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Exposure of humans to microplastics in the environment and the risks of adverse effects.

Preamble

Information included in the following sections was identified through a comprehensive search of published and grey literature. Published literature was identified using two databases, Scopus and PubMed, which were interrogated using the following search string, applied to the Title, Abstract or Keywords for an unlimited period of time:

microplastic* OR nanoplastic* AND Human

The search resulted in 451 papers, the titles and abstracts of which were screened for relevance. First tier screening provided 104 papers considered suitable for secondary screening through review of the full paper.

Of the 451 papers identified in the initial search, 11 related to nanoplastics either specifically or in conjunction with microplastics, with 6 of these addressing a potential impact on human health following exposure through all routes.

Grey literature, including, for example, government and industry reports/publications, opinions from authoritative bodies, white papers and working papers, were identified through a general 'Google' search and by interrogation of specific websites including, but not limited to, the US EPA, ECHA, EFSA, WHO, and the Water Research Foundation. Screening of the identified grey literature was then carried out and information considered of relevance was included in this document.

1.0 What do we mean by microplastics?

Synthetic polymers provide a wide range of mechanical and functional properties that are not possible to achieve with naturally occurring polymers such as proteins and cellulose. As a consequence, they have become one of the most important classes of materials in modern society, being used in numerous commercial applications ranging from packaging materials to medical devices (Andrady and Neal., 2009; Thompson et al., 2009). In Europe, sector-specific plastic usage has been reported as around 40% for packaging, 20% for building and construction, 10% for the automotive industry, 6% for electrical and electronic products, 4% for household leisure and sports, 3% for agriculture and 17% for all other uses (Plastics Europe, 2017[1]).

Four classes of synthetic polymers have previously been defined, namely: (i) thermoplastic polymers or "plastics"; (ii) thermosetting polymers or "thermoplastics"; (iii) elastomers; and (iv) synthetic fibres. Of these, members of group (ii) and some that fit into groups (iii) and (iv) are not strictly considered as plastics as they do not show thermoplastic behaviours. Although thermoplastic polymers (including polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinylchloride (PVC), polyethyleneterephtalate (PET) and polyurethane (PUR)) are most

[1] https://www.plasticseurope.org/en/about-plastics/healthcare).

frequently found in the environment, polymer particles in the environment stem from all types of synthetic polymers and are all referred to as 'plastics' in the literature and by the scientific community. Some newly-introduced bio-based plastics (for example, polylactic acid) and also biodegradable plastics (for example, oxo-degradable polyolefins) are also likely to be found as microplastics in the environment as degradation of these is not complete under environmental conditions (Lambert and Wagner, 2017).

In addition to residual monomers, commercial synthetic polymers are formulated with small amounts of additives (around 4% of total weight) which depend on the end use (Lehner et al., 2019). Additives can include plasticisers (phthalates), inert fillers, brominated flame retardants, bisphenol analogues, surfactants, antioxidants, pigments, dispergents, lubricants, antistatics, nanoparticles or nanofibers, biocides and fragrances, many of which are considered hazardous to human health (Bouwmeester et al., 2015). Additives are, in the main, not bound to the polymer and are free to migrate to the surface of the plastic and be released (Kolemans et al., 2014); for example, leaching of bisphenol A has been shown from polycarbonate plastic during its lifecycle (Sajiki and Yonekubo, 2003). Although efforts have been made to reduce the use of additives considered to be hazardous, these substances may be present in the environment as a result of historical use.

The widespread use of plastics has led to an increase in plastic waste which has accumulated in the environment. Macroplastic objects (i.e. >5mm) degrade into microplastics (< 5 mm) due to a combination of chemical and physical processes (Gewert et al., 2015). These include: photodegradation by UV in sunlight which is able to break chemical bonds (Yousif and Haddad, 2013); oxidation, which increases the absorption of UV (Cao et al., 1999); hydrolysis of polyesters and polyamides which results in reduced mechanical strength, causing bulk and surface stress gradients that lead to cracking (Maniar et al., 1991; Merdas et al., 1993); and mechanical forces that contribute to the fragmentation process. It is important to note that the degradation process can also affect the additives present in the synthetic polymers, resulting in changes to their chemical structure and physical properties (Lehner et al., 2019).

Microplastics thus comprise a highly heterogeneous population varying in size, shape, density and chemical composition. An internationally recognised definition of microplastics has not been derived; typical dimensions of between 1 µm and 5000 µm (da Costa et al., 2016; Kolemans et al., 2019), between 0.1 µm and 1000 µm (Wright and Kelly, 2017) and between 0.1 µm and 5000 µm (EFSA, 2016) have been proposed in the literature. A distinction is made between primary microplastics that are purposely manufactured as such, and secondary microplastics that originate from fragmentation of larger items (EFSA, 2016). It is also acknowledged that microplastics continue to degrade to form plastic nanomaterials (Gigault et al., 2016; Koelmans et al., 2015; Lehner et al., 2019) that may differ in chemical and physical properties compared to the macroscopic materials (Murty et al., 2013) and in their interaction with living organisms, including humans (Zhang et al., 2012). Currently available literature is unable to provide clarity on many issues relating to nano-sized plastic materials and their potential impacts, which inhibits our ability to carry out human health risk assessments. Deficiencies include, but are not limited to: understanding of the fate of nanoplastics in the aquatic environment; the long-term fate of ingested nanoplastics in both aquatic organisms

and humans; the occurrence of further degradation following ingestion; the ability of nanoparticles to cross the gut-intestinal epithelial barrier; and the toxicity of nanoplastic particles in humans or experimental species. Although nano-sized plastic materials may therefore be of potential concern to human health, the data are currently not available to assess this, and the question is not considered further here.

2.0 How are humans potentially exposed to microplastics?

Lehner et al., (2019) report that the production of polymers (including thermoplastics, thermosets, elastomers, biodegradable and bio-based plastics) has increased significantly over the last 60 years (data to 2016), reaching 335 million metric tons worldwide in 2016. Concurrent with this increase in production has been the accumulation of plastics and their degradation products in the environment, particularly of plastics designed for single-use. Although macroplastics constitute the main source of plastic litter and are known to impact on wildlife, microplastics affect a greater number of organisms, including primary consumers in the food chain (Cole et al., 2013; Li, et al., 2015; Bråte et al., 2016). The trophic transfer of microplastics has been reported in the wild (Welden et al., 2018) and under laboratory conditions (Farrell and Nelson 2013; Setälä et al., 2013; Mattsson et al., 2017; Nelms et al., 2018) suggesting a possible increased risk to top predators (Ferreira et al., 2018).

In addition to microplastics produced by fragmentation of macroplastics, microplastic materials have been purposely manufactured in the form of microbeads for incorporation into personal care products and as plastic microfibres for clothing. All are directly released into the environment through waste water effluent, and although reduction in content occurs during conventional waste water treatment (>98%), Murphy et al. (2016) estimated that 65 million microplastics are released into receiving waters daily at one site. It should be noted that some countries have introduced bans and/or restrictions on the use of microbeads which will impact on future levels, but not historic releases. Microplastics have become ubiquitous in the environment, being reported in waters worldwide (marine and freshwater) including remote locations and deep-sea habitats (Obbard et al., 2014; Lusher et al., 2015; Ivar do Sul et al., 2013; Eerkes-Medrano et al., 2015; Akdogan and Guven, 2019).

Galafassi et al. (2019) have reviewed the available literature relating to the major sources of environmental microplastics, including plastic litter, microbeads in PCPs, washing of synthetic clothes, tyre dust and the weathering of some paints. There is increasing evidence for exposure of humans to microplastics through all routes, with ingestion (diet and drinking water) and, potentially, inhalation predominating (Wright and Kelly, 2017). These are explored in further detail in the sections below; however, it should be noted that, as discussed by Toussaint et al. (2019), estimates of human dietary exposure are limited due to a lack of standardised methodologies.

2.1 Oral exposure to microplastics

2.1.1 Foods

Limited data are available on the occurrence of microplastics in a diverse range of foods including seafoods (fish, shrimp and bivalves), honey, beer and table salt. Comparison between studies is often difficult due to differences in the way that microplastic content is measured and expressed, e.g. some studies report the number of particles per organism and in others as numbers of particles per g wet weight, etc.

Seafood is an important dietary component worldwide, providing around 20% of animal protein intake to approximately 3 billion people (FAO, 2012). Fish studies have demonstrated ingestion of microplastics in the laboratory setting and *in situ* by commercial species including herring, whiting, haddock, cod and tuna. Authors reported that the ingestion of particles by fish as a percentage of the sample population ranged from a minimum of 2.6% (North Sea) to a maximum of 36.5% (English Channel); however, the numbers of particles ingested per individual were low, with a highest mean of 2. A number of microplastic types were identified, including PE, PP, PET, SA, PA, PS and PVC, with sizes ranging between 130 and >10,000 µm (Foekema et al., 2013; Lusher et al., 2013; Boerger et al., 2010; Romeo et al., 2015; Avio et al., 2015).

Microplastics present in the gastrointestinal tract (GIT) of fish and/or crustaceans are unlikely to result in direct exposure of humans as fish gut is not normally consumed. However, recent studies have shown microplastics to be present in edible tissues of commercially important species of fish (Akhbarizadeh et al., 2018; Abassi et al., 2018) and in crustaceans (Abassi et al., 2018), which may be of higher concern for human consumers. Akhbarizadeh et al. (2018) estimated the mean intake of microplastics through consumption of 300g fish muscle per week (recommended intake portion) to be 555, 240, 233 and 169 'particles' for *P. incus, E.coioides, A. djedaba and S. jello* species respectively. Abassi et al. (2108) estimated microplastic levels in the fish species *P. indicus*, *S.tumbil*, *S. sihama, C. abbreviatus* and in the crustacean *P. semisulcatus* (tiger prawn) to be from 0.16 'particles' per g in *C. abbreviatus* up to 1.5 'particles' per g in *P. semisulcatus.*

At the current time, a more significant source of human dietary exposure to microplastics is considered to be through the consumption of shellfish (bivalve molluscs) as these organisms filter large volumes of water and retain particles for ingestion. In contrast to fish, the GIT of shellfish is usually consumed when eaten by humans. Laboratory studies and those *in situ* show evidence to support the capture and ingestion of microplastics by bivalves. China has the greatest general aquaculture production volume (>60%) worldwide and it has been reported that commercially popular shellfish species show a mean number of 4 particles per g. Particles were shown to be comprised of PE, PET and PA, with 60% in the size range 5 - 250µm (maximum 5000µm) (Li et al., 2015). The presence of microplastics in wild and farmed mussels from Canada and Belgium have also been reported (Mathalon and Hill, 2014; Van Cauwenberghe and Janssen, 2014; De Witte et al., 2014). Higher numbers of particles were identified in farmed compared to wild mussels (375 per 5 mussels compared to 175 per 5 mussels, respectively) in Canada, which was suggested by Mathalon and Hill to be due to PP culture lines, although no particle composition analysis was carried out. In comparison, the mean number of microplastic particles reported in wild mussels from two Belgian studies

were much lower (0.37 and 0.36 - 0.47 particles/g). No compositional analyses were carried out for these; however, the most common class sizes were reported as between 5 – 25µm and 200 – 1500µm by Van Cauwenberghe and Janssen, and De Witte and colleagues respectively.

Other potential human dietary sources of microplastics have been reported. Synthetic microfibres and fragments have been identified in honey and sugar. Average numbers of fibres (minimum 40 µm in length) and fragments (10 – 20 µm in length) per kg of honey were measured as 174 and 8 respectively. In sugar, levels of 217 fibres and 32 fragments per kg were reported. The authors confirmed the fibres and fragments to be of synthetic origin (using negative staining with Rose Bengal), although compositional analysis was not carried out. The authors concluded that synthetic microfibres and microplastics must be airborne in order for such contamination to occur, and further showed fibres and fragments to be present in rain water and on flowers (Liebezeit and Liebezeit, 2013). A number of German beer brands (n=24) were reported to contain microplastics, with counts ranging from 0.002 to 0.079 fibres/mL, 0.012 to 0.109 fragments/mL and 0.002 to 0.066 granules/mL, although these were not confirmed as being plastic using spectrophotometric methods. The authors considered likely sources to be airborne particles, materials used during beer processing, impurities on bottle surfaces, and contamination of raw materials (Liebezeit and Liebezeit, 2014). Sea-salt for human consumption has also been found to contain microplastics, thought to originate from coastal water contamination. PET and PE types have mainly been reported, with levels between 0.55 and 0.681 particles/g salt and size range of 45 – 4300 µm (Yang et al., 2015).

Although there is a lack of experimental data on the impact of processing on microplastic levels in foods, EFSA considers that it is possible for levels to increase due to the release of microplastics from processing aids, water, air, machinery and textiles (EFSA, 2016).

2.1.2 Drinking water and sources

Microplastics have been shown to be widely distributed in freshwater bodies, including on the water surface, in the water column and in lake sediments, at levels similar to those found in the marine environment (Eerkes-Medrano et al., 2015; Li et al., 2018). The concentrations of microplastics in freshwaters and sediments shows considerable variation and may be associated with levels of human activity (Eerkes-Medrano et al., 2015; Li et al., 2018; Rezania et al., 2108). Levels ranging from a few microplastic particles to thousands/m^3 have been reported in freshwaters (Horton et al., 2017; Rezania et al., 2018; Di et al., 2019; Novotna et al., 2019) and up to several thousand particles/kg in sediment (Hurley et al., 2018; Rezania et al., 2018; Di et al., 2019; Novotna et al., 2019).

A number of studies have reported the presence of microplastics in bottled and tap drinking water from different sources (for example, Kosuth et al., 2018; Mason et al., 2018; Mintenig et al., 2019; Schymanski et al., 2018; Pivokonsky et al., 2018;) at levels between zero and 10^4 microplastic particles/L. The most commonly identified microplastics were comprised of PP, nylon, PS, PE and PEST, with a range of shapes including fragments, film, fibre, foam and pellet. A comparison with levels reported in freshwater is not possible as freshwater studies

targeted larger particles (compared with < 300 µm in drinking water studies), meaning that total particle numbers were much lower as smaller particles were not captured.

In a comprehensive review of literature, Kolemans and colleagues (2019) identified around 50 studies that provided concentration data for microplastics in drinking water or its freshwater sources (surface, ground and waste waters). As the studies varied considerably in sampling methods, isolation, purification and identification of microplastics and in the level of quality assurance employed, the authors used a scoring system to carry out a quantitative evaluation of study quality to find consensus in the data reported. Their findings showed that microplastics are frequenly found in fresh and drinking waters with a range of measured concentrations between 1 x 10^{-2} and 10^{8} particles/m^3; this wide range may have been partly due to the generally inconsistent quality assurance in sampling and analysis. Of the microplastics present globally, the most common types were PE and PP, with PS > PVC > PET, reflecting global use patterns and the higher densities of the latter two plastics which settle at a faster rate. A range of shapes were identified including fragments, fibres, film, foam and pellets.

2.2 Exposure to microplastics through inhalation

There is growing evidence that inhalation is an important human route of exposure to microplastics in the environment. Around 60 million metric tons of synthetic plastic fibres were produced in 2016 for the textile industry, which included an increased level of fine-diameter (1 – 5 µm) plastic fibres (Gasperi et al., 2018). These types of fibres have been shown to be shed into the environment during wear and/or washing and drying (Cesa et al., 2017; Napper and Thompson, 2016) and are subject to degradation, fragmenting into finer, inhalable particles. Fibrous microparticles also settle as dust on floors and surfaces which may be ingested, especially by infants and children.

Sludge by-products from WWTPs, that are applied to agricultural lands as a standard practice, have been reported to contain synthetic clothing fibres that persist in the sludge and soil up to 5 years post application, although some have been detected in soils 15 years post application (Zubris et al., 2005). This has been proposed to represent a persistent terrestrial contaminant, potentially allowing wind-driven transport from dried sludge-based fertilizers to occur; other proposed sources are the release of fibres from degraded PE agricultural sheets and from drying clothes (Wright and Kelly, 2017).

Atmospheric fallout in two suburbs of Paris has been shown to contain microplastics, comprised mainly of fibres, with around 30% confirmed as being of plastic origin. The abundance of fibres was found to be higher in urban areas than in suburban areas, with an average of 110 ± 96 particles/m^2/d; rainfall was associated with the highest levels recorded which indicates the potential for atmospheric particles to be washed out and contribute to other soil/ water levels. The diameter of fibres varied between 7 and 15 µm and length between 100 and 500 µm (50 µm limit of detection) (Dris et al., 2016). In a subsequent study the authors compared fibres found in indoor and outdoor air. Concentrations of fibres in indoor air ranged between 1.0 and 60.0 fibres/m^3 compared with a range of 0.3 to 1.5 fibres/m^3 in outdoor air.

Of the fibre types identified in indoor air, one third were of plastic origin. Settled dust found in the indoor environment contained between 190 and 670 fibres/mg, which the authors state may be a source of exposure in children through ingestion (Dris et al., 2017).

Tyre dust is increasingly acknowledged as a source of microplastics in air, as synthetic rubber is considered a variation on plastic (hydrocarbon-based polymer) (Sommer et al., 2018; Kole et al., 2017; Wright and Kelly, 2017). Tyre abrasion products are present in ambient particulate matter (PM), making up between 0.05 and 0.70 mg/m^3 of the PM10 fraction in studies across Japan, Europe and the USA (Unice et al., 2012; Panko et al., 2013); tyre wear particles also contribute significantly to man-made particles in the aquatic environment (Wagner, 2018). Deposited urban dust in Tehran was reported to contain microplastic particles at a concentration of between 88 and 605 particles per 30g dust, with size distribution 250 – 500 µm (Dehghani et al., 2017). Abbasi and colleagues (2019) assessed ingestible and/or inhalable microplastic particles (MP) and microrubber particles (MR) in street and airborne dust samples in a city in Iran. In street dust particles < 5 mm an average of 900 and 250 MP and MR particles were measured, ranging in size between < 100 and >1000 µm. In comparison, airborne dust contained around 1 MP per m^3 in the size range 2 to 100 µm, with only MR fragments present (Abbasi et al., 2019).

Occupational studies in polymer textile workers show that the potential risk through inhalation exposure is dependent on size, shape and concentration of particles. Workers in the nylon flock industry have shown a higher prevalence of respiratory irritation (Warheit et al., 2001); also, Pimentel et al. (1975) reported interstitial fibrosis and granulomatous lesions considered to contain acrylic, polyester and/or nylon dust, in lung biopsies from textile workers (including nylon, polyester, ploy olefin and acrylic) who presented with symptoms comparable to allergic alveolitis. Although the exposure levels experienced by the workers were considerably higher than environmental levels, the study showed uptake and persistence of microplastics triggering localised biological responses. The bio-persistence of plastic microfibres in lung tissue has also been reported in non-neoplastic and malignant lung tissue, with fibres present in the deep lung (Pauly et al., 1998)

Fibre dimension is relevant to potential toxicity, as fibres longer than 15 to 20 µm are inefficiently cleared from the lung by either alveolar macrophages or the mucociliary escalator (Warheit et al., 2001). Porter et al. (1999) showed that nylon fibres of a respirable size (average 2 µm diameter by 14 µm length) were retained for up to 29 days in exposed rats and caused an acute inflammatory response. Warheit et al. (2003) found no significant changes to lung weight, pulmonary inflammation or macrophage function in male rats exposed to shorter and wider nylon fibres (mean 9.8 µm length and 1.6 µm diameter). It has been suggested that the level of fibres present, the site of deposition and the potential for chemical desorbtion from the fibre all have the potential to contribute to overall toxicity (Pauly et al., 1998).

The ability of microplastics to accumulate is also a factor that will impact potential toxicity. They are resistant to chemical degradation *in v*ivo, with retention time being dependent on microplastic characteristics such as size, shape, solubility and surface chemistry (including

wettability), biological factors including the site of deposition, and particle interactions with biological structures.

2.3 Exposure to microplastics through the dermal route

Dermal contact with microplastics is feasible through direct application of, for example, personal care products including facial scrubs, or indirect exposure via water containing microplastics during washing. However, as uptake across the skin requires penetration of the *stratum corneum*, which is limited to particles <100 nm, skin absorption of microplastics is unlikely. It is feasible, however, for nanoplastics to have a higher potential for dermal absorption (Sykes et al., 2014).

3.0 Microplastics analysis

The prevalence of microplastics in the environment has been well documented; however, there are considerable differences in the levels reported which are likely to stem from the present inherent difficulties in carrying out such measurements. This impacts on study comparison and indicates the need to develop and implement standardised methods for the sampling, quantification and characterisation of microplastics has been recognised (Silva et al., 2018).

From a human perspective, accurate exposure measurements are required to enable health risk assessments to be made. At the current time, microplastics in extracts from biological samples are separated for size using filtration devices or sieves with different mesh sizes; a filter with pore sizes between 1 and 1.6 µm is commonly used to collect all microplastics. Visual sorting using categories such as source, shape, erosion and colour is often carried out prior to quantitation. Quantitation is achieved through counting, with or without the use of tagging dyes. Visual assisted microscopy can allow a detection limit in the low µm range, with smaller particles requiring electron microscopic techniques (Hidalgo-Ruz et al., 2012; Fries et al., 2013). Identification of microplastics is achieved using Fourier Transform Infra-red spectroscopy (FTIR) or Raman spectroscopy, allowing detection of particles of between 10-20 µm and 1-20 µm, respectively. Pyrolysis and GC/MS are also used for determination of particles, according to their mass, typically of size > 500 µm and provide information on the polymer and additives present; liquid chromatography/ MS is mostly used for analysis of chemicals bound to microplastics (Renner et al., 2019; Silva et al., 2018).

4.0 Potential toxicity of microplastics

4.1 Toxicokinetics

Based on the current level of knowledge, the main route of human exposure to microplastics is likely to be through ingestion of food and drinking water, with some intake via inhalation of indoor and outdoor air also possible.

The gut wall has an epithelial lining that prevents direct transport of microplastics into the body, and paracellular uptake (i.e. through the tight junctions of the epithelial cell layer) is not considered possible due to the small size of the tight junction channels (1.5 nm). Uptake of microplastics (0.1 to 10 µm) from the GIT is proposed to occur via endocytosis (i.e. formation of internal vesicles by the cell plasma membrane) by the M cells of Peyer's patches (lymphoid nodules in the mucosa of the small bowel), with subsequent transport to mucosal lymphoid tissue, or via paracellular uptake with subsequent phagocytosis (a type of larger scale endocytosis by cells (macrophages) that have this specific function) and transport to lymphatic systems, with eventual elimination from the body (Galloway, 2015); however, specific data to support this for microplastics is limited. Particle size is recognised as a critical factor in both the pathway and the extent of absorption. Yoo and colleagues (2011) has proposed that for endocytosis the upper particle size limit is around 0.5 µm and that phagocytosis occurs with particles > 0.5 µm (Yoo et al., 2011).

Translocation of microplastics across the gut into the lymphatic system has been shown in humans for particles between 0.2 and 150 µm diameter, in dogs for particles between 3 and 100 µm, in rabbits for particles between 0.1 and 10 µm and in rodents for particles between 30 and 40 µm (Hussain et al., 2001). Absorption is however limited. In rats, an *in vivo* study using 2 µm latex particles administered as either a single oral dose or through extended feeding showed that only between 0.04 – 0.3% of particles were absorbed. The site of absorption differed with length of exposure, being at villous sites after a single dose and Peyer's patch sites after multiple feeds (Carr et al., 2012). An *in vitro* study with healthy human rectal mucosal tissue, reported that 0.2% of 3 µm polylactide-co-glycolide microparticles were absorbed. This increased to 0.45% in tissue from individuals with inflammatory bowel disease, indicating the increased permeability of the gut associated with this condition (Schmidt et al., 2013).

Less information is available regarding the distribution of microplastics following absorption (any route). Yoo et al. (2011) reported that microparticles of > 0.2 µm in lymph undergo elimination via splenic filtration whilst microplastics in the blood are removed via the liver into bile and faeces. Only the smallest microplastics (< 1.5 µm) are thought to be able to penetrate into organs (Yoo et al., 2011). EFSA and the FAO considered that the absorption of microplastics via the GIT is low, estimating that >90% is eliminated via the faeces. Uptake of microplastics > 150 µm in size was suggested to be unlikely, whilst that of microplastics < 150 µm is limited to ≤ 0.3%; only those particles < 20 µm in size were thought to be able to reach organs. Both organisations comment that absorption and distribution may be more significant for nanoplastics, but the data are too limited to determine this at present (EFSA, 2016; FAO, 2017).

Deng and colleagues (2017) have reported the uptake and distribution of 5 and 20 µm fluorescent PS microplastics in mice exposed for 4 weeks via the oral route to doses of 0.01, 0.1 and 0.5 mg/day (Deng et al., 2017). Translocation to the liver and kidney was apparent, with particles detected one week following cessation of exposure. These findings have however been questioned, with the dose considered very high in comparison to human

exposure levels and the test groups too small for meaningful conclusions to be drawn (Braeuning, 2018).

In the lung, mucociliary clearance is most likely for inhaled microplastics > 1 µm, with uptake across the epithelium possible for smaller particles. For particles small enough to deposit in the deep lung, penetration of the thinner lung lining fluid and contact with the epithelium is plausible, allowing translocation via diffusion or active cellular uptake into epithelium (Ruge et al., 2013). It is known that for some poorly soluble particles and fibres (e.g. silica, asbestos) inhalation can result in adverse effects in the lung. The importance of a range of physical properties, including size, shape, surface area and surface properties, in determining the degree of response to exposure is well reported in the literature (Wright and Kelly, 2017).

Toxicity-based toxicokinetic/toxicodynamic (TBTK/TD) modelling has been used to estimate organ bioaccumulation and biomarker responses following exposure of mice to 5 or 20 µm PS microplastics; published datasets were used. The authors reported that the gut had the highest bioaccumulation factor (BCF) of 8 when exposed to 5 µm microplastics, with a mean residence time of 17 days. Threshold concentrations for the most sensitive biomarkers were 8 ± 5 and 0.71 ± 0.14 µg/g bw for 5 and 20 µm particles respectively, indicating that particle size influences TK/TD behaviour in mice (Yang et al., 2019).

4.2 Potential toxicity of microplastic constituents

Laboratory studies with freshwater species exposed to microplastics have shown toxicity related to both physical and chemical properties (SAPEA, 2019). The relevance to human health impact assessment of studies on aquatic organisms is undetermined but in general mammals are consider more appropriate models for humans. In a meta-analysis, Foley et al. (2019) assessed the potential impacts of microplastic exposure on consumption (and feeding), growth, reproduction and survival of fish and aquatic invertebrates (Foley et al., 2019). The authors reported that negative effects were found for all categories; however, the effects were highly variable across taxa, with the most consistent being a reduction in consumption of natural prey. Similar laboratory studies have also been conducted in a number of marine species. Negative effects have been reported on feeding efficiency (zooplankton, lungworms and fish), oxygen consumption (lungworms and crabs), and early stage development of marine biota, and in molluscs for a range of toxicities related to the immune response, oxidative stress and neurotoxicty (SAPEA, 2019).

One of the major limitations of laboratory studies is considered to be the high concentrations of microplastics used, which are significantly higher than reported environmental levels. Indeed, FAO concludes that in wild aquatic organisms, microplastics have only been found in the GIT in small numbers and that there is currently no evidence to suggest that ingestion will impact negatively on wild and farmed populations (FAO, 2017). In addition, the studies have tended to use small spherical polystyrene microplastics which are not representative of those found in the environment (Lambert et al., 2017). The impact on a wider range of aquatic organisms is unknown, particularly at different trophic levels (SAPEA, 2019).

Although plausible routes of exposure of humans to microplastics have been described, it remains unknown whether microplastics (and their associated component and adsorbed chemicals) are transferred to humans via the diet and/or inhalation (Wright and Kelly, 2017). A number of potential adverse effects in humans following microplastic exposure have been explored and reported in the literature, and these are detailed below.

4.2.1 Physical effects

The physical effects of ingested microplastics are less well defined than the chemical effects. Currently available data suggest several potentially hazardous effects including local inflammation, disruption of the gut microbiome and altered lipid metabolism (Smith et al., 2018).

Physical properties including size, shape, surface functional groups, surface charge, buoyancy and hydrophobicity affect the uptake of microplastics, and hence potential toxicity. The potential for translocation increases with decreasing particle size, as does the surface area to volume ratio which allows increased cellular interactions and cellular uptake and adsorption of biologically significant molecules and proteins. This may include adsorption of environmental toxins (see section below). Increased surface area can lead to enhanced degradation, potentially generating smaller particles that are more easily absorbed, although the extent to which this can happen in humans is not clear (Gewert et al., 2015). Although it is known that the shape of particles and fibres influences uptake and clearance in the lung, the impact of these following ingestion is unclear.

As with other particles and fibres, Wright and Kelly (2017) propose that the biopersistence of microplastics *in vivo* has the potential to lead to a number of biological responses including inflammation, genotoxicity, oxidative stress, apoptosis and necrosis. In turn, these conditions, when sustained, can lead to tissue damage, fibrosis and carcinogenesis (Wright and Kelly, 2017). As reported by Deng et al. (2017), administration of PS particles (5 and 20 µm) to mice for 28 days by oral gavage was associated with inflammation of the liver, coincident with the presence of lipid droplets at doses of 0.1 and 0.5 mg/day. Lu et al. (2018) also reported altered lipid metabolism and gut microbiota diversity (compared to controls) in male mice exposed for 5 weeks to PS particles of 0.5 and 50 µm at a level of 1 mg/L in drinking water. A reduced level of intestinal mucus secretion and impaired intestinal barrier function has been reported in mice exposed to PS particles (5 µm) at either 100 or 1000µg/L in drinking water for 6 weeks (Jin et al., 2019); as noted by Lu et al., (2018) altered gut microbiota diversity was also apparent. Interpretation of all these findings for human relevance is difficult as the levels used are considerably higher than those found environmentally; however, they are consistent with a prolonged presence in the gut lumen.

4.2.2 Chemical toxicity

Chemical toxicity resulting from exposure to microplastics could be due to polymer composition, the leaching of unbound chemicals and residual monomers, endogenous additives, or adsorbed hydrophobic organic contaminants.

4.2.2.1 Polymers

The WHO reported that the most prevalent polymers detected in fresh and drinking waters are polypropylene, polyethylene, polystyrene, polyvinylchloride and polyethyleneterephthalate (WHO, 2019). A brief summary of available toxicity data of relevance to oral exposure is given below.

4.2.2.1.1 Polypropylene (PP)

ECETOC (1994) reported that PP has low acute toxicity with an oral LD_{50} in rats of > 5000 mg/kg bw (no further details given). Pulmonary toxicity was not apparent in rats administered PP fibres at doses of 0, 15, 30 or 60 mg/m^3 (fibres of geometric mean diameter 1.6 µm with 46% <1µm and geometric mean length of 30.3 µm) for 90 days (6h/d, 5d/w). Carcinogenicity studies are not available for PP, however the monomer, propylene, has been shown not to increase tumour incidence in Fischer 344/N rats exposed by inhalation (6hd, 5d/w) for 103 weeks to propylene at doses of 0, 8600 and 17,200 mg/m^3 in a study carried out to NTP protocols (NTP, 1985). Similarly, in B6C3F1 mice treated under the same conditions and at the same doses, no evidence of an increase in tumour incidence was recorded (NTP, 1985). These findings are supported by evidence from human epidemiology studies, the combined weight of which does not support a link between polypropylene exposure and (colorectal) cancer (ECETOC, 1994). PP has been evaluated by IARC as "*not classifiable as to its carcinogenicity in humans*" (Group 3).

In vitro studies reported by Hwang et al. (2019) have been carried out to assess the cytotoxicity of PP microplastic particles of around 20 µm and between 20 and 200 µm diameter at concentrations up to 500 µg/L. In parallel studies, DMSO was added to the PP microplastic particles to improve dispersibility, thereby increasing the chance of contact with cells, and a powdered form of the particles was also prepared. Cytotoxicity was assessed against a range of cell types (human dermal fibroblasts, macrophages, murine macrophages and red blood cells) through analysis of cytokine production, ROS production, polarization and cell proliferation. The authors reported that PP microplastic particles and the powdered form showed low cytotoxicity. However, when treated with DMSO, particles in the size range of around 20 µm showed cytotoxicity to peripheral blood mononuclear cells (PBMCs) and murine macrophages as a result of increased ROS production, which was size and concentration dependent. The importance of direct contact was therefore demonstrated, which allows induction of cytokines from immune cells rather than the microplastic particles causing direct toxicity.

4.2.2.1.2 Polyethylene (PE)

The toxicity of PE has been reviewed by The Cosmetic Ingredient Review (CIR) Expert Panel (CIR, 2007). With regard to oral exposure specifically, PE has low acute toxicity which is influenced by molecular weight; an oral LD_{50} of >2000 mg/kg was reported in rats for PE with an average molecular weight of 450, which increased to > 5000 mg/kg for PE with an average molecular weight of 655 (CIR, 2007). The CIR Expert Panel also reported a lack of adverse effects in male and female rats administered PE (unknown molecular weight) at 7.95 g/kg bw (single dose gavage) or at levels of 1.25%, 2.50%, and 5.00% in the diet for 90 days (no further details given). In mutagenicity studies, PE with a molecular weight of 450 did not increase

mutation frequency in *Salmonella typhimurium* strains TA1535, TA1537, TA98, and TA100 or in *E. coli* WP2uvrA when tested at concentrations of 1, 10, 30, 100, 300, and 1000 µg/plate. As IARC has also evaluated PE as "*not classifiable as to its carcinogenicity in humans*" (Group 3), it is therefore not considered to be genotoxic.

4.2.2.1.3 Polystyrene (PS)

Luo et al. (2019) evaluated the effects of maternal exposure to PS microplastic particles of 5 µm diameter at concentrations of 100 and 1000 µg/L in drinking water, in ICR mice during pregnancy and lactation (compliance to OECD guidelines was not stated by the authors). Potential effects on offspring were evaluated in the F1 (at PND 42 and 280) and F2 (at PND 42) generations. The authors reported that maternal exposure to PS microplastic particles was associated with altered glycolipid metabolism-related physiological indexes in serum and liver of dams and the F1 and F2 generations. In addition, in exposed dams, metabolic disorder associated with gut microbiota dysbiosis and gut barrier dysfunction was reported.

Polystyrene has been shown to be negative for mutagenicity in *Salmonella typhimurium* strains TA100, TA1535, TA97 and TA98 in the presence and absence of S9 at doses up to 10,000 µg/plate, with assays carried out to OECD Guideline 471 (NTP, 2019[2]).

4.2.2.1.4 Polyvinylchloride (PVC)

IARC has evaluated the available evidence for the carcinogenicity of PVC and concluded that it is "*not classifiable as to its carcinogenicity in humans*" (Group 3).

4.2.2.1.5 Polyethyleneterephthalate (PET)

In a subchronic study, rats were administered technical grade PET at levels between 5 and 400 mg/kg bw/day, or pure PET at levels between 5 and 100 mg/kg bw/day, for 12 weeks (no further details given). No changes in behaviour, body weight gain, biochemical indices of blood serum, urine, or haematology analyses, or in relative weights of internal organs, was apparent (HSDB, 2009).

PET was tested as a potential mutagen when used for the manufacture of beverage bottles. Leachates were obtained using mineral water stored under static (up to 6 months storage at 25^{o}c) conditions, with or without daylight or under dynamic (shaking at 40^{o}C for up to 48h) conditions. Mutagenic potential of concentrated leachate samples was assessed according to the Ames protocol (pre-OECD Guidelines) using *Salmonella typhimurium* strains TA98 and TA100, with and without S9 activation. Mutagenicity was apparent in TA98 with S9 activation for samples stored for 1 month under static conditions in daylight and in the dark. This correlated with a peak measurement of total organic carbon. The authors considered this to be evidence of 'slight mutagenicity' of the leachate, with storage under daylight conditions giving higher activity. However, supporting evidence to confirm the presence of mutagenic compounds migrating from PET bottles using unconcentrated samples in direct tests (i.e. *Salmonella* strains grown directly in sterilised PET bottles and in glass flasks) did not show positive results, which the authors concluded was due to low levels present in unconcentrated

[2] https://ntp.niehs.nih.gov/whatwestudy/testpgm/status/ts-9003536.html

leachate. For risk assessment purposes these findings are considered inconclusive and are not included for further consideration.

Merski et al. (2008) carried out a 90-day oral toxicity study to OECD Guideline 408 with a spunbound PE and PET polymer fabric. Spraque-Dawley CD rats were administered ground fabric in the diet at levels of 0.5, 2.5 and 5%. No toxicologically relevant treatment related effects were apparent. In addition, the authors performed a *Salmonella* reverse mutation assay to OECD Guideline 471 using an extraction of the ground fibre. No mutagenic response was found in either the presence or absence of S9 in *Salmonella* strains TA98, TA100, TA102, TA1535 and TA1537.

4.2.2.2 Unbound monomers and additives

Monomers present as a result of incomplete polymerisation, or chemical additives included during manufacture, can leach from microplastics into the surrounding medium (including animal tissues following ingestion), as they are not chemically bound within the polymer matrix (Browne et al., 2013; Rochman et al., 2013). Commonly used additives include organophosphorus flame retardants (OPFRs). Deng et al., reported findings from a 90-day study in which mice where concurrently exposed to two OPFRs and PE and PS microplastics (2 µg/L in drinking water). The authors reported increased toxicity of OPFRs in the presence of microplastic particles and proposed that the action of the microplastics on the gut mucosa enhanced the uptake of OPFRs, resulting in increased toxicity (Deng et al., 2018). However, it is unclear whether the effects were due to the OPFRs or caused by the presence of the microplastics themselves.

4.2.2.3 Adsorbed components

Microplastics have a hydrophobic surface which facilitates the adsorption and concentration of organic contaminants and heavy metals also present in environmental milieu, thereby having the potential to act as a vector. These include priority pollutants listed under the Stockholm Convention, namely: polycyclic aromatic hydrocarbons (PAHs), organochlorine pesticides, polychlorinated biphenyls (PCBs), cadmium, zinc, nickel and lead (Mato et al., 2001; Ogata et al., 2009; Holmes et al., 2012; Rochman et al., 2014). Mato et al. estimated the concentration factor of POPs by microplastics to be in the order of 10^6 (Mato et al., 2001), and high levels of PCBs, PAHs and organochlorine pesticides in microplastics have been reported (Bouwmeester et al., 2015). Concerns have been raised that microplastics allow the transfer of hazardous POPs to aquatic animals and subsequently to humans. Data on the levels of metals associated with microplastics are limited.

4.2.3 Biofilms

The surfaces of microplastics in the environment are rapidly colonised by microbes, with biofilms becoming well established after 7 days in water (Harrison et al., 2014; Lobelle and Cunliffe, 2011). The plastic-associated communities are also referred to as “plastispheres”. Physicochemical properties of microplastics that encourage biofilm formation include surface roughness (Nauendorf et al., 2016) and hydrophobicity (Rummel et al., 2017). The composition of the biofilms associated with microplastics has been reported to contain lower

taxon richness, diversity and evenness in comparison to those on non-plastic substrates (McCormick et al., 2016). Interestingly, a large proportion of the bacterial and fungal strains identified on microplastics represent genera able to degrade plastic polymers, including *Pseudomonas*, *Arcobacter spp.*, *Erythrobacter*, *Streptococcus*, *Staphylococcus*, *Aspergillus*, *Penicillium*, and *Phanerochaete* (Bhardwaj et al., 2012; McCormick et al., 2014). Zettler et al. (2013) reported that biofilms on microplastics could also contain harmful pathogens (e.g. *Vibrio spp.*) and Arias-Andres and colleagues that microplastics could potentiate the distribution of antibiotic resistance determinants in the environment (Arias-Andres et al., 2018).

5.0 Existing risk assessments of human health effects following exposure to microplastics

Microplastics have been most widely studied in the context of marine pollution, with potential human exposure pathways and associated risks to health only being more recently recognised. Thus, the database relating to any adverse health effects resulting from exposure of humans to environmental microplastics through any route is limited. In addition, when assessing risk, it should also be noted that reported measurements of exposure may be underestimated due to current technical limitations in sampling and analysis. Also, microplastics are also present as a mixture of particles that vary in size, shape and chemical composition, and in the degree to which POPs and biofilms are adsorbed to their surface. All of these present challenges to traditional human health risk assessment approaches.

The WHO has published a summary of evidence examining the potential risks to human health from exposure to microplastics in drinking water (WHO, 2019). They considered the potential hazards of microplastics to be: the particles themselves, which present a physical hazard; chemicals (unbound monomers, additives, and sorbed chemicals from the environment); and microorganisms that may attach to and colonize microplastics - known as biofilms. With regard to microplastic particles posing a physical hazard, the WHO considered that there was insufficient data to draw any firm conclusions; however, they also noted that those studies judged as reliable did not indicate any adverse health effects.

As the residual levels of monomers present in microplastics have not been determined, WHO was unable to assess these against available guidance values. For additives and sorbed chemicals that had been reported to be present in microplastics, were considered to be of toxicological concern and for which adequate/accepted points of departure had been derived, an MOE assessment was undertaken. This was carried out using a conservative drinking water exposure scenario and indicated that health impacts were likely to be low. When assessing potential health risks from biofilms present on microplastic particles, the WHO considered that the relative contribution from these, compared to other particles that bind pathogens and human/livestock waste present in drinking water, was likely to be low. The WHO report highlighted the need for robust toxicological and/or epidemiological studies that could inform more accurate human health risk assessment for microplastic ingestion, including from drinking water.

In an evaluation of the potential health impact to humans of microplastics in food, Bouwmeester et al. (2015) considered that any such assessment should distinguish between particle toxicity *per se* and that of the additives and/or adhering contaminants. The authors acknowledged that fish and shellfish are likely to be an important dietary source of microplastics in the human diet, but quantitative data on the levels of microplastics are not available for a large proportion of these to allow dietary exposure assessment. Other foods were also suggested to contribute to total dietary exposure, with microplastics being found in honey, sugar, salt and beer. As the toxicity of the particles has not been studied, a full risk assessment is not possible. The authors suggest that due to the size of microplastics, transport across cellular membranes is unlikely and any adverse effects are expected to be local effects on the immune system and inflammation of the gut (Bouwmeester et al., 2015).

The authors acknowledged the unique nature of microplastics in containing adsorbed POPs and leachable additives that require separate consideration. They estimated that consumption of 300 g of mussels (average portion) from the Belgian coast would result in ingestion of 300 plastic particles containing 0.25 pg of PCBs. If all of this was released following consumption it would contribute only 0.0001% of the average daily dietary exposure to PCBs. In the same way, Bouwmeester and colleagues (2015) estimated that the same portion of mussels would contain around 0.06 µg of BPA, contributing approximately 0.25% of daily dietary exposure. Based on the very limited data available, the authors concluded that other additives and adsorbed POPs would give similar levels of exposure which they considered negligible (Bouwmeester et al., 2015).

In a Scientific Opinion on the presence of microplastics in seafood, EFSA (2016) assessed the possible transfer of additives and adsorbed chemical contaminants to edible tissues and carried out an estimation of human exposure through this route. They reported that some information is available to estimate exposure for bisphenol A, polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs), but data on metals and other contaminants is lacking. EFSA estimated that consumption of an average portion of Chinese mussels (225 g) would be associated with an intake of 900 plastic particles, representing 7 µg of plastics. In turn, this would result in an increase in exposure to PCBs of <0.006% and to PAHs of <0.004%, assuming worst case exposure levels and complete release from the microplastics following consumption. Using the same intake data, EFSA calculated that the intake of additives from 7 µg of plastics would be 4% of the total weight, or 0.28 µg. Using BPA as the only additive, in a worst-case scenario, this would contribute < 2% of dietary exposure; the authors commented that the exposure to other additives would be at a similar level and was considered as a small effect (EFSA, 2016).

In a review of cross-discipline scientific literature, Wright and Kelly (2017) evaluated the potential human health impacts of exposure to microplastics through the diet and/or inhalation. They suggested that uptake of microplastics through these routes is plausible, supported by evidence of plastic microfibres in lung biopsies and demonstration of biopersistent particles < 100 µm being able to cross the GIT epithelium. They consider that microplastics <2.5 µm and fibres are of the highest concern in the lung. In the GIT, larger microplastics are considered to be of concern due to the ability of M cells in Peyer's patches

to engulf microplastics of micrometer size, and also due to persorption. Wright and Kelly (date?) consider that any toxicity of microplastics is likely to be dose dependent and due to inflammation caused by their biopersistence and unique hydrophobicity and surface chemistries. The importance of recognising deposited and airborne microplastics and microrubbers in ambient air as a source of human exposure through both inhalation and ingestion to enable an understanding of human health impacts, has been emphasised by Abbasi et al. (2019).

Welle and Franz (2018) evaluated current literature on microplastics in bottled mineral water, assessing human exposure from this source and the potential for adverse health effects to occur following ingestion. The authors estimated exposure to microplastics using reported levels and, assuming total release of unbound components, found no concern for consumer safety. Further, it was considered that based on available toxicokinetic data, absorption from the GI tract was likely to be marginal, if occurring at all. The requirement for better data on which to base exposure estimates and risk assessments was again highlighted.

Eerkes-Medrano et al. (2019) have carried out a review of data relating to microplastics in drinking water to assess whether the impact of this on human health can be determined. The authors identified large data gaps in both human exposure measurements and hazard data which, they say, precludes adequate risk characterisation of microplastics from any route of exposure at the current time. They conclude that improved exposure assessments would require advances in QA, QC, the development of proficiency testing schemes (including appropriate certified standards) and advances in analytical capacity to enable the measurement of nano-microplastics. In addition, in terms of hazard characterisation, toxicological data are required to understand the toxicokinetics of microplastics, potential mechanisms of toxicity and dose-response relationships, and also to identify any subpopulations that may be at an increased risk from exposure.

6.0 Summary of findings in relation to human health effects

- The presence of microplastics in the environment is widespread but any associated risks to human health are difficult to quantify.
- One of the key issues in assessing risks to human health is the considerable variability in the physical and chemical properties of microplastics to which humans are exposed.
- Standard methods for the identification, quantification and analysis of microplastics in foods and biological specimens are not available, making comparison of study findings difficult.
- Epidemiological studies to assess uptake and potential effects following exposure to microplastics are not available.
- It is estimated that uptake of microplastics in the GIT is restricted to those < 150 µm and limited to around ≤ 0.3% of the dose. Only particles < 20 µm in size are thought to be able to reach organs.

- There is very limited data from experimental studies to assess the toxicokinetics and potential toxicity of microplastics, though animal studies on toxicity of some common polymers are generally reassuring.
- At the current level of understanding, the following hazards and potential effects are considered to be relevant to humans exposed to microplastics through the diet or inhalation:
    - Physical effects which may be associated with local inflammation, altered gut microbiome and altered lipid metabolism;
    - Chemical hazards associated with residual monomers and/or additives that have known adverse human health effects. The contribution from microplastics of these chemicals to total daily exposure from the diet is expected to be low or insignificant;
    - Chemical hazards associated with adsorbed POPs that have known adverse human health effects. The contribution from microplastics of these chemicals to daily exposure from the diet is expected to be low or insignificant;
    - Adsorbed microbial pathogens associated with biofilms, are thought to be of low risk.
    - There is potential risk to the lungs from any suitably small low solubility particle or fibre inhaled in sufficient quantity, however this is considered unlikely for microplastics in the environment.

References

Abbasi, S., Keshavarzi, B., Moore, F., Turner, A., Kelly, F. J., Dominguez, A. O. & Jaafarzadeh, N. 2019. Distribution and potential health impacts of microplastics and microrubbers in air and street dusts from Asaluyeh County, Iran. *Environmental Pollution***,** 153-164.

Abbasi, S., Soltani, N., Keshavarzi, B., Moore, F., Turner, A. & Hassanaghaei, M. 2018. Microplastics in different tissues of fish and prawn from the Musa Estuary, Persian Gulf. *Chemosphere,* 205**,** 80-87.

Akdogan, Z. & Guven, B. 2019. Microplastics in the environment: A critical review of current understanding and identification of future research needs. Environ Pollut. 254(Pt A):113011, pp24.

Akhbarizadeh, R., Moore, F. & Keshavarzi, B. 2018. Investigating a probable relationship between microplastics and potentially toxic elements in fish muscles from northeast of Persian Gulf. *Environmental Pollution,* 232**,** 154-163.

Andrady, A. L. & Neal, M. A. 2009. Applications and societal benefits of plastics. *Philos Trans R Soc Lond B Biol Sci,* 364**,** 1977-84.

Arias-Andres, M., Rojas-Jimenez, K. & Grossart, H. P. 2018. Collateral effects of microplastic pollution on aquatic microorganisms: An ecological perspective. *TrAC - Trends in Analytical Chemistry*.

Avio, C. G., Gorbi, S. & Regoli, F. 2015. Experimental development of a new protocol for extraction and characterization of microplastics in fish tissues: First observations in commercial species from Adriatic Sea. *Marine Environmental Research,* 111**,** 18-26.

Boerger, C. M., Lattin, G. L., Moore, S. L. & Moore, C. J. 2010. Plastic ingestion by planktivorous fishes in the North Pacific Central Gyre. *Mar Pollut Bull,* 60**,** 2275-8.

Bouwmeester, H., Hollman, P. C. H. & Peters, R. J. B. 2015. Potential Health Impact of Environmentally Released Micro- and Nanoplastics in the Human Food Production Chain: Experiences from Nanotoxicology. *Environmental Science and Technology,* 49**,** 8932-8947.

Braeuning, A. 2019. Uptake of microplastics and related health effects: a critical discussion of Deng et al., Scientific reports 7:46687, 2017. *Arch Toxicol,* 93**,** 219-220.

Bråte, I. L. N., Eidsvoll, D. P., Steindal, C. C. & Thomas, K. V. 2016. Plastic ingestion by Atlantic cod (Gadus morhua) from the Norwegian coast. *Marine Pollution Bulletin,* 112**,** 105-110.

Browne, Mark a., Niven, Stewart j., Galloway, Tamara s., Rowland, Steve j. & Thompson, Richard c. 2013. Microplastic Moves Pollutants and Additives to Worms, Reducing Functions Linked to Health and Biodiversity. *Current Biology,* 23**,** 2388-2392.

Cao, H., Yuan, J.-P., Zhang, R., Huang, C.-M., Sandreczki, T.C., Jean, Y.C. 1999. Degradation of Polymer Coating Systems Studied by Positron Annihilation Spectroscopy. 3. Wavelength Dependence of UV Irradiation Effect. *Macromolecules,* 32**,** 9.

Carr, K. E., Smyth, S. H., Mccullough, M. T., Morris, J. F. & Moyes, S. M. 2012. Morphological aspects of interactions between microparticles and mammalian cells: intestinal uptake and onward movement. *Prog Histochem Cytochem,* 46**,** 185-252.

Cesa, F., Turra, A. & Baruque-Ramos, J. 2017. Synthetic fibers as microplastics in the marine environment: A review from textile perspective with a focus on domestic washings. *Sci Total Environ,* 598**,** 1116-1129.

Cole, M., Lindeque, P., Fileman, E., Halsband, C., Goodhead, R., Moger, J. & Galloway, T. S. 2013. Microplastic Ingestion by Zooplankton. *Environmental Science & Technology,* 47**,** 6646-6655.

CIR (2007) Cosmetics Industry Review. Final report on the safety assessment of polyethylene. Int J Toxicol. 26 (Suppl 1), 115-27.

Da Costa, J. P., Santos, P. S. M., Duarte, A. C. & Rocha-Santos, T. 2016. (Nano)plastics in the environment - Sources, fates and effects. *Science of the Total Environment,* 566-567**,** 15-26.

De Fusco, R., Monarca, S., Biscardi, D., Pasquini, R. & Fatigoni, C. 1990. Leaching of mutagens into mineral water from polyethyleneterephthalate bottles. *Sci Total Environ,* 90, 241-248.

De Witte, B., Devriese, L., Bekaert, K., Hoffman, S., Vandermeersch, G., Cooreman, K. & Robbens, J. 2014. Quality assessment of the blue mussel (Mytilus edulis): Comparison between commercial and wild types. *Marine Pollution Bulletin,* 85**,** 146-155.

Dehghani, S., Moore, F. & Akhbarizadeh, R. 2017. Microplastic pollution in deposited urban dust, Tehran metropolis, Iran. *Environmental Science and Pollution Research,* 24**,** 20360-20371.

Deng, Y., Zhang, Y., Lemos, B. & Ren, H. 2017. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. *Scientific Reports,* 7.

Deng, Y., Zhang, Y., Qiao, R., Bonilla, M. M., Yang, X., Ren, H. & Lemos, B. 2018. Evidence that microplastics aggravate the toxicity of organophosphorus flame retardants in mice (Mus musculus). *J Hazard Mater,* 357**,** 348-354.

Di, M., Liu, X., Wang, W. & Wang, J. 2019. Manuscript prepared for submission to environmental toxicology and pharmacology pollution in drinking water source areas: Microplastics in the Danjiangkou Reservoir, China. *Environ Toxicol Pharmacol,* 65, 82-89.

Dris, R., Gasperi, J., Mirande, C., Mandin, C., Guerrouache, M., Langlois, V. & Tassin, B. 2017. A first overview of textile fibers, including microplastics, in indoor and outdoor environments. *Environmental Pollution,* 221**,** 453-458.

Dris, R., Gasperi, J., Saad, M., Mirande-Bret, C. & Tassin, B. 2016. Synthetic fibers in atmospheric fallout: A source of microplastics in the environment? *Marine Poll Bull,* 104, 290-293.

Eerkes-Medrano, D., Leslie, H.A. & Quinn, B. 2019. Microplastics in drinking water: A review and assessment. *Current Opinion in Environmental Science & Health*, 7, 69-75.

Eerkes-Medrano, D., Thompson, R. C. & Aldridge, D. C. 2015. Microplastics in freshwater systems: A review of the emerging threats, identification of knowledge gaps and prioritisation of research needs. *Water research,* 75**,** 63-82.

FAO 2012. World review of fisheries and aquaculture: The state of world fisheries and aquaculture.

FAO 2017. Microplastics in fisheries and aquaculture: Status of knowledge on their occurrence and implications for aquatic organisms and food safety. Rome.

Farrell, P. & Nelson, K. 2013. Trophic level transfer of microplastic: Mytilus edulis (L.) to Carcinus maenas (L.). *Environmental Pollution,* 177**,** 1-3.

Ferreira, G. V. B., Barletta, M., Lima, A. R. A., Morley, S. A., Justino, A. K. S. & Costa, M. F. 2018. High intake rates of microplastics in a Western Atlantic predatory fish, and insights of a direct fishery effect. *Environmental Pollution,* 236**,** 706-717.

Foekema, E. M., De Gruijter, C., Mergia, M. T., Van Franeker, J. A., Murk, A. J. & Koelmans, A. A. 2013. Plastic in North Sea Fish. *Environmental Science & Technology,* 47**,** 8818-8824.

Foley, C. J., Feiner, Z. S., Malinich, T. D. & Hook, T. O. 2018. A meta-analysis of the effects of exposure to microplastics on fish and aquatic invertebrates. *Sci Total Environ,* 631-632**,** 550-559.

Fries, E., Dekiff, J. H., Willmeyer, J., Nuelle, M.-T., Ebert, M. & Remy, D. 2013. Identification of polymer types and additives in marine microplastic particles using pyrolysis-GC/MS and scanning electron microscopy. *Environmental Science-Processes & Impacts,* 15**,** 1949-1956.

Galafassi, S., Nizetto, L. & Volta P. 2019. Plastic sources: A survey across scientific and grey literature for their inventory and relative contribution to microplastics pollution in natural environments, with an emphasis on surface water. *Sci Total Environ,* 693, 133499.

Galloway, T. S. 2015. Micro- and nano-plastics and human health.

Gasperi, J., Wright, S. L., Dris, R., Collard, F., Mandin, C., Guerrouache, M., Langlois, V., Kelly, F. J. & Tassin, B. 2018. Microplastics in air: Are we breathing it in? *Current Opinion in Environmental Science & Health,* 1**,** 1-5.

Gewert, B., Plassmann, M. M. & Macleod, M. 2015. Pathways for degradation of plastic polymers floating in the marine environment. *Environ Sci Process Impacts,* 17**,** 1513-21.

Gigault, J., Pedrono, B., Maxit, B. & Ter Halle, A. 2016. Marine plastic litter: the unanalyzed nano-fraction. *Environmental Science: Nano,* 3**,** 346-350.

Harrison, J. P., Schratzberger, M., Sapp, M. & Osborn, A. M. 2014. Rapid bacterial colonization of low-density polyethylene microplastics in coastal sediment microcosms. *BMC microbiology,* 14**,** 232-232.

HSDB (Hazardous Substances Database) 2009. Polyethylene terephthalate. Available at: https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+7712 [accessed November 2019].

Hidalgo-Ruz, V., Gutow, L., Thompson, R. C. & Thiel, M. 2012. Microplastics in the Marine Environment: A Review of the Methods Used for Identification and Quantification. *Environmental Science & Technology,* 46**,** 3060-3075.

Holmes, L. A., Turner, A. & Thompson, R. C. 2012. Adsorption of trace metals to plastic resin pellets in the marine environment. *Environ Pollut,* 160**,** 42-8.

Horton, A. A., Walton, A., Spurgeon, D. J., Lahive, E. & Svendsen, C. 2017. Microplastics in freshwater and terrestrial environments: Evaluating the current understanding to identify the knowledge gaps and future research priorities. *Sci Total Environ,* 586**,** 127-141.

Hurley, R., Woodward, J. & Rothwell, J. J. 2018. Microplastic contamination of river beds significantly reduced by catchment-wide flooding. *Nature Geoscience,* 11**,** 251-257.

Hwang, J., Choi, D., Han, S., Choi, J. & Hong, J. 2019. An assessment of the toxicity of polypropylene microplastics in human derived cells. *Sci Total Environ*, 684, 657-669.

Ivar Do Sul, J. A., Costa, M. F., Barletta, M. & Cysneiros, F. J. A. 2013. Pelagic microplastics around an archipelago of the Equatorial Atlantic. *Marine Pollution Bulletin,* 75**,** 305-309.

Jin, Y., Lu, L., Tu, W., Luo, T. & Fu, Z. 2019. Impacts of polystyrene microplastic on the gut barrier, microbiota and metabolism of mice. *Sci Total Environ,* 649**,** 308-317.

Koelmans, A., Besseling, E. & Foekema, E. 2014. Leaching of plastic additives to marine organisms. *Environmental Pollution*, 187, 49-54.

Koelmans, A. A., Besseling, E. & Shim, W. J. 2015. Nanoplastics in the Aquatic Environment. Critical Review. *In:* BERGMANN, M., GUTOW, L. & KLAGES, M. (eds.) *Marine Anthropogenic Litter.* Cham: Springer International Publishing.

Koelmans, A. A., Mohamed Nor, N. H., Hermsen, E., Kooi, M., Mintenig, S. M. & De France, J. 2019. Microplastics in freshwaters and drinking water: Critical review and assessment of data quality. *Water Res,* 155**,** 410-422.

Kole, P. J., Lohr, A. J., Van Belleghem, F. G. a. J. & Ragas, A. M. J. 2017. Wear and Tear of Tyres: A Stealthy Source of Microplastics in the Environment. *International Journal of Environmental Research and Public Health,* 14**,** 1265-1265.

Lambert, S. & Wagner, M. 2017. Environmental performance of bio-based and biodegradable plastics: the road ahead. *Chem Soc Rev,* 46**,** 6855-6871.

Lehner, R., Weder, C., Petri-Fink, A. & Rothen-Rutishauser, B. 2019. Emergence of Nanoplastic in the Environment and Possible Impact on Human Health. *Environmental science & technology*.

Li, J., Liu, H. & Paul Chen, J. 2018. Microplastics in freshwater systems: A review on occurrence, environmental effects, and methods for microplastics detection. *Water research,* 137**,** 362-374.

Li, J., Yang, D., Li, L., Jabeen, K. & Shi, H. 2015. Microplastics in commercial bivalves from China. *Environmental Pollution,* 207**,** 190-195.

Liebezeit, G. & Liebezeit, E. 2013. Non-pollen particulates in honey and sugar. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess,* 30**,** 2136-40.

Liebezeit, G. & Liebezeit, E. 2014. Synthetic particles as contaminants in German beers. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess,* 31**,** 1574-8.

Lobelle, D. & Cunliffe, M. 2011. Early microbial biofilm formation on marine plastic debris. *Marine Pollution Bulletin,* 62**,** 197-200.

Lu, L., Wan, Z., Luo, T., Fu, Z. & Jin, Y. 2018. Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. *Science of the Total Environment,* 631-632**,** 449-458.

Luo, T., Wang, C., Pan, Z., Jin, C., Fu, Z., Jin, Y. 2019. Maternal Polystyrene Microplastic Exposure during Gestation and Lactation Altered Metabolic Homeostasis in the Dams and Their F1 and F2 Offspring. *Environ Sci Technol.* 53(18), 10978-10992.

Lusher, A. L., Mchugh, M. & Thompson, R. C. 2013. Occurrence of microplastics in the gastrointestinal tract of pelagic and demersal fish from the English Channel. *Mar Pollut Bull,* 67**,** 94-9.

Lusher, A. L., Tirelli, V., O'connor, I. & Officer, R. 2015. Microplastics in Arctic polar waters: the first reported values of particles in surface and sub-surface samples. *Sci Rep,* 5**,** 14947.

Maniar, M. L., Kalonia, D. S. & Simonelli, A. P. 1991. Determination of specific rate constants of specific oligomers during polyester hydrolysis. *J Pharm Sci,* 80**,** 778-82.

Mason, S. A., Welch, V. G. & Neratko, J. 2018. Synthetic Polymer Contamination in Bottled Water. *Frontiers in Chemistry,* 6**,** 407-407.

Mathalon, A. & Hill, P. 2014. Microplastic fibers in the intertidal ecosystem surrounding Halifax Harbor, Nova Scotia. *Marine pollution bulletin,* 81**,** 69-79.

Mato, Y., Isobe, T., Takada, H., Kanehiro, H., Ohtake, C. & Kaminuma, T. 2001. Plastic resin pellets as a transport medium for toxic chemicals in the marine environment. *Environ Sci Technol,* 35**,** 318-24.

Mattsson, K., Johnson, E. V., Malmendal, A., Linse, S., Hansson, L. A. & Cedervall, T. 2017. Brain damage and behavioural disorders in fish induced by plastic nanoparticles delivered through the food chain. *Sci Rep,* 7**,** 11452.

Mccormick, A. R., Hoellein, T. J., London, M. G., Hittie, J., Scott, J. W. & Kelly, J. J. 2016. Microplastic in surface waters of urban rivers: Concentration, sources, and associated bacterial assemblages. *Ecosphere,* 7.

Merdas, I., Thominette, F. & Verdu, J. 2003. Hydrolytic ageing of polyamide 11. Effect of carbon dioxide on PA11 hydrolysis. *Polymer Degradation and Stability*, 79, 419-425.

Merski, J.A., Johnson, W.D., Muzzio, M., Lyang, N.L. & Gaworski, C.L. 2008. Oral toxicity and bacterial mutangenicity studies with a spunbond polyethylene and polyethylene terephthalate polymer fabric. *Intern J Toxicol*, 27, 387–395.

Mintenig, S. M., Löder, M. G. J., Primpke, S. & Gerdts, G. 2019. Low numbers of microplastics detected in drinking water from ground water sources. *Science of the Total Environment,* 648**,** 631-635.

Murphy, F., Ewins, C., Carbonnier F., Quinn B. (2016) Wastewater Treatment Works (WwTW) as a Source of Microplastics in the Aquatic Environment*. Environmental Science & Technology*, 50 (11), 5800-5808.

Murty, B. S., Shankar, P., Raj, B., Rath, B. B. & Murday, J. 2013. Unique Properties of Nanomaterials. *In:* MURTY, B. S., SHANKAR, P., RAJ, B., RATH, B. B. & MURDAY, J. (eds.) *Textbook of Nanoscience and Nanotechnology.* Berlin, Heidelberg: Springer Berlin Heidelberg.

Napper, I. E. & Thompson, R. C. 2016. Release of synthetic microplastic plastic fibres from domestic washing machines: Effects of fabric type and washing conditions. *Marine Pollution Bulletin,* 112**,** 39-45.

Nauendorf, A., Krause, S., Bigalke, N. K., Gorb, E. V., Gorb, S. N., Haeckel, M., Wahl, M. & Treude, T. 2016. Microbial colonization and degradation of polyethylene and biodegradable plastic bags in temperate fine-grained organic-rich marine sediments. *Mar Pollut Bull,* 103**,** 168-178.

Nelms, S. E., Galloway, T. S., Godley, B. J., Jarvis, D. S. & Lindeque, P. K. 2018. Investigating microplastic trophic transfer in marine top predators. *Environmental Pollution,* 238**,** 999-1007.

Novotna, K., Cermakova, L., Pivokonska, L., Cajthaml, T. & Pivokonsky, M. Microplastics in drinking water treatment - Current knowledge and research needs. *Sci Total Environ*, 667, 730-740.

Obbard, R. W., Sadri, S., Wong, Y. Q., Khitun, A. A., Baker, I. & Thompson, R. C. 2014. Global warming releases microplastic legacy frozen in Arctic Sea ice. *Earth's Future,* 2**,** 315-320.

Ogata, Y., Takada, H., Mizukawa, K., Hirai, H., Iwasa, S., Endo, S., Mato, Y., Saha, M., Okuda, K., Nakashima, A., Murakami, M., Zurcher, N., Booyatumanondo, R., Zakaria, M. P., Dung Le, Q., Gordon, M., Miguez, C., Suzuki, S., Moore, C., Karapanagioti, H. K., Weerts, S., Mcclurg, T., Burres, E., Smith, W., Van Velkenburg, M., Lang, J. S., Lang, R. C., Laursen, D., Danner, B., Stewardson, N. & Thompson, R. C. 2009. International Pellet Watch: global monitoring of persistent organic pollutants (POPs) in coastal waters. 1. Initial phase data on PCBs, DDTs, and HCHs. *Mar Pollut Bull,* 58**,** 1437-46.

Panko, J., Chu, J., Kreider, M. & Unice, K. 2013. Measurement of airborne concentrations of tire and road wear particles in urban and rural areas of France, Japan, and the United States. *Atmospheric Environment*, 72, 192-199.

Pauly, J. L., Stegmeier, S. J., Allaart, H. A., Cheney, R. T., Zhang, P. J., Mayer, A. G. & Streck, R. J. 1998. Inhaled cellulosic and plastic fibers found in human lung tissue. *Cancer Epidemiol Biomarkers Prev,* 7**,** 419-28.

Pimentel, J. C., Avila, R. & Lourenco, A. G. 1975. Respiratory disease caused by synthetic fibres: a new occupational disease. *Thorax,* 30**,** 204-19.

Pivokonsky, M., Cermakova, L., Novotna, K., Peer, P., Cajthaml, T. & Janda, V. 2018. Occurrence of microplastics in raw and treated drinking water. *Science of the Total Environment,* 643**,** 1644-1651.

Porter, D. W., Castranova, V., Robinson, V. A., Hubbs, A. F., Mercer, R. R., Scabilloni, J., Goldsmith, T., Schwegler-Berry, D., Battelli, L., Washko, R., Burkhart, J., Piacitelli, C., Whitmer, M. & Jones, W. 1999. Acute inflammatory reaction in rats after intratracheal instillation of material collected from a nylon flocking plant. *J Toxicol Environ Health A,* 57**,** 25-45.

Renner, G., Nellessen, A., Schwiers, A., Wenzel, M., Schmidt, T. C. & Schram, J. 2019. Data preprocessing & evaluation used in the microplastics identification process: A critical review & practical guide. *TrAC - Trends in Analytical Chemistry,* 111**,** 229-238.

Rezania, S., Park, J., Md Din, M. F., Mat Taib, S., Talaiekhozani, A., Kumar Yadav, K. & Kamyab, H. 2018. Microplastics pollution in different aquatic environments and biota: A review of recent studies. *Marine pollution bulletin,* 133**,** 191-208.

Rochman, C. M., Hentschel, B. T. & Teh, S. J. 2014. Long-term sorption of metals is similar among plastic types: implications for plastic debris in aquatic environments. *PLoS One,* 9**,** e85433.

Rochman, C. M., Hoh, E., Kurobe, T. & Teh, S. J. 2013. Ingested plastic transfers hazardous chemicals to fish and induces hepatic stress. *Scientific reports,* 3**,** 3263-3263.

Rochman, C. M., Kross, S. M., Armstrong, J. B., Bogan, M. T., Darling, E. S., Green, S. J., Smyth, A. R. & Verissimo, D. 2015. Scientific Evidence Supports a Ban on Microbeads. *Environ Sci Technol,* 49**,** 10759-61.

Romeo, T., Pietro, B., Pedà, C., Consoli, P., Andaloro, F. & Fossi, M. C. 2015. First evidence of presence of plastic debris in stomach of large pelagic fish in the Mediterranean Sea. *Marine pollution bulletin,* 95**,** 358-361.

Ruge, C. A., Kirch, J. & Lehr, C. M. 2013. Pulmonary drug delivery: from generating aerosols to overcoming biological barriers-therapeutic possibilities and technological challenges. *Lancet Respir Med,* 1**,** 402-13.

Rummel, C. D., Löder, M. G. J., Fricke, N. F., Lang, T., Griebeler, E. M., Janke, M. & Gerdts, G. 2016. Plastic ingestion by pelagic and demersal fish from the North Sea and Baltic Sea. *Marine pollution bulletin,* 102**,** 134-141.

Sajiki, J., Yonekubo, J. 2003. Leaching of bisphenol A (BPA) to seawater from polycarbonate plastic and its degradation by reactive oxygen species. *Chemosphere,* 51**,** 55-62.

Sapea 2019. A scientific perspective on microplastics in nature and society. Berlin, Germany.

Schymanski, D., Goldbeck, C., Humpf, H. U. & Fürst, P. 2018. Analysis of microplastics in water by micro-Raman spectroscopy: Release of plastic particles from different packaging into mineral water. *Water research,* 129**,** 154-162.

Setälä, O., Fleming, V. & Lehtiniemi, M. 2013. Ingestion and transfer of microplastics in the planktonic food web. *Environmental Pollution*, 185, 77-83.

Silva, A. B., Bastos, A. S., Justino, C. I. L., Da Costa, J. P., Duarte, A. C. & Rocha-Santos, T. a. P. 2018. Microplastics in the environment: Challenges in analytical chemistry - A review. *Anal Chim Acta,* 1017**,** 1-19.

Smith, M., Love, D. C., Rochman, C. M. & Neff, R. A. 2018. Microplastics in Seafood and the Implications for Human Health. *Current environmental health reports,* 5**,** 375-386.

Sommer, F., Dietze, V., Baum, A., Sauer, J., Gilge, S., Maschowski, C. & Gieré, R. 2018. Tire Abrasion as a Major Source of Microplastics in the Environment. *Aerosol and Air Quality Research*, 18, 2014-2028.

Sykes, E. A., Dai, Q., Tsoi, K. M., Hwang, D. M. & Chan, W. C. W. 2014. Nanoparticle exposure in animals can be visualized in the skin and analysed via skin biopsy. *Nature Communications,* 5**,** 3796.

Thompson, R. C., Swan, S. H., Moore, C. J. & Vom Saal, F. S. 2009. Our plastic age. *Philos Trans R Soc Lond B Biol Sci,* 364**,** 1973-6.

Toussaint, B., Raffael, B., Angers-Loustau, A., Gilliland, D., Kestens, V., Petrillo M., Rio-Echevarria, IM., Van den Eede, G. 2019. Review of micro- and nanoplastic contamination in the food chain. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*. 36(5), 639-673.

Unice, K. M., Kreider, M. L. & Panko, J. M. 2012. Use of a deuterated internal standard with pyrolysis-GC/MS dimeric marker analysis to quantify tire tread particles in the environment. *Int J Environ Res Public Health,* 9**,** 4033-55.

Van Cauwenberghe, L. & Janssen, C. R. 2014. Microplastics in bivalves cultured for human consumption. *Environmental Pollution,* 193**,** 65-70.

Warheit, D. B., Hart, G. A., Hesterberg, T. W., Collins, J. J., Dyer, W. M., Swaen, G. M. H., Castranova, V., Soiefer, A. I. & Kennedy, G. L. 2001. Potential Pulmonary Effects of Man-Made Organic Fiber (MMOF) Dusts. *Critical Reviews in Toxicology,* 31**,** 697-736.

Warheit, D. B., Webb, T. R., Reed, K. L., Hansen, J. F. & Kennedy, G. L., Jr. 2003. Four-week inhalation toxicity study in rats with nylon respirable fibers: rapid lung clearance. *Toxicology,* 192**,** 189-210.

Welden, N. A., Abylkhani, B. & Howarth, L. M. 2018. The effects of trophic transfer and environmental factors on microplastic uptake by plaice, Pleuronectes plastessa, and spider crab, Maja squinado. *Environmental Pollution,* 239**,** 351-358.

Welle, F., & Franz, R. 2018. Microplastic in bottled natural mineral water – literature review and considerations on exposure and assessment. Food Addit Contam: Part A , Anal Control Expo Risk Assess. 35(12), 2482-2492.

WHO. 2019. Microplastics in drinking water. Geneva: World Health Organization. Licence: CCBY-NC-SA 3.0 IG0

Wright, S. L. & Kelly, F. J. 2017. Plastic and Human Health: A Micro Issue? *Environmental Science and Technology,* 51**,** 6634-6647.

Yang, D., Shi, H., Li, L., Li, J., Jaben, K. & Kolandhasamy, P. 2015. Microplastic Pollution in Table Salts from China. *Environ Sci Technol,* 49**,** 13622-7.

Yang, Y. F., Chen, C. Y., Lu, T. H. & Liao, C. M. 2019. Toxicity-based toxicokinetic/toxicodynamic assessment for bioaccumulation of polystyrene microplastics in mice. *Journal of hazardous materials***,** 703-713.

Yoo, J.-W., Doshi, N. & Mitragotri, S. 2011. Adaptive micro and nanoparticles: Temporal control over carrier properties to facilitate drug delivery. *Advanced Drug Delivery Reviews,* 63**,** 1247-1256.

Yousif, E. & Haddad, R. 2013. Photodegradation and photostabilization of polymers, especially polystyrene: review. *Springerplus,* 2**,** 398.

Zettler, E. R., Mincer, T. J. & Amaral-Zettler, L. A. 2013. Life in the "plastisphere": microbial communities on plastic marine debris. *Environ Sci Technol,* 47**,** 7137-46.

Zhang, X. Q., Xu, X., Bertrand, N., Pridgen, E., Swami, A. & Farokhzad, O. C. 2012. Interactions of nanomaterials and biological systems: Implications to personalized nanomedicine. *Adv Drug Deliv Rev,* 64**,** 1363-84.

Zubris, K. A. & Richards, B. K. 2005. Synthetic fibers as an indicator of land application of sludge. *Environ Pollut,* 138**,** 201-11.