The concentrations of OPEs were reported from several ng/L to hundreds of ng/L in
219 drinking water worldwide (Andresen and Bester, 2006; Benotti et al., 2009; Kim et al.,

220 2007; Li et al., 2014; Rodil et al., 2012). Comparatively, OPEs were found at a high
221 level in tap water in the present study. It is speculated that the high levels of OPEs in
222 tap water come from contamination in source water. Eastern China is an important
223 area of production and consumption of OPEs in China. Application of large amounts
224 of OPEs would lead to increasing release and high levels in environmental matrices,
225 including surface water. Indeed, we detected a slightly high level of OPEs in surface
226 water collected from one of rivers in the sampling area (data not shown). Another
227 probable contributor may be the limited removal for OPEs during purification
228 processes applied in drinking water treatment plants (DWTPs) in the sampling area.
229 To the best of our knowledge, only two out of five DWTPs employed advanced
230 purification processes, such as activated carbon filtration and membrane processes in
231 the sampling area (HWHG, 2014). However, it remains a hypothesis, since no
232 investigation about the efficiency of different drinking water treatment processes in
233 removal of OPEs in this area is conducted yet.

234 **3.1.2. Concentrations of OPEs in direct drinking water**

235 The residues of OPEs in the direct drinking water were compared with the paired
236 tap water from the same families or community (Figure 1). A paired T-test revealed
237 that the sum OPE concentrations were significantly lower in the direct drinking water
238 ($p < 0.01$). OPEs in the tap water seemed to be partly removed by the additional
239 devices applied in producing direct drinking water and resulted in the decrease of
240 OPEs in the direct drinking water. The elimination rates varied from 4.6 to 93.3%,
241 depending on the purification devices involved. Obviously, the removal of OPEs by

242 public purifying machines (P1-P10, average 81.8%) was better than household
243 filtering apparatuses (H1-H7, averagely 28.0%). The public purifying machines
244 adopted multiple filtration processes and a reverse osmosis system which may be
245 more effective to remove OPEs (Kim et al., 2007). Comparatively, less filtration was
246 used in most household filtering apparatuses and therefore resulted in poorer
247 elimination rates. In addition, the elimination efficiency of OPEs is also depended on
248 the service time since various efficiencies were observed among the same group
249 (P1-P10) with the same type of purification device.

250 For individual OPEs, all major detected compounds were significantly ($p<0.01$)
251 lower in direct drinking water except TEP ($p<0.05$). As shown in Figure 2, direct
252 drinking water purification devices provided less effective elimination on TEP (40.0%,
253 median) than others (e.g. TDCIPP and TnBP, 91.7% and 91.0%, respectively,
254 median).

255 **3.1.3. Concentrations of OPEs in well water**

256 In contrast to the tap water, OPEs were detected at much lower levels in the well
257 water from rural areas. This reduction in contamination probably resulted from natural
258 purification during ground water recharge (Stepien et al., 2013). It was reported that
259 effective elimination (ca. 90%) was achieved for both chlorinated and non-chlorinated
260 OPEs when natural purification processes, such as slow underground passage, soil
261 passage, and bank filtration were involved in the DWTPs (Andresen and Bester,
262 2006). The adsorption capacity and biological activity in soil should intercept most of
263 the OPEs during ground water recharge from surface water.

264 **3.1.4. Concentrations of OPEs in bottled and barreled water**

265 The OPE concentrations in the bottled water were similar to the well water and ranged
266 between 0.9 and 11.2 ng/L. The results revealed that the manufacturing processes (e.g.
267 reverse osmosis) for the bottled water were effective. In addition, clean source water
268 should be another contributor, since some of producers of bottled water announced
269 that their clean source water comes from natural protected areas. Comparatively,
270 however, OPEs exhibited a higher and broader concentration ranging from 1.5 to 71.9
271 ng/L in the barreled water. The observation is believed to result in part from the
272 diversity of manufacturing techniques (such as reverse osmosis vs. ultrafiltration)
273 employed in the production of barreled water. In China, most barreled
274 water-producing manufactures are regional, and thus may apply different
275 manufacturing techniques depending on their enterprise scale and money. For the
276 prosperous and large scale manufactures, advanced technologies are employed and
277 result in satisfactory removal of OPEs.

278 **3.2. Patterns of OPE compounds in drinking water**

279 Three OPE compounds, namely TEP, TCEP and TPhP, were detected in all drinking
280 water samples. TCPP was detected in most of the samples, with only several
281 exceptions in commercial drinking water (bottled water and barreled water). TEP was
282 the most abundant OPE in tap water and direct drinking water with a median
283 concentration of 50.2 and 30.2 ng/L, respectively, followed by TCEP and TCPP. TCPP
284 was the most abundant OPE in the barreled water and well water with a median
285 concentration of 8.0 and 2.5 ng/L, respectively, followed by TCEP and TEP. However,

286 TPhP was the most abundant OPE in the bottled water. Although the most abundant
287 individual OPEs were different among the five types of drinking water, these four
288 OPEs altogether dominated the total OPE concentrations in all drinking waters and
289 accounted for 72.4% (median, bottled water) to 96.2% (median, direct drinking water)
290 of total OPEs (Figure S2 in Supporting Information).

291 TCEP and TCPP are the two most prevalent chlorinated OPEs used in rigid and
292 flexible polyurethane foams (van der Veen and de Boer, 2012). As a result, they were
293 detected in various matrices, including drinking water. These OPEs have been
294 frequently detected and identified as major contributors in drinking water in previous
295 studies (Benotti et al., 2009; Esteban et al., 2014; Rodil et al., 2012; Schaidler et al.,
296 2014). For example, median concentrations of TCEP and TCPP were 120 and 210
297 ng/L in finished water samples from 19 DWTPs across the U.S. (Benotti et al., 2009)

298 Besides TCEP and TCPP, TDCIPP was another chlorinated OPEs detected in the
299 five types of drinking water samples with a detection frequency and a median
300 concentration ranged from 72.2% and 5.84 ng/L in the tap water to 100% and 0.12
301 ng/L in the well water. The ratio of 3 chlorinated OPEs (TCEP, TCPP and TDCIPP) to
302 the total OPEs was in a range of 7.3% (direct drinking water) to 95.0% (barreled
303 water). The chlorinated OPEs were the main contributors to the total OPEs in most of
304 the drinking water types, except for the direct drinking water. The results were
305 consistent with studies on other matrices since chlorinated OPEs had a high
306 production volume and seemed to be more resistant to both natural and biological
307 degradation in the environment than non-chlorinated OPEs (Reemtsma et al., 2008).

308 Although TEP is not a routine target OPE in either surface water or in drinking
309 water analysis, it showed a high detection frequency with concentrations ranging from
310 several ng/L to more than one hundred ng/L in surface water and drinking water
311 (Bacaloni et al., 2008; Martínez-Carballo et al., 2007; Rodil et al., 2012; Wang et al.,
312 2011). TEP concentrations of about 3 and 5 ng/L in surface water and the
313 corresponding drinking water, respectively, were measured in Galicia, Spain (Rodil et
314 al., 2012). The findings indicated a poor elimination of TEP in drinking water
315 treatment or in the worst case, a release from the water supply piping system. In the
316 present study, TEP was identified as the most abundant OPE in terms of concentration
317 in the tap water and direct drinking water. The presence of TEP results in part from
318 inefficient purification in DWTPs, household filtering apparatuses or public purifying
319 machines during production of tap water or direct drinking water. The
320 compound-specific elimination of OPEs was compared in the paired direct drinking
321 water and tap water samples (Figure 2). It was found that purification apparatus
322 provided a poorer efficiency in TEP elimination compared with other OPEs. This also
323 suggests that TEP is difficult to remove even when advanced purification technologies
324 are employed.

325 TnPP was occasionally detected in the samples with a low detection frequency. The
326 low detection frequency of TnPP was predictable considering its scarce usage. In fact,
327 some analytical methods (Quintana et al., 2008) use TnPP as an internal standard in
328 due to its low occurrence in environment (Rodil et al., 2012).

329 **3.3. Exposure assessment of OPEs through drinking water consumption**

330 The ADD of total OPEs via ingestion of drinking water were calculated and shown in
331 Table 2. The uptake of OPEs through tap water is higher than other drinking water in
332 either adults or children, ranging from 6.1 to 7.1 ng/kg bw/day. Comparatively, the
333 ADDs are at least one order of magnitude lower, and less than 1 ng/kg bw/day for
334 ingestion of the well water and bottled water. Actually, most of people in Chinese
335 cities have to face comparatively high ADDs since they usually drink tap water or
336 boiled tap water instead of other drinking waters. The effect of boiling on OPEs in tap
337 water is discussed in the Supporting Information and is shown in Figure S3. There are
338 no significant differences found between adults and children among all types of
339 drinking water. However, exposure doses of OPEs are found to be slightly higher in
340 males than in females, for both adults and children (Table 2).

341 Compared with airborne exposure via particulate matter inhalation (Yang et al.,
342 2014) and dust ingestion (Cao et al., 2014) in China, which were averagely calculated
343 at 3.4 and 12.6 ng/kg bw/day, respectively, for adults (Supporting Information), the
344 exposure doses of OPEs through drinking water were in a similar range. For children,
345 the doses were higher and were 5.7 and 127.9 ng/kg bw/day for particulate matter
346 inhalation and dust ingestion, respectively (Supporting Information). Conversely, for
347 children, uptake of OPEs through airborne exposure was higher than from drinking
348 water. Nevertheless, drinking water is probably one of the important pathways for
349 exposure to OPEs for Chinese people.

350 **3.4. Risk assessment of OPEs through drinking water consumption.**

351 Given the ubiquitous presence of OPEs in all types of drinking water in Eastern China,

352 it is crucial to estimate the potential risks of OPEs to local residents through drinking
353 water. However, there is still no reference doses (RfD) suggested for OPEs by
354 authoritative institutions such as USEPA, NIH and WHO due to the limited data in
355 toxicity information of OPEs on humans. Therefore, the RfD values used in the
356 present assessment were calculated by dividing chronic no-observed adverse effect
357 levels (NOAELs) by a safety factor of 1,000, which was calculated by Ali et al. (2012)
358 except for TEP. The RfD of TEP was calculated from its lowest no-observed effect
359 level (NOEL) suggested by Organization for Economic Cooperation and
360 Development (OECD, 2005).

361 The hazard quotient (HQ), which indicates the non-carcinogenic risk, was
362 calculated for each OPE (shown in Figure 3). The estimated HQ of individual OPEs
363 from drinking water are all within acceptable level ($HQ < 1$) in both average and high
364 exposure scenarios. Actually, the values are generally at 10^{-4} - 10^{-7} , indicating a 4-7
365 orders of magnitude safety margin to the theoretical risk threshold. Therefore, it is
366 suggested that there is a negligible non-cancer risk to local residents arising from OPE
367 exposure through drinking water. The results also revealed that the presence of
368 chlorinated OPEs in drinking water should be of major concern, because the three
369 chlorinated analogs (TCEP, TCPP and TDCIPP) always showed a higher HQ value
370 than non-chlorinated OPEs in all types of drinking water.

371 In addition to the non-carcinogenic risk, the carcinogenic risk from TCEP was also
372 assessed. Only TCEP could be assessed because it was the only OPE with an
373 available SFO. The result indicates a very low risk ($< 10^{-7}$) for all types of drinking

374 water (Figure 4). The highest carcinogenic risk of TCEP was found at 7.3×10^{-8} to
375 8.5×10^{-8} for gender and age specific category from exposure to the tap water.

376 The assessment reveals that the risk originating from exposure to OPEs through
377 ingestion of drinking water is currently low in Eastern China. Among the five types of
378 drinking water, the well water and bottled water posed the lowest non-cancer and
379 carcinogenic risks from OPEs, while tap water poses the highest. Drinking well water
380 and bottled water is unreasonable for most of urban residents in eastern China due to
381 the limits of transportation and cost. Therefore, barreled water or direct drinking water
382 may be an alternative for urban residents to reduce their health risk from OPEs.

383

384 ■ **ASSOCIATED CONTENT**

385 Descriptions for types of drinking water, effect of boiling on OPEs in drinking
386 water and calculation of OPEs exposure via suspended particulate matter and dust
387 ingestion. Two tables, three figures and references are included.

388

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392 **Notes:** The authors declare no competing financial interest.

393

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399

400 **References**

401 Ali, N.; Dirtu, A.C.; Eede, N.V.D.; Goosey, E.; Harrad, S.; Neels, H., et al. 2012.

402 Occurrence of alternative flame retardants in indoor dust from New Zealand:

403 Indoor sources and human exposure assessment. *Chemosphere* 2012; 88:1276-82.

404 Andresen, J.; Bester, K. 2006. Elimination of organophosphate ester flame retardants

405 and plasticizers in drinking water purification. *Water Res* 2012; 40:621-9.

406 Bacaloni, A.; Cucci, F.; Guarino, C.; Nazzari, M.; Samperi, R.; Laganà, A. 2008.

407 Occurrence of Organophosphorus Flame Retardant and Plasticizers in Three

408 Volcanic Lakes of Central Italy. *Environ Sci Technol* 2008; 42:1898-903.

409 Benotti, M.J.; Trenholm, R.A.; Vanderford, B.J.; Holady, J.C.; Stanford, B.D.; Snyder,

410 S.A. 2009. Pharmaceuticals and Endocrine Disrupting Compounds in U.S.

411 Drinking Water. *Environ Sci Technol* 2009; 43:597-603.

412 Cao, Z.; Xu, F.; Covaci, A.; Wu, M.; Wang, H.; Yu, G., et al. 2014. Distribution

413 Patterns of Brominated, Chlorinated, and Phosphorus Flame Retardants with

414 Particle Size in Indoor and Outdoor Dust and Implications for Human Exposure.

415 *Environ Sci Technol* 2014; 48:8839-46.

416 Core Team of R. 2014. R: A language and environment for statistical computing. R

417 Foundation for Statistical Computing, Vienna, Austria. <http://www.R-project.org/>

418 (Accessed Jul. 10, 2014).

419 Cristale, J.; García Vázquez, A.; Barata, C.; Lacorte, S. 2013a. Priority and emerging
420 flame retardants in rivers: Occurrence in water and sediment, *Daphnia magna*
421 toxicity and risk assessment. *Environ Int* 2013; 59:232-43.

422 Cristale, J.; Katsoyiannis, A.; Sweetman, A.J.; Jones, K.C.; Lacorte, S. 2013b.
423 Occurrence and risk assessment of organophosphorus and brominated flame
424 retardants in the River Aire (UK). *Environ Pollut* 2013; 179:194-200.

425 Dishaw, L.V.; Powers, C.M.; Ryde, I.T.; Roberts, S.C.; Seidler, F.J.; Slotkin, T.A., et
426 al. 2011. Is the PentaBDE replacement, tris (1,3-dichloro-2-propyl) phosphate
427 (TDCPP), a developmental neurotoxicant? Studies in PC12 cells. *Toxicol Appl*
428 *Pharm* 2011; 256:281-9.

429 Esteban, S.; Gorga, M.; González-Alonso, S.; Petrovic, M.; Barceló, D.; Valcárcel, Y.
430 2014. Monitoring endocrine disrupting compounds and estrogenic activity in tap
431 water from Central Spain. *Environ Sci Pollut R* 2014; 21:9297-310.

432 European Union. 2008. Risk assessment report of tri (2-Chloroethyl) phosphate, 2008.
433 CAS No: 115-96-8 EINECS No: 204-118-5.

434 Fries, E.; Mihajlović, I. 2011. Pollution of soils with organophosphorus flame
435 retardants and plasticizers. *J Environ Monitor* 2011; 13:2692-4.

436 Fu, J.; Han, J.; Zhou, B.; Gong, Z.; Santos, E.M.; Huo, X., et al. 2013. Toxicogenomic
437 Responses of Zebrafish Embryos/Larvae to Tris(1,3-dichloro-2-propyl) Phosphate
438 (TDCPP) Reveal Possible Molecular Mechanisms of Developmental Toxicity.
439 *Environ Sci Technol* 2013; 47: 10574-82.

440 Greaves, A.K.; Letcher, R.J. 2014. Comparative Body Compartment Composition and
441 In Ovo Transfer of Organophosphate Flame Retardants in North American Great
442 Lakes Herring Gulls. *Environ Sci Technol* 2014; 48:7942-50.

443 Helsel, D.R. 2006. Fabricating data: how substituting values for nondetects can ruin
444 results, and what can be done about it. *Chemosphere* 2006; 65:2434-9.

445 Hangzhou Water Holding Group CO., LTD. 2014. <http://www.hzwgc.com/> (In
446 Chinese, accessed Oct. 25, 2014).

447 Kanazawa, A.; Saito, I.; Araki, A.; Takeda, M.; Ma, M.; Saijo, Y., et al. 2010.
448 Association between indoor exposure to semi-volatile organic compounds and
449 building-related symptoms among the occupants of residential dwellings. *Indoor*
450 *Air* 2010; 20:72-84.

451 Kim, S. D.; Cho, J.; Kim, I. S.; Vanderford, B. J.; Snyder, S. A. 2007. Occurrence and
452 removal of pharmaceuticals and endocrine disruptors in South Korean surface,
453 drinking, and waste waters. *Water Res* 2007; 41:1013-21.

454 Lee, L. 2014. NADA: Nondetects and Data Analysis for environmental data. R
455 package version 1.5-6. 2014. <http://CRAN.R-project.org/package=NADA/>
456 (Accessed Jul 10, 2014).

457 Li, J.; Yu, N.; Zhang, B.; Jin, L.; Li, M.; Hu, M., et al. 2014. Occurrence of
458 organophosphate flame retardants in drinking water from China. *Water Res* 2014;
459 54:53-61.

460 Liu, X.; Ji, K.; Jo, A.; Moon, H.; Choi, K. 2013. Effects of TDCPP or TPP on gene
461 transcriptions and hormones of HPG axis, and their consequences on reproduction

462 in adult zebrafish (*Danio rerio*). *Aquat Toxicol* 2013; 134-135:104-11.

463 Marklund, A.; Andersson, B.; Haglund, P. 2003. Screening of organophosphorus
464 compounds and their distribution in various indoor environments. *Chemosphere*
465 2013; 53:1137-46.

466 Martínez-Carballo, E.; González-Barreiro, C.; Sitka, A.; Scharf, S.; Gans, O. 2007.
467 Determination of selected organophosphate esters in the aquatic environment of
468 Austria. *Sci Total Environ* 2007; 388:290-9.

469 Meeker, J.D.; Stapleton, H.M. 2009. House Dust Concentrations of Organophosphate
470 Flame Retardants in Relation to Hormone Levels and Semen Quality Parameters.
471 *Environ Health Persp* 2009; 118:318-23.

472 Ministry of Environmental Protection of the P.R.C. (MEPC) 2013. Exposure factors
473 handbook of Chinese population: China Environmental Science Press: 2013 (In
474 Chinese).

475 OECD 2005. Screening information data set (SIDS) for high production volume
476 chemicals: triethylphosphate. 2005.
477 <http://www.inchem.org/documents/sids/sids/78400.pdf>. (Accessed Jan. 29,
478 2015). .

479 Ou, Y. 2011. Developments of organic phosphorus flame retardant industry in China.
480 *Chem Ind Eng Prog* 2011; 30:210-5.

481 Quintana, J.B.; Rodil, R.; Reemtsma, T.; García-López, M.; Rodríguez, I. 2008.
482 Organophosphorus flame retardants and plasticizers in water and air II. Analytical
483 methodology. *TrAC-Trend Anal Chem* 2008; 27:904-15.

484 Reemtsma, T.; Quintana, J.B.; Rodil, R.; Garcı A-López, M.; Rodrı Guez, I. 2008.
485 Organophosphorus flame retardants and plasticizers in water and air I.
486 Occurrence and fate. *TrAC-Trend Anal Chem* 2008; 27:727-37.

487 Rodil, R.; Quintana, J.B.; Concha-Graña, E.; López-Mahía, P.; Muniategui-Lorenzo,
488 S.; Prada-Rodríguez, D. 2012. Emerging pollutants in sewage, surface and
489 drinking water in Galicia (NW Spain). *Chemosphere* 2012; 86:1040-9.

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

492 Salamova, A.; Ma, Y.; Venier, M.; Hites, R.A.; 2014. High Levels of
493 Organophosphate Flame Retardants in the Great Lakes Atmosphere. *Environ Sci*
494 *Technol Lett* 2014; 1:8-14.

495 Schaider, L.A.; Rudel, R.A.; Ackerman, J.M.; Dunagan, S.C.; Brody, J.G. 2014.
496 Pharmaceuticals, perfluorosurfactants, and other organic wastewater compounds
497 in public drinking water wells in a shallow sand and gravel aquifer. *Sci Total*
498 *Environ* 2014; 468-469:384-93.

499 Shi, W.; Zhang, F.; Zhang, X.; Su, G.; Wei, S.; Liu, H., et al.; 2011. Identification of
500 trace organic pollutants in freshwater sources in Eastern China and estimation of
501 their associated human health risks. *Ecotoxicology* 2011; 20:1099-106.

502 Stapleton, H.M.; Sharma, S.; Getzinger, G.; Ferguson, P.L.; Gabriel, M.; Webster,
503 T.F., et al. 2012. Novel and High Volume Use Flame Retardants in US Couches
504 Reflective of the 2005 PentaBDE Phase Out. *Environ Sci Technol* 2012;
505 46:13432-9.

506 Stepien, D.K.; Regnery, J.; Merz, C.; Püttmann, W. 2013. Behavior of
507 organophosphates and hydrophilic ethers during bank filtration and their potential
508 application as organic tracers. A field study from the Oderbruch, Germany. *Sci*
509 *Total Environ* 2013; 458-460:150-9.

510 Sundkvist, A.M.; Olofsson, U.; Haglund, P. 2010. Organophosphorus flame retardants
511 and plasticizers in marine and fresh water biota and in human milk. *J Environ*
512 *Monitor* 2010; 12:943-51.

513 USEPA. 2005. Environmental profiles of chemical flame-retardant alternatives for
514 low-density polyurethane foam. (Accessed Dec. 9, 2014).

515 USEPA. 2013a. Toxic substances control act (TSCA) work plan and action plan: risk
516 assessments and data collection activities. (Accessed Oct. 10, 2013).
517 http://www.epa.gov/oppt/existingchemicals/pubs/assessment_chemicals_list.html

518 USEPA. 2013b. Mid Atlantic risk assessment. Regional screening level (RSL)
519 summary table. Washington DC. 2013.

520 Van den Eede, N.; Dirtu, A.C.; Neels, H.; Covaci, A. 2011. Analytical developments
521 and preliminary assessment of human exposure to organophosphate flame
522 retardants from indoor dust. *Environ Int* 2011; 37:454-61.

523 Van den Eede, N.; Neels, H.; Jorens, P.G.; Covaci, A. 2013. Analysis of
524 organophosphate flame retardant diester metabolites in human urine by liquid
525 chromatography electrospray ionisation tandem mass spectrometry. *J Chromatogr*
526 *A* 2013; 1303:48-53.

527 Van der Veen, I.; de Boer, J. 2012. Phosphorus flame retardants: Properties,

528 production, environmental occurrence, toxicity and analysis. *Chemosphere* 2012;
529 88: 1119-53.

530 Wang, X.; He, Y.; Lin, L.; Zeng, F.; Luan, T. 2014. Application of fully automatic
531 hollow fiber liquid phase microextraction to assess the distribution of
532 organophosphate esters in the Pearl River Estuaries. *Sci Total Environ* 2014;
533 470-471:263-9.

534 Wang, X.; Liu, J.; Yin, Y. 2011. Development of an ultra-high-performance liquid
535 chromatography– tandem mass spectrometry method for high throughput
536 determination of organophosphorus flame retardants in environmental water. *J*
537 *Chromatogr A* 2011; 1218:6705-11.

538 Wei, G.; Li, D.; Zhuo, M.; Liao, Y.; Xie, Z.; Guo, T., et al. 2015. Organophosphorus
539 flame retardants and plasticizers: Sources, occurrence, toxicity and human
540 exposure. *Environ Pollut* 2015; 196:29-46.

541 Wensing, M.; Uhde, E.; Salthammer, T. 2005. Plastics additives in the indoor
542 environment-flame retardants and plasticizers. *Sci Total Environ* 2005;
543 339:19-40.

544 WHO. 1998. Environmental Health Criteria 209: Flame retardants: Tris(chloropropyl)
545 phosphate and tris(2-chloroethyl) phosphate. World Health Organization: Geneva,
546 Switzerland.

547 Yang, F.; Ding, J.; Huang, W.; Xie, W.; Liu, W. 2014. Particle Size-Specific
548 Distributions and Preliminary Exposure Assessments of Organophosphate Flame
549 Retardants in Office Air Particulate Matter. *Environ Sci Technol* 2014; 48:63-70.

550 Table 1. Detection frequency (DF, %) and concentration range (ng/L) of OPEs in different drinking water.

551

	Bottled water		Barreled water		Direct drinking water		Tap water		Well water	
	DF	Range (median)	DF	Range (median)	DF	Range (median)	DF	Range (median)	DF	Range (median)
TEP	100	0.0-0.8 (0.1)	100	0.2-8.0 (2.3)	100	0.8-96.9 (30.2)	100	13.0-124 (50.2)	100	0.1-4.1 (0.3)
TnPP	4.4	nd-0.2 (nd)	5.3	nd-0.0 (nd)	5.6	nd-0.0 (nd)	33.3	nd-0.2 (nd)	22.2	nd-0.0 (nd)
TnBP	91.3	nd-0.4 (0.1)	73.7	nd-1.6 (0.1)	100	0.2-6.6 (0.9)	100	3.9-76.3 (9.5)	100	0.1-0.4 (0.2)
TCEP	100	0.1-5.9 (0.5)	100	0.2-44.2 (6.9)	100	1.9-48.5 (9.1)	100	28.5-139 (48.5)	100	0.1-3.5 (0.5)
TCPP	95.7	nd-3.6 (0.6)	94.7	nd-48.5 (8.0)	100	1.6-26.5 (6.7)	100	21.5-109 (43.0)	100	1.3-3.8 (2.5)
TPhP	100	0.3-2.1 (0.8)	100	0.0-0.9 (0.2)	100	0.0-1.8 (0.2)	100	0.3-4.0 (1.4)	100	0.0-0.5 (0.2)
TCrP	30.4	nd-0.2 (nd)	15.8	nd-0.1 (nd)	27.8	nd-0.6 (nd)	85.7	nd-0.8 (0.3)	94.4	nd-0.3 (0.1)
TBEP	91.3	nd-2.1 (0.2)	36.8	na-0.3 (nd)	94.4	nd-5.3 (0.3)	100	1.4-6.6 (3.7)	100	0.0-0.6 (0.2)
TDCIPP	91.3	nd-4.0 (0.6)	84.2	nd-7.0 (0.5)	77.8	nd-6.6 (0.5)	100	5.4-6.8 (5.8)	72.2	nd-1.1 (0.1)
ΣOPEs		0.9-11.2 (4.0)		1.5-71.9 (27.6)		17.2-126 (59.2)		123-338 (192)		2.5-8.4 (4.5)

552

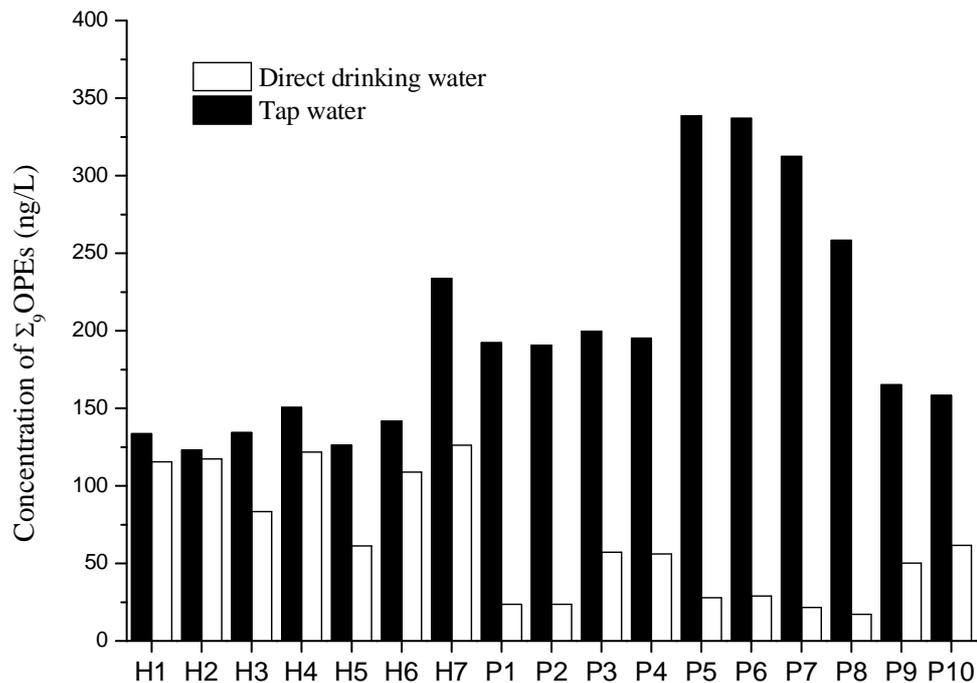
553 Table 2. Average daily doses (ng/kg bw/day) of total OPEs via ingestion of different
 554 types of drinking water in two exposure scenarios.

555

	adult ^a				child ^b			
	man		woman		boy		girl	
	average	high	average	high	average	high	average	high
Tap water	7.07	11.56	6.06	9.91	6.95	11.37	6.80	11.13
Well water	0.17	0.27	0.14	0.23	0.16	0.27	0.16	0.26
Direct drinking water	2.22	4.20	1.91	3.60	2.19	4.13	2.14	4.04
Bottled water	0.16	0.35	0.14	0.30	0.16	0.34	0.15	0.33
Barreled water	1.06	2.14	0.91	1.83	1.05	2.10	1.02	2.06

556 a: exposure factor values were from Exposure Factors Handbook of Chinese Population;

557 b: exposure factor values were from Shi et al.³⁸



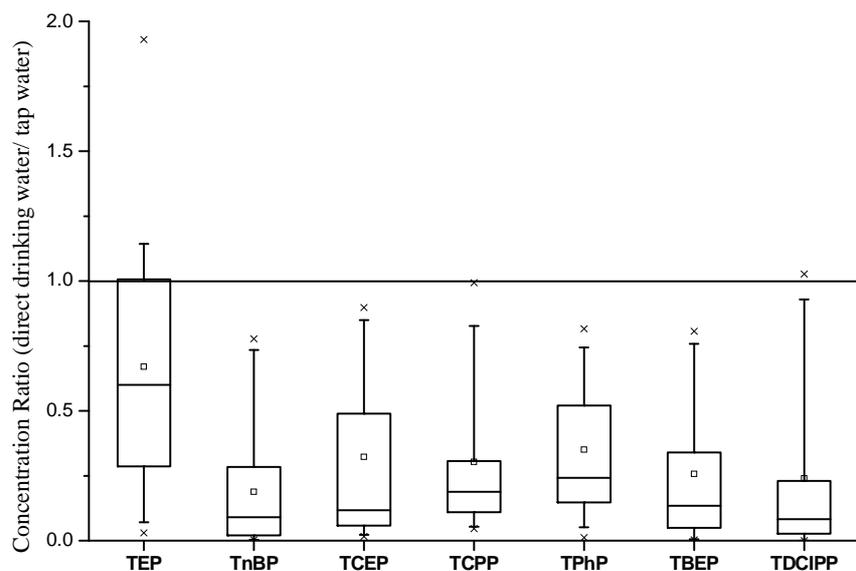
558

559 Figure 1. Comparison of Σ OPEs in paired direct drinking water and tap water samples.

560 H1-H7 standards for direct drinking water which was produced by household filtering

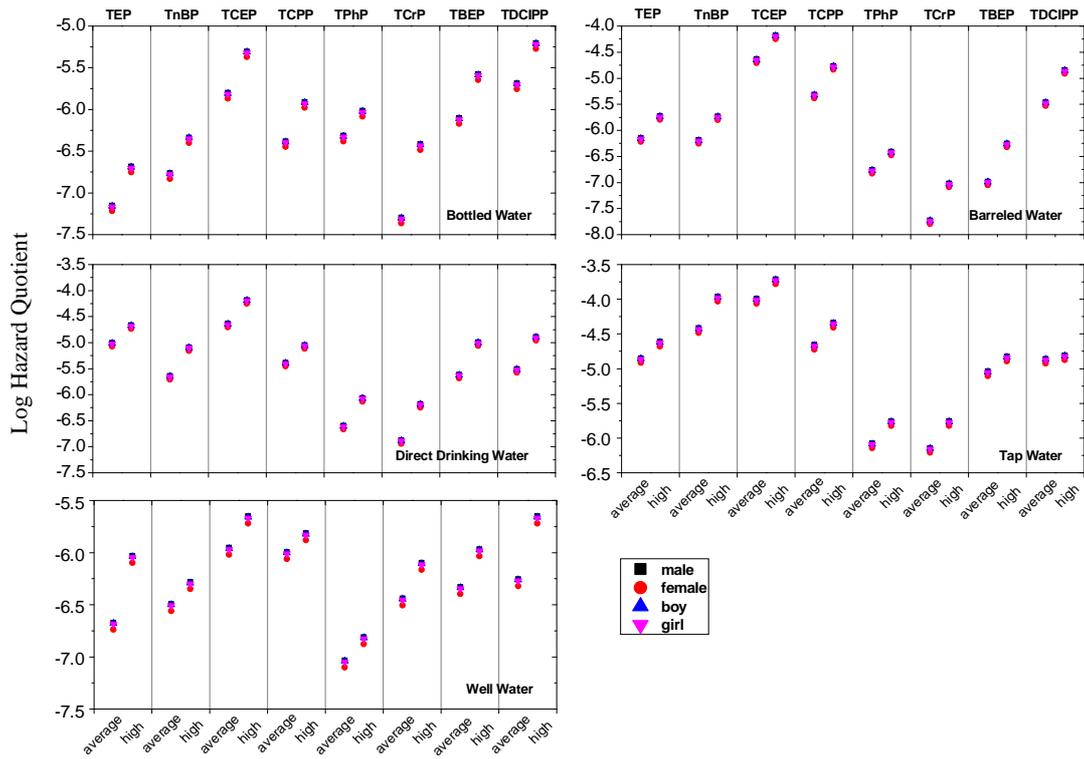
561 apparatuses while P1-P10 produced by public purifying machines. See details in

562 Supporting Information.



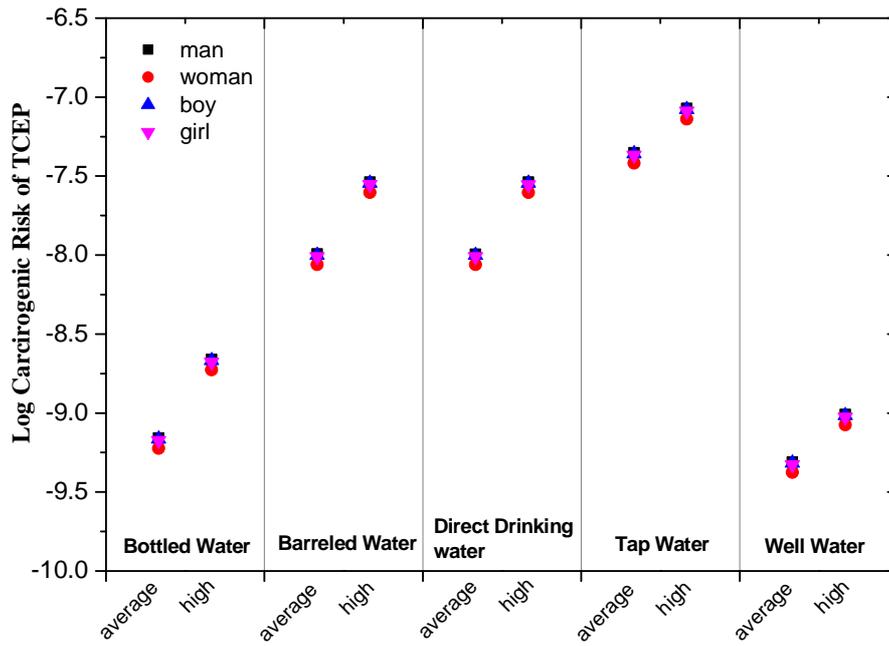
563

564 Figure 2. Comparison of OPE concentrations in paired direct drinking water and tap
 565 water samples. The data are reported as a box/whiskers plot, where the upper, middle,
 566 and lower levels of the box represent the 75th, 50th, and 25th percentiles and the
 567 whiskers represent the 90th and 10th percentile. □ stands for mean value and ×
 568 stands for maximum and minimum value.



569

570 Figure 3. Non-cancer risks of OPEs via different drinking water types.



571

572 Figure 4. Carcinogenic risks posed by TCEP via different types of drinking water.