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Abstract

Workers involved in the processing of electronic waste (e-waste) are potentially exposed to toxic chemicals, including phthalates and alternative plasticizers (APs). Dismantling and shredding of e-waste may lead to the production of dust that contains these plasticizers. The aim of this study, which was part of the European Human Biomonitoring Initiative (HBM4EU), was to assess the exposure to phthalates (e.g. di-(2-ethylhexyl) phthalate (DEHP), diethyl phthalate (DEP), di-butyl phthalate (DBP), butyl-benzyl phthalate (BBzP), di-isononyl phthalate (DiNP), di-isodecyl phthalate (DiDP) and cyclohexane-1,2-dicarboxylic di-isononyl ester (DINCH) in e-waste workers from ten European companies. This was achieved by (i) analysing urine samples from 106 e-waste workers collected at the beginning and at the end of the work week, (ii) comparing these with urine samples from 63 non-occupationally exposed controls, and (iii) analysing settled floor dust collected in e-waste premises. Significantly higher urinary concentrations of seven out of thirteen phthalates and DINCH metabolites were found in the e-waste workers compared to the control population. However, no significant differences were found between pre- and post- shift concentrations in the e-waste workers. Concentrations of DBP, DEHP and DiDP in dust were weakly to moderately positively correlated with their corresponding urinary metabolite concentrations in the e-waste workers (Spearman's ρ= 0.4, 0.3 and 0.2, respectively). Additionally, significantly lower urinary concentrations of nine phthalates and DINCH metabolites were found in e-waste workers using respiratory protective equipment (RPE) during their work activities, reflecting the potential benefits of RPE to prevent occupational exposure to phthalates and DINCH. The estimated daily intake (EDI) values obtained in this study were lower than the corresponding tolerable daily intake (TDI) adopted by the European Food Safety Authority (EFSA) for the general population, suggesting that the risk for negative health consequences in this population of e-waste workers from exposure to phthalates and DINCH is expected to be low. This was confirmed by the urinary metabolite concentrations of all workers being lower than the HBM4EU guidance values derived for the occupational exposed and general population. This study is one of the first to address the occupational exposure to phthalates and DINCH in Europe in e-waste dismantling workers, combining a human biomonitoring approach with analysis of settled indoor dust.

Keywords

- Plasticizers
- Occupational exposure
- Human biomonitoring
- E-waste
- Indoor dust
- Human risk assessment

Highlights

- Urine biomonitoring suggests higher exposure in e-waste workers compared to controls
- Use of respiratory protective equipment resulted in significantly reduced exposure
- A weak to moderate indication that floor dust contributes to exposure was found
- Highest concentrations in dust from e-waste facilities were found for DEHP and DiNP

Abbreviations

ACN	Acetonitrile
APs	Alternative plasticizers
ASE	Accelerated solvent extraction
BBzP	Butyl-benzyl phthalate
BMI	Body mass index
CLP	Classification Labelling and Packaging
DEHP	Di-(2-ethylhexyl) phthalate
DEP	Di-ethyl phthalate
DBP	Di-butyl phthalate
DF	Detection frequency
DI	Daily intake
DiDP	Di-isodecyl phthalate
DINCH	Cyclohexane-1,2-dicarboxylic di-isononyl ester
DiNP	Di-isononyl phthalate
dMRM	Dynamic multiple reaction monitoring
ECHA	European Chemicals Agency
EDC	Endocrine disrupting chemical
EDI	Estimated daily intake
EEE	Electronics and electronical equipment
EFSA	European Food Safety Authority
ESI	Electrospray ionization
E-waste	Electronic waste
GC-MS	Gas chromatography–mass spectrometry
G-EQUAS	German External Quality Assessment Scheme
GV	Guidance values
HBM4EU	Human Biomonitoring for the European Union
IS	Internal standard
LC-MS	Liquid chromatography – mass spectrometry
LOQ	Limit of quantification
MBzP	Mono-benzyl phthalate
MEP	Mono-ethyl phthalate
MEHP	Mono-(2-ethylhexyl) phthalate
5OH-MEHP	Mono-(2-ethyl-5-hydroxyhexyl) phthalate
5oxo-MEHP	Mono-(2-ethyl-5-oxohexyl) phthalate
5Cx-MEPP	Mono-(2-ethyl-5-carboxypentyl) phthalate
MeOH	Methanol
MiBP	Mono-iso-butyl phthalate
MSD	Mass Spectrometer Single Quadrupole
OH-MiDP	Mono-hydroxy-isodecyl phthalate
Cx-MiOP	Mono-carboxy-isooctyl phthalate
Cx-MINCH	Cyclohexane-1,2-dicarboxylate-mono(7-carboxylate-4-methyl) heptylester
OH-MINCH	Cyclohexane-1,2-dicarboxylate-mono(7-hydroxy-4-methyl) octylester
Cx-MiNP	Mono-carboxy-isononyl phthalate
MnBP	Mono-n-butyl phthalate
PPE	Personal protective equipment
QA	Quality assurance
QC	Quality control
REACH	Registration, Evaluation, Authorization, and Restriction of Chemicals regulation
RMMs	Risk management measures
RPE	Respiratory protective equipment
RSD	Relative standard deviation
TDI	Tolerable daily intake
UPW	Ultrapure water
UV	Urinary volume

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Study approval

The study was conducted in accordance with the Declaration of Helsinki. Study protocols have been approved by ethical review boards in each of the participating countries, with the approvals granted before recruiting the study participants. The ethical boards reviewing and approving the study are as follows: For Belgium, the Ethics Committee Research UZ/KU Leuven, approved on 8th of October 2020 (Reference number: S64321). For the Netherlands, the CMO Regio Arnhem-Nijmegen, approved on 20th of January 2021 (Reference number: 2020-7089; National registry: NL67044.091.18). For Luxembourg, the National Research Ethics Committee, approved on the 4th of August 2021, and the Ministry of Health approved on 17th of November 2021 (Reference number: 83bx30c66). For Latvia, Rīga Stradiņš University Research Ethics Committee, approved on 14th of April 2021 (Reference number: 22-2/250/2021). For Finland, Coordinating Ethics Committee, HUS Joint Authority, approved on 2nd of June 2021 (Reference number: HUS/1357/2021). For Portugal, Ethical Committee of the National Institute of Health Dr. Ricardo Jorge (Ethics Committee for Health, INSA), approved on 13th of March 2020, and Ethical Committee of the Lisbon School of Health Technology, approved on 22nd of September 2021.

Introduction

Phthalates and alternative plasticizers (APs) are widely incorporated in materials to enhance their flexibility and durability. They are found in many everyday products such as flooring, wires and cables, medical equipment, cosmetics, food packaging, children's toys etc. (1–3). As these plasticizers are not covalently bonded to the products, they can easily leach out of their source materials into the environment (4). Phthalate plasticizers (including di-(2-ethylhexyl) phthalate (DEHP), di-ethyl phthalate (DEP), dibutyl phthalate (DBP) and butyl-benzyl phthalate (BBzP)) have been considered as hazardous compounds due to numerous reports on toxicological effects, including endocrine disruption, carcinogenicity and developmental defects (4–6). Additionally, they have been associated with type II diabetes, obesity, allergies and asthma and interference with neurological development in children (7,8). These reports raised increasing concerns regarding human health risks due to phthalate exposure, which led to global regulations to limit the use of phthalates in consumer products and decrease human exposure (9,10). DEHP, DBP, DiBP and BBzP have been classified as reproductive toxicants in category 1B under the Annex VI to the European Classification, Labelling and Packaging (CLP) regulation. This has led to the addition of these phthalates to the list of substances of very high concern (Annex XIV EC, 1907/2006) in the EU, and are therefore subjected to authorization under the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) regulation. In addition, in July 2020, the restriction of these phthalates in a wide range of products with concentrations greater than or equal to 0.1% in the European Union was implemented (11).

As a result of the efforts to restrict the use of these reproductive toxic phthalates, novel compounds were introduced as substitutes. This class of alternative plasticizers includes chemicals with a phthalate backbone but altered sidechains, such as di-isononyl phthalate (DiNP) and di-isodecyl phthalate (DiDP), and compounds with a non-phthalate backbone including adipates, benzoates, phosphate esters, citrates, sebacates, terephthalates, trimellitates and cyclohexane dicarboxylic acids (i.e. cyclohexane-1,2-dicarboxylic di-isononyl ester (DINCH)) (3). However, also phthalates in this newer class have been associated with endocrine disruption, leading to their restriction in i.e. children's toys and other consumer products in the European Union (12,13). In this study, DEHP, DEP, DBP and BBzP were grouped as phthalates, while DiNP, DiDP and DINCH were grouped as APs.

Due to the widespread exposure to phthalates and DINCH, their metabolites are frequently analysed in human biomonitoring studies. Pharmacokinetic studies show a fast excretion of these compounds from the human body, with a half-life of less than 24 h (14,15). Phthalates and DINCH are mainly excreted as conjugated monoesters, and can undergo secondary metabolism, including oxidative transformation, prior to urinary excretion (14). The presence of these primary and secondary metabolites in urine has been widely reported in multiple studies to assess human exposure to phthalates and DINCH (16,17).

Due to the increasing use of newer APs, the number of studies investigating their presence in environmental matrices increased over the recent years (2,3). As we spend most time indoors, the indoor environment has been recognized as an important source of (industrial) chemicals such as plasticizers (18). Indoor dust is one of the main sources of human exposure to plasticizers, and multiple studies have reported high phthalates and DINCH levels in indoor dust (18–20). Previous studies have suggested correlations between phthalates concentrations in indoor dust and asthma and allergy symptoms in children (19,21,22).

Multiple studies have investigated the occupational exposure to phthalates and, to a smaller extent, APs in the e-waste dismantling sector (23). Zhang et al. (2019) (24) showed significantly higher urinary concentrations of five phthalate metabolites in participants living in e-waste dismantling sites compared to a non-industrial area in Southern China. Moreover, some biomonitoring studies have been performed to study reproductive or endocrine disrupting effects in highly exposed polyvinylchloride workers, suggesting the possible negative health outcomes of exposure to these compounds (25,26). However, the studies evaluating exposure to phthalates were mostly located in different parts of Asia, with very few studies addressing occupational exposure in the e-waste sector in Europe (23). Moreover, there is a lack in uniform approaches which could facilitate comparisons between studies, as for now experimental designs still differ largely. Additionally, new phthalates and APs should be included to further assess the human exposure to these compounds in occupational settings (27).

The primary objectives of this study were (i) to compare the exposure level of phthalates and DINCH of e-waste workers to a control population, to investigate further the differences between pre-shift and post-shift samples, and additionally evaluate if the exposure levels are different amongst e-waste workers performing different tasks and activities, (ii) to investigate the correlations between the concentrations of phthalates and DINCH in urine and the corresponding indoor dust samples from working environments, and (iii) to assess how the daily intake estimated from both internal and external exposure compare with available tolerable daily intake (TDI) adopted by the European Food Safety Authority (EFSA) for use in food contact materials (28,29). Additionally, urinary metabolite concentrations will be compared to guidance values (GV) determined by the European Human Biomonitoring Initiative (HBM4EU) for the exposure to phthalates and DINCH in the general population and the occupationally exposed population (30).

Materials and methods

Study population

This exploratory study on occupational exposure to hazardous chemicals from e-waste processing was part of the HBM4EU Initiative. A detailed study protocol and further information regarding HBM4EU Legal and Ethics Policy has been previously published (27,31). The target population consisted of 106 e-waste workers and a control population of 63 participants which were recruited from ten companies in six European countries namely Belgium, the Netherlands, Luxembourg, Portugal, Finland, and Latvia. These companies were involved in various e-waste processing activities, including sorting, dismantling, shredding, and pre-processing of metal and non-metal components.

Additional information on the e-waste workers was collected using questionnaires including personal information, such as sex, age, body weight, height, smoking, home location (rural/urban) and the presence of industrials plants, incinerators or landfill sites within a radius of 10 km from the home location. The recruitment of the companies and workers was performed after following the dedicated SOP for the selection of participants, recruitment, informing participants and obtaining informed consent (Scheepers et al (27)). Common information leaflets and informed consent forms were developed and translated in the national languages. Study protocols were submitted for approval by ethics review boards in each of the participating countries with the approvals being granted before recruiting the study participants. Detailed demographic information and details on the questionnaires can be found in Supplementary Information A and B, respectively.

E-waste workers were qualified to participate in the study if they were involved in one or more of the following activities: 1) sorting e-waste from household or industrial sources either manually or in a semi-automatic way, 2) dismantling electronic components, 3) shredding and pre-processing, and 4) recycling of electronic components to recover precious metals or obtain granulated plastic for further processing, re-use or resale. Five subcategories of e-waste workers were set based on the type of electronic waste they came into contact with most often during their work shifts. These subcategories included batteries, white goods (refrigerators, washing machines, microwaves, etc.), brown goods (televisions, radios, computers, cell phones, etc.), metals and plastics, and miscellaneous e-waste (AC adapters, keyboards, computer mice, etc.). The control population consisted of individuals from the same geographical area, but neither involved in e-waste processing nor in activities with known occupational exposure to emissions from e-waste processing activities. Moreover, the control group was subdivided into two categories based on the occupation of the subjects: controls working in the same companies e.g., working in offices and performing administrative tasks on the same industrial site as the exposure workers, but have no known exposure to emissions from e-waste processing ("within" the e-waste industry), and those who worked in industries not associated with e-waste processing, such as healthcare, technology, research and development, among others ("outwith" control).

Sample collection

In total, 212 and 63 urine samples were collected from 106 e-waste workers and 63 control group participants, respectively. Detailed sampling strategy is described by Scheepers et al. (2021)(27). Briefly, the first sample represents the baseline (after 48 h off work) and was collected before the start of the first shift on the first day of the workweek (pre-shift). The second sample (post-shift) reflects the contribution of the exposure during the workweek and was collected immediately after the end of the shift towards the end of the workweek. For the participants in the control group (n=63), only one pre-shift urine sample was collected to assess a baseline level in a comparable group of workers with no known exposure as a reference. All urine samples were transported on dry ice to the Toxicological Centre (University of Antwerp, Belgium) and stored at -20°C prior to analysis. General information about the participants including age, gender, height, body weight, and their work tasks was obtained through three detailed questionnaires (Supplementary Information B).

Settled dust samples (n=43) were collected from the ten companies according to the protocol described by Scheepers et al. (2021) (27), towards the end of a given work shift using a University Products Museum-Vac type 561-1997 vacuum cleaner (Adams, MA, USA). Dust samples were taken from premises of the participating e-waste processing facilities where workers perform most of the e-waste related activities. To avoid cross contamination, the vacuum crevice head tool was first thoroughly cleaned with isopropyl alcohol and dry paper towels. HEPA filter bags were pre-weighted prior to field visit. To collect enough dust, one m^2 of bare floor was vacuumed cleaned for 2 min. If the collected sample amount was insufficient, additional areas were included for further sampling. If more than one exposure group was identified in the participating e-waste processing facility involved in performing different tasks, additional samples were collected. After collection, settled dust samples were kept at room temperature and protected from light in a clean box until transportation to the Laboratoire National de Santé (Luxemburg) for analysis.

Chemicals and reagents

Detailed descriptions of the chemicals and materials used in this study are reported in the Supplementary Information C.

Sample preparation

Urine samples were analysed according to the methodology previously described and validated at the Toxicological Centre (Dirtu et al., 2013; Been et al., 2019). One mL of urine was added to a clean glass tube and spiked with 50 µL of internal standard (IS) solution (25 ng for phthalate metabolites, 5 ng for APs metabolites). To ensure complete deconjugation of the targeted metabolites, 25 µL of β-glucuronidase (from *E. coli* powder (Supelco), 2 mg/mL in phosphate buffer) and 1 mL of phosphate buffer solution (pH 6) were added to the sample and the mixture was incubated at 37 °C for 90 min. Analytes were extracted using Oasis MAX cartridges (30 mg, 3 mL, Waters, Milford, MA, USA) previously conditioned with 3 mL of dichloromethane, 3 mL of methanol (MeOH) and 3 mL of MilliQ water. Afterwards, the sorbent was washed with 3 mL of MilliQ water containing 5% ammonium hydroxide followed by 1 mL MilliQ water and then dried under vacuum for 30 min. Elution was performed using 8 mL of MeOH containing 2% formic acid. The eluate was evaporated to near dryness, reconstituted in 100 µL of acetonitrile (ACN):MilliQ water (1:1 V:V) and filtered over a 0.20 µm filter prior to instrumental analysis.

Dust samples were weighed and sieved with a Retsch AS 200 digit vibratory sieve shaker in order to analyse only the fine fraction (< 63 µm). For 9 out of the 43 samples, the amount of dust < 63 µm was not sufficient for determination, and the fraction < 2 mm was then selected. After sieving, 100 mg of fine fraction dust sample was weighed in ASE cell filled with diatomaceous earth, spiked with a mixture of deuterated analogues (1 µg of DEP-D4, DBP-D4, BzBP-D4 and 10 µg of DEHP-D4) and submitted to accelerated solvent extraction with n-hexane/acetone (90:10, v/v). The extract collected was then evaporated at 40 °C under N_2 flow to reduce and adjust the final extract volume to 1 mL (transfer and adjustment in a 1-mL graduated amber flask with ethyl acetate). It was transferred in a 2-mL amber glass vial for injection into the gas chromatography–mass spectrometry (GC-MS) system.

Instrumental analysis

Analysis of targeted phthalate metabolites was carried out using an Agilent 1290 Infinity liquid chromatography system coupled to an Agilent 6460 Triple Quadrupole mass spectrometer (LC-MS/MS, Agilent, Santa Clara, USA) equipped with an electrospray ionization source in negative mode (ESI-). Analysis of targeted APs metabolites was carried out using an Agilent 1290 Infinity liquid chromatography system coupled to an Agilent 6495 Triple Quadrupole mass spectrometer (LC-MS/MS, Agilent, Santa Clara, USA) equipped with an electrospray ionization source in negative mode (ESI-). The separation of the targeted metabolites was achieved using a Phenomenex Kinetex Biphenyl column (2.1 × 100 mm, 2.6 µm, Phenomenex, Torrance, USA) using MilliQ water (A) and ACN (B), both containing 0.1% acetic acid, as mobile phase. The acquisition was carried out in dynamic multiple reaction monitoring (dMRM). Quantification of target metabolites was performed using multi-level calibration curves ranging from 0.1 ng to 125 ng for phthalate metabolites and 0.05 ng to 25 ng for APs metabolites.

The dust analysis was performed with an Agilent 7890 gas chromatograph equipped with a HP-5MS UI capillary column (30 m, 0.25 mm I.D., 0.25 µm film thickness) and an ALS 7683 autosampler, coupled to an Agilent 5975C InertXL Mass Spectrometer Single Quadrupole (MSD).

Method details are described in the Supplementary Information D.

Quality assurance (QA) and quality control (QC)

The internal QA and QC for urine analysis was performed by regular analyses of procedural blanks (minimum one blank per batch of 20 samples) and spiked samples (10 ng/mL). Additionally, solvent blanks and spiked samples were injected regularly throughout the instrumental run. Procedural blank concentrations were analysed to check the background contamination potentially coming from plastic containers and the laboratory environment. Blank values were subtracted from metabolite concentrations in samples. Limits of quantification (LOQs) were calculated as the concentration corresponding to a signal-to-noise ratio of 10 in low-level QC samples. The external quality control was assured through successful participation to inter-laboratory comparison exercises German External Quality Assessment Scheme (G-EQUAS) and Human Biomonitoring for Europe External Quality Assurance Scheme (HBM4EU ICI/EQUAS). Further details of the QC parameters and results are presented in Supplementary Information E.

Statistical analysis

Statistical analysis was performed for compounds with detection frequencies (DFs) greater than 60%. The urinary concentrations of targeted analytes were corrected by individual urinary creatinine (crea) concentration. Concentrations below the LOQ were substituted with 1/2 of respective LOQ (medium bound approach). Because targeted compounds in both dust and urine in this study did not show normal distribution according to Kolmogorov Smirnov test, nonparametric tests were selected for univariate analyses. To test the disparities among concentrations between categories or groups, Mann-Whitney U tests or Kruskal-Wallis tests were used. For each worker, a rank was calculated from the pre- and post-shift urinary metabolite concentrations that was subsequently used in a Wilcoxon test. The possible correlation between urinary metabolite concentrations in e-waste workers and their representative settled dust concentrations was analysed using Spearman's rank correlation test. Comparison of the estimated daily intake (EDI) values between control and pre- or post-shift was done using Wilcoxon test. Statistical significance was set at $p < 0.05$ throughout the study. All statistical tests are applied using SPSS Statistics 28.0.0.0 software (IBM, Inc., Chicago, IL, USA).

Estimated daily intake (EDI)

The EDI of phthalates and APs from e-waste workers was calculated in two ways (i) through the concentrations of the parent compounds in dust samples of the working environment (ii) through the urinary metabolite concentrations in the e-waste workers, reflecting the total exposure to phthalates and APs. In this way it is possible to estimate the contribution of exposure to plasticizers through dust ingestion in e-waste workers.

The EDI through the ingestion of dust (EDI_{dust}) was calculated based on previous publications of Ait Bamai et al. (2016)(21), Kasper-Sonnenberg et al. (2019)(32), Christia et al. (2021)(33) and Li et al. (2020)(34). This resulted in one EDI_{dust} value for every e-waste worker, based on the mean dust concentration of their working environment.

$$EDI_{dust}\ [ng/kg/day] = \frac{C\ dust\ [ng/g] \times Ba \times m\ ingest\ dust\ [g/day]\ x\ EF}{BW\ [kg]}$$

with Ba the theoretical bioaccessibility, assumed to be 0.8 in case of an octanol water partition coefficient (LogKow) < 5, and 0.2 in case of $LogK_{ow} > 8$ (Dong et al. (2019)(35) and Christia et al. (2021)(36)); $m_{ingest\ dust}$ as the daily dust ingestion rate, which was assumed to be 0.060 g

per day for occupational workers (Li et al., 2020)(34)); BW as body weight of worker in kg and EF as the exposure fraction (hours spent in a certain environment divided by 24 h). The body weight of the e-waste worker was provided through the questionnaire, as well as the generalised duration of the shifts, which was eight hours (Supplementary Information Table F.1).

The total estimated daily intake (EDI_{urine}) was based on the urinary metabolite concentrations of e-waste workers and controls. This value reflects the total estimated daily intake of phthalates and APs and is based on previous publications by Ait Bamai et al. (2016)(21), Kasper-Sonnenberg et al. (2019)(32) and Hua et al. (2022)(37). This resulted in two EDI_{urine} values for every e-waste worker based on the metabolite concentrations in the pre-shift and post-shift urine samples. Additionally, one EDI_{urine} value was obtained for every participant in the control group.

$$EDI_{urine}\ [ng/kg/day] = \frac{\frac{Cmetabolite\ (ng/L)}{MWm} \times UV\ (L/day) \times MWp}{Body\ weight\ (kg) \times Sum\ Fue}$$

with UV as daily urinary volume, assumed as 1.7 L for men and 1.6 L for women (Hua et al. 2022)(37), MWp as molecular weight of the parent compound, MWm as molecular weight of the metabolite and Fue as percentage of metabolites excreted in urine (Supplementary Information Table F.2).

Based on the median EDI_{dust} and EDI_{urine} values calculated for the e-waste workers, it is possible to estimate the contribution of exposure to phthalates and APs through dust ingestion by using the following formula:

$$\%DI = \frac{EDIdust[ng/kg/day]}{EDIurine[ng/kg/day]} * 100$$

Obtained results were compared with the respective tolerable daily intakes (TDIs) for use in food contact materials established by EFSA in 2019 (28,29).

Results and discussion

In this study, pre- and post-shift urine samples of e-waste dismantling workers and corresponding dust samples from their work environment were collected from ten companies located in six European countries involved in handling of e-waste, namely Belgium, the Netherlands, Luxembourg, Portugal, Finland, and Latvia. A human biomonitoring approach was used in which the concentrations of eight phthalate metabolites (MEP, MnBP, MiBP, MBzP, MEHP, 5OH-MEHP, 5oxo-MEHP, and 5Cx-MEPP) and five metabolites of APs (Cx-MiOP, Cx-MiNP, OH-MiDP, OH-MINCH, and Cx-MINCH) were analysed in urine samples of 106 e-waste workers and 63 controls from six European countries. Additionally, the concentrations of the corresponding parent phthalates (DEP, DBP, BBzP, and DEHP) and APs (DiNP, DiDP and DINCH) were analysed in dust samples collected from the different e-waste dismantling environments.

Concentrations of phthalates and DINCH in urine and dust

Detection frequencies (DF) of all phthalate and DINCH metabolites were > 60% in both the e-waste worker group (pre-shift and post-shift), and control group (only pre-shift)(Table 1). In the e-waste workers, the highest concentrations were found for metabolites of DEP, DnBP and DiBP with median concentrations of 20.0 µg/g creatinine, 14.1 µg/g creatinine and 9.2 µg/g creatinine, respectively. The same trend was observed for the control population, with

concentrations of 12.3 µg/g crea, 7.54 µg/g crea and 6.69 µg/g crea, for DEP, DnBP and DiBP metabolites, respectively. This is followed with median concentrations above 1 µg/g crea for all individual DEHP metabolites, except MEHP, in both groups. The other metabolites (MBzP, MEHP, and metabolites of DiNP, DiDP and DINCH) had median concentrations below 1 µg/g crea in both groups.

The obtained urinary metabolite concentrations are in the same order of magnitude as reported by Wang et al. (2018)(38) who analysed urine samples of 165 workers of an e-waste plastic recycling site and 152 controls in China. Results of Wang et al. (2018)(38) showed mean concentrations of workers vs controls (µg/g creatinine) for MEP (52.3 vs 33.2), MBP (94.8 vs 106), MBzP (1.88 vs 1.30), MEHP (16.6 vs 14.5), 5OH-MEHP (76.1 vs 44.6) and 5oxo-MEHP (12.5 vs 9.3). Especially urinary metabolites of DEHP in the study of Wang et al. (2018) showed higher concentrations compared to the results obtained in this study, which may reflect higher exposure to DEHP in e-waste workers in Asia, due to the less strict policies regarding plasticizers use in EEE.

Table 1 Urinary concentrations of phthalate and DINCH metabolites in pre-shift and post-shift samples of e-waste workers and controls (µg/g creatinine)

Parent com-pounds	Metabo-lites	LOQ	E-waste worker samples (n=212)					Control samples (n=63)				
			DF (%)	25th	Median	75th	Range	DF (%)	25th	Median	75th	Range
DEP	MEP	0.4	100	8.13	20.0	45.2	1.41-1553	100	4.07	12.3	24.5	0.86-485
DnBP	MnBP	0.2	100	6.83	14.1	32.7	1.14-490	100	3.99	7.54	13.6	1.2-138
DiBP	MiBP	0.2	100	5.01	9.17	20.9	<LOQ-144	100	3.41	6.69	11.0	0.53-112
BBzP	MBzP	0.2	89	0.41	0.9	2.42	<LOQ-294	79	0.24	0.64	1.48	<LOQ-35.5
DEHP	MEHP	0.2	90	0.49	1.03	2.14	<LOQ-37.5	88	0.33	0.57	0.95	<LOQ-7.95
	5OH-MEHP	0.2	100	2.33	4.15	7.39	0.37-132	100	1.14	2.48	6.09	0.23-19.5
	5oxo-MEHP	0.2	100	1.55	2.58	4.57	0.32-77.7	97	0.80	1.61	3.59	<LOQ-15.9
	5Cx-MEPP	0.2	100	3.45	5.51	9.71	0.85-171	100	1.36	4.13	6.75	0.39-28.9
DiNP	Cx-MiOP	0.4	60	<LOQ	0.66	2.23	<LOQ-555	62	0.20	0.45	1.63	<LOQ-7.62
DiDP	OH-MiDP	0.2	85	0.3	0.96	2.39	<LOQ-1239	84	0.36	0.64	1.62	<LOQ-6.00
	Cx-MiNP	0.2	78	<LOQ	0.36	0.85	<LOQ-54.8	67	0.10	0.26	0.71	<LOQ-7.39
DINCH	OH-MINCH	0.2	94	0.49	0.89	1.67	<LOQ -471	90	0.42	0.62	1.25	<LOQ-23
	Cx-MINCH	0.2	76	0.2	0.66	1.66	<LOQ -65.5	81	0.20	0.79	2.01	<LOQ-27.3

In total, 43 dust samples from ten e-waste working environments were analysed for concentrations of phthalates and DINCH (Table 2). All compounds were found with a DF > 60%, except for DEP and DINCH. This could be due to the limited use of DEP as plasticizer in electrical devices due to its volatile characteristic. Because of its low molecular weight, DEP is prone to evaporate and is more used as plasticizer in personal care products, such as perfumes (39). The low detection frequency of DINCH could be due to its lower leachability potential from electronic devices compared to other plasticizers, which in turn resulted in lower concentrations found in indoor dust or simply due to its limited use in various products.

In dust from the e-waste facilities, the highest concentrations were found for DEHP and DiNP with median concentration of 105 µg/g dust and 141 µg/g dust, respectively. The predominance of these plasticizers in dust was previously reported by Li et al. (2023)(40), analysing 46 indoor

dust samples collected from five villages located in South China where e-waste dismantling and recycling activities have been conducted for decades, and Shi et al. (2023)(41), analysing 66 indoor dust samples collected from e-waste working facilities located in Central China. However, in both studies lower median concentrations of DEHP and DiNP (21.9 µg/g dust and 7.6 µg/g dust reported by Li et al. (2023), and 98 µg/g dust and 37.3 µg/g dust reported by Shi et al.(2023), respectively) compared to results from this study.

Additionally, median concentrations of phthalates in indoor dust from e-waste dismantling facilities were within the range previously reported by Muenhor et al. (2017)(42). This study analysed indoor and outdoor dust samples from manual e-waste dismantling facilities in Thailand. Both studies report median concentrations for DEP, DBP and BBzP below 10 µg/g dust, and above 100 µg/g dust for DEHP. Although the range of phthalates concentrations in indoor dust is similar, the maximum values of DEP, DBP, BBzP and DEHP were higher in European dust samples (5.0, 35.1, 115 and 5883 µg/g dust, respectively) compared to Thai dust samples (0.7, 8.0, 1.1 and 780 µg/g dust, respectively).

Table 2 Phthalate and DINCH concentrations (µg/g dust) in dust samples from European e-waste working environments

Compound	LOQ	Dust samples (n=40)				
		DF (%)	25th	Median	75th	Range
DEP	1	33	<LOQ	<LOQ	1.35	<LOQ-5.00
DBP	1	78	3.27	7.53	17.7	<LOQ -35.1
BBzP	1	65	0.87	3.83	9.11	<LOQ -115
DEHP	1	97	14.9	105	296	<LOQ-5883
DINCH	0.1	55	<LOQ	5.16	23.0	<LOQ-1303
DiNP	1.5	88	59.0	141	317	<LOQ-6905
DIDP	0.4	85	17.4	47.0	147	<LOQ-1732

E-waste workers vs control population

When comparing post-shift urinary data of the e-waste workers with the control population, significantly higher concentrations were observed in e-waste workers for MEP, MnBP, MiBP, all DEHP metabolites and the molar sum of DEHP and DiDP metabolites. Figure 1 shows a comparison of the concentrations for the molar sum of DEHP metabolites (MEHP + 5OH-MEHP + 5oxo-MEHP + 5Cx-MEPP) between e-waste workers (pre- and post-shift) and the control group. Concentrations of the molar sum of DEHP metabolites in both pre- and post-shift e-waste workers (median: 68 nmol/L and 54 nmol/L, respectively) were significantly higher than the control population (30 nmol/L). This reflects the additional exposure of e-waste workers to DEHP during working activities. An overview of median urinary metabolite concentrations for these three groups (pre- and post-shift, and control) is shown in Table G.1 (Supplementary Information). A high occupational exposure to DEHP in workers from plastic manufacturing workers has also been reported by Petrovicova et al. (2016)(43) with significantly higher urinary concentrations of MEHP, 5OH-MEHP, 5oxo-MEHP, the molar sum of DEHP metabolites, as well as for MiBP, which are in line with the findings of this study.

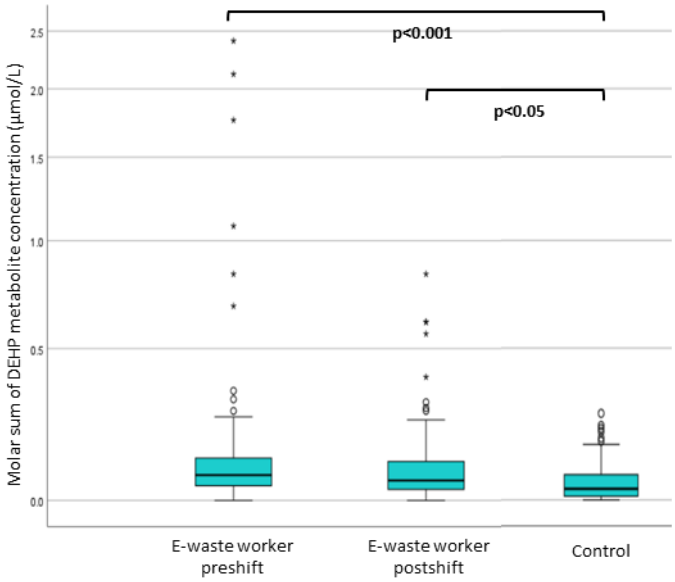

Figure 1 Comparisons of urinary concentrations of molar sum of DEHP metabolites in pre-shift (n=106) and post-shift of e-waste workers (n=106) and control group (n=63) urine samples. Sum of DEHP metabolites = Σ (MEHP + 5OH-MEHP + 5oxo-MEHP + 5Cx-MEPP). The end of the whisker indicates the minimum or maximum value that is not an outlier. The boxplot represents the first quartile, median and third quartile. Mild (>1.5 x interquartile range) and extreme outlier (>3.0 x interquartile range) are represented by circles and asterisks, respectively.

E-waste workers subcategories vs control population

The pre-shift urinary metabolite concentrations of five work subcategories were compared with those of the control population. Five subcategories of e-waste workers were set based on the type of electronic waste they came into contact with most often during their work shifts. These subcategories included batteries, white goods (refrigerators, washing machines, microwaves, etc.), brown goods (televisions, radios, computers, cell phones, etc.), metals and plastics, and miscellaneous e-waste (AC adapters, keyboards, computer mice, etc.).

The urinary concentration of all metabolites, except MEP, Cx-MiOP, OH-MiDP and OH-MINCH, was significantly higher in the e-waste worker group handling metals and plastics than in the control group (Table G.1). Also, battery workers showed significantly higher concentrations of all metabolites compared to the control group, except for MiBP, MnBP, MEHP, and Cx-MINCH. This is followed by workers handling brown goods, where significantly higher concentrations were found for MnBP, MiBP and MBzP in the worker group. It should be noted that e-waste workers handling white goods showed significantly higher urinary concentrations of MEHP, whereas urinary Cx-MiNP and Cx-MINCH concentrations were higher in the control group. This may reflect other exposure sources for these plasticizers, such as personal care products, food contact materials, etc. (44). No significant differences were found between e-waste workers handling miscellaneous e-waste and controls.

E-waste workers pre-shift vs post-shift

By comparing the pre- and post-shift urine samples of the e-waste workers, the contribution of the exposure during the work week could be estimated. It should be noted that, even though e-waste workers are exposed to plasticizers to a higher degree during the work week, significantly higher urinary metabolite concentrations were not always found in the post-shift sample. This is in contrast with previous studies such as Fong et al. (2014)(45) and Fong et al. (2015)(46) for which post-shift levels of all DEHP metabolites showed significantly higher concentrations for all PVC production workers from three facilities in Taiwan. This could be

due to overall low urinary metabolite concentrations found in e-waste workers, which made it difficult to differentiate behind the variation in background exposure. Additionally, peak excretion after the exposure might take place later in the evening of the working day, as described by Porras et al. (2020)(47) analysing urine samples of plastic product manufacturing workers in Finland. However, when the e-waste workers were divided in subcategories, significant differences in the creatinine-normalized concentrations could be seen between pre- and post-shift samples for all urinary metabolites, except for MBzP, Cx-MiOP, Cx-MiNP and Cx-MINCH, for at least one subcategory of e-waste worker (Table G.1). Interpretation of these results should be done with caution, as subcategory groups are smaller.

Parameters influencing exposure in e-waste workers

Associations between post shift urinary metabolite concentrations of phthalates and DINCH in e-waste workers and their demographic information are shown in Table G.1. As for the determinants, sex, age, BMI, smoking, home location (rural/urban) and the presence of industrials plants, incinerators, or landfill sites within a radius of 10 km from the home location were considered. No significant differences were seen based on age, smoking or home location in a rural or urban environment. Significantly higher urinary Cx-MINCH concentrations were found in e-waste workers with a BMI above 30 (median: 1.37 µg/g creatinine) compared to workers with a BMI below 25 (0.44 µg/g creatinine). Additionally, urinary MiBP concentrations were significantly higher in e-waste workers with at least one industrial plant, incinerator, or landfill site within a radius of 10 km from the home location (median: 19.1 µg/g creatinine) than not (5.89 µg/g creatinine).

The influence of the number of years the e-waste workers were active in the e-waste dismantling sector and the use of respiratory protective equipment (RPE) during at least 50% of the work activities is shown in Table G.1. No significant differences in urinary metabolite concentrations were found between e-waste workers working less than 5 years, 6 to 14 years or more than 15 years in the e-waste dismantling sector. However, significantly higher urinary concentrations of MEP, MnBP, MiBP, MBzP, 5OH-MEHP, 5oxo-MEHP, 5Cx-MEPP, Cx-MiNP and Cx-MINCH were found in e-waste workers not wearing RPE in at least 50% of their work activities (Figure 2). This may reflect the higher exposure to phthalates and DINCH of e-waste workers not protected by RPE. These findings are in line with results of Wang et al. (2018)(38) and Fong et al. (2014)(45) which recommended local ventilation systems and personal protection equipment to decrease phthalate exposure in plastic waste recycling workers.

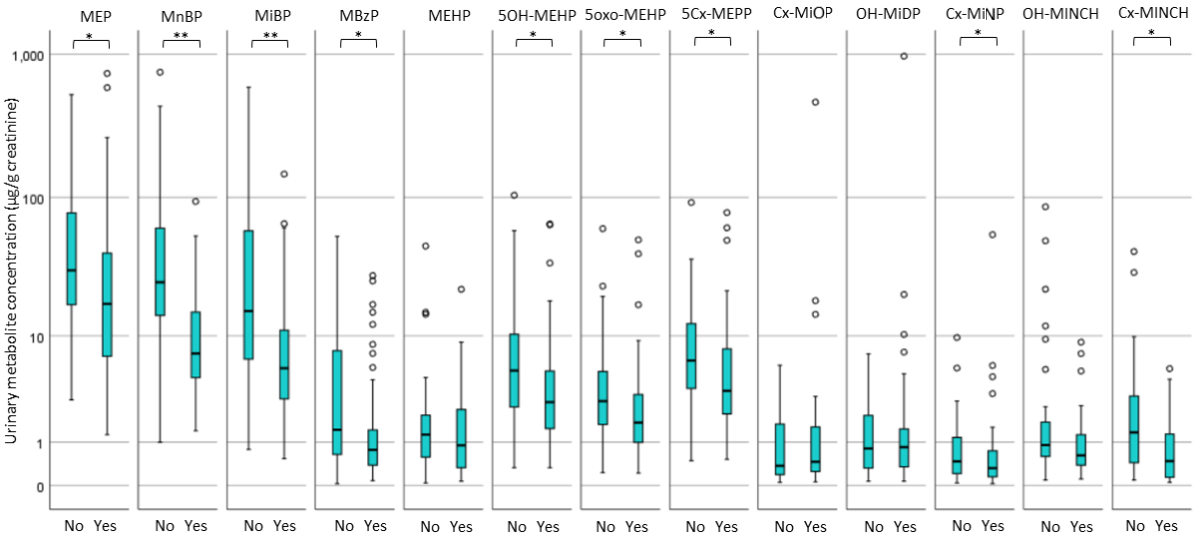

*Figure 2 Urinary metabolite concentrations of phthalate and DINCH metabolites of e-waste workers wearing RPE during at least 50% of their working activities (Yes) compared with workers who do not (No). Mann Whitney U test; * p<0.05 ; ** p<0.001. Use: n=64; No use: n=32. The end of the whisker indicates the minimum or maximum value that is not an outlier. The boxplot represents the first quartile, median and third quartile. Mild (>1.5 x interquartile range) and extreme outlier (>3.0 x interquartile range) are represented by circles.*

Correlation with dust data

An overview of the number of collected settled dust samples per e-waste company, together with the number of participating e-waste employers working at the company are shown in Supplementary Information H. The Spearman's rank correlation test showed a weak, but positive correlation between the urinary metabolite of plasticizer concentrations of e-waste workers and their corresponding concentrations in dust samples of their working environment (Table 5). A significant positive correlation was shown for MiBP with DBP in dust with a Spearman's correlation coefficient of 0.4 (p< 0.001), followed by MEHP, 5Cx-MEPP, MnBP and Cx-MiNP with correlation coefficients between 0.2 and 0.3 (p<0.05) with their correspondent parent compounds in dust. A significant, but weak negative correlation with correlation coefficient -0.3 between settled dust data and urinary metabolite concentrations was shown for Cx-MINCH. Considering that correlations vary between metabolites, and are only weak to moderately strong for a limited number of metabolites, it seems that dust levels did not correlate well with their corresponding urinary metabolite concentrations. This could be due to multiple reasons, for example that human biomonitoring data reflects internal exposure to plasticizers from all sources (personal care products, food contact materials, indoor and outdoor dust,…) and by all routes (ingestion, inhalation, dermal absorption,…) (44). Another plausible reason is the use of PPE, which helped to limit the systemic exposure of plasticizers to this occupationally exposed population.

*Table 5 Spearman's correlation coefficient of urinary metabolite concentrations of plasticizers in e-waste workers (n=106) with their parent compounds levels in dust (n=40) from the correspondent working environment. (PH: phthalates, AP: alternative plasticizers; *: p< 0.05, **: p< 0.01; bold coefficients reflect significant correlations)*

Dust concentration (µg/g dust)	Urinary metabolite concentration (µg/g creatinine)																
	MEP	MnBP	MiBP	MBzP	MEHP	5OH MEHP	5oxo MEHP	5Cx MEPP	ΣDEHP m.	ΣPH m.	OH MINCH	Cx MINCH	Cx MiOP	OH MiDP	Cx MiNP	ΣDIDP m.	Σ APm.
DEP	-0.01																
DBP		**0.21***	**0.41****														
BBzP				-0.19													
DEHP					**0.32****	0.14	0.14	**0.23***	0.17								
ΣPH										0.17							
DINCH											-0.19	**-0.29****					
DiNP													0.10				
DiDP														0.05	**0.21***	0.03	
ΣAP																	0.05

Exposure assessment through estimated daily intake

The distribution of the calculated EDI $_{dust}$ (ng/kg bw/day) and EDI $_{urine}$ (ng/kg bw/day) values are shown in Supplementary Information I. EDI $_{dust}$ values ranged from 1.57 to 69.67 ng/kg/day for

the sum of phthalates and from 3.55 to 90.12 ng/kg bw/day for the sum of APs. Highest EDI_{dust} values were obtained from DEHP, DiNP and DiDP.

EDI_{urine} values ranged from 188 to 132,660 ng/kg bw/day for the sum of phthalates and 110 ng/kg bw/day to 321780 ng/kg bw/day for the sum of alternative plasticizers. Highest EDI_{urine} values were obtained for DEHP, DEP and DBP.

Comparison with results of Zhang et al. (2019)(24) shows lower median EDI_{urine} values for DEP (150 ng/kg bw/day) and DBP (3810 ng/kg bw/day) compared to the medians obtained from this study (1047 and 825 ng/kg bw/day, respectively). However, EDI_{urine} values for DEHP show higher medians in e-waste workers from China as reported by Zhang et al. (2019)(24) compared to European e-waste workers included in this study (2780 vs 563 ng/kg bw/day, respectively).

When comparing EDI_{dust} values of e-waste workers using RPE during at least 50% of their working activities, significantly higher median values were observed for DEP, BBzP, DEHP and the sum of the phthalates and the sum of the APs, in the group which was not protected. This indicates that e-waste workers are exposed to plasticizers during their working activities, such as through dust ingestion due to hand to mouth contact. Risk management measures (RMMs) such as general and local exhaust ventilation, cleaning of the floor and surfaces following standard operating procedures and hygienic measures (i.e. frequently washing of hands and face) could help to reduce this potential occupational exposure. Use of RPE might have complementary benefits to the reduction of plasticizer exposure. However, in this study, other (confounding) factors, which may cause this association, were not considered which is why interpretation of the results should be done with caution.

When comparing the total EDI_{urine} values of the pre-shift worker samples, post-shift worker samples and control samples, significantly higher values were observed in the pre shift e-waste worker group compared to the control group, for all phthalates and APs, except for DINCH (Figure 3).

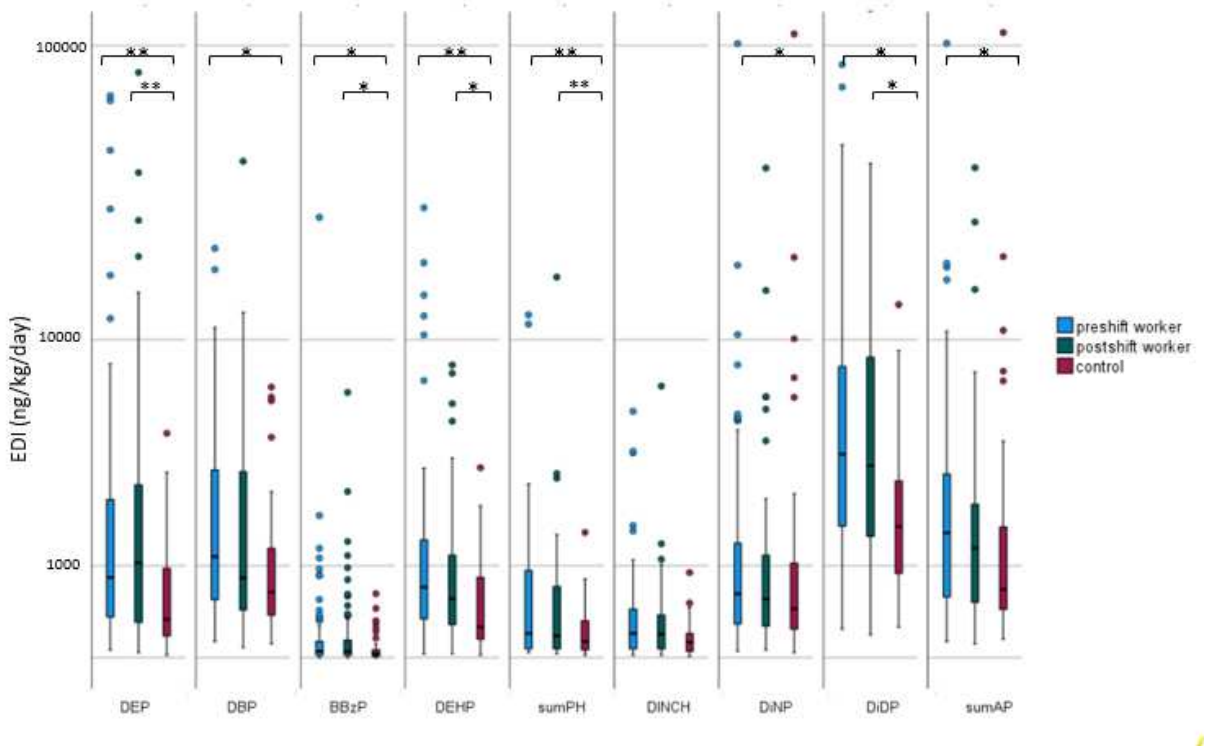

*Figure 3 Estimated daily intake (EDI: ng/kg/day) of phthalates (PH) and alternative plasticizers (AP) for pre-shift (n=106), post-shift (n=106) and control (n=46) urine samples. Wilcoxon signed rank test; *p<0.05 ; **p<0.001. The end of the whisker indicates the minimum or maximum value that is not an outlier. The boxplot represents the first quartile, median and third quartile. Mild (>1.5 x interquartile range) and extreme outlier (>3.0 x interquartile range) are represented by circles.*

Significantly higher median EDI_{urine} values were shown for the post-shift e-waste worker group when compared with the control group medians for DEP, BBzP, DEHP and DiDP. No significant differences were found between EDI_{urine} values based on pre-shift and post-shift e-waste workers. This indicates that e-waste workers are occupationally more exposed to plasticizers during their working activities compared to the control population.

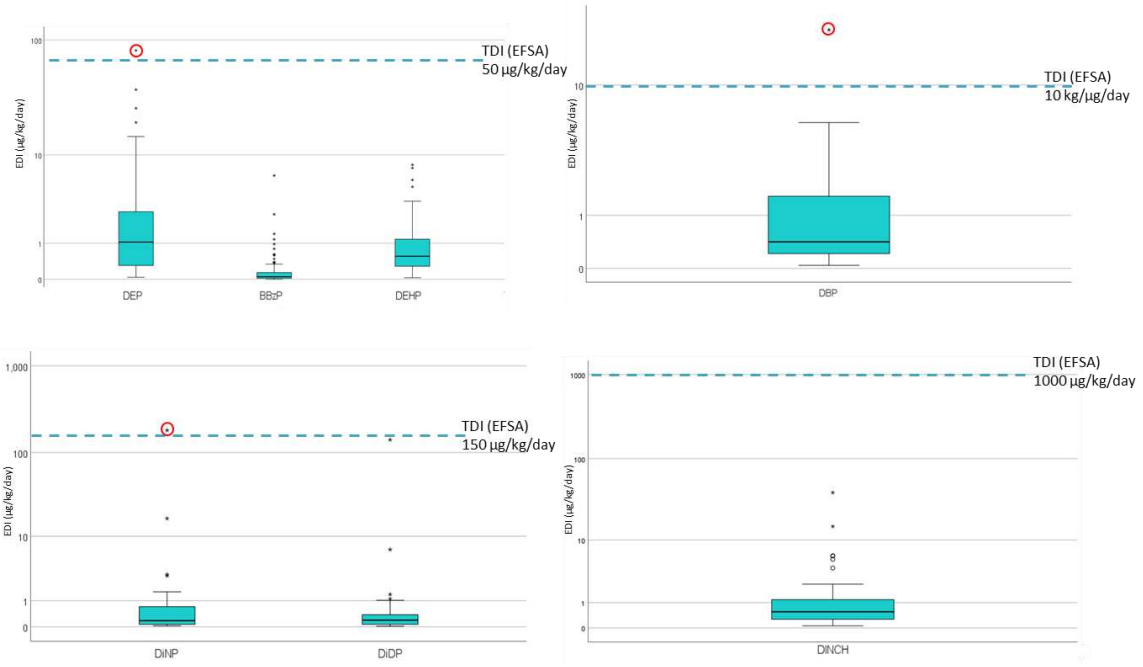

Figure 4 Estimated daily intake (EDI) (µg/kg/day) of phthalates and APs from post-shift worker samples (n=106) compared to tolerable daily intake (TDI) (µg/kg/day) according to the European Food Safety Authority (EFSA, 2019). Red circled values represent EDI > TDI. The end of the whisker indicates the minimum or maximum value that is not an outlier. The boxplot represents the first quartile, median and third quartile. Mild (>1.5 x interquartile range) and extreme outlier (>3.0 x interquartile range) are represented by circles.

The EDI $_{urine}$ values reflect the total exposure of this population to plasticizers. As described earlier, phthalates and DINCH are suspected to interfere with the human endocrine hormonal system, affecting fertility. To estimate the possible negative health consequences for the target population, the EDI $_{urine}$ values obtained in this study were compared to the TDIs adopted for the general population by the European Food Safety Authority (EFSA) in 2019 (48). As shown in Figure 4, one e-waste worker exceeded the TDI for DEP (81.5 µg/kg bw/day) and DBP (41.24 µg/kg bw/day) and one e-waste worker exceeded the TDI for DiNP (180.83 µg/kg bw/day). These two e-waste workers had no outstanding characteristics compared with other e-waste workers included in this study, except that they both were involved in dismantling brown goods, such as televisions, radios, computers, cell phones, etc. This indicates that negative health consequences from occupational exposure to phthalates and DINCH in this population of e-waste workers are expected to be limited. Especially considering that the TDIs have been adopted by EFSA to protect the general population (including small children and foetuses) from the hazards of phthalates. During the foetal stage, phthalates can affect foetal testosterone production with negative consequences in fertility later in life. Therefore, especially exposure of pregnant females to phthalates should be minimised in contract to our study population composed mostly of males.

The assumption of limited toxicological health consequences was confirmed when comparing urinary metabolite concentrations with guidance values (GV) determined by the HBM4EU Initiative for the exposure to selected phthalates and DINCH in the general and occupationally exposed population. For the working population, the GV for 5Cx-MEPP, MnBP, MiBP and MBzP were 0.6, 3.0, 3.5 and 3.0 mg/L, respectively. For the general population, the GV for the sum of 5oxo-MEHP and 5OH-MEHP, the sum of 5Cx-MEPP and 5-OH-MEHP, and the sum of OH-MINCH and Cx-MINCH were 0.50, 0.57 and 4.50 mg/L. None of the obtained urinary metabolite concentrations from pre- or post-shift e-waste worker samples, nor control samples exceeded these GV. Nonetheless, exposure levels of the population to phthalates and DINCH must be assessed to timely implement necessary measures. Furthermore, the monitoring of restricted phthalates and their alternatives is essential to evaluate the effectiveness of the regulations in place and adopt new regulations if necessary.

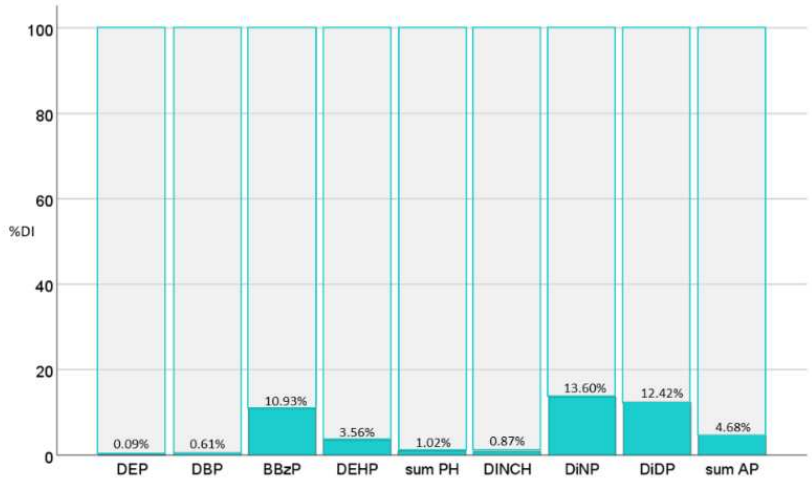

Figure 5 Contribution of exposure to phthalates (PH) and alternative plasticizers (AP) through dust ingestion in e-waste workers (n=106)

The EDI for each e-waste worker was calculated in two ways: from dust concentrations reflecting the exposure through ingestion of dust, and from their urinary concentrations reflecting the total exposure to phthalates and APs. The ratio of the median contribution of dust to the total exposure is illustrated in Figure 5. The distribution of the obtained daily intake percentages can be found in Supplementary Information Figure I-3. This contribution is rather low (<5%) for all phthalates and APs, except for BBzP (10.9%), DiDP (12.4%) and DiNP (13.6%). The high results for BBzP are remarkable, as both concentrations in urine and dust were lower compared to other compounds. Although other exposure routes have not been considered in this study, dust ingestion might be an important exposure source for BBzP in this occupational setting. Additionally, the high contributions of BBzP and DiNP through dust ingestion are remarkable, since only weak to moderate significant correlations between urinary metabolite concentrations and dust data was observed. We assume that the contribution of exposure to phthalates and DINCH from different sources (personal care products, food packaging materials,…) and through different routes (ingestion, inhalation and dermal contact) have influenced these correlations. Additionally, the use of personal protective equipment, and other personal hygiene aspects (frequency of washing hands,…) might limit the exposure of workers to phthalates and DINCH, influencing the correlation between urine and dust data. These results should be interpreted with caution as the EDI_{dust} was calculated based on the average dust concentrations from the working environment and is the same for all workers of one e-waste dismantling company, in contrast to EDI_{urine}, which are calculated individually and are specific for one e-waste worker.

Conclusions

Both phthalate and DINCH metabolites were measured in the urine of e-waste workers at the beginning and at the end of the shift towards the end of the workweek. The significantly higher urinary concentrations of MEP, MnBP, MiBP, MEHP, 5OH-MEHP, 5oxo-MEHP and 5Cx-MEPP observed in the e-waste worker group compared to the control group reflects the occupational exposure of these workers to phthalates. However, no significant differences were found between pre- and post-shift concentrations of phthalate and DINCH metabolites in the e-waste workers in contrast to previous studies. Sex, age, BMI, smoking, rural or urban home environment and the presence of industrial sources of emission within a radius of 10 km from the home location had no to limited influence on the exposure to phthalates and DINCH. However, higher urinary concentrations of several phthalates and DINCH metabolites were found in e-waste workers not wearing respiratory protective equipment in at least 50% of their work activities, reflecting inadvertent exposure. Comparison of the estimated EDI_{urine} values with the corresponding TDIs adopted by EFSA (28), and the urinary metabolite concentrations with HBM4EU guidance values for the general and occupationally exposed population, suggests that the risk for negative health consequences in this population of e-waste workers from exposure to phthalates and DINCH is expected to be low. Nonetheless, exposure levels of the population to phthalates and DINCH must be assessed to timely implement necessary measures. Furthermore, the monitoring of restricted phthalates and their alternatives is essential to evaluate the effectiveness of the regulations in place and adopt new regulations if necessary.

Conflict of interest

None

Acknowledgments

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Supplementary Materials

Supporting information can be found in the Supplementary Materials.

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