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Obesogens in consumer products

Part 1 Cosmetics and detergents

RIVM report 2026-0111
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H.S. Hendriks (author), RIVM
L.F.H. Fransen (author), RIVM
M.C. Bouwmeester (author), RIVM
P.C.E. Van Kesteren (author), RIVM
H. Proquin (author), RIVM
L. Dings (author), RIVM
I.M.E. Bakker-'t Hart (author), RIVM

Contact:
H.S. Hendriks
Centrum Veiligheid Stoffen en Producten/Centre for Safety of Substances and Products
hester.hendriks@rivm.nl

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Synopsis

Obesogens in consumer products

Part 1 Cosmetics and detergents

Severe overweight (obesity) is caused by many different factors, the most significant among them being diet, lifestyle, and family history. Studies in recent years have shown that, in some cases, the body stores more fat when it is exposed to certain chemical substances known as 'obesogens'. It is not yet fully understood how these substances contribute to obesity or to what extent they influence an individual's obesity risk.

To gain more insight into this problem, the National Institute for Public Health and the Environment (RIVM) has defined what it classifies as obesogens. On the basis of this definition, RIVM identified which chemical substances are involved. It also developed a method to measure the levels of eighteen potential obesogens in consumer products. For this purpose, obesogen levels were measured in a wide range of consumer products. This report includes the results for personal care products (such as deodorant and cosmetics) and cleaning products. The results for levels in toys (stuffed toys) and food packaging will be published later.

RIVM found sixteen out of the eighteen identified substances in the consumer products that were analysed. The levels found in personal care products and cleaning products are very low when an individual product is considered but added together, they could contribute to the onset of obesity. There are considerable differences in how this happens. For example, an obesogen might disrupt hormone production, stimulate the production of fat cells, or cause people to become inactive. Unborn and young children are especially sensitive to these effects on their health.

Examples of those sixteen substances include bisphenols and plasticisers (phthalates), parabens, and octocrylene. One notable finding was that certain substances were discovered in personal care products even though their presence is not permitted in those products. These substances could have found their way into the product accidentally during the production process or may have migrated from the packaging. As such contamination is often not stated on the label, consumers do not know what they are exposed to.

RIVM believes it is important that more research is carried out. This research requires a scientific definition of obesogens that is supported internationally, plus a description of the effects concerned. More research is also needed to find out at what levels obesogens contribute to the onset of obesity.

Keywords: obesity, overweight, chemical substances, consumer products, exposure, personal care products, cosmetics, cleaning products

Publiekssamenvatting

Obesogene stoffen in consumentenproducten

Deel 1 Cosmetica en reinigingsmiddelen

Ernstig overgewicht (obesitas) ontstaat door veel verschillende factoren. De belangrijkste zijn voeding, leefstijl en erfelijkheid. De laatste jaren zijn er aanwijzingen dat het lichaam in sommige gevallen meer vet opslaat als het aan bepaalde chemische stoffen wordt blootgesteld. Deze stoffen heten obesogene stoffen. Het is nog niet duidelijk hoe ze werken en hoeveel ze bijdragen aan het ontstaan van obesitas.

Om hier meer inzicht in te krijgen, heeft het RIVM beschreven wat het verstaat onder obesogene stoffen. Op basis van deze definitie heeft het RIVM in kaart gebracht om welke chemische stoffen het gaat. Ook ontwikkelde het een methode om achttien mogelijk obesogene stoffen te meten in consumentenproducten. Daarvoor is in verschillende soorten consumentenproducten gemeten. In dit rapport staan de resultaten voor verzorgingsproducten, zoals deodorant en cosmetica, en schoonmaakmiddelen. De resultaten van metingen in speelgoed (knuffels) en voedselverpakkingen worden later gepubliceerd.

Het RIVM vond zestien van de achttien stoffen in de onderzochte consumentenproducten. De gevonden hoeveelheden in verzorgingsproducten en schoonmaakmiddelen zijn per product heel laag, maar bij elkaar opgeteld zouden ze kunnen bijdragen aan het ontstaan van obesitas. Hoe dat gebeurt, verschilt sterk. Bijvoorbeeld omdat een stof een hormoonverstorend effect heeft, de aanmaak van vetcellen stimuleert, of omdat mensen er inactief door worden. Vooral ongeboren en jonge kinderen zijn gevoelig voor deze effecten.

Voorbeelden van de zestien stoffen zijn bisfenolen en weekmakers (ftalaten), parabenen en octocryleen. Het viel op dat een aantal stoffen in heel kleine hoeveelheden in verzorgingsproducten zijn gevonden hoewel ze daar niet in mogen worden gebruikt. De stoffen kunnen tijdens de productie per ongeluk in het product zijn terechtgekomen, of vanuit de verpakking. Zulke verontreinigingen staan vaak niet op het etiket vermeld. Daardoor weten consumenten niet dat ze eraan worden blootgesteld.

Het RIVM vindt het belangrijk dat er meer onderzoek wordt gedaan. Hiervoor is een wetenschappelijke definitie van obesogene stoffen nodig die internationaal wordt gesteund. En een beschrijving van de effecten waarom het gaat. Ook is er meer onderzoek nodig naar de mate waarin obesogene stoffen bijdragen aan het ontstaan van obesitas.

Kernwoorden: obesitas, overgewicht, chemische stoffen, consumentenproducten, blootstelling, persoonlijke verzorgingsproducten, cosmetica, schoonmaakmiddelen

Foreword

The Dutch Ministry of Health, Welfare and Sport (VWS) aims to protect and promote the health of the Dutch population. The national Health Policy Memorandum 2020-2024 emphasises the importance of health protection to achieve a healthy living environment and promote well-being [1]. There is a particular need for more information on common diseases such as cancer, obesity, and dementia in relation to exposure to chemicals.

This report focusses on obesity, which has a significant impact on people's health and well-being. Several factors play a role in the development of obesity: genetic factors, diet, lifestyle, and chemicals. The Ministry of VWS wants to better understand the contribution made by chemicals in consumer products to the development of obesity. Therefore, the project aims to identify chemicals with potential obesogenic properties and to quantify consumer exposure to these substances through a literature review, targeted substance selection, and analytical measurements in consumer products. This initial report presents measurement results for cosmetics, a medical device, and several cleaning products, while subsequent reports are planned for toys (soft toys) and food contact materials.

Contents

Summary

The development of obesity is influenced by multiple factors, including genetics, diet, lifestyle, and exposure to environmental chemicals. However, the extent to which chemical exposure contributes to obesity remains unclear. This report aims to identify which chemicals present in consumer products may play a role in the development of obesity.

Chemicals that may contribute to the development of obesity are so-called 'obesogens'. In this context, particular attention should be given to prenatal and early-life exposure, as foetuses, infants, and young children are especially vulnerable due to their developing organ systems, higher exposure relative to body weight, and immature detoxification mechanisms. Early-life exposure to chemicals such as bisphenols, phthalates, and persistent organic pollutants has been increasingly linked to a higher risk of obesity later in life. These effects may be further amplified by gene-environment interactions.

In this study, a clear definition of obesogens was established, forming the foundation for a comprehensive literature review that identified a range of chemicals associated with the development of obesity. Then, the presence of these chemicals in consumer products was assessed, providing insight into potential everyday exposure routes.

A subsequent literature review focussed on mechanistic evidence and the determination of critical effect values for obesogenic outcomes. These values were compared to points of departure (PoDs) for other toxicological endpoints to determine which chemicals should be given priority for further research in relation to the induction of obesogenic effects.

To further assess consumer exposure, a GC-MS analytical method was developed and applied to quantify eighteen selected potential obesogens in consumer products. In this report, chemicals were measured in personal care products and cosmetics, detergents, and a medical device. Research on presence of these chemicals in toys (stuffed animals) and food contact materials is ongoing.

Sixteen out of the eighteen chemicals were detected in at least one product; only dihexyl phthalate (DHP) and triphenyl phosphate (TPP) were absent. For most chemicals, detected levels were low, while octocrylene in sunscreen showed the highest concentration (0.6219% w/w). Measurements below 0.001% (w/w) were considered negligible for risk assessment. However, the detection of low levels of prohibited chemicals in numerous products is significant; such chemicals may be inadvertently introduced during manufacturing or through packaging migration. Importantly, these chemicals are not always listed on product labels, especially in personal care products and cosmetics, leaving consumers unaware of their exposure.

Analysis of exposure data from literature indicated that personal care products and cosmetics, dietary intake, children's mouthing behaviour

(e.g. from toys), house dust, and air are the primary sources of obesogen exposure. Combining critical effect values, mechanistic evidence, prevalence in consumer products, and exposure data, seven obesogens were selected for further research: bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bis(2-ethylhexyl) phthalate (DEHP), methylparaben (MeP), triphenyl phosphate (TPP), and 4-nonylphenol (4NP). These candidates for further research can be used as a test set to address initial data gaps, needs for standardising definitions and testing methodologies for obesogens, and quantification approaches.

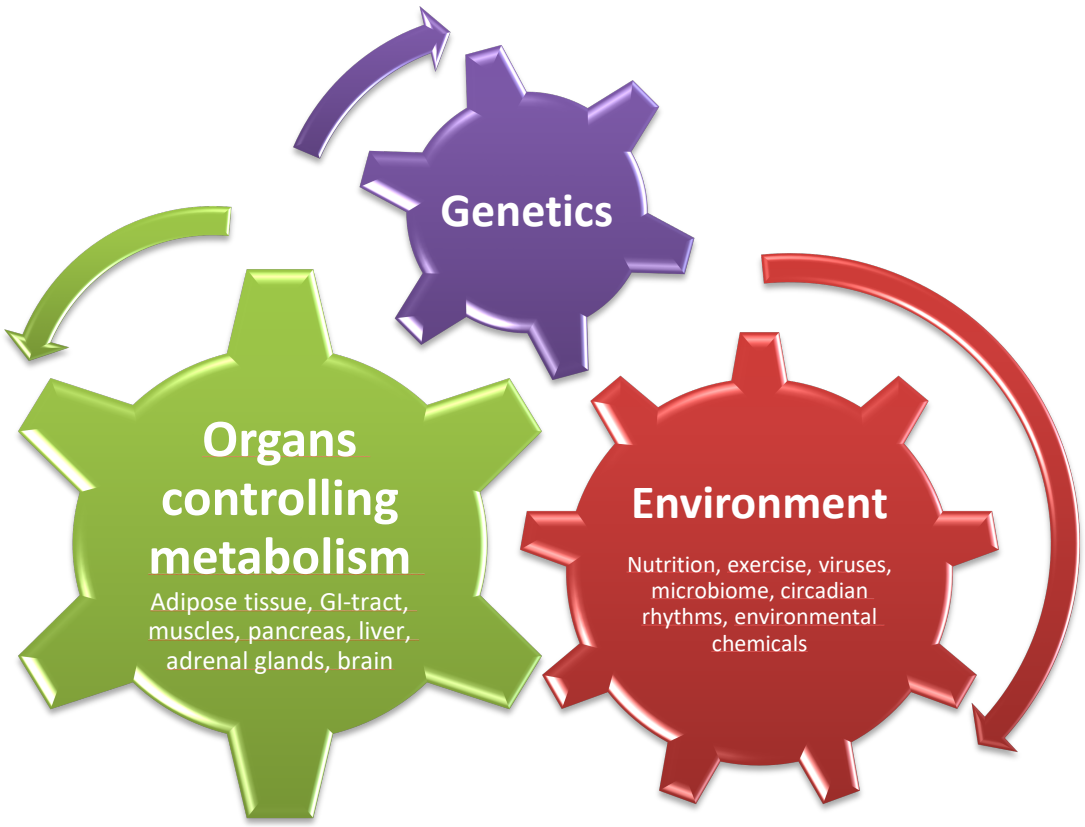
This report places the findings within the broader context of obesity risk factors. While lifestyle and diet remain the primary, well-established drivers of obesity, there is growing recognition that obesogens represent an additional risk. Obesogens typically act via hormonal disruption, altering metabolic pathways and increasing susceptibility to weight gain. Despite increasing evidence, the quantitative contribution of obesogens at the population level remains unclear and is an important area for future research.

1 Introduction

1.1 Obesity

Obesity (severe overweight) is a chronic disease characterised by an excessive accumulation of body fat, to such an extent that it involves health risks. Obesity is defined as having a Body Mass Index (BMI) of ≥30. BMI is calculated by dividing body weight in kilograms by the square of height in meters. After smoking, overweight and obesity are the leading causes of disease in the Netherlands. In 2021, one in two Dutch adults was overweight, and over 14% had obesity. The proportion of Dutch individuals with overweight is expected to increase further, and by 2050, 64% of the population is projected to have a BMI over 25 [2]. This obesity pandemic trend poses a substantial threat to the public health and well-being of people worldwide. Obesity is associated with a variety of health complications, including an increased risk of chronic conditions such as cardiovascular diseases, diabetes, and musculoskeletal disorders [3]. Beyond the physical health implications, obesity can also exert a profound impact on mental well-being, contributing to conditions such as depression, diminished quality of life, and, as a result, has a considerable impact on the societal costs [4, 5].

Figure 1 Factors that are involved in the development of obesity



Many tissues/organs, hormones, pathways, and mechanisms that play essential roles in metabolism to induce adipose tissue are involved in the development of obesity (Figure 1). An overview of the molecular and biochemical mechanisms associated with obesity is described in the reviews by Lustig et al. 2022 [6] and Heindel 2011 [7], and is summarised below.
Both genetic and environmental factors can affect the development of obesity. Environmental factors include nutrition, exercise, viruses, microbiome, circadian rhythms, and the exposure to specific chemicals ('obesogens'). These factors act on the complex interacting organ systems that control metabolism, including adipose tissue, the gastrointestinal tract, muscles, pancreas, adrenal glands, liver, and various parts of the brain, for instance, that integrate the control of eating habits.
Control of adipose tissue development, as well as the number and size of adipocytes, depends on the activity and interaction of a variety of liver transcription factors, including the two master regulators of adipogenesis: PPARγ (peroxisome proliferation-activated receptor gamma) and RXR (retinoid X receptor), which can activate adipogenesis, either alone or together with PPARγ.
The hormones insulin, estrogen, androgen, glucocorticoid, and thyroid hormone also play important roles in metabolism and adipogenesis by binding to their receptors. Other liver transcription factors modulate specific metabolic signals, which can result in disease when dysfunctional. For example, LXR (liver X receptor) regulates adipocyte differentiation, cholesterol transport, and triglyceride accumulation. PXR (pregnane X receptor) and CAR (constitutive androstane receptor) appear to act in conjunction with PPARγ and regulate glucose and energy homeostasis and immune and lipid metabolism. FXR (farnesoid X receptor) regulates bile acid synthesis and lipid metabolism, and AhR (aryl hydrocarbon receptor) can result in hepatic insulin resistance. Activation of these receptors can result in hyperinsulinemia, leptin resistance, and weight gain.

The tissues and organs controlling metabolism, and therefore energy homeostasis, communicate via a network of hormones and neurotransmitters elicited from adipocytes, the stomach, the gastrointestinal tract, the pancreas, the brain, and endocrine glands.

In short, there are several factors that play a part in the development of obesity: genetic factors, diet, lifestyle and the exposure to environmental chemicals. Since the contribution made by exposure to chemicals to the development of obesity is not clear, this report sets out to investigate which chemicals found in consumer products may contribute to obesity development.

1.2 Purpose of the study

The aim of this project is to gain insight into which chemical substances may have obesogenic properties ('obesogens') and into the extent of exposure to these substances through consumer products. A literature review will provide an overview of what is known about chemical substances in consumer products and their relationship to obesity. On the basis of the literature review and other relevant information on

obesogens, a selection will be made of substances that may contribute to obesity and that are expected to be present in consumer products. Based on this list, measurements of the levels of selected potential obesogens in various consumer products will be conducted. This will ultimately provide an up-to-date overview of consumer exposure to these substances via consumer products. This initial report describes the results of measurements in cosmetics, a medical device, and several cleaning products. Subsequent reports will describe the results of measurements in toys (stuffed animals) and food contact materials.

1.3 How to read this report

Chemicals that may contribute to the development of obesity are so-called 'obesogens'. The current study is a multifaceted investigation that aims to contribute valuable insights into understanding and addressing the role that obesogens in consumer products play in the development of obesity.
To this end, it is essential to formulate a clear working definition of 'obesogens' in the current study. This definition is inferred from existing definitions in earlier research that have been explored and described.

Chapter 2 of the current report starts with the description of existing definitions of obesogens, following which the working definition for the current study is presented. Next, the well-documented roles of lifestyle, diets, and genetics, together with the exacerbating influence of obesogens on obesity risk is described. It is also highlighted why children in the prenatal period and early childhood are uniquely vulnerable to obesogen exposure that can increase lifelong susceptibility to obesity.

Chapter 3 describes a comprehensive literature review on obesogens in which findings from both toxicological and epidemiological studies are integrated to identify chemicals that exhibit a plausible link to obesity. On the basis of the results of this thorough literature analysis, a selection of potential obesogens is made, focussing on those with a substantiated connection to weight-related health issues. Next, the relevance of these selected potential obesogens to consumer products is explored, providing an initial indication of their potential impact on public health through exposure in everyday consumer items.

Chapter 4 summarises the several regulatory frameworks within the European Union (EU) and the Netherlands that are relevant for chemicals in non-food consumer products as well as an overview of restrictions of the prioritised chemicals in these EU frameworks.

In **Chapter 5,** the results of a second literature review on supporting mechanistic information are presented. An overview is provided of the general toxicity of the selected potential obesogens, as well as of the mechanisms of action for the obesogenic endpoints and critical effect values.

Measurements of the selected potential obesogens in a selection of consumer products are described in **Chapter 6.** First, the development of the GC-MS method is described, followed by the actual results of the

measurements of eighteen selected potential obesogens in personal care products, medical devices, and detergents.

In **Chapter 7,** the results of the literature review and laboratory measurements are explained, interpreted, and clarified to place them in context.
Finally, the results of the study are discussed, and recommendations are made for further research in **Chapter 8**.

2 Obesogens

2.1 Definitions of 'obesogens'

To better understand how the environment affects obesity, researchers have introduced the concept of 'obesogens'. Although obesogens are generally defined as (environmental) chemicals, encompassing both natural and synthetic chemicals, that promote obesity, details of the definition vary between studies. Please note that the overview of studies given below is not an exhaustive list of all studies that have discussed and defined 'obesogens'.

The role of chemicals in the development of obesity was already suggested by Baillie-Hamilton in 2002 [8]. In 2006, Grun and Blumberg introduced the term 'chemical obesogens', referring to 'molecules that inappropriately regulate lipid metabolism and adipogenesis to promote obesity'. Their work laid the foundation for understanding the impact of certain chemicals on the body's metabolic processes [9]. Building upon the initial concept, the 'obesogen hypothesis' underwent expansion and transformation into the 'metabolic disruptor hypothesis'. This hypothesis posits that 'environmental chemicals can induce metabolic changes leading to obesity, type 2 diabetes, or fatty liver in animals, including humans' [10]. In the current study, we focus on the promotion of obesity and the role of chemicals with potential obesogenic properties in consumer products herein; therefore, our working definition is limited to effects on obesity only.

In 2011, Janesick and Blumberg defined obesogens as 'chemicals (natural, pharmaceutical, or xenobiotic) that promote obesity by increasing the number of fat cells or the storage of fat into existing fat cells'. They noted that obesogens can also act on adipocytes indirectly 'by changing the basal metabolic, by shifting energy balance to favour the storage of calories, and by altering hormonal control of appetite and satiety' [11].

In 2014, Heindel and Schug reviewed the current status of the obesogen hypothesis and described obesogens as 'a subclass of endocrine-disrupting chemicals that interfere with hormonally regulated metabolic processes, especially during early development' [12]. Egusquiza and Blumberg (2020) built on this concept and argued that, whereas most obesogens are a subset of metabolism-disrupting chemicals, not all metabolism-disrupting chemicals can be defined as obesogens. They recognised that obesogens may also have more diverse effects apart from inducing obesity, although obesity may be a key contributor to those effects. Furthermore, they distinguished between 'bona fide' and 'potential' obesogens. They defined bona fide obesogens as chemicals that induce white adipose tissue storage *in vivo* and potential obesogens as chemicals that have only been shown to promote adipogenesis in *in vitro* studies [13].

Kolatorova et al. (2018) defined obesogens as 'chemicals that promote obesity by increasing the number of fat cells (and increasing fat in

existing cells), by changing the amount of calories burnt during resting metabolism and by interfering with mechanisms that affect appetite and satiety' [14]. Audouze et al. (2020) contributed to the understanding of obesogens through the OBERON project, emphasising their role as 'a specific class of endocrine-disrupting (ED) chemicals that promote obesity by altering adipocyte tissue development, lipid homeostasis, and hormonal physiology' [15]. Mohajer et al. (2021) noted that obesogens may cause susceptibility to weight gain, lipid storage, and energy imbalances, ultimately resulting in obesity [16].

In this report, the working definition of obesogens is:

Working definition of obesogens:
'Chemicals that promote obesity by affecting the control of adipose development due to, among others, changes in lipid storage, and/or disruption of involved receptors such as PPAR or RXR.'

2.2 Obesogens versus lifestyle, diet and genetics

Lifestyle and diet are the primary, best-documented causes of the global rise in overweight and obesity and explain most of the variation in population prevalence [17-21]. Lifestyle and diet cause positive energy balance through sustained excess calorie intake, frequent consumption of energy-dense processed foods, sedentary behaviour, and sleep deficiency, leading directly to fat accumulation.

Obesogens may be an additional risk factor that can contribute to effects due to lifestyle, especially when exposure occurs prenatally or in early childhood. Obesogens often act as hormone-like agents that affect insulin, thyroid, or oestrogen pathways, promote pre-adipocyte differentiation, alter appetite regulation, and increase metabolic susceptibility to weight gain. Their effects are typically subtle and interact with diet. Evidence for their contribution is growing but less quantitatively established than for lifestyle factors [13].

Genetic factors influence individual susceptibility to weight gain and interact with lifestyle, diet, and obesogens to determine obesity risk. Genetic contributions range from rare single-gene disorders that cause severe early-onset obesity to common polygenic variation that shifts population risk modestly but cumulatively [19, 22, 23]. In addition, genetic factors influence the vulnerability to endocrine-disrupting chemicals or obesogens. As a result of genetic variation, the same exposure may produce larger metabolic or developmental effects in genetically susceptible people [19, 22, 23].

In Table 1, a comparison is made between obesogens, lifestyle, diet, and genetics, based on key features. For individual consumers, diet and activity are most likely to be the dominant factors; obesogens can increase risk or sensitivity but generally are not the primary trigger in adults. For a minority, genetics is the primary determinant and requires specialised management.
At the population level, lifestyle and diet remain the dominant, modifiable drivers of obesity, but widespread environmental exposure to

chemicals may help explain why some groups gain weight more rapidly despite similar lifestyle patterns.

Table 1 Comparison of key features for obesity of obesogens vs. lifestyle, diet, and genetics (based on information from [23])

Feature	Lifestyle and diet	Obesogens	Genetics
Main mechanisms	Energy surplus; dietary composition; physical activity	Hormone disruption; adipogenesis; metabolic dysregulation	Inherited variation in appetite, energy expenditure, fat distribution; monogenic or syndromic defects
Strength of evidence	Very strong; consistent epidemiology and randomised interventions	Moderate and growing; experimental and epidemiological studies	Strong for monogenic and syndromic causes; large evidence for polygenic influence
Population impact	Largest direct driver of population prevalence	Unknown, may already have an effect *in utero* and in early life; contributes to background risk	Major determinant of interindividual susceptibility; does not fully explain secular rise
Modifiability	High: behavioural change, environmental and policy interventions	Limited individually; requires regulatory and exposure-reduction measures	Low for inherited variants
Time profile of effect	Immediate to long-term; direct and reversible with behaviour change	Critical windows prenatally and early childhood; cumulative lifelong effects	Lifelong influence from conception onward; early-onset in monogenic/syndromic cases

2.3 Prenatal and early-life exposure to obesogens

A group that requires specific attention in this respect are the unborn, infants, and young children. There are various reasons for this increased concern, as summarised below.

First, foetuses, infants, and young children have developing systems. They have rapid growth, ongoing organ and neuroendocrine development, and immature detoxification systems. As a result, the impact of obesogen exposure may be higher compared to adults:

- Early-life periods, especially prenatal and the first years after birth, are critical windows when exposure can permanently alter energy balance regulation, appetite circuits, adipocyte number, and metabolic setpoints [24, 25].
- Obesogens can interfere with hormone systems during early-life and may increase adipocyte differentiation and number, reprogramme hypothalamic appetite regulators, and alter insulin and thyroid signalling, thereby raising lifelong susceptibility to fat accumulation [26].
- Some obesogens also modify epigenetic marks during developmental windows, producing persistent changes in metabolic gene expression [16, 24, 25, 27]. This makes

metabolic and hormonal disturbances more impactful and longer lasting.

Chemicals that disrupt early metabolic and hormonal development and increase lifelong susceptibility to excess fat accumulation and obesity may be called developmental obesogens.

Second, foetuses, infants and young children differ from adults in physical aspects. Through placental transfer, breastfeeding, mouthing behaviour, contaminated dust, and diet, they are exposed to environmental chemicals per kg body weight more intensively than adults [28]. Lower body mass and developing routes of excretion may result in higher internal concentrations for the same external exposure, increasing biological effect potential.

Epidemiologic and experimental studies increasingly associate prenatal and early postnatal exposure to chemicals, such as bisphenols, certain phthalates, persistent organic pollutants (e.g. organochlorine pesticides), and tobacco smoke, with higher risk of greater adiposity, rapid infant weight gain, or later childhood obesity. Systematic reviews and scoping reviews summarise a growing but heterogeneous evidence base that is biologically plausible and strongest for early-life exposure [27-29]. Several recent reviews propose obesogen-centric models of developmental origins of obesity and call for prioritising early-life exposure reduction in prevention strategies [16, 26].

Genetic susceptibility and obesogenic diets or sedentary environments interact with early chemical exposure, so that children with higher genetic risk or unhealthy nutritional environments may show stronger effects from the same chemical exposure; this gene-environment-chemical interplay helps explain variation in outcomes between children with similar chemical exposure.

3 Obesogens in consumer products

3.1 Literature search on obesogens

As a starting point for the literature search on specific obesogens, lists of possible obesogens were taken from a workshop held in September 2022. This pivotal workshop organised by the Healthy Environment and Endocrine Disruptors Strategies (HEEDS) programme was bringing together key experts from the topics of obesity and toxicology research [30]. The collaborative effort set out to facilitate dialogue and knowledge exchange among experts in these fields. Central to the discussions was a comprehensive review of the current state of scientific knowledge concerning the role of obesogens in contributing to the global obesity pandemic. The lists of possible obesogens resulting from the workshop mostly contained chemicals that fall outside the scope of this report since they are not relevant for consumer products, such as pharmaceuticals. Still, several insights into obesogens and their possible mechanisms of actions were gained.

The list of obesogens relevant for consumer products obtained from the HEEDS workshop was expanded with chemicals studied in the *in vitro, in vivo*, epidemiological, and review studies found in the literature search. In Appendix 1 the search strategies and criteria for inclusion are described.

The literature search resulted in identifying 78 chemicals that were included in *in vitro*, *in vivo*, or epidemiological studies on obesity or obesogenic effects. Out of these chemicals, 48 (see Appendix 2) were identified as meeting the criteria of potential obesogens in at least one study.
Although mono-(2-ethylhexyl) phthalate and mono-ethyl phthalate were identified as possible obesogens from the literature, they were excluded further on in the study as these compounds are major metabolites of bis(2-ethylhexyl) phthalate (DEHP) and diethyl phthalate, respectively. Therefore, they are not likely to be present in consumer products. Instead, their parent compounds were included in the list of possible obesogens.

3.2 Obesogens in consumer products

Several databases were accessed to gain information on the presence of the possible obesogens identified in the previous step in non-food consumer products, such as personal care products including cosmetics, food contact materials (FCMs), and toys.

The search strategy is further explained in Appendix 3. The chemicals that were present in at least one database were selected for further examination for their obesogenic potential (see highlighted chemicals in Table A3, Appendix 2).

In total, 38 chemicals were selected for their presence in consumer products (see **Fout! Verwijzingsbron niet gevonden.**). Notably,

several groups of chemicals are more prevalent, including several bisphenols (6), phthalates (5), and parabens (4).

3.2.1 *Mintel Global New Products Database*

The Mintel Global New Products Database (GNPD)[1] was used as source for product information from the categories Beauty & Personal Care, Household products, and Health. Please note, however, that products that are added to this database once they enter the market are not excluded from the database when they are withdrawn from the market. Initially, the search was performed without any restrictions on published dates of the products to have an indication in which (types) of products the substance may occur. For some chemicals, the published date was restricted to 'Last complete 3 years' to narrow the search to products that are likely to still be available on the market.

3.2.2 *Migration from Food Contact Materials*

The Food Contact Chemicals Database (FCCdb)[2] created by the non-profit organisation Food Packaging Forum Foundation (FPF) was used to determine whether chemicals are intentionally added to food contact materials (FCM). For chemicals that were identified within the FCCdb, information on migration of chemicals from FCM was gathered from the Database on Migrating and Extractable Food Contact Chemicals (FCCmigex)[3]. Data from the database is shown in Table 2 per substance as 'data entries that indicated migration / total data entries' to give an indication of whether migration of the substance from FCMs is likely.

3.2.3 *Chemicals in toys*

The Database on Chemicals in consumer products[4] created by the Danish EPA was used to gain information on the presence of chemicals in toys.

3.2.4 *SPIN database*

The Substances in Products in the Nordic Countries (SPIN) database[5] is a publicly accessible database with information from companies on mixtures they bring to market. This database was used to gain further information on the presence of chemicals in chemical consumer products, such as paints, together with the production volume and, mainly, the consumer use index of the products. The consumer use index gives an indication on the potential 'worst-case' exposure. Where there are multiple uses with different exposure scenarios, the index for the most critical use was selected within the database. Inhalation is assumed to be the dominant uptake route for consumer exposure. The use index has been divided on a scale of 1-5 as follows:

- Use index 1 or 2: The registered product use does not indicate direct exposure.
- Use index 3: One or several product uses indicate a potential exposure.

[1] https://www.mintel.com
[2] https://www.foodpackagingforum.org/fccdb
[3] https://www.foodpackagingforum.org/fccmigex
[4] https://eng.mst.dk/chemicals/chemicals-in-products/consumer-and-consumer-products/chemicals-in-consumer-products-database
[5] http://spin2000.net/

- Use index 4: One or several product uses indicate a probable exposure.
- Use index 5: One or several product uses indicate a very probable exposure.

Table 2 List of possible obesogens and their presence in databases on consumer products (databases checked in October 2023)

Chemical (CAS nr)	**Beauty & personal care products[1,2]**		**Household products[1,2]**		**Health products [1,2]**		**Food Contact Materials (FCCmigex[1])**	**Toys (Danish EPA database)[1,3]**	**SPIN database**	**References**
	Last 3 years	No time limit	Last 3 years	No time limit	Last 3 years	No time limit	Positive studies/Total studies	Positive samples/Total samples	Consumer exposure index	
Aromatic hydrocarbons										
Benzo[a]pyrene (50-32-8)	-	-	-	-	-	-	2/7	--	4 to 5	[31]
Styrene (100-42-5)	1	3	0	0	0	0	61/85	23/43	5	[32]
Toluene (108-88-3)	0	1	0	0	0	0	35/43	49/89	5	[32]
Tonalide (1506-02-1)	0	1	0	0	0	0	-	-	5	[16]
Bisphenols										
Bisphenol A (80-05-7)	0	0	0	0	0	0	159/217	1/27	4	[13, 16, 29, 33-51]
Bisphenol F (620-92-8)	-	-	-	-	-	-	10/43	--	3	[13, 33, 36, 38, 42, 52]
Bisphenol S (80-09-1)	-	-	-	-	-	-	10/53	--	3	[13, 16, 33, 36, 38, 51, 53-56]
Tetrabromobisphenol-A (79-94-7)	-	-	-	-	-	-	2/9	--	2 to 4	[57-59]

Chemical (CAS nr)	**Beauty & personal care products[1,2]**		**Household products[1,2]**		**Health products [1,2]**		**Food Contact Materials (FCCmigex[1])**	**Toys (Danish EPA database)[1,3]**	**SPIN database**	**References**
	Last 3 years	No time limit	Last 3 years	No time limit	Last 3 years	No time limit	Positive studies/Total studies	Positive samples/Total samples	Consumer exposure index	
Tetrabromobisphenol-A sulfate	-	-	-	-	-	-	-	-	-	[57]
Tetrachlorobisphenol-A (79-95-8)	-	-	-	-	-	-	-	-	-	[57]
Heavy metals										
Arsenic (7440-38-2)	0	0	0	0	0	1	32/50	0/15	4	[41, 42, 60-66]
Cadmium (7440-43-9)	0	0	0	0	0	0	54/88	0/15	4	[16, 41, 42, 67, 68]
Lead (7439-92-1)	-	-	-	-	-	-	88/109	5/14	4	[41, 69, 70]
Organophosphates										
2-ethylhexyl diphenyl phosphate (1241-94-7)	-	-	-	-	-	-	7/12	--	3 to 4	[71, 72]
Triphenylphosphate (115-86-6)	1	49	0	0	0	0	12/18	--	4 to 5	[42]
Parabens										
Butylparaben (94-26-8)	10	518	0	5	0	7	1/3	1/1	4 to 5	[16, 38, 73]
Ethylparaben	24	719	0	8	0	11	1/3	1/1	4 to 5	[33, 74]

Chemical (CAS nr)	**Beauty & personal care products[1,2]**		**Household products[1,2]**		**Health products [1,2]**		**Food Contact Materials (FCCmigex[1])**	**Toys (Danish EPA database)[1,3]**	**SPIN database**	**References**
	Last 3 years	No time limit	Last 3 years	No time limit	Last 3 years	No time limit	Positive studies/Total studies	Positive samples/Total samples	Consumer exposure index	
(120-47-8)										
Methylparaben (99-76-3)	1775	101	10	0	62	0	1/3	3/3	5	[26, 75, 76]
Propylparaben (94-13-3)	7	67	0	7	0	23	2/4	1/2	5	[33, 73]
Phenols										
3-tert-Butyl-4-hydroxyanisole (121-00-6)	0	0	0	0	0	0	2/3	-	3	[77]
4-nonylphenol (104-40-5)	-	-	-	-	-	-	19/32	--	3	[38, 42, 78-80]
Butylated hydroxytoluene (128-37-0)	254	1740	0	0	2	0	44/76	19/39	5	[32]
Triclosan (3380-34-5)	2	67	0	0	0	0	2/3	--	5	[41, 42, 81]
Phthalates										
Di-n-butyl phthalate (84-74-2)	-	-	-	-	-	-	121/170	8/95	4	[42, 79, 82]

Chemical (CAS nr)	**Beauty & personal care products[1,2]**		**Household products[1,2]**		**Health products [1,2]**		**Food Contact Materials (FCCmigex[1])**	**Toys (Danish EPA database)[1,3]**	**SPIN database**	**References**
	Last 3 years	No time limit	Last 3 years	No time limit	Last 3 years	No time limit	Positive studies/Total studies	Positive samples/Total samples	Consumer exposure index	
Bis(2-ethylhexyl) phthalate (117-81-7)	-	-	-	-	-	-	137/186	30/129	3 to 5	[13, 34, 38, 39, 41, 73, 79, 83-87]
Dicyclohexyl phthalate (84-61-7)	-	-	-	-	-	-	-	-	-	[16, 41]
Benzyl butyl phthalate (85-68-7)	-	-	-	-	-	-	44/87	1/15	4	[41, 85]
Dioctyl terephthalate (6422-86-2)	0	0	0	0	0	0	2/6	5/27	3 to 4	[33]
Bis(2-ethylhexyl) tetrabromophthalate (26040-51-7)	-	-	-	-	-	-	-	-	3 to 4	[88]
Phthalic acid (88-99-3)	0	0	0	0	0	0	6/6	2/27	3 to 4	[79]
UV-filters										
Benzophenone-3 (131-57-7)	55	262	0	0	0	0	5/28	-	5	[74, 85]
Octocrylene (6197-30-4)	70	368	0	0	0	3	3/7	-	4 to 5	[85]
Other chemicals										
Acetyl tributyl citrate	29	177	0	0	0	0	57/70	-	5	[89]

Chemical (CAS nr)	**Beauty & personal care products[1,2]**		**Household products[1,2]**		**Health products [1,2]**		**Food Contact Materials (FCCmigex[1])**	**Toys (Danish EPA database)[1,3]**	**SPIN database**	**References**
	Last 3 years	No time limit	Last 3 years	No time limit	Last 3 years	No time limit	Positive studies/Total studies	Positive samples/Total samples	Consumer exposure index	
(77–90–7)										
Cyclohexanone (108-94-1)	-	-	-	-	-	-	5/12	38/86	4 to 5	[32]
Dioctyl sodium sulfosuccinate (577-11-7)	5	11	0	0	0	1	-	--	5	[13, 16, 42, 90]
Monosodium glutamate (142-47-2)	5	9	1	1	0	0	-	-	3 to 5	[91]
Perfluorooctanoic acid (335-67-1)	-	-	-	-	-	-	23/32	--	2	[34, 92, 93]
Permethrin (52645-53-1)	0	0	1	4	0	0	-	--	4 to 5	[42]

1 '-' indicates the compound was not present in the database
2 '0' indicates that the compound was present in the database, but was not found in the ingredient list in the selected product categories
3 '--' indicates that the compound was present in the database, but was not tested in the selected product categoriesPlease note that no ingredient lists are available for products in the categories Food Contact Materials, and Toys.

3.3 Selection of obesogens for further testing

As this research continued with quantitative analysis of potential obesogens in consumer products, chemicals mentioned in **Fout! Verwijzingsbron niet gevonden.** were selected for inclusion in the analytical method for measurement. This selection was based on the following factors:

- Feasibility of measurements
  Measurements will be performed in consumer products by Gas Chromatography-Mass Spectrometry (GC-MS); therefore, only chemicals that are measurable by this equipment were considered for the selection.
- Strength of evidence of obesogenic potential
  Some groups of chemicals were selected due to strong evidence supporting their obesogenic effects. The largest numbers of studies identifying a link with obesity or obesogenic mechanisms were found for bisphenols and phthalates (28 and 16 studies, respectively).
- Occurrence in consumer products
  The likelihood of consumer exposure was considered by taking into account the occurrence of obesogens in consumer products. Chemicals such as parabens, octocrylene (OC), and butylated hydroxytoluene (BHT) in cosmetics were selected, as these are expected to have a higher likelihood of exposure despite less robust evidence for their obesogenic effects compared to bisphenols.

The research focusses on four key categories of consumer products – cosmetics (personal care products), household products, food contact materials, and toys – on the basis of their significant contribution to consumer exposure to chemicals. The (groups of) chemicals selected for measuring in specific product groups are shown in Table 3. In this report, the results of measurements in cosmetics (personal care products), a medical device, and household products are described.

Table 3 Chemical selection for quantitative analysis in specific product groups

Chemical	Abbreviation	CAS number	Matrix
Bisphenols			
Bisphenol A	BPA	80-05-7	Toys Food contact materials
Bisphenol F	BPF	620-92-8	
Bisphenol S	BPS	80-09-1	
Tetrabromobisphenol-A*	TBBPA	79-94-7	
Tetrachlorobisphenol-A*	TCBPA	79-95-8	
Phthalates			
Di-n-butyl phthalate	DBP	84-74-2	Toys Food contact materials
Bis(2-ethylhexyl) phthalate	DEHP	117-81-7	
Dicyclohexyl phthalate	DCHP	84-61-7	
Benzyl butyl phthalate	BBP	85-68-7	
Dioctyl terephthalate	DOTP	6422-86-2	
Dihexyl phthalate**	DHP	84-75-3	

Chemical	Abbreviation	CAS number	Matrix
Bis(2-ethylhexyl) tetrabromophthalate*	TBPH	26040-51-7	
Parabens			
Butylparaben	BP	94-26-8	
Ethylparaben	EtP	120-47-8	Cosmetics
Methylparaben	MeP	99-76-3	
Propylparaben	PP	94-13-3	
Other			
Octocrylene	OC	6197-30-4	Cosmetics Food Contact Materials Household products
Butylated hydroxytoluene	BHT	128-37-0	
Triphenyl phosphate	TPP	115-86-6	
4-nonylphenol	4NP	104-40-5	
Styrene	Styr	100-42-5	
Toluene*	Tol	108-88-3	

*For various reasons (e.g. not suitable for GC-MS method or poor reproducibility) these chemicals, although initially selected, were ultimately not included in the developed method to measure obesogens in consumer products (see Chapter 6).
**DHP was added after prohibited phthalates and metabolites were detected in a recent German national biomonitoring survey [94].

4 Relevant legislation

Several regulatory frameworks within the European Union and the Netherlands are relevant for chemicals in non-food consumer products. These include:

- The REACH Regulation: Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Annex XVII of this regulation lists chemicals that are not allowed in products for consumers and substances whose uses are subject to specific restrictions. In addition, REACH includes a list of Substances of Very High Concern (SVHC) and an Authorisation List (Annex XIV); substances on these lists may only be used if explicit authorisation has been granted.
- The Classification Labelling and Packaging (CLP) Regulation, the regulation on classification, labelling and packaging of substances and mixtures (EC No 1272/2008). Generic concentration limits are shown in Table 1.1 of Annex I of the CLP legislation and specific concentration limits are set in Annex 1, Part 3 of the CLP regulation.
- The General Product Safety Regulation (GPSR): Regulation (EU) 2023/988 of the European Parliament and of the Council of 10 May 2023 on general product safety (replaced Directive 2001/95/EC) aims to provide for a high level of consumer protection and to improve the functioning of the internal market. It addresses the product safety challenges of emerging technologies, including the use of artificial intelligence (AI) and connected devices, and establishes clear obligations for online marketplaces. The GPSR is a safety net for products intended for consumers or requirements that are not included in one of the following product-specific directives:
  - The Cosmetics Product Regulation (CPR) ((EU) No 1223/2009)
  - The Medical Devices Regulation ((EU) No 2017/745)
  - The Detergents Regulation ((EC) No. 648/2004)

This first report focusses on cosmetics, medical devices, and detergents. Subsequent reports will describe the relevant legislations for toys (stuffed animals) and food contact materials.

Legislation is regularly updated. For instance, butylated hydroxytoluene (BHT) is now included in CPR Annex III (List of chemicals that cosmetic products must not contain except subject to the restrictions laid down). This means that from 1 July 2023, cosmetic products containing BHT and not complying with the restrictions (restrictions in mouthwash, toothpaste and other leave-on and rinse-off products) shall not be placed on the Union market, and from 1 January 2024, cosmetic products containing BHT and not complying with the restrictions shall not be made available on the Union market. Furthermore, due to concerns for endocrine-disrupting properties, concentration limits for octocrylene (OC) in cosmetics are in place. Interestingly, France has

submitted an intention for an OC restriction on the basis of environmental concerns.[6]
These changes are important to include in the analysis of obesogens in relation to consumer products that are currently used, as well as with regard to the expected exposure.

Table 4 provides an overview of the legal restrictions on selected chemicals, as determined by the CLP Regulation, REACH Regulation, Medical Devices Regulation, and Cosmetics Products Regulation. For details and any changes/updates regarding concentration limits or restrictions, please consult the relevant legislation.

4.1 Cosmetics Product Regulation

The Cosmetics Products Regulation (CPR) sets out the requirements for placing cosmetics on the market. The regulation establishes rules to be complied with by any cosmetics product made available on the market, to ensure the functioning of the internal market and a high level of protection of human health. Restrictions for chemicals are listed in the Annexes of the CPR. As a result, every cosmetics product is assessed for safety before it is placed on the market. To determine whether a product is safe, the manufacturer must carry out a risk assessment. The risk of using a product that contains a certain substance needs to be assessed, rather than merely the hazard of the substance in pure and concentrated form. Warnings that are necessary for safe use must be clearly stated on the label.

Annex II of the CPR lists chemicals that are prohibited in cosmetics. However, Article 17 states that small quantities of prohibited chemicals may inadvertently be present due to impurities of natural or synthetic ingredients, the manufacturing process, storage, or migration from packaging. Their presence is only permitted if this is technically unavoidable in good manufacturing practice (GMP). These small quantities are permitted provided that such presence is in conformity with Article 3 (‘a cosmetic product made available on the market shall be safe for human health when used under normal or reasonably foreseeable conditions of use’). In the case of traces of prohibited chemicals, evidence for their technical unavoidability should also be included in the cosmetic product safety report.

4.2 Medical devices

While cosmetic products are subject to strict rules as to which chemicals may or may not be present in the product and in what concentration, this is less detailed for medical devices. Medical devices are regulated in the Medical Devices Regulation ((EU) No 2017/745). The regulation states that medical devices shall not contain >0.1% (w/w) Carcinogenic, Mutagenic or toxic to Reproduction (CMR) chemicals category 1A or 1B (following Annex VI of the CLP Regulation) or chemicals having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health. The regulation requires that if CMR and/or endocrine-disrupting chemicals are present in the product, they must be clearly indicated on the device itself and/or on the label.

[6] Registry of restriction intentions until outcome - ECHA

4.3 Detergents

Cleaning products such as detergents and cleaning agents are regulated in the Detergents Regulation ((EC) No 648/2004). The regulation sets requirements for the environment (biodegradability of surfactants) and requires that certain information must be available to consumers and professional users on the label and/or in other places. The packaging of detergents and cleaning agents indicates which ingredients the product contains. Often the name of the chemicals themselves is not stated, but categories of chemicals are shown, such as perfumes, anionic surfactants, or oxygen-based bleaching agents. The manufacturer must provide exactly which chemicals the product contains on a website. Manufacturers must always state on the label any perfumes and allergenic fragrances that are known to cause allergies, when present in concentrations exceeding 0.01%.

Table 4 Legal restrictions on selected chemicals, as determined by CLP Regulation, REACH Regulation, Medical devices Regulation, and Cosmetics Products Regulation by March 2026

Chemical (CAS nr)	**CLP Regulation (harmonised classification, Annex VI)**	**REACH Regulation**	**Medical Devices Regulation**	**Cosmetic Products Regulation**
Bisphenols				
BPA (80-05-7)	Repr. 1B STOT SE 3 Eye Dam. 1 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	Identified as SVHC (Repro, ED human health and environment), on candidate list for authorisation Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3% Restriction on use in thermal paper to <0.02% w/w	<0.1%	Prohibited (Annex II)
BPF (620-92-8)	Proposed classification: Repr. 1B[7]	-	-	-
BPS (80-09-1)	Repr. 1B	Identified as SVHC (Repro, ED human health and environment), on candidate list for authorisation Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%	<0.1%	Prohibited (Annex II)
Phthalates				
DBP (84-74-2)	Repr. 1B Aquatic Acute 1	Identified as SVHC (Repro, ED human health and environment), requires authorisation Restricted to <0.1% individually or in any combination with DEHP, DBP, BBP and/or DIBP	<0.1%	Prohibited (Annex II)

[7] https://chem.echa.europa.eu/100.009.691/activities/clhProcess/110916ab4b12e12da03bf9e22ec961a0?searchText=bisphenol%20f

Chemical (CAS nr)	CLP Regulation (harmonised classification, Annex VI)	REACH Regulation	Medical Devices Regulation	Cosmetic Products Regulation
		in toys, childcare articles and articles in prolonged contact with human skin Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%		
DEHP (117-81-7)	Repr. 1B	Identified as SVHC (Repro, ED human health and the environment), requires authorisation Restricted to <0.1% individually or in any combination with DEHP, DBP, BBP and/or DIBP in toys, childcare articles and articles in prolonged contact with human skin Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%	<0.1%	Prohibited (Annex II)
DCHP (84-61-7)	Repr. 1B Skin Sens. 1	Identified as SVHC (Repro, ED human health), on candidate list for authorisation Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%	<0.1%	Prohibited (Annex II)
BBP (85-68-7)	Repr. 1B Aquatic Acute 1 Aquatic Chronic 1	Identified as SVHC (Repro, ED human health), requires authorisation Restricted to <0.1% individually or in any combination with DEHP, DBP, BBP and/or DIBP	<0.1%	Prohibited (Annex II)

Chemical (CAS nr)	CLP Regulation (harmonised classification, Annex VI)	REACH Regulation	Medical Devices Regulation	Cosmetic Products Regulation
		in toys, childcare articles and articles in prolonged contact with human skin Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%		
DOTP (6422-86-2)	-	-	-	-
DHP (84-75-3)	Repr. 1B	Identified as SVHC (Repro) requires authorisation Restricted on use in consumer mixtures other than, for example, cosmetics and medical devices to <0.3%	<0.1%	Prohibited (Annex II)
Parabens				
BP (94-26-8)	-	Identified as SVHC (ED human health), on candidate list for authorisation	-	Maximum concentration allowed in cosmetics: 0.14 % (as acid) for the sum of the individual concentrations 0.8 % (as acid) for mixtures of chemicals mentioned in entries 12 and 12a. Not to be used in leave-on products designed for application on the nappy

Chemical (CAS nr)	CLP Regulation (harmonised classification, Annex VI)	REACH Regulation	Medical Devices Regulation	Cosmetic Products Regulation
				area of children under the age of three years.
EtP (120-47-8)	-	-	-	Maximum concentration allowed in cosmetics: 0.4 % (as acid) for single ester 0.8 % (as acid) for mixtures of esters
MeP (99-76-3)	-	-	-	Maximum concentration allowed in cosmetics: 0.4 % (as acid) for single ester 0.8 % (as acid) for mixtures of esters
PP (94-13-3)	-	ED expert group concluded; ED for environment but not for human health[8]	-	Maximum concentration allowed in cosmetics: 0.14 % (as acid) for the sum of the individual concentrations 0.8 % (as acid) for mixtures of chemicals mentioned in entries 12 and 12a. Not to be used in leave-on products designed for application on the nappy

[8] https://chem.echa.europa.eu/100.002.098/activities/edAssessment/42c8e8a294a80684675a619f2e02f1be?searchText=propylparaben

Chemical (CAS nr)	CLP Regulation (harmonised classification, Annex VI)	REACH Regulation	Medical Devices Regulation	Cosmetic Products Regulation
				area of children under the age of three years.
Other				
OC (6197-30-4)	-	Proposal for restriction in cosmetic products submitted by France[9]	-	Maximum concentration allowed in cosmetics (Annex VI): 9% in propellant spray products 10% in other products
BHT (128-37-0)	-	-	-	Maximum concentration allowed in cosmetics (Annex III): 0.001% in mouthwash 0.1% in toothpaste 0.8% in other leave-on and rinse-off products
TPP (115-86-6)	-	Identified as SVHC (ED environment), on candidate list for authorisation	-	Prohibited (Annex II): products with TPP must be removed from the EU market by January 1, 2027 (placed) and July 1, 2028 (made available).
4NP (104-40-5)	-	Restricted to <0.1% in products such as cleaning agents, textiles and cosmetic products	-	Prohibited (Annex II)

[9] https://chem.echa.europa.eu/100.025.683/activities/restrictionProcess/b8d969652bfd4fc7bea25fbe8d2beef4?searchText=octocrilene

Chemical (CAS nr)	CLP Regulation (harmonised classification, Annex VI)	REACH Regulation	Medical Devices Regulation	Cosmetic Products Regulation
		Identified as SVHC (ED environment), on candidate list for authorisation		
Styr (100-42-5)	Flam. Liq. 3 Repr. 2 Acute Tox. 4 STOT RE 1 Skin Irrit. 2 Eye Irrit. 2	-	-	Prohibited (Annex II)

5 Obesogenic effects of selected chemicals

This chapter provides information on the obesogenic effects of each of the eighteen selected potential obesogens[10]. The information is organised by chemical-group (Chapters 5.1 – 5.4): Bisphenols, Phthalates, Parabens and Other obesogens. For each chemical, the following aspects are discussed: General toxicity, Mechanism of action of obesogenic effects, Limit values from other studies, and Critical effect value.

An overview of the mechanisms of action of obesogenic effects of all eighteen chemicals is provided in Chapter 5.5. In Chapter 5.6, an overview of the data on the critical effect value (if available) and its limitations is shown for all chemicals. Moreover, this critical effect value is compared to established points of departure (PoDs) for other endpoints as documented in the scientific literature.

General toxicity and Mechanisms of action

For each chemical, an overview of the *general toxicity* is provided, as well as the *mechanism of action* for obesogenic endpoints. Please note that this is not an exhaustive overview of all available studies. As described in Chapter 3.1, a literature search was conducted to identify obesogens, which served as the starting point for the review of each chemical. For each selected chemical, additional searches were performed, although these were not systematic or comprehensive. Furthermore, a recently published overview of epidemiological studies on obesogens was also included [95].

Limit values from other studies and Critical effect value

In the section *Limit values from other studies*, reference values were described for each chemical (if available), which have been published by regulatory or scientific bodies, such as the European Food Safety Authority (EFSA), the Scientific Committee on Consumer Safety (SCCS) or the United States Environmental Protection Agency (US EPA).

While the derivation of a formal point of departure (PoD) for obesogenic effects falls outside the scope of this study (see Appendix 4 for more information on PoDs in toxicological risk assessment and their application to obesogens), *critical effect values* (i.e. doses at which obesity-related effects are seen in in vivo studies) were identified from the literature.

Critical effect values for obesity are dose levels at which obesity-related effects are observed in *in vivo* studies.

Because the organs and endocrine systems of infants, children, and adolescents are still developing, these age groups are more susceptible to obesogens. Early-life exposure can also change adipocyte

[10] I.e. the obesogens which were ultimately included in the analytical measurements of obesogenic substances in consumer products as mentioned in Chapter 6..

development, energy balance regulation, and gut microbiota that may persist into adulthood and increase the lifelong risk of obesity [96]. Additionally, due to their higher intake of food, dust, and consumer products relative to their body weight, children may experience higher internal doses compared to adults at the same environmental exposure levels. For these reasons, critical effect values derived from juvenile studies observing an increase in body weight or other obesogenic endpoints were preferred. In case no juvenile studies were available, studies with adult animals for these endpoints were used to derive a critical effect value.

5.1 Bisphenols

Bisphenols are widely used in the production of durable, heat-resistant plastics and epoxy resins. They play an important role in the production of polycarbonate plastics, which are found in items such as shatterproof windows, electronics, and water bottles. Epoxy resins containing bisphenols are used for coatings on metal food cans, pipes, and adhesives. Bisphenols are also present in other products, including thermal paper, PVC, and medical devices.
Due to the increased evidence regarding the adverse health effects of bisphenol A (BPA), many alternatives have arisen with structural and functional similarity to BPA, such as bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol E (BPE), and bisphenol AF (BPAF).

5.1.1 Bisphenol A (BPA)

Bisphenol A (BPA) is an organic chemical widely used in the production of plastics, epoxy resins, and various consumer products, including food contact materials, thermal paper, toys, and textiles [97]. Since December 2024, BPA and other bisphenols are banned from food contact materials in the EU (Regulation (EU) 2024/3190).

5.1.1.1 General toxicity

BPA has received increased public attention due to its harmful effects on development, reproduction, metabolism, and cardiovascular and immune systems, among others [98]. BPA, a ubiquitous xenoestrogen, exerts toxicity primarily through endocrine disruption by binding to oestrogen receptors (ERα, ERβ, GPER), androgen receptors, and thyroid hormone receptors, thereby dysregulating reproduction, metabolism, and neurodevelopment. It induces oxidative stress via elevated reactive oxygen species (ROS), causing mitochondrial dysfunction, DNA damage, and activation of apoptotic/autophagic pathways, as observed in embryonic and mammalian cell models. Additional mechanisms include epigenetic alterations (e.g. DNA methylation changes via Dnmt3a/b and histone modifications), endoplasmic reticulum stress, membrane perturbation due to its lipophilicity, and downstream effects on adipogenesis, carcinogenesis, and neurotoxicity. Collectively, these pathways underpin BPA's links to metabolic syndrome, developmental defects, and hormone-dependent diseases [99-101].

On the basis of animal evidence under CLP, the ECHA Committee for Risk Assessment (RAC) has classified BPA as a Category 1B reproductive toxicant from 2014 onwards, indicating it is presumed to impair fertility.

5.1.1.2 Mechanism of action of obesogenic effects

Epidemiological studies indicate that BPA exposure is associated with changes in adipokine levels that are involved in the regulation of appetite and satiety [38, 42, 102]. Numerous *in vivo* studies have been published concerning the pathophysiology of obesity following BPA exposure in animals [38, 42, 102]. Animals treated with low doses of BPA presented metabolic dysfunctions associated with obesity. This includes increased expression of genes involved in fatty acid metabolism, cholesterol, and triglyceride biosynthesis. *In vitro* studies have identified molecular targets and signalling pathways that may be involved in the pathogenesis of obesity following BPA exposure [38, 42, 102]. However, a clear conclusion on the obesogenic potential of BPA is difficult as studies are looking at a wide range of parameters relating to obesity and almost every study uses other variables, such as differences in strain and in species, type of diet, number of animals used, etcetera. [103]. Metabolic effects are often studied in animal models using specific conditions such as high fat, high carbohydrate, species, and strain [103].

5.1.1.3 Limit values from other studies

Depending on the specific endpoint/mechanism of action, several values are derived from studies. For example, BPA is classified under CLP as Reprotoxic Category 1B for the endpoint of sexual function and fertility. The NOAEL of 2.5 mg/kg bw/day, based on relevant effects on histopathology in ovaries and uterus [104], was recently used as PoD for the calculation of an 8h-TWA (Time Weighted Averages, an occupational exposure limit value) for fertility by RAC [105].

The European Food Safety Authority (EFSA) on the other hand, established a TDI of 0.2 ng/kg bw/day on the basis of immune effects [106, 107].

Uric acid is the degradation product of the metabolism of purines. As purines are constituents of the diet, which contains nucleic acids, increased levels of uric acid in blood (hyperuricaemia) can result from increased dietary uptake. In the study by Ma et al. (2018), a dose-dependent increase in hepatic and serum concentration of uric acid was observed in two separate mice strains (with a ratio dose/BMDL of 3.1 for the hepatic uric acid concentration, and 12.8 for the serum uric acid concentration) [108].

5.1.1.4 Critical effect value

Several studies indicate effects of BPA relating to metabolic diseases in developing organisms. For example, in the study by Yang et al. (2016), 5-week-old male and female C57BL/6J mice showed significantly increased body weight and fat mass when fed a chow diet (LOAEL 5 µg/kg bw/day; increase in body weight only shown in a figure) [109]. However, no significant difference in body weight and fat mass was observed in either male or female mice fed a high-fat diet, suggesting that BPA may interact with diet in promoting obesity risk. In this regard, RAC recently concluded that currently none of the studies focussing on developing obesogenic effects of BPA is adequate for the derivation of a PoD [88].

5.1.2 Bisphenol F (BPF)

Bisphenol F (BPF), a structural analogue and common substitute for BPA, is used in the production of rigid polymers for household appliances, automotive parts, protective coatings, and dental sealants. While BPA exposure is decreasing, human biomonitoring studies show increasing BPF and BPS levels [110].

5.1.2.1 General toxicity

Most available data on BPF's toxicity profile derives from comparative studies with BPA, as comparable to or slightly less potent than BPAs, leveraging their close chemical resemblance (both diphenylmethane derivatives with phenolic groups) to infer similar effects, including endocrine disruption, neurotoxicity, inflammation via pro-inflammatory cytokines, and reproductive impairment [38, 111, 112]. It can bind to oestrogen receptors, particularly ERβ (oestrogen receptor β), and act as a weak oestrogen, resulting in hormonal imbalance [113]. Animal studies demonstrate that BPF exposure is associated with gonadal toxicity, such as testicular damage, reduced sperm quality, and disturbances in reproductive hormones such as GnRH, LH, FSH, and testosterone [113]. In addition to reproductive toxicity, like lipophilic BPA, BPF is likely to cross the blood-brain barrier, where it accumulates and can cause neurobehavioural changes, cognitive deficits, and disrupt neuronal developmental processes in zebrafish embryos [114, 115]. Furthermore, BPF is known to induce oxidative stress and inflammation by increasing pro-inflammatory markers and promoting apoptotic signalling pathways [113].

In 2024, RAC proposed to classify BPF as toxic for reproduction (Category 1B), which has only recently been included in Annex VI of the CLP Regulation[11]. BPF shows mechanistic and functional overlaps with BPA [116], and in 2024, RAC acknowledged the adverse effects of BPF on fertility [117].

5.1.2.2 Mechanism of action of obesogenic effects

As studies show that the endocrine-disrupting properties of other bisphenols are similar to BPA, this may also be the case for the obesogenic properties [118, 119]. The obesogenic mechanisms of BPF involve its capacity to disrupt adipose tissue homeostasis and promote adipogenesis. Experimental studies show that BPF can induce preadipocyte differentiation into mature adipocytes, augmenting lipid accumulation and upregulating adipogenic genes such as lipoprotein lipase (Lpl), fatty acid binding protein 4 (Fabp4), and perilipin (Plin) [120]. The principal molecular pathway implicated in these effects is the activation of peroxisome proliferator-activated receptor gamma (PPARγ), a transcription factor that governs fat cell formation and lipid metabolism [38, 42]. *In vivo* studies suggest that BPF may stimulate adipocyte proliferation and increase overall fat mass. Overall, while laboratory models establish the mechanistic basis for BPF's obesogenic potential, further research is needed to clarify the relevance and impact of these findings in human populations [121, 122].

[11] https://echa.europa.eu/documents/10162/68c20fdb-05b1-132b-ae49-357575aebdc4

5.1.2.3 Limit values from other studies
No reference values have been published by EFSA, the SCCS, or US EPA.

5.1.2.4 Critical effect value
In an *in vivo* study, adolescent male rats were exposed to BPF via drinking water for five weeks. At 152.5 µg/kg bw/day, results showed an increased body growth (5%, LOAEL), abdominal adiposity, and urine output in male rats, suggesting a heightened risk for future metabolic diseases, even in the absence of increased caloric intake [123].

5.1.3 Bisphenol S (BPS)
Bisphenol S (BPS), a structural analogue and replacement for BPA, is used in polyethersulfone (PES) plastics, rigid plastic components, cleaning products, electrical coatings, and textiles, and is also used to enhance colourfastness in fabrics [124]. BPS is found in a wide range of consumer products, including those marketed as 'BPA-free', while human biomonitoring data shows increasing exposure levels [110].

5.1.3.1 General toxicity
Various studies have demonstrated that BPS exhibits multiple toxicological effects. Endocrine disruption is evident, as BPS acts as an agonist of oestrogen receptors (ERα) [125]). Reproductive toxicity includes alterations in oestrous cycles, reduced fertility, impaired reproductive performance, and developmental deformities [126, 127]. Neural toxicity is characterised by neural alterations, disrupted neurogenesis, and behavioural changes [125]. BPS exposure also induces cardiovascular defects [128]. Hepatic effects involve elevated serum liver enzymes, increased liver weight, and alterations in lipid and carbohydrate metabolism [119, 128, 129]. Immunotoxicity is reflected by increased secretion of pro-inflammatory cytokines and suppression of anti-inflammatory cytokines [126, 128]. Notably, these adverse effects have been observed even at low concentrations. Several reviews have concluded that the biological disruptive effects of BPS are comparable to, or even exceed, those of BPA [127-129].

BPS is classified under CLP as toxic for reproduction (Category 1B). Moreover, it is listed as reprotoxic, ED to human health and ED to the environment on the Candidate List of SVHC for Authorisation.

5.1.3.2 Mechanism of action of obesogenic effects
Studies show that the endocrine-disrupting properties of bisphenols are similar to BPA; this may also be the case for the obesogenic properties, see, for instance, [127]. This review shows that studies in mouse, sheep, and embryonic stem cells identify that BPS causes increased body weight via the activation of preadipocytes, adipogenic differentiation, and increased cellular expression of adipogenic genes with accumulation of triglycerides, respectively. Additionally, studies show that BPS stimulates the differentiation of adipocytes *in vitro* by activating PPARγ [38, 42]. In addition, like BPA, BPS is associated with interference induction of obesity *in vivo*, and promotion of transgenerational inheritance of obesity [38, 111].

5.1.3.3 Limit values from other studies

At a LOAEL of 20 mg/kg bw/day, irregular oestrus cycles with a decreased pro-oestrus stage and an increased dioestrus phase were observed in rats [130].
The RAC CLH opinion from 2020 shows effects in rats, such as a decreased fertility index, decrease in number of implantation sites, and irregular oestrus cyclicity. These effects are found at doses of approximately 180 mg/kg bw/day in standard guideline studies [130].
Post-implantation loss and reduced litter size are reported at 60 mg BPS/kg bw/day and over in rats [130].
Other studies show effects on sperm parameters as well as on folliculogenesis (as described following exposure with BPA), which are reported at lower levels (in µg BPS/kg bw/day) (for an overview see the 2020 RAC CLH opinion [130]). Moreover, indications of effects of BPS on mammary glands, immunotoxicity, neurotoxicity, and metabolic diseases were noted in an available review, which is based on several studies [112]. Similarly to BPA, these effects are noted at low dose levels, but a PoD is not always possible to derive.

5.1.3.4 Critical effect value

In Beausoleil et al. (2022), eighteen studies assessing *in vivo* metabolic effects were conducted on young animals or involved exposure during early development periods. These included different protocols, dose ranges, species, sex and metabolic outcomes studied [131]. It was concluded that BPS could be a metabolic disruptor targeting several metabolic organs at both neural and peripheral levels (liver, adipose tissue, and muscle); in several studies, males proved more susceptible. In one of the reviewed studies, exposure of mice to BPS at doses of 1.5 and 50 µg/kg bw/day from gestational day 1 through to adulthood resulted in increased body weight and fat mass in male offspring at 22 weeks of age, specifically when they were fed a high-fat diet [55].

5.2 Phthalates

Phthalates are commonly used as plasticisers in plastic consumer products such as toys and food contact materials. Phthalates are known for their ability to enhance the flexibility and durability of plastic products. Notably, these plasticisers are typically not bound to the matrix, making them prone to migration from the product and more relevant for human exposure [132].

5.2.1 Di-n-butyl phthalate (DBP)

Di-*n*-butyl phthalate (DBP) is a low-molecular weight phthalate historically used as a plasticiser in various consumer products.

5.2.1.1 General toxicity

Subchronic rodent studies note decreased body weights and increased liver and kidney weights, indicating systemic toxicity at high dose levels [133]. A NOAEL of 50 mg/kg/day for developmental effects was established in a rat study where DBP was administered by gavage during gestational days 12 to 21 [134].

DBP and its primary metabolite, monobutyl phthalate (MBP), are known endocrine-disrupting chemicals that interfere with androgen signalling

by inhibiting (foetal) testosterone synthesis, leading to reproductive tract malformations [135]. In a dietary study by Lee et al. (2004), pregnant rats exposed to DBP from gestational day 15 to postnatal day 21 produced male offspring with minimal but detectable reproductive changes at the lowest tested dose of 20 ppm (approximately 2.5 mg/kg/day) [136].

DBP is classified under the CLP regulation as toxic for reproduction (Category 1B) and as acutely toxic to aquatic environments. Furthermore, it is listed on the REACH SVHC Candidate list as an endocrine-disrupting chemical for human health.

5.2.1.2 Mechanism of action of obesogenic effects

Manikkam et al. (2013) demonstrated, using an *in vivo* rat model, that exposure to a mixture of plastic-derived endocrine-disrupting chemicals (BPA, DEHP, and DBP) can induce epigenetic transgenerational effects, leading to increased body weight and abdominal adiposity in third-generation offspring [82]. However, as a mixture of chemicals was used, it cannot be concluded that these effects were caused by DBP exposure. In epidemiology studies, Choi et al. (2014) demonstrated a positive association between serum levels of DBP and rates of childhood obesity in young Korean girls [79]. In this study, no associations were found between serum levels and obesity for BPA and DEHP. However, even though obese and non-obese children from the same school were studied, no other potentially confounding factors were taken into account in this study.

Harley et al. (2017) and Philips et al. (2020) have shown a link between *in utero* DBP exposure and outcomes such as an increased BMI and risk of childhood obesity [137-139], although the mechanisms remain unknown. Proposed mechanisms of action include disruption of lipid metabolism, altered expression of genes regulating adipogenesis, and epigenetic modifications influencing energy homeostasis.
Exposure to low doses of DBP during pregnancy in mice is suggested to promote obesity in the offspring through participation of endoplasmic reticulum stress by suppressing Uncoupling Protein 1 (UCP)1 (essential for brown fat cells to perform their heat-production functions) [140]. This effect was mostly reversed when the mice were treated with tauro ursodeoxycholic acid, a compound known to relieve ER stress.

5.2.1.3 Limit values from other studies

The European Food Safety Authority (EFSA, 2019) has established a TDI for DBP of 0.01 mg/kg bw/day, based on reproductive toxicity observed in rats. This TDI was derived from a LOAEL of 2 mg/kg bw/day for reduced spermatocyte development and effects on mammary glands [133]. In comparison, dietary exposure was estimated to average 0.042 to 0.769 µg/kg bw/day, with a P95 of 1.503 µg/kg bw/day by EFSA. For drinking water, RIVM estimated a maximum permissible concentration to be 35 µg/L [141], based on a TDI of 0.01 mg/kg.

Additionally, the U.S. Agency for Toxic Substances and Disease Registry (ATSDR, 2001) has derived a minimal risk level (MRL) of 0.5 mg/kg/day for acute oral exposure, based on a NOAEL of 50 mg/kg/day for developmental effects in rats [134, 135]. The ATSDR did not derive an

intermediate or chronic MRL for DBP, because of non-appropriate or missing studies [135].

Within the authorisation process, ECHA RAC (2013) derived a reference DNEL for DBP of 0.007 mg/kg bw/day for the general population, based on a LOAEL of 2 mg/kg bw/day in a developmental toxicity study in rats [142].

5.2.1.4 Critical effect value

No critical effect value could be derived for early-life exposure to DBP, as no studies in juvenile animals were found that observed an increase in body weight or other obesogenic endpoints. However, several studies have shown DBP effects in adults or of *in utero* exposure to DBP on offspring body weight:

- A subacute 4-week study found that male rats given 10 mg/kg bw/day DBP by oral gavage gained significantly more weight and had higher feed efficiency [143]. However, this effect was not observed at higher dose levels in this study. Body weight was not significantly increased in this study.
- In a developmental toxicity rat study, gestational and lactational exposure to DBP resulted in decreased body weight in the F0 generation. However, this study showed increased body weight and visceral fat in F1 offspring from postnatal day 7 persisting into adulthood in a dose-dependent manner. The lowest tested dose of 33 mg/kg bw/day DBP showed effects on body weight in this study up until the second month (+16.8%), whereas the body weight increase in the highest tested dose of 132 mg/kg bw/day persisted until at least the third month (+7.2%) [144].
- A perinatal exposure study showed increased body weight in female offspring upon DBP exposure (5 mg/kg bw/day), an effect that persisted into adulthood. This effect was, however, not shown for male offspring [145].
- A mouse study demonstrated that *in utero* exposure to 5 mg/kg bw/day DBP resulted in increased offspring body weight and fat mass, as well as in other markers for obesity [140].

Overall, the results are not consistent, and no dose response can be established. The evidence may suggest using the LOAEL of 5 mg/kg bw/day as a critical effect value for obesogenic effects resulting from *in utero* exposure to DBP. Both animal studies and epidemiological data have linked prenatal exposure to changes in body weight and other indicators of obesity.

5.2.2 Bis(2-ethylhexyl) phthalate (DEHP)

Bis(2-ethylhexyl) phthalate (DEHP) is a plasticiser used in PVC products.

5.2.2.1 General toxicity

DEHP targets the liver in rodents by activating PPARα. This receptor activation induces peroxisome proliferation, hepatocellular hypertrophy, and changes in lipid metabolism [146]. Kidney and liver weight increases have also been reported across repeated dose studies, typically at higher exposure levels. Histopathological liver changes, such as hepatocellular hypertrophy and fatty infiltration, are considered sensitive endpoints for DEHP exposure [146].

The most sensitive toxicological endpoint of DEHP exposure is male reproductive toxicity. Reproductive and developmental toxicity in male rodents include reduced foetal testosterone, disrupted male reproductive tract development, and decreased fertility from doses of 4.8 mg/kg bw/day [146-148]. The interference with testosterone biosynthesis observed in these studies also demonstrates an endocrine-disrupting effect of DEHP. Furthermore, epidemiological studies have linked DEHP metabolites to reduced sperm quality and testosterone in men [149, 150].

DEHP is classified under the CLP regulation as toxic to reproduction (Category 1B). Furthermore, it is listed on the REACH SVHC Candidate list as an endocrine-disrupting chemical for the environment and human health.

5.2.2.2 Mechanism of action of obesogenic effects

A systematic review and meta-analysis performed in 2017 linked early-life exposure to DEHP to increased fat weight in rodents; however, it concluded that there was too much heterogeneity across studies to link DEHP exposure to body weight changes [151].

DEHP activates PPARα in the liver, leading to increased fatty acid oxidation. In an *in vivo* mouse model, this activation has been associated with protection against diet-induced obesity. However, in humanised PPARα mouse models, DEHP exposure exacerbated diet-induced obesity, indicating species-specific responses [152]. An *in vivo* rat model has shown that DEHP exposure results in statistically significant increases in body weight, glucose, and insulin levels, reinforcing its obesogenic potential [153]. *In vitro* studies have shown that DEHP's primary metabolite mono(2-ethylhexyl) phthalate (MEHP) activates PPARγ, a key regulator of adipogenesis, promoting adipocyte differentiation and lipid accumulation [154]. DEHP itself was inefficient in promoting adipogenesis *in vitro* [84]. In the latter study, *in vivo* experiments in mice showed that DEHP exposure resulted in increased body weight and adiposity, confirming the obesogenic effects observed *in vitro* [84].

In vivo studies in mice have demonstrated that DEHP exposure impairs insulin tolerance and alters adipose tissue function, including changes in adiponectin and leptin levels [155].

Using an *in vivo* rat model, Manikkam et al. (2013) demonstrated that exposure to a mixture of plastic-derived endocrine-disrupting chemicals (BPA, DEHP, and DBP) can induce epigenetic transgenerational effects, resulting in increased body weight and abdominal adiposity in third-generation offspring [82]. However, as a mixture of chemicals was used, it cannot be concluded that these effects were caused by DEHP exposure

5.2.2.3 Limit values from other studies

EFSA (2019) has established a TDI for DEHP of 0.05 mg/kg body weight per day, based on reproductive toxicity.
A NOAEL of 4.8 mg DEHP/kg bw/day, based on effects on the testis in F1 animals, was identified from a three-generation reproductive toxicity

study in rats. By applying an uncertainty factor of 100, the TDI was set to 0.05 mg/kg bw/day [133].

The U.S. Food and Drug Administration (FDA, 2001) has similarly adopted a TDI of 0.04 mg/kg bw/day for DEHP [146], whereas the World Health Organization (WHO) recommends a slightly more conservative TDI of 0.025 mg/kg bw/day, based on a NOAEL of 2.5 mg/kg bw/day for peroxisomal proliferation in the liver in rats, and an uncertainty factor of 100 for interspecies and intraspecies variation. This entails a drinking water guideline of 0.008 mg/L [156].

Additionally, the ATSDR has derived a minimal risk level (MRL) of 0.003 mg/kg/day for acute oral exposure, based on a LOAEL of 1 mg/kg/day for developmental effects (altered glucose homeostasis), and an intermediate MRL of 0.0001 mg/kg bw/day, based on a LOAEL of 0.04 mg/kg bw/day for developmental effects [134]. The ATSDR did not derive a chronic MRL for DEHP [135, 146].

Within the authorisation process, ECHA RAC (2013) derived a reference DNEL for DEHP of 0.034 mg/kg bw/day for the general population, based on a NOAEL of 4.8 mg/kg bw/day on testicular toxicity from a 3-generation rat study [157].

5.2.2.4 Critical effect value

Currently, no clear PoD for obesogenic effects of DEHP can be established on the basis of juvenile animal studies:

- In a study by Wang et al. (2024), exposure of prepubertal male mice to DEHP from postnatal day 22 resulted in testicular injury; however, only a slight, non-significant increase in body weight was observed, suggesting minimal obesogenic impact under the tested conditions [158].
- Kang et al. (2021) reported a modest increase in body weight up to postnatal day 30 in mice exposed to DEHP from week 3 onwards, followed by a slight decrease at later time points. These findings do not provide consistent or significant evidence of sustained body weight gain or adiposity linked to DEHP exposure during juvenile development [159].
- Hao et al. (2013) showed an increased body weight (+6.6%) in female offspring upon *in utero* exposure to 0.25 mg DEHP/kg bw/day. This effect was, however, not observed for lower or higher concentrations [84].
- A perinatal exposure study showed a non-significant trend for increased body weight and fat mass in female offspring upon DEHP exposure (5 mg/kg bw/day), effects that persisted into adulthood. However, this trend was not shown for male offspring [145].
- Another study using female mice showed significantly increased body weight, increased food intake, and increased visceral fat tissue at the lowest tested dose of 0.05 mg DEHP/kg bw/day [160].
- Klöting et al. (2015) showed 0.05 mg DEHP/kg bw/day exposure for 10 weeks in mice (11-week-old adults) resulted in statistically significantly increased body weight and impaired insulin,

increased fat mass and effects on metabolic function, such as Pparg and adiponectin in female mice [155].

Despite some transient effects on body weight, none of these juvenile studies supports a reliable PoD for obesogenic effects from juvenile exposure to DEHP. A LOAEL of 0.05 mg/kg bw/day could be considered, as this resulted in increased body weight and fat mass in adult mice.

5.2.3 Dicyclohexyl phthalate (DCHP)

Dicyclohexyl phthalate (DCHP) is a plasticiser in consumer products. It is classified under the CLP regulation as toxic to reproduction (Category 1B) and as skin sensitising (Category 1). Furthermore, it is listed on the REACH SVHC Candidate list as an endocrine-disrupting chemical for human health.

5.2.3.1 General toxicity

Repeated oral exposure in rodents caused increases in liver, kidney, and thyroid weights, as well as histopathological alterations [161]. Effects on the developing male reproductive system have been identified as the most sensitive effect following oral exposure. Several rodent studies have identified a NOAEL ranging between 10 and 30 mg/kg bw/day for this effect [162].

5.2.3.2 Mechanism of action of obesogenic effects

DCHP has been shown to activate the nuclear receptor pregnane X receptor (PXR). This receptor plays a role in lipid metabolism, and its activation by DCHP leads to increased expression of lipogenic genes and genes involved in ceramide synthesis in the intestine. As a result, DCHP exposure has been linked to elevated serum ceramide levels and hyperlipidemia in mice [163, 164]. These findings suggest that DCHP may promote metabolic disturbances relevant to obesity, although no *in vivo* studies have demonstrated direct weight gain effects.

5.2.3.3 Limit values from other studies

Regulatory or scientific bodies have not determined reference values for DCHP.

5.2.3.4 Critical effect value

No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.2.4 Benzyl butyl phthalate (BBP)

Benzyl butyl phthalate (BBP) is plasticiser mainly used to soften polyvinyl chloride (PVC) in a wide range of consumer and industrial products.

5.2.4.1 General toxicity

Subchronic toxicity studies in rodents [165, 166] have reported liver and kidney weight increases upon BBP exposure, along with histological changes in liver tissue.

BBP has been found to cause reproductive tract malformations in male offspring in a developmental and reproductive toxicity rat study with 0.75 g/kg bw/day BBP from day 14 of gestation to day 3 of lactation, indicating its anti-androgenic potential [167]. A rat multigeneration study showed testicular toxicity and a reduction in anogenital distance in F1 and F2 males upon 250 mg/kg bw/day BBP exposure [133].

BBP is classified under the CLP regulation as toxic to reproduction (Category 1B) and as toxic to aquatic environment (Acute 1 and Chronic 1). Furthermore, it is listed on the REACH SVHC Candidate list as an endocrine-disrupting chemical for human health.

5.2.4.2 Mechanism of action of obesogenic effects

In 3T3-L1 preadipocyte cells, BBP exposure led to increased lipid accumulation and upregulation of adipogenic markers (e.g. PPARγ), suggesting its role in promoting adipocyte differentiation [168, 169]. Pereira-Fernandes et al. (2014) identified BBP as an obesogenic compound in toxicogenomic screens of the same cell line, reinforcing its role in activating adipocyte-specific gene expression [73].

Park et al. (2025) has shown that BBP exposure (169 µg/kg bw/day) resulted in statistically significantly increased body weight in young, but not in adult mice [170]. Other potentially obesogenic endpoints were, however, not analysed in this study.

5.2.4.3 Limit values from other studies

EFSA has identified a NOAEL of 50 mg/kg bw/day, based on a rat multigeneration study, where testicular toxicity and reductions in anogenital distance were observed in F1 and F2 males at 250 mg/kg bw/day. Applying a standard uncertainty factor of 100, EFSA set a TDI of 0.5 mg/kg bw/day [133].

Within the REACH authorisation process, ECHA RAC (2013) derived a reference DNEL for the general population of 0.5 mg/kg bw/day for BBP. This was based on an oral NOAEL of 50 mg/kg bw/day for developmental toxicity from a rat 2-generation study [171].

5.2.4.4 Critical effect value

No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.2.5 Dioctyl terephthalate (DOTP)

Dioctyl Terephthalate (DOTP), also known as bis(2-ethylhexyl) terephthalate (DEHT), is a non-phthalate plasticiser commonly used as a safer alternative to phthalates like DEHP. DOTP is a structural isomer of DEHP but exhibits a different metabolic and toxicological profile.
In contrast to DEHP, metabolism of DOTP does not result in significant formation of monoesters. Its monoester analogue, mono(2-ethylhexyl) terephthalate (MEHT), has shown similar *in vitro* toxicity to mono(2-ethylhexyl) phthalate (MEHP), a known active metabolite of DEHP.

5.2.5.1 General toxicity

In 90-day dietary rat studies, no adverse effects were observed at doses up to 561 mg/kg bw/day in males and 617 mg bw/kg/day in females; only adaptive liver weight increases were observed. A 2-generation reproductive study established a NOAEL of 868 mg/kg bw/day (females) with no effects on fertility, offspring development, or endocrine markers observed [172]. The Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR, 2015) considers a NOAEL of 142 mg/kg bw/day, based on hyperplasia of the urinary bladder and adenomas in the uterus in a chronic toxicity study in rats [173].

DOTP currently has no harmonised classification under the CLP Regulation.

5.2.5.2 Mechanism of action of obesogenic effects

There is no *in vivo* or epidemiological data indicating obesogenic or metabolic effects of DOTP. However, in an *in vitro* study using 3T3-L1 preadipocytes, Choi et al. (2021) demonstrated that DOTP exposure significantly increased lipid accumulation during adipocyte differentiation. This was accompanied by upregulation of key adipogenic transcription factors, such as PPARγ [33].

5.2.5.3 Limit values from other studies

Regulatory or scientific bodies have not determined reference values for DOTP.

5.2.5.4 Critical effect value

No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.2.6 Dihexyl phthalate (DHP)

Dihexyl phthalate (DHP) is used as a plasticiser in flexible PVC products.

5.2.6.1 General toxicity

In rodent studies, DHP is considered to be a liver toxicant, inducing hepatic lipid accumulation, and hepatocellular necrosis at high doses. DHP undergoes hepatic metabolism and shares metabolic pathways with other phthalates, including initial hydrolysis to monoesters [174, 175].

Toxicological data from a one-generation mouse study indicates that DHP is a developmental toxicant at high doses. Adverse reproductive effects were observed at 380 mg/kg bw/day, which was the lowest dose tested [174]. Rat studies have also shown decreased testosterone production upon *in utero* DHP exposure [176, 177].

DHP is classified under the CLP regulation as toxic to reproduction (Category 1B; H360FD). DHP is placed on the SVHC candidate list for its effects on reproduction.

5.2.6.2 Mechanism of action of obesogenic effects

There is no epidemiological, *in vivo,* or *in vitro* evidence linking DHP to adipogenesis, obesogenic effects, or metabolic dysfunction at

environmentally relevant doses. However, structural similarities to other phthalates may indicate potential obesogenic effects.

5.2.6.3 Limit values from other studies
Regulatory or scientific bodies have not determined reference values for DHP.

5.2.6.4 Critical effect value
No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.3 Parabens

Parabens are a group of chemicals that are widely used as preservatives in personal care products, pharmaceuticals, and the food industry [178]. Parabens are esters of para-hydroxybenzoic acid, resulting in several congeners including, methylparaben, butylparaben, ethylparaben, and propylparaben. Parabens are often used in combination, particularly methylparaben and propylparaben are often used together and are available as a mixture.

5.3.1 Butylparaben (BP)

Butylparaben (BP) is a commonly used long-chain alkyl paraben with antimicrobial properties, found in cosmetics, personal care products, and pharmaceuticals.

5.3.1.1 General Toxicity
The SCCS (2013) considered the NOEL for BP to be 2 mg/kg/day in male juvenile rats, based on a subcutaneous exposure study by Fisher (1999). The SCCS has updated this in 2023 with a conservative NOAEL value of 325 mg/kg bw/day, based on reproductive and developmental effects [179].

BP does not have a classification as a hazardous chemical under CLP. It has higher estrogenic activity than methylparaben and ethylparaben, and is considered an endocrine-disrupting chemical under REACH.

5.3.1.2 Mechanism of action of obesogenic effects
In vitro studies show that BP increases lipid accumulation in 3T3-L1 preadipocytes and promotes adipogenic differentiation [73, 76, 180]. It has also been shown to redirect multipotent mesenchymal stem cells toward the adipocyte lineage, suggesting it may influence early cell fate decisions relevant to fat accumulation [181]. A structure-related mechanism of action has been suggested, in which the potency of obesogenic activity increases with alkyl chain length, placing BP among the more active parabens [73].

In an epidemiological study, prenatal exposure to BP has been associated with increased body fat percentage and android fat mass at the age of 7 in boys, but not in girls [182]. Additional studies also found associations between prenatal BP exposure and childhood overweight, although many of these studies have limitations, including small sample

sizes, co-exposure, reliance on single spot urine samples, lack of dietary or postnatal exposure data, and potential selection bias [183, 184].

5.3.1.3 Limit values from other studies

The SCCS (2023) has considered the decrease of anogenital distance (AGD) in males, which was observed in an oral rat study reviewed by Boberg et al. (2016), as the critical endpoint, resulting in a BMDL5% of 24.5 mg/kg bw/day [179]. On the basis of a comprehensive safety assessment of all available data, including concerns relating to endocrine activity, the SCCS concluded that the use of BP as a preservative in cosmetic products is safe at concentrations up to 0.14% (expressed as acid). The SCCS (2025) concluded that BP is safe for children of all age groups if the aggregate exposure does not exceed 0.245 mg/kg bw/day. Therefore, the SCCS concluded that the concentration of BP should remain at 0.14% (as acid) in rinse-off products, but be reduced to 0.002% in leave-on products and to 0.092% in oral care products for children [185].

5.3.1.4 Critical effect value

In a juvenile mouse study assessing post-weaning exposure to BP (100 mg/kg bw/day), no effects on adiposity, body weight or serum leptin levels were shown. However, significant alterations in metabolic gene expression were observed, indicating potential subclinical metabolic disturbances [75]. Another mouse study showed a non-significant increase in body weight in female, but not in male offspring upon maternal BP (1.75 µg twice per week s.c.) [182]. In this study, the fat mass was statistically significantly increased in female, but not in male offspring.

5.3.2 Ethylparaben (EtP)

Ethylparaben EtP is a short-chain alkyl paraben used as a preservative in personal care products, food, and pharmaceuticals.

5.3.2.1 General Toxicity

It exhibits estrogenic activity but is generally considered less potent than longer-chain parabens such as butyl- or propylparaben [186, 187]. Up to dose levels of 1000 mg/kg bw/day, EtP was shown not to adversely affect male reproductive function or the secretion of sex hormones [188].

EtP does not currently have a harmonised classification as hazardous under CLP.

5.3.2.2 Mechanism of action of obesogenic effects

Currently, there are no *in vivo* rodent studies that specifically demonstrate the obesogenic effects of EtP, such as increased body weight or adiposity. However, *in vitro* research has shown that EtP can promote lipid accumulation in 3T3-L1 adipocytes, indicating a potential for adipogenic activity, possibly through PPARy activation [33, 73]. Additionally, some epidemiological evidence suggests possible metabolic effects, although with inconsistent results. For instance, a positive association between urinary EtP concentrations and body weight has been reported in boys [189].

5.3.2.3 Limit values from other studies

EFSA (2004) considers an ADI of 10 mg/kg bw/day for the combined total of methylparaben and EtP [190]. This is based on a NOAEL of 1000 mg/kg bw/day observed in long-term toxicity studies and in studies on the male reproductive organs in juvenile rats.

5.3.2.4 Critical effect value

No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.3.3 Methylparaben (MeP)

Methylparaben (MeP) is widely used as a preservative in cosmetics, personal care products, food, and pharmaceuticals.

5.3.3.1 General Toxicity

All repeated dose toxicity studies reviewed by the SCCS in 2023 indicate a NOAEL of 1000 mg/kg bw/day for repeated dose toxicity. Additional studies, including combined repeated dose and reproductive toxicity studies, largely confirmed this NOAEL, although a ninety-day study suggested some endocrine-mediated effects and impacts on male reproductive parameters, but without related tissue damage. More recent studies did not confirm earlier findings of reproductive effects but did observe a reduced anogenital distance (AGD) in F2 pups at the highest dose, which is indicative of an anti-androgenic mode of action. This, along with observed effects on sperm, induced one study to identify a lower NOAEL of 300 mg/kg bw/day [191].

While MeP is generally considered to have low acute toxicity and does not currently have a harmonised classification as hazardous under CLP, concerns have been raised about its potential endocrine-disrupting properties. An intention for harmonised classification and labelling for ED environment and human health was submitted in June 2025 and withdrawn[12].

5.3.3.2 Mechanism of action of obesogenic effects

MeP is suspected of promoting adipogenesis via endocrine-disrupting mechanisms. *In vitro* studies indicate that MeP can shift the fate of multipotent mesenchymal stem cells towards the adipocyte lineage, contributing to increased fat cell differentiation [181]. An *in vivo* study in mice supports these findings, showing increased body weight (small effect), increase in fat mass, elevated leptin levels (2-fold), and upregulation of some lipogenic genes following early-life exposure [75].

5.3.3.3 Limit values from other studies

The SCCS (2023) considers the BMDL5% of 374 mg/kg bw/day, derived from the observed reduction in AGD in male F2 pups, to be the PoD for margin of exposure calculations. On the basis of a comprehensive safety assessment of all available data, including concerns relating to endocrine activity, the SCCS concluded that the use of MeP as a preservative in

[12] https://chem.echa.europa.eu/100.002.532/activities/clhProcess/8fb9139a35d436494d52caa6c3fc23f4?searchText=methylparaben

cosmetic products is safe at concentrations up to 0.4% (expressed as acid). Furthermore, its use is also considered safe at up to 0.4% in mixtures of esters, provided the total concentration of all esters does not exceed 0.8% (as acid) [191].

EFSA (2004) considers an ADI of 10 mg/kg bw/day for the combined total of MeP and EtP [190]. This is based on a NOAEL of 1000 mg/kg bw/day observed in long-term toxicity studies and studies on the male reproductive organs in juvenile rats.

5.3.3.4 Critical effect value

A study by Hu et al. (2016) provides a potential critical effect value for obesogenic effects of MeP. In this study, juvenile mice orally exposed to 100 mg/kg bw/day of MeP from postnatal day 21 to adulthood (8 weeks) exhibited increased adiposity, body weight, elevated serum leptin levels, and upregulation of lipogenic genes under a standard diet. However, no effects were observed in animals fed a high-fat diet, and no lower doses were tested, limiting dose-response characterisation [75]. Overall, the evidence suggests using the LOAEL of 100 mg/kg bw/day as a critical effect value for obesogenic effects in juvenile mice.

5.3.4 Propylparaben (PP)

Propylparaben (PP) is a widely used preservative in cosmetics, pharmaceuticals, and food products.

5.3.4.1 General Toxicity

Even though it is less estrogenic than BP, PP still exhibits endocrine-disrupting properties [186, 187].
In a 2013 opinion (SCCS/1514/13), the SCCS considered that the NOEL for BP of 2 mg/kg/day in male juvenile rats, based on a subcutaneous exposure study by Fisher (1999), could be used for PP. However, after reviewing additional studies published since that opinion, the SCCS suggested in 2021 that data on reproductive toxicity, neurotoxicity, and immunotoxicity in rats supports a higher NOAEL of 1000 mg/kg/day [192].

PP does not currently have a harmonised classification as hazardous under CLP.

5.3.4.2 Mechanism of action of obesogenic effects

Increased lipid accumulation has been observed in 3T3-L1 preadipocyte cells following exposure to PP, suggesting a potential for promoting adipogenesis [73]. The same study proposed a structure-related mechanism of action for BPA and PP, where longer alkyl chain length was associated with greater obesogenic potential. These findings suggest that PP may act as a metabolic disruptor, though *in vivo* confirmation remains limited.

Some epidemiological studies have explored associations between PP exposure and obesity-related outcomes. For instance, one study showed that maternal urine concentrations of propylparaben were associated with higher childhood BMI and obesity status [193].

5.3.4.3 Limit values from other studies

EFSA (2004) has stated that it was unable to recommend an ADI for PP due to the absence of a clear NOAEL for this substance. This decision reflects uncertainties in the available toxicological data, particularly regarding the identification of a safe exposure threshold, and highlights the need for further research to better characterise the safety of PP when used in food [190]. In 2021, however, according to the SCCS subsequent studies suggested a NOAEL of 1000 mg/kg bw/day [192]. On the basis of its safety assessment and considering concerns relating to the potential endocrine-disrupting properties of PP, the SCCS has concluded that PP is safe for use as a preservative in cosmetic products at concentrations up to a maximum of 0.14% [192].

5.3.4.4 Critical effect value

Sivaraman et al. (2018) investigated early-life oral exposure to PP in mice (10, 100, or 1000 mg/kg bw/day from postnatal days (PND) 4 to 90). No significant differences in body weight were observed until PND35. However, a slight but consistent increase in body weight was noted in treated groups thereafter. Although slight and not statistically significant, the observed trend during a critical developmental window suggests potential long-term metabolic disruption [194].

5.4 Other obesogens

5.4.1 Octocrylene (OC)

Octocrylene (OC) is an organic compound widely used as a UV filter in sunscreens and other cosmetic products.

5.4.1.1 General toxicology

OC has no harmonised classification under the CLP regulation for human health hazards. However, some studies have suggested that OC may degrade into benzophenone, a substance with known toxicological concerns [195, 196].

There are indications that OC may have endocrine-disrupting properties [196], based on *in vitro* and *in vivo* studies. Kunz and Fent (2006) tested a set of eighteen UV filters including OC using *in vitro* recombinant yeast systems with either a human oestrogen (hERα) or androgen receptor (hAR). In this study, OC was mainly associated with anti-androgenic/androgenic activities [197].

5.4.1.2 Mechanism of action of obesogenic effects

There is no *in vivo* or epidemiological data indicating obesogenic or metabolic effects of OC. One *in vitro* study by Ko et al. (2022) showed an increase in lipid accumulation in bone marrow-derived mesenchymal stem cells as well as in PPARγ nuclear receptor binding upon OC exposure [85], indicating that OC may have obesogenic effects.

5.4.1.3 Limit values from other studies

The SCCS (2021) jas evaluated OC as safe when used as a UV filter in cosmetic products at a concentration up to 9% in spray products and up to 10% in other applications [195, 196]. This was based on a EOGRT study showing reproductive toxicity with a NOAEL of 153 mg/kg.

However, the SCCS noted that benzophenone as an impurity and/or degradation product of OC should be kept at trace levels.

5.4.1.4 Critical effect value

No critical effect value (for the obesogenic endpoint in young animals) could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.4.2 Butylated hydroxytoluene (BHT)

Butylated hydroxytoluene (BHT) acts as a synthetic antioxidant, preventing oxidation in various products. It inhibits the oxidation process by scavenging and neutralising free radicals, preventing the breakdown of lipids, and inhibiting the formation of rancid flavours. It preserves food odour, colour, and flavour.

5.4.2.1 General toxicology

It should be noted that BHT exhibits complex metabolic pathways, with significant interspecies differences in metabolism. In humans, major metabolites are formed via oxidation of one or both tert-butyl groups of BHT, followed by glucuronidation. Pharmacokinetic studies in humans, involving two male subjects administered a single oral dose of BHT, demonstrated that cumulative excretion ranged from 63% to 67% of the administered dose. Additionally, BHT has been reported to accumulate in adipose tissue [198].

The endocrine-disrupting properties of butylated hydroxytoluene have been discussed in literature [199-201] as well as in regulatory instances such as EFSA and the SCCS, and consensus about the ED properties of BHT has not been found. Although BHT currently has no harmonised classification under the CLP Regulation, BHT is on Annex III (restricted substances) with specific maximum concentrations for certain product types of the Cosmetic Product Regulation.

5.4.2.2 Mechanism of action of obesogenic effects

Toxicological studies indicate that high doses of BHT can cause both renal and hepatic damage, with effects such as proteinuria, enzymuria, and histopathological changes observed in animal models [201-203]. These toxic effects are dose-dependent and raise concerns about the safety of long-term exposure, particularly for populations already at risk for obesity-related metabolic disorders.
Furthermore, according to Wada et al. (2004), BHT has estrogenic activity *in vitro* in 293 T cells from a concentration of 50 µmol/L [204]. Little is known about the potential obesogenic effects of this compound. One epidemiological study showed that mixture exposure to BHT with hexane, styrene, cyclohexanone, and 2-butoxyethanol was associated with obesity [32].

5.4.2.3 Limit values from other studies

EFSA established an ADI for BHT of 0.25 mg/kg bw/day. This ADI was derived from a NOAEL of 25 mg/kg bw/day, identified in 2 2-generation reproductive toxicity studies in rats [198]. The critical effects observed were dose-dependent reductions in litter size and pup body weight gain during the lactation period. An uncertainty factor of 100 was applied to

account for inter- and intra-species variability. The selected NOAEL also covers the increased incidence of hepatocellular adenomas and carcinomas observed in the studies [198].
The SCCS concurred with EFSA in their 2021 opinion [201]. BHT has been considered to be safe when used as a preservative in cosmetic products at a concentration up to 0.001% in mouthwash, 0.1% in toothpaste, and 0.8% in other leave-on and rinse-off products [201].

5.4.2.4 Critical effect value

There is currently no established PoD from juvenile or developmental toxicity studies for BHT in mammals. Reviews and regulatory assessments indicate that published studies investigating the developmental or reproductive toxicity of BHT via oral exposure in (juvenile) mammals are lacking, and therefore, no PoD for developmental or reproductive endpoints has been identified [203, 205].

5.4.3 Triphenyl phosphate (TPP)

Triphenyl phosphate (TPP) is an organophosphate and is used as a flame retardant and plasticiser, as well as in adhesives, sealants and in cosmetic products. In cosmetics, it is mainly used to soften polymers. It can be found in, for example, nail products such as nail polish [206]. Probably due to its use as a flame retardant, it can also be found in house dust [207].

5.4.3.1 General toxicity

TPP has shown to induce liver toxicity and endocrine disruption, and there are some indications of neurotoxicity and developmental toxicity [206, 208-210].

- Liver toxicity: TPP induced centrilobular hypertrophy and an increase in liver weight at ≥105 mg/kg bw in rats.
- Neurotoxicity: a decrease of cholinesterase activity has been reported, but no other neurotoxicity effect has been recorded. It is noted that delayed neuropathy of TPP may not be sufficiently assessed on the basis of the available data.
- Developmental toxicity: malformations are seen in rodents exposed to TPP at 200 mg/kg bw/day, but data was insufficient to draw conclusions.
- Endocrine disruption: TPP interacts with nuclear receptors (ERα and ERβ agonistic activity, AR antagonistic activity, GR antagonistic activity, and PXR agonistic activity) *in vitro*. Moreover, there are some *in vitro*, *in vivo,* and *in silico* data on possible effects of TPP on thyroid maternal hormones, also reflected by modifications to the expression of some of the related genes and proteins of fishes. However, the data is considered insufficient for conclusions due to a lack of *in vivo* data.

TPP has no harmonised classification under the CLP. TPP is included in the SVHC Candidate List under REACH. It meets the criteria of substances of very high concern as set out in Article 57f of REACH, on

the basis of endocrine-disrupting properties for the environment[13]. In 2026, the process for placing TPP on Annex XIV started[14].

5.4.3.2 Mechanism of action of obesogenic effects

Perinatal exposure to TPP triggers metabolic disturbances characterised by enhanced weight gain and enhanced adiposity that could be connected to enhanced plasma levels of leptin and possibly to leptin resistance explaining an enhanced food intake. As such, TPP may be considered to be a developmental obesogen.

One hypothesis for the mode of action is that TPP acts as a PPARγ activator by binding to this receptor. PPARγ affects the differentiation of precursors into adipocytes, thereby stimulating adipogenesis. This will result in obesity as an adverse outcome. However, the evidence is insufficient and it is uncertain whether PPARγ activation is the sole mechanism involved and whether this activation shown at a very high concentration will be sufficient to result in obesity [211].

Another possible MoA is lipid metabolism disorder through the activation of the epidermal growth factor receptor (EGFR) [212, 213]. EGFR has been implicated in the regulation of adipocyte function and differentiation. The available data suggests a mechanism in which TPP promotes adipocyte differentiation *in vitro* and metabolic dysfunctions in mice through activation of the EGFR, but also AKT, a downstream effector of EGFR that is critical to the regulation of adipocyte metabolism and differentiation.

Interestingly, France performed a Risk Management Option Analysis (RMOA) on TPP in 2019. They concluded, among other things, that TPP may be considered to be a developmental obesogen [214] on the basis of enhanced weight gain and enhanced adiposity, as observed in a perinatal exposure study [215].

5.4.3.3 Limit values from other studies

No TDI is derived for TPP. The U.S. Food and Drug Administration (FDA) included TPP on the list of indirect food additives.

In 2024, the SCCS published their opinion on TPP. On the basis of the currently available information, it was not possible for the SCCS to conclude on the safety of TPP because a genotoxicity potential could not be excluded [206].

In 2024, a Maximum Permissible Risk value (in Dutch: Maximaal Toelaatbaar Risiconiveau; MTR) of 0.12 mg/m^3 was derived for TPP, based on liver and thyroid hypertrophy detected in a 90-day oral rat study [216].

5.4.3.4 Critical effect value

Several studies have shown effects of TPP exposure on body weight or other parameters that may be related to obesity:

[13] https://chem.echa.europa.eu/100.003.739/obligations/candidateList/details
[14] https://chem.echa.europa.eu/100.003.739/activities/authorisationProcess/7c5d4300b09c14e84b067644ff4f9b42?searchText=triphenyl%20phosphate

- Wang et al. (2019) exposed pregnant ICR mice to TPP at gestation days 6-21 via oral gavage. An increased body weight (no quantitative data) was seen in 4-10-week-old mice exposed to 100 and 1000 µg/kg bw. The highest dose was tested in a second experiment, and showed induction of increased liver weight and fat mass, hepatic steatosis, impaired glucose homeostasis, insulin resistance, and increased mRNA levels of genes involved in lipid metabolism, especially lipogenesis and lipid accumulation in 10-week-old mice.
- In another study, C57BL/6 mice were exposed to 1 or 5 mg/kg bw/day TPP during gestation days 0-18 and offspring was investigated at PND48. Gestational TPP exposure induced hyperlipidemia in male offspring, it dose-dependently increased the weight of body and liver, levels of serum lipid, and enlarged lipid droplets in white adipose tissue [217].
- Female rats were exposed to 170 µg/animal/day of TPP via food, from gestational day 8.5 to weaning. A statistically significant increase in body and fat mass was observed in 3.5-month-old male and female rats (no quantitative data), while leptin and cumulative energy intake were elevated in males and females, respectively. Independent of body mass, perinatal TPP exposure accelerated the onset of type 2 diabetes mellitus in males and increased plasma non-esterified-fasting fatty acids (Green et al., 2017).

In accordance with the available data, a critical effect value of <100 µg/kg bw/day may be considered, based on a body weight increase in 10-week-old mice at 100 µg/kg bw/day.

5.4.4 4-nonylphenol (4NP)

4-nonylphenol (4NP) is an organic compound, mainly used in the production of nonylphenol ethoxylates, which are common surfactants in for instance industrial detergents and paints.

5.4.4.1 General toxicology

4NP has no harmonised classification as hazardous under the CLP regulation. 4NP is listed on the REACH SVHC Candidate list as an endocrine-disrupting chemical for the environment. Furthermore, the use of 4NP in concentrations above 0.1% is restricted under REACH for consumer products such as detergents, textiles, and cosmetics.

A multigeneration study in rats showed increased incidences of renal tubular degeneration in both sexes and across all generations. This effect was observed at the lowest tested dose level, 15 mg/kg bw/day, which is therefore considered to be the LOAEL. Furthermore, for endocrine disruptive effects of 4NP, a NOAEL of 15 mg/kg bw/day was established in rats [218], based on reproductive effects in a multigeneration study.

5.4.4.2 Mechanism of action of obesogenic effects

Hao et al. (2012) demonstrated an obesogenic mode of action for 4NP *in vitro* and *in vivo*. In 3T3-L1 preadipocytes, low concentrations of 4NP were found to induce adipocyte differentiation and upregulate the expression of PPARγ as well as its target genes required for

adipogenesis. *In vivo*, Hao et al. (2012) showed that perinatal exposure to 4NP (0.05 mg/kg bw/day) in mice resulted in increased body weight in both male and female offspring. Furthermore, increased fat pad accumulation was observed at 0.25 mg/kg body weight per day in female offspring; this effect was also seen in males at the lower dose of 0.05 mg/kg body weight per day [78].

Interestingly, Zhang et al. (2023) showed that 4NP (5 µg/kg bw/day) in first-generation (F1) rats and a high-fat diet in F1 offspring synergistically regulate weight gain, adiposity, and expression of lipid metabolism genes in F2 offspring [219].

These findings suggest that exposure to 4NP during critical developmental periods may raise the risk of obesity, possibly by disrupting hormonal processes involved in fat storage and body weight regulation [78]. However, an epidemiology study showed that the urinary or serum levels of 4NP did not significantly differ between obese and reference populations, whereas other compounds in this study were [79].

5.4.4.3 Limit values from other studies

The Danish Environmental Protection Agency has established a TDI of 0.005 mg/kg bw/day, based on a LOAEL of 15 mg/kg/day for reproductive effects and kidney toxicity observed in an oral 3-generation study in rats, and assessment factors of 3000 in total [218, 220].

5.4.4.4 Critical effect value

The study by Hao et al. (2012) provides a potential critical effect value for obesogenic effects of 4NP. In this study, perinatal exposure to 0.05 mg/kg bw/day 4NP resulted in statistically significant increases in body weight in male and female offspring (+18% and +17%, respectively) and increased fat pad accumulation in male offspring [78].

5.4.5 Styrene (Styr)

Styrene (Styr) is a volatile organic compound and is mainly used as a pre-cursor for the plastic polystyrene. Consumers can be exposed to styrene via low levels of naturally occurring styrene in food or from transfer of Styr-based packaging [221]. Further, children may be exposed to Styr via mouthing of toys that contain Styr [222].

5.4.5.1 General toxicity

Styr has a harmonised classification for skin and eye irritation (Category 2), acute toxicity (Category 4, inhalation), specific target organ toxicity upon repeated exposure (STOT RE 1; hearing organs), and reproduction toxicity (Category 2; developmental toxicity).

Concerns are raised about the possible genotoxicity and carcinogenicity of styrene. In 2019, the IARC concluded that Styr is probably carcinogenic to humans (IARC Group 2A), with strong evidence of genotoxicity [223]. In addition, the Dutch Health Council recommends a European classification for carcinogenicity Category 1B and mutagenicity Category 2 [224]. However, EFSA evaluated the oral genotoxicity of Styr and concluded that there is no evidence of oral genotoxicity by Styr [225].

Serious effects on the respiratory system are observed in humans upon repeated exposure to styrene, which needs further evaluation by regulatory agencies.

Styr was identified as an endocrine disruptor by The Endocrine Disruption Exchange Research Institute (TEDX, 2011) [226]. However, other evaluations conclude that Styr does not cause endocrine disruption. In the RAR (2002), it was concluded that there is no evidence that Styr has significant endocrine disruption potential. Further screening of a broader range of studies was performed by Denmark (2014); however, the outcome of this screening was that the initial ED concern could not be confirmed [227]. More recently, Borgert (2023) concluded that Styr cannot be deemed an endocrine disruptor [228].

5.4.5.2 Mechanism of action of obesogenic effects

One epidemiological study showed an association of higher Styr concentrations in a classroom and obesity in children [32]. The OR for obesity was 1.78, with a 95% CI of 1.52-2.10. The median Styr concentration in the class room was 0.36 µg/m^3, with a range of 0-6.97 µg/m^3. Furthermore, a cross-sectional study showed an association between the concentration of two styrene metabolites (i.e. phenylglyoxylic acid and mandelic acid) in urine and obesity in adults. [229].

5.4.5.3 Limit values from other studies

WHO (1984) has established a TDI of 7.7 µg/kg bw/day derived from a NOAEL of 7.7 mg/kg bw/day for reduced body weight in a 2-year drinking water study [156].

Styr is authorised to be used as a monomer and/or starting material for the manufacture of plastic food contact materials (FCM) and is currently listed in Annex I of Regulation (EU) No 10/2011, without a specific migration limit (SML).

In view of the remaining uncertainty regarding the genotoxicity of Styr and the lack of a migration limit combined with a high migration potential, the Commission is preparing a measure to lay down a migration limit of 40 ppb in foods, based on the guidance value established for Styr in drinking water set by the WHO [225].

5.4.5.4 Critical effect value

No critical effect value could be derived, as no studies in (juvenile) animals were found that observed an increase in body weight or effects on other obesogenic endpoints.

5.5 Overview mechanisms of action of obesogens

In this section, an overview is given of studies suggesting (possible) obesogenic mechanisms of the selected chemicals (Table 5). Please note that this is not a complete overview of all available studies. In addition, the studies underwent a non-comprehensive quality assessment on the basis of expert judgement.

The table provides an overview of evidence from *in vitro*, *in vivo*, and epidemiological studies investigating the obesogenic potential of the selected chemicals. For each chemical, *in vitro* studies are summarised with a focus on mechanisms of action, such as PPARγ agonism and other relevant signalling pathways, given their pivotal roles in adipocyte differentiation and lipid storage. Activation of these pathways serves as an early marker for obesogenic activity. Additionally, the table notes effects on lipid accumulation and adipocyte differentiation observed in *in vitro* models, as these endpoints demonstrate direct effects on fat cell development. *In vivo* studies are presented by highlighting changes in body weight, adiposity, and metabolic gene expression, which collectively indicate a physiological impact. Metabolic parameters, including leptin, insulin, glucose, cholesterol, and triglyceride levels, are also included, as alterations in these markers are important for assessing disruptions in energy balance and overall metabolic health. Last, epidemiological studies that investigate chemical effects on body weight and/or BMI are included to provide supporting evidence from human populations, thereby strengthening and complementing the findings from experimental models.

Explanation of the signs used in the table:

↑	Statistically significant increase found in referenced studies (for metabolic gene expression, significantly altered metabolic gene expression found)
↔	No statistically significant effects found in referenced studies
↓	Statistically significant decrease found in referenced studies

Table 5 Overview of literature describing parameters and effects that may be related an obesogenic mechanism

Chemical	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
Bisphenols									
BPA	↑ [33, 73, 230, 231] ↔ [44, 232-234]	↑ GR [234] ↑LXR/RXR [230, 235] ↑FABP4 [231]	↑ [33, 34, 231, 233, 234] ↔ [236] ↓ [236]	↑ [109, 237-242] ↔ [237, 238, 242-244] ↓ [238]	↑ [109, 237-240, 243] ↔ [237, 238]	*Glucose* ↑ [240, 243, 244] ↔ [109, 240, 243, 244] *Cholesterol* ↔ [239, 244] *Triglyceride* ↑ *[244]* ↔ [239] *Leptin*	↑ [109, 237, 239, 240, 242]	↑ [29, 36, 37, 138] ↔ [29, 74, 79, 138, 245, 246] ↓ [29]	Yes, *in vitro*, *in vivo* and epidemiological studies

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
						↑ [238, 240] ↔ [238] *Insulin* ↑ [238, 240, 243, 244] ↔ [238]			
BPF	↑ [33] ↔ [233]		↑ [33, 233]	↑ [123] ↔ [113] ↓ [247]	↑ [123]	*Cholesterol* ↑ [113] ↓ [247]		↑ [36] ↔ [36, 245] ↓ [245]	Yes, *in vitro* and epidemiological studies
BPS	↑ [33, 233]	↑ FABP4 [233] ↑LXR/RXR	↑ [33, 233]	↑ [53, 248, 249] ↔	↑ [53, 248]	*Glucose* ↑ [53, 55] ↔	↑ [53, 55, 248]	↑ [36] ↔	Yes, *in vitro*, *in vivo*, and epidemiological studies

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
		[235]		[248, 249]		[248] *Cholesterol* ↑ [53, 55, 248] *Triglyceride* ↑ [53, 55] ↔ [248] *Leptin* ↑ [55, 248] *Insulin* ↑ [55, 248]		[36, 74, 245, 246]	
Phthalates									
DBP	↑ [250]	↑PPARa [250]		↑ [140, 143, 144]	↑ [140]	*Glucose* ↑ [140, 251]	↑ [140]	↑ [79, 137-139]	Yes, *in vitro*, *in vivo*, and

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
	Metabolite (MBP) ↔ [250]			↔ [143, 145] ↓ [144]	↔ [145]	*Insulin* ↑ [140] *Leptin* ↑ [140] *Triglycerides* ↑ [140, 251]		Metabolite (MBP) ↔ [79]	epidemiological studies
DEHP	↔ [250, 252] *Metabolite (MEHP)* ↑ *[154, 232, 253, 254]*	↑ Pi3k [155] ↑ PXR [255] *Metabolite (MEHP)* ↑ *PPARa*	↑ [85, 155, 236] ↔ [84] ↓ [252]	↑ [83, 84, 145, 155, 160, 257] ↔ [84] ↓	↑ [155] ↔ [145] ↓ [152]	*Glucose* ↑ [84, 251] ↔ [152] *Cholesterol* ↑ [84, 257]	↑ [83, 84, 155, 160, 257, 258]	↔ [79, 259] *Metabolite (MEHP)* ↑ *[260]* ↔ *[79]*	Yes, *in vitro*, *in vivo*, and epidemiological studies

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
		[232, 250] ↑ PXR [255, 256]	*Metabolite (MEHP)* ↑ *[154, 232]*	[152] *Metabolite (MEHP)* ↑ *[154]*	*Metabolite (MEHP)* ↑ *[154]*	*Triglyceride* ↑ [84, 257] ↓ [152, 155, 257] *Leptin* ↑ [160, 257] *Insulin* ↑ *[257]* ↓ [152]			
DCHP	↑ [234]	↑ GR [234] ↑ PXR [163]	↑ [164, 234]	↔ [175, 261]	↔ [261]	*Cholesterol* ↑ [163] ↔ [175]	↑ [163, 164, 261]		Yes, *in vitro* and *in vivo* studies

Chemical	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
						Triglyceride ↑ [175] ↔ [163] *Glucose* ↔ [175]			
BBP	↑ [73, 168, 169, 262, 263]	↑ miR-34a-5p [264]	↑ [85, 168, 169, 262-265]	↑ [170] ↔ [170]					Yes, *in vitro* and *in vivo* studies
DOTP			↑ [33]					↔ [259]	Yes, *in vitro* study
DHP				↔ [175]		↑ *Triglyceride* [175] ↔ *Cholesterol*			Yes, *in vivo* study

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
						[175]			
Parabens									
BP	↑ [73, 180, 232, 266] ↔ [182]	↑ GR [180]	↑ [73, 76, 180, 181, 232]	↔ [75, 182]	↑ [182] ↔ [75, 182]	*Leptin* ↑ [182] ↔ [75] *Glucose* ↔ [75, 182] *Insulin* ↔ [75, 182] *Triglyceride* ↔ [75]	↑ [75]	↑ [182-184] ↔ [74, 182]	Yes, *in vitro*, *in vivo*, and epidemiological studies
EtP	↔ [180]		↑ [33, 180]					↑ [189]	Yes, *in vitro*, and

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
								↔ [74]	epidemiological studies
MeP	↔ [180, 267]		↑ [181, 267] ↔ [33, 180]	↑ [75, 268]	↑ [75]	*Leptin* ↑ [75] *Glucose* ↔ [75] *Insulin* ↔ [75] *Triglyceride* ↔ [75]	↑ [75]	↔ [74]	Yes, *in vitro* and *in vivo* studies
PP	↑ [73, 180, 267]		↑ [180, 267]	↔ [194]				↑ [193].	Yes, *in vitro*, and

Chemi-cal	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
			↔ [33]					↔ [74]	epidemiological studies
Other									
OC	↑ [85]		↑ [85]						Yes, *in vitro* study
BHT				↓ [269]				↔ [32]	Insufficient
TPP	↑ [213, 270, 271] ↔ [254]	↑ EGFR [212]	↑ [212, 213, 270, 271]	↑ [272, 273] ↔ [212, 213, 274]	↑ [212, 213, 272, 273] ↔ [274]	*Insulin* ↑ [212, 272] *Glucose* ↑ [212] ↔ [213] *Triglycerides* ↑ [213, 272]	↑ [212, 213, 272, 273, 275]		Yes, *in vitro* and *in vivo* studies

Chemical	***In vitro* studies**			***In vivo* studies**				**Epidemiological studies**	**Evidence obesogenic potential**
	PPARγ agonism	*Other pathways*	*Lipid accumulation or adipocyte differentiation*	*Body weight*	*Adiposity*	*Leptin, insulin, glucose, cholesterol, or triglyceride levels*	*Change in metabolic gene expression*	*Body weight and/or BMI*	
						Cholesterol ↑ [213]			
4NP	↑ [78, 80]	↓ Wnt [80]	↑ [78, 80] ↓ [80]	↑ [78, 219]	↑ [78, 219, 276]	*Cholesterol* ↑ [78, 276] *Glucose* ↑ [78, 219] *Triglyceride* ↔ [78, 219] *Leptin* ↑ [219, 276]	↑ [78, 219, 276]	↔ [79]	Yes, *in vitro* and *in vivo* studies
Styr								↑ [32, 229]	Yes, epidemiological study

5.6 Overview of critical effect values related to obesity

Table 6 Overview of critical effect values related to obesity and points of departure in current assessments

Chemical	Critical effect value	Limitations	Point of departure (PoD) (relevant effect)	Critical effect value < PoD?
Bisphenols				
BPA	LOAEL: 5 µg/kg bw/day Based on increased body weight[1] [109]. • Species: C57BL/6J • Exposure: Five-week-old mice for 30 days • Diet: chow diet (10% kcal in fat) vs. high fat diet (45 kcal in fat)	Extrapolation LOAEL to NOAEL required No significant difference in body weight and fat mass High-fat diet	NOAEL: 0.475 µg/kg bw/day Based on immune effects [106].	Though several studies indicate (developmental) obesogenic effects of BPA, no clear critical effect value could be derived
BPF	LOAEL: 152.5 µg/kg bw/day Increased body growth (5%), abdominal adiposity, and urine output in male rats [123]. - Species: male N:NIH heterogeneous stock (HS) rats - Exposure: Three-week-old rats for five weeks - Diet: diet formulated to be devoid of phytoestrogens	Extrapolation LOAEL to NOAEL required	LOAEL: 5 mg/kg bw/day Based on endocrine and reproductive effects [247].	Yes (although for indication a PoD was selected, no reference values have been published)
BPS	LOAEL: 1.5 µg/kg bw/day Increased body weight and fat mass in males[1] [55]. - Species: C57Bl/6 mice - Exposure: treatment began at gestational day 0 and continued in offspring up to 23 weeks of age	Extrapolation LOAEL to NOAEL required High-fat diet	NOAEL: 20 mg/kg bw/day Based on developmental toxicity [130].	Yes (although critical effect value is based on high-fat diet study)

Chemical	Critical effect value	Limitations	Point of departure (PoD) (relevant effect)	Critical effect value < PoD?
	- Diet: offspring mice were fed with a standard or high fat diet			
Phthalates				
DBP	LOAEL: 5 mg/kg bw /day Based on increased body weight, fat mass, insulin resistance and effects on lipid metabolism[1] [140]. - Species: obesity-prone SPF C57BL/6J mice - Exposure: Gestational day 12 until postnatal day 7 - Diet: Standard diet containing (g%): 22.60% protein, 50.87% carbohydrate, 3.37% lipid, 3.33% fibres, 6.88% mineral and 12.95% water Effect on body weight was observed at same concentration level (5 mg/kg bw/day) in another study (although only in female offspring), which showed effects persisted until adulthood [145].	Single dose tested, dose-response not possible Extrapolation LOAEL to NOAEL required Limited methodology reporting on analysis, possibility of inflated statistical power	LOAEL: 2 mg/kg bw/day Based on reduced spermatocyte development and effects on mammary glands in a developmental study in rats. [133].	No
DEHP	LOAEL: 0.05 mg/kg bw/day Based on increased body weight[1], fat mass[1], impaired insulin tolerance, and altered metabolic function in female mice [155]. - Species: obesity-resistant 129S6 (F28) mice - Exposure: 10 weeks - Diet: Standard diet, not specified	Exposure during adult life stage is potentially less sensitive compared to exposure during development Single dose tested, dose-response not possible Gender-specific effects: effects on body weight and fat mass not observed in male mice	NOAEL: 4.8 mg/kg bw/day Based on effects on the testis observed in F1 in a three-generation reproductive toxicity study in rats [133].	Yes

Chemical	Critical effect value	Limitations	Point of departure (PoD) (relevant effect)	Critical effect value < PoD?
	A LOAEL of 0.05 mg/kg bw/day was also found for increased food intake (+20%), body weight[1] and increased visceral adipose tissue in another study in female mice and increased visceral adipose tissue F1 offspring (male and female) [160]. *In utero* exposure (5 mg/kg bw/day) resulted in transient increases in body weight in males [251].	Effects on body weight were transient Extrapolation needed LOAEL to NOAEL		
DCHP	-	-	NOAEL: 10 mg/kg bw/day [162].	No critical effect value could be derived
BBP	-	-	NOAEL: 50 mg/kg bw/day [133].	No critical effect value could be derived
DOTP	-	-	NOAEL: 868 mg/kg bw/day [172].	No critical effect value could be derived
DHP	-	-	LOAEL: 380 mg/kg bw/day [174].	No critical effect value could be derived
Parabens				
BP	-	-	BMDL5%: 24.5 mg/kg bw/day [179].	No critical effect value could be derived
EtP	-	-	NOAEL: 1000 mg/kg bw/day [188].	No critical effect value could be derived
MeP	LOAEL: 100 mg/kg bw/day Based on increased adiposity and body weight[1] [75]. - Species: obesity-prone C57BL/6J mice - Exposure: 12 weeks	Extrapolation LOAEL to NOAEL Single (high) dose tested, dose-response not possible Gender-specific effects: only female mice were tested Diet-specific effects: No effects of MP exposure observed when using a high fat diet	BMDL5%: 374 mg/kg bw/day Based on reduction in AGD in F2 pups in EOGRTS and effects on sperm in an oral 90-day repeated dose toxicity study [191].	Yes

Chemical	Critical effect value	Limitations	Point of departure (PoD) (relevant effect)	Critical effect value < PoD?
	- Diet: Standard with minimal natural phytoestrogens (2020X) or high-fat diet (TD.120059) An increase in body weight upon 300 µg/kg bw/day methylparaben exposure was also observed in another study in male adult mice, however adiposity was not analysed [268].			
PP	-	-	NOAEL: 1000 mg/kg bw/ day [192].	No critical effect value could be derived
Other				
OC	-	-	NOAEL: 76.5 mg/kg bw/ day [196].	No critical effect value could be derived
BHT	-	-	NOAEL: 25 mg/kg bw/day [198].	No critical effect value could be derived
TPP	LOAEL: 100 µg/kg bw/day NOAEL: 10 µg/kg bw/day Based on increased body weight in juvenile mice[1] [272]. - Species: ICR mice - Exposure: Gestational day 6 until postnatal day 21 - Diet: not specified (high dose, 1000 µg/kg bw/day, tested with both low-fat and high-fat diet) Effects on adiposity observed in multiple studies, albeit at higher doses [212, 213, 273].	Gender-specific effects: only male mice were tested Limited methodology reporting on analysis, possibility of inflated statistical power	NOAEL: 20 mg/kg bw/day Based on liver effects in an oral 90-day repeated dose toxicity study in rats [206].	Yes
4NP	LOAEL: 0.05 mg/kg bw /day	Extrapolation LOAEL to NOAEL Effects not observed at high dose (0.5 mg/kg bw/day)	LOAEL: 15 mg/kg bw/day Based on endocrine disruptive effects upon oral exposure	Yes

Chemical	Critical effect value	Limitations	Point of departure (PoD) (relevant effect)	Critical effect value < PoD?
	Based on increase in body weight in male (+18%) and female (+17%) offspring [78]. - Species: obesity-prone C57BL/6J mice - Exposure: Gestational day 12 until postnatal day 7 - Diet: not specified Effects observed in other studies, high fat diet exacerbated effects [219, 276].	Limited methodology reporting on analysis, possibility of inflated statistical power	observed in a multigenerational study in rats and renal toxicity observed in a 20 week repeated dose study in rats [218].	
Styr	-	-	NOAEL: 7.7 mg/kg bw/day [156].	No critical effect value could be derived

1 Results only presented in figures, % cannot be calculated.

6 Measurements in consumer products

6.1 Analytical method

6.1.1 Method development

The method development was performed on a GC-MS of Agilent Technologies, GC-7890B/MS-5977C with an Agilent PAH select column (select PAH, CP7462, length 30m, 0.25 mm in diameter and film thickness 0.15 µm) and certified standards. Ethyl acetate was chosen as the extraction solvent. GC-MS settings are described in Appendix 5.

Initially, 22 obesogens were selected for method development. However, tetrabromobisphenol-A (TBBPA) and bis(2-ethylhexyl) tetrabromophthalate (TBPH) did not fit into the same method with the other chemicals from the list since these chemicals were not volatile enough for GC-MS. After a run time of 90 minutes, only a very weak signal for these brominated compounds has been observed. This has been verified by other research groups, which have also found that TBBPA is not measurable (without derivatisation) using GC-MS [277]. For TBBPA and TBPH, an HPLC method (coupled with UV or MS) would be more suitable. Therefore, these chemicals were excluded from the GC-MS measurements. The other 20 chemicals could be properly separated and selectively identified.

Research was done to derive one to three suitable internal standards. It was decided to include ethyl paraben-d4 and dibutyl phthalate-d4 as suitable internal standards, which were separated at various locations in the chromatogram.

As a number of the selected potential obesogens are used in plastics and to prevent contamination by release from plastics, glass was used as much as possible. Blanks were included to correct for any background and to exclude carry-over.

Both liquid-liquid extraction with water and ethyl acetate and single liquid extraction with ethyl acetate were tested. It was established that both methods gave comparable results in the amount of extracted substance. Ethyl acetate was chosen as the extraction solvent, as this saved a drying step in the process.

6.1.2 Validation

Limits of detection (LOD) and quantification (LOQ) were determined by 3x and 10x the standard deviation (SD) of 10 injections at 500 ng/mL, respectively (see also Figure A1 in Appendix 6). LOD and LOQ are statistical thresholds that separate true analytical signals from random measurement noise. A common pragmatic convention is to define the LOD as the level of signal that exceeds the background variability by about 3 times the standard deviation (3xSD), and the LOQ as the level that exceeds background variability by 10 times the SD (10xSD).

Calibration curves consisted of the following levels: 0 – 10 – 50 – 100 – 500 - 1000 ng/ml and showed good linearity ($r^2 > 0.99$).

Because cosmetic products cover a wide range of matrices, it was impossible to perform a complete validation for each matrix separately. The sample set for validation consisted of six separate products: two lip balms, two face creams and two deodorant rollers. These three matrices were used to represent the entire product group of cosmetic products. For pragmatic reasons, a standard mix of the components of a known concentration was chosen, as well as a few repetitions per day for spike recovery and within-lab reproducibility. Validation experiments were performed on three days (one day, experiments were performed in duplicate, while on the other two days, samples were analysed once). Every sample was extracted both without a spike and spiked with 500 ng and 1000 ng of the standard mix.

Approximately 300-500 mg of each sample was weighed for validation. For follow-up research, approximately 500 mg per sample was used per extraction, extracted by 15 mL ethyl acetate as extraction solvent.

After adding the solvent to the samples, they were mixed by swirling/shaking. Subsequently, the samples were shaken for 30 minutes (firm but without splashing in a shaking machine, 120 rpm). The Erlenmeyer flasks containing the extraction are then left for 30 minutes to allow solid particles to settle and the extraction layer to become clear. Then 3 mL of the upper layer was removed and passed through a 0.2 µm filter. The first few drops went into a waste bin; the remainder went into a vial.
Results were expressed as the amount of component per weight of product (w/w).

6.1.3 Results method development

Table 7 reports the LOD and LOQ of the twenty selected potential obesogens.

Table 7 Limits of detection (LOD) and limits of quantification (LOQ) of the twenty selected potential obesogens in the GC-MS method

Chemical	**LOD (ng/mL)**	**LOQ (ng/mL)**	**LOD (µg/g) in sample**	**LOQ (µg/g) in sample**
Bisphenols				
BPA	5	17	0.15	0.51
BPF	3	11	0.10	0.33
BPS	4	12	0.11	0.37
TCBPA	11	36	0.32	1.07
Phthalates				
DBP	5	18	0.16	0.54
DEHP	5	55	0.14	1.65
DCHP	6	20	0.18	0.59
BBP	10	15	0.31	0.45
DOTP	3	9	0.08	0.27
DHP	9	29	0.26	0.86
Parabens				

Chemical	LOD (ng/mL)	LOQ (ng/mL)	LOD (µg/g) in sample	LOQ (µg/g) in sample
BP	11	35	0.32	1.05
EtP	9	29	0.26	0.88
MeP	6	21	0.19	0.62
PP	7	22	0.20	0.66
Other				
OC	4	15	0.13	0.45
BHT	5	16	0.15	0.49
TPP	3	11	0.10	0.34
4NP	5	15	0.14	0.46
Styr	4	12	0.11	0.37
Tol	3	11	0.10	0.34

LOD and LOQ (ng/mL) were determined by the standard deviations (SD) of a 10-fold injection of the analytes at a concentration of 500 ng/ml.
SDx3 = LOD, SDx10 = LOQ.
LOD and LOQ are also expressed in µg analyte/g sample, based on a 500 mg sample extracted by 15 mL ethyl acetate.

Both bisphenols and parabens (80-120%) showed good recovery without any outliers. After exclusion of one or more outliers, also Styr, BHT, TPP, DOTP, DCHP, and OC showed good recoveries (80-120%). For Tol, both low recoveries (60-64%) and multiple outliers were reported while no viable recovery results were obtained for TCBPA.

The reproducibility was found to be good (relative standard deviation <20%) for most components and spike levels. OC had a reproducibility of 30% at the lower and 13% at the higher spike concentration. The reproducibility for Tol was poor (120% and 114% for the lower and higher pike concentrations, respectively) and TCBPA did not have any viable reproducibility results.

As both Tol and TCBPA showed poor recoveries and reproducibility in the validation experiments, these substances were excluded in further analysis in this study. As a result, eighteen potential obesogens were selected for analysis.

6.2 Selection of consumer products for chemical analysis

In this study, measurements of selected potential obesogens were conducted in a range of consumer products. This first report describes the results of measurements in cosmetics, a medical device, and several cleaning products. Subsequent reports will describe the results of measurements in toys (stuffed animals) and food contact materials.

The decision which consumer products to include in the categories cosmetics, medical devices and cleaning products was based on expert judgement, considering several key criteria. Primarily, product groups were chosen on the basis of their relative daily exposure (expressed in mg/kg body weight/day) and the proportion of the population using these products [278-281]. Priority was given to products with significant dermal exposure, although products associated with inhalatory and oral

exposure were also considered. Additionally, products for which the use is actively promoted by governmental health campaigns, such as sunscreen and toothpaste, were included in the analysis.

On the basis of these criteria, the following cosmetic product groups were selected for chemical measurements:

- Body lotion
- Deodorant (roller)
- Foundation
- Hand soap
- Perfume
- Shower gel
- Sunscreen
- Toothpaste

To broaden the scope of the analysis, several non-cosmetic consumer products were also included:

- Medical devices
  - Lubricants
- Detergents
  - Dishwashing liquid (for hand washing)
  - Fabric softener
  - Laundry detergent

Within each product group, specific types or brands were selected according to additional considerations. Preference was given to the most frequently sold products, as indicated by online sales data from major (drug)stores. Furthermore, products were chosen on the basis of the presence of one or more target chemicals, namely BP, EtP, MeP, PP, OC, BHT, TPP, and Styr. Special attention was also paid to variants specifically marketed for men and for children.

This systematic approach ensured that the products selected for analysis were both relevant in terms of consumer exposure and representative of the products available on the market.

6.3 Results

6.3.1 Cosmetics

An overview of the presence and levels of the eighteen selected potential obesogens in cosmetics is shown in Appendix 7, Table A.5-A.12. The absence of a component is reported as n.a. and results ranging between the LOD (limit of detection) and the LOQ (limit of quantification) are shown as <LOQ. Levels are expressed in % (w/w) (for conversion to µg/g: x10.000).

In general, no excessive concentrations of obesogens were detected in the tested products. Values >0.001% (w/w) were considered relevant for further analysis.

6.3.1.1 Body lotion

In two of the analysed body lotions, none of the potential obesogens were detected >0.001% (w/w). In one of the other products, 0.00373% (w/w) BPF, 0.00189% (w/w) EtP, 0.00115% (w/w) OC, and 0.0012%

(w/w) BHT were found. In the other body lotion, 0.00228% (w/w) BPS, 0.1332% (w/w) MeP, and 0.00129% (w/w) BHT were found.

6.3.1.2 Deodorant

In one of the analysed deodorants, none of the potential obesogens were detected >0.001% (w/w). In one of the other products, 0.00144% (w/w) BHT was found. In another deodorant, 0.00259% (w/w) EtP, 0.00237% (w/w) MP, 0.0015% (w/w) OC, and 0.0011% (w/w) BHT were found. In the last tested deodorant, 0.00112% (w/w) BHT was found.

6.3.1.3 Foundation

In one of the analysed foundations, none of the potential obesogens were detected >0.001% (w/w). In one of the other analysed foundations, 0.00167% (w/w) BPF, 0.0017% (w/w) BBP, 0.0109% (w/w) dioctyl terephthalate (DOTP), and 0.00102% (w/w) BHT were found. In another product only 0.00153% (w/w) 4NP was found. In the foundation tested last, only 0.25053% (w/w) MP was found.

6.3.1.4 Hand soap

In two out of the four analysed hand soap products, 0.00102 and 0.00143% (w/w) BHT was found.

6.3.1.5 Perfume

In one analysed perfume, only BHT was found (0.0482% (w/w). In another perfume, EtP (0.00181% (w/w)), MP (0.0346% (w/w)), BHT (0.0198% (w/w)), and Styr (0.00196% (w/w)) were found. In another perfume sample, 0.00302% (w/w) PP, 0.0482% (w/w) BHT, and 0.03300% (w/w) Styr were found, although the latter measurement concerns a level estimate as it was not or hardly found upon remeasurement after dilution. Remeasurement took place a couple weeks later. The results of the first measurement is above the calibration line and therefore concerns an estimate. In the perfume analysed last, 0.00189 % (w/w) DBP, 0.00152% (w/w) EtP, 0.00223% (w/w) BP, and 0.0357% (w/w) BHT were found.

6.3.1.6 Shower gel

In one of the analysed shower gels, none of the potential obesogens were detected >0.001% (w/w). Two shower gels both contained BHT (0.00144 and 0.00112% (w/w)). And another sample contained 0.00259% (w/w) EtP, 0.00237% (w/w) MP, and 0.00110% (w/w) BHT.

6.3.1.7 Sunscreen

In one of the analysed sunscreens, none of the potential obesogens were detected >0.001% (w/w). In one product 0.6219% (w/w) OC was found. In another sunscreen, 0.0144% (w/w) BPF, 0.00259% (w/w) BBP, and 0.00186% (w/w) PP were found. Another sunscreen sample contained 0.0785% (w/w) BPF, 0.00143% (w/w) PP, and 0.0026% (w/w) 4NP.

6.3.1.8 Toothpaste

In three out of the four tested toothpastes, BHT was found at concentrations >0.001% (w/w) (up to 0.00163% (w/w)). None of the other obesogens were detected >0.001% (w/w).

6.3.2 Medical devices

An overview of the presence and levels of the eighteen selected potential obesogens in tested medical devices is presented in Appendix 7, Table A.13. The absence of a component is reported as n.a. and results ranging between the LOD (limit of detection) and the LOQ (limit of quantification) are shown as <LOQ. Levels are expressed in % (w/w) (for conversion to µg/g: x10.000). Values >0.001% (w/w) were considered relevant for further analysis.

In two of the analysed lubricants, none of the obesogens were detected >0.001% (w/w). In another lubricant, 0.00130% (w/w) DCHP, 0.00135% (w/w) BHT, and 0.07230% (w/w) Styr were found. Another lubricant sample contained BPA, BPS, DEHP, DCHP, DOTP, EtP, PP, MP, OC, and Styr at levels >0.001% (w/w).

6.3.3 Detergents

An overview of the presence and levels of the eighteen selected potential obesogens in tested detergents is given in Appendix 7, Table A.14-A16. The absence of a component is reported as n.a. and results ranging between the LOD (limit of detection) and the LOQ (limit of quantification) are shown as <LOQ. Levels are expressed in % (w/w) (for conversion to µg/g: x10.000).
None of the tested obesogens were indicated on the labels of the products. Values >0.001% (w/w) were considered relevant for further analysis.

6.3.3.1 Dishwashing liquid

In one of the analysed dishwashing liquids, none of the obesogens were detected >0.001% (w/w). In one product, 0.00117% (w/w) BBP was found. In another dishwashing liquid sample, 0.0113% (w/w) BPF and 0.00111% (w/w) Styr were found. Yet another product contained 0.00165% (w/w) BPF, 0.00173% (w/w) BHT, and 0.00273% (w/w) Styr.

6.3.3.2 Fabric softener

One of the analysed fabric softeners contained 0.00386% (w/w) MP and 0.00214% (w/w) BHT. In another product, 0.00105% (w/w) EtP and 0.00248% (w/w) MP were found. The third fabric softener sample contained 0.00198% (w/w) MP and 0.00303% (w/w) BHT. Another sample contained 0.00114% (w/w) BPA and 0.00308% (w/w) BHT.

6.3.3.3 Laundry detergent

None of the tested potential obesogens were detected at concentrations >0.001% (w/w) in laundry detergent.

6.3.4 Summary of results

Table 8 shows an overview of the top concentrations of the range of measured concentrations (concentrations >0.001% (w/w)) of the eighteen selected potential obesogens in all three product categories.

Table 8 Overview of the top measured concentrations of eighteen selected potential obesogens present in cosmetic products (n=32), medical devices (lubricant, n=4), and detergents (n=12) (concentration and product only provided when >0.001% (w/w))

Chemical	Cosmetics	Medical Devices	Detergents
Bisphenols			
BPA	- (found in 0/32 products)	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products)	Up to 0.00114% (w/w) in fabric softener (found in 1/12 products)
BPF	Up to 0.0785% (w/w) in sunscreen (found in 4/32 products)	- (found in 0/4 products)	Up to 0.0113% (w/w) in dishwashing liquid (found in 2/12 products)
BPS	Up to 0.00228% (w/w) in body lotion (found in 1/32 products)	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products)	- (found in 0/12 products)
Phthalates			
DBP	Up to 0.00189% (w/w) in perfume (found in 1/32 products)	- (found in 0/4 products)	- (found in 0/12 products)
DEHP	- (found in 0/32 products)	Up to 0.01260% (w/w) in lubricant (found in 1/4 products)	- (found in 0/12 products)
DCHP	- (found in 0/32 products)	Up to 0.00200% (w/w) in lubricant (found in 2/4 products)	- (found in 0/12 products)
BBP	Up to 0.00259% (w/w) in sunscreen (found in 2/32 products)	- (found in 0/4 products)	Up to 0.00117% (w/w) in dishwashing liquid (found in 1/12 products)
DOTP	Up to 0.0109% (w/w) in foundation (found in 1/32 products)	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products)	- (found in 0/12 products)
DHP	- (found in 0/32 products)	- (found in 0/4 products)	- (found in 0/12 products)
Parabens			
BP	Up to 0.00223% (w/w) in perfume (found in 1/32 products)	- (found in 0/4 products)	- (found in 0/12 products)

Chemical	Cosmetics	Medical Devices	Detergents
EtP	Up to 0.00259% (w/w) in deodorant (found in 5/32 products)	Up to 0.01780% (w/w) in lubricant (found in 1/4 products)	Up to 0.00105% (w/w) in fabric softener (found in 1/12 products)
MeP	Up to 0.2053% (w/w) in foundation (found in 5/32 products)	Up to 0.10720% (w/w) in lubricant (found in 1/4 products)	Up to 0.00386% (w/w) in fabric softener (found in 3/12 products)
PP	Up to 0.00302% (w/w) in perfume (found in 3/32 products)	Up to 0.00923% (w/w) in lubricant (found in 1/4 products)	- (found in 0/12 products)
Other			
OC	Up to 0.6219% (w/w) in sunscreen (found in 3/32 products)	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products)	- (found in 0/12 products)
BHT	Up to 0.1257% (w/w) in perfume (found in 18/32 products)	Up to 0.00135% (w/w) in lubricant (found in 1/4 products)	Up to 0.00308% (w/w) in fabric softener (found in 4/12 products)
TPP	- (found in 0/32 products)	- (found in 0/4 products)	- (found in 0/12 products)
4NP	Up to 0.0026% (w/w) in sunscreen (found in 2/32 products)	- (found in 0/4 products)	- (found in 0/12 products)
Styre	Up to 0.00196% (w/w) in perfume (found in 2/32 products)	Up to 0.07230% (w/w) in lubricant (found in 2/4 products)	Up to 0.00273% (w/w) in dishwashing liquid (found in 2/12 products)

'-' indicates that no relevant concentrations were measured

7 Evaluation of the results

Substances can enter consumer products in various ways. For instance, they may be intentionally added as ingredients, as contaminants, or, inadvertently, through migration from packaging materials. The exact concentrations of these substances in products are often not publicly available, which makes it challenging to gain a complete picture of potential exposure.

For example bisphenol A (BPA) in cosmetics. Although BPA is not allowed in cosmetics, traces of BPA may be present as a result of

- Packaging: BPA can migrate from plastic packaging into the product, especially during long-term storage or exposure to heat.
- Contamination during production: BPA can enter the product as an unintended contaminant via machinery or raw materials.

The migration of chemicals from the packaging to the finished product is tested in the Compatibility Test, one of the safety tests that should be part of the Product Information File (PIF) of a cosmetic product. Among their obligations when compiling the PIF, the Responsible Person of a cosmetic product should ensure that the migration of any chemical from the packaging is kept at levels below detection limits. However, as technologies develop, increasingly smaller quantities of a chemical substance can be detected (Regulation (EC) No 1223/2009).

In this chapter, measured concentrations will be compared to legal limit values. In addition, measurements from other European studies and exposure estimates are discussed in this chapter to provide a broader context. Furthermore, it discusses how this information can be used to establish priorities for further research.

7.1 Limit values from legislation

Depending on the regulatory framework for specific consumer products, maximum limits are established for certain substances. This chapter addresses the question of how the detected concentrations (Chapter 6) can be compared to applicable legal requirements regarding maximum levels of substances in consumer products. Reference values in legislation are described in Chapter 4, Table 4.

Also, for any substance without a legal limit value that is present in a product at a (very) low concentration, it is assumed that the substance has no function in the product and has ended up in the final product as a contamination from the production process or via migration from the packaging. Therefore, practical cut-off values (0.001% w/w) are used to determine which measured values are relevant for further research.

Table 9 provides an overview of the measured obesogens per product category. Using colours, it is indicated whether the results are selected for further research on the risks associated with the presence of the substance in a product. This first selection is based on the criteria as mentioned below.

Concentrations measured in this study will not be selected for further research if:

- A prohibited substance in cosmetics is present at <0.001% (w/w);
- A substance without restrictions in cosmetics, which is not declared on the label is, <0.001% (w/w);
- A substance with a concentration limit in cosmetics is a factor of ten below the concentration limit;
- A substance with CMR 1A/1B classification in the medical device and/or detergents is present at <0.001% (w/w).

Table 9 Overview of the top measured concentrations and their selection for further analysis, based on compliance with regulations

Chemical	Cosmetics	Medical Devices	Detergents	Candidate for further research?
Bisphenols				
BPA	- (found in 0/32 products) *	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products) ***	Up to 0.00114% (w/w) in fabric softener (found in 1/12 products) **	Yes, measured in this study
BPF	Up to 0.0785% (w/w) in sunscreen (found in 4/32 products) **	- (found in 0/4 products) *	Up to 0.0113% (w/w) in dishwashing liquid (found in 2/12 products) **	Yes, measured in this study
BPS	Up to 0.00228% (w/w) in body lotion (found in 1/32 products) ****	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products) ***	- (found in 0/12 products) *	Yes, measured in this study and some measurements do not comply with legislation
Phthalates				
DBP	Up to 0.00189% (w/w) in perfume (found in 1/32 products) ****	- (found in 0/4 products) *	- (found in 0/12 products) *	Yes, measured in this study and some measurements do not comply with legislation
DEHP	- (found in 0/32 products) *	Up to 0.01260% (w/w) in lubricant (found in 1/4 products) ****	- (found in 0/12 products) *	Yes, measured in this study and some measurements do not comply with legislation
DCHP	- (found in 0/32 products) *	Up to 0.00200% (w/w) in lubricant (found in 2/4 products) **	- (found in 0/12 products) *	Yes, measured in this study
BBP	Up to 0.00259% (w/w) in sunscreen (found in 2/32 products) ****	- (found in 0/4 products) *	Up to 0.00117% (w/w) in dishwashing liquid (found in 1/12 products) **	Yes, measured in this study and some measurements do not comply with legislation

Chemical	Cosmetics	Medical Devices	Detergents	Candidate for further research?
DOTP	Up to 0.0109% (w/w) in foundation (found in 1/32 products) **	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products) ***	- (found in 0/12 products) *	Yes, measured in this study
DHP	- (found in 0/32 products) *	- (found in 0/4 products) *	- (found in 0/12 products) *	No, not measured (at relevant concentrations) in this study
Parabens				
EtP	Up to 0.00259% (w/w) in deodorant (found in 5/32 products) *	Up to 0.01780% (w/w) in lubricant (found in 1/4 products) **	Up to 0.00105% (w/w) in fabric softener (found in 1/12 products) **	Yes, measured in this study
BP	Up to 0.00223% (w/w) in perfume (found in 1/32 products) **	- (found in 0/4 products) *	- (found in 0/12 products) *	Yes, measured in this study
PP	Up to 0.00302% (w/w) in perfume (found in 3/32 products) **	Up to 0.00923% (w/w) in lubricant (found in 1/4 products) **	- (found in 0/12 products) *	Yes, measured in this study
MeP	Up to 0.2053% (w/w) in foundation (found in 5/32 products) **	Up to 0.10720% (w/w) in lubricant (found in 1/4 products) **	Up to 0.00386% (w/w) in fabric softener (found in 3/12 products) **	Yes, measured in this study
Other				
OC	Up to 0.6219% (w/w) in sunscreen (found in 3/32 products) **	One measurement >0.001% (but not or hardly found after dilution) (found in 1/4 products) ***	- (found in 0/12 products) *	Yes, measured in this study
BHT	Up to 0.1257% (w/w) in perfume	Up to 0.00135% (w/w) in lubricant (found in 1/4 products) **	Up to 0.00308% (w/w) in fabric softener (found in 4/12 products) **	Yes, measured in this study

Chemical	Cosmetics	Medical Devices	Detergents	Candidate for further research?
	(found in 18/32 products) **			
TPP	- (found in 0/32 products) *	- (found in 0/4 products) *	- (found in 0/12 products) *	No, not measured (at relevant concentrations) in this study
4NP	Up to 0.0026% (w/w) in sunscreen (found in 2/32 products) *	- (found in 0/4 products) *	- (found in 0/12 products) *	Yes, measured in this study
Styr	Up to 0.00196% (w/w) in perfume (found in 2/32 products) ****	Up to 0.07230% (w/w) in lubricant (found in 2/4 products) **	Up to 0.00273% (w/w) in dishwashing liquid (found in 2/12 products) **	Yes, measured in this study and some measurements do not comply with legislation

Colour codes in the table:
Green (*): measured value is not relevant for further analysis
Blue (**): measurement complies with legislation but might be interesting for risk assessment
Orange (***): measurement may be unreliable
Red (****): measurement does not comply with legislation

7.2 Concentration data from other European studies

A concise literature review was conducted to identify European studies that measured one or more of the obesogens quantified in this study in similar products or product categories. The objective was to assess whether previous European monitoring and exposure investigations detected these chemicals in comparable matrices, thereby providing a broader context to our findings.
The review focussed on peer-reviewed articles, government and agency monitoring reports, and high-quality surveillance studies published in Europe. It should be noted that this is not a comprehensive overview, but rather a focussed search intended to quickly identify relevant studies.
The results from the literature search (concentrations of obesogens in similar product categories) are summarised in Table A.17.

7.3 Exposure sources and concentrations in Europe

The presence of an obesogen in a consumer product does not necessarily imply that the use of that product will lead to a significant internal exposure level. Actual exposure depends on factors such as the concentration of the obesogen, route of exposure (ingestion, inhalation, dermal), frequency and duration of use, routes of contact, etcetera. Furthermore, consumers may be exposed to obesogens via other routes and sources than the consumer products evaluated in this report (e.g. toys, food contact materials, diet, indoor air, and house dust).
To provide an initial estimate of consumer exposure to the obesogens for which critical effect values for obesity have been established (Chapter 5.6), estimated exposure concentrations from various European studies across different exposure sources are summarised in Table A.18.

7.4 Qualitative interpretation of the results

The margin of exposure (MOE) approach in risk assessment is the use of a ratio of a health-based reference point (point of departure, or PoD), derived from either *in vitro* (cell-based) or *in vivo* (animal) studies, to the estimated human exposure. The MOE value provides a quantitative measure of risk; higher values indicate greater safety, while lower or negative values suggest a higher potential for concern and may warrant further investigation. Although the MOE does not directly equate a risk, it helps to prioritise chemicals for further research or regulatory action and it helps to put the severity of the effect into perspective [282].
A MOE is calculated by dividing the PoD by the estimated human exposure level.

Although we have gained some insight into the possible exposure via a (selection of) consumer products through our own and existing measurement data, the endpoint obesogenic effect is not routinely investigated in *in vivo* studies. There is a lack of both standardised definitions for 'obesogenic effects' and criteria to determine when changes in metabolic and developmental parameters constitute an 'adverse effect'. Consequently, there is a lack of testing protocols and regulatory approaches (see also Chapter 8.2). These limitations hinder accurate risk assessment resulting in little or no reliable data for deriving an (*in vivo*) PoD on obesogenic endpoints. Consequently,

calculating an MOE could give distorted results. Due to the lack of information, it was decided to interpret the results in this study qualitatively.

Although often no PoD can be derived for an obesogenic endpoint, critical effect values (effects that may be related to obesity) can be used from the literature to assess the results. To determine which chemicals are most interesting for further research, the data on the critical effect value was compared to PoD values for other endpoints as documented in the literature (see Chapter 5.6). The largest difference between critical effect value for an obesogenic parameter and the PoD for other effects was found for BPF and BPS, indicating that existing reference values for these chemicals may not be sufficiently protective against obesogenic effects
Subsequently, the strength of the evidence that a substance has obesogenic properties, based on *in vitro*, *in vivo*, and/or epidemiological studies, was assessed (see Chapter 5.5). Furthermore, it was determined whether the substance has been measured in consumer products and, if so, at what concentrations, and what this means for the ultimate internal exposure. These three criteria together help determine whether a substance warrants further research as it raises concerns about obesogenic effects.

An obesogen is selected for further research because there is a trigger for concern about obesogenic effects if:

- The critical effect value related to obesity < PoD general;
- There is strong evidence of obesogenic effects (*in vitro* and/or *in vivo*);
- The obesogen is present in consumer products and results in (significant) exposure.

Table 10 presents summarising information on critical effect values for obesogenic endpoints, the strength of obesogenic evidence, the presence in consumer products (measurements in this or other studies), insight into consumer exposure estimation, specific legislative information, and an informative decision whether the eighteen selected potential obesogens should be included for further research (based on previous tables in this report). These obesogens selected as 'candidate for further research' can be used as a test set to address initial data gaps and needs for standardisation and quantification (see also Chapter 8.2). Subsequently, chemicals exhibiting limited or inconclusive evidence of obesogenic effects should be subjected to further investigation.

Table 10 Integrated overview of key effect values, measurement data, exposure appraisal, and regulatory decisions informing research priorities

Chemical	**Critical effect value lower than PoD?** (Table 6)	**Evidence obesogenic potential** (Table 5)	**Presence in consumer products** (Table 8 and Table A.17)	**Exposure** (Table A.18, only included when critical effect value has been established)	**European legislation** (Table 4)	**Candidate for further research?**
Bisphenols						
BPA	Although several studies indicate (developmental) obesogenic effects of BPA, no clear critical effect value could be derived	Yes, *in vitro*, *in vivo*, and epidemiological studies	Yes, measured in this study	Mainly via diet, dust, and indoor air	Identified as SVHC (Repro, ED human health and env), classified as CMR 1B, prohibited in cosmetics, restriction in thermal paper, restriction in FCM (upcoming)	**Yes**, there is sufficient evidence for the obesogenic potential of BPA and despite the (recent) restrictions for use in consumer products, exposure via various sources is inevitable even though it is already regulated in several products. BPA can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
BPF	Yes (although for indication a PoD was selected, no reference values have been published yet)	Yes, *in vitro* and epidemiological studies	Yes, measured in this study	-	Proposed classification Repr. 1B	**Yes**, there is evidence for the obesogenic potential of BPF, comparable to BPA. BPF is not yet regulated. Further research into its presence in consumer products, exposure, and potential obesogenic effects, (and ultimately potential legal regulations), is recommended. Subsequently, BPF can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
BPS	Yes (although critical effect value is based on high-fat diet study)	Yes, *in vitro*, *in vivo*, and epidemiological studies	Yes, measured in this study	Via thermal paper receipts and dust	Identified as SVHC (Repro, ED human health and env), classified as CMR 1B, prohibited in cosmetics	**Yes**, there is evidence for the obesogenic potential of BPS and despite the (recent) restrictions for use in consumer products, exposure via various sources is inevitable. BPS can be used to address data gaps,

Chemical	**Critical effect value lower than PoD?** (Table 6)	**Evidence obesogenic potential** (Table 5)	**Presence in consumer products** (Table 8 and Table A.17)	**Exposure** (Table A.18, only included when critical effect value has been established)	**European legislation** (Table 4)	**Candidate for further research?**
						standardisation needs, and quantification approaches (see also Chapter 8.2).
Phthalates						
DBP	No	Yes, *in vitro*, *in vivo*, and epidemiological studies	Yes, measured in this study and others	Mainly via perfume, dust, and indoor air	Identified as SVHC (Repro, ED human health and env), classified as CMR 1B, prohibited in cosmetics, restricted in toys	No, the critical effect value related to obesity that was derived in this study is higher than the PoD.
DEHP	Yes	Yes, *in vitro*, *in vivo*, and epidemiological studies	Yes, measured in this study and others	Mainly via perfume, diet, dust, and indoor air	Identified as SVHC (Repro, ED human health and env), classified as CMR 1B, prohibited in cosmetics, in toys, and childcare products, requires authorisation	**Yes**, obesity may be a sensitive outcome and – despite restrictions on use in consumer products – several studies show that there are various sources of exposure to DEHP. DEHP can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
DCHP	No critical effect value could be derived	Yes, *in vitro* and *in vivo* studies	Yes, measured in this study	n/a	Identified as SVHC (Repro, ED human health), classified as CMR 1B, prohibited in cosmetics	No, there is insufficient data to determine the obesogenic potential of and exposure to DCHP. Once follow-up research has addressed data gaps and definitions have been standardised, DCHP can subsequently be investigated for its obesogenic properties.
BBP	No critical effect value could be derived	Yes, *in vitro* and *in vivo* studies	Yes, measured in	n/a	Identified as SVHC (Repro, ED human health), classified as	No, there is insufficient data to determine the obesogenic potential of and exposure to BBP. Once follow-up research has

Chemical	**Critical effect value lower than PoD?** (Table 6)	**Evidence obesogenic potential** (Table 5)	**Presence in consumer products** (Table 8 and Table A.17)	**Exposure** (Table A.18, only included when critical effect value has been established)	**European legislation** (Table 4)	**Candidate for further research?**
			this study and others		CMR 1B, prohibited in cosmetics, toys, and childcare products, requires authorisation	addressed data gaps and definitions have been standardised, BBP can be investigated for its obesogenic properties.
DOTP	No critical effect value could be derived	Yes, *in vitro* study	Yes, measured in this study	n/a	-	No, there is insufficient data to determine the obesogenic potential of and exposure to DOTP. Once follow-up research has addressed data gaps and definitions have been standardised, DOTP can be investigated for its obesogenic properties.
DHP	No critical effect value could be derived	Yes, *in vivo* study	No	n/a	Identified as SVHC (Repro), classified as CMR, prohibited in cosmetics, requires authorisation	No, there is insufficient data to determine the obesogenic potential of and exposure to DHP. Once follow-up research has addressed data gaps and definitions have been standardised, DHP can be investigated for its obesogenic properties.
Parabens						
BP	No critical effect value could be derived	Yes, *in vitro*, *in vivo*, and epidemiological studies	Yes, measured in this study and others	n/a	Identified as SVHC (ED human health), on candidate list for authorisation, maximum concentration in cosmetics	No, there is insufficient data to determine the obesogenic potential of and exposure to BP. Once follow-up research has addressed data gaps and definitions have been standardised, BP can be investigated for its obesogenic properties.
EtP	No critical effect value could be derived	Yes, *in vitro*, and epidemiological studies	Yes, measured in this study and others	n/a	Maximum concentration in cosmetics	No, there is insufficient data to determine the obesogenic potential of and exposure to EtP. Once follow-up research has addressed data gaps and definitions have been

Chemical	**Critical effect value lower than PoD?** (Table 6)	**Evidence obesogenic potential** (Table 5)	**Presence in consumer products** (Table 8 and Table A.17)	**Exposure** (Table A.18, only included when critical effect value has been established)	**European legislation** (Table 4)	**Candidate for further research?**
						standardised, EtP can be investigated for its obesogenic properties.
MeP	Yes	Yes, *in vitro* and *in vivo* studies	Yes, measured in this study and others	Via cosmetics and diet	Maximum concentration in cosmetics	**Yes**, obesity may be a sensitive outcome and – despite restrictions on use in cosmetics – studies show that there are various sources of exposure to MeP. MeP can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
PP	No critical effect value could be derived	Yes, *in vitro*, and epidemiological studies	Yes, measured in this study and others	n/a	Maximum concentration in cosmetics	No, there is insufficient data to determine the obesogenic potential of and exposure to PP. Once follow-up research has addressed data gaps and definitions have been standardised, PP can be investigated for its obesogenic properties.
Other						
OC	No critical effect value could be derived	Yes, *in vitro* study	Yes, measured in this study	n/a	Maximum concentration in cosmetics	No, there is insufficient data to determine obesogenic potential of and exposure to OC. Once follow-up research has addressed data gaps and definitions have been standardised, OC can be investigated for its obesogenic properties.
BHT	No critical effect value could be derived	Insufficient	Yes, measured in this study	n/a	Maximum concentration in cosmetics	No, there is insufficient data to determine obesogenic potential of and exposure to BHT. Once follow-up research has addressed data gaps and definitions have been standardised, BHT can be investigated for its possible obesogenic properties.

Chemical	**Critical effect value lower than PoD?** (Table 6)	**Evidence obesogenic potential** (Table 5)	**Presence in consumer products** (Table 8 and Table A.17)	**Exposure** (Table A.18, only included when critical effect value has been established)	**European legislation** (Table 4)	**Candidate for further research?**
TPP	Yes	Yes, *in vitro* and *in vivo* studies	Yes, measured in other studies	Via cosmetics and diet	SVHC (ED environment), will be prohibited in cosmetics	**Yes**, obesity may be a sensitive outcome. Although TPP was not detected in this study, TPP is also used as flame retardant in consumer products, warranting exposure via house dust. TPP can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
4NP	Yes	Yes, *in vitro* and *in vivo* studies	Yes, measured in this study, complies with legislations	Via cosmetics, household products, diet and air	SVHC (ED environment), restriction (<0.1%), prohibited in cosmetics	**Yes**, obesity may be a sensitive outcome, 4NP is present in consumer products and exposure to 4NP is significant. 4NP can be used to address data gaps, standardisation needs, and quantification approaches (see also Chapter 8.2).
Styr	No critical effect value could be derived	Yes, epidemiological study	Yes, measured in this study and others	n/a	Classified as CMR 2, prohibited in cosmetics	No, there is insufficient data to determine obesogenic potential of and exposure to Styr. Once follow-up research has addressed data gaps and definitions have been standardised, Styr can be investigated for its obesogenic properties.

7.5 Conclusions

The study aimed to gain more insight into which chemical substances have obesogenic properties and into the extent of exposure through consumer products. Therefore, a working definition of obesogens was established: 'Chemicals that promote obesity by affecting the control of adipose development due to, among others, changes in lipid storage and/or disruption of involved receptors such as PPAR or RXR'. A comprehensive literature review on specific obesogens was conducted which resulted in a list of chemicals that were identified in studies to obesity or obesogenic effects and met the criteria of potential obesogens in at least one study.
The relevance of the selected potential obesogens to consumer products was explored, using a selected number of databases, providing an indication of exposure to the obesogens via everyday consumer items. A second literature review resulted in the collection of supporting mechanistic information, enabling the derivation of critical effect values for obesogenic effects for the selected substances. In addition, the critical effect values for obesogenic effects were compared to PoD values for other endpoints or most critical use as documented in the literature. The largest difference between critical effect value for an obesogenic parameter and the PoD for other effects was found for BPF and BPS, indicating that existing reference values for these chemicals may not be sufficiently protective against obesogenic effects.

Next, eighteen obesogens were quantitatively determined in a selection of cosmetic products, detergents, and a medical device, after developing a new GC-MS method: sixteen out of the eighteen obesogens were detected in one or more of the tested consumer products (only dihexyl phthalate (DHP) and triphenyl phosphate (TPP) were not detected). The highest detected concentration was octocrylene (OC) in sunscreen: 0.6219% (w/w). Measured values <0.001% (w/w) were considered to be excluded for further analysis. It is, however, noteworthy that low concentrations of prohibited chemicals were found in many products. These can enter the product during the manufacturing process or through migration from the packaging. Because these chemicals are not declared on the label (at least in the case of cosmetics), consumers are not aware of being exposed (even if minimally) via the product.

From the consulted exposure studies, it was concluded that cosmetics, mouthing behaviour of children (e.g. from toys), diet, dust, and indoor air are relevant sources for exposure to obesogens present in consumer products.

Finally, obesogens designated as candidates for further research were selected. These obesogens can serve as an initial test set to address data gaps, standardisation needs, and quantification approaches (see Chapter 8.2). Subsequently also chemicals with limited or inconclusive evidence for a link with obesogenicity can be prioritised for further investigation.
To determine which obesogens are most interesting for further research, critical effect values, the evidence strength of the obesogenic properties, the presence in consumer products, and exposure data were used. On

the basis of the defined criteria, seven obesogens were recommended as candidates for further research:

- Bisphenol A (BPA)
- Bisphenol F (BPF)
- Bisphenol S (BPS)
- Bis(2-ethylhexyl) phthalate (DEHP)
- Methylparaben (MeP)
- Triphenyl phosphate (TPP)
- 4-Nonylphenol (4NP)

Targeted follow-up studies of specific product categories (stuffed animals and food contact materials) may alter the current selection. New measurements of chemical presence, migration, and use patterns in these matrices, together with updated exposure estimates (including age-specific intake and mouthing behaviour), could identify additional substances of concern or change the relative importance of the seven selected candidates. Consequently, the test set should be considered provisional and subject to revision in following reports.

8 Discussion and recommendations

Despite growing concern about the potential role of chemicals in the development of obesity, significant gaps remain in the scientific understanding of their effects, mechanisms, and impacts.
This chapter summarises current evidence on chemical contributors to obesity, identifies key data and methodological gaps, and sets out practical research priorities. It covers (i) the need for standardised definitions and test methods for obesogenic effects, (ii) criteria for defining adversity for obesity-relevant endpoints, (iii) priority data gaps – with emphasis on early-life vulnerability, (iv) approaches to quantifying the contribution of obesogens at substance and class levels, and (v) exposure assessment needs, including targeted monitoring and source-apportionment. The aim is to provide a clear, actionable roadmap for researchers and policymakers to generate comparable hazard and exposure data that can inform risk assessment and public health measures.

8.1 Literature review

The systematic review of available literature in this study was mainly hampered by the fact that not all studies focussing on the relation between exposure to chemicals and the development of obesity use the term 'obesogens'. While conducting the literature study, it was noticed that specific research groups provide many publications on this subject. Accordingly, the identification of obesogens in literature is prone to potential bias. Therefore, additional searches were performed on the main mechanisms related to obesity. Despite the additional literature search, and bearing in mind the potential bias, this study mainly resulted in the identification of the 'usual suspects'. These are chemicals that have recently been or are being researched extensively, i.e. all chemicals prioritised for further studies are authorised under REACH and/or have restrictions laid down in EU regulations (see Table 4). Future research could aim to develop screening methods to identify new (frequently used) chemicals in consumer products that may act as obesogens. For instance, by developing Integrated Approaches for Testing and Assessment (IATA). IATAs combine multiple sources of information to conclude on the toxicity of chemicals[15]. IATAs may include existing information from the scientific literature or other resources, along with newly generated data resulting from novel or traditional toxicity testing methods to fill data gaps. Additionally, adverse outcome pathways (AOPs) can be helpful to organise data collected from different methods. An overview of relevant *in vitro* and *in vivo* assays is presented in the review by Mohajer et al. 2021 [16].

Several databases were accessed to gain information on the presence of chemicals in consumer products. Although the databases provide an overview of the chemicals in consumer products, information on contaminants in for example cosmetics are not reported.

[15] https://www.oecd.org/chemicalsafety/risk-assessment/iata/

As mentioned in Chapter 4, regulations are updated regularly. Consequently, the datasets consulted may contain records of chemicals present in consumer products that have since become restricted or banned; products placed on the market before the end of the legal transition period may still be available for purchase. For example, although the Mintel database indicated that several products on the Dutch market contained butylated hydroxytoluene (BHT), no toothpastes with BHT were found in stores (January 2024).

8.2 Improving understanding of obesogens: directions for further research

Despite growing concern about the potential role of chemicals in the development of obesity, significant gaps remain in the scientific understanding of their effects, mechanisms, and impact. Currently, obesogenic effects are not systematically assessed in toxicological studies, and there is a lack of standardised definitions, testing protocols, and regulatory approaches. These limitations hinder accurate risk assessment and the development of effective public health policies. This section outlines the main data gaps and standardisation needs in obesogen research and highlights the importance of quantifying their contribution to obesity. By addressing these challenges, future studies can provide a stronger scientific foundation for evaluating the obesogenic potential of chemicals.

8.2.1 Standardisation

Currently, the endpoint 'obesogenic effect' is not routinely investigated in *in vivo* toxicology studies. To improve risk assessment and gain more insight into the hazard of obesogens, comprehensive standards for the definition, testing, and regulatory evaluation of obesogens need to be developed.

Recommendations to achieve this are:

- Standardise the definition of 'obesogen' and specify the mechanistic pathways that qualify a chemical as obesogenic.
- Fill hazard information gaps by testing for multiple relevant mechanisms of action. Current test batteries rarely cover the full range of pathways implicated in obesogenesis, although adverse outcome pathways (AOPs) exist for some related key events relevant to adipogenesis and metabolic disruption [283].
- Develop an OECD test guideline or equivalent that includes obesogenic endpoints to harmonise testing across laboratories and jurisdictions. It is also feasible to incorporate key parameters into OECD Test No. 443: Extended One-Generation Reproductive Toxicity Study (EOGRTS) [284], since this design captures both *in utero* and early-life exposure. In addition, the diet-induced obese (DIO) C57BL/6 mouse model can be used for interactions between chemicals and diet [285].
- Report body weight as an (adverse) endpoint in animal studies. Currently, increased body weight is not always perceived as a potential adverse effect. Results relating to weight gain are often presented only in figures or in supplementary materials, rather than explicitly mentioned as an effect. Inconsistent reporting increases the difficulty of assessing weight gain and accurately assessing the obesogenic potential of substances

8.2.2 Defining adversity for obesity relevant endpoints in chemical safety assessment

Harmonised criteria are required to determine when changes in metabolic and developmental parameters (see definition in Chapter 8.2.1) constitute an 'adverse effect'. Adversity should be assessed on the basis of biological plausibility, magnitude and persistence, dose response and reproducibility, functional consequence, developmental timing, and population relevance rather than statistical significance alone. For example, an increase in body weight following exposure to a putative obesogen should be considered adverse when it is sustained and accompanied by increased adiposity or metabolic dysfunction. Similarly, an increase in fat mass is more likely to be adverse when it involves visceral or ectopic depots, adipocyte hypertrophy, inflammation, or impaired adipose function. Changes in biomarkers such as leptin, glucose, insulin, and lipids should be interpreted in the context of functional tests (e.g. a glucose tolerance test (GTT) or insulin tolerance test (ITT)), tissue pathology, and persistence over time [286]. Molecular endpoints (receptor binding, transactivation, gene expression) provide important mechanistic evidence and strengthen causal inference when they are temporally and dose concordant with downstream phenotypic key events, but they are insufficient on their own for regulatory action [287]; therefore, integration through AOP frameworks and a formal weight of evidence approach is recommended to translate molecular signals into regulatory relevant adverse outcomes.

8.2.3 Data gaps

Aside from the need for standardisation (E. Marra (auteur), RIVM), continued research is needed to gain insights into potential obesogens and to understand their underlying mechanisms.
Recommendations to achieve this are:

- Identification of reference materials that are (suspected) obesogens:
  - Identify chemicals frequently used in consumer products with obesogenic potential.
  - Deriving points of departure (PoDs) for obesogens following standard toxicological practice. This requires careful endpoint selection and evaluation, which is currently not standard practice for obesogenic endpoints (see also Chapter 8.2.1and 8.2.2). As an interim approach, published critical effect values – concentrations at which obesity-related effects are induced – can be used to contextualise findings. This way, an initial estimate of the obesogenic potential of a substance can be made without performing additional studies.
- Prioritisation of studies that address early-life vulnerability:
  - Improve understanding of the lifelong consequences of early-life exposure: does exposure *in utero* or during infancy produce persistent changes in adipocyte programming, energy homeostasis, or gut microbiota that increase lifetime obesity risk?
  - Determine whether it should be standardised that juvenile studies should also be performed for (suspected) developmental obesogens.

- Investigate differences between animal models and humans to improve extrapolation of hazard and dose-response relationships.

To provide a practical framework for implementing the recommendations above, the seven chemicals selected for further research – bisphenol A (BPA), bisphenol F (BPF), bisphenol S (BPS), bis(2-ethylhexyl) phthalate (DEHP), methylparaben (MP), triphenyl phosphate (TPP), and 4-nonylphenol (4NP) – can serve as benchmark chemicals. These chemicals have evidence of obesogenic potential and, for most, exposure through consumer products is plausible, making them suitable as an initial test set to address data gaps, standardisation needs, and quantification approaches. Targeted studies on this test set can be used to refine endpoint selection, determine the magnitude of effect required for it to be considered adverse, validate testing protocols, and develop eventually *in silico* to *in vivo* exposure-to-effect extrapolation methods. Subsequently, chemicals with current limited or inconclusive evidence of obesogenic activity should be prioritised for follow-up investigation to determine whether they nonetheless warrant classification as obesogens.

8.2.4 Quantification of the contribution to obesity

Obesogens are one of several determinants of obesity alongside lifestyle, diet, and genetic predisposition. Because the magnitude of the chemical contribution to population or individual risk remains uncertain, it is important to quantify that contribution and to evaluate whether exposure levels plausibly constitute a significant public health risk. Quantification can be undertaken at the level of an individual substance (e.g. a single compound with obesogenic activity) and at the level of substance classes or groups (e.g. bisphenols, phthalates, PFAS) to capture cumulative or class effects.

Currently, there is no single, universally accepted animal model that fully reproduces human obesity induced by chemical exposure. The diet-induced obese (DIO) C57BL/6 mouse can be used for studying chemical effects on weight gain, adiposity and metabolic dysfunction [285]. As phenotypic effects of obesogens are often amplified or only become apparent under nutritional stress, developmental exposure paradigms can be combined with a dietary challenge (high-fat or obesogenic diet) to reveal chemical/diet interactions.

An initial quantification study might focus on a single, well-characterised obesogen selected from this study, while subsequent work might extend to substance groups to assess aggregate contributions. Such studies should explicitly consider susceptible subpopulations (for example, individuals with genetic variants, pre-existing metabolic disease, or other vulnerabilities) because these groups may experience larger effects at lower exposure. Quantitative estimates should integrate toxicokinetic data, dose-response relationships, and population exposure metrics to support risk-based conclusions about the public health significance of obesogenic chemical exposure.

8.2.5 Exposure

Accurate characterisation of human exposure is essential to quantify the contribution of obesogens to the development of obesity. As noted in Chapter 7.2 and 7.3, exposure estimates of some obesogens are available for a range of matrices (consumer products, indoor air, house dust, food), but this data is incomplete and heterogeneous. To improve temporal and spatial resolution of exposure information, targeted monitoring programmes can be implemented using existing surveillance networks to track concentrations in consumer products, indoor environments, and food. Such monitoring will also permit evaluation of the effectiveness of eventual regulatory or voluntary risk management measures by documenting trends in environmental and product concentrations over time. Particular attention should be given to products intended for infants and children, who may experience higher exposure per body weight and greater vulnerability, and pregnant women.

To support source apportionment and to identify the product categories that contribute most to internal exposure measured in human biomonitoring (HBM) studies, pilot source mapping projects are recommended for the selected potential obesogens in this study. These pilots should combine product-level measurements, environmental sampling, and exposure modelling with HBM data to quantify relative contributions from different sources and pathways.

European initiatives such as HBM4EU[16] and PARC[17] have strengthened the infrastructure for exposure assessment by harmonising HBM protocols, assembling comparable population data, and developing tools for the interpretation of internal concentrations (HBM guidance values and dashboards) and for integrated exposure assessment. The legacy of HBM4EU and the ongoing activities within PARC provide a valuable framework for coordinated monitoring, mixture selection, and exposure-to-dose reconstruction that can be applied to obesogen research.

8.3 Concluding remarks and next steps

This chapter discussed the findings and recommendations regarding the role of obesogens in human health. The literature review revealed challenges in identifying obesogens due to inconsistent terminology and possible research biases. Most identified chemicals are already regulated, but there is a need for new screening methods to discover additional obesogens in consumer products.
While lifestyle, diet, and genetics are the primary factors driving obesity, obesogens can enhance the risk, especially when exposure occurs early in life. Obesogens act through hormone disruption and metabolic changes, but their overall impact is less well quantified than diet and activity. Genetics can also influence individual sensitivity to obesogens. Special concern is given to prenatal and early-life exposure, as developing children are more vulnerable to long-lasting metabolic effects from obesogens. Exposure during critical windows can permanently alter

[16] https://www.hbm4eu.eu/what-we-do/exposure-and-health/
[17] https://www.eu-parc.eu/thematic-areas/risk-assessments/monitoring

fat regulation and increase lifelong obesity risk, especially in genetically susceptible individuals.
Despite growing evidence, significant gaps remain. Obesogenic effects are not routinely tested in toxicology studies, and there is a lack of standardised definitions, testing protocols, and regulatory guidelines.

The main recommendations of this study are:

1. **Standardise the definition and testing of obesogens,** including criteria to define adversity for obesity-relevant endpoints.
2. **Prioritise studies on early-life exposure** and sensitive populations.
3. **Use the seven chemicals selected for further research** to identify/fill data gaps, develop screening methods (e.g. IATA), and derive points of departure.
4. **Quantify the contribution of obesogens to obesity,** alongside genetics, diet, and lifestyle.
5. **Improve human biomonitoring and exposure monitoring** in consumer products, indoor environments, and food, with special attention to children's products.

Addressing these gaps will strengthen risk assessment and will ultimately inform public health strategies to minimise the impact of obesogens.

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References

1. Ministerie van Volksgezondheid Welzijn en Sport. *Landelijke nota gezondheidsbeleid 2020-2024: pipeline naar een gezonder Nederland*. 2020. Available from: https://www.rijksoverheid.nl/documenten/beleidscrossers/2020/05/18/landelijke-nota-gezondheidsbeleid-2020-2024
2. van der Lucht, F.d.B., G. Buijs, M. Deuning, C., Hilderink, H., Plasmans, M., Poos, R., Zwakhals, L., Couwenbergh, C. *Trendscenario Volksgezondheid Toekomst Verkenning 2024*. 2024. Available from: https://www.volksgezondheidtoekomstverkenning.nl/vtv-2024/trendscenario/determinanten
3. Piché, M.E., A. Tchernof, and J.P. Després, *Obesity Phenotypes, Diabetes, and Cardiovascular Diseases.* Circ Res, 2020. **126**(11): p. 1477–1500.
4. Avila, C., et al., *An Overview of Links Between Obesity and Mental Health.* Curr Obes Rep, 2015. **4**(3): p. 303–10.
5. Hecker, J., et al., *Burden of disease study of overweight and obesity; the societal impact in terms of cost-of-illness and health-related quality of life.* BMC Public Health, 2022. **22**(1): p. 46.
6. Lustig, R.H., et al., *Obesity I: Overview and molecular and biochemical mechanisms.* Biochemical Pharmacology, 2022. **199**.
7. Heindel, J.J., *The obesogen hypothesis of obesity: overview and human evidence.* Obesity Before Birth: Maternal and prenatal influences on the offspring, 2011: p. 355–365.
8. Baillie-Hamilton, P.F., *Chemical toxins: a hypothesis to explain the global obesity epidemic.* J Altern Complement Med, 2002. **8**(2): p. 185–92.
9. Grün, F. and B. Blumberg, *Environmental obesogens: Organotins and endocrine disruption via nuclear receptor signaling.* Endocrinology, 2006. **147**(6): p. S50–S55.
10. Heindel, J.J., R. Newbold, and T.T. Schug, *Endocrine disruptors and obesity.* Nature Reviews Endocrinology, 2015. **11**(11): p. 653–661.
11. Janesick, A. and B. Blumberg, *Endocrine disrupting chemicals and the developmental programming of adipogenesis and obesity.* Birth Defects Research Part C - Embryo Today: Reviews, 2011. **93**(1): p. 34–50.
12. Heindel, J.J. and T.T. Schug, *The Obesogen Hypothesis: Current Status and Implications for Human Health.* Current Environmental Health Reports, 2014. **1**(4): p. 333–340.
13. Egusquiza, R.J. and B. Blumberg, *Environmental obesogens and their impact on susceptibility to obesity: New mechanisms and chemicals.* Endocrinology (United States), 2020. **161**(3).
14. Kolatorova, L., et al., *Parabens and their relation to obesity.* Physiol Res, 2018. **67**(Suppl 3): p. S465–s472.
15. Audouze, K., et al., *Integrative strategy of testing systems for identification of endocrine disruptors inducing metabolic disorders—An introduction to the oberon project.* International Journal of Molecular Sciences, 2020. **21**(8).

16. Mohajer, N., et al., *Obesogens: How They Are Identified and Molecular Mechanisms Underlying Their Action.* Frontiers in Endocrinology, 2021. **12**.
17. Kleijne, I. *Leefstijl, omgeving én genen bepalen obesitas*. 2024. Available from: https://www.medischcontact.nl/actueel/laatste-nieuws/artikel/leefstijl-omgeving-en-genen-bepalen-obesitas
18. Loketgezondleven. *Cijfers en feiten overgewicht*. 2024. Available from: https://www.loketgezondleven.nl/gezondheidsthema/overgewicht/werk-planmatig-aan-terugdringen-van-overgewicht/cijfers-en-feiten-overgewicht
19. Richtlijnendatabase. *Overgewicht en obesitas bij volwassenen en kinderen*. 2023. Available from: https://richtlijnendatabase.nl/richtlijn/overgewicht_en_obesitas_bij_volwassenen_en_kinderen/volwassenen.html
20. Kong, Y., et al., *Obesity: pathophysiology and therapeutic interventions.* Molecular biomedicine, 2025. **6**(1): p. 25.
21. Młynarska, E., et al., *Obesity as a multifactorial chronic disease: molecular mechanisms, systemic impact, and emerging digital interventions.* Current Issues in Molecular Biology, 2025. **47**(10): p. 787.
22. Van den Berg, S., M.E.T. Dolle, and J.M.A. Boer, *Genetic contribution to obesity: a literature review.* 2008.
23. Loos, R.J. and G.S. Yeo, *The genetics of obesity: from discovery to biology.* Nature Reviews Genetics, 2022. **23**(2): p. 120–133.
24. Celik, M.N. and O. Yesildemir, *Endocrine disruptors in child obesity and related disorders: early critical windows of exposure.* Current Nutrition Reports, 2025. **14**(1): p. 14.
25. Merrill, M.L. and L. Chatzi, *Chemical Obesogens and Obesity*, in *Textbook of Children's Environmental Health*, R.A. Etzel and P.J. Landrigan, Editors. 2024, Oxford University Press. p. 0.
26. Heindel, J.J., et al., *Obesogens: a unifying theory for the global rise in obesity.* International Journal of Obesity, 2024.
27. Shin, M.W. and S.-H. Kim, *Hidden link between endocrine-disrupting chemicals and pediatric obesity.* Clinical and Experimental Pediatrics, 2024. **68**(3): p. 199.
28. Amon, M., T. Kek, and I.V. Klun, *Endocrine disrupting chemicals and obesity prevention: scoping review.* Journal of Health, Population and Nutrition, 2024. **43**(1): p. 138.
29. Vafeiadi, M., et al., *Association of early life exposure to bisphenol A with obesity and cardiometabolic traits in childhood.* Environmental Research, 2016. **146**: p. 379–387.
30. Heindel, J.J., et al., *Obesogens and Obesity: State-of-the-Science and Future Directions Summary from a Healthy Environment and Endocrine Disruptors Strategies Workshop.* The American Journal of Clinical Nutrition, 2023.
31. Li, Y., et al., *Low-dose benzo [a] pyrene exposure induces hepatic lipid deposition through LCMT1/PP2Ac-mediated autophagy inhibition.* Food and Chemical Toxicology, 2023: p. 113986.
32. Paciência, I., et al., *Exposure to indoor endocrine-disrupting chemicals and childhood asthma and obesity.* Allergy: European Journal of Allergy and Clinical Immunology, 2019. **74**(7): p. 1277–1291.

33. Choi, S.I., et al., *Environmental obesogens (bisphenols, phthalates and parabens) and their impacts on adipogenic transcription factors in the absence of dexamethasone in 3T3-L1 cells.* Journal of Steroid Biochemistry and Molecular Biology, 2021. **214**.
34. Franco, M.E., et al., *Metabolomic-based assessment reveals dysregulation of lipid profiles in human liver cells exposed to environmental obesogens.* Toxicology and Applied Pharmacology, 2020. **398**.
35. Wang, B. and Y. Zhou, *[Relationship between environmental endocrine-disrupting chemicals and obesity epidemic].* Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine], 2013. **47**(4): p. 297–300.
36. Choi, J.Y., et al., *Urinary bisphenol concentrations and its association with metabolic disorders in the US and Korean populations.* Environmental Pollution, 2022. **295**.
37. Metwally, F.M., et al., *The impact of bisphenol a (BPA) as environmental obesogen on lipids and lipids metabolism.* International Journal of Pharmaceutical and Clinical Research, 2016. **8**(9): p. 1323–1330.
38. Amato, A.A., H.B. Wheeler, and B. Blumberg, *Obesity and endocrine-disrupting chemicals.* Endocrine Connections, 2021. **10**(2): p. R87–R105.
39. Biemann, R., M. Blüher, and B. Isermann, *Exposure to endocrine-disrupting compounds such as phthalates and bisphenol A is associated with an increased risk for obesity.* Best Practice and Research: Clinical Endocrinology and Metabolism, 2021. **35**(5).
40. Boudalia, S., et al., *Relationship between endocrine disruptors and obesity with a focus on bisphenol A: A narrative review.* BioImpacts, 2021. **11**(4): p. 289–300.
41. González-Casanova, J.E., et al., *Adipogenesis Regulation and Endocrine Disruptors: Emerging Insights in Obesity.* BioMed Research International, 2020. **2020**.
42. Heindel, J.J., et al., *Obesity II: Establishing causal links between chemical exposures and obesity.* Biochemical Pharmacology, 2022. **199**.
43. Kurşunoğlu, N.E. and B.P.S. Yurekli, *Endocrine disruptor chemicals as obesogen and diabetogen: Clinical and mechanistic evidence.* World Journal of Clinical Cases, 2022. **10**(31): p. 11226–11239.
44. Longo, M., et al., *Low-dose Bisphenol-A Promotes Epigenetic Changes at Pparγ Promoter in Adipose Precursor Cells.* Nutrients, 2020. **12**(11): p. 3498.
45. Kim, K.Y., E. Lee, and Y. Kim, *The association between bisphenol A exposure and obesity in children—a systematic review with meta-analysis.* International journal of environmental research and public health, 2019. **16**(14): p. 2521.
46. Naomi, R., et al., *Bisphenol A (BPA) leading to obesity and cardiovascular complications: A compilation of current In vivo study.* International journal of molecular sciences, 2022. **23**(6): p. 2969.
47. Pu, Y., et al., *Sex-specific extracellular matrix remodeling during early adipogenic differentiation by gestational bisphenol A exposure.* Chemosphere, 2022. **302**: p. 134806.

48. Salehpour, A., et al., *Bisphenol A enhances adipogenic signaling pathways in human mesenchymal stem cells.* Genes and Environment, 2020. **42**(1): p. 1–8.
49. Wu, W., et al., *Bisphenol A and the risk of obesity a systematic review with meta-analysis of the epidemiological evidence.* Dose-Response, 2020. **18**(2): p. 1559325820916949.
50. Hoepner, L.A., *Bisphenol a: A narrative review of prenatal exposure effects on adipogenesis and childhood obesity via peroxisome proliferator-activated receptor gamma.* Environmental research, 2019. **173**: p. 54–68.
51. Gao, P., et al., *Peroxisome proliferator-activated receptor gamma (PPARγ) activation and metabolism disturbance induced by bisphenol A and its replacement analog bisphenol S using in vitro macrophages and in vivo mouse models.* Environment international, 2020. **134**: p. 105328.
52. Wang, J., et al., *Bisphenol F induces nonalcoholic fatty liver disease-like changes: Involvement of lysosome disorder in lipid droplet deposition.* Environmental Pollution, 2021. **271**: p. 116304.
53. Brulport, A., et al., *Multigenerational study of the obesogen effects of bisphenol S after a perinatal exposure in C57BL6/J mice fed a high fat diet.* Environmental Pollution, 2021. **270**.
54. Brulport, A., et al., *Obesogen effect of bisphenol S alters mRNA expression and DNA methylation profiling in male mouse liver.* Chemosphere, 2020. **241**.
55. Ivry Del Moral, L., et al., *Obesogen effects after perinatal exposure of 4,4′-sulfonyldiphenol (Bisphenol S) in C57BL/6 mice.* Toxicology, 2016. **357-358**: p. 11–20.
56. Qin, J.-Y., et al., *Unraveling the mechanism of long-term bisphenol S exposure disrupted ovarian lipids metabolism, oocytes maturation, and offspring development of zebrafish.* Chemosphere, 2021. **277**: p. 130304.
57. Riu, A., et al., *Halogenated bisphenol-a analogs act as obesogens in zebrafish larvae (Danio rerio).* Toxicological Sciences, 2014. **139**(1): p. 48–58.
58. Chappell, V.A., et al., *Tetrabromobisphenol-A promotes early adipogenesis and lipogenesis in 3T3-L1 cells.* Toxicological Sciences, 2018. **166**(2): p. 332–344.
59. Yu, Y., et al., *Potential obesogenic effects of TBBPA and its alternatives TBBPS and TCBPA revealed by metabolic perturbations in human hepatoma cells.* Science of The Total Environment, 2022. **832**: p. 154847.
60. Rehman, M.Y.A., et al., *Transcriptome responses in blood reveal distinct biological pathways associated with arsenic exposure through drinking water in rural settings of Punjab, Pakistan.* Environment international, 2020. **135**: p. 105403.
61. Bibha, K., et al., *Metabolic Derangement by Arsenic: a Review of the Mechanisms.* Biological Trace Element Research, 2023: p. 1–11.
62. Calderón-DuPont, D., et al., *Impaired white adipose tissue fatty acid metabolism in mice fed a high-fat diet worsened by arsenic exposure, primarily affecting retroperitoneal adipose tissue.* Toxicology and Applied Pharmacology, 2023. **468**: p. 116428.

63. Farkhondeh, T., S. Samarghandian, and M. Azimi-Nezhad, *The role of arsenic in obesity and diabetes.* Journal of Cellular Physiology, 2019. **234**(8): p. 12516–12529.
64. Song, Y.-P., et al., *DNA hydroxymethylation reprogramming of β-oxidation genes mediates early-life arsenic-evoked hepatic lipid accumulation in adult mice.* Journal of Hazardous Materials, 2022. **430**: p. 128511.
65. Zhong, Q., et al., *Multiple metal exposure and obesity: A prospective cohort study of adults living along the Yangtze River, China.* Environmental Pollution, 2021. **285**: p. 117150.
66. Meiqin, Z., et al., *Association of urinary metals levels with obesity in urban preschoolers in Shiyan of Hubei Province.* Journal of Environmental and Occupational Medicine, 2021. **38**(9): p. 986–993.
67. Nguyen, J., et al., *Diabetogenic and Obesogenic Effects of Cadmium in Db/Db Mice and Rats at a Clinically Relevant Level of Exposure.* Toxics, 2022. **10**(3).
68. Jackson, T.W., et al., *Gestational Cd exposure in the CD-1 mouse induces sex-specific hepatic insulin insensitivity, obesity, and metabolic syndrome in adult female offspring.* Toxicological Sciences, 2020. **178**(2): p. 264–280.
69. Zhao, Y., et al., *SIRT1/mTOR pathway-mediated autophagy dysregulation promotes Pb-induced hepatic lipid accumulation in HepG2 cells.* Environmental Toxicology, 2022. **37**(3): p. 549–563.
70. Hernández-Mendoza, H., et al., *Serum lead levels and its association with overweight and obesity.* Journal of Trace Elements in Medicine and Biology, 2022. **72**: p. 126984.
71. Yang, R., et al., *2-Ethylhexyl Diphenyl Phosphate Causes Obesity in Zebrafish by Stimulating Overeating via Inhibition of Dopamine Receptor D2.* Environmental Science & Technology, 2023. **57**(38): p. 14162–14172.
72. Yue, J., et al., *Downregulation of miRNA-155–5p contributes to the adipogenic activity of 2-ethylhexyl diphenyl phosphate in 3T3-L1 preadipocytes.* Toxicology, 2023. **487**: p. 153452.
73. Pereira-Fernandes, A., et al., *Toxicogenomics in the 3T3-L1 cell line, a new approach for screening of obesogenic compounds.* Toxicological sciences : an official journal of the Society of Toxicology, 2014. **140**(2): p. 352–363.
74. Xue, J., et al., *Urinary levels of endocrine-disrupting chemicals, including bisphenols, bisphenol A diglycidyl ethers, benzophenones, parabens, and triclosan in obese and non-obese Indian children.* Environmental Research, 2015. **137**: p. 120–128.
75. Hu, P., et al., *Differential effects on adiposity and serum marker of bone formation by post-weaning exposure to methylparaben and butylparaben.* Environmental Science and Pollution Research, 2016. **23**(21): p. 21957–21968.
76. Pereira-Fernandes, A., et al., *Evaluation of a Screening System for Obesogenic Compounds: Screening of Endocrine Disrupting Compounds and Evaluation of the PPAR Dependency of the Effect.* PLoS ONE, 2013. **8**(10).
77. Wang, X., et al., *3-tert-Butyl-4-hydroxyanisole Perturbs Differentiation of C3H10T1/2 Mesenchymal Stem Cells into Brown Adipocytes through Regulating Smad Signaling.* Environmental Science & Technology, 2023. **57**(30): p. 10998–11008.

78. Hao, C., et al., *The endocrine disruptor 4-nonylphenol promotes adipocyte differentiation and induces obesity in mice.* Cellular Physiology and Biochemistry, 2012. **30**(2): p. 382–394.
79. Choi, J., et al., *Association between some endocrine-disrupting chemicals and childhood obesity in biological samples of young girls: A cross-sectional study.* Environmental Toxicology and Pharmacology, 2014. **38**(1): p. 51–57.
80. Zhang, Q., et al., *Effects of 4-nonylphenol on adipogenesis in 3T3-L1 preadipocytes and C3H/10T1/2 mesenchymal stem cells.* Journal of Applied Toxicology, 2022. **42**(4): p. 588–599.
81. Sun, L., et al., *Triclosan-induced abnormal expression of miR-30b regulates fto-mediated m6A methylation level to cause lipid metabolism disorder in zebrafish.* Science of the Total Environment, 2021. **770**: p. 145285.
82. Manikkam, M., et al., *Plastics derived endocrine disruptors (BPA, DEHP and DBP) induce epigenetic transgenerational inheritance of obesity, reproductive disease and sperm epimutations.* PLoS ONE, 2013. **8**(1).
83. Buerger, A.N., et al., *Examining the responses of the zebrafish (Danio rerio) gastrointestinal system to the suspected obesogen diethylhexyl phthalate.* Environmental Pollution, 2019. **245**: p. 1086–1094.
84. Hao, C., et al., *Perinatal exposure to diethyl-hexyl-phthalate induces obesity in mice.* Frontiers in Bioscience - Elite, 2013. **5 E**(2): p. 725–733.
85. Ko, H., et al., *Sunscreen filter octocrylene is a potential obesogen by acting as a PPARγ partial agonist.* Toxicology Letters, 2022. **355**: p. 141–149.
86. Su, H., et al., *Long-term chronic exposure to di-(2-ethylhexyl)-phthalate induces obesity via disruption of host lipid metabolism and gut microbiota in mice.* Chemosphere, 2022. **287**: p. 132414.
87. Hsu, J.-W., et al., *Phthalate exposure causes browning-like effects on adipocytes in vitro and in vivo.* Food and Chemical Toxicology, 2020. **142**: p. 111487.
88. Zhou, Y., et al., *Bis(2-ethylhexyl)-tetrabromophthalate induces zebrafish obesity by altering the brain-gut axis and intestinal microbial composition.* Environmental Pollution, 2021. **290**: p. 118127.
89. Zhang, W., et al., *Characterizing the obesogenic and fatty liver-inducing effects of Acetyl tributyl citrate (ATBC) plasticizer using both in vivo and in vitro models.* Journal of Hazardous Materials, 2023. **445**.
90. Temkin, A.M., et al., *Increased adiposity, inflammation, metabolic disruption and dyslipidemia in adult male offspring of DOSS treated C57BL/6 dams.* Scientific reports, 2019. **9**(1): p. 1530.
91. Shannon, M., et al., *In vitro bioassay investigations of suspected obesogen monosodium glutamate at the level of nuclear receptor binding and steroidogenesis.* Toxicology Letters, 2019. **301**: p. 11–16.
92. Schlezinger, J., et al., *Perfluorooctanoic acid activates multiple nuclear receptor pathways and skews expression of genes regulating cholesterol homeostasis in liver of humanized PPARα mice fed an American diet.* Toxicology and applied pharmacology, 2020. **405**: p. 115204.

93. Murase, W., et al., *Effects of perfluorooctanoic acid (PFOA) on gene expression profiles via nuclear receptors in HepaRG cells: Comparative study with in vitro transactivation assays.* Toxicology, 2023: p. 153577.
94. des Umweltbundesamtes, B., *Ableitung von HBM-I-Werten für den Di-n-hexylphthalat (DnHexP) Monoester-Metaboliten MnHexP.* Bundesgesundheitsblatt-Gesundheitsforschung-Gesundheitsschutz, 2025. **9**: p. 1088.
95. Jaskulak, M., et al., *Understanding the role of endocrine disrupting chemicals as environmental obesogens in the obesity epidemic: A comprehensive overview of epidemiological studies between 2014 and 2024.* Ecotoxicology and Environmental Safety, 2025. **299**: p. 118401.
96. Nicolaou, M., et al., *Obesogens in Adolescence: Challenging Aspects and Prevention Strategies.* Children, 2024. **11**(5): p. 602.
97. EFSA, *Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs.* EFSA Journal 21(4), 2023.
98. Molina-López, A.M., et al., *An Overview of the Health Effects of Bisphenol A from a One Health Perspective.* Animals, 2023. **13**(15): p. 2439.
99. Cimmino, I., et al., *Potential mechanisms of bisphenol A (BPA) contributing to human disease.* International journal of molecular sciences, 2020. **21**(16): p. 5761.
100. Coppola, L. and C. La Rocca, *Special Issue "Molecular Mechanisms of Bisphenol A Toxicity and Effects of Environmental Levels on Health".* International journal of molecular sciences, 2023. **24**(9): p. 8028.
101. Guo, J., et al., *The possible molecular mechanisms of bisphenol A action on porcine early embryonic development.* Scientific reports, 2017. **7**(1): p. 8632.
102. Legeay, S. and S. Faure, *Is bisphenol A an environmental obesogen?* Fundamental and Clinical Pharmacology, 2017. **31**(6): p. 594–609.
103. Rubin, B.S., C.M. Schaeberle, and A.M. Soto, *The Case for BPA as an Obesogen: Contributors to the Controversy.* Front Endocrinol (Lausanne), 2019. **10**: p. 30.
104. Camacho, L., et al., *A two-year toxicology study of bisphenol A (BPA) in Sprague-Dawley rats: CLARITY-BPA core study results.* Food Chem Toxicol, 2019. **132**: p. 110728.
105. RAC. *Opinion on scientific evaluation of occupational exposure limits for4,4-Isopropylidenediphenol (Bisphenol A) and screening of other Bisphenols*. ECHA/RAC/ OEL-O-0000007530-80-01/F 2025. Available from: https://echa.europa.eu/documents/10162/d1fe96a0-c47b-aa63-abda-4ec109327700
106. Luo, S., et al., *Gestational and lactational exposure to low-dose bisphenol A increases Th17 cells in mice offspring.* Environ Toxicol Pharmacol, 2016. **47**: p. 149–158.
107. EFSA. *Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs*. EFSA Journal 21(4) 2023. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2023.6857

108. Ma, L., et al., *Bisphenol A promotes hyperuricemia via activating xanthine oxidase.* The FASEB Journal, 2018. **32**(2): p. 1007–1016.
109. Yang, M., et al., *Bisphenol A promotes adiposity and inflammation in a nonmonotonic dose-response way in 5-week-old male and female C57BL/6J mice fed a low-calorie diet.* Endocrinology, 2016. **157**(6): p. 2333–2345.
110. HBM4EU. *Policy brief bisphenols*. 2022. Available from: https://www.hbm4eu.eu/wp-content/uploads/2022/06/HBM4EU_Policy-Brief-Bisphenols.pdf
111. Mohajer, N., et al., *Epigenetic Transgenerational Inheritance of the Effects of Obesogen Exposure.* Frontiers in Endocrinology, 2021. **12**.
112. Chen, H., et al., *Transcriptome changes and potential immunotoxicity analysis in RAW264. 7 macrophages caused by bisphenol F.* Frontiers in pharmacology, 2022. **13**: p. 846562.
113. Odetayo, A.F., W.J. Adeyemi, and L.A. Olayaki, *In vivo exposure to bisphenol F induces oxidative testicular toxicity: role of Erβ and p53/Bcl-2 signaling pathway.* Frontiers in Reproductive Health, 2023. **5**: p. 1204728.
114. Yuan, L., et al., *Bisphenol F-induced neurotoxicity toward zebrafish embryos.* Environmental science & technology, 2019. **53**(24): p. 14638–14648.
115. Engdahl, E., et al., *Bisphenol A inhibits the transporter function of the blood-brain barrier by directly interacting with the ABC transporter breast cancer resistance protein (BCRP).* International Journal of Molecular Sciences, 2021. **22**(11): p. 5534.
116. Rugard, M., et al., *Deciphering Adverse Outcome Pathway Network Linked to Bisphenol F Using Text Mining and Systems Toxicology Approaches.* Toxicol Sci, 2020. **173**(1): p. 32–40.
117. RAC. *Opinion proposing harmonised classification and labelling at EU level of 4,4'-methylenediphenol; bisphenol F, EC Number: 210-658-2, CAS Number: 620-92-8*. CLH-O-0000007440-81-01/F 2024. Available from: https://echa.europa.eu/documents/10162/68c20fdb-05b1-132b-ae49-357575aebdc4
118. Pelch, K., et al., *A scoping review of the health and toxicological activity of bisphenol A (BPA) structural analogues and functional alternatives.* Toxicology, 2019. **424**: p. 152235.
119. Rochester, J.R. and A.L. Bolden, *Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes.* Environmental health perspectives, 2015. **123**(7): p. 643–650.
120. Singh, M., et al., *Tetra methyl bisphenol F: another potential obesogen.* International Journal of Obesity, 2024. **48**(7): p. 923–933.
121. Reina-Perez, I., et al., *Bisphenol F and bisphenol S promote lipid accumulation and adipogenesis in human adipose-derived stem cells.* Food and Chemical Toxicology, 2021. **152**: p. 112216.
122. Zhang, Y., et al., *Bisphenol F promoted the differentiation of preadipocytes via ER-mediated PI3K/AKT pathway.* Food and Chemical Toxicology, 2025: p. 115678.
123. Wagner, V.A., et al., *Bisphenol F Exposure in Adolescent Heterogeneous Stock Rats Affects Growth and Adiposity.* Toxicol Sci, 2021. **181**(2): p. 246–261.

124. Biomonitoring California. *Bisphenol S (BPS) Fact Sheet*. 2018. Available from: https://biomonitoring.ca.gov/sites/default/files/downloads/BisphenolSFactSheet.pdf
125. Akash, M.S.H., et al., *Toxicological evaluation of bisphenol analogues: preventive measures and therapeutic interventions.* RSC advances, 2023. **13**(31): p. 21613–21628.
126. Kim, J.-J., et al., *Bisphenols as a legacy pollutant, and their effects on organ vulnerability.* International journal of environmental research and public health, 2020. **17**(1): p. 112.
127. Thoene, M., et al., *Bisphenol S in food causes hormonal and obesogenic effects comparable to or worse than bisphenol A: a literature review.* Nutrients, 2020. **12**(2): p. 532.
128. Pant, J., R. Agarwal, and L. Mohan, *Bisphenol S: A potential toxicant in daily use.* World Academy of Sciences Journal, 2023. **5**(3): p. 17.
129. Wu, N., et al., *The environmental occurrence, human exposure, and toxicity of novel bisphenol S derivatives: A review.* Ecotoxicology and Environmental Safety, 2025. **296**: p. 118182.
130. RAC. *Opinion proposing harmonised classification and labelling at EU level of 4,4'-sulphonyldiphenol; bisphenol S, EC Number: 201-250-5, CAS Number: 80-09-1*. CLH-O-0000006929-56-01/F 2020. Available from: https://echa.europa.eu/documents/10162/03fac9dc-94e7-a81c-fed5-1c5008a1c1bc
131. Beausoleil, C., et al., *Regulatory and academic studies to derive reference values for human health: The case of bisphenol S.* Environmental Research, 2022. **204**: p. 112233.
132. Fasano, E., et al., *Migration of phthalates, alkylphenols, bisphenol A and di(2-ethylhexyl)adipate from food packaging.* Food Control, 2012. **27**(1): p. 132–138.
133. EFSA. *Update of the risk assessment of di-butylphthalate (DBP), butyl-benzyl-phthalate (BBP), bis (2-ethylhexyl) phthalate (DEHP), di-isononylphthalate (DINP) and di-isodecylphthalate (DIDP) for use in food contact materials*. EFSA journal 2019. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5838
134. Mylchreest, E., et al., *Dose-dependent alterations in androgen-regulated male reproductive development in rats exposed to Di(n-butyl) phthalate during late gestation.* Toxicol Sci, 2000. **55**(1): p. 143–51.
135. ATSDR. *Toxicological profile for di-n-butyl phthalate*. 2001. Available from: https://www.atsdr.cdc.gov/toxprofiles/tp135.pdf
136. Lee, K.-Y., et al., *Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during the period from late gestation through lactation.* Toxicology, 2004. **203**(1-3): p. 221–238.
137. Harley, K.G., et al., *Association of prenatal urinary phthalate metabolite concentrations and childhood BMI and obesity.* Pediatric Research, 2017. **82**(3): p. 405–415.
138. Philips, E.M., et al., *Exposures to phthalates and bisphenols in pregnancy and postpartum weight gain in a population-based longitudinal birth cohort.* Environment international, 2020. **144**: p. 106002.

139. Philips, E.M., et al., *Maternal bisphenol and phthalate urine concentrations and weight gain during pregnancy.* Environment international, 2020. **135**: p. 105342.
140. Li, H., et al., *Intrauterine exposure to low-dose DBP in the mice induces obesity in offspring via suppression of UCP1 mediated ER stress.* Sci Rep, 2020. **10**(1): p. 16360.
141. Bodar, C., *Environmental risk limits for dibutylphthalate (DBP).* 2008.
142. RAC. *24th meeting of the committee for risk assessment, DNEL setting (DBP), RAC/24/2013/09_rev 2 Agreed in written procedure* 2013. Available from: https://echa.europa.eu/documents/10162/21961120/rac_24_dnel_dbp_comments_en.pdf/44ab77fd-d6fa-4d73-b0ed-9317fd6c0422
143. Majeed, K.A., et al., *Effects of Subacute Exposure of Dibutyl Phthalate on the Homeostatic Model Assessment, Thyroid Function, and Redox Status in Rats.* Biomed Res Int, 2021. **2021**: p. 5521516.
144. Zhou, K., et al., *The influence of perinatal maternal exposure to dibutyl phthalate on glucolipid metabolism in adult female offspring.* Obesity Research & Clinical Practice, 2022. **16**(6): p. 500–506.
145. Neier, K., et al., *Longitudinal metabolic impacts of perinatal exposure to phthalates and phthalate mixtures in mice.* Endocrinology, 2019. **160**(7): p. 1613–1630.
146. ATSDR. *Toxicological Profile for Di (2-ethylhexyl) phthalate (DEHP)*. 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK590474/pdf/Bookshelf_NBK590474.pdf
147. Wolfe, G. and K. Layton, *Multigeneration reproduction toxicity study in rats: Di (2-ethylhexyl) Phthalate: multigenerational reproductive assessment by continuous breeding when administered to Sprague-Dawley rats in the diet.* Unaudited draft. Gaithersburg, MD: TherImmune Research Corporation, 2003: p. 7244–200.
148. Parks, L.G., et al., *The Plasticizer Diethylhexyl Phthalate Induces Malformations by Decreasing Fetal Testosterone Synthesis during Sexual Differentiation in the Male Rat.* Toxicological Sciences, 2000. **58**(2): p. 339–349.
149. Meeker, J.D., A.M. Calafat, and R. Hauser, *Urinary Metabolites of Di(2-ethylhexyl) Phthalate Are Associated With Decreased Steroid Hormone Levels in Adult Men.* Journal of Andrology, 2009. **30**(3): p. 287–297.
150. Duty, S.M., et al., *Phthalate Exposure and Human Semen Parameters.* Epidemiology, 2003. **14**(3): p. 269–277.
151. Wassenaar, P.N.H. and J. Legler, *Systematic review and meta-analysis of early life exposure to di (2-ethylhexyl) phthalate and obesity related outcomes in rodents.* Chemosphere, 2017. **188**: p. 174–181.
152. Feige, J.N., et al., *The pollutant diethylhexyl phthalate regulates hepatic energy metabolism via species-specific PPARα-dependent mechanisms.* Environmental Health Perspectives, 2010. **118**(2): p. 234–241.

153. Wang, S., et al., *Exposure to environmental doses of DEHP causes phenotypes of polycystic ovary syndrome.* Toxicology, 2024. **509**: p. 153952.
154. Hao, C., et al., *The endocrine disruptor mono-(2-ethylhexyl) phthalate promotes adipocyte differentiation and induces obesity in mice.* Bioscience reports, 2012. **32**(6): p. 619–629.
155. Klöting, N., et al., *Di-(2-Ethylhexyl)-Phthalate (DEHP) Causes Impaired Adipocyte Function and Alters Serum Metabolites.* PLoS One, 2015. **10**(12): p. e0143190.
156. WHO. *Guidelines for drinking-water quality: incorporating the first and second addenda*. 2022. Available from: https://iris.who.int/server/api/core/bitstreams/69c17edd-ee26-425b-9d34-33799377e886/content
157. RAC. *24th meeting of the committee for risk assessment, DNEL setting (DEHP), RAC/24/2013/08 rev. 2 Agreed in written procedure*. 2013. Available from: https://images.chemycal.com/Media/Files/TBT/rac_24_dnel_dehp_comments_en.pdf
158. Wang, J., et al., *Di-(2-ethylhexyl) phthalate induces prepubertal testicular injury through MAM-related mitochondrial calcium overload in Leydig and Sertoli cell apoptosis.* Toxicology, 2024. **509**: p. 153956.
159. Kang, J.S., et al., *Long-term exposure changes the environmentally relevant bis(2-ethylhexyl) phthalate to be a neuro-hazardous substance disrupting neural homeostasis in emotional and cognitive functions.* Environmental Pollution, 2023. **324**: p. 121387.
160. Schmidt, J.-S., et al., *Effects of di (2-ethylhexyl) phthalate (DEHP) on female fertility and adipogenesis in C3H/N mice.* Environmental health perspectives, 2012. **120**(8): p. 1123–1129.
161. CPSC US. *Toxicity review for dicyclohexyl phthalate (DCHP, CASRN 84–61–7)*. 2010. Available from: https://www.cpsc.gov/s3fs-public/ToxicityReviewOfDCHP.pdf
162. EPA. *Draft Risk Evaluation for Dicyclohexyl Phthalate (DCHP)*. 2024. Available from: https://www.epa.gov/system/files/documents/2025-01/1.-dchp-.-draft-risk-evaluation-.-public-release-.-hero-.-dec-2024.pdf
163. Sui, Y., et al., *Effects of Dicyclohexyl Phthalate Exposure on PXR Activation and Lipid Homeostasis in Mice.* Environ Health Perspect, 2021. **129**(12): p. 127001.
164. Zhang, Y., et al., *Dicyclohexyl phthalate derails trophoblast function and lipid metabolism through NDRG1 by targeting PPARα:RXRα.* Toxicology, 2025. **514**: p. 154124.
165. EPA. *Draft Non-cancer Human Health Hazard Assessment for Butyl Benzyl Phthalate (BBP)*. Technical Support Document for the Draft Risk Evaluation 2024. Available from: https://www.epa.gov/system/files/documents/2025-01/bbp-.-draft-non-cancer-human-health-hazard-tsd-.-public-release-.-hero-.-dec-2024.pdf
166. CPSC US. *Toxicity review for Benzyl-n-Butyl Phthalate (Benzyl Butyl Phthalate or BBP)*. Bethesda, MD: United States Consumer Product Safety Commission 2010. Available from: https://www.cpsc.gov/s3fs-public/ToxicityReviewOfBBP.pdf

167. Gray, L.E., Jr., et al., *Perinatal Exposure to the Phthalates DEHP, BBP, and DINP, but Not DEP, DMP, or DOTP, Alters Sexual Differentiation of the Male Rat.* Toxicological Sciences, 2000. **58**(2): p. 350–365.
168. Yin, L., et al., *Benzyl butyl phthalate promotes adipogenesis in 3T3-L1 preadipocytes: A High Content Cellomics and metabolomic analysis.* Toxicology in Vitro, 2016. **32**: p. 297–309.
169. Buacheen, P., et al., *Protective effect of Anoectochilus burmannicus extracts and its active compound, kinsenoside on adipocyte differentiation induced by benzyl butyl phthalate and bisphenol A.* Scientific Reports, 2023. **13**(1): p. 2939.
170. Park, M.-S., et al., *Age-Dependent Effects of Butyl Benzyl Phthalate Exposure on Lipid Metabolism and Hepatic Fibrosis in Mice.* Cells, 2025. **14**(2): p. 126.
171. RAC. *Application for authorisation: Establishing reference DNELs for BBP, RAC/26/2013/07 Rev.1* 2013. Available from: http://echa.europa.eu/documents/10162/13579/rac_26_reference_dnels_bbp_en.pdf
172. Carlson, K., *CPSC Staff Statement on University of Cincinnati Report: Toxicity Review for Di-2-Ethylhexyl Terephthalate (DEHT).* University of Cincinnati: Cincinnati, OH, USA, 2018.
173. SCENIHR. *The safety of medical devices containing DEHP plasticized PVC or other plasticizers on neonates and other groups possibly at risk (2015 update)*. Regulatory toxicology and pharmacology: RTP 76 2016. Available from: https://health.ec.europa.eu/document/download/d17de743-1077-4654-81a7-b4148667f20c_en?filename=scenihr_o_047.pdf
174. NTP. *NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Hexyl Phthalate (DnHP)*. Ntp Cerhr Mon 2003; i–III90]. Available from: https://ntp.niehs.nih.gov/sites/default/files/ntp/ohat/phthalates/dnhp/dnhp_monograph_final.pdf
175. Aydemir, D., et al., *Effects of the in-utero dicyclohexyl phthalate and di-n-hexyl phthalate administration on the oxidative stress-induced histopathological changes in the rat liver tissue correlated with serum biochemistry and hematological parameters.* Frontiers in endocrinology, 2023. **14**: p. 1128202.
176. Saillenfait, A.M., et al., *Dose-dependent alterations in gene expression and testosterone production in fetal rat testis after exposure to di-n-hexyl phthalate.* J Appl Toxicol, 2013. **33**(9): p. 1027–35.
177. Aydoğan Ahbab, M. and N. Barlas, *Influence of in utero di-n-hexyl phthalate and dicyclohexyl phthalate on fetal testicular development in rats.* Toxicol Lett, 2015. **233**(2): p. 125–37.
178. Wei, F., et al., *Parabens as chemicals of emerging concern in the environment and humans: A review.* Sci Total Environ, 2021. **778**: p. 146150.
179. SCCS. *SCCS OPINION on Butylparaben (CAS No. 94-26-8, EC No. 202-318-7)-SCCS/1651/23–Final Opinion*. 2023. Available from: https://health.ec.europa.eu/document/download/453366da-0b79-48f6-963e-648f8c176000_en?filename=sccs_o_296.pdf
180. Hu, P., et al., *Effects of Parabens on Adipocyte Differentiation.* Toxicological Sciences, 2012. **131**(1): p. 56–70.

181. Hu, P., et al., *Methylparaben and butylparaben alter multipotent mesenchymal stem cell fates towards adipocyte lineage.* Toxicol Appl Pharmacol, 2017. **329**: p. 48–57.
182. Leppert, B., et al., *Maternal paraben exposure triggers childhood overweight development.* Nature Communications, 2020. **11**(1): p. 561.
183. Golestanzadeh, M., et al., *Association between parabens concentrations in human amniotic fluid and the offspring birth size: A Sub-study of the PERSIAN birth cohort.* Environmental Research, 2022. **212**: p. 113502.
184. Højsager, F.D., et al., *Prenatal Exposure to Butyl Paraben Is Associated With Fat Percentage in 7-Year-Old Boys.* J Clin Endocrinol Metab, 2021. **106**(7): p. e2633–e2638.
185. SCCS. *SCCS opinion on Butylparaben (CAS No. 94-26-8, EC No. 202-318-7)-children's exposure-SCCS/1674/25–final opinion*. 2025. Available from: https://health.ec.europa.eu/document/download/453366da-0b79-48f6-963e-648f8c176000_en?filename=sccs_o_296.pdf
186. Boberg, J., et al., *Possible endocrine disrupting effects of parabens and their metabolites.* Reprod Toxicol, 2010. **30**(2): p. 301–12.
187. Nowak, K., et al., *Parabens and their effects on the endocrine system.* Mol Cell Endocrinol, 2018. **474**: p. 238–251.
188. Oishi, S., *Lack of spermatotoxic effects of methyl and ethyl esters of p-hydroxybenzoic acid in rats.* Food and chemical toxicology, 2004. **42**(11): p. 1845–1849.
189. Guo, J., et al., *Urinary paraben concentrations and their associations with anthropometric measures of children aged 3 years.* Environmental Pollution, 2017. **222**: p. 307–314.
190. EFSA. *Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) related to para hydroxybenzoates (E 214–219)*. EFSA Journal 2 (9) 2004. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2004.83
191. SCCS. *SCCS OPINION on Methylparaben (CAS No. 99-76-3, EC No. 202-785-7)-SCCS/1652/23–Final Opinion*. 2023. Available from: https://health.ec.europa.eu/system/files/2023-12/sccs_o_276_final.pdf
192. SCCS. *SCCS Opinion of the scientific committee on consumer safety (SCCS)–final opinion on propylparaben (CAS No 94-13-3, EC No 202-307-7)*. Regulatory toxicology and pharmacology 2021; 105005]. Available from: https://health.ec.europa.eu/system/files/2022-08/sccs_o_243.pdf
193. Berger, K., et al., *Prenatal exposure to mixtures of phthalates, parabens, and other phenols and obesity in five-year-olds in the CHAMACOS cohort.* International journal of environmental research and public health, 2021. **18**(4): p. 1796.
194. Sivaraman, L., et al., *Safety assessment of propylparaben in juvenile rats.* Regulatory Toxicology and Pharmacology, 2018. **92**: p. 370–381.
195. Berardesca, E., et al., *Review of the safety of octocrylene used as an ultraviolet filter in cosmetics.* J Eur Acad Dermatol Venereol, 2019. **33 Suppl 7**: p. 25–33.

196. SCCS. *SCCS OPINION ON Octocrylene-SCCS/1627/21-Final Opinion*. 2021. Available from: https://health.ec.europa.eu/document/download/2928185b-f8b7-474e-937a-052a90a90970_en
197. Kunz, P.Y. and K. Fent, *Estrogenic activity of UV filter mixtures.* Toxicol Appl Pharmacol, 2006. **217**(1): p. 86–99.
198. EFSA. *Scientific Opinion on the re-evaluation of butylated hydroxytoluene BHT (E 321) as a food additive*. EFSA Journal 2012 [cited 10 3]; 2588]. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2012.2588
199. De Abrew, K.N., et al., *A New Approach Methodology (NAM) Based Assessment of Butylated hydroxytoluene (BHT) for Endocrine Disruption Potential.* Toxicol Sci, 2022. **190**(2): p. 227–241.
200. Alofe, O., et al., *Determining the endocrine disruption potential of industrial chemicals using an integrative approach: Public databases, in vitro exposure, and modeling receptor interactions.* Environment International, 2019. **131**: p. 104969.
201. SCCS. *SCCS OPINION on Butylated Hydroxytoluene (BHT)-SCCS/1636/21-Final Opinion*. 2021. Available from: https://health.ec.europa.eu/system/files/2022-08/sccs_o_257.pdf
202. Lanigan, R.S. and T.A. Yamarik, *Final report on the safety assessment of BHT(1).* Int J Toxicol, 2002. **21 Suppl 2**: p. 19–94.
203. Dutch Health Council. *Health-based Reassessment of Administrative Occupational Exposure Limits: 2,6-Di-tert-butyl-p-cresol*. No. 2000/15OSH/101 2004. Available from: https://www.healthcouncil.nl/site/binaries/site-content/collections/documents/2004/03/30/2-6-di-tert-butyl-p-cresol/advisory-report-health-based-reassessment-of-administrative-occupational-exposure-limits-2-6-di-tert-butyl-p-cresol.pdf
204. Wada, H., et al., *In vitro estrogenicity of resin composites.* Journal of dental research, 2004. **83**(3): p. 222–226.
205. EPA. *Provisional Peer-Reviewed Toxicity Values for Butylated Hydroxytoluene (BHT)*. EPA/690/R-13/003F Final 2013. Available from: https://cfpub.epa.gov/ncea/pprtv/documents/Butylatedhydroxytoluene.pdf
206. SCCS. *SCCS Opinion on Triphenyl phosphate (CAS No. 204-112-2, EC No. 115-86-6)-SCCS/1664/24-Final opinion*. 2024. Available from: https://health.ec.europa.eu/document/download/28a3e06e-bd0d-4ee1-add7-252dc2964b0b_en?filename=sccs_o_286.pdf
207. Haglund, P., et al., *Comprehensive characterization of European house dust contaminants: Concentrations and profiles, geographical variability, and implications for chemical regulation and health risk.* Science of The Total Environment, 2024. **957**: p. 177639.
208. MSCA France. *Risk Management Option Analysis Conclusion Document TPP*. 2019. Available from: https://echa.europa.eu/documents/10162/c98e5a7d-2aaa-0b20-1cf1-394a32deeea7
209. Hartwig, A., *MAK Value Documentation, addendum – Translation of the German version from 2023.* 2024.

210. Burnett, C.L., et al., *Safety Assessment of Triphenyl Phosphate as Used in Cosmetics.* International journal of toxicology, 2025. **44**(1_suppl): p. 86S–99S.
211. Beausoleil, C., et al., *Weight of evidence evaluation of the metabolism disrupting effects of triphenyl phosphate using an expert knowledge elicitation approach.* Toxicology and Applied Pharmacology, 2024. **489**: p. 116995.
212. Tachachartvanich, P., et al., *Perinatal triphenyl phosphate exposure induces metabolic dysfunctions through the EGFR/ERK/AKT signaling pathway: mechanistic in vitro and in vivo studies.* Ecotoxicology and Environmental Safety, 2024. **269**: p. 115756.
213. Li, T., et al., *Triphenyl phosphate induces lipid metabolism disorder and promotes obesity through PI3K/AKT signaling pathway.* Environment International, 2025. **198**: p. 109428.
214. ANSES. *Analysis of the most appropriate risk management option (RMOA) for Triphenyl phosphate (TPP) EC n° 204-112-2.* 2019. Available from: https://echa.europa.eu/documents/10162/24222797/ec204-112%202_tpp_rmoa_13147_en.pdf/a6ce7a90-9c01-d3cf-f2c8-04382d7807f9
215. Green, A.J., et al., *Perinatal triphenyl phosphate exposure accelerates type 2 diabetes onset and increases adipose accumulation in UCD-type 2 diabetes mellitus rats.* Reproductive Toxicology, 2017. **68**: p. 119–129.
216. RIVM. *Advies 16191A00 - Indicatief MTR lucht voor trifenylfosfaat*. 2024. Available from: https://rvs.rivm.nl/sites/default/files/2024-07/Advies_16191A00_iMTR_lucht_trifenylfosfaat.pdf
217. Lin, J., et al., *Exposure to triphenyl phosphate during pregnancy: The role of gut-bile acids-liver axis on lipid metabolism in male offspring.* Ecotoxicology and Environmental Safety, 2025. **290**: p. 117554.
218. WHO. *Integrated risk assessment: nonylphenol case study*. 2017. Available from: https://cdn.who.int/media/docs/default-source/chemical-safety/nonylphenol-who-ipcs-ira-1204.pdf?sfvrsn=751c0ddc_2
219. Zhang, H., et al., *High-Fat Diet Promotes Adipogenesis in Offspring Female Rats Induced by Perinatal Exposure to 4-Nonylphenol.* BioMed Research International, 2023. **2023**(1): p. 6540585.
220. Ladefoged, O. and J.E. Jelnes, *Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl, Phosphates and Benzoic Acid.*
221. Guazzotti, V., et al., *Styrene migration from polystyrene for food contact: a case study on the processing chain of yoghurt pots.* Applied Sciences, 2024. **14**(19): p. 9056.
222. OECD, *Estimating Mouthing Exposure in Children – Compilation of Case Studies. ENV/JM/MONO(2019)2.* Environment directorate joint meeting of the chemicals committee and the working party on chemicals, pesticides and biotechnology. Series on Testing and Assessment No. 306, 2019.

223. EFSA. *Assessment of the impact of the IARC Monograph Vol. 121 on the safety of the substance styrene (FCM No 193) for its use in plastic food contact materials*. EFSA journal 2020. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6247
224. Dutch Health Council. *Evaluation of the mutagenicity and carcinogenicity. To: the State Secretary for Participation and Integration. No. 2025/07/.* 2025. Available from: https://www.healthcouncil.nl/site/binaries/site-content/collections/documents/2025/04/25/styrene-evaluation-of-mutagenicity-and-carcinogenicity/07-Styrene_advice.pdf
225. EFSA. *Re-assessment of the risks to public health related to the genotoxicity of styrene present in plastic food contact materials*. EFSA journal 23(6) 2025. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2025.9473
226. TEDX. *TEDX list of potential endocrine disruptors* 2018. Available from: https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list
227. Danish EPA. *Survey of styrene. Part of Louis review. Environmental prject No. 1612*. 2014. Available from: https://www2.mst.dk/Udgiv/publications/2014/11/978-87-93283-17-6.pdf
228. Borgert, C.J., *Hypothesis-driven weight of evidence evaluation indicates styrene lacks endocrine disruption potential.* Critical Reviews in Toxicology, 2023. **53**(2): p. 53–68.
229. Lei, T., et al., *The association analysis between exposure to volatile organic chemicals and obesity in the general USA population: a cross-sectional study from NHANES program.* Chemosphere, 2023. **315**: p. 137738.
230. Boucher, J.G., et al., *Identification of mechanisms of action of bisphenol a-induced human preadipocyte differentiation by transcriptional profiling.* Obesity, 2014. **22**(11): p. 2333–2343.
231. Ariemma, F., et al., *Low-dose bisphenol-A impairs adipogenesis and generates dysfunctional 3T3-L1 adipocytes.* PloS one, 2016. **11**(3): p. e0150762.
232. Taxvig, C., et al., *Differential effects of environmental chemicals and food contaminants on adipogenesis, biomarker release and PPARγ activation.* Molecular and cellular endocrinology, 2012. **361**(1-2): p. 106–115.
233. Martínez, M., et al., *Bisphenol A analogues (BPS and BPF) present a greater obesogenic capacity in 3T3-L1 cell line.* Food and Chemical Toxicology, 2020. **140**: p. 111298.
234. Sargis, R.M., et al., *Environmental endocrine disruptors promote adipogenesis in the 3T3-L1 cell line through glucocorticoid receptor activation.* Obesity, 2010. **18**(7): p. 1283–1288.
235. Boucher, J.G., et al., *Bisphenol A and bisphenol S induce distinct transcriptional profiles in differentiating human primary preadipocytes.* PloS one, 2016. **11**(9): p. e0163318.
236. Biemann, R., et al., *Endocrine disrupting chemicals affect the adipogenic differentiation of mesenchymal stem cells in distinct ontogenetic windows.* Biochemical and biophysical research communications, 2012. **417**(2): p. 747–752.

237. Desai, M., et al., *In vivo and in vitro bisphenol A exposure effects on adiposity.* J Dev Orig Health Dis, 2018. **9**(6): p. 678–687.
238. Angle, B.M., et al., *Metabolic disruption in male mice due to fetal exposure to low but not high doses of bisphenol A (BPA): evidence for effects on body weight, food intake, adipocytes, leptin, adiponectin, insulin and glucose regulation.* Reproductive toxicology, 2013. **42**: p. 256–268.
239. Somm, E., et al., *Perinatal exposure to bisphenol a alters early adipogenesis in the rat.* Environmental health perspectives, 2009. **117**(10): p. 1549.
240. Stoker, C., et al., *Perinatal exposure to bisphenol A (BPA) impairs neuroendocrine mechanisms regulating food intake and kisspetin system in adult male rats. Evidences of metabolic disruptor hypothesis.* Molecular and cellular endocrinology, 2020. **499**: p. 110614.
241. Bansal, A., et al., *Transgenerational effects of maternal bisphenol: a exposure on offspring metabolic health.* Journal of developmental origins of health and disease, 2019. **10**(2): p. 164–175.
242. Tassinari, R., et al., *Juvenile toxicity rodent model to study toxicological effects of bisphenol A (BPA) at dose levels derived from Italian children biomonitoring study.* Toxicological Sciences, 2020. **173**(2): p. 387–401.
243. Susiarjo, M., et al., *Bisphenol a exposure disrupts metabolic health across multiple generations in the mouse.* Endocrinology, 2015. **156**(6): p. 2049–2058.
244. Fadishei, M., et al., *Effects of Nigella sativa oil and thymoquinone against bisphenol A-induced metabolic disorder in rats.* Phytotherapy Research, 2021. **35**(4): p. 2005–2024.
245. Sol, C.M., et al., *Fetal phthalates and bisphenols and childhood lipid and glucose metabolism. A population-based prospective cohort study.* Environment International, 2020. **144**: p. 106063.
246. Kataria, A., et al., *Exposure to bisphenols and phthalates and association with oxidant stress, insulin resistance, and endothelial dysfunction in children.* Pediatric Research, 2017. **81**(6): p. 857–864.
247. Lee, S., et al., *Pharmacokinetics and toxicity evaluation following oral exposure to bisphenol F.* Archives of Toxicology, 2022. **96**(6): p. 1711–1728.
248. Del Moral, L.I., et al., *Obesogen effects after perinatal exposure of 4, 4′-sulfonyldiphenol (Bisphenol S) in C57BL/6 mice.* Toxicology, 2016. **357**: p. 11–20.
249. EFSA. *Assessment of new information on Bisphenol S (BPS) submitted in response to the Decision 1 under REACH Regulation (EC) No 1907/2006*. 2020. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2020.EN-1844
250. Lapinskas, P.J., et al., *Role of PPARα in mediating the effects of phthalates and metabolites in the liver.* Toxicology, 2005. **207**(1): p. 149–163.
251. Venturelli, A.C., et al., *Effects of in utero and lactational exposure to phthalates on reproductive development and glycemic homeostasis in rats.* Toxicology, 2019. **421**: p. 30–40.

252. Schaedlich, K., et al., *DEHP deregulates adipokine levels and impairs fatty acid storage in human SGBS-adipocytes.* Scientific reports, 2018. **8**(1): p. 3447.
253. Riu, A., et al., *Peroxisome proliferator-activated receptor γ is a target for halogenated analogs of bisphenol A.* Environmental health perspectives, 2011. **119**(9): p. 1227–1232.
254. Garoche, C., et al., *Interspecies differences in activation of peroxisome proliferator-activated receptor γ by pharmaceutical and environmental chemicals.* Environmental Science & Technology, 2021. **55**(24): p. 16489–16501.
255. Yasuda, A., et al., *Effects of di-(2-ethylhexyl) phthalate and its metabolites on transcriptional activity via human nuclear receptors and gene expression in HepaRG cells.* Toxicology in Vitro, 2024. **101**: p. 105943.
256. Feige, J.N., et al., *The endocrine disruptor monoethyl-hexyl-phthalate is a selective peroxisome proliferator-activated receptor γ modulator that promotes adipogenesis.* Journal of Biological Chemistry, 2007. **282**(26): p. 19152–19166.
257. Jia, Y., et al., *Effects of di-(2-ethylhexyl) phthalate on lipid metabolism by the JAK/STAT pathway in rats.* International journal of environmental research and public health, 2016. **13**(11): p. 1085.
258. Lv, Z., et al., *DEHP induces obesity and hypothyroidism through both central and peripheral pathways in C3H/He mice.* Obesity, 2016. **24**(2): p. 368–378.
259. Hunt, K.J., et al., *Phthalate and phthalate replacement concentrations in relationship to adiposity in a multi-racial cohort of children.* International Journal of Obesity, 2024. **48**(9): p. 1266–1273.
260. Yaghjyan, L., et al., *Associations of urinary phthalates with body mass index, waist circumference and serum lipids among females: National Health and Nutrition Examination Survey 1999–2004.* International journal of obesity, 2015. **39**(6): p. 994–1000.
261. Liu, J., et al., *Paternal phthalate exposure-elicited offspring metabolic disorders are associated with altered sperm small RNAs in mice.* Environment international, 2023. **172**: p. 107769.
262. Sonkar, R., C.A. Powell, and M. Choudhury, *Benzyl butyl phthalate induces epigenetic stress to enhance adipogenesis in mesenchymal stem cells.* Molecular and cellular endocrinology, 2016. **431**: p. 109–122.
263. Zhang, J. and M. Choudhury, *The plasticizer BBP selectively inhibits epigenetic regulator sirtuin during differentiation of C3H10T1/2 stem cell line.* Toxicology In Vitro, 2017. **39**: p. 75–83.
264. Meruvu, S., J. Zhang, and M. Choudhury, *Butyl benzyl phthalate promotes adipogenesis in 3T3-L1 cells via the miRNA-34a-5p signaling pathway in the absence of exogenous adipogenic stimuli.* Chemical Research in Toxicology, 2021. **34**(11): p. 2251–2260.
265. Sakuma, S., et al., *Curcumin inhibits adipogenesis induced by benzyl butyl phthalate in 3T3-L1 cells.* Toxicology and Applied Pharmacology, 2017. **329**: p. 158–164.
266. Kodani, S.D., et al., *Parabens inhibit fatty acid amide hydrolase: A potential role in paraben-enhanced 3T3-L1 adipocyte differentiation.* Toxicology letters, 2016. **262**: p. 92–99.

267. Elmore, S., G. Cano-Sancho, and M. La Merrill, *Disruption of normal adipocyte development and function by methyl-and propyl-paraben exposure.* Toxicology Letters, 2020. **334**: p. 27–35.
268. Azeredo, D.B.C., et al., *Endocrine-disrupting chemical, methylparaben, in environmentally relevant exposure promotes hazardous effects on the hypothalamus-pituitary-thyroid axis.* Molecular and Cellular Endocrinology, 2025. **598**: p. 112444.
269. Faine, L., et al., *Butyl hydroxytoluene (BHT)-induced oxidative stress: Effects on serum lipids and cardiac energy metabolism in rats.* Experimental and Toxicologic Pathology, 2006. **57**(3): p. 221–226.
270. Cano-Sancho, G., A. Smith, and M.A. La Merrill, *Triphenyl phosphate enhances adipogenic differentiation, glucose uptake and lipolysis via endocrine and noradrenergic mechanisms.* Toxicology in Vitro, 2017. **40**: p. 280–288.
271. Kim, S., et al., *A data-driven transcriptional taxonomy of adipogenic chemicals to identify white and brite adipogens.* Environmental Health Perspectives, 2021. **129**(7): p. 077006.
272. Wang, D., et al., *Effects of triphenyl phosphate exposure during fetal development on obesity and metabolic dysfunctions in adult mice: Impaired lipid metabolism and intestinal dysbiosis.* Environmental Pollution, 2019. **246**: p. 630–638.
273. Liu, Q., et al., *Prenatal Triphenyl Phosphate Exposure and Hyperlipidemia in Offspring: Role of Trophoblast-Derived Extracellular Vesicle PPARγ.* Environmental Science & Technology, 2024. **58**(52): p. 22930–22943.
274. Kim, S., et al., *Triphenyl phosphate is a selective PPARγ modulator that does not induce brite adipogenesis in vitro and in vivo.* Archives of toxicology, 2020. **94**(9): p. 3087–3103.
275. Hong, J., et al., *Prenatal exposure to triphenyl phosphate activated PPARγ in placental trophoblasts and impaired pregnancy outcomes.* Environmental Pollution, 2022. **301**: p. 119039.
276. Zhang, H.-y., et al., *Perinatal exposure to 4-nonylphenol affects adipogenesis in first and second generation rats offspring.* Toxicology letters, 2014. **225**(2): p. 325–332.
277. Schachterle, M.L., et al., *Micro-extraction method for the analysis of flame retardants in dust collected from air filters from HVAC systems.* MethodsX, 2024. **12**: p. 102693.
278. Biesterbos, J.W., et al., *Usage patterns of personal care products: important factors for exposure assessment.* Food and chemical toxicology, 2013. **55**: p. 8–17.
279. Bremmer, H. and J. van Engelen, *Cosmetics fact sheet. To assess the risks for the consumer. Updated version for ConsExpo 4.* 2006.
280. Meesters, J.A., et al., *Cleaning Products Fact Sheet: Default parameters for estimating consumer exposure-Updated version 2018.* 2018.
281. SCCS. *The SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation-12th revision-SCCS/1647/22*. 2023. Available from: https://health.ec.europa.eu/publications/sccs-notes-guidance-testing-cosmetic-ingredients-and-their-safety-evaluation-12th-revision_en

282. EFSA. *Statement on the use and interpretation of the margin of exposure approach*. EFSA Journal 23(8). 2025. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2025.9606
283. *AOP-Wiki, version 2.8*. 2026. Available from: https://aopwiki.org/
284. OECD. *Test No. 443: Extended One-Generation Reproductive Toxicity Study*. 2018. Available from: https://www.oecd.org/en/publications/test-no-443-extended-one-generation-reproductive-toxicity-study_9789264185371-en.html
285. de Moura e Dias, M., et al., *Diet-induced obesity in animal models: points to consider and influence on metabolic markers.* Diabetology & Metabolic Syndrome, 2021. **13**(1): p. 32.
286. Benedé-Ubieto, R., et al., *Guidelines and considerations for metabolic tolerance tests in mice.* Diabetes, Metabolic Syndrome and Obesity, 2020: p. 439–450.
287. EFSA and EMA. *Report on divergent views between EFSA and EMA on EFSA's updated bisphenol A assessment*. 2023. Available from: https://www.efsa.europa.eu/sites/default/files/2023-04/bfr-efsa-art-30.pdf
288. O'Connor, A.M., et al., *Implementation of systematic reviews in EFSA scientific outputs workflow.* EFSA Supporting Publications, 2012. **9**(12): p. 367E.
289. Marteinson, S.C. and K.J. Fernie, *Is the current-use flame retardant, DBE-DBCH, a potential obesogen? Effects on body mass, fat content and associated behaviors in American kestrels.* Ecotoxicology and Environmental Safety, 2019. **169**: p. 770–777.
290. Warner, M., et al., *Obesity in relation to serum persistent organic pollutant concentrations in CHAMACOS women.* Environmental Epidemiology, 2018. **2**(4).
291. Xu, M., et al., *The mechanism underlying pentabromoethylbenzene-induced adipogenesis and the obesogenic outcome in both cell and mouse model.* Environment International, 2023. **178**: p. 108088.
292. Chamorro-Garcia, R., et al., *Ancestral perinatal obesogen exposure results in a transgenerational thrifty phenotype in mice.* Nature Communications, 2017. **8**(1).
293. Chamorro-García, R., et al., *Transgenerational inheritance of increased fat depot size, stem cell reprogramming, and hepatic steatosis elicited by prenatal exposure to the obesogen tributyltin in mice.* Environmental Health Perspectives, 2013. **121**(3): p. 359–366.
294. Chang, R.C., et al., *MiR-223 Plays a Key Role in Obesogen-Enhanced Adipogenesis in Mesenchymal Stem Cells and in Transgenerational Obesity.* Endocrinology (United States), 2023. **164**(5).
295. Jordão, R., et al., *Obesogens beyond vertebrates: Lipid perturbation by tributyltin in the crustacean Daphnia magna.* Environmental Health Perspectives, 2015. **123**(8): p. 813–819.
296. Kirchner, S., et al., *Prenatal exposure to the environmental obesogen tributyltin predisposes multipotent stem cells to become adipocytes.* Molecular Endocrinology, 2010. **24**(3): p. 526–539.

297. Li, X., J. Ycaza, and B. Blumberg, *The environmental obesogen tributyltin chloride acts via peroxisome proliferator activated receptor gamma to induce adipogenesis in murine 3T3-L1 preadipocytes.* Journal of Steroid Biochemistry and Molecular Biology, 2011. **127**(1-2): p. 9–15.
298. Lyssimachou, A., et al., *The mammalian "obesogen" tributyltin targets hepatic triglyceride accumulation and the transcriptional regulation of lipid metabolism in the liver and brain of zebrafish.* PLoS ONE, 2015. **10**(12).
299. Meador, J.P., et al., *Tributyltin and the obesogen metabolic syndrome in a salmonid.* Environmental Research, 2011. **111**(1): p. 50–56.
300. Viñas, P., et al., *Determination of phthalate esters in cleaning and personal care products by dispersive liquid–liquid microextraction and liquid chromatography–tandem mass spectrometry.* Journal of Chromatography A, 2015. **1376**: p. 18–25.
301. Aldegunde-Louzao, N., M. Lolo-Aira, and C. Herrero-Latorre, *Phthalate esters in different types of cosmetic products: a five-year quality control survey.* Molecules, 2024. **29**(20): p. 4823.
302. De Orsi, D., et al., *A environmentally friendly reversed-phase liquid chromatography method for phthalates determination in nail cosmetics.* Analytica Chimica Acta, 2006. **555**(2): p. 238–241.
303. Aldegunde-Louzao, N., M. Lolo-Aira, and C. Herrero-Latorre, *Quality control in cosmetics: A five-year screening survey on the content of phthalates in colognes.* Chemistry Proceedings, 2023. **14**(1): p. 12.
304. Danish EPA. *Kortlægning og eksponering af kemiske stoffer i spraymaling* Kortlægning af kemiske stoffer i forbrugerprodukter Kortlægning nr. 45 2004 2004. Available from: https://www2.mst.dk/udgiv/publikationer/2004/Kortlaegning/045_eksponering_af_kemiske_stoffer_i_spraymaling.pdf
305. Danish EPA. *Kortlægning af pletfjernere*. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 43 2003 2003. Available from: https://www2.mst.dk/udgiv/publikationer/2003/Kortlaegning/043_kemiske_stoffer_i_pletfjernere.pdf
306. Danish EPA. *Fare- og eksponeringsvurdering af produkter til gør-detselv imprægnering*. Kortlægning af kemiske stoffer i forbruger produkter Nr. 189 2023. Available from: https://www2.mst.dk/Udgiv/publikationer/2023/08/978-87-7038-536-7.pdf
307. Affourtit, F., et al. *Aggregate exposure to parabens in personal care products and toys*. 2023. Available from: https://www.rivm.nl/bibliotheek/rapporten/2022-0201.pdf
308. Danish EPA. *Kortlægning og sundhedsmæssig vurdering af kemiske stoffer i sexcreme (pleasure gel)*. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 76 2006 2006. Available from: https://www2.mst.dk/udgiv/publikationer/2006/87-7052-218-9/pdf/87-7052-219-7.pdf
309. Danish EPA. *Kortlægning og sundhedsmæssig vurdering af produkter til indvendig bilpleje* Kortlægning af kemiske stoffer i forbrugerprodukter Nr. 105 2009 2009. Available from: https://www2.mst.dk/udgiv/publikationer/2009/978-87-92548-91-7/pdf/978-87-92548-92-4.pdf

310. Danish EPA. *Kortlægning og risikovurdering af badeprodukter til børn*. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 20 2025. Available from: https://www2.mst.dk/Udgiv/publikationer/2024/12/978-87-7038-693-7.pdf
311. Danish EPA. *Børn og ufødte børns samlede udsættelse for udvalgte kemiske stoffer*. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 159 2017. Available from: https://www2.mst.dk/udgiv/publikationer/2017/04/978-87-93529-85-4.pdf
312. Danish EPA. *Kortlægning og sundhedsmæssigvurdering af kemisk stoffer i skoplejemidler*. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 52 2005 2005. Available from: https://www2.mst.dk/udgiv/publikationer/2005/87-7614-641-3/pdf/87-7614-642-1.pdf
313. Danish EPA. *Kortlægning nr. 39: Afgivelse af kemiske stoffer i røgelse* 2004. Available from: https://www2.mst.dk/udgiv/publikationer/2004/Kortlaegning/039_Afvigelse_af_kemiske_stoffer_i_r%C3%B8gelse.pdf
314. Bakker, J., et al. *Bisphenol A: Part 1. Facts and figures on human and environmental health issues and regulatory perspectives*. RIVM Report 601351001/2014 2014. Available from: https://www.rivm.nl/bibliotheek/rapporten/601351001.pdf
315. EFSA. *Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs*. EFSA Journal 13(1) 2015. Available from: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2015.3978
316. Rime, C., et al., *Assessing bisphenols migration from children's products on the Swiss market: simulated oral exposure and risk implications.* Chemosphere, 2025. **393**: p. 144772.
317. Sogorb, M.A., J. Estévez, and E. Vilanova, *Case study: Is bisphenol S safer than bisphenol A in thermal papers?* Arch Toxicol, 2019. **93**(7): p. 1835–1852.
318. SCCP. *OPINION ON PHTHALATES IN COSMETIC PRODUCTS* SCCP/1016/06 2007. Available from: https://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_106.pdf
319. OECD. *Estimating Mouthing Exposure in Children – Compilation of Case Studies. ENV/JM/MONO(2019)2*. Environment directorate joint meeting of the chemicals committee and the working party on chemicals, pesticides and biotechnology. Series on Testing and Assessment No. 306 2019. Available from: https://www.oecd.org/en/publications/estimating-mouthing-exposure-in-children-compilation-of-case-studies_debe99f0-en.html
320. Danish EPA. *Survey and health assessment of phthalates in toys and other products for children*. Survey on chemicals in consumer products No. 139, 2015 2015. Available from: https://www2.mst.dk/udgiv/publications/2015/06/978-87-93352-44-5.pdf
321. Brandsma, S.H., et al., *Migration of hazardous contaminants from WEEE contaminated polymeric toy material by mouthing.* Chemosphere, 2022. **294**: p. 133774.

322. Brand, W., et al. *Exposure to and toxicity of methyl-, ethyl-and propylparaben: A literature review with a focus on endocrine-disrupting properties*. 2017. Available from: https://www.rivm.nl/bibliotheek/rapporten/2017-0028.pdf
323. Li, J., et al., *A review on organophosphate Ester (OPE) flame retardants and plasticizers in foodstuffs: Levels, distribution, human dietary exposure, and future directions.* Environment International, 2019. **127**: p. 35–51.
324. European Chemicals Bureau. *European Union Risk Assessment Report: 4-nonylphenol (branched) and nonylphenol*. 2002. Available from: https://www.bfr.bund.de/cm/343/4_nonylphenol_und_nonylphenol.pdf

List of abbreviations

4NP	4-nonylphenol
ADI	Acceptable Daily Intake
AGD	Anogenital Distance
AhR	Aryl hydrocarbon Receptor
AI	Artificial Intelligence
AOP	Adverse Outcome Pathway
ATSDR	U.S. Agency for Toxic Substances and Disease Registry
BBP	Benzyl butyl phthalate
BHT	Butylated hydroxytoluene
BMD	Bench Mark Dose
BMDL	Bench Mark Dose Level
BMI	Body Mass Index
BP	Butylparaben
BPA	Bisphenol A
BPF	Bisphenol F
BPS	Bisphenol S
bw	Body weight
CAR	Constitutive androstane receptor
CLP	Classification Labelling and Packaging
CMR	Carcinogenic, Mutagenic or toxic to Reproduction
CPR	Cosmetic Products Regulation
DBP	Di-n-butyl phthalate
DCHP	Dicyclohexyl phthalate
DEHP	Bis(2-ethylhexyl) phthalate
DHP	Dihexyl phthalate
DIO	Diet Induced Obese
DNEL	Derived No-Effect Level
DOTP	Dioctyl terephthalate
ECHA	European Chemicals Agency
ED	Endocrine Disrupting
EFSA	European Food Safety Authority
EGFR	Epidermal Growth Factor Receptor
EOGRTs	Extended One-Generation Reproductive Toxicity Study
EtP	Ethylparaben
EU	European Union
Fabp4	Fatty acid binding protein 4
FCCdb	Food Contact Chemicals Database
FCCmigex	Database on Migrating and Extractable Food Contact Chemicals
FCM	Food Contact Materials
FDA	U.S. Food and Drug Administration
FPF	Food Packaging Forum Foundation
FXR	Farnesoid X receptor
GC-MS	Gas Chromatography-Mass Spectrometry
GNPD	Mintel Global New Products Database
GPSR	General Product Safety Regulation
GR	Glucocorticoid receptor
HBM	Human Biomonitoring
HEEDS	Healthy Environment and Endocrine Disruptors Strategies
IATA	Integrated Approaches to Testing and Assessment

LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
LOQ	Limit of Quantification
Lpl	Lipoprotein lipase
LXR	Liver X receptor
MBP	Monobutyl phthalate
MeP	Methylparaben
MEHP	Mono(2-ethylhexyl) phthalate
MoA	Mode of Action
MOE	Margin of Exposure
MRL	Minimal Risk Level
MTR	Maximaal Toelaatbaar Risico
NOAEL	No Observed Adverse Effect Level
OC	Octocrylene
OECD	Organisation for Economic Co-operation and Development
PI3K	Phosphoinositide 3-kinase
Plin	Perilipin
PND	Postnatal day
PoD	Point of departure
PP	Propylparaben
PPARα	Peroxisome proliferation-activated receptor alpha
PPARγ	Peroxisome proliferation-activated receptor gamma
PXR	Pregnane X receptor
RAC	ECHA Committee for Risk Assessment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RfC	Reference Concentration
RfD	Reference Dose
RIVM	Dutch National Institute for Public Health and the Environment
RMOA	Risk Management Option Analysis
ROS	Reactive Oxygen Species
RXR	Retinoid X receptor
SCCS	Scientific Committee on Consumer Safety
SD	Standard Deviation
SML	Specific Migration Limit
SPIN	Substances in Products in the Nordic Countries
SVHC	Substances of Very High Concern
TBBPA	Tetrabromobisphenol-A
TBPH	Bis(2-ethylhexyl) tetrabromophthalate
TDI	Tolerable Daily Intake
TWA	Time Weighted Average
US EPA	United States Environmental Protection Agency

Appendix 1 Method literature search on obesogens

Literature search

A literature search was performed in July 2023 in Embase using the following search criteria and focussing on studies that included terms relating to obesity (Table A.1). In total, 325 studies were included in the literature search.

Table A.1 Search strategy of the literature search

No.	Query	Results
#1	chemically induced disorder'/exp OR 'chemical* induc*':ti	124801
#2	obesity'/exp/mj	297367
#3	obes*':ti	209444
#4	#1 AND #2 AND #3	398
#5	#1 AND #2 AND #3 AND [humans]/lim	100
#6	environmental exposure'/exp/mj	35962
#7	obesogen*':ti	1074
#8	#6 AND #7	13
#9	chemicals and drugs'/exp/mj	17183512
#10	expos*':ti	304717
#11	#7 AND #9 AND #10	41
#12	obesogenic diet*':ti,ab	1046
#13	#11 NOT #12	29
#14	obesity'/exp	665376
#15	metabolic disorder'/exp/mj AND 'metabolic disorder*':ti	4565
#16	environmental exposure'/exp	128730
#17	oberon*':ti,ab	67
#18	#9 AND #14 AND #17	3
#19	#9 AND #14 AND #15 AND #16	10
#20	chemical obesogen*':ti,ab	12
#21	environmental obesogen*':ti	28
#22	('chemical*' NEAR/3 'obesogen*'):ti	9
#23	chemic*':ti AND 'induc*':ti AND 'obes*':ti	24
#24	endocrin*':ti AND 'disrup*':ti AND 'obes*':ti	97
#25	obesogen':ti OR 'obesogens':ti	129
#26	obesogen hypothesis':ti,ab	41
#27	#5 OR #8 OR #13 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	403
#28	#27 AND [2005-2023]/py	**325**

An additional literature search was performed in October 2023 to ensure that studies were included that focussed on a mechanism of action of certain chemicals (e.g. PPARγ or RXRα) that could be related to obesity. A total of 441 additional studies [2018-2023] were selected from an additional literature search with 458 results (see Table A.2).

Table A.2 Search strategy of the additional literature search

No.	Query	Results
#1	'chemically induced disorder'/exp OR 'drug induced disease'/exp OR 'chemical* induc*':ti,ab OR 'drug induc*':ti,ab	344176
#2	'obesity'/exp	680428
#3	'obesi*':ti,ab OR 'obeso*':ti,ab	462308
#4	#1 AND #2 AND #3	1521
#5	'environmental exposure'/exp	130720
#6	'obesi*':ti OR 'obeso*':ti	145557
#7	#5 AND #6	516
#8	('chemical compound'/exp OR 'peptides and proteins'/exp/mj OR 'antibiotic agent'/exp OR 'environmental chemical'/exp OR 'metal'/exp OR 'vitamin d'/exp OR 'metalloid'/exp OR 'phenol derivative'/exp OR 'phathalic acid' OR 'phthal*':ti OR 'plasticizer'/exp OR '4,4` isopropylidenediphenol'/exp OR 'flavoring agent'/exp OR 'fatty acid'/exp OR 'nonmetal'/exp OR 'chemical*':ti) NOT (drug:ti,ab OR drugs:ti,ab)	14307278
#9	'expos*':ti	309706
#10	#6 AND #8 AND #9	402
#11	#4 OR #7 OR #10	2360
#12	'mechanism of action'/exp OR 'mechanism of action*':ti,ab OR 'action mechanism*':ti,ab OR 'mechanism*':ti	520906
#13	#11 AND #12	64
#14	'lipid storage'/exp/mj OR 'lipid storage*':ti OR 'lipid accumulat*':ti OR 'fat accumulat*':ti OR 'body weight gain'/exp/mj OR 'weight gain*':ti OR 'gain weight*':ti OR 'adipogenesis'/exp/mj OR 'adipogen*':ti	36649
#15	'peroxisome proliferator activated receptor alpha'/exp/mj OR 'peroxisome proliferator activated receptor gamma'/exp/mj OR (('peroxisome proliferator activated receptor alpha'/exp OR 'peroxisome proliferator activated receptor gamma'/exp) AND 'ppar*':ti,ab)	32580
#16	'rxra gene'/exp OR 'rxra gene*':ti,ab OR 'rxrb gene'/exp OR 'rxrb gene*':ti,ab OR 'rxrg gene'/exp OR 'rxrg gene*':ti,ab	193
#17	'retinoid x receptor alpha'/exp OR 'retinoid x receptor beta'/exp OR 'retinoid x receptor gamma'/exp	2761
#18	'obesogen'/exp OR 'obesogenic environment'/exp	287
#19	'obesity'/exp/mj AND ('obesi*':ti OR 'obeso*':ti)	130517

No.	Query	Results
#20	'environmental exposure'/exp/mj	36825
#21	('chemical compound'/exp OR 'peptides and proteins'/exp/mj OR 'antibiotic agent'/exp OR 'environmental chemical'/exp OR 'metal'/exp OR 'vitamin d'/exp OR 'metalloid'/exp OR 'phenol derivative'/exp OR 'phathalic acid' OR 'phthal*':ti OR 'plasticizer'/exp OR '4,4` isopropylidenediphenol'/exp OR 'flavoring agent'/exp OR 'fatty acid'/exp OR 'nonmetal'/exp OR 'chemical*':ti) NOT (drug:ti,ab OR drugs:ti,ab)	14307278
#22	#14 AND (#20 OR #21)	15416
#23	#15 AND (#20 OR #21)	24240
#24	#16 AND (#20 OR #21)	107
#25	#17 AND (#20 OR #21)	2072
#26	#18 AND (#20 OR #21)	115
#27	#19 AND (#20 OR #21)	35693
#28	'exposure'/exp OR 'expos*':ti,ab	2121675
#29	#22 AND #28	1296
#30	#23 AND #28	2511
#31	#24 AND #28	9
#32	#25 AND #28	205
#33	#26 AND #28	54
#34	#27 AND #28	2232
#35	#29 OR #30 OR #31 OR #32 OR #33 OR #34	5837
#36	'chemically induced disorder'/exp OR 'drug induced disease'/exp OR 'chemical* induc*':ti,ab OR 'drug induc*':ti,ab	344176
#37	'mechanism of action'/exp OR 'mechanism of action*':ti,ab OR 'action mechanism*':ti,ab OR 'mechanism*':ti	520906
#38	'hypothesis'/exp OR 'hypothe*':ti,ab OR 'eviden*':ti,ab	4314316
#39	#35 AND #36	28
#40	#35 AND #37	214
#41	#35 AND #38	1655
#42	#13 OR #39 OR #40 OR #41	1867
#43	'diet-induced obesity'/exp OR 'diet induc*':ti,ab	38785
#44	#42 NOT #43	1704
#45	'air pollut*':ti OR 'neurology'/exp OR 'neuro*':ti OR 'genital system'/exp/mj	1396917
#46	#44 NOT #45	1618
#47	#46 AND ('article'/it OR 'article in press'/it OR 'review'/it)	1161
#48	#46 AND ('article'/it OR 'article in press'/it OR 'review'/it) AND [2010-2023]/py	919
#49	#46 AND ('article'/it OR 'article in press'/it OR 'review'/it) AND [2015-2023]/py	655

No.	Query	Results
#50	#46 AND ('article'/it OR 'article in press'/it OR 'review'/it) AND [2018-2023]/py	458

The research papers were categorised into four distinct groups to facilitate a systematic analysis of the available literature:

- epidemiological studies,
- *in vivo* studies,
- *in vitro* studies, and
- reviews.

Each set of papers underwent screening, focussing on the identification of specific chemicals, as well as the potential mechanisms through which these chemicals operate and their subsequent effects on obesity.

PECO analysis

A PECO analysis was performed to screen the obtained literature for relevance using the following PECO statements [288]:

- Population: *in vivo*, *in vitro,* epidemiology;
- Exposure: chemicals that are not environmental pollutants, pharmaceuticals, or restricted in the EU;
- Comparator: control versus exposed in experimental settings;
- Outcome: obesity and/or obesogenic effects.
-

Studies were first screened on the basis of title, followed by an abstract and full text screening.

- Inclusion criteria: studies that contain the aspects as set out in the PECO statements;
- Exclusion criteria: studies focussing on food, microplastics, and air pollution.

Appendix 2 Overview of possible obesogens

Overview of chemicals with indications for an obesogenic mechanism of action found in literature. Highlighted chemicals were found in consumer product databases and were included in **Fout! Verwijzingsbron niet gevonden.** in the report.

Table A.3 Chemicals with indications for an obesogenic mechanism of action found in the literature search

Chemical	CAS number	Reference
1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane	3322-93-8	[289]
2-ethylhexyl diphenyl phosphate	1241-94-7	[71, 72]
3,4-Dihydroxybenzoic acid	99-50-3	[74]
3-tert-Butyl-4-hydroxyanisole	121-00-6	[77]
4-nonylphenol	104-40-5	[38, 42, 78-80]
Acetyl tributyl citrate	77–90–7	[89]
Arsenic	7440-38-2	[41, 42, 60-66]
Benzo[a]pyrene	50-32-8	[31]
Benzophenone-3	131-57-7	[74, 85]
Benzyl butyl phthalate	85-68-7	[41, 85]
Bis(2-ethylhexyl) tetrabromophthalate	26040-51-7	[88]
Bisphenol A	80-05-7	[13, 16, 29, 33-51]
Bisphenol F	620-92-8	[13, 33, 36, 38, 42, 52]
Bisphenol S	80-09-1	[13, 16, 33, 36, 38, 51, 53-56]
Butylated hydroxytoluene	128-37-0	[32]
Butylparaben	94-26-8	[16, 38, 73]
Cadmium	7440-43-9	[16, 41, 42, 67, 68]
Cyclohexanone	108-94-1	[32]
Dibutyltin	1002-53-5	[13, 16, 38, 42]
Dicyclohexyl phthalate	84-61-7	[16, 41]
Bis(2-ethylhexyl) phthalate	117-81-7	[13, 34, 38, 39, 41, 73, 79, 83-87]
Di-*n*-butyl phthalate	84-74-2	[42, 79, 82]
Dioctyl sodium sulfosuccinate	577-11-7	[13, 16, 42, 90]
Dioctyl terephthalate	6422-86-2	[33]
Ethylparaben	120-47-8	[33, 74]
Lead	7439-92-1	[41, 69, 70]
M/p-xylene	108-38-3	[32]
Methylparaben	99-76-3	[26, 75, 76]
Mono-(2-ethylhexyl) phthalate	4376-20-9	[79, 154]
Mono-ethyl phthalate	2306-33-4	[79]
Monosodium glutamate	142-47-2	[91]
Octocrylene	6197-30-4	[85]
Pentabromodiphenyl ether	32534-81-9	[290]

Chemical	CAS number	Reference
Pentabromoethylbenzene	85-22-3	[291]
Perfluorooctanoic acid	335-67-1	[34, 92, 93]
Permethrin	52645-53-1	[42]
Phthalic acid	88-99-3	[79]
Propylparaben	94-13-3	[33, 73]
Styrene	100-42-5	[32]
Tetrabromobisphenol-A	79-94-7	[57-59]
Tetrabromobisphenol-A sulfate	-	[57]
Tetrachlorobisphenol-A	79-95-8	[57]
Tetrachloroethylene	127-18-4	[32]
Toluene	108-88-3	[32]
Tonalide	1506-02-1	[16]
Tributyltin	688-73-3	[34, 73, 85, 154, 292-299]
Triclosan	3380-34-5	[41, 42, 81]
Triphenylphosphate	115-86-6	[42]

Appendix 3 Methods inventory of chemicals in consumer products

Search strategy Mintel Global New Products Database

The Mintel Global New Products Database (GNPD)[18] was used as a source for product information. GNPD delivers detailed data on new products launched in the food, beverage, beauty and personal care, healthcare, household goods, and pet care markets. It covers 270 subcategories, 140 product claims, 200 packaging attributes, and over 46,000 ingredients.

In this study, we primarily focussed on the categories Beauty & Personal Care, Household products, and Health. The search was performed in October 2023 with the following settings:

- Market matches Netherlands;
- Category matches one or more of Beauty & Personal Care, Household, Health;
- Ingredient matches CAS number of the substance.

Initially, the search was performed without any restriction on published date of the product to have an indication in which (type of) products the substance may occur. For some chemicals, the date published was limited to 'Last complete 3 years' to limit the search to products that are likely to still be available on the market.

Information on the migration of chemicals from FCMs

The Food Contact Chemicals Database (FCCdb)[19] created by the Food Packaging Forum Foundation (FPF) was used to determine if chemicals are intentionally added to food contact materials (FCMs). This database compiles data from 67 different sources, which include regulatory lists and industry inventories. In its latest version (version 5.0), it identifies 12,285 distinct chemicals that are potentially used in the production of food contact materials and articles.

For chemicals that were identified within the FCCdb, information on migration of chemicals from FCMs was gathered from the Database on Migrating and Extractable Food Contact Chemicals (FCCmigex)[20]. The FCCmigex database is updated periodically by the FPF. It was first published in May 2022 and has since been updated in April 2023.

At the time of our research, a total of 10,850 entries in the FCCmigex database were related to migration into food or food stimulations. This corresponds to 2081 chemicals and 956 studies. The following types of food contact materials are included in the database:

- Plastics;
- Paper and board;
- Metals;

[18] https://www.mintel.com/
[19] https://www.foodpackagingforum.org/fccdb
[20] https://www.foodpackagingforum.org/fccmigex

- Multi-materials;
- Glass and ceramic;
- Other FCMs (i.e. silicone, wood, rubber).

In addition, 2067 database entries corresponding to 715 chemicals are related to adhesives, coatings, plastic laminates, printing inks, and wax.

For this research, chemicals that were detected as migrating substances in food and food simulants were of interest, while chemicals detected in extraction experiments were not considered. In the database, the number of database entries per chemical depicts the number of times that chemical has been detected in migration samples from a FCM. Information regarding the level of migration and the testing strategy are not provided directly, however, the original scientific references for all database entries are included in the tool.

Data from the database is displayed per substance as 'data entries that indicated migration / total data entries' to give an indication of whether migration of the substance from FCMs is likely.

Information on chemicals in toys

The Database on Chemicals in consumer products[21] created by the Danish EPA was used to gain information on the presence of chemicals in toys (accessed on 25 October 2023). The database includes data from Danish surveys of chemicals in consumer products, such as toys. A total of 10,141 entries across all product categories were included. The product categories squishy toys (226 entries), slimy toys, (128 entries), wooden toys (133 entries) and other toys (214 entries) were considered for the current study.

SPIN database consumer exposure index

The SPIN database[22] was used to gain further information on the presence of chemicals in chemical consumer products, such as paints, together with the production volume and, mainly, the consumer use index (accessed 10 November 2023) of the products. The SPIN database contains information on 31,738 chemicals used in the Nordic countries, including quantities, industries in which the chemical is used, and the function of the chemicals. In contrast to information on chemical products and preparations, information on chemicals in articles is not included. Furthermore, the reported quantities in the Nordic countries (Sweden, Denmark, Finland, and Norway) may only be used as a rough estimation for the situation in other EU countries.

The consumer use index, included in the database, gives an indication on the potential 'worst-case' exposure. In cases where there are multiple uses with different exposure scenarios, the index for the most critical use was selected within the database. In the SPIN database, the use index 'consumer' relates to dispersal that causes direct exposure to consumers during the use of products. Inhalation is assumed to be the

[21] https://eng.mst.dk/chemicals/chemicals-in-products/consumer-and-consumer-products/chemicals-in-consumer-products-database
[22] http://spin2000.net/

dominant uptake route for consumer exposure. The use index has been divided on a scale of 1-5 as follows:

- Use index 1 or 2: The registered product use does not indicate direct exposure.
- Use index 3: One or several product uses indicate a potential exposure.
- Use index 4: One or several product uses indicate a probable exposure.
- Use index 5: One or several product uses indicate a very probable exposure.

Appendix 4 Points of departure in toxicological risk assessment and their application to obesogens

Normally, a point of departure (PoD) is the dose or exposure level identified from toxicological data that marks the start of extrapolation to a safe human exposure level. It is selected from the dose-response data as a low-effect or no-effect level and then adjusted for uncertainty to derive reference values, such as a reference dose (RfD), reference concentration (RfC), derived no-effect level (DNEL), tolerable daily intake (TDI), or acceptable daily intake (ADI). In European chemical and food safety regulations, PoDs are the basis for health-based guidance values.
Common types of PoDs are:

- NOAEL (No Observed Adverse Effect Level): highest tested dose with no observed adverse effects,
- LOAEL (Lowest Observed Adverse Effect Level): lowest tested dose with observed adverse effects,
- BMD (Benchmark Dose) and BMDL (lower confidence limit): model-derived dose associated with a predefined change in response (benchmark response); BMDL is the lower confidence bound and is preferred because it uses the full dose-response curve and quantifies uncertainty.

To derive a PoD, high-quality studies, preferably carried out or generated according to generally valid and/or internationally accepted testing guidelines, are required. Deriving PoDs for obesogens needs to follow standard toxicological practice and requires careful endpoint selection and evaluation. This is beyond the scope of the present study. Therefore, rather than deriving a PoD for obesity, critical effect values for obesity (i.e. dose levels at which obesity-related effects are observed in *in vivo* studies) were selected from the literature.

Appendix 5 GC-MS settings

The GC-MS settings of the analytical measurements are described in Table A.4.

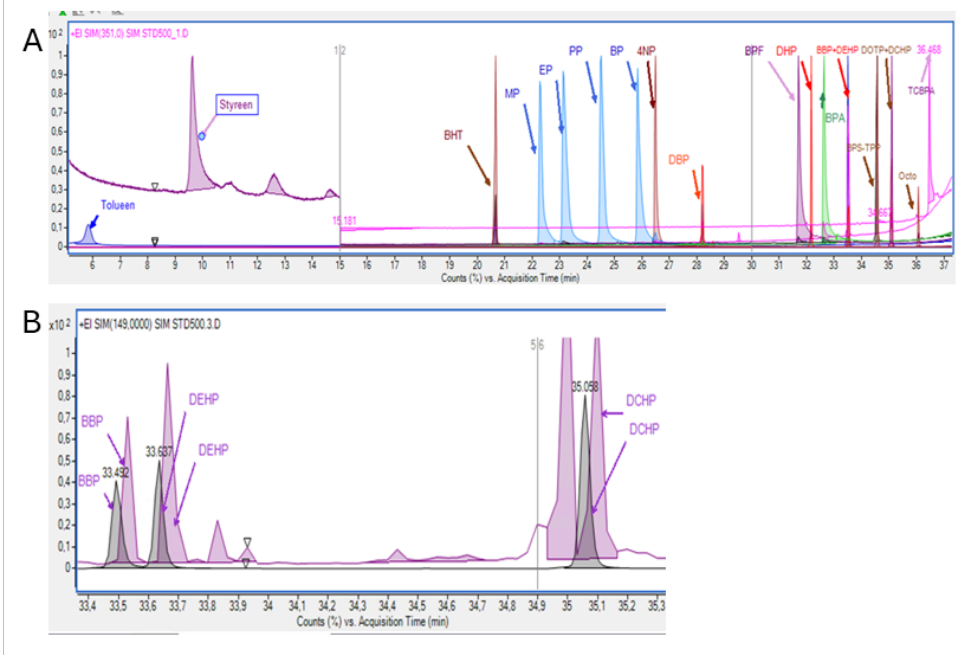
Table A.4 GC-MS settings of the analytical measurements

Agilent GC 7890B system	
Autosampler	
Injection volume	2 µl
# of rinses with solvent (pre-run)	3
# of rinses with solvent (post-run)	2
# of rinses with sample	1
Viscosity delay	0.0 sec
Plunger speed (Injection)	6000 µl/min
Syringe insertion speed	High
Injection mode	Standard
Pumping times	3 times
Injection port dwell time	0.0 sec
Terminal air gap	yes
Plunger washing speed	300 µl/min
Injector	
Injection Mode	Pulsed Splitless
Temperature	320 °C
Carrier Gas	He
Flow Control Mode	Standard
Pressure	9,1189 psi
Total Flow	64,201 ml/min
Column Flow	1,201 ml/min
Linear velocity	39,739 cm/sec
Purge Flow	3,0 ml/min
Injection Pulse Pressure	25 psi
Purge Flow to Split Vent	60 mL/min
Column oven	
Initial Temperature	40°C
Equilibration time	1 min
Temperature program	

Agilent GC 7890B system	
Total programme time	41,75 min
Start Temperature	40 °C
Hold time	7 min
Rate ramp 1	15 °C/min
Temperature ramp 1	100 °C
Hold time ramp 1	2 min
Rate ramp 2	8°C/min
Temperature ramp 2	280 °C
Hold time ramp 2	0 min
Rate ramp 3	20 °C/min
End temperature ramp 3	325 °C
Hold time ramp 3	4 min
Detector: MS	
MS source temperature	230 °C
MS Quad temperature	150 °C
Scan time	13 scans/sec
Ionisation mode	EI
Scan type	SIM
SIM Time Segment 1	Time: 10 min. Group name: 1. Ions: 91, 105 Dwell time: 100 ms. Resolution: High
SIM Time Segment 2	Time: 15 min. Group name: 2. Ions: 107,110,121,125,135,141,149,152,153,200,205,213,223,229,351,465. Dwell time: 100 ms per ion. Resolution: High
SIM Time Segment 3	Time: 10 min. Group name: 3. Ions: 54,91,110,135,141,149,152,167,180,200,205, 213,223,229,261,326,351,465,529 Dwell time: 100 ms per ion. Resolution: High
Mass Range Scan	50-550 m/z
Tune type	EI

Appendix 6 Chromatograms of obesogens

Figure A.1 GC-MS chromatogram (Selected Ion Monitoring: SIM) with 20 obesogens at level 500 ng/mL (A) and zoomed in on the time window 33.4-35.3 minutes (B)



Abbreviations: 4NP, 4-nonylphenol; BBP, benzyl butyl phthalate; BHT, butylated hydroxytoluene; BPA, bisphenol A; BPF, bisphenol F; BPS, bisphenol S; BP, butylparaben; DBP, di-n-butyl phthalate; DCHP, dicyclohexyl phthalate; DEHP, bis(2-ethylhexyl) phthalate; DHP, dihexyl phthalate; DOTP, dioctyl terephthalate; EP, ethylparaben; MP, methylparaben; Octo, octocrylene; PP, propylparaben; Styr, styrene; TCBPA, tetrachlorobisphenol A; Tol, toluene; TPP, triphenyl phosphate.

Peaks with similar colours have a similar quantifier mass. Next to a quantifier, a qualifier ion is required for identification. Qualifiers are not shown in the chromatograms. Purple-coloured peaks are spiked chemicals in lip balm (the sample set for validation consisted of six distinct products: two lip balms, two face creams and two deodorant rollers. These three matrices were used as representative of the entire product group of cosmetic products) and the dark grey peaks are the reference standards BBP, DEHP, and DCHP.

Appendix 7 Results measurements

This appendix describes the results of the measured concentrations of the obesogens in the products of the different categories (cosmetics, medical devices, and detergents).

Explanation of the result tables below:

- Levels are expressed in % (w/w).
- The absence of a component is shown as n.a., and results ranging between the LOD (limit of detection) and the LOQ (limit of quantification) are shown as <LOQ.
- Levels >0.001% (w/w) have a light-green shade.
- Ingredients listed in the ingredients list on the label of the product are in italics.

Measured levels in cosmetics

Table A.5 Measured concentrations of eighteen selected potential obesogens in four body lotion products

Chemical	**Product number**			
	A226317	A226318	A226319	A226320
Bisphenols				
BPA	0.00087	0.00009	0.0002	0.00022
BPF	0.00373	0.0001	0.0001	0.0001
BPS	0.00022	0.00057	0.00018	0.00228
Phthalates				
DBP	0.00027	0.00055	n.a.	n.a.
DEHP	0.00051	< LOQ	< LOQ	< LOQ
DCHP	0.00006	0.00006	n.a.	n.a.
BBP	0.00012	0.0001	n.a.	< LOQ
DOTP	n.a.	n.a.	0.00009	0.00007
DHP	< LOQ	0.00021	< LOQ	< LOQ
Parabens				
BP	< LOQ	< LOQ	< LOQ	< LOQ
EtP	0.00189	0.00048	n.a.	n.a.
MeP	0.00035	0.00008	0.00013	*0.1332*
PP	0.00009	0.0001	0.00068	*0.00211*
Other				
OC	0.00115	0.00021	n.a.	n.a.
BHT	0.0012	*0.00069*	*0.00059*	0.00129
TPP	0.00006	0.00006	n.a.	n.a.
4NP	0.00006	0.00007	0.00011	0.00007
Styr	n.a.	n.a.	n.a.	n.a.

Table A.6 Measured concentrations of eighteen selected potential obesogens in four deodorant products

Chemical	**Product number**			
	A226305	A226306	A226307	A226308
Bisphenols				
BPA	0.00032	0.0001	0.0001	0.00064
BPF	0.00019	0.0001	0.0001	0.00032
BPS	0.00012	0.00006	0.00005	n.a.
Phthalates				
DBP	0.00008	n.a.	0.00008	n.a.
DEHP	< LOQ	< LOQ	< LOQ	< LOQ
DCHP	< LOQ	< LOQ	< LOQ	n.a.
BBP	< LOQ	0.00012	0.00008	< LOQ
DOTP	0.00007	0.00017	0.00012	0.00004
DHP	< LOQ	< LOQ	0.0001	< LOQ
Parabens				
BP	n.a.	< LOQ	0.00012	n.a.
EtP	n.a.	0.00259	0.00008	< LOQ
MeP	< LOQ	0.00237	0.00006	n.a.
PP	n.a.	0.0002	n.a.	< LOQ
Other				
OC	0.00009	0.0015	0.00022	< LOQ
BHT	0.00144	0.0011	0.00052	*0.00112*
TPP	< LOQ	0.00006	0.00006	< LOQ
4NP	n.a.	0.00007	0.00026	0.00003
Styr	0.00008	n.a.	0.0004	n.a.

Table A.7 Measured concentrations of eighteen selected potential obesogens in four foundation products

Chemical	**Product number**			
	A226321	A226322	A226323	A226324
Bisphenols				
BPA	0.00013	n.a.	n.a.	0.00011
BPF	0.00011	0.00167	0.0001	0.0001
BPS	n.a.	0.00007	0.00005	n.a.
Phthalates				
DBP	< LOQ	n.a.	0.00005	0.00006
DEHP	0.00018	< LOQ	< LOQ	< LOQ
DCHP	< LOQ	0.00007	n.a.	< LOQ
BBP	< LOQ	0.0017	0.0001	< LOQ
DOTP	0.0003	*0.0109*	0.00015	0.00059
DHP	< LOQ	< LOQ	< LOQ	< LOQ
Parabens				

Chemical	**Product number**			
	A226321	A226322	A226323	A226324
BP	< LOQ	n.a.	n.a.	n.a.
EtP	n.a.	0.00015	< LOQ	0.00014
MeP	0.00023	< LOQ	< LOQ	*0.2053*
PP	n.a.	n.a.	n.a.	n.a.
Other				
OC	0.00006	n.a.	n.a.	0.00006
BHT	0.00039	0.00102	0.00069	0.00072
TPP	< LOQ	n.a.	n.a.	< LOQ
4NP	0.00005	0.00005	0.00153	0.00005
Styr	< LOQ	n.a.	n.a.	n.a.

Table A.8 Measured concentrations of eighteen selected potential obesogens in four hand soap products

Chemical	**Product number**			
	A229201	A229202	A229203	A229204
Bisphenols				
BPA	0.00018	0.00018	n.a.	n.a.
BPF	0.00008	0.00008	n.a.	n.a.
BPS	0.00006	0.00006	n.a.	n.a.
Phthalates				
DBP	n.a.	n.a.	0.00006	n.a.
DEHP	0.00014	< LOQ	< LOQ	< LOQ
DCHP	0.00014	0.00012	n.a.	n.a.
BBP	0.00009	0.00008	0.0001	0.00009
DOTP	0.00012	0.00012	< LOQ	0.00005
DHP	0.0002	0.00027	0.00009	n.a.
Parabens				
BP	< LOQ	< LOQ	0.00005	0.00017
EtP	0.00012	0.00006	n.a.	< LOQ
MeP	0.0001	0.00018	< LOQ	< LOQ
PP	0.00007	< LOQ	< LOQ	< LOQ
Other				
OC	0.00011	0.00015	n.a.	0.00015
BHT	0.00078	0.0007	0.00143	0.00102
TPP	0.00004	0.00004	n.a.	n.a.
4NP	0.00005	0.00005	0.00011	< LOQ
Styr	n.a.	0.00047	n.a.	n.a.

Table A.9 Measured concentrations of eighteen selected potential obesogens in four perfume products

Chemical	**Product number**			
	A226313	A226314	A226315	226316
Bisphenols				
BPA	0.00033	0.0001	0.00029	0.00027
BPF	0.00009	n.a.	n.a.	0.0001
BPS	0.00003	0.00003	0.00003	0.00004
Phthalates				
DBP	n.a.	0.00011	0.00008	0.00189
DEHP	< LOQ	< LOQ	< LOQ	< LOQ
DCHP	< LOQ	< LOQ	< LOQ	< LOQ
BBP	0.00006	0.00013	0.00011	0.00006
DOTP	0.00017	0.00015	0.00007	0.00016
DHP	< LOQ	< LOQ	< LOQ	< LOQ
Parabens				
BP	0.00066	< LOQ	< LOQ	0.00223
EtP	0.00181	0.00053	0.00009	0.00152
MeP	0.0346	< LOQ	< LOQ	0.0007
PP	0.00035	0.00302	0.0001	0.00022
Other				
OC	n.a.	0.00037	0.00005	n.a.
BHT	*0.0198*	*0.0482*	*0.1257*	*0.0357*
TPP	0.00005	n.a.	n.a.	0.00005
4NP	0.00046	0.00005	0.00021	0.00043
Styr	0.00196	0.03300*	0.00009	0.00079

*: Not or hardly found upon remeasurement after dilution. Remeasurement took place a couple of weeks later. The result of the first measurement is above the calibration line and concerns a level estimate.

Table A.10 Measured concentrations of eighteen selected potential obesogens in four shower gel products

Chemical	**Product number**			
	A226305	A226308	A226305	A226307
Bisphenols				
BPA	0.00032	0.00064	0.00010	0.00010
BPF	0.00019	0.00032	0.00010	0.00010
BPS	0.00012	n.a.	0.00006	0.00005
Phthalates				
DBP	0.00008	n.a.	n.a.	0.00008
DEHP	< LOQ	< LOQ	< LOQ	< LOQ
DCHP	< LOQ	n.a.	< LOQ	< LOQ
BBP	< LOQ	< LOQ	0.00012	0.00008
DOTP	0.00007	0.00004	0.00017	0.00012

Chemical	Product number			
	A226305	A226308	A226305	A226307
DHP	< LOQ	< LOQ	< LOQ	0.00010
Parabens				
BP	n.a.	n.a.	< LOQ	0.00012
EtP	n.a.	< LOQ	0.00259	0.00008
MeP	< LOQ	n.a.	0.00237	0.00006
PP	n.a.	< LOQ	0.00020	n.a.
Other				
OC	0.00009	< LOQ	0.00150	0.00022
BHT	0.00144	0.00112	0.00110	0.00052
TPP	< LOQ	< LOQ	0.00006	0.00006
4NP	n.a.	0.00003	0.00007	0.00026
Styr	0.00008	n.a.	n.a.	0.00040

Table A.11 Measured concentrations of eighteen selected potential obesogens in four sunscreen products

Chemical	Product number			
	A226301	A226302	A226303	A226304
Bisphenols				
BPA	0.0001	0.00014	n.a.	0.00011
BPF	0.00024	0.0144	0.0785	n.a.
BPS	0.00003	0.00008	0.00007	0.00003
Phthalates				
DBP	0.00034	n.a.	0.00017	0.00032
DEHP	< LOQ	0.00034	< LOQ	< LOQ
DCHP	n.a.	0.00007	n.a.	< LOQ
BBP	0.0008	0.00259	n.a.	0.00013
DOTP	0.00017	0.00008	0.00007	0.00007
DHP	0.00027	0.00023	n.a.	0.00013
Parabens				
BP	< LOQ	0.00011	< LOQ	< LOQ
EtP	n.a.	n.a.	< LOQ	< LOQ
MeP	n.a.	< LOQ	0.00019	n.a.
PP	n.a.	0.00186	0.00143	n.a.
Other				
OC	*0.6219*	0.00035	0.00039	*0.00012*
BHT	0.00065	0.00065	0.00074	0.00036
TPP	0.0001	n.a.	n.a.	0.00018
4NP	0.00008	0.00007	0.0026	0.00011
Styr	n.a.	n.a.	n.a.	n.a.

Table A.12 Measured concentrations of eighteen selected potential obesogens in four toothpaste products

Chemical	**Product number**			
	A226309	A226310	A226311	A226312
Bisphenols				
BPA	0.00013	0.00071	0.00012	0.00012
BPF	0.00011	0.00011	0.00012	0.00012
BPS	0.00003	0.00004	0.00003	0.00003
Phthalates				
DBP	n.a.	n.a.	< LOQ	n.a.
DEHP	< LOQ	< LOQ	< LOQ	< LOQ
DCHP	< LOQ	< LOQ	0	0
BBP	0.00006	0.00035	0.00007	0.00007
DOTP	0.00009	0.00009	0.00006	0.00006
DHP	< LOQ	< LOQ	< LOQ	< LOQ
Parabens				
BP	< LOQ	< LOQ	n.a.	< LOQ
EtP	n.a.	n.a.	n.a.	n.a.
MeP	< LOQ	< LOQ	n.a.	n.a.
PP	< LOQ	< LOQ	n.a.	n.a.
Other				
OC	0.00009	n.a.	0.00005	0.00005
BHT	0.00135	0.00163	0.00088	0.0013
TPP	0.00005	0.00005	n.a.	n.a.
4NP	0.00006	0.00006	0.00009	0.00005
Styr	0.00012	0.00004	0.00014	0.00002

Measured levels in medical devices

Table A.13 Measured concentrations of eighteen selected potential obesogens in four lubricants

Chemical	**Product number**			
	A228901	A228902	A228903	A228904
Bisphenols				
BPA	0.00009	0.00010	0.00009	0.00291 *
BPF	0.00008	n.a.	0.00008	0.00010
BPS	0.00006	0.00009	0.00005	0.00990 *
Phthalates				
DBP	n.a.	0.00002	n.a.	0.00099
DEHP	< LOQ	< LOQ	< LOQ	0.01260
DCHP	< LOQ	0.00130	< LOQ	0.00200
BBP	0.00012	< LOQ	< LOQ	n.a.

Chemical	Product number			
	A228901	A228902	A228903	A228904
DOTP	n.a.	0.00008	n.a.	0.00360 *
DHP	< LOQ	< LOQ	< LOQ	0.00012
Parabens				
BP	< LOQ	< LOQ	< LOQ	< LOQ
EtP	< LOQ	n.a.	< LOQ	*0.01780*
MeP	< LOQ	< LOQ	< LOQ	*0.10720*
PP	n.a.	n.a.	n.a.	*0.00923*
Other				
OC	n.a.	0.00016	n.a.	0.00470 *
BHT	0.00060	0.00135	0.00068	0.00070
TPP	n.a.	n.a.	n.a.	0.00014
4NP	0.00005	0.00005	0.00005	n.a.
Styr	n.a.	0.07230	n.a.	0.00008

*: Not or hardly found upon remeasurement after dilution. Remeasurement took place a couple of weeks later. The result of the first measurement is above the calibration line and concerns a level estimate.

Measured levels in detergents

Table A.14 Measured concentrations of eighteen selected potential obesogens in four dishwashing liquid products

Chemical	Product number			
	A229101	A229102	A229103	A229104
Bisphenols				
BPA	0.0001	n.a.	n.a.	0.00013
BPF	0.00055	0.0113	0.00165	0.00017
BPS	0.00007	< LOQ	0.00004	0.00011
Phthalates				
DBP	0.00006	n.a.	< LOQ	0.0001
DEHP	0.00013	n.a.	n.a.	0.00024
DCHP	< LOQ	n.a.	< LOQ	0.0001
BBP	0.00117	0.00006	0.00009	0.00025
DOTP	0.00012	< LOQ	n.a.	0.0002
DHP	0.00009	n.a.	n.a.	0.00018
Parabens				
BP	< LOQ	n.a.	n.a.	0.0002
EtP	0.00005	n.a.	n.a.	0.00019
MeP	0.00012	n.a.	< LOQ	0.00023
PP	< LOQ	n.a.	n.a.	0.00014
Other				
OC	n.a.	0.00056	0.00025	0.00015

Chemical	Product number			
	A229101	A229102	A229103	A229104
BHT	0.00074	0.00089	0.00173	0.00066
TPP	0.00006	n.a.	n.a.	0.00011
4NP	0.00005	n.a.	0.00056	0.00009
Styr	n.a.	0.00111	0.00273	0.00018

Table A.15 Measured concentrations of eighteen selected potential obesogens in four fabric softener products

Chemical	Product number			
	A229001	A229002	A229003	A229004
Bisphenols				
BPA	n.a.	n.a.	0.00028	0.00114
BPF	n.a.	n.a.	0.00037	0.00038
BPS	0.00005	0.00003	0.00006	0.00006
Phthalates				
DBP	0.00009	0.00008	0.00015	0.00017
DEHP	n.a.	n.a.	0.00017	< LOQ
DCHP	n.a.	n.a.	0.00008	0.00009
BBP	0.00005	0.00006	0.00009	0.00008
DOTP	n.a.	n.a.	0.00013	0.00012
DHP	n.a.	n.a.	0.00009	< LOQ
Parabens				
BP	0.00014	0.00014	0.00021	< LOQ
EtP	0.00033	0.00105	0.00007	n.a.
MeP	0.00386	0.00248	0.00198	< LOQ
PP	0.00007	n.a.	0.00012	< LOQ
Other				
OC	0.00017	0.00014	0.00019	0.00019
BHT	0.00214	0.0008	0.00303	0.00308
TPP	n.a.	n.a.	n.a.	n.a.
4NP	0.00013	0.00008	0.00007	0.00006
Styr	0.00006	0.00011	n.a.	n.a.

Table A.16 Measured concentrations of eighteen selected potential obesogens in four laundry detergent products

Chemical	**Product number**			
	A228801	A228802	A228803	A228804
Bisphenols				
BPA	n.a.	n.a.	0.00022	0.00023
BPF	n.a.	n.a.	0.00013	0.00011
BPS	< LOQ	n.a.	0.00006	0.00006
Phthalates				
DBP	0.00006	0.00006	n.a.	n.a.
DEHP	< LOQ	< LOQ	< LOQ	< LOQ
DCHP	n.a.	n.a.	0.00009	0.00008
BBP	0.00012	0.00017	0.00008	0.00008
DOTP	n.a.	n.a.	0.00012	0.00012
DHP	< LOQ	< LOQ	0.00009	< LOQ
Parabens				
BP	n.a.	n.a.	< LOQ	< LOQ
EtP	0.00022	0.00013	0.00003	n.a.
MeP	0.00007	0.00009	0.00008	n.a.
PP	n.a.	n.a.	< LOQ	0.00007
Other				
OC	0.00016	0.00015	0.0001	0.00014
BHT	0.00075	0.00087	0.00078	0.00065
TPP	n.a.	0.00007	0.00007	0.00005
4NP	0.00015	0.00007	n.a.	n.a.
Styr	0.00004	0.00013	0.00034	0.00019

Appendix 8 Concentration data from other European studies

Table A.17 A non-comprehensive overview of obesogen concentrations in consumer products based on peer-reviewed articles, government and agency monitoring reports, and high-quality surveillance studies published in Europe (2003-2025)

Chemical	Cosmetics	Medical Devices (lubricant)	Detergents
Bisphenols			
BPA	-	-	-
BPF	-	-	-
BPS	-	-	-
Phthalates			
DBP	• Cosmetics: 0.0001618-0.0017504 % (w/w) [300] 0.0001-0.0006 % (w/w) [301] • Nail products: 0.7-2.1% (w/w) [302] • Perfumes: 0.0001-0.0020 % (w/w) [303]	-	• Spray paint: 0.01% (w/w) [304] • Stain remover: 0.0012-0.0014% (w/w) [305] • Dishwasher detergent: 0.0000877-0.000187% (w/w) • Laundry detergent: 0.0006943-0.0008410% (w/w) • Floor cleaner: 0.0000125-0.0009648% (w/w) [300]
DEHP	• Cosmetics: 0.000089-0.0003558% (w/w) [300] 0.0001-0,0217% (w/w) [301] • Nail products: 0.3-1.7% (w/w) [302] • Perfumes: 0.0001 – 0.1785% (w/w) [303]	-	• Dishwasher detergent: 0.0000224-0.0000267% (w/w) • Laundry detergent: 0.000048% (w/w) • Floor cleaner: 0.0000112-0.0008261% (w/w) [300] • Impregnation agent: 0.2-2.1% [306]
DCHP	-	-	-
BBP	-	-	• Dishwasher detergent: 0.0000529-0.0001035% (w/w) • Laundry detergent: 0.0001483-0.0009948% (w/w) • Floor cleaner: 0.0001015-0.0003572% (w/w) [300]
DOTP	-	-	-
DHP	-	-	-
Parabens			
BP	• Face mask: 0.020% (w/w)	Found in lubricant	-

Chemical	Cosmetics	Medical Devices (lubricant)	Detergents
	• Shower gel: 0.026% (w/w) • Shampoo: 0.026% (w/w) [307]	(concentration unknown) [308]	
EtP	• Face mask: 0.031% (w/w) • Shower gel: 0.12% (w/w) • Shampoo: 0.12% (w/w) [307]	Found in lubricant (concentration unknown) [308]	-
MeP	• Face mask: 0.083% (w/w) • Shower gel: 0.11% (w/w) • Shampoo: 0.11% (w/w) • Eye contour: 0.13% (w/w) • Toothpaste: 0.051% (w/w) [307]	Found in lubricant (concentration unknown) [308]	Glass cleaner: 2.6% (w/w) [309]
PP	• Face mask: 0.018% (w/w) • Shower gel: 0.034% (w/w) • Shampoo: 0.034% (w/w) • Eye contour: 0.062% (w/w) [307]	-	-
Other			
OC	-	-	-
BHT	• Bathing products: 0.000001-0.005% (w/w) [310] • Body lotion: 0.0002-0.23% (w/w) • Deodorant (roll-on): 0.052-0.23% (w/w) • Face cream: 0.0071-0.22% (w/w) • Sunscreen: 0.0009-0.32% (w/w) [311]	-	• Leather cleaner: 0.032% (w/w) [309] • Shoe care product: 0.12% (w/w) [312]
TPP	• Nail products: 0.49-1.68% (w/w) [302]	-	-
4NP	-	-	-
Styr	-	-	Incense: Emission [313]

Appendix 9 Exposure sources

Table A.18 Estimated exposure calculation for exposure sources relevant for consumers and concentrations of the eighteen selected potential obesogens in studies performed in Europe as per December 2025

Chemical	Estimated exposure through cosmetics (µg/kg bw/day)	Estimated exposure through household products (µg/kg bw/day)	Estimated exposure through toys (µg/kg bw/day)	Estimated exposure through food contact materials, diet and drinking water (µg/kg bw/day)	Estimated exposure through indoor air and dust (µg/kg bw/day)
Bisphenols					
BPA	Cosmetics: 0.002-0.005 [314] *(2014)* Cosmetics Adults: 0.0012 Teenagers: 0.0015 Infants: 0.0029 [107] *(2023)*	Thermal paper receipts: Adolescents: 0.003 Teenagers: 0.001 [315] *(2015)*	Toys: Average: 0.00002-0.0003 High: 0.0005-0.0012 [314] *(2014)* Toys: 0.0032 *[316] (2025)* Toys: 0.0003 Pacifiers: 0.0066 *[315] (2015)*	Diet: Average: 0.12-0.38 High: 0.34-0.86 [314] *(2014)* Average: 0.375 High: 0.857 [107] *(2023)*	Dust Average: 0.0006-0.008 High: 0.001-0.015 Indoor air Average: 0.0002-0.0007 High: 0.0003-0.0014 [314] *(2014)*
BPF	-	-	-	-	-
BPS	-	Thermal paper receipts: 0.013-0.025 [317] *(2019)*	-	-	-
Phthalates					
DBP	Perfume: 0,2 Worst case all cosmetics: 1.48 [318] *(2007)*	-	Infant exposure through mouthing of toys and childcare products: Average: 27.8 Worst case: 169.9 [319] *(2019)*	Diet: 0,042–0,769 [133] *(2019)*	Dust Median: 0.04 Max: 0.64 Indoor air Median: 0.38 Max: 1.02 Total Median: 0.41

Chemical	Estimated exposure through cosmetics (µg/kg bw/day)	Estimated exposure through household products (µg/kg bw/day)	Estimated exposure through toys (µg/kg bw/day)	Estimated exposure through food contact materials, diet and drinking water (µg/kg bw/day)	Estimated exposure through indoor air and dust (µg/kg bw/day)
					Max: 1.66 [320] *(2015)*
DEHP	Perfume: 2.47 [318] *(2007)*	-	Mouthing: Median: 0.0014 High: 0.0143 [321] *(2022)*	Diet: 0.446-3.459 [133] *(2019)*	Dust Median: 0.53 Max: 16.78 Indoor air Median: 0.09 Max: 0.23 Total Median: 0.62 Max: 17.01 [320] *(2015)*
Parabens					
MeP	Cosmetics: Adults: 790 Infants: 1010 [322] *(2018)*	-	-	Diet: Adults: 0.36 Infants: 1.38 [322] *(2018)*	-
Other					
TPP	Nail polish: 0.04 [206] *(2024)*	-	-	Diet (Belgium): 0.0466 [323] *(2019)*	Dust Median: 0.00251 High: 0.0136 [207] *(2024)*
4NP	Hair dyes: 0.1 [324] *(2002)*		-	Diet: 2 Food packaging materials: 0.2 [324] *(2002)*	

(This overview only includes the obesogens for which a critical effect value has been established in Chapter 5.6.)
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