

NON-TOXIC HEALTH CARE:

Alternatives to Hazardous Chemicals in Medical Devices: Phthalates and Bisphenol A

SECOND EDITION (2019)





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FOREWORD

Modern healthcare makes use of a wide range of plastic-based medical products to provide high quality and effective treatment to patients. As a consequence high volumes of plastic single-use products and complex plastic composites are routinely used by the European health sector and it is becoming increasingly important to understand the impact these materials have on human health.

We have known for decades that certain hazardous chemicals leach out of medical devices, such as phthalates in plastic tubing. One of Health Care Without Harm (HCWH) Europe's first campaigns focused on the elimination of DEHP, the most commonly used phthalate, in intravenous drips. Our work in this area has also highlighted the high exposure to bisphenol A (BPA) of new-borns receiving medical treatment using multiple devices.

The endocrine-disrupting properties of these chemicals are now well established; we have seen an increase in endocrine-related diseases such as breast and testicular cancers, thyroid disorders, infertility, and diabetes throughout Europe over the last decades.

This second edition of *Non-toxic Healthcare* forms an important part of HCWH Europe's work to raise awareness about the presence of hazardous substances in medical devices and the consequent risks to patients. This report also contains a new chapter specifically examining the health impact of plastics in healthcare.

HCWH Europe promotes the substitution of harmful substances by demonstrating that many alternatives with safer toxicological profiles are available on the market. We aim to accelerate the shift towards substitution within the European healthcare sector, supported by research, evidence, collaboration, and greater awareness. Progressive manufacturers, governments, health systems, hospitals, and health practitioners are starting to come together to lead this change; many European healthcare providers have already moved to eliminate PVC, DEHP, and BPA from healthcare practice. HCWH Europe has highlighted a number of examples in recent years, some of which are listed in this report.

Importantly, the move towards substitution needs to be further encouraged and supported by strong political and regulatory action, such as in France for example, where tubes and pipes containing DEHP are banned in paediatric, neonatal, and maternity departments in hospitals. The new Medical Devices Regulation introduces provisions that would help phase out endocrine disrupting chemicals, carcinogenic, mutagenic and reprotoxic substances, and particularly phthalates in medical devices, if safer alternatives are available and technically feasible. This is a positive step and one that HCWH Europe will continue to follow and support through its implementation.

Prevention is always better than cure, and this theme is central to the recommendations laid out in this report. Opting for safer alternatives in healthcare to prevent patients (particularly children and other vulnerable groups), from being exposed to toxic chemicals will help prevent devastating lifelong long-term health consequences in these groups. In doing the healthcare sector will be fulfilling its duty to first do no harm.

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EXECUTIVE SUMMARY

Medical devices play a critical role in healthcare but may contain hazardous substances in their composition that can leach into patients during their use and compromise patient safety. Concerns have been raised by different societal groups including governmental bodies, healthcare professionals, scientists and civil society organisations, regarding the potential health impacts of chemical exposure from medical devices, particularly for vulnerable population groups.

In 2017, the European Council adopted the Medical Devices Regulation (MDR), fully applicable to medical devices placed on the EU market as of 26 May 2020. Importantly, some of the provisions within this regulation have the potential to act as an engine for substituting medical devices that contain harmful chemicals with safer alternatives.

Phthalates and Bisphenol A (BPA) are substances of particular concern that are often found in medical devices. Phthalates are commonly used as plastic softeners in PVC-based medical devices, whilst BPA is used to produce certain plastics such as polycarbonates and epoxy resins that have applications in the medical device industry. A major concern surrounding these substances is that they are known endocrine disrupting chemicals (EDCs), which may interfere with the normal functioning of the human endocrine system and therefore present a hazard to different physiological and developmental processes. EDCs can impact upon the human body at very low concentrations and can combine with other endocrine disruptors to produce additive effects. Despite difficulties to demonstrate a causal link, some associations between EDC exposure and diseases are apparent: evidence shows that foetuses, children, and pregnant women are the most vulnerable groups.

Awareness of actions to eliminate harmful plastics must be increased within the healthcare sector, highlighting that a high level of patient care and safety can be maintained. Furthermore, as some of the most highly trusted community figures, healthcare professionals have the capacity and moral obligation to educate the communities they serve and help trigger widespread beneficial behaviour changes in plastic use.

Within this report, HCWH Europe examines the health impact of plastics in healthcare, and presents a number of recommendations for policy makers, competent authorities, notified bodies and healthcare providers, to move towards non-toxic healthcare and minimise the risk to patients without compromising medical care:

- European legislation must protect the most vulnerable groups. Consistent technical implementation of Annex I.II.10.4 of the MDR must therefore be ensured. The benefit-risk assessment of the presence of hazardous chemicals in certain medical devices should therefore be subject to the most stringent conformity assessment procedures by a Notified Body
- Devices should be subject to stringent compliance assessment of required labelling by a Competent Authority. Information labelled in accordance with the MDR must be accessible to the public via the revamped European Database on Medical Devices (EUDAMED)
- The market authorisation process for medical devices needs increased transparency
- Sustainable procurement guidelines should provide incentives for the substitution of hazardous chemicals in medical devices
- Funding for research and development of alternative substances and products and for clinical and epidemiological projects that compare the performance of these alternatives should be prioritised.

INTRODUCTION

Medical devices are an essential feature of modern healthcare, playing an important role in prevention, diagnosis, monitoring, and treatment of diseases and disabilities. Hazardous chemicals are often present in medical devices to improve plastic performance e.g. plasticisers, flame-retardants, fillers, colourings, impact modifiers, and stabilisers. These harmful chemicals can represent a high percentage of the final product (in some cases up to 80%) and can leach out of products and have adverse effects on human health and the environment.

Concerns regarding hazardous chemical exposure through medical devices are particularly relevant to

groups of vulnerable patients that undergo multiple medical interventions or are exposed chronically over extended periods, including infants in neonatal care or dialysis patients.

Substances that are commonly found in medical devices and are of particular concern are phthalates and Bisphenol A (BPA). These substances have been the subject of intense political debate in recent years due to their widespread use in consumer products and the risks they pose to human health and the environment. The endocrine-disrupting properties of these chemicals are also well established.

Hazard of chemicals contained in medical devices

Humans are exposed to environmental contaminants from several sources and exposure pathways, including consumption of contaminated food and water, air and dust inhalation/ingestion, and dermal absorption. Human biomonitoring studies have detected hazardous chemicals like phthalates and BPA in almost every individual analysed and in a variety of human tissues and fluids such as placental tissue, breast milk, amniotic fluid, urine, blood, cord blood, sperm, and saliva.^{2 3 4 5 6 7 8 9} The majority of studies show widespread exposure to phthalates in unborn children and infants across Europe. The new European Human Biomonitoring (HBM4EU) Initiativeⁱ (2017-2021) aims to coordinate and advance human biomonitoring in Europe. The project represents a joint effort of Member States, the European Environment Agency, and the European Commission. One of the objectives of HBM4EU is to generate scientific evidence on the causal relationships between exposure to prioritised chemicals (including phthalates and bisphenols) and the adverse health effects and public health implications.

One of the major reasons for concern surrounding phthalates and BPA is that they are known endocrine disrupting chemicals (EDCs) that can mimic or otherwise interfere with hormone production or function. EDCs can therefore interfere with organ formation and growth, sexual maturation, stress response, and behaviour.¹⁰ As traditional risk assess-

ment procedures lack integration of endocrinology concepts, the effects of EDCs in human health and the environment are mostly dismissed in the existing risk assessment framework. In particular, effects from early life, chronic low-dose, and/or multiple simultaneous exposures are not taken into consideration. Increased incidence of diseases and illnesses in humans from neonatal/infancy through to adulthood has been associated with exposure to these substances.^{4 10} In 2015, the Endocrine Society reviewed the latest science and declared that the evidence for adverse reproductive effects is strong and mounting for effects in areas such as neuroendocrine, sexual development, obesity, metabolism, thyroid systems, and insulin resistance. Further, the effects may also be transmitted to future generations.¹¹

A European Parliament study reviewed the scientific evidence of endocrine disruption, the extent of EDC exposure, and the associated health effects and consequent costs of treatment. Published in May 2019, the study concluded that after several decades of multidisciplinary research in endocrinology, ecotoxicology, toxicology, epidemiology, clinical research, epigenetics, environmental sciences and other disciplines, endocrine disruption is now an important and validated scientific concept.¹² The evidence therefore justifies classifying EDCs as a specific class of hazard, equivalent to that of carcinogenic, mutagenic, reprotoxic chemicals (CMRs). Researchers and healthcare practitioners are particularly concerned that exposure to EDCs from medical devices compounds adds to the existing exposure from other sources: EDCs are ubiquitous and the entire population is already exposed. Furthermore, vulnerable population groups such as neonates, infants, pregnant and breast-feeding women, and the elderly are not adequately protected from the risk of exposure to these chemicals. The most at risk groups comprises dialysis patients and neonates in intensive care units, as they experience frequent and intimate contact with a number of medical devices containing EDCs. Premature babies and infants are particularly sensitive to phthalate effects, as their reproductive system is still developing and they have much higher relative phthalates intakes. In addition, the unborn and young children are not able to metabolise chemical substances in the same way as adults, due to the on-going development of their organs and maturation of the different systems (see Box 5).

Despite claims that exposure to hazardous chemicals through medical devices represents a small proportion of an individual's overall exposure, this

exposure can be harmful for patients as they will be primarily from the vulnerable populations and/or maybe rendered more susceptible to toxic insult through (critical) illness. A precautionary approach and eliminating exposure to hazardous chemicals wherever possible is therefore appropriate in the case of medical devices and recognised under the

BOX 1

EU definition of a medical device

(Regulation 2017/745 on medical devices¹)

Any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- Diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability
- Investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
- Providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood, and tissue donations

This does not include devices/treatments that achieve the principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but a medical device may be assisted in its function by such means.

ⁱ www.hbm4eu.eu

BOX 2

What are phthalates?

Phthalates are a group of chemical substances, primarily used as plasticisers (softeners) in plastics to make them more flexible. Depending on the number of carbon atoms in their alkyl side-chains they are divided into:

- High-chain length - with more than six carbons (e.g. DINP, DIDP, DPHP, and DIUP)
- Transitional-chain length - with three to six carbons (e.g. DEHP, DBP, DIBP and BBP)
- Low-chain length - fewer than three carbons. (e.g. DEP and DMP)

Phthalates are abundant in polyvinyl chloride (PVC) medical devices such as blood bags, intravenous bags, tubing, catheters, respiratory masks, or disposable gloves - approximately 40% of all plastic-based medical devices are made from PVC.¹³

Di-2-ethylhexyl phthalate (DEHP) has for many years been the most commonly used phthalate ester plasticiser in medical devices. A 2014 survey in the Danish Medical Device Industry found that 95% of products contained DEHP.¹⁴ DEHP can contribute up to 40% of weight of intravenous bags and up to 80% of weight in medical tubing.¹⁵ Leaching of DEHP from PVC medical devices has been documented since the late 1960s.^{16 17 18} Use of PVC medical devices may lead to a higher exposure to DEHP than everyday sources affecting the general population.¹⁹

BOX 3

What is Bisphenol A?

Bisphenol A (4,4-dihydroxy-2,2-diphenylpropane or BPA) is a chemical substance used as a monomer in the production of polymers such as polycarbonate, epoxy resins, polysulfone, and polyacrylate. BPA is also used as an antioxidant and inhibitor in the polymerisation of PVC and as a precursor for the synthesis of the flame retardant tetrabromobisphenol A (TBBPA). Up to 1 million tonnes of BPA is manufactured and/or imported in the European Economic Area (EEA) annuallyⁱⁱ, from which over 95% of BPA is used in the production of polycarbonates and epoxy resins.^{20 21}

BPA has applications in medical devices that have both direct and indirect contact with patients including those made of polycarbonate, polysulfone, and PVC such as medical tubing, catheters, haemodialysers, newborn incubators, syringes and blood oxygenators. BPA has been shown to leach from medical devices into liquids.^{22 23} European PVC manufacturers informed the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) that they no longer use BPA as stabiliser or antioxidant in PVC production.²³

ii <https://echa.europa.eu/>

Hazard for human health

There is growing evidence that many phthalates and BPA can present a hazard to human health and are recognised in the EU as endocrine-disrupting compounds. Evidence comes from *in vitro* and animal studies as well as clinical and epidemiological studies encompassing both prenatal and postnatal exposures.

The effects of DEHP in animals has been thoroughly reviewed by Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)¹⁹ which concluded that i) the testis toxicity of DEHP is age dependent, with immature animals being more susceptible to testicular toxicity by DEHP than older mature animals; ii) even low-level exposures to DEHP during pregnancy can affect male genital development.²⁴

A review of human epidemiology studies found a

higher risk of male reproductive disorders after prenatal and postnatal exposure to phthalates.²⁵ It has been proven that phthalates can transfer from mothers to fetuses and neonates through placenta and breast milk.²⁶ Exposure to DEHP and DBP has been linked with reproductive alteration including low sperm concentration, shortened anogenital distances (a measure of feminisation of external genitalia), endometriosis, hypospadias, shorter pregnancy duration, changes in neurobehaviour in neonates, infants and children, cholestasis, dermatitis, heart disease and perturbations in inflammatory responses.^{27 28 29 30 31 32} A recent comprehensive and critical review addressed the health hazards posed by phthalates on children and adolescents, including reproductive toxicity in women and men, cancer, insulin resistance and type II diabetes, overweight and obesity, allergy and asthma.⁶ Growing evidence suggests that prenatal phthalate exposures may have neurodevelopmental consequences^{33 34 35 36} and can affect IQ, attention, hyperactivity, and social communication of children.^{37 38}

Exposures to BPA are associated with many health effects in humans, including reproductive effects (erectile dysfunction, miscarriage), cardiovascular diseases, thyroid, immune and metabolic diseases (diabetes), childhood obesity as well as general/abdominal obesity and hypertension, neurodevelopment impairments, respiratory conditions and behaviour alterations (anxiousness, hyperactivity, depression).^{39 40 41 42 43} BPA has recently also been suggested to be an emerging threat to male infertility.⁴⁴

Particularly worrying is the fact that exposure to phthalates and Bisphenol A can lead to cumulative adverse effects on future generations such as neural and immune disorders, infertility, and late-onset complex diseases (cancers and diabetes).⁴⁵

Exposure through medical devices

Exposure to hazardous chemicals through medical devices can be enteral (via the digestive tract), parenteral (intravenously), transcutaneous (via the skin), or through inhalation. Dietary exposure to phthalates and BPA is expected to account for the majority of human exposure. Several studies have described phthalates, (particularly DEHP), leaching from medical devices and recorded levels in urine and blood. The leaching of DEHP from medical plastic devices into body fluids and subsequent migration into human tissues was first reported in the late 1960s.¹⁶ Nearly 60 years after this discovery, regulators are still struggling to define and manage

the potential human health risks posed by DEHP in medical devices.

According to the SCENIHR premature neonates in neonatal intensive care units, infants subjected to repeated medical treatment using medical devices, and patients undergoing haemodialysis are at risk of DEHP-induced effects.¹⁹ Patients in a neonatal intensive care unit (NICU) are exposed to phthalate mixtures through the complex materials used concurrently in NICU care: respiratory circuits, intravenous equipment, enteral feeding supplies, and incubators are likely vehicles of phthalate exposure.⁴⁶

Whilst evidence of BPA leaching into patients is more limited, dialysers, dental materials, circulation equipment, neonatal care medical devices, and urinary catheters have demonstrated releases of BPA.²³ Length of contact time (duration of exposure), temperature and pH, among other parameters, has been shown to increase the release of BPA from polycarbonate.²³ The SCENIHR opinion on the safety of the use of Bisphenol A in medical devices concluded that there is a risk when BPA is directly available for systemic exposure after non-oral exposure routes, especially for neonates in intensive care units, infants undergoing prolonged medical procedures, and for dialysis patients.²³ The risk of adverse effects due to BPA may exist in patients undergoing dialysis treatment since BPA accumulates in systemic circulation due to reduced renal clearance. Although the benefit of medical devices has also to be considered, the SCENIHR recommends that, where practical, medical devices that do not leach BPA should be used.²³ With the exception of dialysis patients (for which treatment is repeated over long time periods and can be considered similar to chronic exposure), the exposure to BPA via medical devices is generally of limited duration (representative of acute to sub-chronic exposure in a toxicological context).

A number of observations from the scientific literature are available, confirming the link between use of plastics in medical devices and exposure of patients to phthalates and/or BPA. A strong association was found between the use of DEHP-containing medical devices and urinary concentrations of three DEHP metabolites in infants receiving care in two neonatal intensive care units.⁴⁷ DEHP leached from endotracheal tubes immediately after use in high-risk neonates.⁴⁸ Premature neonates receiving treatment through feeding tubes and endotracheal tubes had increased levels of DEHP in their urine.⁴⁹

Certain vulnerable patients groups such neonates / children are exposed during intense care to multiple invasive medical procedures and therefore to

multiple medical devices simultaneously, sequentially, or intermittently.^{50 51} Neonates in intensive care are exposed to DEHP at much higher levels than existing safe limits, which might contribute to common early and chronic complications of prematurity.⁵²

Premature infants in neonatal intensive care units undergoing treatment were also found to have BPA levels 10 times higher than the general population, presumably from BPA leaching from medical devices.⁵³ Infants in neonatal intensive care units using a large number of PVC-containing medical devices had also higher concentrations of urinary BPA (one order of magnitude higher than the median concentration of the general population in the US).⁵⁴

Recent clinical studies provide information about the overall significant exposure to BPA during haemodialysis treatment in patients suffering from end-stage renal disease (ESRD).⁵⁵ A recent study demonstrated overexposure to BPA and its chlorinated derivatives of patients with ESRD during online haemodiafiltration (OL-HDF) due to BPA leaching from different medical devices.⁵⁶

The materials used in medical devices are also an important factor. In one study, BPA concentrations among infants in one healthcare unit were approximately 17 times higher than another unit.⁵⁴ Patients undergoing regular continuous ambulatory peritoneal dialysis using plasticiser-free devices had reduced levels of phthalates in urine and blood.⁵⁷ Moreover, the level of cholestasis in neonates was reduced from 50% to 13% in neonates fed through a DEHP-free catheter.⁵⁸

A growing number of studies suggest the link between exposure of patients to phthalates and/or BPA from medical devices and adverse effects in exposed patients. There is emerging evidence that the use of medical devices containing DEHP is potentially harmful for the brain development and function of critically ill children. Belgian clinicians identified a clear link between previously hospitalised children's long-term neurocognitive test results and their individual exposure to the phthalate DEHP during their stay in intensive care.⁵⁹ Critically ill children had very high circulating levels of phthalate metabolites, explained by leaching from medical devices, and these levels were associated with the significant attention-deficit observed four years later.

Another recent study highlighted the impact of acute mono-2-ethylhexyl phthalate (MEHP, the primary metabolite of DEHP) exposure on cardiac electrophysiology in the heart. It concluded that heightened

clinical exposure to plasticised medical products might have cardiac safety implications.⁶⁰ Several clinical observations point to the possible involvement of BPA/DEHP exposure in dialysis patients increased cardiovascular (CV) mortality and sudden cardiac death (SCD).⁶¹ As emphasised by the authors, importantly, BPA/DEHP exposure may be a modifiable risk factor for SCD in dialysis as alternatives to BPA and DEHP do exist and could potentially be used as replacements for dialysis procedures. Replacement of BPA- and DEHP-leaching plastics may reduce morbidity and mortality of patients with ESRD undergoing dialysis and of other patients undergoing invasive interventions with prolonged exposure to plastics (e.g. cardiac surgery). Prospective clinical studies and randomised controlled trials are needed to test this hypothesis.

These data strongly support SCENIHR's recommendation to use medical devices with low DEHP and BPA release potential, whenever possible.



BOX 4

Medical procedures with potential for high exposure to DEHP¹⁹ and BPA²³

- Exchange transfusion of blood in neonates
- Extracorporeal membrane oxygenation (ECMO) treatment of neonates and of adults
- Total Parenteral Nutrition (TPN) in neonates
- Multiple procedures in sick neonates
- Haemodialysis
- Enteral nutrition in neonates and adults
- Heart transplantation or coronary artery bypass graft surgery
- Massive blood transfusion of red blood cells and plasma
- Peritoneal dialysis

Six scenarios considered as representative situations of release of BPA from medical devices:

1. External contact with a medical device containing BPA
2. Contact with oral/dental material and/or orthodontic equipment
3. Contact with implants such as valves, pacemakers and insulin dispensers made from polycarbonate
4. Haemodialysis
5. Prolonged surgical procedures such as bypass operations and transplantations
6. Prolonged exposure to different sources of BPA in intensive care units.

BOX 5

Why neonates and children are more vulnerable

The levels of exposure to hazardous chemicals are of particular concern for unborn children, neonates, and children. These groups are being exposed to hazardous chemicals at a highly vulnerable moment when important aspects of their development can be altered, perhaps with lifelong consequences. Furthermore, their low body weight means the exposure can be relatively higher than for adults. Premature babies are subject to an even higher risk due to their lower birth weight combined with the fact they require many medical interventions. In addition, the unborn and young are not able to metabolise chemical substances in the same way as adults, due to the on-going development of their organs and maturation of the different systems. For example, the glucuronidation mechanisms that are responsible for the excretion of some phthalate metabolites are not fully developed before the age of 3 months.³ Finally, expected longer life spans could mean that this group will be exposed for a longer time to these substances. All these factors may put this group at an increased risk of suffering deleterious effects.

Hazards for the environment

Phthalates and BPA have been detected in aquatic and marine environments, terrestrial ecosystems and in the atmosphere in concentrations that are likely to adversely affect a number of species.^{62 63} These substances have also been shown to bioaccumulate in some species of molluscs and crustaceans.⁶⁴ Phthalates have been measured in a range of environmental matrices, including sludge, dust, soil, air, and water, and are ubiquitous contaminants in the environment. Phthalates and BPA can reach the environment from industrial discharges, sewage, landfill leachates and natural breakdown of plastics in the environment.

DEHP (authorisation list)⁶⁵ and BPA (candidate list)⁶⁶ are both classified by the European Commission as "toxic to aquatic life with long lasting effects" and endocrine disrupting chemical for environment. Data collected from wildlife studies, laboratory ex-

periments and *in vitro* studies show that exposure to environmentally relevant concentrations of BPA have shown detrimental effects in invertebrates and all vertebrate classes.⁶³ Similarly, exposure to different phthalates and/or their metabolites has caused adverse effects at various endpoints in aquatic organisms at environmentally relevant exposures.⁶⁷ There are studies that indicate that BPA can especially affect development, reproduction, immune function and metabolism in aquatic species.⁶⁸ Besides the chemical contamination of a wide range of natural habitats, these compounds also create a waste management problem. The disposal of PVC medical waste can release dioxins and other persistent environmental pollutants, which can have a detrimental impact on human health and the environment.

The European legal framework on hazardous chemicals in medical devices

European medical devices manufacturers have to comply not only with the EU Medical Devices Regulation 2017/745 but also with a number of chemical regulations – the EU Regulation 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and the EU Directive 2011/65/EU on the Restriction of Hazardous Substances in Electrical and Electronical Equipment (RoHS II).

The REACH Regulation

The REACH regulation makes a distinction between medical devices that are:

- Chemical substances, either on their own or as mixtures. Examples of mixtures include lubricants, dental filling materials and bone cements.
- Articles (that is, objects with a function determined by their shape, surface or design rather than their chemical composition (Article 3.3)). Examples include catheters, contact lenses and medical implants.

In practice, most medical devices are likely to qualify as articles under REACH.

A medical device that qualifies as a substance/mixture is subject to most of the requirements of REACH, including registration. Pursuant to Articles 60(2) and 62(6) of REACH, an application for authorisation is not required for a substance used in a medical device. Article 60(2) states that the Commission shall not consider the risks to human health

arising from the use of a substance in a medical device regulated by the MDR. Nonetheless, suppliers, distributors or retailers of medical devices have the duty to communicate information about the presence of Substances of Very High Concern – SVHCs if requested by a consumer in 45 days (Article 33).

Several phthalates are classified as toxic for reproduction under the EU Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (the CLP Regulation) and are listed on the Candidate List of SVHCs under REACH (see Table 1). Seven of those phthalates had subsequently been added to the Authorisation List (Annex XIV of REACH) due to their classification as toxic for reproduction (see Table 1).

The European Chemicals Agency (ECHA) has recently submitted a recommendation to the European Commission to amend Authorisation List entries by adding the endocrine disrupting properties of DEHP, BBP, DBP, and DIBP.⁶⁹ They were identified as substances of very high concern (SVHCs) due to endocrine disrupting properties with effects on human health. DEHP was also identified for its effects on the environment. One important impact of this is that the REACH authorisation process will be able to address – and work to phase out in the longer term – the use of DEHP in medical devices. The authorisation process places significant emphasis on the substitution of affected substances. The actual amendment of the entries including the final decision on the dates, by which companies will need to apply for authorisation to ECHA and on exemptions of uses, will be made by the European Commission in collaboration with the Member States and the

European Parliament.

In the case of BPA, this has been classified as toxic for reproduction, an EDC for human health and an EDC for environment, and listed on the Candidate List of SVHCs under REACH in 2017. However, PlasticsEuropeⁱⁱⁱ (the leading pan-European industrial association) brought a case to the EU court against BPA's classification as a SVHC and against the identification of BPA as an endocrine disruptor with impact on health. This year, the General Court of the EU dismissed both claims. PlasticsEurope also challenged the identification of BPA as an endocrine disruptor with impact on the environment in a third case (the judgment is expected in November 2019).

ⁱⁱⁱ <https://www.plasticseurope.org/en>



TABLE 1

Phthalates in the Candidate List of Substances of Very High Concern (REACH)⁶⁶

Phthalate	CAS number	Reason for inclusion
DCHP (Dicyclohexyl phthalate)	84-61-7	Toxic for reproduction; Endocrine disrupting properties for human health
DHP (Dihexyl phthalate)	84-75-3	Toxic for reproduction
DPP (Dipentyl phthalate)	131-18-0	Toxic for reproduction
1,2-benzenedicarboxylic acid, dipentylester, branched and linear	CAS 84777-06-0	Toxic for reproduction

Phthalates in the Authorisation List⁶⁵

Phthalate	CAS number	Reason for inclusion
DIPP: Diisopentyl phthalate	CAS 605-50-5	Toxic for reproduction
DIBP: Diisobutyl phthalate	CAS 84-69-5	Toxic for reproduction; Endocrine disrupting properties for human health
BBP: Benzylbutyl phthalate	CAS 85-68-7	Toxic for reproduction; Endocrine disrupting properties for human health
DEHP: Bis(2-ethylhexyl) phthalate	CAS 117-81-7	Toxic for reproduction; Endocrine disrupting properties for human health; Endocrine disrupting properties for environment
DBP: Dibutyl phthalate	CAS 84-74-2	Toxic for reproduction; Endocrine disrupting properties for human health
PIPP: n-pentyl-isopentyl phthalate	CAS 776297-69-9	Toxic for reproduction
DMEP: Bis(2-methoxyethyl) phthalate	CAS 117-82-8	Toxic for reproduction

RoHS II Directive

The RoHS II Directive (2011/65/EU) was adopted to limit the concentration of six hazardous substances (including lead, mercury and toxic flame retardants) in electrical and electronic equipment with a view to contributing to the protection of human health and the environment. From July 2014, the RoHS II Directive also applies to electrical and electronic medical devices. *In vitro* medical devices are covered from July 2016 and active implantable medical devices are exempted. Additional exemptions have been added (Annex IV), specific to medical devices and monitoring and control instruments for which a reliable alternative was not available.

Directive (EU) 2015/863 (often referred to as "RoHS 3") amends Directive 2011/65/EU adding four substances to the original six restricted substances – Bis(2-ethylhexyl) phthalate (DEHP), Butyl benzyl phthalate (BBP), Dibutyl phthalate (DBP) and Diisobutyl phthalate (DIBP) – in view of their negative impact on recycling and on human health and the environment during electrical and electronic waste management operations. The longer innova-

tion cycles for medical devices and monitoring and control instruments were taken into account while determining the transitional period. Consequently, the restriction of the use of DEHP, BBP, DBP and DIBP applies to medical devices, including *in vitro* medical devices, and monitoring and control instruments, including industrial monitoring and control instruments, from 22 July 2021.

The Medical Devices Regulation (MDR)

The new MDR aims to create a modernised and more robust EU legislative framework to ensure better protection of public health and patient safety and include, among others, stronger rules on clinical and performance evaluation, reinforced designation and oversight processes of Notified Bodies, establishment of a comprehensive EU database on medical devices (EUDAMED) to be made publicly available, and stricter requirements related to the use of hazardous substances. When the MDR takes effect in May 2020, manufacturers will have to comply with new rules for almost every kind of product

in the medical device spectrum.

According to the new EU Medical Devices Regulation, “Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device.”

Annex I.II.10.4 of the MDR introduces provisions that would help phase out endocrine disrupting chemicals (EDCs), carcinogenic, mutagenic and reprotoxic substances (CMRs), and phthalates in medical devices if safer alternatives are available and technically feasible. Manufacturers of medical devices are required to provide adequate justification (benefit-risk assessment) to the Notified Body for the presence of those substances if they are present above a certain concentration (see Box 6). The term “notified body” refers to the typically private companies charged with evaluating the quality and safety of medical devices in the EU.

The Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) of the European Commission prepared the *Guidelines on the benefit-risk assessment of the presence of phthalates in certain medical devices covering phthalates, which are carcinogenic, mutagenic, and toxic to reproduction (CMR) or have endocrine disrupting (ED) properties.*⁷⁰

Before a justification can be accepted as valid, several steps need to be taken, including giving consideration to the possible use of alternative substances, materials, designs, and medical treatments. In addition, the risk in terms of hazards associated with such alternatives should be weighed against the risk of the use of CMR 1A/1B and/or ED identified phthalates covered under MDR Annex I Chapter II point 10.4.1. However, the risk by itself is not the only parameter to consider; an evaluation must also be made of the impact of the possible alternatives on the functionality, the performance and the overall benefit-risk ratio of the medical device.

These Guidelines are intended to be used by the relevant stakeholders, e.g. manufacturers, notified bodies and regulatory bodies. The approach taken in these Guidelines may also be used for a benefit-risk assessment of other CMR/ED substances present in medical devices. As foreseen by the MDR, adherence to these Guidelines will become mandatory.

BOX 6

Regulation (EU) 2017/745, Annex I.II.10.4 (Substances: 10.4.1. Design and manufacture of devices):

Devices, or those parts thereof, or those materials used therein that:

- Are invasive and come into direct contact with the human body
- (Re)administer medicines, body liquids or other substances, including gases, to/ from the body, or transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body

Shall only contain the following substances in a concentration that is above 0,1 % w/w where justified:

- Category 1 Carcinogen, Mutagen, Reproductive Toxins (CMRs)
- Endocrine disrupting chemicals

The presence of hazardous substances (subject to justification) will have to be indicated on the medical devices’ labelling (in accordance with provisions laid down in Annex I.II.10.4.5). It also specifies that, if such devices are intended to treat children or pregnant or nursing women, the manufacturer should provide information on residual risks for these patient groups and if applicable on appropriate precautionary measures (see Box 7).

Information labelled in accordance with this annex is one of the mandatory Unique Device Identifiers (UDI) data elements to be provided by the manufacturer to the UDI database. This information on the devices will be accessible to the public via the European Database on Medical Devices (EUDAMED).

EUDAMED’s purpose is to strengthen market surveillance and transparency in the field of medical devices, by providing national Competent Authorities with fast access to information. EUDAMED in current form contains data on medical devices that have been collected and entered by Competent Authorities and the European Commission and is currently only accessible by these parties. The MDR, however, calls for EUDAMED to be revamped: the information will be more comprehensive and ac-

cess will be extended. The database will not only be used by the Competent Authorities and the European Commission, it will also be accessed by the Medical Devices Coordination Group (MDCG), Notified Bodies, Economic Operators (manufacturers, authorised representatives, importers, sponsors), experts, and the public, including medical institutions.

Creating greater transparency will allow for a better understanding of what medical devices are placed on the EU market and who is ultimately responsible for them. The level of access, however, will differ between the types of user.

Theoretically, procurers (such as hospitals and Competent Authorities) will be able to access, search, and filter the content of EUDAMED to identify safer medical devices for their procurement process.

Originally, the new database’s launch was supposed to coincide with the date of application for the MDR in May 2020. However, in October 2019, the Commission announced that the launch would be delayed by two years. The Commission plans to have the new database ready when another piece of legislation — the *in vitro* diagnostics regulation — comes into full effect in May 2022.

BOX 7

Regulation (EU) 2017/745, Annex I.II.10.4 (Substances: 10.4.5. Labelling):

Where devices, parts thereof or materials used therein as referred to in Section 10.4.1. contain substances referred to in points (a) or (b) of Section 10.4.1. in a concentration above 0,1 % weight by weight (w/w), the presence of those substances shall be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances.

If the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials, information on residual risks for those patient groups and, if applicable, on appropriate precautionary measures shall be given in the instructions for use.

Why update this report now?

Many alternative substances and materials have appeared in recent years for many of the most hazardous chemicals used in medical devices, including for phthalates and BPA. There is a choice now to be made between safer alternatives or ignoring the potential dangers to patients. The new European legislation was long in the making, but with the MDR there is a real opportunity to accelerate the process of phasing-out phthalates and BPA and minimise patients, and in particular vulnerable groups, exposure to these harmful chemicals.

We are all exposed to endocrine disrupters from multiple sources, but healthcare should not be one of these. As Kambia and co-authors stated already more than fifteen years ago, **when exposures to hazardous chemicals in medical devices can be avoided through careful selection of materials, not doing it is both unprofessional and undesirable.**⁷¹



CHAPTER 1

Substituting hazardous chemicals in medical devices

Exposure to phthalates or BPA can be minimised by adopting a precautionary approach and replacing medical devices with phthalate-free and BPA-free devices, which can fulfil the same function. The precautionary principle is enshrined in Article 191 of the Treaty on the Functioning of the European Union (EU) and aims to ensure a high level of environmental, consumer and human health protection through preventive decision-making in the case of risk. Nevertheless, the decision whether or not to apply the precautionary principle appears to be poorly defined, with ambiguities inherent in determining what level of uncertainty and significance of hazard justifies invoking it.⁷² Decision makers prefer to wait until overwhelming scientific evidence is gathered, often taking a long time to achieve, and potentially delaying action to a point where risks and effects cannot be undone.

On the European market, several manufacturers offer products where phthalates/PVC or BPA have been replaced by alternative materials or substances. In the case of the phthalates, phthalate-free or PVC-free medical devices are available for nearly all product categories except blood bags (see Box 8).

Many hospitals have already made considerable progress, having adopted phase-out policies and committing to using products that are less harmful for patients. However, most of these initiatives are only happening due to the commitment of individuals and in spite of a lack of political or regulatory impetus.

In a project for the European Commission's Directorate General Environment, the Swedish Environmental Management Council developed a set of EU Green Public Procurement (GPP) criteria with regards to electrical and electronic medical devices. In 2014, the creation of Green Public Procurement Criteria about electrical and electronic medical devices missed the opportunity to incorporate a criterion on phasing out BPA due to insufficient scientific evidence and supply chain transparency. Given the growing amount of data and new tools available to track the presence of substances, updating this policy tool would better support sustainable procurement strategies aimed at phasing out hazardous chemicals.

BOX 8

PVC-free Blood Bag project

The PVC-free Blood Bag Project (www.pvcfree-bloodbag.eu) was a Life+ collaborative initiative between industry and the healthcare sector that aimed to demonstrate that it is possible to produce a blood bag without using PVC. The project, which was completed in 2017, has shown that it is possible to produce a completely PVC-free set of four bags, which can store red blood cells and fulfil the requirement specifications including a gap analysis for CE-marking.⁷³

The majority of Swedish healthcare providers and other organisations, including Health Care Without Harm Europe, supported this Initiative, and Karolinska University Hospital is now working towards a PVC-free blood processing and storage system. Their objective is to identify a partner with the ability to launch PVC-free blood bags on the European market. Demonstrating widespread demand is critical to achieving that goal and other European healthcare providers are invited to show support for this initiative by signing a Letter of Intent, available here:

(<https://www.karolinska.se/en/karolinska-university-hospital/about-karolinska/environment-and-sustainability/pvc-free-blood-bag/>).

Progress made by the industry

Eastman Chemical Company has teamed up with BloodCenter of Wisconsin (BCW) on a clinical trial evaluating a new plasticiser for blood bags. The aim of the trial is to evaluate the stability of red blood cells in di-2-ethylhexyl terephthalate (DEHT) plasticised containers compared with standard di-2-ethylhexyl phthalate (DEHP) plasticised containers. The trial expanded upon the use of DEHT as an alternative to DEHP for bags to store red blood cells in AS-1 and PAGGSM preservative solutions. The trial concluded that DEHT, a non-phthalate general-purpose plasticizer, is a viable alternative to DEHP. Although structurally and functionally similar to DEHP, DEHT (or Eastman 168 SG) is metabolically distinct with a comprehensive and benign toxicology profile.⁷⁴

*"PVC blood bags without phthalates of concern are just around the corner"*⁷⁵

Governmental Initiatives

Three European countries – Denmark, France and Germany – have taken legislative steps to reduce the use of phthalates and/or BPA. All three countries have addressed, to varying degrees, the issue of DEHP-containing medical devices and provide political support to efforts to improve healthcare in this regard. The Nordic Council of Ministers, the official inter-governmental body for cooperation in the Nordic Region also promotes the Swan Ecolabel, which among other product categories also includes certain healthcare products.

As all cases were described in the previous edition of Non-toxic Healthcare report⁷⁶, and only new information has been included in 2019 edition.

Since 1 July 2015 tubing/pipes containing DEHP have been banned for use in paediatric, neonatal,

and maternity departments in hospitals in France. This law also paves the way for a future ban on DEHP and other phthalates in all medical devices if alternative materials are available and the equipment's safety can be guaranteed.

The French National Agency for the Safety of Medicines and Health Products (ANSM) tested medical devices on the French market, targeting 3 therapeutic areas in which PVC devices were presented as DEHP-free: haemodialysis, enteral feeding and infusion.⁷⁷ During market surveillance ANSM observed that a large number (around 70%) of these devices in which DEHP was not added as plasticiser, actually contained residual quantities of DEHP, with however, concentrations lower than 1,000 ppm (0.1%) being observed for most of them.

Non-Governmental Initiatives

The Safer Medical Devices Database by HCWH Europe

One of the issues that hospitals face when starting a phase-out programme for phthalates or BPA is knowing what alternatives are available and the impact and effectiveness of the alternative. Engagement and communication with manufacturers is therefore essential. To enable healthcare procurers to identify medical devices that do not contain PVC and/or DEHP or BPA, and that are already available on the European market, HCWH Europe launched in 2014 an online listing of DEHP-free, PVC-free or BPA-free medical products available in the European market – the Safer Medical Devices Database (safermedicaldevices.org). Manufacturers, procurers and anyone else working in the healthcare sector that would like to provide information about PVC-, DEHP- or BPA-free medical devices, are invited to do so.

The Swedish Substitution List by the Substitution group on chemicals

The Swedish regions and counties and the Swedish Environmental Management Council, through the

CHAPTER 2

national Substitution Group on chemicals, maintain and regularly update a Substitution List for hazardous substances in the healthcare sector, available online.⁷⁸ The Substitution List compiles information on products available in the Swedish market to help healthcare procurers make healthier and more informed choices. Products are organised by product category (use), and possible alternatives of the hazardous substances are listed for each product, including at least one supplier.

The Substitution Portal by Kooperationsstelle Hamburg IFE GmbH and partners

The Substitution Support Portal – SUBSPORT (<http://www.subsport.eu>) – is a multi-lingual collaborative project coordinated by Kooperationsstelle Hamburg IFE GmbH (a consultancy based in Germany), the International Chemical Secretariat – ChemSec (a non-profit organisation based in Sweden), Grontmij (a consultancy based in Denmark) and the Instituto Sindical de Trabajo, Ambiente y Salud – ISTAS (a technical body of one of the Spanish workers unions). The project aims to provide useful information on substitution and provide resources to those interested in substituting hazardous chemicals in products. The Case Story database in the portal includes the assessment of alternative substances for ten substances or groups of substances of high concern – including BPA – plus several case studies from hospitals.

The GreenScreen® Chemicals Alternative Assessment and the Plastics Scorecard by the Clean Production Action

The GreenScreen® for Safer Chemicals⁷⁹, developed by the non-profit organisation Clean Production Action⁸⁰, employs an open, transparent methodology to perform chemical hazard assessment. A wide range of professionals, governmental and non-governmental bodies and manufacturers use it to assess the hazard of chemicals and their potential effect on human health and the environment. The goal is to push for the substitution of hazardous chemicals by safer alternatives.

The ChemSec Marketplace

The Marketplace (<https://marketplace.chemsec.org/>) is a business to business website where buyers and sellers of alternatives to hazardous chemicals can interact. Not only does it provide a unique market opportunity for producers of safer alternatives, but also a one-stop shop for downstream user companies looking to substitute hazardous chemicals in their products.

Chemicals substitution by INERIS

This website (<https://substitution.ineris.fr/en>), set up by the French National Institute for Industrial Environment and Risks (INERIS) provides support to economic operators engaged in a substitution approach in order to promote the dissemination and sharing of information. The website currently offers information provided by companies on the alternatives available for three families of substances: bisphenols, phthalates and alkylphenol ethoxylates. They are illustrated by concrete applications and include medical devices.



Alternatives to phthalates

Alternative substances for replacing phthalates exist for a number of products, including the majority of applications in medical devices. Several companies already manufacture DEHP-free medical devices, either by using PVC plasticisers other than DEHP or by avoiding the use of PVC material altogether.¹⁵

A survey of the Denmark medical industry showed that in 2014, 95% of the manufacturers still used DEHP.⁸¹ However, 60% of the companies had also products that do not contain phthalates, and 80% of those using phthalates believed that substitution should not be problematic over a period of 3-5 years.⁸¹

No clinical studies have systematically compared the health outcomes of different substances used in medical devices, particularly comparing DEHP and other phthalates with alternatives. Nonetheless, a number of studies from manufacturers, regulatory agencies, researchers and NGOs have looked into alternatives for phthalates or PVC in medical devices.^{19 82 83}

In 2014, the Danish Environmental Protection Agency published a report looking at alternative plasticisers in medical devices to DEHP, BBP, DBP and DIBP. The overall purpose of the report was to come up with a list of alternatives to help guide manufacturers of medical devices to substitute these plasticisers.¹⁴ The report screened available information existing in the REACH registration dossiers for a list of substances and found that the values of the “no effect level” (DNEL) for the general population were all higher in comparison with DEHP, meaning these substances would in principle be safer than DEHP.¹⁴ In the *Plastics Scorecard: Evaluating the Chemical Footprint of Plastics* report, the plastic footprint of polyolefin and PVC in IV bags was compared.⁸³ The results of the comparison showed that the substitution of PVC bags by polyolefin-based polymers greatly reduced the chemical footprint of the products.

The plasticisers industry has been investing and developing alternatives to DEHP in medical devices. These alternatives have been included in the

European Pharmacopoeia since 2018. Today, other plasticisers such as Di-isononyl cyclohexanoate (DINCH), Tri-2-ethylhexyl trimellitate (TEHTM), and Dioctyl Terephthalate (DOTP) are being proposed in medical applications, such as medical tubing and blood bags.

Tables summarising the applications, advantages, disadvantages, toxicity and main knowledge gaps relating to known alternative plasticisers to phthalates or known alternative polymers to PVC were included in the previous edition of Non-toxic Healthcare report.⁷⁶ These have been moved to the Safer Medical Devices Database (safermedicaldevices.org) with the intention of keeping them updated as and when appropriate evidence becomes available.

A concern that has been raised by a study from Genay et al. (2011).⁸⁴ and by the French National Agency for the Safety of Medicines and Health Products⁷⁷ is that not all DEHP-free devices are in practice DEHP-free, as DEHP was present in small quantities (below 0.1% by weight). These results point to the necessity for manufacturers to verify the purity of raw materials for all plastics used in the composition of the various parts of a medical device and not just PVC.

CHAPTER 3

Alternatives to BPA

The hazardous properties of BPA and those of some of its alternatives have been reviewed in several studies.^{21 23} The substitution of BPA can be done by replacing BPA with chemical alternatives or by substituting the plastic polymer with another plastic polymer or material.

Other bisphenols have been indicated as potential substitutes for BPA. This is the case for bisphenol S, bisphenol F and bisphenol AP. However, existing data shows that due to their similar structure they can have similar or even worse health effects than BPA.^{21 85 86 87} Therefore, when evaluating the safety of compounds for consumer use, it may be prudent to consider entire classes instead of individual compounds.⁸⁸

The SCENIHR report on BPA in medical devices made only a brief overall note of existing studies on both bisphenol S and bisphenol F toxicity.²³ One common conclusion from all the reviews is that because BPA is used ubiquitously, there is no single replacement for all industrial solutions. Known alternatives to BPA or to the plastic polymer con-

taining BPA that are used in medical devices include many of the alternatives for phthalates such as polyethylene, polypropylene, polyurethane, silicone and acetylo-nitrile-butadiene-styrene. Other common replacements include ceramic, stainless steel, glass and acrylic.

The information available for the alternatives to BPA in medical devices is considerably less than that existing for phthalate alternatives. More specific BPA alternatives have only appeared more recently and information about them is much more sparse and the data gaps much larger. Manufacturers already replacing BPA in their medical devices include Didactic⁸⁹, Technoflex⁹⁰, Mamivac, Nipro Europe. Tables summarising the applications, advantages, disadvantages, toxicity and main knowledge gaps of possible alternatives to BPA in medical devices were printed in the previous edition of Non-toxic Healthcare report⁷⁶. These have been moved to the Safer Medical Devices Database (safermedicaldevices.org) with the intention to keep them updated as and when appropriate evidence becomes available.



CHAPTER 4

Best practices in European healthcare

Healthcare facilities and professionals play an important role in the substitution of hazardous chemicals. They have both an ethical responsibility to use products that are less hazardous for patients and the purchasing power to push manufacturers towards safer and lower impact products. In Europe, public procurement of goods accounts for 16% of the total European market.⁹¹

Hospitals throughout Europe are working to minimise the exposure of their patients to hazardous chemicals. The first step of many hospitals has been to identify which products contain substances of concern and develop an internal substitution strategy or policy. Many have launched substitution projects, particularly targeting DEHP and PVC in medical devices. These strategies and policies help hospitals in their purchasing decisions.

HCWH Europe's factsheet *PVC/DEHP phase-out is possible anywhere in Europe: Model hospitals show how to succeed*, shows that already in 2007, hospitals across Europe (Austria, Denmark, Sweden, Czech Republic, Slovakia, France, Italy, the Netherlands) were phasing out PVC medical devices in order to protect patients from DEHP and other alternative plasticisers.⁹²

In 2008, HCWH published a report with information, examples, and guidance for healthcare facilities to improve their purchasing decisions regarding chemicals – *Guide to Choosing Safer Products and Chemicals: Implementing Chemicals Policy in Health Care*.⁹³ In 2018, HCWH Europe published *Guidelines for the procurement of safer medical devices*.⁹⁴

In the 2014 edition of this report, HCWH Europe collated information on best practices in European hospitals and approaches towards non-toxic healthcare (HCWH 2014). Initiatives taken by the Hospital of Southern Jutland (Denmark), Stockholm County Council (Sweden), the Westfriesgasthuis Hospital (The Netherlands), the Vienna Hospitals Association (Austria) were described.

Only new information has been included in 2019 update.



Non-toxic Healthcare:

Alternatives to Phthalates and Bisphenol A in Medical Devices



PVC-free initiative of Helsinki University Hospital (Finland)

One of the environmental objectives at Helsinki University Hospital (HUS) is responsible procurement, taking into consideration important ecological and social aspects and giving priority to products that are considered more sustainable. Medical gloves are a product's group completely PVC-free now. HUS aims to radically reduce the use of PVC in all product groups by the end of 2020, where replacement is possible, particularly medical tubing, which conventionally contains PVC.⁹⁵ PVC-free tubing has already been requested in procurement specifications.⁹⁶

How hospital districts in Finland are taking steps to reduce the use of PVC

KEINO Competence Centre for sustainable and innovative public procurement (<https://www.hankintakeino.fi/en>) and HUS invited hospital districts to a meeting in March 2019, to create a vision of a responsible procurement.^{97 98} During this meeting, hospitals presented a range of different sustainable procurement objectives. Among these, the reduction of PVC use received a lot of support.⁹⁸

CHAPTER 5

The health impacts of plastics in healthcare

The increased global focus on plastics can be explained by the growing awareness of the environmental consequences of plastics production and consumption, particularly in relation to plastic waste generation. The human dependence on plastics in everyday life is reflected in its ubiquitous presence as litter in the environment.

Plastic pollution has drawn significant attention from the media, the public, and scientists spanning diverse fields, including polymer science, ecology, and toxicology. To date the impacts of plastic have been primarily studied within marine environments⁹⁹, and whilst plastic contamination was first reported on nearly 50 years ago, the United Nations Environment Programme only identified plastic debris in the ocean as an emerging issue in 2011.¹⁰⁰

More recently, microplastics in freshwater¹⁰¹ and terrestrial¹⁰² environments has become an emerging concern. There is also a new research exploring the impact of plastics on antimicrobial resistance.^{103 104}

Single-use plastics and plastic packaging present a substantial part of this problem. Short-term use with long-term environmental consequences, with most plastic waste currently disposed of in landfills or incinerated. Plastics and the chemicals used in their manufacture now contaminate our soils, rivers, oceans, air, and increasingly our food supply. This significant societal challenge has stimulated research on plastic uses and its impacts on human health.¹⁰⁵

This chapter discusses the state of understanding of medical plastics used in healthcare and their impact on health. We aim to present a picture about how plastics are being used in healthcare and the effects of plastics on human health, from production through to end-of-life. We also ask whether it is possible to reduce plastic use and plastic waste in the healthcare sector and what healthcare institutions are doing to address this emerging global challenge.

General background

What are plastics?

In the EU, plastic is defined as *“a material consisting of a polymer as defined in point 5 of Article 3 of Regulation (EC) No 1907/2006, to which additives or other substances may have been added, and which can function as a main structural component of final products, with the exception of natural polymers that have not been chemically modified”*.¹⁰⁶

It is important to understand that plastics are not a single, specific material, although they are often referred to as such. Plastics are a large family of chemicals, composed of a great variety of materials designed to meet thousands of very different needs and applications. Over 5,300 polymer formulations are commercially available¹⁰⁷ and more than 4,000 known chemicals are associated with plastic packaging alone.¹⁰⁸ In principle, plastics can be developed with virtually any combination of properties to accommodate almost any application. Plastics are therefore increasingly being used in diverse applications such as packaging, building and construction, mobility and transport, electronics, agriculture, healthcare, sport and leisure, and energy.¹⁰⁹

Plastics are chains of molecules (monomers) linked together in chains called polymers. The vast majority of plastics are composed of polymers of carbon and hydrogen, either alone or with oxygen, nitrogen, chlorine, fluorine or sulphur.¹¹⁰ Those polymers follow a different production process (e.g. condensation and cross-linking), have different chemical structure (e.g. acrylics, polyesters, polyolefins, silicones, polyurethanes and halogenated plastics), and all have different properties, which make it impractical for different polymers to be recycled together. Generally speaking, plastics can be divided into four key groups: oxo-degradable plastics, biodegradable plastics, bioplastics, and microplastics (see Box 9). In addition, two main categories of polymers can be clearly distinguished: thermoplastics and thermosets (see Table 2).

Plastics can contain various additives to improve their behaviour during manufacturing (lubricants, catalysts, stabilisers, solvents, and aids for polymere-

risation or recycling). Additives can also be used for specific properties defining their application (e.g. hardness, softness, resistance to ultraviolet light, flame formation resistance). A joint project by ECHA and the plastics industry listed over 400 functional additives or pigments currently used in plastics, including information on the polymers they are most commonly found in and the typical concentration ranges.¹¹¹

BOX 9

Main types of plastics

Oxo-degradable plastics include additives which, through oxidation, lead to fragmentation into micro-fragments or to chemical decomposition.¹⁰⁶

Biodegradable plastics are capable of decomposing physically and biologically, ultimately into carbon dioxide (CO₂), biomass, and water. In accordance with European standards for packaging, these plastics are recoverable through composting and anaerobic digestion.¹⁰⁶

Bioplastics: (also known as biopolymers) are made from renewable plant feedstocks (e.g. corn, sugar beet, or sugar cane). Bioplastics can consist of mixtures including other plastic(s) and are not necessarily biodegradable; however, they do generally present a lower risk to the environment in comparison to conventional plastic.¹⁰⁵ Polylactic acid (PLA), plant-derived polyethylene terephthalate (PET), and polyhydroxyalkanoate (PHA) are all bioplastics.

Microplastics are not a specific kind of plastic but rather any type of plastic solid particle smaller than 5mm¹¹². Particles smaller than 0.1mm are defined as nanoplastics¹¹³. Primary microplastics are materials deliberately designed and manufactured to be of small size (e.g. cosmetic microbeads), while secondary microplastics are unintentionally formed through the wear and tear of larger pieces of plastic, including synthetic textiles, that have undergone fragmentation and weathering, during their use or disposition in the environment.¹¹⁴

Table 2.

Two main categories of polymers.^{110 115}

Thermoplastics can be melted and hardened reversibly	Thermosets undergo a chemical change during heating – they cannot be re-melted and reformed)
Common examples Polyethylene terephthalate (PET) Polypropylene (PP) Polystyrene (PS) Polyethylene (PE) Polyvinyl chloride (PVC) Fluoropolymers	Common examples Polyurethane (PUR) Epoxy resins Unsaturated polyester Acrylic resins Silicone Vinyl ester

Plastic production and pollution

Plastics are used almost everywhere. It has been estimated that a total of 8,300 million metric tonnes of virgin plastic has been produced globally so far, of which only 30% of it is still in use.¹¹⁶ In 2017, global plastic production reached 348 million tonnes, of which 64.4 million tonnes was in Europe (EU28, Norway, and Switzerland). Packaging and building/construction accounted for 39.7% and 19.8% of the total plastics respectively, whilst 16.7% of the total plastics produced in 2017 were used to produce medical equipment together with other non-medical uses, such as furniture and technical parts used for mechanical engineering.¹¹⁵

High production volumes of plastic and high demand have led to the global problem of plastic pollution in the environment. In 2015, there was 6,300 million metric tonnes of plastic waste produced, of which only 9% was recycled.¹¹⁶ With regards to plastic packaging, 95% of material value is estimated to be lost (not recycled).¹¹⁷ Globally, plastic production and plastic incineration is estimated to produce 400

million tonnes of CO₂ a year.¹¹⁸ In Europe, 41.6% of collected plastic (27.1 million tonnes) is used for energy recovery whilst 27.3% ends up in landfill.¹¹⁵ The remaining 31.1% of plastic waste is recycled with 63% of recycling occurring in the EU.¹¹⁵

It is important to recognise that the global trade in waste plastics has seen the movement of significant volumes of plastic waste from developed countries to developing countries, where environmentally unsound recycling and disposal practices can exacerbate exposure to toxic compounds. China's decision to ban the import of contaminated plastic waste is predicted to result in the displacement of 111 million metric tonnes of plastic waste by 2030.¹¹⁹ In 2019, human exposure to persistent organic pollutants due to poor management of imported plastics was noted in Ghana with sampling at a 'recycling site' revealing some of the highest levels of dioxins ever recorded.¹²⁰

Plastics can enter marine, freshwater, and terrestrial environments, reaching air, soils, rivers and lakes.¹⁰⁵ It has been estimated that there are 5.25 trillion particles of plastics in the oceans globally, weighing 268,940 tonnes.¹²¹ Of the plastic debris detected in the western North Pacific Ocean 89% came from single-use plastic items.¹²² In the EU, 80-85% of marine litter plastic, half of which is single-use plastic. Within the EU, 75,000 – 300,000 tonnes of microplastics end up in the environment annually¹¹⁸, and a 2019 study suggested that atmospheric transportation and deposition of microplastics is contributing to the contamination.¹²³

Single-use plastics are a growing problem, yet whilst biodegradable and compostable plastics were designed as a potential solution, these plastics also pose problems to ecosystems.¹²⁴

Despite the fact that huge amounts of polymers are produced, imported, and used in Europe and there is wide exposure, companies currently have no obligation to register these chemicals and therefore provide information on their health and environmental hazards. At the time of the REACH regulation's adoption in 2007, polymers were considered to be less hazardous than monomers and were therefore exempted.

Global initiatives related to mitigation of plastics impact on the environment

As the global use of plastics rises, so too do initiatives to mitigate the environmental and health impacts of plastics. Global conventions to tackle plastic pollution have been suggested by the Center for International Environmental Law (CIEL) and their

partners¹²⁵, and Adelphi.¹²⁶

The United Nations Environment Programme's Global Plastic Platform, launched in September 2018, seeks to reduce plastic pollution through new commitments. The network also promotes the transition to a circular economy in which design, production, consumption and disposal of plastics are taken into account.¹²⁷

In October 2018, the New Plastics Economy Global Commitment was launched, led by the Ellen MacArthur Foundation¹²⁸. As of 2019 this has over 400 signatories including businesses and governments.¹²⁹

The World Economic Forum (WEF) also launched a platform in 2018 for public-private actions towards a circular economy¹³⁰, which includes plastics. The partnership's ambition is to prevent plastic pollution reaching the sea by 2025.¹³⁰

As China reduced imports of nearly a million tons of mixed plastic waste in 2018, waste-exporting nations turned to South East Asian countries, which soon became overwhelmed. In May 2019, world governments supported developing countries to refuse toxic mixed plastic waste shipments through the UN Basel Convention.¹³¹ The majority of the world's governments created new regulations requiring waste exporters to declare the content of mixed waste shipments and enable receiving countries to refuse plastic waste imports.

The European legal framework

The European Strategy for Plastics in a Circular Economy

In December 2015, the European Commission adopted an EU action plan for the Circular Economy and identified plastics as a priority area. The action plan stated that plastic recycling is necessary in a circular economy.¹³²

In January 2018, the European Commission released the European Strategy for Plastics in a Circular Economy¹¹⁸, which lays out the vision for Europe's new plastics economy. Under the strategy key players should improve the design of plastic products so that at least 50% of plastic waste is recycled by 2030.

Modernising and developing markets for recycled products should also be addressed.¹²⁴

EU Directive (2018/852) on packaging and packaging waste

In July 2018, the revised legislative framework on waste entered into force setting recycling rate targets for plastic in packaging waste: 65% by 2025

and 70% by 2030.¹³³

EU Directive (2019/904) on the reduction of the impact of certain plastic products on the environment

In June 2019, the European Commission adopted a Directive on the reduction of the impact of certain plastic products on the environment.¹³⁴ The Directive lays down market restrictions of single-use plastic products, as well as oxo-degradable plastic products, including cotton bud sticks, straws, and food and beverage containers made of expanded polystyrene.

Restriction under consideration: Microplastics

ECHA has prepared an Annex XV restriction report¹³⁵ on the use of intentionally added microplastic particles in consumer or professional use products.¹³⁶ The public consultation on microplastics ran until 20 September 2019.¹³⁷

Industry initiatives

Globally, industry efforts are only focussing on end-of-life plastics, increasing the use of recycled content with the intention of keeping materials in the value chain longer. In practice, this means that materials are being recycled that were never optimised for human and environmental health.¹³⁸ Polymeric materials such as foam, plastic food packaging and

textiles for example can contain flame-retardants, plasticisers, coatings, modifiers, catalysts, and other performance enhancing additives and residuals. When recycled into new products, the output tends to be non-homogeneous and highly contaminated, and therefore not suitable for use in toys, food contact materials, and other applications.¹³⁸

Voluntary actions from the European plastics industry also focus only on recycling and reusing of plastics.¹³⁹ Whilst important components of working towards a circular economy, other aspects, such as reduction of plastics use (and single-use plastic in particular), and 'detoxification' of plastics need to be addressed as well.

The Alliance to End Plastic Waste (AEPW), comprising over 35 global companies from different parts of the plastics value chain, has a mission is to "eliminate plastic waste in the environment".¹⁴⁰ Crucially, however, the reduction of single-use plastic is not to be found in the AEPW plans.

The Circular Plastics Alliance was launched in December 2018, bringing together public and private stakeholders from the plastics value chain. The alliance's target is to annually re-use 10 million tonnes of recycled plastics in products and packaging by 2025.¹⁴¹ The declaration of the alliance was adopted on 20 September 2019, with more than 100 signatories.¹⁴¹



Impact of plastics on human health

The presence of toxic or potentially toxic substances in plastic products has a negative impact on the environment and human health, and affects all phases of the life cycle of plastic products. Persistent organic pollutants (POPs) are used as additives in a large volume of plastic polymers.¹³⁸ Short Chain Chlorinated Paraffins (SCCPs) used in PVC and ethylene-vinyl acetate (EVA), for example, have already been listed under the Stockholm Convention. Several other chemicals (e.g., cadmium, lead, polycyclic aromatic hydrocarbons) are also used as additives or found as contaminants in plastics.

Evidence concerning the health risks posed by plastics is mounting. It is important to recognise that plastics can cause risks to human health during their whole lifecycle, through the different exposure routes: inhalation, ingestion, and contact with skin. Challenges of the life cycle management of plastics and their impact on health have been recently addressed in detail by Center for International Environmental Law.¹⁰⁵

Human exposure during the extraction and transportation of fossil feedstock required for producing plastic can be linked to cancer, neurotoxicity, and reproductive and developmental toxicity. During the refinement and production of plastic resins and additives, impairment of the nervous system, leukaemia, and low birth weight have been reported. Incineration, co-incineration, gasification, and pyrolysis cause toxic chemicals to be released into the air, water, and soils. These releases can cause cancers, as well as neurological and immune damage. During use, consumers can ingest and inhale microplastics together with other toxic substances (such as additives), which can potentially cause cancers, diabetes, and developmental toxicity.¹⁰⁵

The review of known plastic-associated chemicals and their hazards concluded that of the 906 chemicals likely associated with plastic packaging, 63 rank highest for human health hazards and 68 for environmental hazards according to the harmonised hazard classifications assigned by the European Chemicals Agency within the Classification, Labelling and Packaging (CLP).¹⁴² Further, 7 of the 906 substances are classified in the European Union as persistent, bioaccumulative, and toxic (PBT), or very persistent, very bioaccumulative (vPvB), and 15 as endocrine disrupting chemicals (EDC). Of the 906 chemicals, 34 are also recognised as EDC or potential EDC in the recent EDC report by the United Nations Environment Programme. The identified hazardous chemicals are used in plastics as monomers,

intermediates, solvents, surfactants, plasticizers, stabilizers, biocides, flame-retardants, accelerators, and colorants, among other functions.¹⁴²

Most plastic-associated chemicals are not covalently bound to the polymer, so they can be released at all stages of the plastics' lifecycle via migration to liquids or solids or via volatilisation. This can result in a transfer of chemicals from products/packaging to consumer e.g. via food. A recent comprehensive scientific study on the toxicity of chemicals present in plastic products confirmed toxicity of complex chemical content.¹⁴³ Researchers analysed 34 widely used consumer products made from plastics, including products coming in contact with food such as refillable water bottles and food wraps. This analysis covers eight major polymer types: polyvinyl chloride (PVC), polyurethane (PUR), polyethylene terephthalate (PET), polystyrene (PS), Polypropylene (PP), high-density polyethylene (HDPE), low-density polyethylene (LDPE) and polylactic acid (PLA). Researchers found toxic compounds in a majority of the plastic extracts and proposed a prioritisation of chemicals entering into their composition according to their toxicity.

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906 chemicals likely associated with plastic packaging

Findings showed that¹⁴³:

- 74% of the plastic extracts contained chemicals triggering at least one endpoint relevant for assessing health impacts – including baseline toxicity (62%), oxidative stress (41%), cytotoxicity (32%), estrogenicity (12%), or antiandrogenicity (27%).
- Plastics contain large mixtures of chemicals – many of those are unknown and difficult to identify.
- Out of 260 chemicals tentatively identified (including monomers, additives, and non-intentionally added substances,) 27 of were prioritised based on high *in vitro* toxicity, including well-known additives such as benzophenones, butylated hydroxytoluene or triethyl phosphate, as well as less known isomers such as decanoic acid.
- Extracts of polyvinyl chloride (PVC) and polyurethane (PUR) were observed to induce the highest toxicity at most endpoints from the eight polymer types investigated.
- All “bioplastics” made of polylactic acid (PLA) were also observed to be of toxicity levels similar to that of PVC and PUR.
- The toxicities of low-density polyethylene (LDPE), polystyrene (PS), and polypropylene (PP) varied depending on the endpoint measured.

Compared with chemicals used in plastics, even less is known about the toxic effects of plastic particles in the human body.¹⁴⁴ A scientific literature review on health impacts and human exposure to plastic through diet and inhalation revealed that microplastics might accumulate and exert localised particle toxicity by inducing or enhancing an immune response.¹⁴⁵ If inhaled or ingested, chemical toxicity could occur due to the localised leaching of component monomers, endogenous additives, and adsorbed environmental pollutants.

Chronic exposure is anticipated to be of greater concern due to the accumulative effect that could occur. This is expected to be dose-dependent but a robust evidence-base of exposure levels is currently lacking.¹⁴⁵ A literature review by Smith et al. (2018) focused on exposure to microplastics through seafood and the potential implications for human health. The authors concluded that the toxicity associated with consuming microplastics is likely de-

pendent on size, associated chemicals, and dose. As with the previous study, recommendations for future research are provided.¹⁴⁶ In general, microplastics to which human are exposed via different routes can potentially cause inflammation, genotoxicity, oxidative stress and cell necrosis, and over time, these effects could also lead to tissue damage, fibrosis, and cancer.¹⁰⁵

A 2019 report by Science Advice for Policy by European Academies: *Scientific Perspective on Microplastics in Nature and Society*¹¹³ and the report from the World Health Organization *Microplastics in drinking water*¹¹⁴ concluded that, based on the information currently available, there are no emerging health concerns relating to microplastics. However, both reports outline that further research is needed.

Particularly worrying is fact that that plastic particles and plastic associated chemicals are found almost in every human studied. Recent reports suggest that microplastics are entering the human body through drinking water, food, and air. A 2018 study from the Medical University of Vienna and the Environment Agency of Austria analysed stool samples from participants across eight countries and found microplastics and up to nine different types of plastic resins in every sample tested.¹⁴⁷

Another study showed alarming levels of plastic in children's bodies. According to a study by the German Environment Ministry and the Robert Koch Institute, plastic by-products were found in 97% of blood and urine samples from 2,500 children tested between 2014 and 2017.¹⁴⁸ Younger children were reported to be the most affected by plastic ingestion. The study has not yet been published, and the results were made available by the government upon request by a Green Party inquiry into the effects of chemicals on public health.¹⁴⁸

It should be broadly understood that toxic additives need to be substituted with non-chemical alternatives or non-toxic substances to reduce human exposure, as well as to make recycling easier.¹³⁸

Currently ZonMw, the Netherlands Organisation for Health Research and Development, coordinates 15 short-term projects investigating the effects of micro- and nanoplastics on human health, and focusing in particular on uptake via ingestion and inhalation and effects of, potential translocation to brain and placenta, and potential effects on immune system.¹⁴⁹

Plastics in healthcare - Medical plastics

The market in plastic medical devices and pharmaceutical packaging continues to grow. A key benefit in medicine and public health is the versatility of these materials which, when combined with an extremely low cost, has enabled the mass production of disposable single-use health care products that are both functional and hygienic. The industry points out that modern healthcare would be impossible without many plastic-based medical products.^{150 151}

Fibres and resins used in medical applications include polyvinyl chloride (PVC), polypropylene (PP), polyethylene (PE), polystyrene (PS) as well as nylon, polyethylene terephthalate (PET), polyamide (PA), polycarbonate (PC), acrylonitrile butadiene (ABS), polyetheretherketone (PEEK) and polyurethane (PU). The most widely used plastic material in medical applications is PVC followed by PE, PP, PS and PET. PVC is most widely used in pre-sterilised single-use medical applications.¹⁵¹

Traditionally, metals, glass and ceramics were used for medical implants, devices and supports. However, polymers are often better suited to certain applications as they offer lighter weight and better biocompatibility. Plastics are for example key components of modern prosthetic devices offering greater flexibility, comfort and trouble-free mobility. Plastic packaging, with its excellent barrier properties, lightweight, low cost, durability, and transparency, is particularly suitable for medical applications.

Today, medical plastics are everywhere, from examination gloves to sterile syringes and IV tubes or heart valves. There is also an array of plastic disposable medical products in use, including bed pans, insulin pens, IV tubes, tube fittings, plastic cups and pitchers, eye patches, surgical and examination gloves, inflatable splints, inhalation masks, tubing for dialysis, disposable gowns, wipes and droppers, urine continence and ostomy products.

Importantly, innovations in plastics are making more and more new procedures possible. Plastics are now being used as orthopaedic devices, where they align, support or correct deformities. Thin tubes called catheters are used to unblock blood vessels. Synthetic material also plays a vital role for diseased arteries that cannot be helped via vessel support, whereby the affected section of the aorta is removed and the gap bridged by a flexible plastic prosthesis. Artificial corneas made from special silicone, flexible and made of biomechanics similar to a natural cornea can restore clear vision again.¹⁵¹

Modern healthcare uses many plastic-based medical products to provide high quality treatments and solutions. However, this exerts pressure on environment throughout the supply chain, which includes plastic packaging, single-use products made of different (often mixed) plastics and materials frequently containing hazardous chemicals. Plastics used in healthcare therefore pose a direct risk to patients and staff, and produces a significant volume of waste, which contributes to wider environmental harm.

There has been a gradual transformation from re-useable non-plastic to disposable plastic products in healthcare over the last 30 years, with most common arguments for this transition being an increased focus on infection prevention and control and cost effectiveness.¹⁵² It remains unclear whether what is required is more effective sterilisation procedures, rather than disposable equipment. Use of re-useable devices can often reduce costs in the long run, as well as reducing packaging and clinical waste.¹⁵² Further evidence in the form of whole-life costing calculations undertaken during procurement exercises is required.

In the study of Minoglou et al. (2017)¹⁵³ healthcare waste generation rates (kg/bed/day) of some European countries are presented: Latvia: 1.18, Netherlands: 1.7, Bulgaria: 2, France and UK: 3.3, Germany and Greece: 3.6, Norway: 3.9, Italy: 4, and Spain: 4.4. Overall, plastic waste generation in the EU in 2016 reached 17,590,000 tonnes, and healthcare and biological waste generation was 2,020,000 tonnes.^{iv}

Plastic use and waste disposal varies across healthcare providers in Europe and there is a lack of precise data showing the extent of medical and non-medical plastics use and volumes of waste. Where evidence has been gathered, the need for transformative action is clear. The UK's National Health Service, for example, recovers only about 5% of plastic waste and pays to dispose of 133,000 tonnes of plastic each year, significantly contributing to its £700m annual waste disposal bill.¹⁵⁴ Whilst general public awareness of plastics' harmful impacts is increasing in Europe, the healthcare sector is largely unaware of the impacts from its own plastic consumption and how to go about reducing this. Recent studies have challenged received wisdom concerning the use of single-use plastics in infection prevention and control, and demonstrate the potential to reduce, reuse, and recycle at a much higher rate.¹⁵²

The Healthcare Plastics Recycling Council has prepared a guidance document to inform and educate

^{iv} Eurostat. (2019) <https://ec.europa.eu/eurostat/home?>

plastics recyclers and processors about the common streams of plastic waste (see Box 10) generated in clinical settings.¹⁵⁵

BOX 10

The most common recyclable healthcare plastic waste streams¹⁵⁵:

- Polypropylene (PP) (product: sterilisation wraps which are used for surgical instruments to prevent contamination)
- Homo-polymer PP (product: containers such as pitchers, basins, and cups)
- Polypropylene (PP) or high-density polyethylene (HDPE) (product: irrigation bottles)
- Polyethylene terephthalate glycol (PETG) or high impact polystyrene (HIPS) (product: trays)
- Low-density polyethylene (LDPE) or high-density polyethylene (HDPE) (product: flexibles such as Non-Woven and Film Plastics)

Impacts of medical plastics

In the previous chapters of this report, the focus has been on plastic medical devices containing phthalates and BPA and the possible risks they pose to patients during medical treatments. This chapter outlines how toxic chemicals are generated throughout the lifecycle of plastic medical products, for example, dioxins generated during PVC production and disposal, which can also pose a risk to human health.

Although beyond the scope of this report, it is important to emphasise that the use of plastics in healthcare is not limited to medical devices and other medical products. Electronics, upholstered furniture, cups and cutlery used in the staff canteen, and PVC coverings in hospitals are entirely or partially made from plastic materials.^{156 157 158}

Medical plastics comprise a diverse and heterogeneous group of polymers and each product has an individual and complex chemical composition (i.e. one or more polymers, multiple additives such as

plasticisers, flame retardants, stabilisers, antioxidants – for examples see Box 11). Unfortunately, due to a lack of full transparency in the supply chain and incompleteness of publicly available information on both the use and amount of numerous substances in medical plastics, our knowledge is currently limited.

While hazard, exposure and epidemiological data on a small number of prominent plastic-associated chemicals such as DEHP and BPA is abundant and growing, it remains challenging to form a true assessment of the chemical safety of medical plastics, despite this being an important source of patient exposure. At the same time, the breadth of research identifying negative human health impacts of many of the plastic additives present in widely used consumer products is conclusive that there

BOX 11

Some examples of devices / additives used in healthcare

- PVC medical devices/ Plasticisers: DEHP⁵¹
- PVC medical devices/ Alternative plasticisers (APs): TOTM, DEHT, DINCH, DEHA, ATBC, DiDP, DiNP, and DPHP⁵¹
- Continuous venovenous hemofiltration (CVVH) and extracorporeal membrane oxygenation (ECMO) medical devices/ Phosphate flame retardants (PFRs)¹⁵⁹
- Linear polyethylene surgical sutures/ Colour additive: Chromium-cobalt-aluminum oxide¹⁶⁰
- Polypropylene sutures, Polybutester sutures, Polybutylene terephthalate sutures/ Colour additive: [Phthalocyaninato(2-)] copper¹⁶⁰
- Medical devices of different types: Fillers, Reinforcement, Composites; Release Agents; Slip Additives/Internal Lubricants; Catalysts; Impact Modifiers and Tougheners; Radiation Stabilizers; Optical Brighteners; Pigments, Extenders, Dyes, Mica; Coupling Agents; Thermal Stabilizers; and Antistats¹⁶¹
- Medical devices and medical textiles where PTFE is used: PFOA as impurity from manufacturing¹⁶²

are significant risks to human health and a precautionary approach is warranted.¹⁰⁵

This section describes emerging groups of chemicals used in plastic production due to their known impacts on human health. It deals with groups of chemicals rather than individual substances, in order to focus on the reduction in the use of entire classes rather than the phasing out of individual problematic chemicals one at a time. Such an approach helps develop coordinated strategies for reducing the production and use of chemicals of concern and prevents regrettable substitutions.

BOX 12

Perfluorinated chemicals

Per- and polyfluoroalkyl substances (PFAS) are a group of man-made chemicals that includes PFOA, PFOS, GenX, and many other chemicals. PFAS have been manufactured and used in a variety of industries around the globe, including in the United States since the 1940s. The widespread use of PFAS and their ability to remain intact in the environment means that over time PFAS levels from past and current uses can result in increasing levels of environmental contamination.

PFOA and PFOS have been the most extensively produced and studied of these chemicals. Both chemicals are persistent, bioaccumulative, and toxic substances (PBT). Due to these properties it may cause severe and irreversible adverse effects on the environment and human health. PFOA and a number of PFOA-related substances are found throughout the environment, including remote areas, since they can be transported over long distances via water and air. Based on their PBT and CMR properties, PFOA and its salt (APFO) have been identified as substances of very high concern (SVHC) under REACH. Certain PFAS chemicals are no longer manufactured in the United States as a result of phase-outs including the PFOA Stewardship Program in which eight major chemical manufacturers agreed to eliminate the use of PFOA and PFOA-related chemicals in their products and as emissions from their facilities. Currently, the use of both PFOS and PFOA is restricted under the Stockholm



Convention, a treaty to control and phase out major persistent organic pollutants (POPs).

Flame-retardants

Polybrominated diphenyl ethers (PBDEs) are organobromine compounds that are used as flame-retardants. They are structurally similar to the PCBs and other polyhalogenated compounds, consisting of two halogenated aromatic rings. PBDEs are classified according to the average number of bromine atoms in the molecule. Since the 1990s, environmental concerns were raised because of the high hydrophobicity of PBDEs and their high resistance to degradation processes. Swedish scientists first reported substances related to pentaBDE were accumulating in human breast milk.¹⁶³ Halogenated phosphate flame retardant, Tris (1,3-dichloro-2-propyl) Phosphate (TDCPP) and its blends are used as flame-retardants in the manufacture of polyurethane foam.

Perfluoroalkyl and polyfluoroalkyl substances (PFAS)

PFASs contain a wide group of substances¹⁶⁴ of which a significant amount have no CAS number (the unique reference number that allows chemical substances to be identified).¹⁶⁵ It has been estimated that there are nearly 5,000 types of PFAS in the global market with plenty different applications.¹⁶⁶ Unfortunately, applications within the healthcare sector are much less well known (see Box 13).¹⁶⁵

BOX 13

Examples of healthcare applications of PFAS^{162 165 167 168}

- Dental restorative material
- Medical devices (e.g. sensors, cardiovascular devices, vascular catheters, protection tubing, implants and orthopaedic devices)
- Invasive medical devices (e.g. guide wires, balloon catheters and introducer sheets)
- Radiopaque catheters (e.g. catheters for angiography and indwelling needle catheters)
- Medical textiles (e.g. surgical gowns and drapes, masks and caps, medical implants, surgical patches)

Exposure to PFASs has been associated with hepatic, cardiovascular, endocrine, immune, reproductive, and developmental effects.¹⁶⁹ One recent study showed that exposure to eight PFAS compounds was associated with altered kidney and thyroid functioning.¹⁷⁰ The most known PFASs are perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), extremely persistent (also called 'forever chemicals') and toxic chemicals that became also global contaminants.¹⁷¹ PFOS, PFOA and related substances are included in the Stockholm Convention.

A considerable number of adverse health effects have been linked with PFOA exposure in humans: increased cholesterol levels, ulcerative colitis, thyroid disease, cancers, pregnancy-induced hypertension, and reduced birth weight.¹⁷² Strong evidence has been found in toxicology and epidemiology studies that humans exposed to PFOA and PFOS are at risk for immunosuppression.¹⁷³ A literature review summarised the epidemiological evidence for the influence that pre- and postnatal exposures to PFASs may have on health outcomes in offspring, with a particular focus on birth outcomes and postnatal growth, immunomodulatory effects and neurodevelopment.¹⁷⁴ Studies on health impacts in children found associations with PFAS exposure and dyslipidemia, vaccine response asthma, renal function, and the onset of menstruation.¹⁷⁵

The European Food Safety Agency (EFSA) recent-

ly set the provisional tolerable weekly intakes for PFOA at 6 nanograms (ng) per kilogram of body weight, lowering it from 1,500 ng daily – a clear acknowledgement that these chemicals are much more damaging to human health than previously thought. A large portion of the EU population already exceeds these new safety levels.¹⁷²

Flame-retardants

There are many different types of flame retardants, which are used to protect products from burning. In the healthcare sector, polybrominated diphenylethers (PBDEs) are used most frequently; their chlorine analogs are polychlorinated diphenyl ethers (PCDEs). Halogenated phosphate flame retardants were reported in some applications as well. The PBDEs family contains 209 substances, which are termed congeners. Each is a mixture of brominated substances.¹⁷⁶ Because of their toxicity and persistence, the industrial production of some PBDEs (decaBDE, hexaBDE, heptaBDE, tetraBDE, pentaBDE,) is restricted under the Stockholm Convention).^{177 178 179}

To date, PBDEs impacts on human health is limited, as most studies have been conducted on animals.¹⁷⁶ The impact of PBDEs on developing nervous and reproductive system, developing and mature endocrine system, and the liver and the male reproductive system, have raised concerns in animal studies.¹⁷⁶ PBDEs have been shown to have hormone-disrupting effects, in particular, on oestrogen and thyroid hormones.¹⁸⁰ The studies have shown that even a single dose administered to rat during development of the brain can cause permanent changes in behaviour of offspring and permanently impaired spermatogenesis.¹⁸¹

The health hazards of PBDEs have attracted increasing scrutiny, and have been shown to reduce fertility in humans at levels found in typical households.¹⁸² The studies in humans found effects of (PBDEs) on thyroid regulation during pregnancy¹⁸³, neurodevelopment effects¹⁸⁴, and behavioural development in children.¹⁸⁵ Moreover, it has been reported that memory domains in early adolescence can be affected following prenatal and postnatal exposure to PBDEs.¹⁸⁶ Some epidemiological results indicate that PBDEs could act as developmental neurotoxicants.¹⁸⁷ In general, more research, in particular epidemiology studies, is needed to obtain greater support for associations between PBDEs and certain health impacts in humans.

Recently, the phosphate flame retardant (PFR) metabolites were found in urine samples from patients

in intensive care unit (ICU): 4-hydroxyphenyl phenyl phosphate (4-HO-DPHP), 4-hydroxyphenyl diphenyl phosphate (4-HO-TPHP), bis(2-butoxyethyl) phosphate (BBOEP), and bis(2-butoxyethyl) 30-hydroxy-2-butoxyethyl phosphate (3-HO-TBOEP).¹⁵⁹ Overall, the levels of the metabolites were higher in urine samples from intensive care unit (ICU) patients in comparison to urine samples from the control group.¹⁵⁹ The results of this study are preliminary (there are no previous studies), but as the highest PFRs levels were found in patients that were in contact with continuous venovenous hemofiltration (CVVH) and extracorporeal membrane oxygenation (ECMO), this study could suggest that PFRs are originating from indwelling medical devices used in the ICU.¹⁵⁹ Further research into the possible toxic effects of these chemicals released from medical devices is urgently needed.

Case studies of plastic waste management in European hospitals

The following examples describe initiatives already being undertaken to address many plastic material streams in European healthcare providers.

Aarhus University Hospital (Denmark)

Aarhus University Hospital (AUH) is investigating new approaches to manage plastic packaging waste through increased recycling and circular economy of plastic packaging.¹⁸⁸ Through collaboration with industry, focus is put on the development and testing of a value chain model for the creation of environmental and commercial values out of hospital plastic packaging waste.^{188 189} Preliminary recommendations are as follows¹⁸⁸: reduce the number of polymers; prioritise use of recyclable polymers, and consider recycling of resources in the design of packaging.

Helsinki University Hospital (HUS, Finland)

In 2018, waste prevention was addressed in a new group of HUS called Ekologinen ATeK. This group is working towards an operating room model, which is as environmentally sustainable as possible, in different areas of activity.⁹⁶

In a press release in June 2019¹⁹⁰, HUS highlighted that most of its plastic waste originates from operating rooms dealing with musculoskeletal surgery. This is because all of the equipment used is packaged separately (including individual screws).

At the outset, the difficulties in sorting plastics were related to insufficient or unclear labelling on packaging.¹⁹⁰ The plastics are currently sorted into three containers depending on the following plastic types: PET-plastic 01, PE-LD-plastic 04, PE-HD-plastic 02 and PP-plastic 05.

University Hospital of Leuven (UZ Leuven, Belgium)

Every year Belgian hospitals throw away millions of baby feeding bottles after a single use, creating more than 300 tonnes of high-quality plastic material which are then incinerated. Sirris, a Belgian non-profit organisation, together with a working group of interested parties, started the 'Baby Bottle Reborn' pilot project in 2013 at the University Hospital of Leuven (UZ Leuven).¹⁹¹ The project aimed to recycle this material stream by identifying and solving the legal, technical and logistical obstacles in the way. The result is that the disposable bottles are now sorted at the hospital before being recycled into new raw materials. From the experiences gathered in this project, it is hoped that the project can be rolled out to other hospitals.¹⁹²

Onze Lieve Vrouwe Gasthuis Hospital in Amsterdam (OLVG, The Netherlands)

An analysis of the plastic waste stream from OVLG hospital in Amsterdam was conducted by the social enterprise, Circle Economy¹⁹³ as part of the Dutch Ministry of Infrastructure and Environment's Nederland Circulair initiative.¹⁹⁴ The analysis of nine bags from OVLG's operating room was performed, and concluded that disposables packaging makes up over 50% of plastic waste, and is composed of nearly 15 different types of plastic materials.¹⁹⁵ The largest estimated plastic type used in disposables packaging based on weight were Polypropylene (PP), followed by Polyethylene Terephthalate (PET), Mixed High Density Polyethylene (HDPE) with Coated Medical Grade Paper, and Polyvinyl chloride (PVC).¹⁹⁵ In addition, 45% of plastic products were not labelled and nearly 20% of the plastic waste was composed of mixed materials either (different kinds of plastic or plastic combined with other materials such as paper and aluminium).¹⁹⁵

Initiatives from the medical devices industry

Halyard Health has developed a BLUE RENEW* Sterilization Wrap Recycling Program. The program started in 2010 with the aim of helping healthcare

facilities recycle the HALYARD* Sterilization Wrap used in operating rooms. The wrap consists of polypropylene fabric, which is recyclable. In North America there are now nearly 300 healthcare facilities, which together prevent 4 million pounds of wrap ending up in landfills.¹⁹⁶

In Australia and New Zealand, Kimberley-Clark has initiated a KIMGUARD* Sterile Wrap recycling program together with SITA-MediCollect. Used, clean, and uncontaminated KIMGUARD* Sterile Wrap products are collected by SITA MediCollect, which recycles the products into polypropylene pellets. These pellets are then used to make buckets, rain drains and corrugated packaging.¹⁹⁷

PVCMed Alliance (The European Council of Vinyl Manufacturers) describes challenges and opportunities of PVC plastic recycling in hospitals.¹⁹⁸ PVC Recycling in Hospitals estimates that PVC-based medical products are estimated to represent about one-quarter of all plastic waste.¹⁹⁹ PVCMed states that medical-grade PVC is a high-quality compound that can be recycled into many new soft PVC applications, however, the presence of DEHP plasticiser may compromise recycling. This will become less of an issue as the use of DEHP is phased out. Currently, in the UK, more than 10 hospitals are part of the RecoMed scheme²⁰⁰, funded by the European PVC industry's sustainable development programme VinylPlus®.²⁰¹



The way forward / The urgency to act on plastics

“Use of plastic goods in the healthcare sector has become ‘epidemic’ and most of it is being used in the name of low cost and patient safety”.¹⁵²

Plastics, plasticisers, and other additives to polymers are ubiquitous in modern society, however, their increasing use causes environmental harm and poses a clear and defined risk to human health. In the healthcare sector, plastics are used in medical devices and other medical applications because they fulfil number of specific performance and safety requirements. Unfortunately, certain specialist healthcare devices contain plastics made using toxic materials, despite the availability of safer alternatives. Further, high volumes of plastic waste, including single-use products, packaging, and complex plastic composites (often made from toxic materials), are generated in healthcare facilities. Due to fear of contamination, recycling of medical devices has often been considered a “no-go” option in the waste industry.²⁰²

Further work towards phasing out of hazardous chemicals and substitution with non-toxic alternatives should be encouraged and supported, highlighting that a high level of patient care and safety must be maintained. Elimination of toxic chemicals

is also important in order to encourage a circular economy; to reduce the risk to primary consumers’ health in the first instance, but also and to avoid the presence of banned toxic chemicals in products made from recycled materials, thereby reducing secondary risk to human health and the environment.

The success of the plastics circular economy in Europe does not rely on recycling and reuse only and there is a need to reduce the unnecessary use of plastics, particularly in healthcare. A growing number of hospitals and healthcare providers are making efforts to reduce single-use and non-essential plastics, and increasing recycling wherever possible. For those medical devices where it is currently essential to use plastics, safer plastics can often be substituted. Elimination of problematic or unnecessary plastics should happen through design/re-design, innovation, and new delivery models. Proper diversion and recycling are also crucial for plastics use reduction. In the future, all essential plastics should be 100% reusable, recyclable, or compostable.

The European healthcare sector, with 12,990 hospitals and over 2.8 million hospital beds, is a major purchaser of goods and services. The sector, therefore, has the potential to drive transformation in the production and consumption of plastics by le-

veraging its combined purchasing power. Through strategic partnerships and collective action, European healthcare can stimulate adoption and development of new products and packaging and lead us out of the current plastics crisis.

Awareness about actions to eliminate harmful plastics must be raised within the healthcare sector, highlighting that a high level of patient care and safety can be maintained. Furthermore, as some of the most highly trusted figures in society, healthcare professionals have the capacity and moral obligation to educate the communities they serve and trigger widespread beneficial behaviour changes in plastic use. We recommend the following immediate actions for European healthcare providers:

- Educate staff and patients about environmental and health hazards of plastic usage.
- Undertake baseline assessments to improve understanding of the scale of plastic use and waste.
- Discourage use of plastic-related material unless absolutely necessary; encourage the use of reusable instruments and materials hospitals (whilst safeguarding patient care), informed by whole-life costing evaluations.

- Focus on quick-win substitutions. For example, phase-out non-medical single-use plastics and substitute harmful medical plastics with existing safer alternatives.
- Facilitate dialogue between manufacturers, suppliers, procurement specialists, clinicians and recyclers to assess the full scope of opportunity across the value chain in healthcare.
- Establish an overarching strategy for plastics substitution and reduction using the 5 Rs concept (reduce, replace, reuse, recycle, rethink).
- Identify how plastics reduction in healthcare can align with work in other sectors and the broader movement.



CHAPTER 6

Conclusions and recommendations

A number of governments, regulatory authorities, healthcare systems, hospitals, healthcare professionals and medical devices manufacturers have endorsed a move towards medical devices that are free from hazardous chemicals, so that patients do not have to be exposed to unnecessary risks when safer alternatives are available. This is even more important when patients' exposure can be minimised without compromising medical care, for example by opting for a safer alternative that performs the same function. The phase-out of hazardous chemicals in medical devices is supported by international and European organisations representing more than 500 hospitals, medical institutions and healthcare systems and 16 million healthcare professionals.²⁰³

Conclusions

Citizens' exposure to DEHP and BPA during medical procedures contributes to a continuous, long-term, and low-level exposure to a mixture of different hazardous chemicals, which causes or enhances adverse effects on human health and the environment. European manufacturers of medical devices, under some regulatory pressure, have increased the development of alternatives to both phthalates and BPA in medical devices. Most medical devices containing phthalates can be substituted relatively easily with less hazardous alternatives at an affordable cost.²⁰⁴ Several companies already manufacture DEHP-free medical devices either by using PVC plasticisers other than DEHP or not using PVC material at all.

Since widely available and safer alternative medical devices exist, we can protect fetuses, neonates, pre-pubescent children, and other vulnerable patients from exposure to DEHP by insisting on DEHP-free, PVC-free and BPA-free products. The use of DEHP should not be granted to any medical device when safer alternatives are available.

Further development of safer medical devices by manufacturers, along with greater demand by caregivers and hospitals, could result in a complete transition away from DEHP and BPA.

HCWH Europe's Recommendations

- Apply the precautionary principle in EU legislation so that hazardous chemicals, such as phthalates and BPA contained in medical devices, are phased-out if safer alternatives are available and technically feasible. European legislation must protect the safety of patients and healthcare workers and, in particular, the most vulnerable groups.

Consistent technical implementation of Annex I.II.10.4 of the MDR must be ensured, in particular to protect the most vulnerable groups. The benefit-risk assessment of the presence of hazardous chemicals in certain medical devices should therefore be subject to the most stringent conformity assessment procedures by a Notified Body.

Legislation has a crucial double role in both protecting patients and consumers from exposure to hazardous chemicals and in sparking innovation. The adoption of progressive legislation can be a considerable driver of innovation leading to the development of safer alternatives.^{205 206} The inclusion of certain phthalates in the Authorisation List under REACH, for example, has led to an increase in the number of patented alternatives.²⁰⁷ The MDR's requirement for manufacturers to provide justification for the use of hazardous chemicals above certain thresholds in invasive medical devices, in addition to the need for application for authorisation expected in the near future for DEHP, should also ultimately lead to an increase in innovation and substitution in the health technology sector.

- Increase transparency of the market authorisation process for medical devices and improve the access to the authorisation data on medical devices.

The market authorisation for medical devices needs to be improved to ensure that approved medical devices are both efficient and safe for patients. The expanded labelling of hazardous substances introduced in the new MDR should be a driver for substitution by raising awareness in the healthcare community about the chemical composition of medical devices. Those devices should be subject to stringent compliance assessment of required labelling

by a Competent Authority. Information labelled in accordance with the MDR should be publicly available via the revamped European Database on Medical Devices (EUDAMED), so that procurers, researchers and other stakeholders have easy access to data on the devices. Clinical data used to approve devices should also be made publicly available so that healthcare professionals can better evaluate the risks and benefits of the medical products and make informed decisions.

Improved disclosure of product ingredients would allow healthcare professionals to better understand where hazardous substances are present and to prioritise their replacement.

- Avoid regrettable substitutions.
- Implement data requirements for medical devices approval and registration in the EUDAMED.

The safety evaluation of medical devices needs to be improved. The substitution of a hazardous chemical with a structurally similar substance to minimise impact on the manufacturing of the product or with a substance for which toxicity data is not available must be avoided.²⁰⁶

The existing data requirements on chemicals used in medical devices (for instance the lack of a requirement to provide information about alternatives used in a device) hamper the development of adequate data on the use, performance and safety of those alternatives. Furthermore, if a compound has a history of use, then its on-going use is assured. For example, continued use of DEHP is justified on the grounds that it has been used for many years and that it helps in the treatment of patients, regardless of its proven negative health impacts. Better evidence concerning the technical performance of alternatives is needed to guarantee that safer alternatives are adopted.

- Standards, certifications and tools similar to the EC GPP, the EU Ecolabel and the Nordic Swan label, among others, should be applied to establish harmonised environmental criteria for medical devices and different groups of hazardous chemicals to avoid any gaps and inconsistencies.



- Adopt regional and national strategies and tools to phase out hazardous chemicals in medical devices, such as the substitution group of chemicals created by the Swedish Environmental Management Council and the Swedish County Councils.

Sustainable procurement guidelines should provide incentives for the substitution of hazardous chemicals in medical devices. Procurement practices can contribute to a quicker phase-out of certain hazardous chemicals in medical devices by driving manufacturers to develop alternatives to those chemicals/products and by assessing if the available alternatives are feasible. The healthcare sector is a growing industry with a high demand for equipment that can, through responsible purchasing policies, drive the market. Hospitals are increasingly demanding products that are free of certain groups of chemicals, thereby driving research, innovation and lowering the market price of the products. The introduction of green procurement criteria at the regional, national and European levels can lead to the phase-out of hazardous chemicals in medical devices.

- Make available research funds for clinical and epidemiological studies on chemical exposure, particularly for comparing exposure and outcomes in patients being treated with similar devices but containing different chemicals.

- Prioritise research and innovation funding for the development of safer products that reduce chemical exposure of all types in the health technology sector.

- Provide greater incentives for healthcare facilities to consider substitution.

Funding for research and development of alternative substances and products and for clinical and epidemiological projects that compare the performance of these alternatives should be prioritised. Governmental authorities should support the development of safer alternatives to medical devices containing hazardous chemicals and prioritise funding for the development of those substitutes. The diversion of funding for these alternatives can be complementary to the adoption of stricter regulations.

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