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Potential Health Impact of Phthalates: An Irish Perspective

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Rialtas na hÉireann
Government of Ireland

ENVIRONMENTAL PROTECTION AGENCY

The Environmental Protection Agency (EPA) is responsible for protecting and improving the environment as a valuable asset for the people of Ireland. We are committed to protecting people and the environment from the harmful effects of radiation and pollution.

The work of the EPA can be divided into three main areas:

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We regulate the following activities so that they do not endanger human health or harm the environment:

- waste facilities *(e.g. landfills, incinerators, waste transfer stations)*;
- large scale industrial activities (*e.g. pharmaceutical, cement manufacturing, power plants)*;
- intensive agriculture *(e.g. pigs, poultry)*;
- the contained use and controlled release of Genetically Modified Organisms *(GMOs)*;
- sources of ionising radiation *(e.g. x-ray and radiotherapy equipment, industrial sources)*;
- large petrol storage facilities;
- waste water discharges;
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- Office of Environmental Sustainability
- Office of Environmental Enforcement
- Office of Evidence and Assessment
- Office of Radiation Protection and Environmental Monitoring
- Office of Communications and Corporate Services

The EPA is assisted by an Advisory Committee of twelve members who meet regularly to discuss issues of concern and provide advice to the Board.

EPA RESEARCH PROGRAMME 2021–2030

Potential Health Impact of Phthalates: An Irish Perspective

(2015-HW-MS-3)

EPA Research Report

Prepared for the Environmental Protection Agency

by

Dublin City University Water Institute

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This report is based on research carried out/data from May 2015 to December 2019. More recent data may have become available since the research was completed.

The EPA Research Programme addresses the need for research in Ireland to inform policymakers and other stakeholders on a range of questions in relation to environmental protection. These reports are intended as contributions to the necessary debate on the protection of the environment.

Cover image: A graphical representation of a phthalate molecule spans a range of Irish environmental matrices; landfill, wastewater, surface water and soils.
Image credit: Dr Catherine Allen.

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Executive Summary

This project aimed to examine the environmental sources, fates and body burden of phthalates in Ireland. The three main objectives were to:

- assess the concentrations of phthalates in surface waters, soils, household waste, landfill leachates and wastewater;
- develop methods for the detection of phthalates in wastewater process streams for future compliance monitoring;
- assess human exposure through wastewater-based epidemiology and estimate a related risk.

Phthalates are pervasive in the Irish environment. The concentrations found in this study are consistent with those in other European countries and, therefore, Ireland does not present an increased cause for concern. Nevertheless, 100% detection frequency for 10 of the 11 phthalates studied suggests that further steps need to be taken to reduce this burden on the environment and prevent any further contamination in the ecosystem.

Phthalate esters are synthetic organic chemicals used in many consumer products. They are not chemically bound, so they leach and have become ubiquitous within the environment. As a result of their high level of production and continuous release, humans are constantly exposed to phthalates, with increasing evidence of detrimental health effects. The European Commission is preparing to amend the Authorisation List (Annex XIV to the Registration, Evaluation, Authorisation and Restriction of Chemicals Regulation — REACH) with the addition of four phthalates (diethylhexyl phthalate – DEHP; dibutyl phthalate – DBP; benzyl butyl phthalate – BBP; diisobutyl phthalate — DIBP) that are viewed as substances of very high concern with endocrine-disrupting properties (ECHA, 2019). Other phthalates have yet to be studied extensively. This project assessed the impact of phthalates in an Irish context, including both restricted and less well-studied phthalates.

There has been minimal research into the environmental and human burden of phthalates in Ireland. Among environmental sources of phthalates, wastewater sludge contains the highest concentration of phthalates, ranging from 0.20 to 315.21 mg/kg dry weight. The primary method for sludge disposal in Ireland is land application of biosolids; consequently, this could be a source of phthalates in soil in Ireland.

We found that wastewater treatment plant (WWTP) effluent contained low levels of phthalates, ranging from 0.002 to 1.52 µg/L; for context, the Environmental Quality Standard set for DEHP in surface waters is 1.3 µg/L. The removal of phthalates from influent was efficient (however, phthalates are retained in sludge). Influent WWTP levels showed that phthalates are prevalent in Irish households and industry, with down-the-drain disposal accounting for concentrations of 0.01–95 µg/L, although this could be an underestimate because of in-sewer transformation.

Landfill remains one of the most common means of disposal of municipal waste in Ireland, although the introduction of incineration may have already helped to mitigate some phthalate contamination. Concentrations found in the leachate samples from a closed landfill ranged from 0.01 mg/kg to 15.16 mg/kg; this was shown to be consistent with concentrations in European literature but higher than concentrations in some Scandinavian countries, possibly because of their earlier introduction of incineration practices. This was the only matrix in which diisodecyl phthalate (DIDP) had the highest concentration in comparison with other phthalates. As the landfill site has been shut down for some time, this could indicate a temporal change in phthalate use or that DIDP has a longer residence time in landfill owing to its high octanol/water partition co-efficient (log K_{ow}). Composite samples of recyclable, general and food/garden household waste were also examined.

Recyclable waste had the highest levels of phthalate, as expected, with concentrations ranging from 0.25 to 136.36 mg/kg. In all waste samples, DIBP was found at the highest concentration, and di-*n*-octylphthalate (DNOP) was found at the lowest. Further monitoring of phthalates in recyclable materials should be carried out to assess whether or not restricted phthalates are accumulating in plastics during the recycling process.

The aquatic environment displayed low-level contamination in comparison with other European countries. Phthalate concentrations at the WWTP discharge site were significantly higher than those at other surface water sites, suggesting that WWTP effluent may play a role in phthalate contamination of surface waters. Phthalates in soil were found in higher concentrations than phthalates in surface waters (as expected because of their hydrophobicity). Agricultural soil concentrations were significantly higher than urban samples in this study and were higher than those in other agricultural soils in Europe. Phthalate concentrations in agricultural soils ranged from 0.03 µg/g to 8.45 µg/g, while those in urban soils ranged from 0.01 µg/g to 5.02 µg/g. Similar to other matrices, DIBP and DBP contribute to the highest degree of contamination. These data suggest that, despite legislation, these phthalates remain prevalent in the environment. Although phthalate concentrations measured in most environmental samples are consistent with those in published European data and meet environmental quality standards, further work should be undertaken to examine phthalate levels in soils with an emphasis on agriculture.

A comprehensive and critical review of the literature found that human exposure to phthalates is best assessed through metabolite concentration in biological samples. One study followed urinary phthalate metabolite concentration in Ireland through the DEMOCOPHES project. However, human biomonitoring studies are costly. Therefore, in this study, the feasibility of wastewater-based epidemiology for the assessment of phthalate exposure risk was examined, owing to its cost-effective nature and ready availability of data. Three WWTP influent streams were monitored for phthalate metabolite concentration, and estimated population exposure was calculated using metabolic breakdown factors, flow rate and population served. Total exposure to phthalate ranged from 10.27 µg/inhabitant per day to 418.42 µg/inhabitant per day, with BBP accounting for the lowest body burden and diisononyl phthalate (DINP) accounting for the highest. Risk assessment involved using the hazard quotient (HQ) to assess the toxicological effect of phthalates in Ireland. In terms of HQ, BBP showed the lowest degree of endocrine disruption risk in the studied population, with DIBP deemed the highest risk phthalate, with an average HQ ranging from 0.0023 to 0.0186. All HQ values and the sum of all phthalate HQs – reported as the hazard index– were below levels of concern. This indicates that there is no phthalate-induced risk for the population studied. However, only a selection of phthalate metabolites were monitored, and this may not reflect the risk associated with all phthalates and plasticisers. Wastewater-based epidemiology techniques need to be improved to give a more robust indication of population exposure; however, it is recommended that periodic screening of wastewater for a wide range of metabolites related to contaminants of emerging concern could indicate temporal trends in exposure and give an early indication of a priority area for research or the need for a biomonitoring campaign.

1 Introduction

Phthalates are synthetic organic compounds, commonly used in plastic and particularly used in polyvinyl chloride (PVC) products, with a wide range of end uses including food packaging, cosmetics and personal care products, medical devices, tubing and flooring. They are colourless, odourless compounds that are liquid at room temperature and are added to give a product flexibility and resilience because of their fluidity, stability and low volatility. Phthalates are heavily used throughout PVC manufacturing, with soft PVC containing up to 40% diethylhexyl phthalate (DEHP) (Koch and Calafat, 2009).

Owing to the extensive presence and environmental persistence of phthalates, their effects on health have been frequently studied.

The limited number of data in the Irish context for both environmental occurrence of phthalates and human exposure to phthalates has been the driving force for this research. The objectives of the study were to identify the presence or absence of phthalates in a range of Irish environmental matrices and pioneer the use of wastewater as a mechanism for detection of human exposure to phthalates on a population basis. The research was divided into a number of interlinked work packages dealing with developing methods for phthalate analysis (Chapter 2), testing environmental samples for phthalate presence (Chapter 3), examining the measured levels of phthalate metabolites in wastewater to get an idea of human exposure and risk (Chapter 4), and looking at policy and making recommendations around the usage and monitoring of phthalates in an Irish context (Chapter 5).

It has been found that phthalates act as endocrine disruptors, leading to a range of adverse effects including hypospadias, reduced anogenital distance, cryptorchidism, impaired neurological development in children and precocious puberty, with children and women at the highest risk of exposure (Kay *et al*., 2014). Certain phthalates have been legislated for including benzyl butyl phthalate (BBP), dibutyl phthalate (DBP), DEHP, di-*n*-octylphthalate (DNOP), diisobutyl phthalate (DIBP) and diisodecyl phthalate (DIDP). DIBP, DBP, BBP and DEHP have been banned or limited in manufacturing (in particular for items such as electrical and electronic equipment and children's toys; see section 1.1), and as a result these have typically been the most widely studied phthalates. As a result of this legislation, a number of higher molecular weight plasticisers have been introduced as substitutes in plastic manufacturing. However, new research may indicate that these substitute plasticisers may also have a negative impact on human health, and this warrants further study.

The most common exposure of phthalates in humans identified in the literature is through food consumption (at least 67% of total exposure), but drinking water, air, dermal contact and cosmetics all contribute to total exposure (Das *et al*., 2014). Humans readily metabolise phthalates, generally excreting the phthalate as a number of phthalate metabolites within 1–2 days (Anderson *et al*., 2011). This metabolism occurs in at least two steps: hydrolysis (phase 1) and conjugation (phase 2) (see Figure 1.1). Some of the phthalate metabolites will be excreted as a glucuronide conjugate. These glucuronide conjugates are often broken down by enzymes contained in the matrix; however, all of the metabolites contained in urine will be glucuronide conjugates, as there are no esterases in this matrix. For this reason, urine is the most widely studied matrix for human phthalate metabolite monitoring, although many more (e.g. blood, sweat, breast milk) have been studied. The simpler forms of phthalates such as diethyl phthalate (DEP) and DBP are usually excreted as their corresponding phthalate monoester, whereas highly branched phthalates undergo more extensive biological transformations (Saravanabhavan *et al*., 2012). These phthalate metabolites (or biomarkers) can be monitored to infer a subject's phthalate body burden. Knowledge of the metabolism of phthalates will be important for consideration in identifying biomarkers for phthalate body burden, as only a fraction of the phthalates is excreted is in their unconjugated form (Frederiksen *et al*., 2007). Using the metabolites can therefore give us a more accurate representation of the direct effects on humans. A large quantity of the research looks at monoesters because of their ease of analysis and the evidence human consumption yielded by

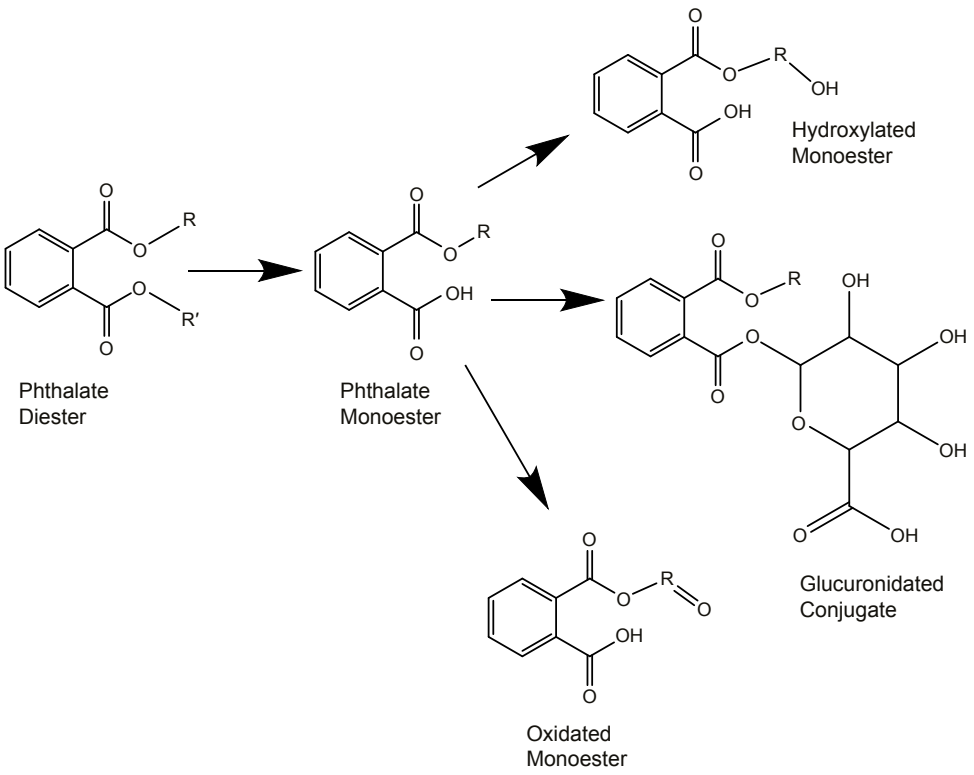


Figure 1.1. Phthalate metabolic pathway.

such analysis. Although further oxidative metabolites may give more accurate information on the human consumption of phthalates (Wang *et al.*, 2019), these more highly conjugated metabolite standards are very difficult to source.

It has been determined that phthalates can produce a “cocktail effect” and can have additive effects. Overall, in studies it was found that, when humans were exposed to a mixture of phthalates, the resulting effect was stronger than if exposure was restricted to the most potent component (CPSC, 2014). Most studies involve focusing on the effects of isolated phthalates. This project aimed to monitor a diverse range of phthalates to give a greater understanding of how these can influence human health. The physical properties of the phthalate and its metabolite will influence how it affects human health and how it is monitored (see Tables 1.1 and 1.2).

1.1 Current Legislation

The REACH Regulation is the European Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (EU, 2006). A number of phthalates that were classified as category 1B reproductive agents were identified as substances of very high concern (SVHCs) and placed on the REACH Candidate List. The REACH Authorisation List (Annex XIV to the REACH Regulation) contains SVHCs that should be controlled and ideally progressively replaced with suitable alternatives. Substances listed in Annex XIV to the REACH Regulation cannot be placed on the market for use or used after a given date (the so-called ‘sunset date’) unless the companies concerned are granted an authorisation for the specific use(s). DEHP, BBP, DBP and DIBP are on the Authorisation List with sunset dates in 2015, while bis(2-methoxyethyl) phthalate, diisopentyl phthalate (DIPP), dipentyl phthalate (DPP) and *N*-pentyl-isopentylphthalate have sunset dates in 2020. Commission Regulation (EU) 2020/171 led to the addition of dihexyl phthalate (DHP) to the Authorisation List in February 2020, with a sunset date in 2023.

In 2019, the European Chemicals Agency (ECHA) proposed adding endocrine-disrupting properties to the SVHC entries of DEHP, DBP, BBP and DIBP, and effects on the environment for DEHP (ECHA, 2019). Should this recommendation be accepted by the Commission, it will mean that authorisations will be necessary for some previously exempted products, such as DEHP in the immediate packaging of medicinal products.

Table 1.1. Characteristics of phthalates proposed for investigation

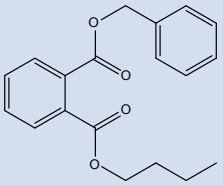
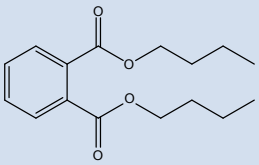
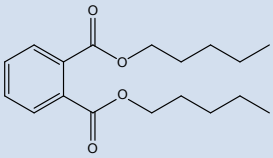
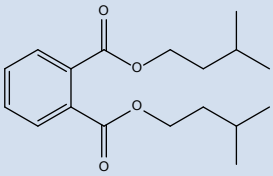
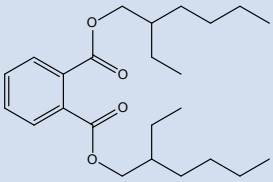
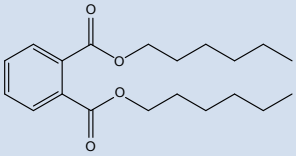
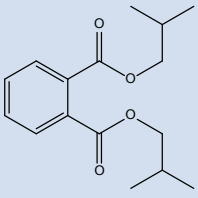
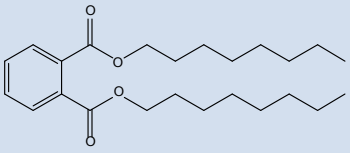
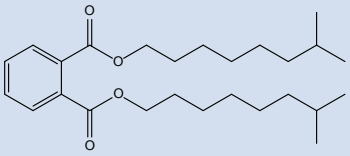
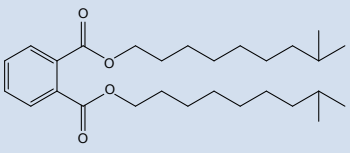
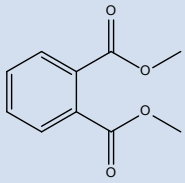
Compound	CAS No.	Structure	Molecular weight (g/mole)	Log K_{ow}
BBP	85-68-7		312.36	4.65
DBP	84-74-2		278.34	4.16
DPP	131-18-0		306.4	4.99
DIPP	605-50-5		306.4	4.82
DEHP	117-81-7		390.56	7.50
DHP	84–75–3		334.46	6.80
DIBP	84-69-5		278.35	4.12
DNOP	117-84-0		390.56	7.50
DINP	28553-12-0		418.62	8.16
DIDP	26761-40-0		446.66	8.99

Table 1.1. Continued

Compound	CAS No.	Structure	Molecular weight (g/mole)	Log K_{ow}
DMP	131-11-3		194.19	1.60

BBP, benzyl butyl phthalate; CAS, Chemical Abstracts Service; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DHP, dihexyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DIPP, diisopentyl phthalate; DMP, dimethyl phthalate; DNOP, di-*n*-octylphthalate; DPP, dipentyl phthalate; log K_{ow}, octanol/water partition coefficient.

The REACH Restriction List (Annex XVII to the REACH Regulation) imposes European Union-wide restrictions on the manufacture, use or placing on the market of substances causing an unacceptable risk to human health or the environment. DEHP, DBP, BBP, DIBP, diisononyl phthalate (DINP), DIDP and DNOP are restricted in that they "shall not be used as substances or as constituents of preparations, at concentration higher than 0.1% by mass of the plasticised material, in toys and childcare articles" because of their reprotoxicity. The phthalates classified as category 1B reproductive agents are also restricted in cosmetic products under the Cosmetics Regulation (EU, 2009).

Internationally, six phthalates (dimethyl phthalate – DMP; DEP; DBP; BBP; DEHP; and DNOP) have been classified as priority pollutants by the US Environmental Protection Agency (US EPA, 2014), and three of them (DEP, DBP and DNOP) have been listed as priority pollutants by the China State EPA (Wang *et al*., 2018). The US EPA has also set the maximum admissible concentration for DEHP in water systems at 6 mg/L.

In the USA, a congressional edict banned DBP, BBP and DEHP from children's articles owing to potential health risks. DINP, DNOP and DIDP were banned from children's toys that can be placed in a child's mouth, or children's toys smaller than 5 cm. The ban applies only to accessible parts of a toy. The Consumer Product Safety Commission's (CPSC) advisory panel now recommends a permanent ban on DINP but says that the ban on DNOP and DIDP should be lifted. In addition, the panel is considering a ban on DIBP, DPP, DHP and DCHP. This legislation is also relevant should Transatlantic Trade and Investment Partnership (TTIP) negotiations be reinstated.

In 2012, the US EPA developed a Phthalates Action Plan based on their toxicity, widespread use and human exposure, focusing on coordination with the Food and Drug Administration (FDA) and the CPSC for regulatory action on the manufacturing, use, sale and distribution of these compounds in the USA. Eight phthalates were included: DBP, DIBP, BBP, di-*n*-pentyl phthalate (DNPP), DEHP, DNOP, DINP and DIDP (US EPA, 2012).

Toxicological limits have been set for DEP, DBP, BBP, DEHP, DNOP, DINP and DIDP (see Table 1.3) in the most recent Chronic Hazard Advisory Panel (CHAP) report on phthalates (CPSC, 2017).

1.2 Occurrence of Phthalates in Environmental Matrices

The phthalates BBP and DEHP have been reported on more frequently than other phthalates owing to their inclusion in the Toxics Release Inventory since 1992; they are, therefore, the only two phthalates for which data on general release into the environment can be found (US EPA, 2012).

Phthalates are relatively volatile; as a result of this, they have been frequently found in air, promoting exposure to phthalates through inhalation. According to the US EPA Toxics Release Inventory for 1987, 147,000 kg of BBP was released into the air, 860 kg was discharged into water and 3900 kg was released onto the land from manufacturing and processing facilities in the USA. By 1993, 170,000 kg was released into air, 620 kg was discharged into water, 38 kg was disposed of by underground injection and 1200 kg was released onto the land (US EPA, 2020). BBP has been detected in surface water, groundwater and drinking water in many locations at levels generally

Table 1.2. Characteristics of phthalate monoester metabolites

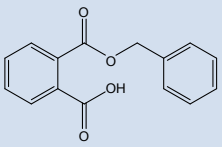
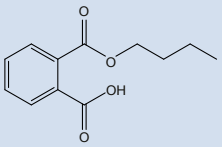
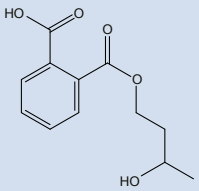
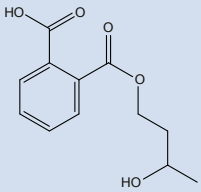
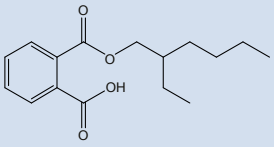
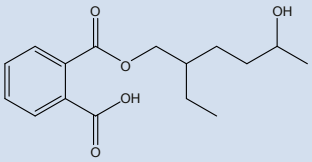
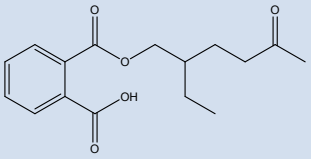
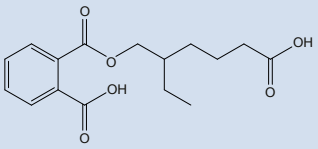
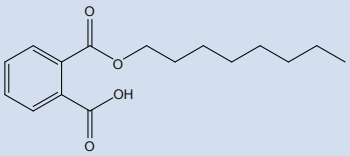
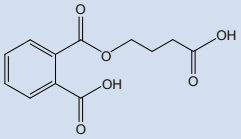
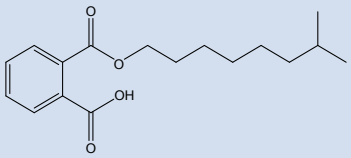
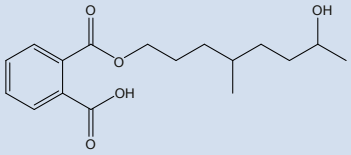
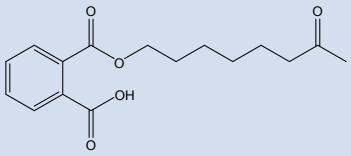
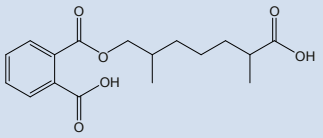
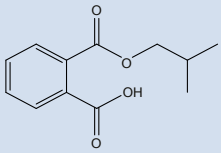
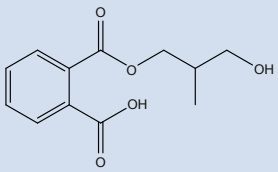
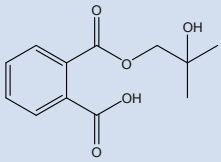
Parent phthalate	Major metabolite(s) monoester	CAS No.	Structure	Molecular weight (g/mol)	Log K_{ow}	pK_a
BBP	MBzP	2528-16-7		256.26	3.14	3.22
DBP	MBP	34-74-2		222.09	2.65	3.292
	Mono(3-hydroxybutyl) phthalate	57074-43-8		238.24	1.32	3.263
	Mono(4-hydroxybutyl) phthalate	17498-34-9		238.24	1.45	3.29
DEHP	MEHP	4376-20-9		278.35	4.3	3.266
	MEHHP	40321-99-1		294.35	3.01	3.266
	MEOHP	40321-98-0		292.33	2.99	3.265
	MECPP	40809-41-4		308.33	3.9	3.266
DNOP	MNOP	5393-19-1		278.35	4.32	3.29
	MCPP	66851-46-5		252.22	1.25	4.471

Table 1.2. Continued

Parent phthalate	Major metabolite(s) monoester	CAS No.	Structure	Molecular weight (g/mol)	Log K_{ow}	pK_a
DINP	MINP	68515-53-7		292.38	4.65	3.289
	MHINP	N/A		294.35	3.02	3.9
	MOINP	N/A		292.33	3.01	3.29
	MCIOP	N/A		294.3	3.5	3.29
DIBP	MIBP	30833-53-5		222.24	3.263	3.278
	3OH-MIBP	N/A		238.24	1.49	3.25
	2OH-MIBP	N/A		238.24	1.43	3.121

BBP, benzyl butyl phthalate; CAS, Chemical Abstracts Service; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DIBP, diisobutyl phthalate; DINP, diisononyl phthalate; DNOP, di-*n*-octylphthalate; log K_{ow}, octanol/water partition co-efficient; MBP, monobutyl phthalate; MBzP, monobenzyl phthalate; MCIOP, mono(carboxyisooctyl) phthalate; MCPP, mono-(3-carboxypropyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MEHP, monoexylhexyl phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MHINP, mono(hydroxyisononyl) phthalate; MIBP, mono-iso-butyl phthalate; MINP, monoisononyl phthalate; MNOP, mono-*n*-octyl phthalate; MOINP, mono(oxoisononyl) phthalate; N/A, not applicable.

well below 10 µg/L. Concentrations ranging from 0.1 to 16 µg/m^3 have been found in indoor air as a result of release from products such as vinyl flooring, caulks and adhesives, and carpets (Tran *et al.*, 2017). It also has been detected at mg/kg levels in foods (González-Sálamo *et al.*, 2018).

The Toxics Release Inventory reports the air emissions of DEHP from 298 industrial facilities in the USA; in 1997 it reported emissions of 107 tonnes. In Canada, these air emissions reached 27 tonnes in 1995, according to the Canadian National Pollutant Release Inventory. DEHP concentrations of up to 790 ng/m^3 have been found in urban and polluted air, but usually the levels in

Table 1.3. Legislation related to phthalates

Legislation	Description
Directive 2005/84/EC of the European Parliament and of the Council	This directive placed restrictions on the use of certain dangerous substances and preparations (phthalates in toys and childcare articles). It stated that "use of certain phthalates in toys and childcare articles should be prohibited due to health risks, also any toys that can be put in the mouth". This directive highlighted the following phthalates: DEHP, DBP, BBP, DINP, DIDP and DNOP (EU, 2005).
Regulation (EC) 1907/2006 of the European Parliament and of the Council concerning Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH); Cosmetics Regulation (EC) 1223/2009 and Cosmetics Directive (76/768/EEC)	DEHP, DBP, BBP, DIBP, DINP, DIDP and DNOP "shall not be used as substances or as constituents of preparations, at concentration higher than 0.1% by mass of the plasticised material, in toys and childcare articles". Eleven phthalates are identified as SVHCs under the REACH Regulation and are classified as reprotoxicants 1B. The phthalates classified as category 1B reproductive agents are also restricted in cosmetic products under the Cosmetics Regulation (EU, 2009).
Regulation on Plant Protection Products (2009) and the Regulation on Biocidal Products (2012)	Ten phthalates are listed.
WFD (2000/60/EC), Directive 2008/105/EC and Directive 2013/39/EU	These identify a list of priority and relevant pollutants and lay down the EQSs. DEHP is listed among the 33 priority substances listed in Directive 2008/105/EC and was amended to classification as a priority hazardous substance in 2011 [2011/0429(COD)]. Directive 2013/39/EU recommended that the annual average concentration of DEHP in surface waters be limited to 1.3 µg/L.
Commission Directive 2007/19/EC	This directive allows for the presence of DEHP in food production facilities, such as in conveyor belts, provided it does not exceed the SML of 1.5 mg per kg of food, although it is prohibited in the manufacture of single-use lips or caps.
Commission Delegated Directive 2015/863/EU, amending Annex II to Directive 2011/65/EU (RoHS legislation)	Commission Delegated Directive 2015/863/EU classes DEHP, BBP, DBP and DIBP as SVHCs, reporting that the available evidence indicates that the SVHC phthalates, when used in EEE, can have a negative impact on recycling and on human health and the environment during EEE waste management operations. The directive also includes a clause to maintain the previous legislation on the restriction of DEHP, BBP and DBP in toys and in concentrations above 0.1% in plasticised material (EU, 2015). Annex II to Directive 2011/65/EU (RoHS legislation) was updated to reflect this.
Commission Regulation (EU) No 10/2011	This regulation restricts the quantities of substances in materials used for food packaging that is able to come into contact with food. The restrictions are known as SMLs and are defined as "the maximum permitted amount of a given substance released from a material or article into food or food simulants" and expressed in mg substance per kg food (Pérez-Outeiral *et al*., 2016)
US EPA (2012)	Six phthalates (DMP, DEP, DBP, BBP, DEHP and DNOP) have been classified as priority pollutants. In 2012, the US EPA developed a Phthalates Action Plan based on their toxicity, widespread use and human exposure. Eight phthalates are included in the Action Plan: DBP, DIBP, BBP, DNPP, DEHP, DNOP, DINP and DIDP (US EPA, 2012). A significant new use rule has since been proposed for DNPP, which requires manufacturers or processors of the chemical to obtain US EPA approval (US EPA/FDA, 2012).
China State EPA	China State EPA lists DEP, DBP and DNOP as priority pollutants (Wang *et al*., 2018).
Consumer Product Safety Improvement Act (US Government, 2008)	DEHP, DBP, and BBP were banned in the USA in children's toys and some childcare articles.
Clean Drinking Water Act	Levels of DEHP in drinking water are regulated with an MCL of 0.006 mg/L for DEHP. DEHP and DBP are also listed as hazardous pollutants under the Clean Air Act. Several phthalates are listed among the risks to public health associated with PVC materials, and the American Public Health Association, which represents a broad array of public health professionals, urges federal and local governments to replace PVC when possible in medical care settings, schools, public housing and building materials (APHA, 2011).

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DEP, diethyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DMP, dimethyl phthalate; DNOP, di-*n*-octylphthalate; DNPP, di-*n*-pentyl phthalate; EEE, electrical and electronic equipment; EQSs, Environmental Quality Standards; MCL, maximum contaminant level; RoHS, Restriction of Hazardous Substances; SMLs, specific migration limits; WFD, Water Framework Directive.

ambient air are well below 100 ng/m^3. A study on DEHP detected emissions over the Atlantic and Pacific Oceans, suggesting that DEHP may be carried for long distances in the troposphere (Giam *et al.*, 1978).

There is currently no defined level for "background" DEHP exposure among the general population. Based on the metabolite levels found in environmental monitoring of DEHP and in controls of occupational studies, levels of monoethylhexyl phthalate (MEHP) higher than 12 µg/L are considered to surpass background levels and can therefore be used to investigate possible occupational exposures. However, other sources of environmental exposure, such as DEHP-containing consumer products, may contribute to this occupational exposure.

Although other phthalates are not on the Toxics Release Inventory, they have been studied extensively in the environment, as they are thought to have similar effects. With increased industrial manufacture of phthalates comes greater release into the environment; they have now been found to occur in atmospheric, terrestrial and aquatic environments of populated regions, and have been repeatedly detected in various compartments of remote areas (Del Bubba *et al*., 2018). For example, DMP has been found in atmospheric particulate matter (up to 10.4 ng/m^3), fresh water (up to 31.7 µg/L), sediments (up to 10.4 ng/m^3), soil (316 µg/kg dry weight) and landfills (solids up to 200 µg/kg dry weight and leachate up to 43.27 µg/L) (Gao and Wen, 2016).

1.3 Phthalate Impacts on Human Health

Phthalate endocrine-disrupting activity has led to an association with a wide range of adverse health effects. There are many complexities in determining the effect of phthalates on human health, leading to a lack of risk assessment data concerning humans. Many studies have been conducted on rats and other mammals; however, relating this risk to humans could possibly present inaccuracies because of interspecies variation. Some *in vitro* studies have been conducted to determine the potency of specific phthalates' effects on binding sites, evaluating their oestrogenic properties. In assessing human health risk from any biomonitoring study, phthalate metabolite concentrations are related to risk data generated from epidemiological studies.

1.3.1 Epidemiological studies

There are three main types of epidemiological studies: cohort, case–control and cross-sectional.

A cohort study is the optimal experimental design for determining the incidence and natural history of a condition (Mann, 2003). Cohort studies are usually prospective or retrospective in nature. In prospective cohort studies, a population without the condition of interest is chosen. The researcher then investigates a variety of variables that may be relevant to the development of the condition. This population is then observed over a period of time to see whether or not they develop the condition. In single-cohort studies, those people who do not develop the outcome of interest are used as internal controls. Where two cohorts are used, one group has been exposed to the agent of interest and the other has not, thereby acting as an external control (Porta, 2008). Alternatively, retrospective cohort studies use data already collected for other purposes. The cohort is "followed up" retrospectively. The study period may be many years, but the time to complete the study is only as long as it takes to collate and analyse the data (Mann, 2003). The relative risk can be found from a cohort study (see equation 1.1). This is the ratio of the risk of occurrence of a disease among exposed people to that among the unexposed (Bonita, 2012). In the case of phthalates, all subjects will have been exposed but the group with the lowest level of exposure will be used as the referent.

$$\text{Relative risk} = \frac{\text{Incidence in exposed}}{\text{Incidence in unexposed}} \qquad (1.1)$$

Case–control studies examine the association between exposure and a health outcome by comparing individuals already ill with the disease of interest (i.e. exposed cases) with a control group that comprises a sample of the same population from which the cases were identified (i.e. exposed non-cases) (Mann, 2003). Case–control studies are the least expensive studies to run, as they intentionally select subjects with the condition of interest, providing more cases. Case–control studies determine the relative importance of a predictor variable in relation to the presence or absence of the disease. As a result of their retrospective nature, they cannot be used to determine the relative risk. They can, however, be used to calculate odds ratios (ORs), which relate to the relative risk (Porta, 2008). OR data form the basis of

the association with health risk (see equation 1.2). An OR above 1 associates that degree of exposure with increased odds of developing that health outcome, whereas an OR of 1 has no association with the outcome (Szumilas, 2010). The confidence interval (CI) must be reported with the OR, as it gives an estimate of the precision of the risk estimate. A 95% CI that reports values both below and above 1 is not significant, as it crosses the "null value", implying that the exposure is both positively and negatively associated with the outcome of interest and therefore the risk estimate is not precise (Viera, 2008). Again, in the case of phthalates, all subjects will have been exposed, but the group with the lowest level of exposure will be used as the referent.

$$\text{OR} = \frac{\text{Exposed cases } (n) \times \text{unexposed non-cases } (n)}{\text{Exposed non-cases } (n) \times \text{unexposed cases } (n)} \quad (1.2)$$

Cross-sectional studies are most frequently used to determine prevalence, although they can also be used to determine causation (Bonita, 2012). Measurements are made at one point in time and the subjects are assessed to determine whether they have the exposure of interest and whether they have the outcome of interest. Some of the subjects will not have been exposed or have the outcome of interest. Therefore, ethical difficulties are greatly reduced as subjects are not purposely exposed or treated, and treatment is not deliberately withheld. This type of study is relatively cheap, as multiple outcomes can be monitored over only one group with minimal data collection (Porta, 2008).

Some epidemiological studies use surveys as a means to divide people into groups with varying degrees of exposure (Bonita, 2012). A hypothetical example would be subjects who use the most cosmetics being classed as the highest exposed group. However, as there are very limited data available on the concentration of phthalates in most consumer products, this does not offer sufficient accuracy. Therefore, only risk data from epidemiological studies that use biomonitoring as their source of exposure, i.e. studies that have accurate exposure data derived from phthalate metabolite levels in a human biological sample, will be analysed. OR data seem to be the most prevalent in the literature, so these values will be used in combination with any relative risk data to assess human health risk in Ireland based on the levels found.

1.4 Biomonitoring as a Tool to Assess Phthalate Exposure

Biomonitoring measures the concentration of each phthalate or phthalate metabolite in human body fluids, e.g. urine, blood and sweat, using analytical techniques. The majority of biomonitoring studies focus on phthalate metabolites rather than parent compounds because there is increasing evidence that as little as 1% of phthalates are excreted unchanged (Frederiksen *et al*., 2007). As there are limited data available on the exact metabolism of phthalates, the selection of an appropriate biomarker of exposure is subjective. There is increasing evidence that selection of the more extensively metabolised analytes offers more accurate results (Anderson *et al*., 2011; Saravanabhavan *et al*., 2012). Monoesters have short half-lives, resulting in lower concentrations in biological samples. In addition, monoesters may be produced through an abiotic process from parent phthalates of outside sources in some human samples that contain esterases (e.g. blood, faeces) but particularly in wastewater effluent, as many enzymes are contained in this matrix (Högberg *et al*., 2008; González-Marino *et al*., 2017). However, preliminary data suggest that the percentage of monoesters formed abiotically is very low, and that they mostly occur near neutral pH. Therefore, if a matrix with esterases is analysed, overestimation of phthalate metabolite concentration should be negligible if pH is controlled (González-Marino *et al*., 2017). Since the choice of metabolite may have a significant influence on the exposure estimate, literature exposure values may vary significantly when they are based on different metabolites (Calafat *et al*., 2010). Phthalates were identified for inclusion in the large-scale human biomonitoring study HBM4EU[1] in 2016, and preliminary assessments in a number of European countries indicate that oxidised metabolites are most suitable for the assessment of high-molecular-weight (HMW) phthalates, while primary metabolites are best for low-molecular-weight (LMW) metabolites. While there were no Irish biomonitoring studies included in HBM4EU, one less recent study followed urinary phthalate metabolite concentration in mother–infant

1 https://www.hbm4eu.eu/ (accessed 4 November 2020).

pairs in Ireland, through the DEMOCOPHES project (Cullen *et al.*, 2017).

An issue that arises when modelling exposure is variability in phthalate exposure between populations. Although this effect on the data may be small when a large population is studied, it may be significant when biomonitoring is performed on smaller samples (Dewalque *et al*., 2015). Skewing the results by making measurements reflect recent exposures might lead to an overestimate of average exposures and thus to the conclusion that risks are higher than they actually are. Another significant limitation of biomonitoring is that it is usually based on a single sample on a particular date and at a particular time, and so it does not provide information about the time course of exposure in that individual or population. This is particularly true for compounds, such as phthalates, that are readily metabolised and change rapidly in concentration over time (Wittasek and Angerer, 2008; Anderson *et al*., 2011).

1.4.1 Consideration of matrices in biomonitoring studies

The matrix examined should be strongly considered when conducting a biomonitoring study. Often the matrix will be preferential to certain phthalates or give accurate information on only long-term or short-term exposure. Each matrix will require a very specific means of sample pre-treatment. Some matrices, e.g. blood, will require a higher level of training for the analyst and will be more invasive for the subject. Urine is by far the most widely studied matrix for the determination of phthalate body burden. Sample collection requires minimal training and is non-invasive. A benefit of urine analysis lies in the fact that urine does not contain the esterases that can break down phthalate parent compounds into metabolites, meaning that contamination is of little to no concern. Urine samples will often be adjusted for creatinine in order to find a more representative phthalate metabolite concentration. Data collected from blood and serum are more difficult to interpret than data from urine. More persistent phthalates may be found in higher concentrations in blood. An issue with this matrix is the presence of esterases. Blood is the only invasive matrix proposed for the analysis of phthalate exposure. A reliable method to analyse phthalate metabolites in serum was developed by Jeong *et al*. using column-switching liquid chromatography–mass spectrometry/mass spectrometry (LC–MS/MS). When urine was analysed through this method, a lower level of variation was found (Jeong *et al*., 2011). Serum was deemed an unreliable matrix when methods without column switching were used, because many samples presented below the limit of detection (LOD) for a variety of phthalates (Högberg *et al*., 2008). Further method development could yield more repeatable results, but data at present resulting from serum analysis should be examined with caution. As male sexual health is one of the most prominent adverse health effects associated with phthalate exposure, it is useful to measure metabolites in seminal fluid to determine exposure at the target organ. The presence of phthalates in seminal fluid has confirmed that the male reproductive system is a target organ of these phthalates. Semen is much less frequently studied; this could be due to more complications regarding ethical approval. The data derived from this matrix offer information on phthalate exposure; in comparison with urine, this is an indicator of longer term exposure. Studies measure metabolite concentration and sperm quality from the same sample, offering reliable information on how the magnitude of exposure affects the target organ (You *et al*., 2015; Wang *et al*., 2016). As neonates and infants are at a higher risk of excessive phthalate body burden, phthalate concentrations in breast milk have been studied mainly to assess the level of phthalates that are being passed on to infants through early stage diet. Studies of breast milk have found primary metabolites in higher concentrations (Kim *et al*., 2015; Adenuga *et al*., 2020). A comparison of phthalate metabolite levels in human urine, breast milk, blood and serum found that blood contained a greater concentration of HMW phthalates (Högberg *et al*., 2008).

Hair and nails have been suggested as potential non-invasive matrices for longer term stable assessment of phthalate exposure (Hsu *et al*., 2015; Alves *et al*., 2016; Giovanoulis *et al*., 2016; He *et al*., 2018; Katsikantami *et al*., 2019).

Phthalate metabolites are found in many human matrices because of the exposure that humans face from the environment. The most common matrix is urine and the least frequently used matrices are hair and nails. However, new matrices to assess

human exposure are constantly being examined, to determine the extent of the human body burden of these endocrine-disrupting compounds. These concentrations provide valuable data on the levels of phthalates expected to be seen in humans and can give an estimate of the global scale of phthalate body burden for multiple phthalates. However, larger sample sizes that large-scale governmental biomonitoring studies contribute usually offer more data-rich sample and subject information, with lower variation due to larger sampling numbers.

1.5 Wastewater-based Epidemiology

Wastewater-based epidemiology (WBE) is an emerging method of gaining insight into human health and behaviour at a population level. This method utilises human excretion products (metabolites/ biomarkers) of certain compounds as they enter the wastewater system. Analysing parent compounds (in this case phthalate diesters) to examine a population's exposure to phthalates is ineffective because of phthalates' extensive metabolism and the large quantity of phthalates that enter the sewage system through industrial disposal. WBE was first used as a means of assessing cocaine use in Italy (Zuccato *et al*., 2005). Since then, it has grown to monitor a wide range of biomarkers for multiple xenobiotics, infectious agents, stress and cancer (Bicchi *et al*., 2009; Yang *et al*., 2015; Ryu *et al*., 2016; Bisseux *et al*., 2018). If the biomarker is considered stable in wastewater, then the calculated level can be attributed to human exposure. This study provides a first assessment of phthalates as a candidate for WBE in Ireland. Human exposure to phthalates is unavoidable, and, as small-study sizes are labour intensive and cannot capture the exposure of the general public, WBE is an attractive method of analysis, as it provides a cost-effective and unbiased means of determining human phthalate body burden on a pooled population level.

The biomarkers used for phthalate exposure are their monoester metabolites (Frederiksen *et al*., 2007). Attribution of phthalate body burden among a population is calculated by multiplying the measured phthalate monoester metabolite concentrations in wastewater by the daily flow rates of the WWTP to find daily sewer loads. From this value, the total consumption of the phthalate is estimated by applying a specific correction factor, which considers the average excretion rate of a given phthalate and the molecular weight (MW) ratio of the parent phthalate diester to its monoester metabolite. Lastly, the daily consumption can be found by dividing these daily values by the number of people served by the WWTP (equation 1.3).

$$\text{Correction factor} = \left(\frac{\text{MW diester}}{\text{\% excreted as monoester}} \times \frac{1}{\text{MW monoester}}\right)$$

$$\text{Estimated daily intake} = \frac{\text{Concentration} \times \text{flow rate} \times \text{correction factor}}{\text{Population}} \quad (1.3)$$

This current model for the analysis of down-the-drain chemicals is very basic and does not account for the in-transit and in-sewer transformations that can occur with unstable metabolite compounds. Down-the-drain metabolites can be lost through degradation or formed through enzymatic formation from their parent compounds in transit to the WWTP. At the treatment plant, there is an even greater likelihood of these transitions occurring as a result of the wastewater treatment process. Although many studies examine the removal and stability of phthalate diesters in WWTPs, very little is known about their monoester metabolites in this environment, with only one study to date investigating phthalate monoesters from a WBE perspective (Gonzalez-Marino *et al*., 2017).

The available literature has illustrated that in-sewer transformation is compound-specific and influenced by environmental factors. Some compounds seen in the literature (e.g. 3,4-methylenedioxy-methamphetamine – MDMA; ketamine; and methylenedioxypyrovalerone – MDPV) remain stable at neutral pH and temperatures up to 20°C. However, drugs such as 11-nor-9-carboxy-Δ9-tetrahydrocannnabinol (THCCOOH), fentanyl, mephedrone and cathinones have higher levels of variability (McCall *et al*., 2016). To compare results between different studies and environments, a standardised method with quality controls/correction factors for the stability of compounds in addition to in-transit and in-sewer transformation should be developed. This will allow for a higher degree of accuracy when informing policy.

1.6 Factors Affecting Phthalate Metabolite Levels Upstream of Wastewater Treatment Plants

1.6.1 Variation in human metabolism

Studies suggest that very few of the phthalates consumed are excreted unchanged. Therefore, in biomonitoring studies it is important to consider phthalate metabolism in the selection of biomarkers. Phthalate metabolism has been extensively described (Saravanabhavan *et al*., 2012). The simpler forms of phthalates, such as DEP and DBP, are usually excreted as monoester phthalates. However, highly branched phthalates undergo more extensive biological transformations, signifying that the use of more extensively oxidised metabolites may prove to be more effective as a result of their higher selectivity and longer half-lives (Frederiksen *et al*., 2007).

As phthalates are readily metabolised and change rapidly in concentration over time, most phthalate monoesters have exhibited substantial within-subject variability. The time of day at which measurements are made may have a significant impact on the results because certain activities, such as the use of personal care products, are likely to mainly occur at certain times of the day (Duty *et al*., 2005). In addition, ethnicity and socioeconomic variables have impacts on exposure (Koo *et al*., 2002). Of the factors that influence monoester levels in urine, sociodemographic and lifestyle factors (class, body weight, education) have been established as superior predictors of phthalate exposure when compared with food habits and cosmetic usage (Valvi *et al*., 2015). These factors are often not reflected in the data, which are generally summary values for particular age groups. In contrast, a heterogeneous population study found that monoester levels do not vary consistently by age or gender (Fromme *et al*., 2007).

Biomonitoring data are not generally available for some populations thought to be particularly at risk, i.e. infants and young children, and most of the data available on conversion – from body fluid concentrations to exposure levels – are from adult-based studies. Children have higher magnitudes of exposure to phthalates and including them in these populations could cause a minor shift in the distribution (Dewalque *et al*., 2014). This is an important consideration to take into account when comparing data from WBE studies with conventional biomonitoring, as these studies generally do not involve children.

The temporal variability of phthalate monoesters in wastewater is unknown. As a result of the evidence of within-subject variability shown in urine, it is estimated that a single grab sample of wastewater influent will not be sufficient for generating a reliable health risk assessment of that community. Further research needs to be conducted to elucidate this factor in the application of sewage epidemiology (Yang *et al.*, 2015; Baz-Lomba *et al.*, 2016; McCall *et al.*, 2016). This suggests that, for biomonitoring purposes, more than a single sample should be analysed to account for variability. A single sample provides information only from a particular date and time, and so it does not provide information about the time course of exposure in that individual or population.

In-pipe transformation of phthalate monoesters in transit to WWTPs has not been investigated. Biofilms contained in the piping systems could possibly account for some in-sewer formation of monoester biomarkers from the degradation of their phthalate diester parent compounds. In addition, some degradation could occur in transit, as the degradation rates of monoesters in wastewater have not been studied. In humans, the half-lives of phthalate monoesters range from 4 h to 8 h for metabolites of DEHP and DINP; however, LMW biomarkers may have shorter half-lives (Anderson *et al*., 2011).

Many studies have looked at the removal rate of phthalate diesters in WWTPs and the pathways by which they break down. All models of this degradation show the transformation of the parent diester to a monoester, as would be seen in human metabolism (Liang *et al*., 2007; Vavilin, 2007; Huang *et al*., 2017). The concentration of monoesters formed during the degradation of these diesters is unknown. The rate of degradation of diesters will depend on the wastewater treatment process involved, with LMW phthalates degrading more readily (Liang *et al*., 2007).

Although individual microbes contribute to the degradation of phthalate esters, the rate at which phthalates degrade in wastewater depends on their breakdown by a combination of many microbes. Phthalates in general have been found to degrade both aerobically and anaerobically, with anaerobic degradation occurring at a slower rate (Liang *et al*.,

2007). With average removal rates ranging from 53% in membrane bioreactors to 97.6% in activated sludge treatment, it is clear that some monoesters are being formed in-sewer as opposed to in-human, although it is not known whether or not this will have a significant impact on results for all treatment plants (Gao and Wen, 2016).

Sewage residence time is the length of time for which wastewater resides in a sewer system prior to being treated. Risk assessments based on wastewater data will have to take this factor into account, as it can have a significant influence on predictions. There are no data available at present on how residence time affects phthalate monoester levels. However, information on monoester stability in storage can relate to time-related variation in monoester concentrations in transit.

No data are available on the effects of temperature on the degradation or formation of phthalate monoesters in WWTPs, although temperature has been long regarded an important variable in the interpretation of WBE data of other down-the-drain compounds.

The levels of analyte of interest found in WWTPs are influenced by pH levels. No data exist on the effects of pH on phthalate monoesters in WWTPs.

The only existing WBE study on phthalates looked at the effect of storage on non-human transformation of monoesters with respect to temperature and pH (Gonzalez-Marino *et al*., 2017). These results can be used primarily to prevent any formation of phthalate monoesters after sampling. However, these data can relate to in-transit degradation, not accounting for flow rates or biological transformation by biofilms. If the study were to be expanded to look at effluent, further examination would be needed as these studies are not representative of bacteria and enzyme levels at each stage of treatment. Metabolites of DBP and BBP [mono-*n*-butyl phthalate (MNBP) and monobenzyl phthalate (MBzP), respectively] were the only monoesters being formed above method qualification levels, but only at natural pH and at very low percentages of the parent compound concentrations after 24 h (Gonzalez-Marino *et al*., 2017). Metabolite stability experiments indicated that only monethyl phthalate (MEP) and monomethyl phthalate (MMP) (metabolites of DEP and DMP, respectively) showed low levels of stability, and that concentrations dropped significantly (up to 35% and 23% of the initial concentration, respectively) after 48 h at room temperature and pH 2. At higher pH, the monoester is primarily found in its ionised form, making it more reactive to other agents in the matrix and causing degradation of the original product. This could present a problem in the case of commonly used 24-h composite sampling, whereby the sample spends an average time of 12 h in the sampling container. To circumvent this, Gonzalez-Marino *et al*. suggest adjusting samples to pH 2 as soon as they are received and storing them at 4 ºC until extraction (performed within 8 h).

No long-term storage degradation studies were carried out; however, best practice dictates that samples should be extracted and analysed as soon as possible. As discussed previously, when phthalates are metabolised, some are excreted in their free forms and some are excreted as glucuronide conjugates. In addition, no studies were conducted to examine the level of glucuronide conjugate metabolites in the influent. It is predicted that this will be quite low because of the enzyme content of this matrix in both influent and effluent (it appears at a higher rate in effluent owing to biological treatment) (Gonzalez-Marino *et al*., 2017). An enzymatic hydrolysis bench study would definitively show whether or not a significant number of bound metabolites are not being analysed; this is also relevant for influent data.

2 Detection of Phthalates in Environmental Matrices

A method was developed for the determination of 11 phthalates in a range of environmental samples. Analysis of phthalates is considered challenging because of the high levels contained in laboratory environments. The majority of phthalate research uses gas chromatography–mass spectrometry (GC–MS) to reduce the amount of instrumentation-related phthalate contamination. However, this project utilised a delay column to remove instrumental contamination, allowing for routine LC–MS analysis. Solid phase extraction (SPE) was used for pre-concentration and clean-up of phthalate samples. Ultrasonication and Soxhlet methods were evaluated for the extraction of solid matrices pre SPE, with ultrasonication showing greater recovery and being a more environmentally friendly method.

2.1 Quality Control

Stringent quality control is essential in any phthalate analysis because ubiquity of phthalates in the environment means that there is a risk of sample contamination and, therefore, overestimation of results (Marega *et al*., 2013; Net *et al*., 2015).

The first step should be to carefully prepare glassware and materials for sampling and analysis. Minimal plastics should be used, replacing them with glass, Teflon, aluminium, stainless steel or PTFE (polytetrafluoroethylene) where possible (Net *et al*., 2015). Any unavoidable plastics will be incorporated into procedural blanks. All glassware must be cleaned prior to analysis, in accordance with the recommendations specified in US EPA Method 506 (Munch, 1995), to reduce phthalate contamination levels. Although glassware is recommended, it should also be noted that longer chain phthalate esters such as dinonyl phthalate (DNP), DNOP and DHP can adsorb to the glassware (Khan, 2014).

2.2 Phthalate Diester Method Development

This project has developed a sensitive and selective LC–MS method to examine 11 phthalates in environmental matrices using an Agilent 6470 Triple-Quadrupole LC–MS. The targets under investigation are BBP, DBP, DPP, DIPP, DEHP, DHP, DIBP, DNOP, DINP and DIDP. Extraction methods have been optimised for a variety of environmental matrices (surface water, wastewater, sludge, soil, leachate and municipal waste). Solid samples have been extracted using ultrasonication paired with offline SPE, with liquid samples using SPE alone.

2.2.1 Solutions and standards preparation

All phthalate standards were procured from Accustandard (New Haven, CT) as liquids. The standards were diluted in 50:50 (v/v) methanol–acetonitrile (ACN) to obtain the concentrations required for the calibration standards. LC–MS-grade methanol and ACN were purchased from Thermo Fischer Scientific (Waltham, MA). Ultrapure water was sourced from a reverse osmosis system with 18.2 MΩ purity. Minimal standard preparation steps were taken, and all processes were carried out in a timely manner to avoid excess exposure to laboratory air. All glassware used was rinsed three times with LC–MS-grade methanol after an overnight bake at 200°C.

2.2.2 Quality control for the prevention of contamination and carry-over

Reduction of contamination

Each new solvent bought in was checked for phthalate contamination before use, even if the brand had passed this check before. The source was surface cleaned daily and deep cleaned weekly by flushing with nebuliser.

Engineering controls

The instrument was retrofitted with stainless steel tubing and pump heads. The degasser was bypassed to prevent a build-up of phthalates in the mobile phase. A delay column was installed after the mixer to push interfering phthalates from the mobile phase and system into a different retention time window and a dynamic multiple reaction monitoring method was

developed, removing any of these interferences from the analysis window. A multi-wash system was used with analytical blanks [a stronger solvent than that used in the mobile phase is injected between runs to ensure that there is no carry-over from the column – isopropyl alcohol (IPA)–ACN 50:50] (Figure 2.1).

2.2.3 Mass spectrometry conditions

Full scans of all target analytes were run to assess precursor and possible product ions. The Agilent Source Optimizer program was then used with these transitions to determine the optimal fragmentor voltages and collision energies for each compound (Table 2.1). This could be done manually by running samples at varying fragmentor voltage and collision energy.

To optimise signal, the source parameters need to be carefully controlled. Agilent Source Optimizer runs a variety of temperatures, flows, voltages and pressures to analyse which settings increase analyte detection. The parameters chosen gave the best average signal for all phthalates (Table 2.2).

2.2.4 Liquid chromatography analysis

Eliminating background phthalate contamination constituted the major analytical challenge in this project. However, the 11 target analytes included three sets of isomeric pairs (DIBP and DBP; DIPP and DPP; and DEHP and DNOP), which required some chromatographic development. Two Agilent columns were trialled for the resolution of these compounds: the Eclipse column and the Poroshell column. Trials on the Eclipse column did not show sufficient resolution of the isomeric pairs at the optimal flow rate and mobile phase. Owing to these co-elutions, the longer and more porous column, Poroshell, was examined for efficiency, with chromatographic conditions optimised as in Table 2.3 and performance illustrated in Figures 2.2 and 2.3.

2.2.5 Sample preparation

Solid phase extraction

Samples were initially filtered with 0.8-µm glass fibre filters, followed by 0.45-µm nylon filters, to remove suspended solids. Internal standards (dibutylphthalate-3,4,5,6-d 4 and bis(2-ethylhexyl)phthalate-3,4,5,6-d, 50 µL, 1 ppb) were then added prior to extraction.

The filtered samples were solid-phase extracted using reverse phase cartridges. Extraction conditions were similar to those described in US EPA Method 537 (Shoemaker *et al.*, 2008). Strata-X cartridges were purchased from Phenomenex (Torrance, CA). Cartridges were conditioned with methanol (LC–MS grade, 2 mL) followed by ACN (LC–MS grade, 2 mL) and water (Milli-Q, 4 mL). Samples (100 mL) were loaded under low vacuum and then washed with water (Milli-Q, 1 mL).

The extract was dried under nitrogen and then adjusted to a total volume of 1 mL with ACN. The

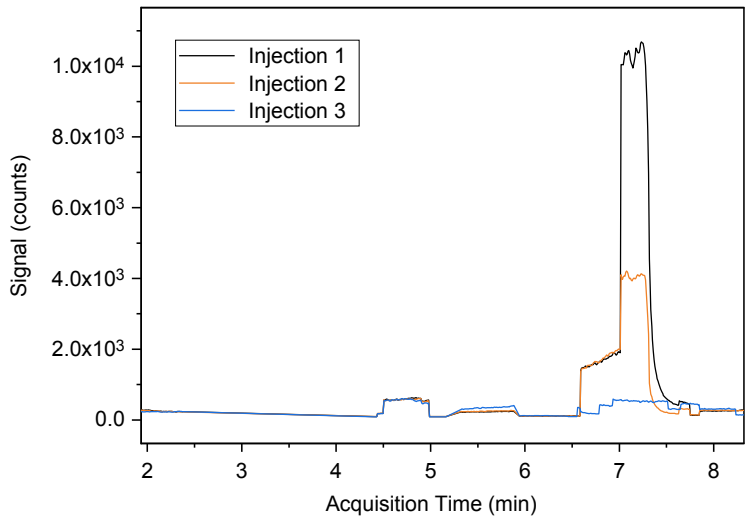


Figure 2.1. Effect of multi-wash and analytical blanks.

Table 2.1. Phthalates mass spectrometry

Phthalate	Peak no.	Retention time (min)	Target transitions (*m/z*)	Fragmentor (V)	Collision energy
DMP	1	2.15	195.1–162.9	62	8
			195.1–77.0	62	40
BBP	2	4.65	313.2–148.9	77	12
			313.2–91.0	77	40
DIBP	3	4.75	279.2–205.1	90	4
			279.2–149.0	90	14
			279.2–57.1	90	14
DBP	4	4.82	279.2–205	50	4
			279.2–148.9	50	12
			279.2–120.9	50	40
DIPP	5	5.50	307.18–149.0	96	20
			307.18–71.1	96	12
DPP	6	5.60	307.2–219.0	96	4
			307.2–148.9	96	20
DHP	7	6.25	335.2–233.0	80	4
			335.2–148.9	80	12
DEHP	8	7.15	391.0–166.9	115	12
			391.0–148.9	115	28
DNOP	9	7.30	391.3–166.9	99	12
			391.3–148.9	99	32
			391.3–120.9	99	60
DINP	10	7.50	419.31–148.9	96	24
			419.31–71.1	96	20
DIDP	11	8.20	447.3–141.1	99	8
			447.3–85.1	99	16

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DHP, dihexyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DIPP, diisopentyl phthalate; DMP, dimethyl phthalate; DNOP, di-*n*-octylphthalate; DPP, dipentyl phthalate; *m/z*, mass to charge ratio.

Table 2.2. Mass spectrometer source conditions

Parameter	Value
Mass spectrometer system	G6470A
Ionisation mode	Positive
Gas temperature	350°C
Gas flow	10 L/min
Nebuliser	35 psi
Capillary	4000 V
Sheath gas temperature	400°C
Sheath gas flow	12 L/min
Nozzle voltage	2000 V

psi, pounds per square inch.

Table 2.3. Chromatographic conditions

Parameter	Value	
System	Agilent	
Delay column	Eclipse Plus C18, 3.5 µm, 4.6 x 50 mm	
Analytical column	Poroshell 120 EC-C18, 2.7 µm, 2.1 x 150 mm	
Injection volume	2 µL	
Column temperature	50°C	
Mobile phase	(A) Water	
	(B) Methanol–ACN (50:50)	
Gradient	Time (min)	%B
	0	60
	2	80
	5	100
Run time	9 min	
Post time	2 min	

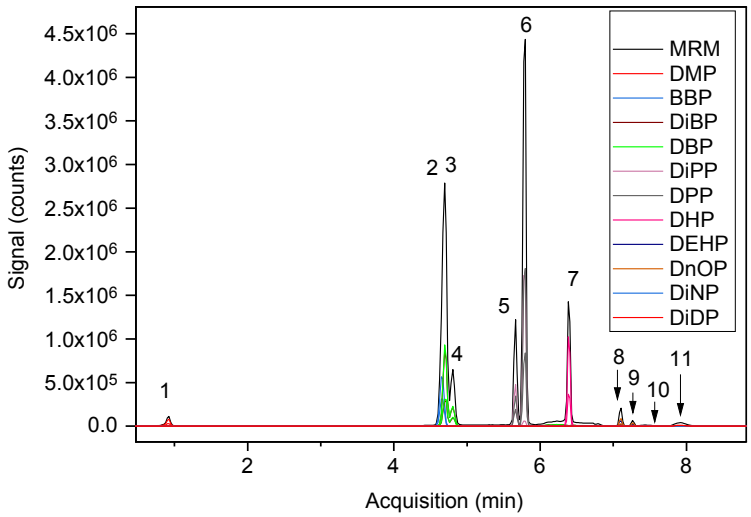


Figure 2.2. Chromatographic performance. MRM, multiple reaction monitoring.

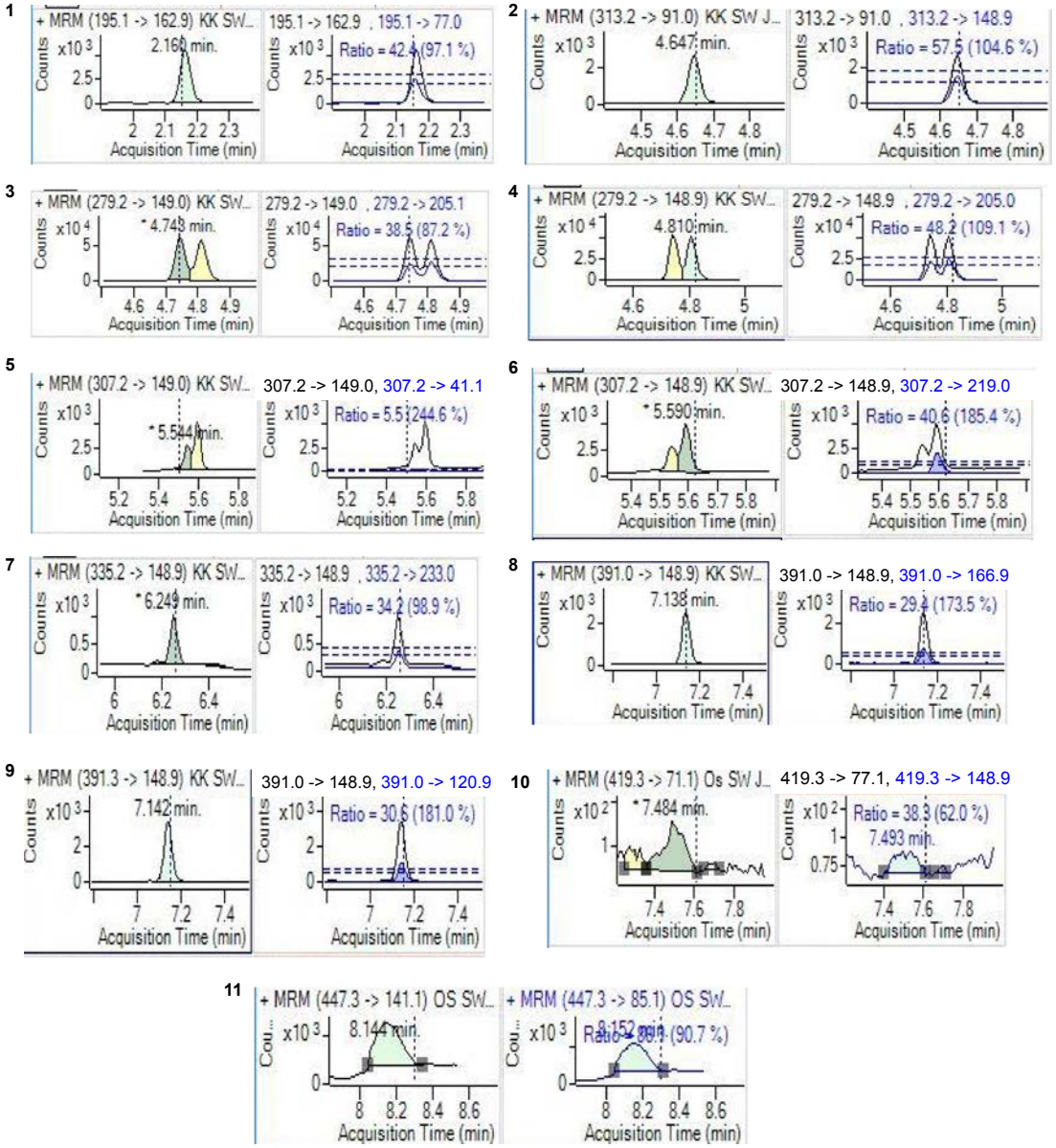


Figure 2.3. Quantifying multiple reaction monitoring transition for all phthalates.

percentage recovery for this method ranged from 70% to 98% (Figure 2.4).

Pre-extraction steps for solid samples

For the extraction of solid samples, an additional extraction prior to SPE must be carried out. Phthalate analysis has mainly used Soxhlet and ultrasonic extraction for these purposes, and both were investigated for this project. The QuEChERS (quick, easy, cheap, effective, rugged and safe) method is increasingly popular for solid matrix extraction, but as this uses a high volume of plastics and additional reagents that are not phthalate free, it was not investigated owing to the probability of introducing high background contamination. Once the matrix was extracted through Soxhlet/ultrasonication, the same SPE method was applied to the extract, with modifications carried out for sample volume loads. Three phthalates were selected: DMP, DEHP and DIDP. These were chosen as they covered the lowest, the mid-range and the highest octanol/water partition co-efficient (log K_{ow}). Ultrasonication was found to be the most efficient and environmentally friendly method for pre-extraction with acceptable recoveries and significantly reduced solvent use.

2.3 Phthalate Monoester Method Development

2.3.1 Solutions and standards preparation

All phthalate monoester standards were procured from Accustandard as solids. The standards were diluted in 50:50 (v/v) ACN–water, and buffered with ammonium acetate and glacial acetic acid to pH 5.5, to obtain the concentrations required for the calibration standards. LC–MS-grade ACN and methanol were purchased from Thermo Fischer Scientific, while LC–MS-grade ammonium acetate and glacial acetic acid were obtained from Sigma-Aldrich (Steinheim, Germany). Ultrapure water was sourced from a reverse osmosis system with 18.2 MΩ purity. Method details are as per Tables 2.4 and 2.5.

2.3.2 Injection programme with multi-wash

To reduce carry-over and increase reproducibility, a multi-wash programme was used. The multi-wash was run at the start and end of every injection and three analytical injection blanks of the mobile phase were carried out between samples (Figure 2.5).

The separation efficiency and details are outlined in Figure 2.6 and Table 2.6.

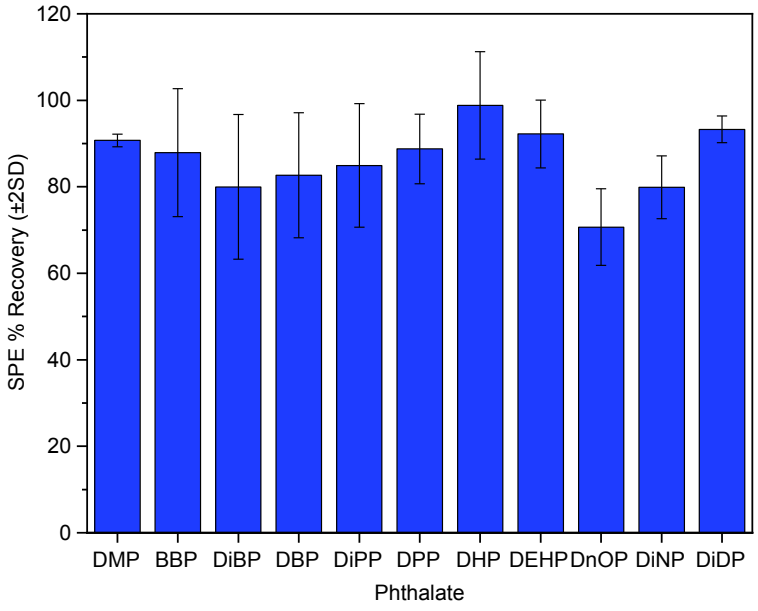


Figure 2.4. SPE percentage recovery.

Repeated injections showed retention time reproducibility, with all compounds remaining within <5% relative standard deviation (RSD) (Figure 2.7). Between each sample, three blanks were run to eliminate sample carry-over. This coupled with the multi-wash system gave a noise-level background for sample analysis (Figure 2.8); sensitivity and linearity of response are outlined in Table 2.7.

Table 2.4. LC conditions

Parameter	Value	
System	Agilent 1290 Infinity II	
Delay column	N/A	
Analytical column	EclipsePlus C18 RRHD, 2.1 x 50 mm, i.d. 1.8 µm	
Injection volume	5 µL	
Column temperature	50°C	
Mobile phase	(A) 5 mM ammonium acetate buffer in water	
	(B) 5 mM ammonium acetate buffer in methanol	
Flow rate	0.4 mL/min	
Gradient	Time (min)	%B
	0	25
	3.5	65
Run time	4.8 min	
Post time	1 min	

N/A, not applicable.

Table 2.5. Mass spectrometry source parameters

Parameter	Value
Mass spectrometer system	Agilent 6470 Triple Quadrupole
Ionisation mode	Negative
Gas temperature	350°C
Gas flow	10 L/min
Nebuliser	35 psi
Capillary	2500 V
Sheath gas temperature	400°C
Sheath gas flow	12 L/min
Nozzle voltage	2000 V

psi, pounds per square inch.

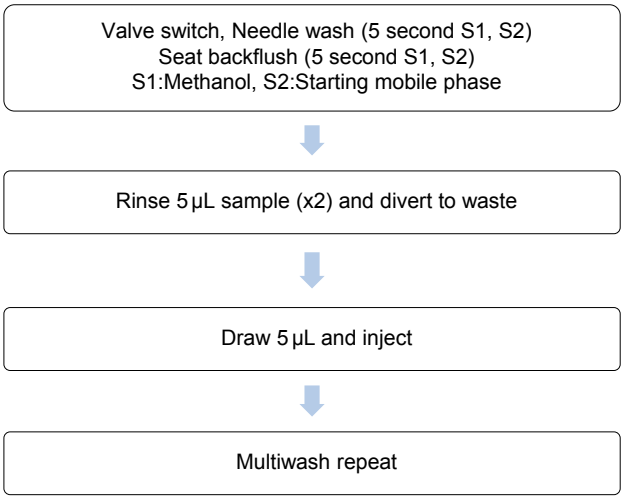


Figure 2.5. Multi-wash programme.

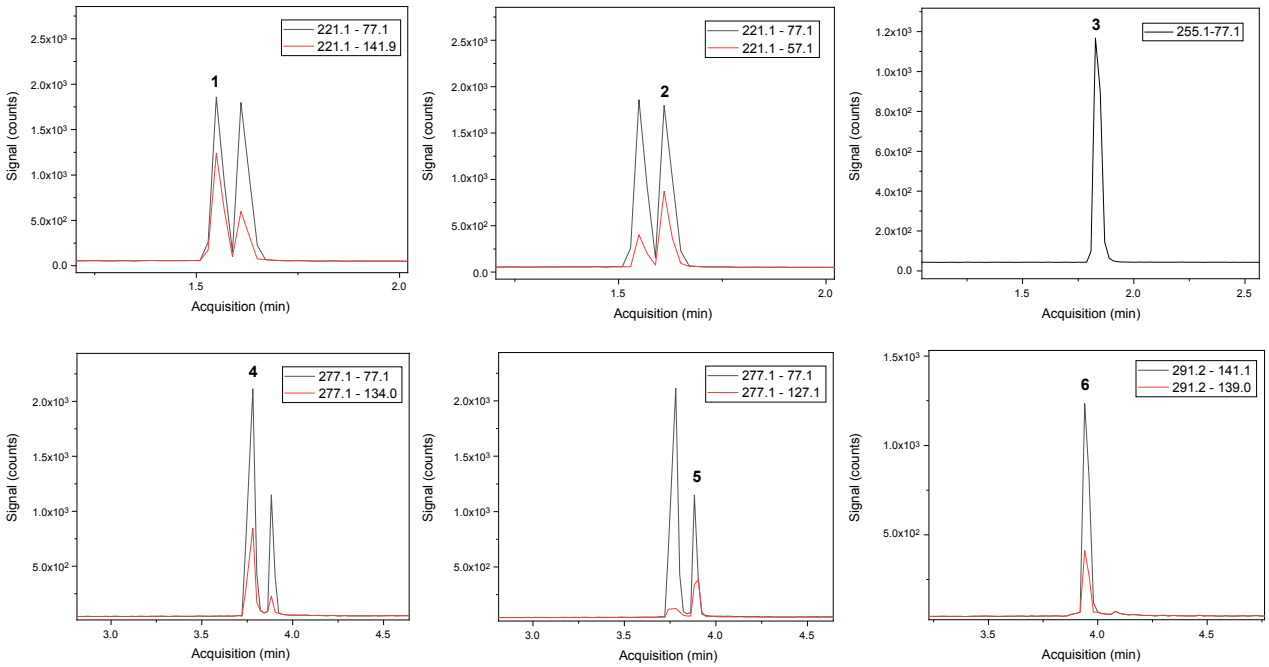


Figure 2.6. Overlay of multiple reaction monitoring for separation of phthalate monoesters. MBP, monobutyl phthalate; MIBP, monoisobutyl phthalate; MINP, monoisononyl phthalate; MNOP, monooctyl phthalat; TIC, total ion current.

Table 2.6. Monoester LC–MS

Compound	Peak no.	Target transitions (*m/z*)	Fragmentor (V)	Collision energy	Retention time (min)
MIBP	1	221.1–77.1	98	0	1.535
		221.1–141.9	98	16	
MBP	2	221.1–77.1	82	20	1.596
		221.1–57.1	99	32	
MBzP	3	255.1–77.1	88	20	1.838
MEHP	4	277.1–77.1	250	0	3.773
		277.1–163.5	103	8	
MNOP	5	277.1–127.1	103	16	3.879
		277.1–134	103	16	
		277.1–77.1	103	24	
MINP	6	291.2–141.1	109	20	3.940
		291.2–139.0	109	16	
		291.2–121.0	109	20	

MBP, monobutyl phthalate; MBzP, monobenzyl phthalate; MEHP, monoethylhexyl phthalate; MIBP, monoisobutyl phthalate, MINP, monoisononyl phthalate; MNOP, monooctyl phthalate.

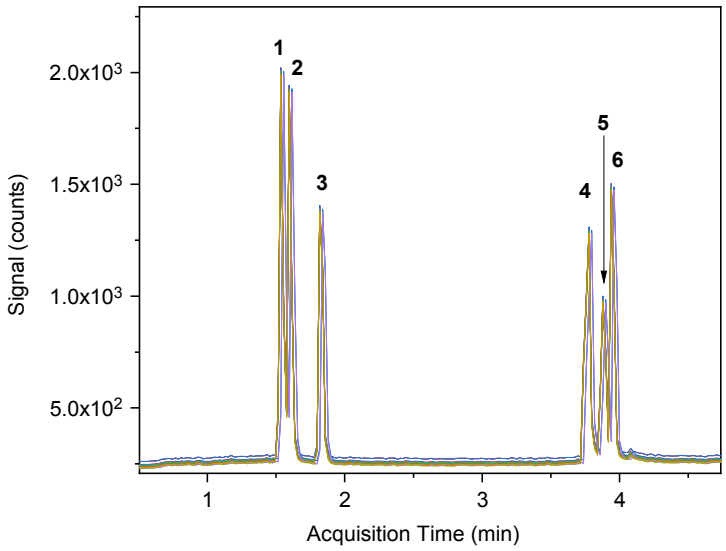


Figure 2.7. Repeated injections of 0.5 ppb standard mix.

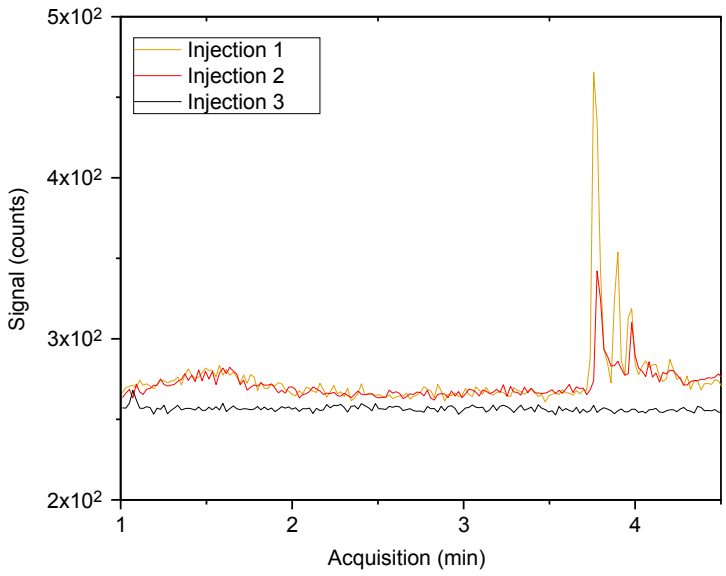


Figure 2.8. Multi-wash and blank monoesters.

Table 2.7. Sensitivity and linearity of response

Peak no.	Compound	Range of linearity (ppb)	R^2 ($n=3$)	CCV RSD (%)	LOD (ppb)	LOQ (ppb)	S/N (at 0.01 ppb)
1	MIBP	0.01–1	0.9922	0.33	0.003	0.1	1.19
2	MBP	0.01–1	0.9855	0.93	0.003	0.1	1.21
3	MBzP	0.01–1	0.9836	0.84	0.0003	0.001	87.28
4	MEHP	0.01–1	0.9866	2.12	0.0005	0.002	54.76
5	MNOP	0.01–1	0.9816	1.80	0.001	0.03	3.27
6	MINP	0.01–1	0.9984	0.08	0.003	0.01	11.51

CCV, Continuing Calibration Verification; LOQ, limit of quantification; MBP, monobutyl phthalate; MBzP, monobenzyl phthalate; MEHP, monoethylhexyl phthalate; MIBP, monoisobutyl phthalate; MINP, monoisononyl phthalate; MNOP, monooctyl phthalate; S/N, signal to noise ratio.

3 Occurrence of Phthalates in Ireland

Phthalates are transported around the environment through various sources, such as WWTP output, leaching, drainage and atmospheric deposition. The occurrence of phthalates in Ireland is relatively unknown. The partitioning of phthalates generally depends on the polarity of the compound, so LMW phthalates are more likely to be concentrated in aqueous matrices such as surface waters and effluents, whereas HMW phthalates are more common in soils and sludges. A very limited study of environmental phthalate contamination was conducted on samples collected in the Irish Midlands Shannon Catchment region during the winter of 2004/2005. Sediments, sludge and leachate were examined for DBP, DEHP, DINP and DIDP. In river sediment, levels of up to 24.4 mg/kg phthalate were found, while in leachate and sludge values of up to 49.8 mg/kg and 174 mg/kg, respectively, were quantified (Reid *et al.*, 2009).

3.1 Municipal Waste

In this study, a representative subsample from household waste collected from an urban area was analysed. Full details of the waste characterisation campaign can be found at http://www.epa.ie/pubs/reports/waste/wastecharacterisation/. Recyclable waste, general waste and food/garden waste were analysed separately. Overall, 75.5% of total phthalates found in household waste was attributed to waste in recycling bins, 21% was from waste in general household waste bins and 3.5% was from waste in food/garden waste bins (Figure 3.1).

The predominant phthalates found in recycled waste are DIBP, DBP and DIDP. For green bin samples, the concentration of BBP in relation to the other phthalates was higher than that seen in other matrices. BBP has been limited in manufacturing (Table 1.3), and, although legislation may have reduced the concentration in environmental samples overall, recycling may keep this compound in circulation for household goods made from recyclate.

Although many recycling and recovery options for the management of general household waste currently exist in Ireland, historically many waste types were disposed of in various landfill facilities. Many of these facilities are now closed, and older facilities may have issues in terms of effective containment of leachate – liquid contaminated by the landfill contents – which can migrate from the landfill to the surrounding subsurface.

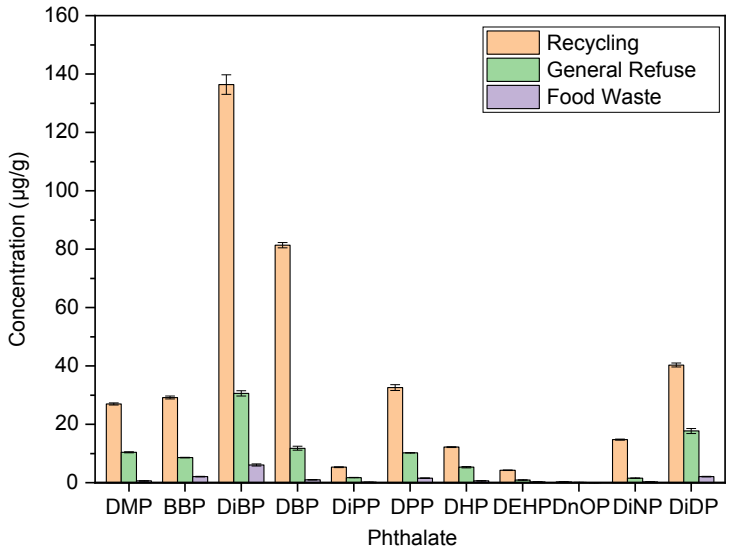


Figure 3.1. Phthalates in household waste.

3.2 Landfill Leachate

The leachate examined in this study came from a now-closed municipal waste landfill that contained lining and included samples from both the sump and the lagoon. Leachate is collected on site and pumped via the leachate sump to the leachate lagoon. Leachate is discharged from the site via the leachate lagoon to the sewer, and it is then transported via a rising main to a WWTP.

DNOP, DINP and DIDP were present in the leachate at relatively higher concentrations than in other environmental matrices (Figure 3.2).

3.3 Wastewater Treatment Plant Influent and Effluent

The influent to WWTPs (i.e. the raw wastewater) can give some indication of the degree of phthalate burden in the catchment area of a WWTP. Run-off (from roads or agricultural land), storm water and landfill leachate can contribute to the levels of phthalates seen at WWTPs, while disposal of phthalates into drains is common owing to the use of these plasticisers in personal care products, household cleaners, etc. The presence of phthalate diesters will not serve to relate directly to human exposure, as less than 1% of phthalates is excreted unchanged. In general, phthalate concentrations in the WWTP influent were highest at the suburban site (Figures 3.3–3.5), with some evidence of temporal variability across sites (potentially attributable to individual WWTP parameters, such as residence time at the time of sampling; it is not possible to confirm spatial or temporal variation statistically without increased data availability). DMP, DIBP and DBP were found in the highest concentrations at all sites.

Estimated removal of phthalates from the watered fraction of WWTPs is shown in Table 3.1.

It is important to note that removal from the watered fraction does not necessarily indicate a breakdown of phthalates in the WWTP; given the range of hydrophobicities, partitioning to sewage sludge does occur. This is further explored in section 3.5.

3.4 Surface Water

Phthalate contamination can be introduced to fresh water through numerous routes. Effluent, surface run-off, industrial discharge, leachate and atmospheric deposition are deemed to be the highest contributors (Wilkinson *et al*., 2017). As a result of their hydrophobicity, phthalates tend to partition in sediments and suspended particulate matter. Sediments and soil therefore act as a source and sink of contamination in fresh water through the re-suspension of particulate matter.

DMP, DEP, DIBP, DMEP, DBP, BBP, DEHP and DNOP are among the most frequently detected phthalates in surface water. Rainfall is associated with the transfer of phthalates in the atmosphere to surface water

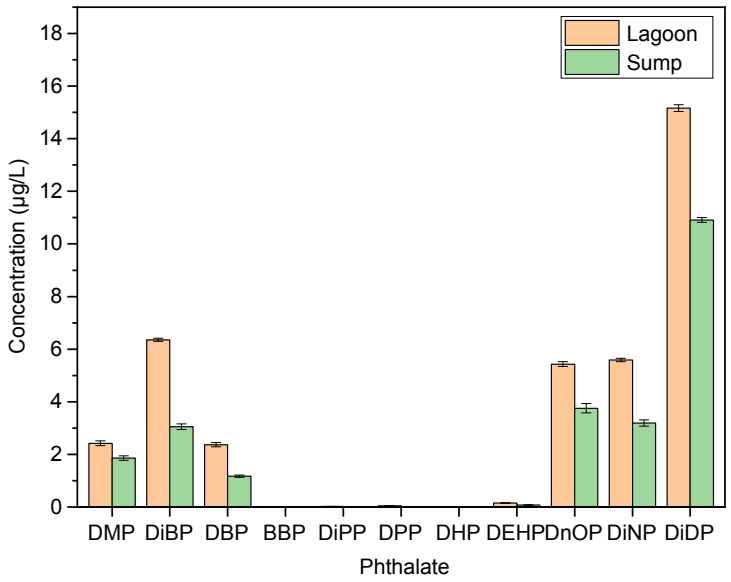


Figure 3.2. Phthalate concentrations in leachate.

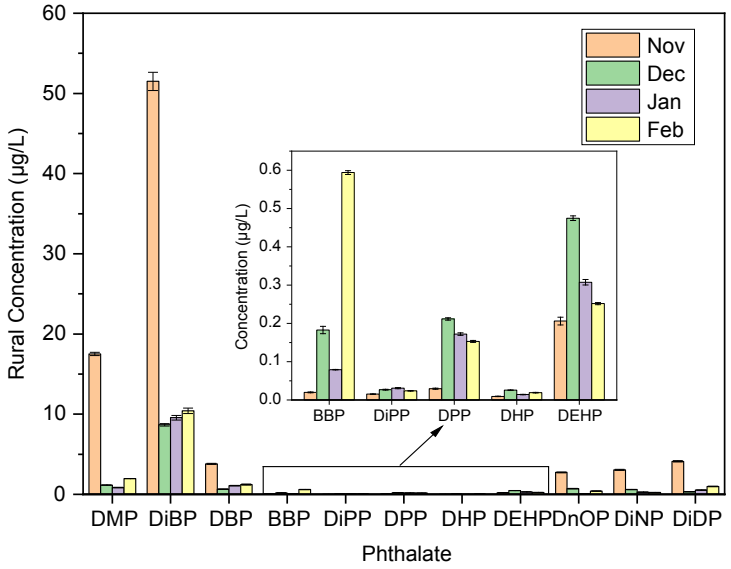


Figure 3.3. Rural influent concentrations.

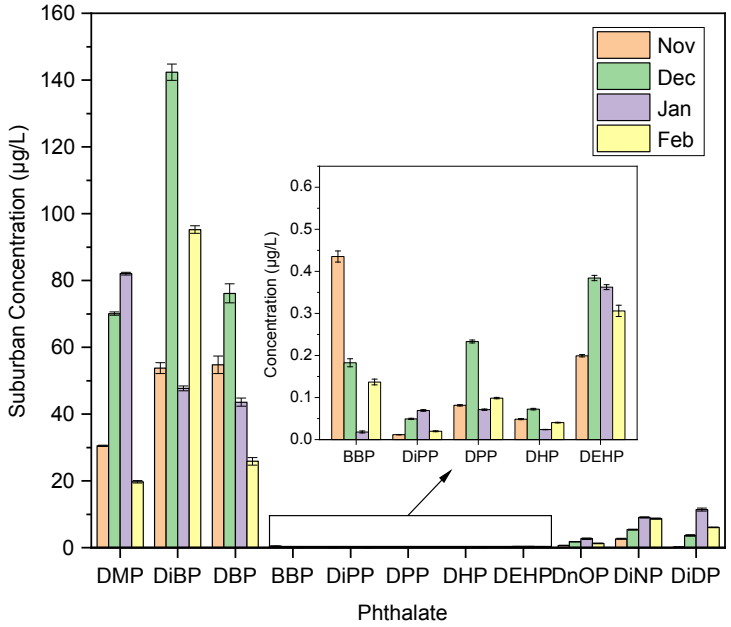


Figure 3.4. Suburban influent concentrations.

and soils, facilitating their accumulation in the wider environment, with higher concentrations of phthalates found in short-term precipitation events (Fernández-Amado *et al*., 2017).

3.4.1 Grab samples

Surface water samples were taken from four sites defined as the following: upstream, receiving waters (point of release downstream from the WWTP), suburban area and estuary (Figure 3.6). Samples from each of these sites were analysed for the months January, June, July and November 2017. These months were chosen because of the high variation in precipitation. The low-precipitation months were January and July, with average rainfall of 0.2 mm/day and 0.5 mm/day, respectively, occurring over the 3 days leading up to sampling. The high-precipitation months were June and November, during which rainfall averaged 10.1 mm/day and 5.7 mm/day, respectively, over the 3 days prior to sampling. It was expected that phthalates would be found in higher concentrations

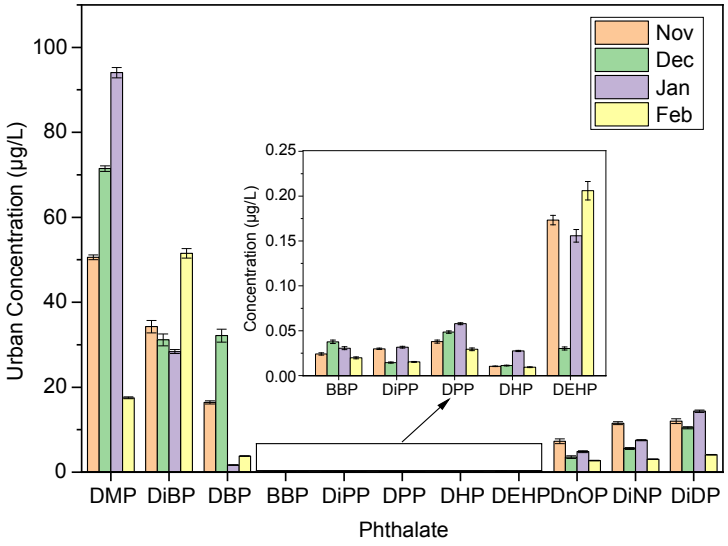


Figure 3.5. Urban influent concentrations.

Table 3.1. Removal of phthalates from the watered fraction at Irish WWTPs

Phthalate	Suburban % removal (*n*=4)	Rural % removal (*n*=4)
DMP	95.59	66.51
BBP	60.77	70.50
DIBP	99.41	93.64
DBP	98.90	69.64
DIPP	81.93	43.02
DPP	96.43	91.32
DHP	86.27	67.30
DEHP	94.19	95.99
DNOP	99.84	87.88
DINP	99.87	94.86
DIDP	99.78	92.98

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DHP, dihexyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DIPP, diisopentyl phthalate; DMP, dimethyl phthalate; DNOP, di-*n*-octylphthalate; DPP, dipentyl phthalate.

during the high-precipitation months and at the wastewater effluent discharge site (receiving waters).

Phthalate concentrations at the receiving water site were higher than those at all other sites, as expected. HMW phthalates showed the highest increase at the receiving water site (a three-fold increase) (Figures 3.7–3.10). Therefore, in Ireland WWTP output can contribute to phthalate contamination in surface waters. From the literature, phthalates are relatively high in wastewater and, while removal rates are efficient, these phthalates have a strong affinity to river sediment and can concentrate at discharge sites, continuously being re-suspended in particulate matter.

From the literature, increased rainfall is associated with greater phthalate concentrations in surface water, possibly owing to run-off increasing the number of suspended solids in the river. This was not seen in the results in this study (Figures 3.7–3.10). However, estuary samples taken in June, during a very high rainfall event, showed a large increase in phthalate concentrations (Figure 3.10).

The Environmental Quality Standard (EQS) for DEHP in surface water is set at 1.3 µg/L, and all surface water samples remained well below this limit for DEHP (Figures 3.7–3.10). According to the ECHA, no predicted no effect concentration (PNEC) is available for DEHP. The phthalates found to have the highest concentrations in the surface water samples were DBP and DIBP. The PNEC of DIBP in freshwater is set at 1 µg/L (ECHA),[2] and thus the concentration observed is close to the PNEC. DBP was found

2 https://echa.europa.eu/brief-profile/-/briefprofile/100.001.412 (accessed 8 May 2020).

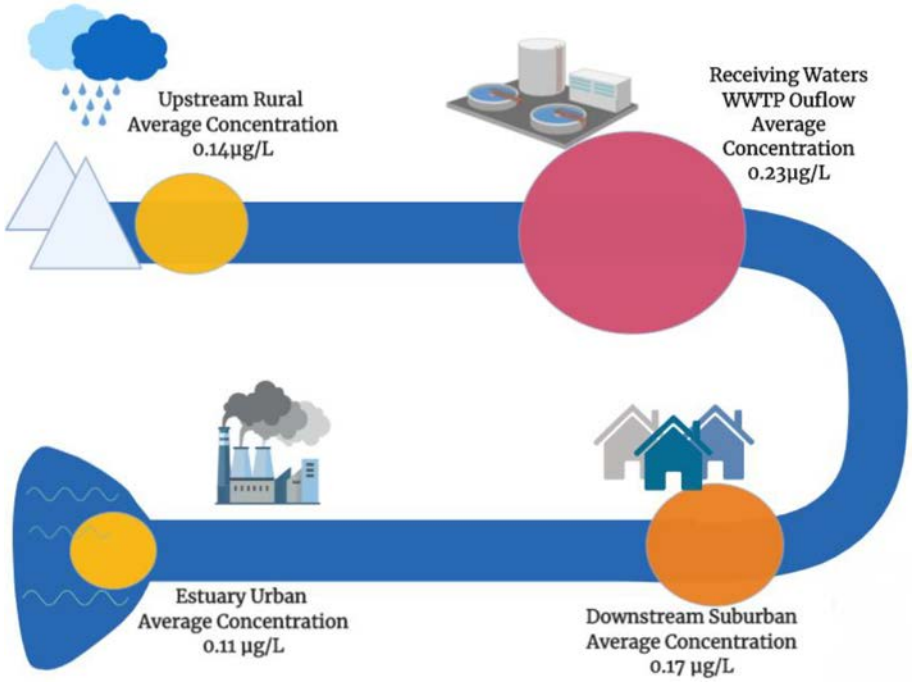


Figure 3.6. Summary of surface water results.

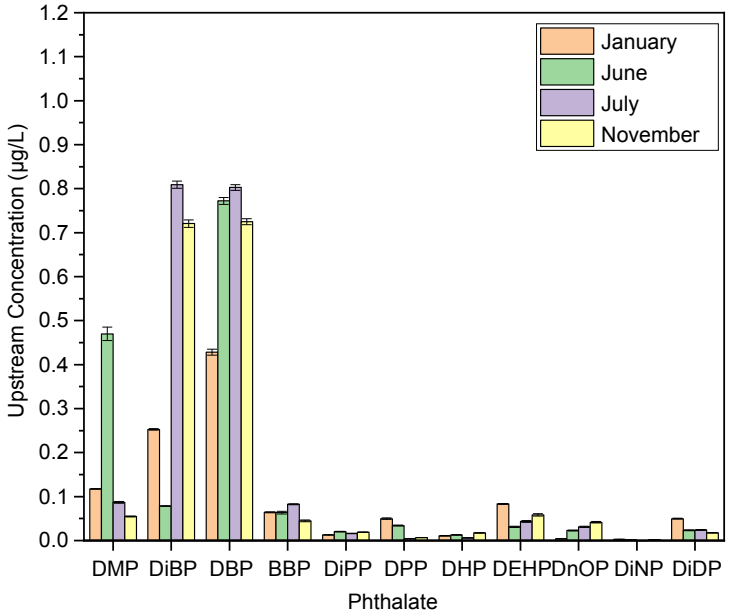


Figure 3.7. Upstream surface water concentrations.

at a comparatively high concentration; however, it was well below the PNEC of 10 µg/L.[3] It is unlikely that the levels of phthalates in surface water pose a risk to freshwater aquatic life in Ireland; however, the concentration of DIBP is potentially a cause for concern.

3.4.2 Passive sampling of receiving waters

To evaluate the potential to use passive sampling rather than grab sampling for monitoring surface water for phthalate contamination, passive sampling of surface water at the WWTP discharge site was carried

3 https://echa.europa.eu/brief-profile/-/briefprofile/100.001.416 (accessed 8 May 2020).

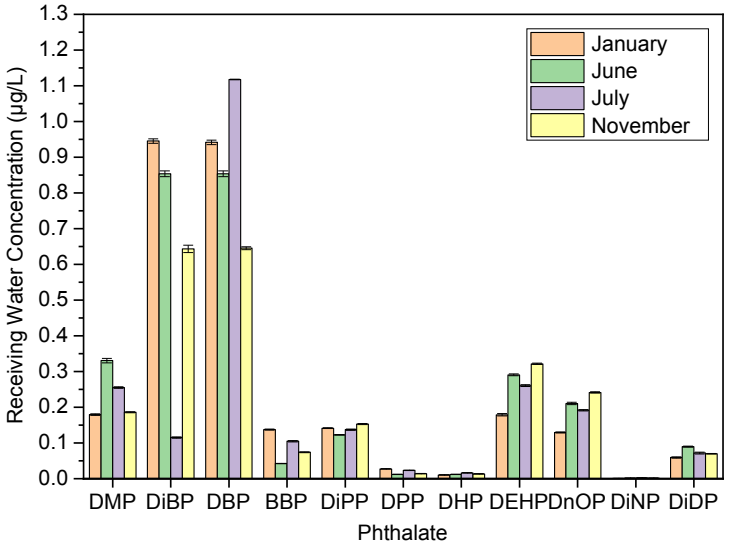


Figure 3.8. Receiving surface water concentrations.

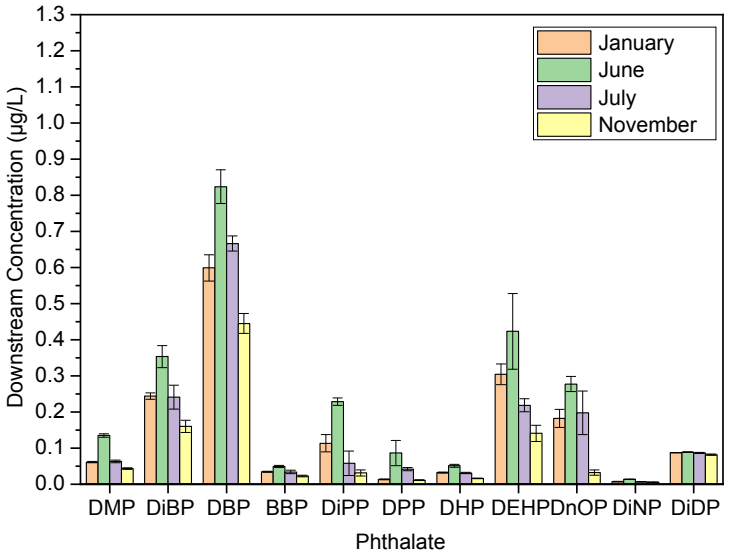


Figure 3.9. Downstream surface water concentrations.

out using commercially available Chemcatcher™ passive sampling devices. Grab samples were also analysed to compare variation between the two methods. Passive sampling can detect phthalates in surface water (Table 3.2).

3.5 Wastewater Treatment Plant Sludge

In wastewater treatment, examining the treated wastewater stream alone to assess the removal of a contaminant does not give sufficient information. Examining the solid waste (sludge) from the WWTP is critical, as contaminants may partition to sludge unchanged, rather than actually being degraded in the WWTP. High removal rates may appear to represent a positive impact on phthalate contamination in the environment; however, although the levels in effluent and thus receiving waters are reduced, levels in sludge are increased, which may lead to higher phthalate burden in soils in some agricultural areas that implement the land spreading of sludge.

The concentration is reported on a µg per g dry weight of sludge basis.

It is clear from assessment of the increased levels of phthalate diesters in sludge that the removal of phthalates from wastewater is partly a partitioning

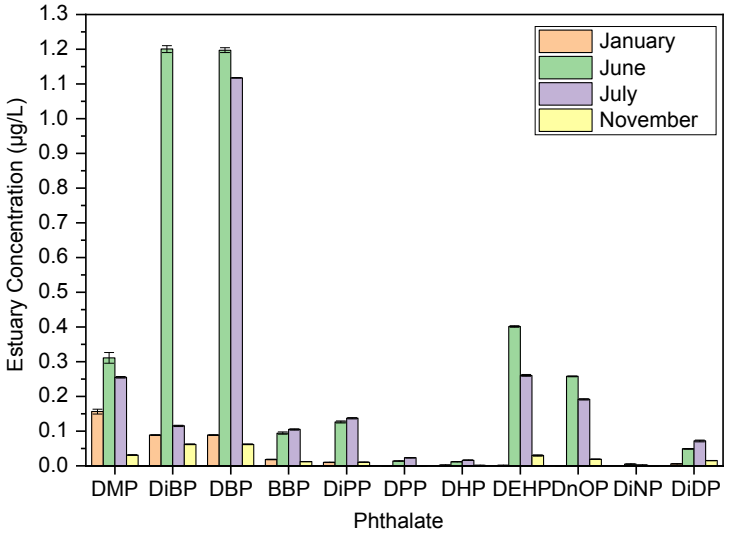


Figure 3.10. Estuary surface water concentrations.

Table 3.2. Estimated concentration of phthalates in surface water through passive sampling

Phthalate	Day 1 (µg/L)	% RSD	Day 7 (µg/L)	% RSD
DMP	0.13	3.88	0.53	3.99
BBP	0.15	3.44	0.30	4.66
DIBP	1.35	3.55	2.48	2.78
DBP	0.47	4.66	0.68	3.51
DIPP	0.10	4.83	0.11	5.83
DPP	0.14	3.36	0.29	1.00
DHP	0.15	3.61	0.29	3.08
DEHP	0.28	3.72	0.63	1.79
DNOP	0.17	3.83	0.34	3.53
DINP	0.001	6.04	0.01	2.73
DIDP	0.09	2.63	0.09	0.52

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DHP, dihexyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DIPP, diisopentyl phthalate; DMP, dimethyl phthalate; DNOP, di-*n*-octylphthalate; DPP, dipentyl phthalate.

effect to the solid matrix, rather than complete removal via degradation. The application of agricultural fertiliser derived from WWTP biosolids gives rise to concern, as further treatment is intended to remove pathogens, not phthalates, and the presence of phthalates in WTTP biosolids is not typically assessed. Sludge processing has been shown to increase the concentration of DEHP, with the level of concentration doubling after thermal treatment is applied to dry the sludge (Mailler *et al.*, 2017). It is worth noting that the level of DEHP in suburban sludge (Figure 3.11) in December was much higher than that in the rural sludge (Figure 3.12), despite the fact that the influent concentration of DEHP in both locations was similar during that month (Figures 3.3 and 3.4). The reason for this difference is not clear; however, as the samples were taken on the same day, it is possible that, given the residence time in the WWTP, the comparatively higher level in the suburban sludge reflects a spike in influent concentration 2–3 days prior to the grab sample being taken.

3.6 Soil

Phthalates can concentrate in soils because of their hydrophobicity. Different farming practices have been hypothesised to affect the concentrations of phthalates in soils, for example the use of plastic crop covers on organic farms. Elsewhere, many studies have looked at the introduction of endocrine-disrupting chemical (EDC) contamination though the treatment of soils with reclaimed wastewater and biosolids. Some studies have shown phthalate uptake in crops from soils, which contaminates the food chain and puts humans at a higher exposure risk. Phthalates have been detected in leaves and fruits at the agricultural source (Ma *et al.*, 2020). This has been widely studied for other EDCs. It should be noted that, in Ireland, there is no use of reclaimed wastewater irrigation; however, land spreading of biosolids is in place at some sites in Ireland.

Three soil samples in triplicate from various sites were analysed (industrial, residential, agricultural)

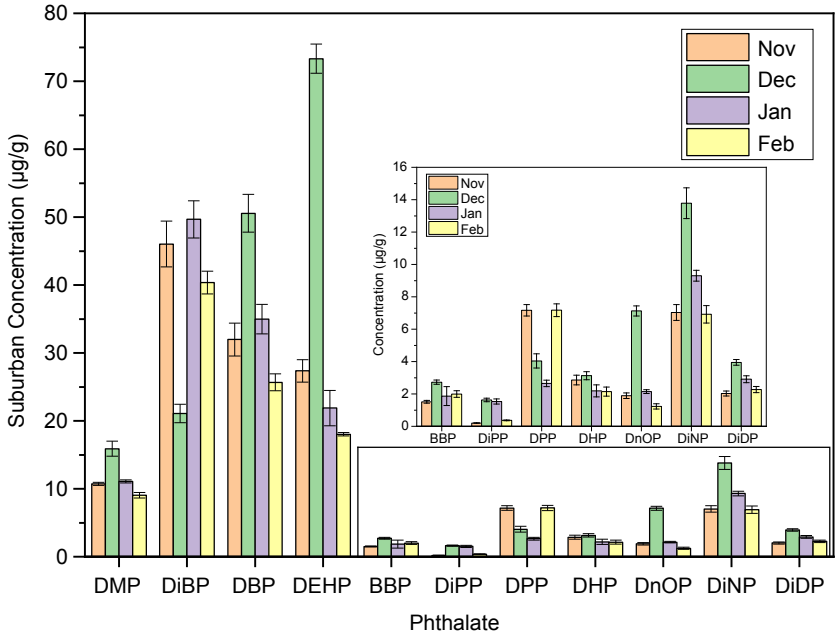


Figure 3.11. Suburban sludge concentrations.

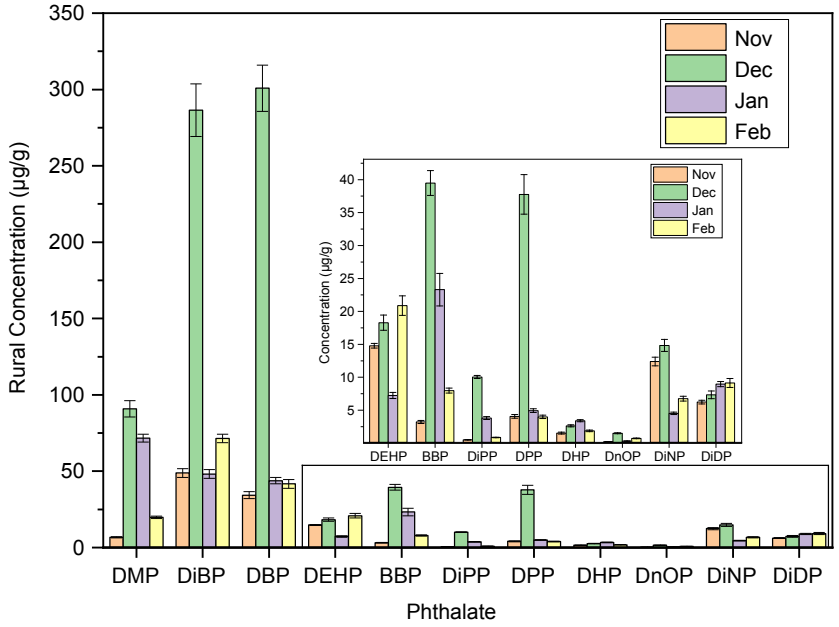


Figure 3.12. Rural sludge concentrations.

(Figure 3.13). It was expected, as a result of the soil's hydrophobicity, that HMW phthalates would concentrate in this matrix. It was also expected that industrial and urban soils would have the highest concentrations of phthalates owing to the association of phthalates with increased industry.

Phthalates were found in the highest concentrations in the farmland samples. This was not as expected, but farming practices could indicate a higher contamination risk. The organic farmland site used plastic sheeting and tyres combined with poly-tunnels to protect soils and retain the farm's organic status. Traditional farms often use land spreading of treated wastewater sludge, although this is not thought to be the case at the farmland sampled. As this type of land spreading causes direct contact with a phthalate-contaminated material in a similar matrix, this could cause increased migration of phthalates to soils,

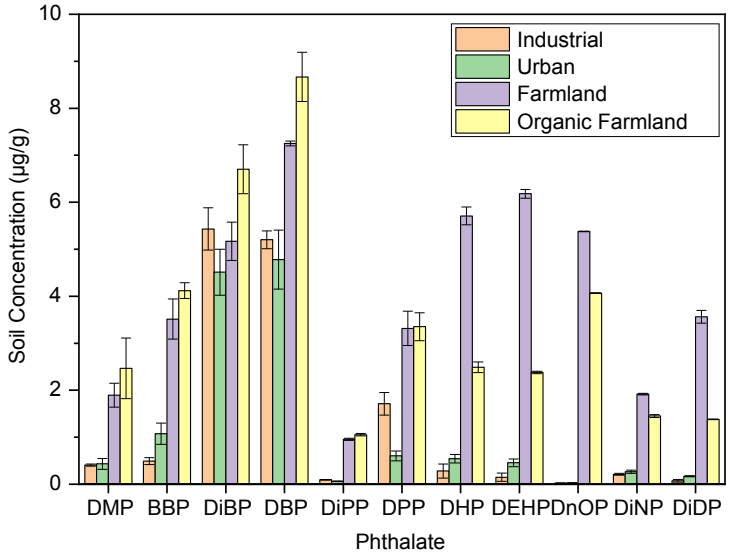


Figure 3.13. Phthalate concentrations in soil.

compared with that seen when covering soil with a plastic sheet, because of the reduced surface area and more resilient material.

As the sources of phthalates into the Irish environment as evidenced by testing of other matrices all contained high levels of DBP and DIBP, these phthalates were also found at the highest levels in soil (Figure 3.13).

4 Human Exposure to Phthalates in Ireland

The concentrations of phthalate monoester metabolites were measured in wastewater influent. Five months of grab samples were analysed at three different WWTPs (Figures 4.1–4.5). Each WWTP represented a rural, suburban or urban population and WWTPs are labelled as such throughout. Grab samples were used because there was a limited amount of composite sample available; this could contribute slightly to monthly variations.

There is temporal and spatial variation for phthalate monoester metabolites in Ireland. Metabolite levels were highest at the suburban site (Figure 4.2), and all sites were significantly different from each other as confirmed by two-way analysis of variance (ANOVA). Although population levels and behaviour at each site are likely to fluctuate, temporal variation could be partly attributable to different degradation kinetics in transit to the WWTPs or variations in residence times before sampling, allowing the degradation of phthalate diester to the monoester metabolite in-sewer.

Concentrations of many metabolites at the suburban site were higher than those at the urban site

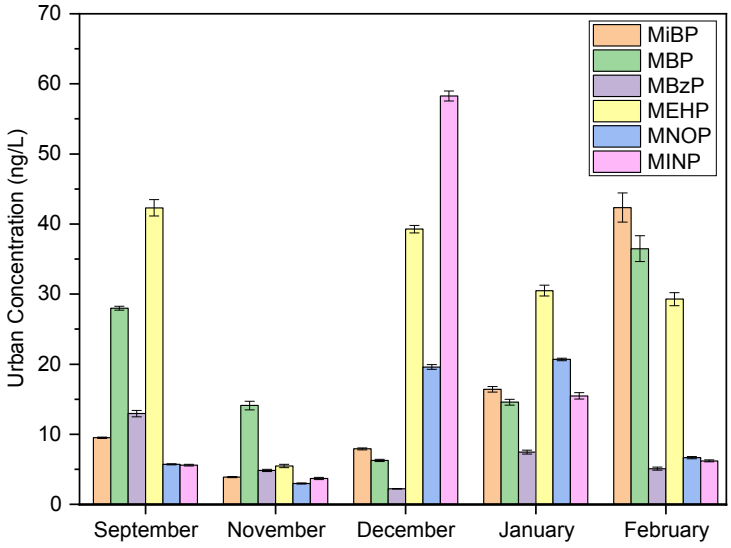


Figure 4.1. Monoester concentrations at the urban site.

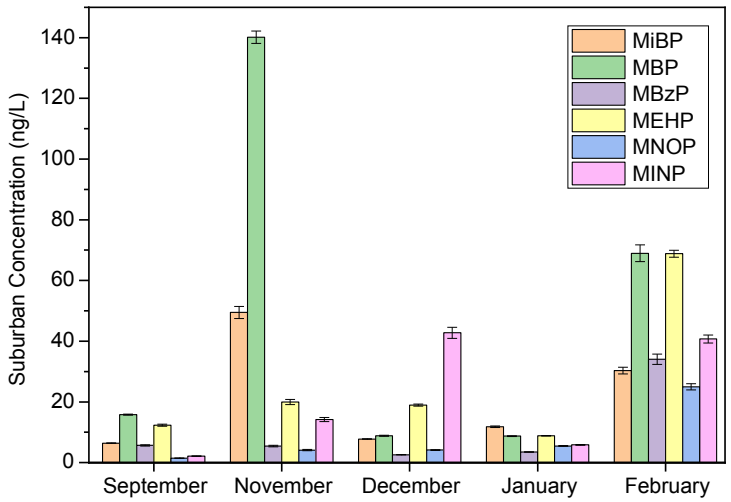


Figure 4.2. Monoester concentrations at the suburban site.

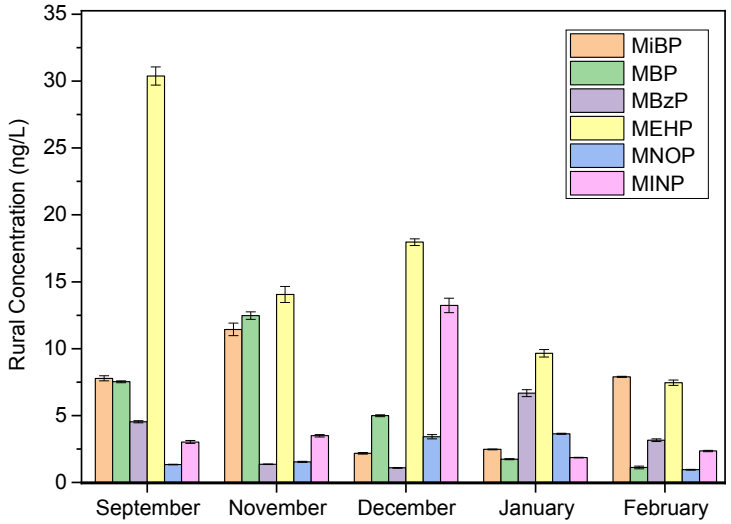


Figure 4.3. Monoester concentrations at the rural site.

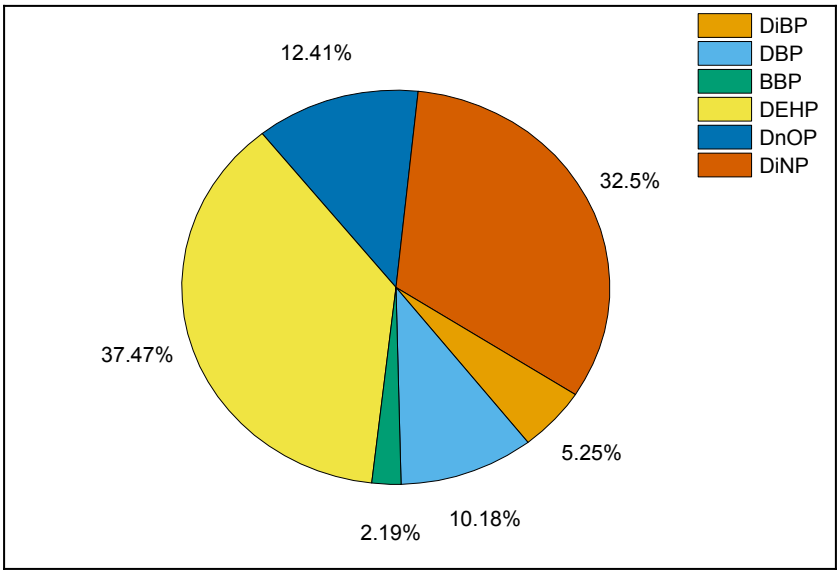


Figure 4.4. Breakdown of exposure to phthalates in Ireland.

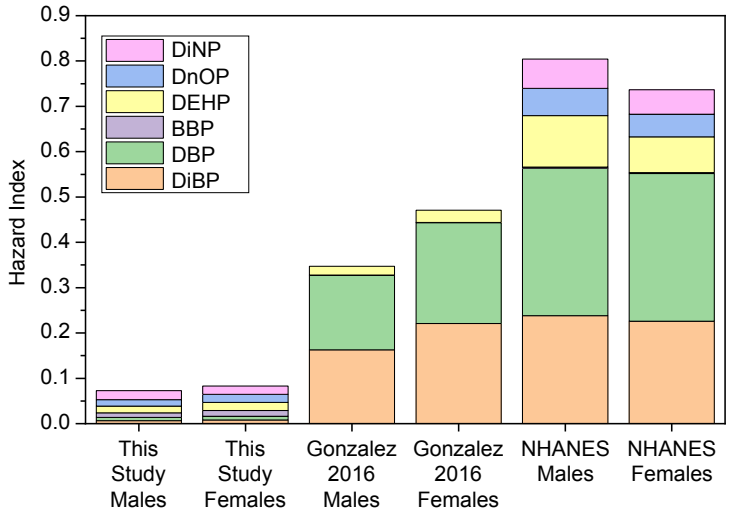


Figure 4.5. Hazard index.

(Figure 4.1), which was not expected. This could be due to agricultural run-off contributing phthalate monoesters from animals or from degraded phthalate parent compounds in soils. There is a high level of hard surface run-off in the suburban area, which could indicate that concentrations from this type of area could overestimate human exposure. However, further data would be required to get a real insight into the significance of spatial and temporal variation, such as apparent increases in MEHP and monoisononyl phthalate in December and February.

The monoester concentrations were converted to the associated population diester exposure, as outlined in Chapter 2, and are reported as an averaged level of phthalate diesters metabolised per person per day (Table 4.1).

From this study, on average, the phthalate that contributes the highest degree of exposure to humans in Ireland is DEHP, followed by DINP and DNOP. The LMW phthalates (DBP, DIBP and BBP) combine to form roughly 18% of total phthalate exposure. Using a crude calculation averaging human body weight in catchment areas at 70 kg, the average estimated exposure is order(s) of magnitude lower than the tolerable daily intake (TDI) of 50 µg per kg body weight per day for DBP, BBP, DEHP and DINP set by the European Food Safety Authority and outlined in Table 4.2.

Table 4.1. Phthalate diesters metabolised (µg/person per day)

Site	Month	DIBP	DBP	BBP	DEHP	DNOP	DINP
Rural	September	1.25	1.21	0.68	22.84	1.01	2.28
	November	5.95	6.64	0.68	34.91	3.84	8.69
	December	0.67	1.57	0.32	26.30	5.01	19.38
	January	0.46	0.33	1.18	8.50	3.22	1.65
	February	1.28	0.19	0.49	5.75	0.74	1.82
Suburban	September	2.87	7.24	2.43	26.29	3.13	4.56
	November	29.25	84.74	3.07	56.39	11.63	40.03
	December	9.35	10.91	2.97	108.92	23.77	245.42
	January	6.31	4.77	1.79	22.57	31.42	33.66
	February	16.37	38.07	17.54	177.25	64.24	104.95
Urban	September	2.31	6.94	3.00	48.98	6.62	6.48
	November	1.58	5.89	1.89	10.64	5.80	7.19
	December	3.68	4.29	0.67	59.09	29.50	87.69
	January	4.82	4.37	2.09	42.72	28.97	21.68
	February	9.53	8.39	1.09	31.44	7.15	6.67

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DIBP, diisobutyl phthalate; DINP, diisononyl phthalate; DNOP, di-*n*-octylphthalate.

Table 4.2. Human phthalate exposure limits

Phthalate	2005 TDI (µg/kg per day)	2019 TDI (µg/kg per day)	TDI rationale (EFSA, 2019)	This study (µg/kg per day)
DBP	10	50	Based on the impact on testosterone in fetuses	0.17
BBP	500	50		0.04
DEHP	50	50		0.65
DINP	150	50		0.56
DIDP	150	150	Based on the effects on the liver	N/A
DIBP	N/A	N/A	N/A	0.09
DNOP	N/A	N/A	N/A	0.21

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DIBP, diisobutyl phthalate; DIDP, diisodecyl phthalate; DINP, diisononyl phthalate; DNOP, di-*n*-octylphthalate; N/A, not applicable.

Source: EFSA (2005, 2019).

The National Health and Nutrition Examination Survey (NHANES) is a programme of studies designed to assess the health and nutritional status of adults and children in the USA (CDC, 2018). The survey is unique in that it combines interviews and physical examinations, providing a wealth of data on each sample collected. As this is a large-scale biomonitoring project, it will form the basis of a total population risk assessment that can be compared with the wastewater data collected in Ireland. NHANES has monitored phthalates since 1999, with the most recent data available coming from the period 2013–2014. An analysis of NHANES biomonitoring data from the period 2001–2010 suggested that population exposure to phthalates changed in the USA during this time frame. A decrease in DBP, BBP and DEHP exposures was observed, while an increase in DINP and DIBP was observed. This indicates a temporal trend, possibly associated with changes in legislation and the impact of advocacy groups on consumer behaviour (Zota *et al*., 2014). Owing to these temporal trends, the most recent phthalate data collected are used for comparison here.

The other studies were chosen as they used WBE and recent European data.

4.1 Hazard Quotient

The hazard quotient (HQ) and the sum of the HQs (known as the hazard index – HI) were calculated. As discussed previously, this serves to relate a degree of exposure to an associated toxicological risk. Any value greater than 1 is deemed to be a risk for toxicity purposes. Any value greater than 0.8 is deemed to be a risk for endocrine disruption, as reported by the US EPA.

Individual HQs for each phthalate were quite low for this study, as suggested by the lower level of exposure (see Table 4.3). The level of exposure was higher among females. The phthalate that contributed the least to toxicological effects was BBP. The phthalate with the highest health impact based on the HQ was DINP, with higher levels of risk associated with the HMW phthalates; this increased risk when compared with LMW phthalates is based on higher magnitudes of exposure. The literature suggests that populations should be less exposed to HMW phthalates because of their reduced leaching abilities. Changes in manufacturing practices may have increased HMW phthalate production to such a degree that we are now at greatest exposure to these compounds in Ireland.

The HI of this study was compared with a NHANES (CDC, 2018) and another European WBE study carried out in 2016 (González-Marino *et al*., 2017) (see Figure 3.4). The HI calculated from the NHANES suggested that the population is at risk of endocrine disruption and possibly further toxicological effects from phthalates, as only the phthalates included in this study were assessed. The Spanish WBE study also showed a higher HI from phthalate exposure. From an investigation into the HQ in Ireland, there is no cause for concern for phthalate exposure from a toxicological endpoint. However, a number of phthalates and other

Table 4.3. HQ of exposure to each phthalate

Gender	Site	DIBP	DBP	BBP	DEHP	DNOP	DINP
Male	Rural	0.0023 (0.005–0.0071)	0.0024 (0.002–0.0079)	No risk	0.0047 (0.0014–0.0083)	0.0007 (0.0002–0.0083)	0.0005 (0.0001–0.0015)
	Suburban	0.0153 (0.0034–0.0348)	0.0347 (0.0057–0.1009)	0.0001 (0–0.004)	0.0186 (0.0054–0.0422)	0.0064 (0.0007–0.0153)	0.0068 (0.0004–0.0195)
	Urban	0.0052 (0.0019–0.0113)	0.0071 (0.0051–0.0100)	No risk (0–0.001)	0.0092 (0.0025–0.0141)	0.0037 (0.0014–0.0070)	0.0021 (0.0005–0.0070)
Female	Rural	0.0028 (0.0007–0.0086)	0.0029 (0.0003–0.0096)	No risk	0.0057 (0.0017–0.0101)	0.0008 (0.0002–0.0015)	0.0007 (0.0002–0.0019)
	Suburban	0.0186 (0.0042–0.0424)	0.0422 (0.0069–0.1228)	0.0002 (0.0001–0.0005)	0.0227 (0.0065–0.0514)	0.0078 (0.0009–0.0186)	0.0083 (0.0004–0.0237)
	Urban	0.0064 (0.0023–0.0138)	0.0087 (0.0062–0.0122)	0.0001 (0–0.0001)	0.0112 (0.0031–0.0171)	0.0045 (0.0017–0.0085)	0.0025 (0.0001–0.0085)

Numbers in brackets signify the range.

BBP, benzyl butyl phthalate; DBP, dibutyl phthalate; DEHP, diethylhexyl phthalate; DIBP, diisobutyl phthalate; DINP, diisononyl phthalate; DNOP, di-*n*-octylphthalate.

plasticisers were not included in this, so assessing a mixture of EDCs in Irish wastewater may show that there is potential for endocrine disruption. Indeed, lower HIs for phthalates (as low as 0.1 or 0.2) have been suggested to account for the combined impact of exposure to the wide spread of EDCs that exist (Apel *et al*., 2020).

4.2 Odds Ratio

The OR conveys the degree of exposure to an associated risk. A detailed literature review surveyed the data with a particular focus on the following health outcomes: pregnancy outcomes, male birth defects, allergy, children's neurological development and precocious puberty in females. From the literature, the strongest evidence in humans is for associations with birth anomalies, precocious puberty in females and allergy, with these studies showing the highest statistical significance > 1.

4.2.1 Risk data collection

Human risk data were collected from the literature. We searched PubMed (NCBI) using the search terms [("Phthalic Acids/adverse effects") AND Humans)] NOT tha], and studies were included or excluded as follows in Figure 4.6.

The remaining 121 papers were reviewed for the quality of the OR/risk ratio. For the purposes of risk data, exposure magnitudes are separated into either tertiles or quartiles – groups containing one-third (tertiles) or one-quarter (quartiles) of the population ranked according to exposure concentration from lowest to highest. In Tables 4.4 and 4.5, ORs for adverse effects associated with various phthalates are divided into tertiles. As all members of the population are exposed to phthalates, the first tertile is not the unexposed group but rather the group with the lowest magnitude of exposure (the referent). These values were used to relate the level of exposure in Ireland to the relevant adverse health effect, i.e. if the concentration exposed falls into the second tertile, then the OR for that tertile can be applied to the Irish population.

The levels of phthalate exposure from this study were compared with the levels found in the literature review and a comparison with the OR was made. This is an approximation and is not based on any

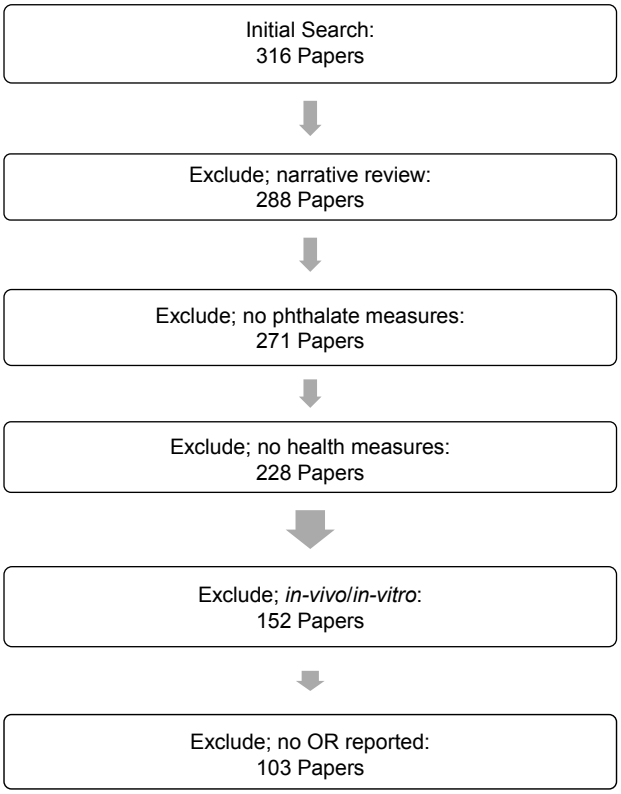


Figure 4.6. Search parameters for human risk data.

health data from the population studied, so it serves as an indication of possible risk only. As exposure in Ireland was lower than that in the NHANES, all risks were lower than those reported from these data. It is assumed that there is no increased risk of a specific health effect from phthalate exposure in Ireland.

4.3 Wastewater-based Epidemiology as a Biomonitoring Tool

There will be many catchment-specific differences between influent samples at WWTPs that may affect the concentrations of metabolites used for exposure assessment. These variations in sewer network residence times could cause different in-transit transformations and therefore partially contribute to international variations in concentrations. The available literature has illustrated that in-sewer transformation is compound specific and influenced by environmental factors. Some compounds seen in the literature (e.g. MDMA, ketamine and MDPV) remain stable at neutral pH and temperatures up to 20°C. However, drugs such as THCCOOH, fentanyl, mephedrone and cathinones have higher levels of variability (McCall *et al*., 2016). To compare results between different studies and environments, a standardised method

Table 4.4. OR (95% CI) data on health effects of LMW phthalates

					MEP			MBP			MIBP			MBzP		
Adverse effect	**Reference**	**Study type**	**Analysis of exposure**	***N***	**1st**	**2nd**	**3rd**	**1st**	**2nd**	**3rd**	**1st**	**2nd**	**3rd**	**1st**	**2nd**	**3rd**
Reduced AGD	Swan *et al*. (2005)	Cohort	Prenatal urinary metabolite analysis by LC–MS/MS	85	1	2.6 (0.9–7.8)	4.7 (1.2–17.4)	1	3.8 (1.2–12.3)	10.2 (2.5–42.2)	1	3.4 (1.1–10.5)	9.1 (2.3–35.7)	1	3.1 (1.002–9.8)	3.8 (1.03–13.9)
Weak NBAS scores	Engel *et al*. (2009)	Prospective birth cohort	Urinary	295	Relative risk LMW 1.05 (0.93, 1.17)											
Autism spectrum disorder	Philippat *et al*. (2015)	Case–control	GC–MS urinary monoester concentration	145	1.13 (0.76–1.66)			1.06 (0.65–1.73)		N/A			1.17 (0.85–1.61)			
Developmental delay					1.18 (0.70–1.98)			1.63 (0.92–2.87)		N/A			1.40 (0.97–2.04)			
ADD	Chopra *et al*. (2014)	Case–control	Urinary metabolites by HPLC–ESI–MS/MS asterix:total parent compound	1493	1.0 (0.6–1.8)			1.8 (0.6–4.8)		N/A			1.5 (0.7–3.4)			
Learning difficulties					1.0 (0.6–1.6)			1.3 (0.6–2.9)		N/A			1.2 (0.6–2.5)			
ADD + learning difficulties					1.7 (0.9–3.3)			3.3 (0.9–12.7)		N/A			2.0 (0.6–6.3)			
Pregnancy loss (exposure pre-conception)	Toft *et al*. (2012)	Prospective cohort	LC–MS/MS analysis of urinary metabolites	430 (114 excluded)	1	0.93 (0.35–2.50)	0.81 (0.31–2.09)	1	0.70 (0.27–1.84)	0.79 (0.32–2.00)	N/A			1	1.38 (0.53–3.62)	0.59 (0.21–1.65)
Pregnancy loss (exposure during conception)	Toft *et al*. (2012)	Prospective cohort	LC–MS/MS analysis of urinary metabolites	430 (114 excluded)	1	1.51 (0.57–3.98)	1.98 (0.74–5.34)	1	1.12 (0.41–3.02)	1.12 (0.43–2.95)	N/A			1	1.72 (0.63–4.69)	2.10 (0.74–5.88)
Preterm birth	Ferguson *et al*. (2014)	Case–control	Urinary metabolites by LC–MS	Visit 1 35,336	0.92 (0.71–1.19)			0.97 (0.62–1.50)		0.92 (0.57–1.47)			1.02 (0.73–1.43)			
Preterm birth	Ferguson *et al*. (2014)	Case–control	Urinary metabolites by LC–MS	Visit 2 31,297	0.96 (0.74–1.26)			1.23 (0.79– 1.93)		0.88 (0.54–1.41)			1.07 (0.73–1.55)			
Preterm birth	Ferguson *et al*. (2014)	Case–control	Urinary metabolites by LC–MS	Visit 3 32,289	0.99 (0.77–1.27)			1.15 (0.77–1.72)		1.00 (0.68–1.48)			1.07 (0.78–1.48)			
Preterm birth	Ferguson *et al*. (2014)	Case–control	Urinary metabolites by LC–MS	Visit 4 15,303	0.88 (0.60–1.29)			0.94 (0.40– 2.22)		1.02 (0.57–1.84)			1.02 (0.64–1.63)			
Elevated triglycerides	Trasande *et al*. (2013)	Cross-sectional	NHANES data; urinary metabolites by LC–MS	705	LMW phthalates 0.85 (0.71–1.01)											
Low HDL	Trasande *et al*. (2013)	Cross-sectional	NHANES data; urinary metabolites by LC–MS	2539	LMW phthalates 1.00 (0.87–1.15)											

ADD, attention deficit disorder; AGD, anogenital distance; ESI–MS, electrospray ionisation–mass spectrometry; HDL, high-density lipoprotein; HPLC, high-performance liquid chromatography; MBP, monobutyl phthalate; MEP, monoethyl phthalate; MIBP, monoisobutyl phthalate; N/A, not applicable; NBAS, Neonatal Behavioural Assessment Scale.

Table 4.5. OR (95% CI) data on health effects of HMW phthalates

Specific effect	Reference	Study type	Analysis of exposure	*N*	MEHP			5-Hydroxy-MEHP			5-oxo-MEHP			5-cx-MEPP			7cx-MMeHP			MCPP		
					1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Reduced AGD	Jensen *et al.* (2015)	Case–control	LC–MS/MS	75 cases, 300 controls	N/A			N/A			N/A			1	0.75 (0.39–1.46)	0.89 (0.44–1.8)	1	1.3 (0.62–2.72)	1.69 (0.78–3.67)	N/A		
Cryptochidism	Jensen *et al.* (2015)	Case–control	LC–MS/MS	270 cases, 300 controls	N/A			N/A			N/A			1	0.70 (0.46–1.08)	0.90 (0.57–1.41)	1	1.06 (0.68–1.63)	1.28 (0.80–2.01)	N/A		
Weak NBAS scores	Engel *et al.* (2009)	Cohort	Urine laboratory	295	Relative risk HMW 0.93 [0.82,1.06]																	
Autism spectrum disorder	Philippat *et al.* (2015)	Case–control	Urine laboratory	145	1.33 (0.78–2.25)		N/A				N/A			N/A			N/A			N/A		
Developmental delay					2.12 (1.10–4.09)		N/A				N/A			N/A			N/A			N/A		
ADD	Chopra *et al.* (2014)	Case–control	Urinary metabolite levels by HPLC–ESI–MS/MS	1493	2.1 (1.1–3.9)									N/A			N/A			N/A		
Learning difficulties					1.5 (0.7–3.0)									N/A			N/A			N/A		
ADD + learning difficulties					2.2 (0.6–7.4)									N/A			N/A			N/A		
Pregnancy loss (exposure pre-conception)	Toft *et al.* (2012)	Cohort	LC–MS/MS analysis of urinary metabolite levels	430	1	0.74 (0.38–1.82)	1.79 (0.47–6.81)	1	1.33 (0.51–3.40)	0.57 (0.22–1.48)	1	2.01 (0.80–5.04)	0.46 (0.16–1.34)	N/A			N/A			N/A		
Pregnancy loss (exposure during conception cycle)					1	0.97 (0.34–2.76)	2.87 (1.09–7.57)	1	0.94 (0.34–2.59)	1.46 (0.56–3.78)	1	1.22 (0.46–3.27)	1.38 (0.51–3.78)	N/A			N/A			N/A		
Preterm birth	Ferguson *et al.* (2014)	Case–control	Urinary metabolite levels by LC–MS	Visit 1 35,336	1.12 (0.85–1.48)			1.14 (0.86–1.52)			1.18 (0.88–1.57)			1.46 (1.10–1.95)			N/A			1.20 (0.90–1.60)		
Preterm birth	Ferguson *et al.* (2014)	Case–control	Urinary metabolite levels by LC–MS	Visit 2 31,297	1.03 (0.75–1.41)			0.99 (0.71–1.39)			1.03 (0.74–1.45)			1.22 (0.90–1.67)			N/A			0.91 (0.64–1.28)		

Table 4.5. Continued

Specific effect	Reference	Study type	Analysis of exposure	*N*	MEHP			5-Hydroxy-MEHP			5-oxo-MEHP			5-cx-MEPP			7cx-MMeHP			MCPP		
					1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
Preterm birth	Ferguson *et al.* (2014)	Case–control	Urinary metabolite levels by LC–MS	Visit 3 32,289	1.07 (0.78–1.48)			1.19 (0.86–1.63)			1.20 (0.87–1.66)			1.32 (0.98–1.78)			N/A			1.18 (0.83–1.69)		
Preterm birth	Ferguson *et al.* (2014)	Case–control	Urinary metabolite levels by LC–MS	Visit 4 15,303	1.02 (0.64–1.63)			0.74 (0.42–1.29)			0.91 (0.52–1.56)			1.29 (0.79–2.11)			N/A			1.24 (0.74–2.09)		
Elevated triglycerides	Trasande *et al.* (2013)	Cross-sectional	NHANES data; urinary metabolite levels by LC–MS	705	Total DEHP metabolites 1.05 (0.90–1.22)															HMW phthalates 1.06 (0.90–1.24)		
Low HDL	Trasande *et al.* (2013)	Cross-sectional	NHANES data; urinary metabolite levels by LC–MS	1493	Total DEHP metabolites 0.94 (0.82– 1.08)															HMW phthalates 0.93 (0.80–1.07)		
Breast cancer	López-Carrillo *et al.* (2010)	Case–Control	Urinary metabolite levels	223 cases, 221 controls	1	1.03 (0.62–1.69)	1.23 (0.75–2.01)	1	0.77 (0.46–1.28)	1.37 (0.84–2.24)	1	0.60 (0.36–1.00)	0.84 (0.52–1.36)	1	1.27 (0.77–2.10)	1.68 (1.01–2.78)	N/A			N/A		

5-cx-MEPP, mono(2-ethyl-5-carboxypentyl)phthalate; 7cx-MMeHP, mono(4-methyl-7-carboxy-heptyl) phthalate; ADD, attention deficit disorder; AGD, anogenital distance; ESI–MS, electrospray ionisation-mass spectrometry; HDL, high-density lipoprotein; HPLC, high performance liquid chromatography; MCPP, mono-(3-carboxypropyl) phthalate; MEHP, monoethylhexyl phthalate; N/A, not applicable; NBAS, Neonatal Behavioural Assessment Scale.

with quality controls/correction factors for the stability of compounds in addition to in-transit and in-sewer transformations should be developed. This will allow a higher degree of accuracy when informing policy.

It is recommended that reference standards of more highly metabolised biomarkers are used for exposure assessment because of their increased resilience to biotic and abiotic formation outside the human body. However, these standards may not be cost-effective (for phthalates, these may be roughly 1000 times more expensive). This method would therefore not be attractive to governmental testing bodies because of the comparatively high cost, although this disparity may be less for other emerging contaminants. The assessment method could also be improved by determining the compound kinetics of degradation. If spiked analytes of interest are added to bioreactors and piping systems that simulate real-life sewer conditions, then accurate degradation rates could be obtained for a range of residence times. Once the kinetics of degradation are published, WBE could be improved by incorporating these into the existing exposure model.

As it stands, the basic method for WBE still serves as a useful diagnostic tool for the prioritisation of contaminants of emerging concern. Within one community, a variety of EDCs can be screened to assess the most critical compound for body burden. Traditional biomonitoring studies are labour intensive, expensive and require patients. With a first step assessment, these studies can be reserved for EDCs that are already known to cause body burden in that society. This evidence should increase the likelihood of these biomonitoring studies, which are much needed to influence policy change, being funded. It is, however, recommended that a large-scale biomonitoring study be carried out in Ireland in the future, as richer data on a population can be obtained and we are far behind our European counterparts in this area of research. One large-scale biomonitoring study could yield information on a wide range of EDCs, and if proper sample management is maintained then retrospective studies on multiple chemicals of emerging concern can be carried out.

5 Recommendations

This project aimed to examine the environmental sources, fates and body burden of phthalates in Ireland. The three main objectives were to:

- assess the concentrations of phthalates in surface waters, soils, household waste, landfill leachates and wastewater;
- develop methods for the detection of phthalates in wastewater process streams for future compliance monitoring;
- assess human exposure through WBE and estimate a related risk.

Phthalates are pervasive in the Irish environment. The concentrations in this study have been found to be consistent with those in other European countries and, therefore, Ireland does not present an increased cause for concern. Nevertheless, 100% detection frequency for 10 of the 11 phthalates studied suggests that further steps need to be taken to reduce this burden on the environment and prevent any further contamination in the ecosystem.

5.1 Reduction of Phthalate Burden

It is possible that restricted phthalates remain in our consumer products because of the recycling process. If recyclable material contains more than the recommended levels of these phthalates, recyclable materials should not be used for the manufacture of food contact materials or children's toys. Therefore, relevant recyclable materials should be carefully tested for restricted phthalates to lessen the risk of phthalate contamination in these materials. If a toxicological concern is raised beyond this endpoint, then incineration of plastics should be considered until these compounds have been eliminated. Landfill should be avoided, and leachate systems need to be controlled and monitored. The recently announced European Commission Green Deal[4] highlights the intention to implement a zero pollution and toxic-free environment, with a circular economy action plan and proposed policy development in the areas of sustainable industry and elimination of pollution; management of phthalates must be a prominent feature of this moving forward.

Wastewater effluent was seen to contribute some degree of phthalate contamination to the wastewater discharge point (river or marine system). The levels at the discharge point were significantly higher than those at other points of the river. However, the levels in effluent are low, with all phthalates being under the EQS for surface water. The findings of this study suggest that no further action to reduce phthalates in wastewater effluent needs to be taken.

The EPA notes that land spreading is the primary removal route of sludge in Ireland. Phthalates are well retained in sludge, and the literature has shown that the transfer of phthalates from fertiliser to soil and hence crops is high. Novel wastewater treatment could be employed to remove these EDCs from sludge; some examples of this are chemical extraction, bioleaching, electroreclamation and supercritical fluid extraction. This will reduce not only the level of phthalates but also the levels of heavy metals and other EDCs retained in sludge that could also contribute to endocrine-disrupting effects. These solutions are currently very expensive, and it is recommended that a technoeconomic analysis of sludge disposal methods versus the benefit to agriculture should be carried out.

5.2 Feasibility of Wastewater-based Epidemiology for Compliance Monitoring

Wastewater analysis is a feasible approach for compliance monitoring. Phthalate levels exhibit a level of temporal variation. The analytical method developed shows that, once significant experimental factors are put in place for the control of outside contamination, there is a simple and robust technique for determining the concentrations in this matrix. This SPE method could be incorporated into an analysis of other compounds once the correct control steps are

4 https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en (accessed 5 June 2020).

put in place. The main recommendations for analysing phthalates by LC–MS are as follows.

- Check each new batch of solvent for phthalate contamination. Triple rinse all glassware with solvent after an overnight bake-out and reduce solvent and sample contact with air and any plastic materials.
- Fischer Optima™ solvents should be considered for solvent choice, as these showed the lowest phthalate contamination of all solvents studied.
- Use a delay column to prevent instrument contamination.
- Conduct daily cleans of the instrument to remove residual phthalate and, if possible, use a multi-wash system to fully clean the needle.
- Include multiple analytical blanks to reduce column carry-over. Ensure that all analytical blanks are clean before sample run; if not, subtract from sample. Include procedural blanks and subtract levels from samples.

If limits are set, this is a reliable method to determine levels at the WWTP and monitor emissions.

5.3 Wastewater as a Biomarker for Human Health

A first-step health risk assessment of phthalates was carried out by monitoring the metabolites of six phthalate esters. These data were then converted to the daily intake rates of the parent phthalates. The average exposure levels found in Ireland were well below the levels of concern from a toxicological endpoint. The exposure rates were lower than those found in the USA, China and Spain, but levels were within an order of magnitude, so this can be attributed to population differences. The analytical method developed was robust and resistant to matrix effects, although it was time-consuming because of the use of standard addition. This offers a cost-effective way to examine the impact of an EDC on a population, with the caveat that changes to the analyte of concern in transit to the WWTP are as yet difficult to quantify. This serves as a useful tool for estimating population exposure and prioritising substances of emerging concern.

5.4 Future Research

- As soils were deemed to have greater phthalate burden, an increased sample size soil survey should be carried out, including monitoring specific sites that utilise land application of biosolids. This will establish whether or not any land spreading practices pose a risk to soil ecology at those sites. It would be beneficial to also examine crop uptake of phthalates through these soils to determine the degree of phthalate contamination introduced to food pre packaging.
- Phthalate metabolites were monitored in this study only as a means to assess human exposure, but recent bioassay research has suggested that the phthalate metabolites themselves exhibit similar levels of endocrine-disrupting properties. If future work is carried out in the area of phthalate contamination in Ireland, phthalate metabolites should be considered to assess the total impact of phthalates on the environment.
- The accuracy of WBE could be improved in further research. One method is by using secondary metabolites for greater selectivity and resistance to transformations in transit to the WTWP. Another method would be to determine the degradation/abiotic formation kinetics of the primary metabolites using bioreactors and model piping systems. This kind of research, once published, would benefit the research community, allowing basic WBE experiments to be carried out with kinetics incorporated into the exposure model to improve accuracy.
- To determine the true human health impact of phthalates, a full-scale biomonitoring study should be carried out in Ireland; this will give detailed health information on the subjects and therefore a targeted risk. A method could be developed to include monitoring of a wide-ranging suite of compounds of emerging concern to maximise the resources. If such a study were conducted, there would be strong evidence to influence policy on emerging EDCs.

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Abbreviations

ACN	Acetonitrile
BBP	Benzyl butyl phthalate
CI	Confidence interval
CPSC	Consumer Product Safety Commission
DBP	Dibutyl phthalate
DEHP	Diethylhexyl phthalate
DEP	Diethyl phthalate
DHP	Dihexyl phthalate
DIBP	Diisobutyl phthalate
DIDP	Diisodecyl phthalate
DINP	Diisononyl phthalate
DIPP	Diisopentyl phthalate
DMP	Dimethyl phthalate
DNOP	Di-*n*-octylphthalate
DNPP	Di-*n*-pentyl phthalate
DPP	Dipentyl phthalate
ECHA	European Chemicals Agency
EDC	Endocrine-disrupting chemical
EPA	Environmental Protection Agency
EQS	Environmental Quality Standard
FDA	Food and Drug Administration
GC–MS	Gas chromatography–mass spectrometry
HI	Hazard index
HMW	High molecular weight
HQ	Hazard quotient
IPA	Isopropyl alcohol
LC–MS/MS	Liquid chromatography–mass spectrometry/mass spectrometry
LMW	Low molecular weight
LOD	Limit of detection
Log K_{ow}	Octanol/water partition co-efficient
MBzP	Monobenzyl phthalate
MDMA	3,4-Methylenedioxy-methamphetamine
MDPV	Methylenedioxypyrovalerone
MEHP	Monoethylhexyl phthalate
MW	Molecular weight
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
PNEC	Predicted no effect concentration
PVC	Polyvinyl chloride
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RSD	Relative standard deviation
SPE	Solid phase extraction
SVHC	Substance of very high concern
TDI	Tolerable daily intake
THCCOOH	11-Nor-9-carboxy-Δ9-tetrahydrocannnabinol

TTIP	Transatlantic Trade and Investment Partnership
WBE	Wastewater-based epidemiology
WWTP	Wastewater treatment plant

AN GHNÍOMHAIREACHT UM CHAOMHNÚ COMHSHAOIL
Tá an Ghníomhaireacht um Chaomhnú Comhshaoil (GCC) freagrach as an gcomhshaol a chaomhnú agus a fheabhsú mar shócmhainn luachmhar do mhuintir na hÉireann. Táimid tiomanta do dhaoine agus don chomhshaol a chosaint ó éifeachtaí díobhálacha na radaíochta agus an truaillithe.

Is féidir obair na Gníomhaireachta a roinnt ina trí phríomhréimse:

Rialú: *Déanaimid córais éifeachtacha rialaithe agus comhlíonta comhshaoil a chur i bhfeidhm chun torthaí maithe comhshaoil a sholáthar agus chun díriú orthu siúd nach gcloíonn leis na córais sin.*

Eolas: *Soláthraímid sonraí, faisnéis agus measúnú comhshaoil atá ar ardchaighdeán, spriocdhírithe agus tráthúil chun bonn eolais a chur faoin gcinnteoireacht ar gach leibhéal.*

Tacaíocht: *Bímid ag saothrú i gcomhar le grúpaí eile chun tacú le comhshaol atá glan, táirgiúil agus cosanta go maith, agus le hiompar a chuirfidh le comhshaol inbhuanaithe.*

Ár bhFreagrachtaí

Ceadúnú
Déanaimid na gníomhaíochtaí seo a leanas a rialú ionas nach ndéanann siad dochar do shláinte an phobail ná don chomhshaol:
- saoráidí dramhaíola *(m.sh. láithreáin líonta talún, loisceoirí, stáisiúin aistrithe dramhaíola)*;
- gníomhaíochtaí tionsclaíocha ar scála mór *(m.sh. déantúsaíocht cógaisíochta, déantúsaíocht stroighne, stáisiúin chumhachta)*;
- an diantalmhaíocht *(m.sh. muca, éanlaith)*;
- úsáid shrianta agus scaoileadh rialaithe Orgánach Géinmhodhnaithe *(OGM)*;
- foinsí radaíochta ianúcháin *(m.sh. trealamh x-gha agus radaiteiripe, foinsí tionsclaíocha)*;
- áiseanna móra stórála peitril;
- scardadh dramhuisce;
- gníomhaíochtaí dumpála ar farraige.

Forfheidhmiú Náisiúnta i leith Cúrsaí Comhshaoil
- Clár náisiúnta iniúchtaí agus cigireachtaí a dhéanamh gach bliain ar shaoráidí a bhfuil ceadúnas ón nGníomhaireacht acu.
- Maoirseacht a dhéanamh ar fhreagrachtaí cosanta comhshaoil na n-údarás áitiúil.
- Caighdeán an uisce óil, arna sholáthar ag soláthraithe uisce phoiblí, a mhaoirsiú.
- Obair le húdaráis áitiúla agus le gníomhaireachtaí eile chun dul i ngleic le coireanna comhshaoil trí chomhordú a dhéanamh ar líonra forfheidhmiúcháin náisiúnta, trí dhíriú ar chiontóirí, agus trí mhaoirsiú a dhéanamh ar leasúchán.
- Cur i bhfeidhm rialachán ar nós na Rialachán um Dhramhthrealamh Leictreach agus Leictreonach (DTLL), um Shrian ar Shubstaintí Guaiseacha agus na Rialachán um rialú ar shubstaintí a ídíonn an ciseal ózóin.
- An dlí a chur orthu siúd a bhriseann dlí an chomhshaoil agus a dhéanann dochar don chomhshaol.

Bainistíocht Uisce
- Monatóireacht agus tuairisciú a dhéanamh ar cháilíocht aibhneacha, lochanna, uiscí idirchriosacha agus cósta na hÉireann, agus screamhuiscí; leibhéil uisce agus sruthanna aibhneacha a thomhas.
- Comhordú náisiúnta agus maoirsiú a dhéanamh ar an gCreat-Treoir Uisce.
- Monatóireacht agus tuairisciú a dhéanamh ar Cháilíocht an Uisce Snámha.

Monatóireacht, Anailís agus Tuairisciú ar an gComhshaol
- Monatóireacht a dhéanamh ar cháilíocht an aeir agus Treoir an AE maidir le hAer Glan don Eoraip (CAFÉ) a chur chun feidhme.
- Tuairisciú neamhspleách le cabhrú le cinnteoireacht an rialtais náisiúnta agus na n-údarás áitiúil *(m.sh. tuairisciú tréimhsiúil ar staid Chomhshaol na hÉireann agus Tuarascálacha ar Tháscairí)*.

Rialú Astaíochtaí na nGás Ceaptha Teasa in Éirinn
- Fardail agus réamh-mheastacháin na hÉireann maidir le gáis cheaptha teasa a ullmhú.
- An Treoir maidir le Trádáil Astaíochtaí a chur chun feidhme i gcomhair breis agus 100 de na táirgeoirí dé-ocsaíde carbóin is mó in Éirinn.

Taighde agus Forbairt Comhshaoil
- Taighde comhshaoil a chistiú chun brúnna a shainaithint, bonn eolais a chur faoi bheartais, agus réitigh a sholáthar i réimsí na haeráide, an uisce agus na hinbhuanaitheachta.

Measúnacht Straitéiseach Timpeallachta
- Measúnacht a dhéanamh ar thionchar pleananna agus clár beartaithe ar an gcomhshaol in Éirinn *(m.sh. mórphleananna forbartha)*.

Cosaint Raideolaíoch
- Monatóireacht a dhéanamh ar leibhéil radaíochta, measúnacht a dhéanamh ar nochtadh mhuintir na hÉireann don radaíocht ianúcháin.
- Cabhrú le pleananna náisiúnta a fhorbairt le haghaidh éigeandálaí ag eascairt as taismí núicléacha.
- Monatóireacht a dhéanamh ar fhorbairtí thar lear a bhaineann le saoráidí núicléacha agus leis an tsábháilteacht raideolaíochta.
- Sainseirbhísí cosanta ar an radaíocht a sholáthar, nó maoirsiú a dhéanamh ar sholáthar na seirbhísí sin.

Treoir, Faisnéis Inrochtana agus Oideachas
- Comhairle agus treoir a chur ar fáil d'earnáil na tionsclaíochta agus don phobal maidir le hábhair a bhaineann le caomhnú an chomhshaoil agus leis an gcosaint raideolaíoch.
- Faisnéis thráthúil ar an gcomhshaol ar a bhfuil fáil éasca a chur ar fáil chun rannpháirtíocht an phobail a spreagadh sa chinnteoireacht i ndáil leis an gcomhshaol *(m.sh. Timpeall an Tí, léarscáileanna radóin)*.
- Comhairle a chur ar fáil don Rialtas maidir le hábhair a bhaineann leis an tsábháilteacht raideolaíoch agus le cúrsaí práinnfhreagartha.
- Plean Náisiúnta Bainistíochta Dramhaíola Guaisí a fhorbairt chun dramhaíl ghuaiseach a chosc agus a bhainistiú.

Múscailt Feasachta agus Athrú Iompraíochta
- Feasacht chomhshaoil níos fearr a ghiniúint agus dul i bhfeidhm ar athrú iompraíochta dearfach trí thacú le gnóthais, le pobail agus le teaghlaigh a bheith níos éifeachtúla ar acmhainní.
- Tástáil le haghaidh radóin a chur chun cinn i dtithe agus in ionaid oibre, agus gníomhartha leasúcháin a spreagadh nuair is gá.

Bainistíocht agus struchtúr na Gníomhaireachta um Chaomhnú Comhshaoil
Tá an ghníomhaíocht á bainistiú ag Bord lánaimseartha, ar a bhfuil Ard-Stiúrthóir agus cúigear Stiúrthóirí. Déantar an obair ar fud cúig cinn d'Oifigí:
- An Oifig um Inmharthanacht Comhshaoil
- An Oifig Forfheidhmithe i leith cúrsaí Comhshaoil
- An Oifig um Fianaise is Measúnú
- Oifig um Chosaint Radaíochta agus Monatóireachta Comhshaoil
- An Oifig Cumarsáide agus Seirbhísí Corparáideacha

Tá Coiste Comhairleach ag an nGníomhaireacht le cabhrú léi. Tá dáréag comhaltaí air agus tagann siad le chéile go rialta le plé a dhéanamh ar ábhair imní agus le comhairle a chur ar an mBord.

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Potential Health Impact of Phthalates: An Irish Perspective

Authors: Catherine Allen, Fiona Regan, Anthony Staines and Jenny Lawler

Identifying Pressures

Phthalates are plasticisers that are ubiquitous in the environment, have the potential to disrupt the endocrine system and are associated with a wide range of adverse health effects. A study of phthalates was undertaken to:

- review the environmental sources and fate of phthalates in Ireland;
- develop robust methods for the analysis of phthalates in multiple environmental matrices;
- investigate the feasibility of applying wastewater-based epidemiology to assess exposure and health risk.

This report identifies that all 11 phthalates studied are currently present in the Irish environment. The levels of human exposure, as assessed via an analysis of phthalate metabolite levels in untreated wastewater, indicate that there is no immediate risk to human health on a population-averaged basis. Treated wastewater at all sites examined was of sufficient quality in terms of phthalate diester levels; however, phthalates are being retained in wastewater biosolids, and an analysis of land spreading practices and their impact on soil and agriculture should be assessed further.

Informing Policy

Seven phthalates (diethylhexyl phthalate – DEHP; dibutyl phthalate – DBP; benzyl butyl phthalate – BBP; diisobutyl phthalate – DIBP; diisononyl phthalate; diisodecyl phthalate; di-n-octylphthalate – DNOP) are currently restricted to certain manufacturing under Annex XVII to the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation [Regulation (EC) No 1907/2006] and the Cosmetics Regulation [Regulation (EC) No 1223/2009]. The European Chemicals Agency has submitted a recommendation to REACH to amend the authorisation list (Annex XIV to REACH), identifying DEHP, DBP, BBP and DIBP as substances of very high concern because of their endocrine disrupting effects (in addition to their reprotoxicity), which may mean that previously exempted usages may require authorisation in the future. DHP was added to Annex XIV to Commission Regulation 2020/1711 of February 2020 because of its toxicity to reproduction. This project has demonstrated that DiBP is one of the most prevalent phthalates contained in the Irish environment. Dipentyl phthalate, a newer phthalate, has been found at some of the lowest concentrations in environmental samples in Ireland, yet it is more present in waste and sludge samples. Legislative restrictions help to prevent further introduction of new replacement phthalates into the environment.

Developing Solutions

A robust LC-MS method allowing background phthalate contamination to be reduced and controlled has been validated. This routine method can now be used to further monitor phthalates in the environment, and for any future compliance assessment of phthalate levels in consumer goods or in the monitoring of emissions levels.

Wastewater-based epidemiology has been developed as a novel means to assess the exposure risk of a population to endocrine disrupting compounds (EDCs). This method offers real-time, readily available and cost-effective data. Owing to the assumptions made during the process, it is best used as a first-step risk assessment or a method for prioritising EDCs. The exposure rates detected, when compared with the reference intakes described for phthalates, indicated that there is no existing risk to the Irish population from exposure to the 11 phthalates assessed in this work.

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