Logika Noise Air Quality CONSULTANTS

The socio-economic Costs of Chemical Pollution to the UK – Final

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EMRC

RPA Risk & Policy Analysts

Peter Fisk Associates

Brunel University London

Document Control

Client	Department for Environment Food and Rural Affairs (Defra)	**Principal Contact**	Ahamad Akbor, Economic Advisor, International Chemicals, Department for Environment, Food and Rural Affairs. Ground floor, Seacole Building, 2 Marsham Street, London, SW1P 4DF

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Prepared By: David Tyrer, Kayleigh Moore, Dr. Liz Nicol and Marko Ristic Smith, Logika Group; Meg Postle, Sophie Garrett, Daniel Vencovsky and Richard Stenning, RPA; Dr. Oliver Warwick, PFA Ltd; Dr. Mike Holland, EMRC; Dr. Olwenn Martin, Brunel University, London.

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Registered Office: 23 Coldharbour Road, Bristol BS6 7JT Tel: 0117 974 1086

24 Greville Street, Farringdon, London, EC1N 8SS Tel: 020 3873 4780

6 Bankside, Crosfield Street, Warrington WA1 1UD Tel: 01925 937 195

Contents

Tables

Figures

Executive Summary

This study

Chemical substances have a wide range of uses and applications, providing functionalities in diverse products and services which we encounter every day. But the exposure to harmful chemicals is also associated with significant adverse health and environmental effects. These effects can be associated with exposure during the chemicals manufacturing process, over the lifetime use of the products in which they are found, after disposal of these products and potentially when chemicals are incorporated into recycled products. Effective management of the risks posed requires good knowledge of the prevalence and relative importance of exposure pathways and effects, and for these to be quantified and monetised where possible, against the costs of regulatory action. For many chemicals, there is a lack of information on exposures and effects, resulting in the need for regulatory controls on the basis of precaution and risk-based judgement. The costs to businesses and wider society of regulatory action are better known, but the benefits of such action may be significant but are poorly understood. As such, this study undertaken by a team from Logika Group (Logika), Risk and Policy Analysts (RPA), Peter Fisk Associates (PFA), Dr Olwenn Martin (Brunel University) and Dr Mike Holland, between October 2021 and January 2022, has three objectives:

1. Based on a rapid review of the existing evidence, to document associations between exposure and effects where these have been translated into monetary estimates of economic and social damage costs.
2. To collate and develop new estimates of the costs of such damage that may be incurred in the United Kingdom (UK) and that can reasonably be associated with past or current chemical exposure, with varying degrees of certainty.
3. To set out key data gaps and research priorities to improve such estimates in the future.

This assessment should not be interpreted as a figure that represents the “total” costs of chemical burden to the UK. Rather it reflects the available evidence, where data on exposure to effects and valuation methods could be applied. There are a significant number of chemicals where evidence on risks and exposure are uncertain, absent or emerging, but cannot be quantified at this stage.

Scope and methodology

This study focuses on chemical substances that can pose a risk to human health or the environment and that are placed on the market in the UK. Transboundary effects are not included. The analysis covers the major endpoints found in regulatory toxicology, intended to result in an assessment of the main pollution effects. But the assessment should not be interpreted as a figure that represents the “total” costs of chemical burden to the UK. The analysis reflects the available evidence, where data on exposure to effects and valuation methods could be applied. Data availability and time constraints meant effects from microplastics, nanomaterials and veterinary medicines were not covered. “Pollution” here is interpreted as negative externalities (i.e. costs incurred by a third party arising from production or consumption). As such, burdens from occupational exposure are included as well as those from environmental and consumer exposure more generally. Both sources have been subject to regulatory action in the UK over many years. The assessment is based on a systematic review of available evidence, where possible drawing conclusions on the magnitude and type of socio-economic costs, to whom they are incurred and when.

Any such assessment needs to be clear what precisely is meant by “cost”. Here it seeks to capture the welfare consequences to wider society of changes to people’s wellbeing. Society places a high value on having a long, healthy and fulfilled life. The most common such approach is calculated using a Disability Adjusted Life Year (DALY) used to quantify the burden of disease. Where appropriate, these consequences

are expressed in monetary terms using market-based or non-market-based approaches. This includes a "cost of illness" approach to estimate the various economic and treatment costs associated with illness. This includes resources foregone, lost output due to illness and medical treatment or health service costs. It also includes revealed or stated preference methods that have elicited "willingness to pay (WTP)" values for good health (one's own or others'), to avoid a health condition, or to capture the value of avoided damage to the environment.

The methodology applied here requires several sequential steps. Each are associated with uncertainty and the quality and extent of evidence differs at each stage and between effects. In several cases UK data are not available. A "top down" attributable fraction (AF) approach can be used to estimate the attributable costs from chemical pollution. There are various sources of these available from the literature, although their scientific basis varies in terms of its robustness. Some of the AFs used in deriving the above estimates are highly uncertain, affecting the reliability of the results.

A "bottom-up approach" can also be applied to determine the impact of specific substances; often those already subject to regulatory control. This relies on the ability to derive a dose-response relationship (DRR) to reflect the relationship between exposures to the chemical and different outcomes. A high level of toxicological and/or epidemiological data is required. As such the use of DRRs is more limited and such an approach is not possible for assessment of environmental effects. Monetary assessment of pollution costs to natural capital suffer from particular methodological challenges in attribution and aggregation. As such, assessment is partial, uncertain, and subject to change as improved evidence becomes available.

What are the likely scale of effects and associated costs to the UK?

The socio-economic costs associated with exposure to harmful chemicals in the UK are significant. Each effect is considered in turn. Note these data are further discussed in a table and an infographic, below.

In terms of cancers: between 7,000 to 21,000 annual UK cancer diagnoses could be attributable to ***past occupational exposure*** to carcinogenic chemicals. The associated monetary costs could be between £3 billion and £32 billion. Intangible effects based on WTP approaches account for the majority of these costs. ***Future burdens associated with current occupational exposure*****,** may account for between 2,000 and 6,000 further diagnoses in 2040, associated with a cost of between £0.7 billion and £7 billion. The range of monetary values reflects both the estimated range of occupational cancer cases and two different monetisation approaches. Insufficient data are available to develop similar estimates for the impact of carcinogens on humans via the environment and consumer products, although significant costs may be expected here as well.

Reproductive effects relate both to sexual function, development of the foetus and effects to offspring. Whilst uncertainties in parts of the analysis are significant, impacts ***via occupational exposures of both male and female workers*** suggest social damage costs in the order of £0.4 million per year due to past and potentially on-going exposures. Costs over £440 million across the most likely exposed worker populations could occur when taking into account possible impacts from ***combined exposures, including those outside the workplace***. In addition:

- Developmental effects in the offspring of potentially exposed female workers (past and on-going) include low birth weights. This accounts for costs of £1.7 million.
- Developmental effects to all potentially exposed female workers have also been assessed. As above, this takes into account possible impacts of combined exposures including those outside the workplace. This is associated with a maximum of 11,500 statistical cases of various reproductive effects, at a cost of £4.3 billion to the UK.
- For consumers and the general public, an alternative approach yields estimates by type of effect for historic and possible on-going exposures. This suggests costs upwards of £85 million

per year from male infertility; between £0.07 million and £2.7 million per year for hypospadias; and cryptorchidism in new-born boys at a cost of around £50 million per year (range between £5 – 127 million).

Published evidence on the effects and costs associated with exposure to **endocrine disrupting chemicals** (EDCs) has been reviewed. A range of substance-effect associations have been documented, with different levels of certainty. Applying the methodologies used in that evidence to the UK results in substantial economic costs ***in the order of tens of billions per year,*** comprising both WTP and cost of illness approaches***. The methodology is associated with some significant uncertainties and further refinement should be considered***.

Documented **neurodevelopmental effects** include IQ loss and incidence of mild mental retardation (MMR), alongside suggested associations with ADHD. Quantitative effects have been studied only for a small number of extensively regulated substances; notably lead and mercury. But evidence is emerging that damage could be caused in children, including in the womb, at levels previously thought to be safe. Economic costs associated with IQ loss and the corresponding effect on productivity and hence lifetime earnings have been suggested, alongside approaches based on DALY valuations for MMR. The extent of effects for lead and mercury is highly dependent on the existence/validity of a threshold for effects, below which damage may not occur. UK exposure levels are expected to generally fall below previously suggested thresholds for effects, but other studies have assumed no such threshold. ***Depending on the validity of reported thresholds for effect, the associated costs in the UK may be negligible at the level of the average individual - or significant in terms of lost lifetime earnings to cohorts of children, arising from current exposure***. However:

- The methodologies upon which these IQ effect estimates are based were developed for assessing benefits of significant decreases in blood lead levels (BLL) associated with action such as banning lead in petrol from the late 1970's. They assume an empirical link between IQ (which is itself challenging to measure and only a proxy for intelligence), productivity and earnings. It is not clear what effect marginal changes in IQ actually have given the challenges in measuring intellectual ability and the complexity of its corresponding relationship to employment outcomes, earnings or performance. Hence it is not clear what socio-economic costs, if any, are occurring. This should be further evaluated.
- Despite this, the assessment indicates that as new evidence emerges, previous assumptions of safe exposure may be challenged. There are larger numbers of substances potentially harmful for neurodevelopment that have not been studied at nearly the level of lead and mercury.
- Although more uncertain, lead, PFCs and arsenic may account for between 11,000 and 18,000 cases of ADHD, associated with combined costs upwards of £2 billion, based on the associated DALYs.

A range of factors affect **cardiovascular health risks**, a major health burden in the UK. Associations between lead and mercury exposure with hypertension, ischaemic heart disease (ISD) and stroke have been documented. As above, the ***extent of UK socio-economic costs from these exposures are significantly affected by the existence and accuracy of documented thresholds for effect***. If reported thresholds are valid, UK exposures appear to be controlled at the level of the average individual, and are associated with only small socio-economic costs. If they are not, ***UK socio-economic costs could be significant in increased hypertension risks, alongside smaller increases in mortality risk, and DALYs associated with stroke and ischaemic heart disease***. Further research would be required to establish the health effect of marginal changes in risk for these diseases and to improve the accuracy of data in a UK context. But the relationship between chemical exposure and cardiovascular health is poorly understood. Further research on a wider range of chemicals, on the medical risks associated with marginal changes in hypertension, as well as ISD and stroke and there potential effect is recommended.

More commonly associated with air pollution, **respiratory effects** are also caused by chemical exposure. Occupational asthma accounts for just under 10% of UK asthma cases. The associated costs are estimated at somewhere over £1 billion (based on DALYs) or around £0.6 billion (based on costs of treatment, and disability claims). The causes of asthma are not fully established, and it is not clear how much of the costs can be attributed to harmful chemical exposure alone, a further area where epidemiological data could be improved. This does not apply to ***asbestosis, which killed some 1,500 people in the UK in 2016-2018***. Annual deaths are only now beginning to decrease, some 20 years after it was banned in the UK. The associated costs are somewhere below £0.3 billion, excluding the significant compensation liability.

Chronic obstructive pulmonary disease (COPD) is a further major health burden in the UK, costing the NHS around £2 billion per year. Several lifestyle and environmental factors are associated with increased risk, including some chemical exposures. Potential costs based on DALYs could be somewhere below £0.3 billion, but the population attributable fraction (PAF) on which this is based is highly uncertain. Further research on the contribution of chemicals exposure to COPD risk is recommended.

Chemicals cause various significant **environmental burdens** in the UK. Attributing these to chemical substances, quantifying aggregate impacts and placing monetary values on impacts are methodologically challenging. Specific examples of damage can be observed. Some 1,500 km of English rivers (3% of the total) are polluted form ***historical mining activities***. One remediation scheme near Middlesbrough is estimated to have prevented some £13 million damage (from recreational value and bathing) over a 25 year period. This assessment provides a framework for deriving future national level estimates of the environmental costs from historic activities.

Some chemicals are of particular concern for the environment because of their ability to ***persist and accumulate*** in surface water, sediment or soil for example, over long periods of time. An assessment has been undertaken on a small number of known substances of very high concern (SVHC) to estimate the environmental load (mass) and concentration in different environmental compartments. This is based on estimated volumes and uses of those substances on the UK market. By assessing this burden at ***steady state (the point at which losses are equal to inputs (releases))*** – it gives an estimation of the environmental burden of specific substances and where they end up in the environment. Estimating the time it takes to reach steady state and for a substance to decrease to half the steady state mass if all inputs ceased ***(its environmental half-life)***, provides insight on substances that will be building up in the environment and how long it takes for the environment to be clear of the substance, should further use be prohibited. The relative concern for the substances in terms of environmental burden can then be identified. Time to steady state based on worst case releases in the UK as well as a comparison for 1kg of release, differ significantly between the SVHCs assessed, from a matter of months to several thousands of years in water and up to 250 years in air.

In this context, none of the ***UKs freshwater bodies, estuaries and coastal water*** meet the good chemicals status Environmental Quality Standard (EQS) under the UK Water Environment Act for polybrominated diphenyl ethers (PBDE). Between 87% and 100% fail for Mercury and around a quarter of freshwater bodies fail for perfluoro octane sulfonate (PFOS). This permits a valuation based on improvements in waterbody status, per KM waterbody affected. Broadly, this may apply to 170,000 km of rivers in England alone. Based on the time period over which 1kg of PBDE and PFOS may degrade to levels below the EQS, this suggests ***damage costs that could be in the order of £20 billion or more***. There are over 130 known substances for which similar characteristics are suspected, but not yet concluded.

Land contaminated by chemical pollution poses a burden on landowners, developers and on UK Local Authorities, who often incur the costs for both analysis and subsequent remediation. This adversely affects brownfield development viability and requires allocation of public funds to offset this. Little current data exists on the extent of UK contamination or costs of remediation. ***EU data indicates average remediation costs of between €50,000-500,000 per site. There may be some 10,000 brownfield sites requiring contamination investigation in England alone***.

Use of **pesticides** has given rise to health and environmental concerns for many years. They are associated with a range of possible effects (reproductive effects, cancers, sensitisation) via chronic occupational exposure as well as to bystanders and consumers. The UK National Poisons Information Service (NPIS), estimates that 886 potential exposure cases occurred in 2019/20. The majority (649 cases) were registered as asymptomatic or mild symptoms. A 2008 study exploring the potential benefits of withdrawal of seven active substances identified up to around £190 million in reduced cancer risk to spray operators and up to £0.7 billion in the wider exposed population. Insufficient epidemiological evidence prevented action at the time but these seven have since been banned in the UK. Other ***substances currently lacking in sufficient evidence may be contributing to ongoing cancer burdens as well as other effects, even at low levels of exposure.*** Other research has pointed to potentially significant adverse effects on groundwater as well as to pollinators (valued as providing £435 million in benefits in 2021).

Skin diseases associated with chemical exposure at work may account for around 10,000 skin disorder cases in the UK, costing the NHS about £17.5 million, per year. Productivity losses from time off work are associated with a further cost to the UK economy of some £35 – 40 million in foregone gross value added (GVA). This is likely an underestimate as larger numbers of less serious cases are not reported, but which may present at GPs and require treatment.

Volatile Organic Compounds (VOCs) impact human health and ecosystems via effects on tropospheric ozone formation resulting from release of non-methane VOCs (NMVOCs). Formation of secondary aerosols are also impacted. The assessment here is based only on some uses in scope (or potentially in scope) given lack of data for specific substances, based on existing damage cost data. It suggests ***damage costs of £375 million per year (in scope) and over £500 million (when further substances are included) based on the central estimates.***

Risks from **Pharmaceuticals in water** have been the subject of a detailed UK analysis in 2015. This is being further explored via the UKWIR chemical investigation programme. ***Areas for further research include concerns that the environment may act as a pathway for microbial resistance; in combination effects of cancer drugs in drinking water; and effects on animals***.

What data and research would improve future assessment?

A further objective of this research to is identify priority areas for future research that could improve similar assessment that may be undertaken in the future. There are several ***cross cutting research needs***.

- The risks associated with the large number of chemicals currently placed on the market need to be better understood. For those known to be of concern, a wider set of risks could be assessed. Impacts associated with substances suspected to be of concern should also be further investigated. More accurate data on the conditions where they may pose particular risks are required, especially where effect thresholds are suspected to exist. Better data on actual chemicals exposures both in occupational settings, from consumer products and via the environment would be just one important step to enable improvements in the development of causal relationships between exposures and different health outcomes.
- The relationship between ***chemical exposure and other environmental and/or lifestyle factors*** needs to be better understood, as does the role that ***occupational versus consumer or environmental exposures might play*** in contributing to combined effects.
- There is a ***significant lack of UK biomonitoring data*** which could provide empirical time series data on concentrations of harmful chemicals in blood, urine, breast milk, or hair, for example. The UK could draw on its involvement in the Human Biomonitoring for EU (HBM4EU) project to develop a more comprehensive biomonitoring system.

- More comprehensive ***socio-economic assessment of environmental effects are a particular priority***. The importance of being able to better assess damage costs becomes clear when considering the increasing number of persistent, bio-accumulative and highly mobile substances being identified due to improvements in scientific understanding.
- There is currently no ***accepted method for the quantification and monetisation of environmental impacts that can be directly applied within the regulatory context***. A framework needs to be developed that is consistent with existing information requirements set down in legislation, that can allow impacts to be estimated and valued. Linking estimations of substance fate (modelling) with estimations of impact (based on extrapolations from ecotoxicity data based on (ecological) consequences of exceeding threshold values) may allow linkage to ecosystem services and natural capital, which could then provide the basis for valuation of impacts. Similarly, there is no methodology available to consider combined and cumulative effects from multiple exposures from several chemicals of concern.

There are several more ***specific research needs, related to improving assessment of specific effects, technical and socio-economic analysis***.

For cancers, there are data gaps for all exposure routes but partially limited evidence for exposure via the environment and consumer exposure. Specific research may include: a systematic review of literature on the environmental presence of specific carcinogens, including in consumer products, specification of UK sites with carcinogenic contamination and derivation of UK specific clean-up cost estimates. Available AF studies for occupational exposure could be updated.

For reproductive effects, a review of grandfathered substances under UK REACH and EU consumer product information to identify reprotoxic substances with greatest use in the UK, separating those associated with past and on-going exposure could be performed. So too could a systematic review to identify both fertility / maternal and developmental effects for which there is most scientific evidence, alongside review with the objective of improving existing AFs.

For EDCs there are both major evidence gaps and scope to improve the existing monetary analysis. These include on effects in fish as well as terrestrial effects. Given the costs of remediation, further assessment of the costs and potential benefits of source control measures may be valuable.

Neurodevelopmental effects assessments are complicated by the limited number of substances that have been assessed. Further research should focus on known and/or suspected neurotoxicants, ascertaining volumes placed on the UK market. Even for well-studied and regulated heavy metals, the debated validity of thresholds for effects complicate damage costs assessment. This is compounded by tenuous associations that have been assumed in the literature between (often marginal) changes in IQ, labour market productivity and earnings. These associations should be systematically reviewed.

Given the scale of the UK health burden from various cardiovascular effects, the role of chemical exposure in these risks has received only limited attention. Similar conclusions apply to respiratory effects, where AFs for occupational asthmagens and COPD assume only a very small role of chemicals exposure.

There are 207 substances or substance groups (510 individual substances) for which persistent bioaccumulate and toxic (PBT) or very persistent and very bio-accumulative (vPvB) or equivalent effects are a concern, results are inconclusive, or for which conclusions are pending. A large number of these substances have the potential to cause environmental harm. The ability to identify substances of potential concern has outpaced the speed at which testing to verify these properties can be undertaken. It is possible, using data on UK tonnage and use to estimate where and how much of substances of concern end up in the environment. But there is no accepted methodology that enables quantification and monetisation of impacts of substances, singularly and in mixtures, on environmental receptors. Such a methodology should be developed, via a scoping study on specific substances, that utilizes existing ecotoxicity data required by legislation. The outlines of such a framework are suggested.

In the UK context there are currently competing valuation figures that may be used in assessment of the same effect. Some of these are under review. We recommend that guidance is provided on appropriate values that should be applied in a UK context, both for policy appraisal as well as for the development of restrictions and the consideration of applications for authorisation under UK REACH. Consistency between the figures recommended for assessment of effects in air quality appraisal, for example, should be explicitly considered, with recommended reference values published.

Table 0-1 Summary of effects assessment

Effect / substance group	Human health/ environmental impacts assessed	Timeframe of effects (historic, current or future burdens)	Methodology used (cost of illness, WTP etc.)	Chemicals in scope	Type of exposure (consumer or occupational)	Scale of costs and timeframe (£)	Evidence and uncertainty rating[1]		
							Role of chemicals in effect[2]	Quant. data on impacts[3]	Methods for valuing effects[4]
Cancer	Cancer cases (occupational exposure)	Current burden (historic exposure)	PAF in relation to UK incidence data (non-market effects derived from WTP)	20-40 carcinogens	Occupational exposure	£3-32 billion (diagnoses in a single year)			
		Future burden (current exposure - burden in 2040)	Adjusted PAFs for future exposure trends (non-market effects derived from WTP)	20-40 carcinogens	Occupational exposure	£0.7-7 billion (diagnoses in 2040)			
	Cancer cases (humans via the environment)		Qualitative assessment – significant data gaps						
	Cancer cases (consumer exposure)		Qualitative assessment – significant data gaps						
Reproductive effects	Infertility, Endometriosis, Ectopic pregnancy, spontaneous abortion/ miscarriages, still births	Current annual burden	Adjusted PAF in relation to UK incidence data (intangible costs derived from WTP)	5 Repro. 1A/1B chemicals	Occupational exposure	£0.5-440 million (2020 prices)	(Male infertility)		
							(Maternal effects)		

[1] Note, the RAG rating has been applied using the author's elicitation. It provides an overall evaluation of the quality and extent of the data and hence the level of caution on particular quantitative estimates. Note, the costs are not necessarily a reflection of the total burden. The costs are determined by what available evidence and valuation methods exist in the literature, and should therefore not be compared against one another.
[2] Extent and quality of evidence on association between chemical exposures and effects
[3] Availability, quality and extent of data including population attributable fractions, dose response functions, case numbers
[4] Methodologies through which these effects can be assigned monetary values

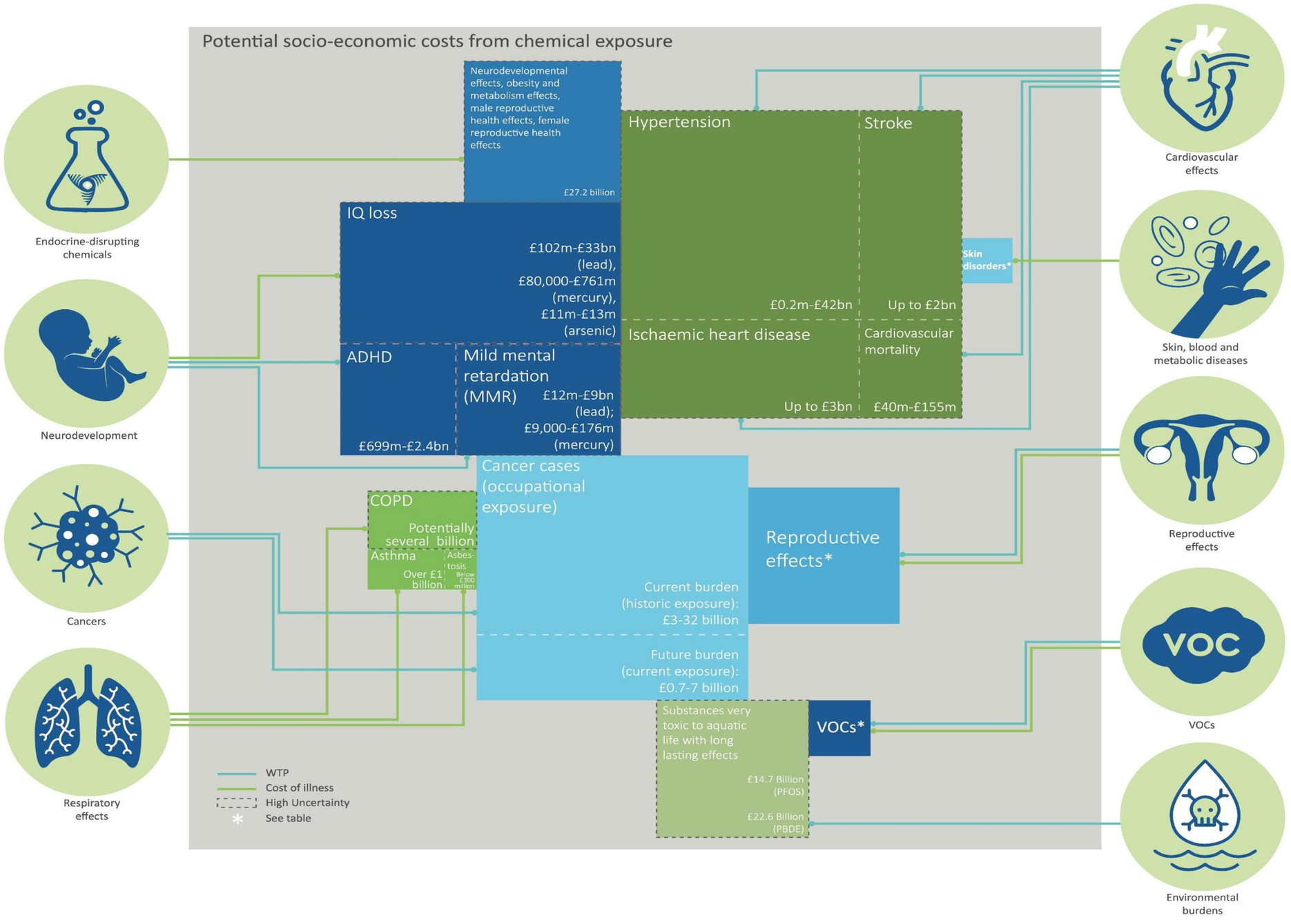
Effect / substance group	Human health/ environmental impacts assessed	Timeframe of effects (historic, current or future burdens)	Methodology used (cost of illness, WTP etc.)	Chemicals in scope	Type of exposure (consumer or occupational)	Scale of costs and timeframe (£)	Evidence and uncertainty rating[1]		
							Role of chemicals in effect[2]	Quant. data on impacts[3]	Methods for valuing effects[4]
	Developmental effects due to maternal exposure	Current annual burden	Case estimates based on Eurocat and Euro peristat	Repro. 1A/1B substances	Occupational maternal exposure	£1.7million - £4.3 billion (2020 prices)			
	Male infertility	Current annual burden	Case estimates based on PAF and ECHA restriction dossiers	Repro. 1A/1B substances	Consumer/ via the environment	£86-195 million (2020)			
	Hypospadias	Current annual burden	Case estimates based on PAF and restriction dossiers	Repro. 1A/1B substances	Consumer/ via the environment	£1.7-2.7 million (2021)			
	Cryptorchidism	Current annual burden	Case estimates based on PAF and restriction dossiers	Repro. 1A/1B substances	Consumer/ via the environment	£5-127 million (2021)			
Endocrine-disruption	Neurodevelopmental effects, obesity and metabolism effects, male reproductive health effects, female reproductive health effects	Current annual burden	Cost of illness	Organophosphate pesticides, PBDE, DEHP, phthalates, benzyl and butylphthalates, bisphenol A, and DDE.	Consumer / via the environment	Potentially in the order of tens of billion. Further assessment advised.			
Neurodevelop mental effects	IQ loss	Current annual burden	Loss of earnings	Lead, mercury, arsenic	Consumer / via the environment	Costs reported in wide ranges based on debated thresholds for effect, impact of marginal changes in IQ and of associations between IQ and earnings.			
	Mild mental retardation (MMR)	Current annual burden	WTP	Lead, mercury	Consumer / via the environment				
	ADHD	Current annual burden	WTP	Lead, PFCs, pesticides	Consumer / via the environment	£699m-£2.4bn (2020)			

Effect / substance group	Human health/ environmental impacts assessed	Timeframe of effects (historic, current or future burdens)	Methodology used (cost of illness, WTP etc.)	Chemicals in scope	Type of exposure (consumer or occupational)	Scale of costs and timeframe (£)	Evidence and uncertainty rating[1]		
							Role of chemicals in effect[2]	Quant. data on impacts[3]	Methods for valuing effects[4]
Cardiovascular effects	Hypertension	Historic annual burden	WTP	Lead	Consumer / via the environment	Costs reported in wide ranges based on debated thresholds for effect and impact of marginal changes in medical risk			
	Cardiovascular mortality	Current annual burden	WTP	Mercury	Consumer / via the environment	£40m-£90m (2019)			
	Ischaemic heart disease	Current annual burden	WTP	Lead	Consumer / via the environment	Costs uncertain based on data quality and impact of marginal changes in medical risk, but could be significant.			
	Stroke	Current annual burden	WTP	Lead	Consumer / via the environment	Costs uncertain based on data quality and impact of marginal changes in medical risk, but could be significant			
Respiratory effects	Asthma	Current annual burden	PAF of DALYs	Some occupational asthmagens.	Occupational	Over £1 billion (2019)			
	Asbestosis	Current annual burden	PAF of DALYs	Asbestos	Consumer and occupational	<£300 million (2019)			
	COPD	Current annual burden	PAF of DALYs	Occupational PMGF (only very small proportion likely to be in scope)	Occupational	Up to several billion (2019)			

Effect / substance group	Human health/ environmental impacts assessed	Timeframe of effects (historic, current or future burdens)	Methodology used (cost of illness, WTP etc.)	Chemicals in scope	Type of exposure (consumer or occupational)	Scale of costs and timeframe (£)	Evidence and uncertainty rating[1]		
							Role of chemicals in effect[2]	Quant. data on impacts[3]	Methods for valuing effects[4]
Skin, blood and metabolic diseases	Skin disorder cases	Current	Cost of illness, productivity losses, WTP	Includes heavy metals (e.g. lead), chromium VI, nickel and cobalt compounds, and formaldehyde.	Consumer	Treatment cost: £17.5 million (2018-19) Productivity loss: £42 million (2019) WTP valuation: £2.5-11.8 million (2020)			
VOCs	Increased tropospheric ozone	Current annual burden	Cost of illness, WTP	Non Methane VOC	Consumer	£54m-£560m (2020)		N/A damage costs used.	
	Formation of secondary aerosols	Current annual burden	Cost of illness, WTP	Non Methane VOC	Consumer				
	Direct effects on human health inc. cancer	Current annual burden	Cost of illness, WTP	Dioxins (PCDD/F)	Consumer	£40,000-£110,000 (2020)			
				Benzene	Consumer	£110-£1,000 (2020)			
				1,3-butadiene	Consumer	£8,600-£78,000 (2020)			
				16PAH	Consumer	£33m-£300m (2020)			
Pesticides	Various risks from exposure and misuse	Current burdens	Literature review conducted, some estimation of values	Substances deemed suitable for use as pesticides	Occupational/Consumer (bystander)	Qualitative assessment			
Environmental burdens - Assessment of SVHC substances	Environmental burden (load) in specific compartments (soil, water, sediment)	Prospective based on volumes and uses.	Modelling of environmental fate	SVHC substances (PBT and of equivalent concern)	Environment	Qualitative assessment			
Other environmental burdens	Substances very toxic to aquatic life with long lasting effects	Current costs to achieve good chemical status	NWEBS values and substance half-life to value social damages	PFOS and PBDE	Environment	-Up to £14.7 Billion (PFOS) -Up to £22.6 Billion (PBDE)			

Effect / substance group	Human health/ environmental impacts assessed	Timeframe of effects (historic, current or future burdens)	Methodology used (cost of illness, WTP etc.)	Chemicals in scope	Type of exposure (consumer or occupational)	Scale of costs and timeframe (£)	Evidence and uncertainty rating[1]		
							Role of chemicals in effect[2]	Quant. data on impacts[3]	Methods for valuing effects[4]
		(from 19 up to 183 years)							

Figure 0-1 Summary of potential socio-economic costs from chemical exposure in the UK[5]



[5] Note, the size of the boxes should not be interpreted as an representation of the total scale of the problem and should not be compared against one another.

1 Introduction

1.1 The purpose of the study

This study has been prepared by a team led by Logika Group (Logika), with Risk and Policy Analysts (RPA), Peter Fisk Associates (PFA), Brunel University London and Dr Mike Holland.

Alongside the benefits of their use, various adverse human health effects and environmental burdens are associated with chemical exposures. These impose various socio-economic costs on society. This study evaluates the human health and environmental effects of chemical pollution in the United Kingdom. Illnesses and diseases identified in epidemiological and toxicological evidence and which have been associated with exposure to harmful chemicals include cancers, reproductive, neurodevelopmental, cardiovascular & respiratory effects as well as skin sensitization. Environmental effects include damage to various ecosystem services, fresh and coastal water quality, animal health, and contaminated land. Quantitative estimates of the attributable damage are provided, alongside monetary valuations where data are available.

This report was prepared in a short period, between October 2021 and March 2022. Methodological weaknesses, significant uncertainties, data and evidence gaps are identified. A series of recommendations to improve future analyses are made.

Any such assessment reflects the nature of chemicals pollution, existing risk management activities and regulations that have applied in the UK over several decades. This is characterised by:

- an evolving process where public awareness of and concerns over the protection of public health and the environment changes over time;
- a constantly changing chemical landscape, with scientific advancements and industrial innovation. Whilst innovations can remove or reduce chemical pollution, it can create new substances or processes that are later found to be polluting;
- an ongoing process of chemical risk assessment, as evidence on the risks and exposure to these develop over time and as methods for risk assessment evolve;
- impacts which manifest over time and space – often many years after initial exposure and far from the original source– and which pose challenges in the attribution of harm to specific causal factors;
- The evidence base on chemical use, exposure, risk, and effect is characterised by significant data gaps; and
- action is often taken on the basis of the precautionary principle and on a preventative basis.

To reflect this changing environment, chemical legislation equally needs to be dynamic to ensure the safe and sustainable use of chemicals. The evidence base deepens over time, regularly showing both new effects and a more developed understanding of previously known effects. Regulatory changes to reflect this are required, and so chemical regulation evolves over time. As such chemical emissions/contamination deemed acceptable in previous decades is regularly overtaken by more recent regulatory standards. These actions are then reflected in avoided or reduced exposure as well as substitution for less harmful substances. However, this occurs alongside ongoing damage caused by substances that are not yet regulated, their risk are not yet fully understood, or from substances that turn out to pose similar risks to those that have been substituted – so called regrettable substitution.

The intention of this report is to examine the overall burden from chemicals exposure to the UK. This includes current burdens from past exposure, which have persisted, sometimes decades after those substances have been removed from the market. They include acute and chronic effects associated with

recent exposure which may manifest now and in the future. It also includes possible future burdens arising from current exposure, taking into account gaps in understanding of the risk posed by many chemicals in use today.

Each chapter considers a particular disease category or burden from chemicals in different environmental compartments. But the risks posed by chemical substances tend not to be confined to one disease category, or environmental compartment, but several. The assessment seeks to focus on the tangible, where protection is manifestly in the public interest: avoiding cancer, protecting reproductive health and the cognitive development of children, the safety of food we eat, the air we breathe and the water we drink.

1.2 Context and current status

Since the late 1960s, both independently as a signatory to international treaties and via membership of the European Union, the UK has implemented a large body of chemicals legislation. This reflects the hazards and risk associated with chemicals, the wide use of chemicals in society and the various benefits they confer. This legislation has sought to avoid damage to human health and the environment from harmful chemicals, whilst ensuring international trade of substances, in mixtures and articles in a competitive and innovative chemicals industry. Several publications have sought to establish what this body of legislation has achieved and what ongoing burdens may be occurring under that current legislation. The most recent was published in 2017 by the European Commission[6], which assessed a body of legislation which applied in the UK at that time. Three key findings of that study were:

- That ***chemicals legislation over the last 50 years has delivered significant benefits in terms of protecting human health and safeguarding the environment. The monetary value of all of these benefits were likely in the high tens of billions of Euro per year, perhaps more***. Moreover, this reflects only a subset of avoided damage, largely due to a lack of data available to quantify the physical impacts of chemical releases (especially on the environment). As methods to aggregate monetary values, particularly for environmental end points, are improved and as more data becomes available, the authors' expected these identified benefits to increase, perhaps significantly;
- Despite these achievements, ***there continued to be significant ongoing damage to human health and the environment caused by chemicals exposure*** under the current legislative regime; and
- ***New threats to health and environment are occurring because of emerging and evolving risks*** associated with chemical exposure. Moreover, there are still many gaps in knowledge and understanding about the health and environmental hazards and risks of many existing chemicals, including those likely to be used in the UK.

Typologies of socio-economic costs associated with chemicals pollution have been extensively studied, typically in the context of single substances for which regulatory action was being considered. These are often presented in two categories: ***benefits of action*** (estimates of avoided harm from preventative action) and the ***costs of inaction*** (ongoing harm from current exposures to harmful chemicals substances). These studies have typically focussed on the risks from exposure during manufacture (whilst the substance was being produced and/or incorporated into subsequent products); over the course of the lifetime use of the product in question; or – less commonly - after it has been disposed of at "end of life". But there are several significant methodological challenges and evidence gaps hindering a comprehensive assessment of the total aggregate societal burden. These are discussed in each of the chapters that follow.

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[6] European Commission DG ENV (2017) Study on the cumulative health and environmental benefits of chemical legislation https://op.europa.eu/en/publication-detail/-/publication/b43d720c-9db0-11e7-b92d-01aa75ed71a1/language-en

What types of socio-economic costs have been identified?

Socio-economic costs of chemicals pollution identified in the existing literature have focussed on mortality and morbidity, various direct health care costs (time of specialist staff, medication and treatment); lost productivity (from absence, illness/disease and associated with provision of care); and damage to cognitive development reflected in decreased long term earnings potential. It also includes the results of various stated or revealed preference studies (typically expressed in monetary terms via "willingness to pay" methods).

Environmental damage includes various adverse effects to ecosystem services, recreational values, fishing revenues and water treatment costs. These environmental effects are typically harder to quantify and monetise. Risks from release of hazardous substances, especially those that are persistent, bioaccumulative and/or toxic, and the associated health, environmental and clean-up costs have been assessed, typically in specific case-based research. There is some, albeit limited, published research on liability costs and of reputational and litigation costs to business associated with specific chemical pollution incidents.

1.3 Contents

Following this introduction:

- We provide an overall summary of the scope of the study and the **methodology used in chapter 2**. Technical and conceptual terms are also explained.
- **In chapter 0** we review the evidence on **UK cancer burdens** from chemical exposures; followed by assessment of **reproductive effects (chapter 0);** a review of evidence on effects from **endocrine disrupting chemicals (chapter 5); neurodevelopment effects on children (chapter 6); cardiovascular effects (chapter 7**Error! Reference source not found.**) and respiratory effects (chapter 0).**
- Assessment of environmental effects from chemicals exposure is more challenging to quantify and assign monetary values to associated damage. We explore **environmental burdens from chemicals in chapter 9.**
- The final three subsections deal with effects associated with **pesticides (chapter 9); "skin, blood and metabolic diseases" (chapter 11**Error! Reference source not found.**)** and certain **V olatile Organic Compounds (VOCs) in chapter 12**Error! Reference source not found.
- We review key findings from a 2019 study prepared for Defra on effects attributed to **pharmaceuticals in water, in section 12**.
- The appendix contains further details of the calculations, assumptions and input data.

2 Methodology

This section explains the overall scope of the assessment, the structure of the analysis and defines conceptual and technical issues. Specific methodological challenges are discussed in each chapter.

2.1 Scope of analysis

The study focused on all chemical substances which can pose a risk to human health or the environment. This includes those that are likely to be registered under UK REACH[7]. The strength of evidence is assessed and documented in each case and taken into account in the assessment of costs. Consideration of microplastics, nanomaterials or veterinary medicines were excluded from the scope of the study, primarily due to time constraints as well as a lack of evidence.

The assessment here should not be interpreted as a figure that represents the total costs of chemical burden to the UK. That is beyond what is currently methodologically possible. Rather, we systematically consider the available evidence, drawing conclusions where possible on the scale, type and magnitude of damage as well as to whom and when the costs are incurred. The study is limited to impacts in the UK, irrespective of the source of the pollution. Similarly, it doesn't consider damage caused outside the UK which may be attributable to chemical manufacture, use or disposal in the UK.

Typically in a study of this kind, the assessment effects would be prioritized based on a combination of prevalence and significance of effect. In this case the effects considered result from an initial review of the available published literature. These were presented in an unpublished methodology paper discussed with Defra and the Health and Safety Executive (HSE). The effects cover the major endpoints found in regulatory toxicology and hence are driven by data availability. The intention was to explore different types of pollution, so as to provide as comprehensive assessment as possible. The resulting assessment reflects a range of "serious" human health issues such as cancers, associated with high costs in each instance, as well as those which are typically lower order complications such as skin sensitization.

2.2 What is being "valued"?

The economic, human health and environmental costs of pollutants can be calculated through different market-based or non-market-based valuation approaches. A market-based, "cost of illness" approach can be used to estimate the various economic and treatment costs associated with illness. This includes resources foregone, lost output due to illness and medical treatment or health service costs.

In addition, various revealed or stated preference methods have elicited "willingness to pay (WTP)" values for good health (one's own or others'), to avoid a health condition, or to capture the value of avoided damage to the environment. Monetary estimates use a wide range of available unit values based on these WTP data, which includes the values of statistical life (VOSL) as well as monetary valuations which derive from the Disability Adjusted Life Year (DALY) and the Quality Adjusted Life Year (QALY). Assessments using these metrics seek to capture the welfare consequences to wider society of changes to people's wellbeing.

Where benefits relate to productivity and/or healthcare treatment ("direct financial") costs, these can be compared to GDP in national accounts to provide context on their significance. Others reflect "personal valuation" (willingness to pay to avoid certain medical ailments or for ecosystem services, for example). These costs are no less real than those that are linked to GDP: society places a high value on having a long, healthy and fulfilled life. Where appropriate, they are expressed in monetary terms. The most common such

[7] Note Registration under UK REACH is being phased in over several years. Relevant EU REACH registrations have been recognised under UK REACH, this is known as 'grandfathering'. This permits continued access to the GB market, but requires submission of some data to HSE. "Full" UK Registrations have not yet been submitted for many substances.

approach is calculated using a Disability Adjusted Life Year (DALY) which is used to quantify the burden of disease.

Valuation of DALYs, mortality and other effects – Challenges in a UK Context

The DALY measures health burdens, via differences between prevailing health conditions and an ideal state where all live to the standard life expectancy and do so in perfect health[8]. One DALY can be equated to one lost year of "healthy" life. The sum of DALYs across the population - the burden of disease – measures the gap between current health status and an ideal health situation. It is derived by combining Years of life lost (YLL) with Years lived with disability (YLD). YLL, for a specific cause or age, in turn, is calculated by multiplying the number of deaths (N) with standard remaining life expectancy at age of death in years (L). YLD is estimated based on both the incidence (I) and average duration of the disease (L) alongside a weighting (a disability weight – DW) that takes into account different severities of diseases.

$$DALY = YLL\ (NxL) + YLD\ (I\,x\,DW * L)$$

These disability weights reflect societal preferences for different health states and outcomes. For example, diabetes has a lower disability weight than cancer. Studies also take into account other preferences based in discounting (see section 0). These calculations provide population wide DALYs for various diseases states. These can then be assigned monetary values. There is not a single valuation figure for a DALY, however, and different studies have presented significantly different values. The HM Treasury Green Book[9] advises valuing a QALY (Quality Adjusted Life Year) at £60,000. This figure can be applied to a DALY. This is a conservative figure. Nedellec and Rabl (2016) use value of VOLY to estimate monetary value of DALY. The value used is €126,000. The UK figure draws on the results of a single, now very dated UK study that does not reflect the broader literature on valuation. The UK valuation is under review. Given this is a study focused on the UK, we reflect the Green Book valuation.

The same applies to values of a statistical life (VSL). These are derived from stated preference methods which ask people for their willingness to pay to reduce various risks. The OECD conducted a meta-analysis of VSL figures in 2012[10]. This derived a figure of $3.6m (2005 prices). In this study, we have used the OECD mortality valuation report because it is based on a much larger literature than alternatives, although it is dated. The OECD analysis is also currently being updated. The 2005 dollar figure has been converted to GBP using OECD PPP-adjusted exchange rates, then applied UK GDP deflators to adjust for inflation to arrive at a 2020 figure of £3,540,162 (£3.5m).

For many morbidity endpoints we use valuations from a comprehensive WTP study published by the European Chemicals Agency (ECHA)[11]. This study developed monetary estimates for avoiding selected adverse human health outcomes due to exposure to chemicals. The values were based on surveys conducted in four Member States (Italy, the United Kingdom, the Czech Republic, and the Netherlands) with the aim of obtaining representative (average) EU-wide estimates. These values are used in this

[8] WHO (undated). The Global Burden of Disease Concept https://www.who.int/quantifying_ehimpacts/publications/en/9241546204chap3.pdf

[9] HM Treasury (2020). The Green Book. Central Government Guidance on Appraisal and Evaluation. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf

[10] OECD (2012). Mortality Risk Valuation in Environment, Health and Transport Policies. https://www.oecd.org/env/tools-evaluation/mortalityriskvaluationinenvironmenthealthandtransportpolicies.htm

[11] ECHA (2016) Stated-preference study to examine the economic value of benefits of avoiding selected adverse human health outcomes due to exposure to chemicals in the EU. https://echa.europa.eu/support/socio-economic-analysis-in-reach/willingness-to-pay-to-avoid-certain-health-impacts

report, given their relevance to chemical risks and that they are based on survey data that includes the UK.

We recommend that guidance is provided on appropriate values that should be applied in a UK context, both for policy appraisal as well as for the development of restrictions and the consideration of applications for authorisation under UK REACH. Consistency between the figures recommended and those used for assessment of effects in air quality appraisal, for example, should be explicitly considered with recommended reference values published[12].

2.3 Challenges in attribution

Only part of identified health and environmental effects can be attributable to chemical exposure, and there will be many other contributing factors in each case. A "top down" attributable fraction (AF) or population attributable fraction (PAF) approach can be used to estimate the attributable costs associated with chemical pollution. Alternatively, a "bottom-up approach" can be applied to determine the impact of specific substances. Whilst this may be more accurate than the alternative AF approach, it relies on the ability to derive a dose-response relationship (DRR) or a dose response function (DRF) to reflect the relationship between exposures to the chemical and different health outcomes. Derivation of such relationships is difficult, requiring a high level of toxicological and/or epidemiological data. As such DRRs are more limited and such an approach is not currently possible for the assessment of environmental effects.

Attributable Fractions and Population Attributable Fractions

Several studies used in the assessment rely on the use of AFs/PAFs. The AF can be estimated if there is available data on the prevalence of a risk factor and the relative risk of a disease or outcome associated with that risk factor[13,14] :

$$AF = \frac{Prevalence_{risk\ factor}(RR-1)}{1+Prevalence_{risk\ factor}(RR-1)}$$

Here RR is the relative risk of a health effect (morbidity) associated with exposure to a chemical agent. In order to establish AFs for a particular population, a review of epidemiological / toxicological /clinical (cohort) studies, disease rates, and other statistics are required to collate data on:

- The prevalence of risk factors (e.g. exposure to chemicals, consumption habits, confounding factors such as smoking, or obesity); and
- Relative risks / odds ratios for outcomes associated with the risk factor (exposure).

The AFs can then be derived and used to calculate the "fractional contribution" of a risk factor to causation of an outcome (reproductive effects or birth defects), using the following equation[15]:

[12] See for example (2021) Air Quality appraisal: damage costs guidance https://www.gov.uk/government/publications/assess-the-impact-of-air-quality/air-quality-appraisal-damage-cost-guidance

[13] Smith, K. R., Corvalán, C. F., & Kjellström, T. (1999). How much global ill health is attributable to environmental factors?. *Epidemiology (Cambridge, Mass.)*, *10*(5), 573–584.

[14] Trasande, L., Zoeller, R. T., Hass, U., Kortenkamp, A., Grandjean, P., Myers, J. P., DiGangi, J., Hunt, P. M., Rudel, R., Sathyanarayana, S., Bellanger, M., Hauser, R., Legler, J., Skakkebaek, N. E., & Heindel, J. J. (2016). Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. *Andrology*, *4*(4), 565–572. https://doi.org/10.1111/andr.12178

[15] Institute of Medicine (US) Committee for a Planning Study on Ongoing Study of Costs of Environmental-Related Health Effects. Costs of Environment-Related Health Effects: A Plan for Continuing Study. Washington (DC): National Academies Press (US); 1981. Available from: https://www.ncbi.nlm.nih.gov/books/NBK219029/ doi: 10.17226/812

$$Attributable\ disease\ burden = Outcome\ prevalence \times AF \times Population\ size$$

Challenges in using and interpreting Afs and PAFs

AFs are used to estimate the proportion of an outcome caused by a particular risk factor at the level of an exposed population. As such there are various uncertainties, simplification and assumptions made in any one calculation. The risks factors considered in this report typically have a number of underlying causes, which may comprise (non-chemical) environmental factors, lifestyle factors (such as diet or alcohol consumption) as well as generic components. Extent and/or duration of exposure may be affected by occupation, geography, gender as well as socio-economic factors. AFs are typically expressed for single risk factors, but there are specific gaps in knowledge of how risks may differ in combination and cumulatively over time. Uncertainty in the data and methods used to calculate the AF can result in inaccurate AFs being used to determine the effects of a risk factor.

A widely cited paper by Greenland and Robins (1988)[16] outlines various conceptual problems associated with the definition and interpretation of attributable fractions. These include:

- the distinction between "excess fractions", "incidence-density fractions" and "etiologic fractions". An excess case is one that would not have occurred without exposure, whereas an etiologic case is based on exposure as a contributing factor. Calculation of an etiologic fraction requires significantly more biologic assumptions. For most PAFs, an 'excess fraction' will be the most appropriate.

Another dated, but widely cited paper by Rockhill, Newman and Weinberg (1998)[17] discuss the "use and misuse" of PAFs, with specific reference to conceptual and computational errors in their development and use. The purpose of their paper is to highlight the importance of careful interpretation and communication of PAFs.

- They note challenges in the definition of "exposure" (i.e. broad assumptions about extent, categories of exposed people and duration) which can have significant effects on the calculations. Other challenges include computational errors (the authors noted an example where a study attributing US mortality to poverty overstated the association by a factor of three based on a formula error). They note summing PAF estimates for multiple risks tends to overestimate effects, compared to considering each one simultaneously. They also note concern with the extent of epidemiological data used in the derivation of some PAFs.
- They conclude that "the assumptions underlying valid population attributable fraction estimation include the following (further explanations are in brackets):
  - a *causal relationship between the risk factors and disease* (is proven and exists);
  - the *immediate attainment, among those formerly exposed, of the unexposed disease risk following elimination of the exposures* (is possible in practice);
  - and independence of the considered risk factors from other factors that influence disease risk so that it is possible to conceive of changing the population distributions of the considered factors only".

Dose Response Relationships

Several of the relevant studies have relied upon the use of DRRs to estimate the number of cases of ill-health associated with exposure to specific substances/concentrations. The DRR is the algorithm

[16] Greenland, S., & Robins, J. M. (1988). Conceptual problems in the definition and interpretation of attributable fractions. *American journal of epidemiology*, *128*(6), 1185–1197. https://doi.org/10.1093/oxfordjournals.aje.a115073
[17] Rockhill, B., Newman, B., & Weinberg, C. (1998). Use and misuse of population attributable fractions. *American journal of public health*, *88*(1), 15–19. https://doi.org/10.2105/ajph.88.1.15

indicating the proportion of (e.g.) workers that will develop a health effect (endpoint) when exposed to a certain exposure level; when multiplied by the number of exposed workers operating at this exposure level, the number of cases of ill-health is estimated.

Challenges in use of Dose Response Relationships

Many of the same challenges apply to DRRs. They require data, often over man years (or even decades) on exposure, which often don't exist or are methodologically inconsistent. Occasionally, these data are extrapolated back in time to overcome this, which introduces further uncertainty. Errors in attribution and study biases occur, given the range of confounding factors. Where epidemiological data do exist, they may be based on a small number of disease occurrences (particularly for less common diseases). As such they are available for only a small number of chemical substances, often those that have been extensively studies (and regulated) in the past[18].

Particular challenges relate to the discovery and representation of non-linear relationships between increased dose and the corresponding response[19] as well as the presence of thresholds for effect, under which no/negligible risk is expected to occur and where there are confounded effects, which applies to most health outcomes.

Are reported effect associations "true"?

A paper by Ioannidis (2008)[20] explores general challenges in reporting and interpreting any research findings that are based on reported effect associations. The focus of the paper is whether associations (between e.g. endocrine disrupting chemical and obesity) do not just reflect chance or bias, or contingent conditions at the time of discovery but are in fact "true" representations of those effects more generally. The paper explores a series of systematic biases (including publication biases) which can serve to inflate (exaggerate) effects, alongside a briefer survey of those that serve to deflate (understate) effects. These are:

- They review evidence for **inflated effect sizes in "newly discovered" associations**. The authors note that the first study to report effect associations often reports larger effects than later ones.
- **When a claim is based on crossing a threshold of statistical significance and the discovery study has an insufficient sample size** (which can be offset by meta-analyses). Inflation of effects can occur when a study has an insufficient sample size (is "underpowered") to make the discovery at the required threshold of statistical significance. Inflation occurs when there is both a focus on crossing a threshold of statistical significance and the sample size is insufficient.
- **Selective reporting and flexible analysis leading to a range in effects ("vibration of effects")** A significant range in effects can occur if alternative analytical approaches are used in the analysis. There are a range of options in statistical modelling and data selection can also play a role.

[18] Mundt, K (2005) Statistical Challenges in Evaluating Dose-Response using Epidemiological Data https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2477196/

[19] May, S and Bigelow, C (2006). Modelling nonlinear dose-response relationships in epidemiologic studies: statistical approaches and practical challenges https://pubmed.ncbi.nlm.nih.gov/18648629/

[20] Ioannidis J. P. (2008). Why most discovered true associations are inflated. *Epidemiology (Cambridge, Mass.)*, *19*(5), 640–648. https://doi.org/10.1097/EDE.0b013e31818131e7

- **Inflated interpretation of results** (e.g. by extrapolation or generalisation, or downplaying caveats) are a further issue.
- However, the **opposite can also be true**, with the effects of associations sometimes being deflated. This could be due to early analysis of data which only on later analysis passes a threshold for significance, misclassification of results due to measurement errors, or the underreporting of results due to reverse biases, e.g. results which do not fit with certain perspectives.

For all these reasons, the authors advocate several guiding principles when interpreting results such as those in this study. These include; being cautious about the certainty of assumed effect sizes; questioning the underlying data used to derive the results (was it based on a small sample size, who undertook and published the research; is the evidence based on several studies, conducted over time etc?). Maximising free access of relevant data is recommended. As such in this study, calculations are transparent and the uncertainties, limitations and key assumptions required in the calculations are explained.

2.4 Past, current and future burdens

Some studies estimating cancer, EDC and reprotoxic effects express results as annual values only. Further, some published literature are not clear on precisely the period over which effects are assessed or presented. This results in the loss of valuable information on the time period over which impacts will actually occur. Studies often adopt a timeframe of 40 years for worker exposures, 70 years for general population exposures and in some cases 80 years to also account for impacts occurring on new-borns or from early childhood exposures.

Studies dealing with morbidity effects often express impacts in annual terms, even though impacts may have been calculated over a long time period to account for the need for medical intervention at certain points in time or ongoing treatment. Environmental impacts may be expressed either as annual, annualised damage or as present values, depending on the broader analysis.

Two types of studies can be identified: those that are retrospective in nature and are aimed at establishing the current burden of disease due to past exposures; and those that are prospective in nature and are aimed at assessing the future burden of disease associated with current and ongoing future exposures. Retrospective studies can provide an indication of the burden of disease linked to already regulated substances, thereby providing a post-hoc justification for earlier action. Prospective studies are aimed at assessing – or providing - justification for regulatory action. Both types of study can be valuable in demonstrating the importance of a proactive chemicals risk management framework. Both have been referred to and where they are used, the basis of the analysis is explained.

Current prices

Unless otherwise specified we have uprated costs to 2020 prices using HMT GDP deflators[21]. Where unit costs/valuations are converted from foreign currency to Sterling, this is based on the prevailing exchange rates at the time of publication of the relevant study, before uprating to current prices. Details are provided in each case.

Discounting

The discount rates used in the original studies vary from zero to 4% (i.e. studies prepared for/by the European Commission). Some studies adopt a declining rate, or a low rate for latent human health effects.

[21] https://www.gov.uk/government/collections/gdp-deflators-at-market-prices-and-money-gdp

We have adopted current advice on discount rates from HMT Green Book[22] and supplementary guidance, unless otherwise specified. We have used a 0% discount rate, for illustrative purposes as part of a sensitivity assessment for some neurodevelopmental effects. The rationale is to demonstrate the effect of the discount rate, give the intergenerational nature of harm. We use consistent valuation(s) for the same effects, unless specified and explained. We have taken into account methods agreed by the Interdepartmental Group on Costs and Benefits (IGCB) on valuation of Air Quality work[23].

2.5 Structure of analysis in the following chapters

The wider cycle in which the assessment of risk and regulation of chemicals takes place is shown in (Figure 2-1). The overall aim is protection of human health and the environment (1) from various chemicals substances that are known or suspected to cause harm (2). Where exposure occurs, this can result in impacts on human health and/or the environment (3). The body of regulation and legislation is applied and evolves over time (4). This results in changes in the production and consumption of hazardous substances, alongside changes in emissions/releases and in concentrations of some of these substances in the body, where such "biomarker" data are available (5). But ongoing damage occurs under current legislative controls (6).

A consistent structure has been adopted for each chapter. This adapts the Impact Pathway Assessment (IPA)[24] Framework as it provides a logical and sequential structure to the analysis, whilst highlighting key evidence gaps. Several adjustments have been necessary to this approach to ensure the analysis is manageable and coherent. For each impact, we:

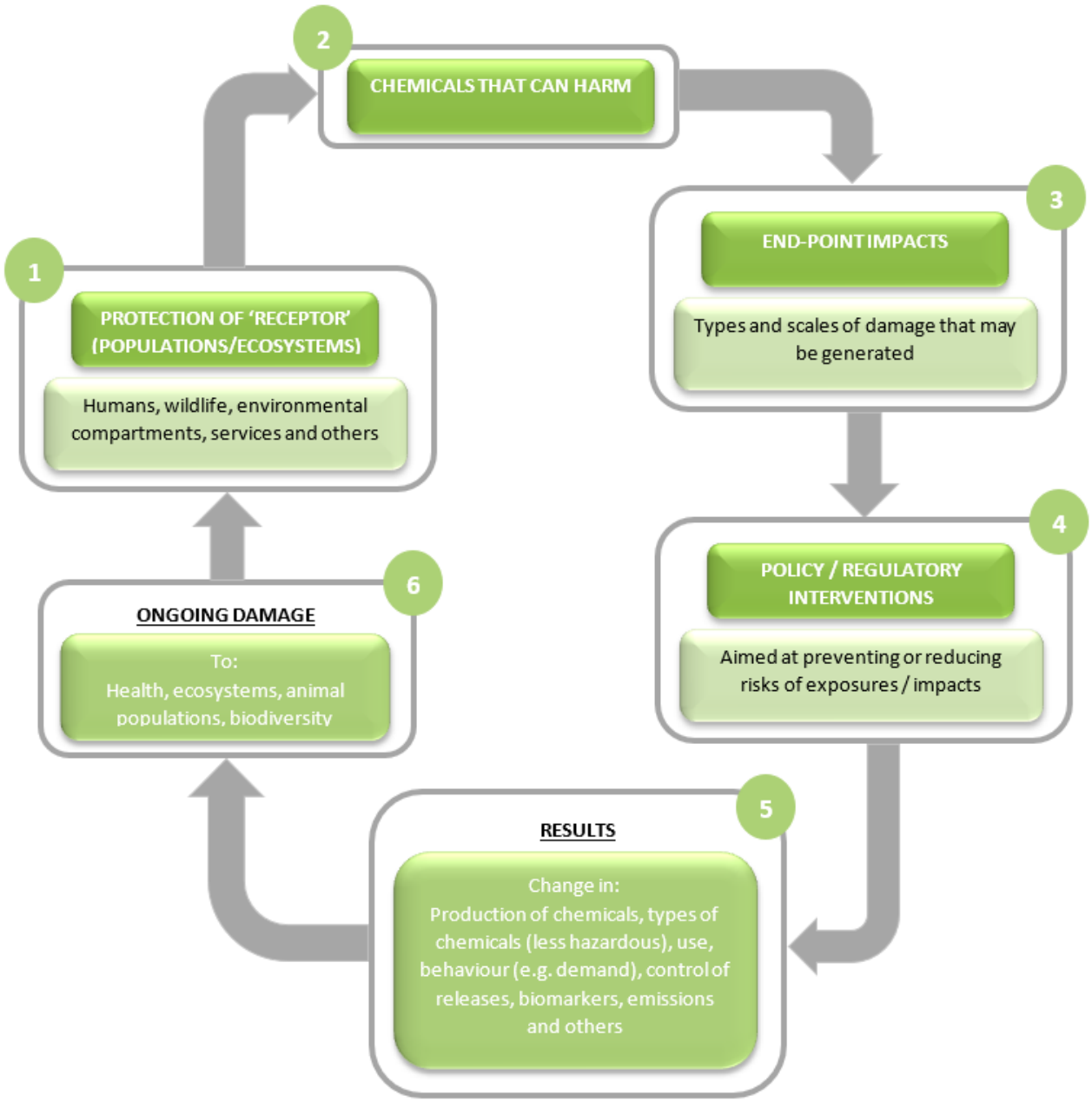
- Note the **specific effects** that are considered and **evaluate the strength of the relationship** between it and the substance(s) in question. This is relatively brief; the focus of the study is not on evaluating this evidence base, which is extensive and dynamic.
- For those substance/human health effects where damage can be quantified, we describe the **UK incidence or prevalence**; and the UK data on the **severity of effects** (e.g. DALYs, number of cases/treatments etc), using AF or DRR's. For effects that cannot be quantified, a qualitative assessment was made, drawing conclusions on the likely importance (severity and extent) of the impact where possible.
- For a specific number of SVHCs, we assess **environmental releases** and associated burden adjusting to UK as a 'region', using standard environment model (EUSES). This is supplemented with qualitative assessment.
- Where possible, effects are quantified in monetary terms, setting out key assumptions, uncertainties, limitations of the approach and - in some cases – criticisms that have been made of the methods used and of their relevance to the UK.

[22] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf. This recommends a discount rate of 1.5% for valuing health in the first 30 years, which then incrementally decreases for much longer term effects.

[23] Most recently summarised in 'Air Quality damage cost update 2019' https://uk-air.defra.gov.uk/assets/documents/reports/cat09/1902271109_Damage_cost_update_2018_FINAL_Issue_2_publication.pdf.

[24] See Defra IPA Guidance https://www.gov.uk/government/publications/assess-the-impact-of-air-quality/air-quality-appraisal-impact-pathways-approach

Figure 2-1 Simplified Impact Pathway



3 Cancer

3.1 Effects

Carcinogenic chemicals give rise to a wide range of effects through different types of threshold and non-threshold modes of action. Cancer is typically classified by site and/or cell type. For example, RPA (2017)[25] and Rushton et al (2012)[26] estimate the incidence of occupational cancer for around 25 cancer sites[27] such as lung, bladder, breast cancer, etc.

Many carcinogenic chemicals can give rise to cancer at more than one site. For example, available research suggests that up to eight cancer sites may be relevant to Polycyclic aromatic hydrocarbons (PAHs), although it is recognised that the strength of evidence of carcinogenicity varies between these cancer sites (RPA, 2017).

3.2 Substances of concern

Under Classification, Labelling and Packaging (CLP), human carcinogens are classified based on the strength of the evidence:

- **Category 1 A: known** to have a carcinogenic potential for humans, based largely on **human evidence**
- **Category 1 B: presumed** to have a carcinogenic potential for humans, based largely on **experimental animal data**
- **Category 2: suspected** to have a carcinogenic potential for humans

Over 1,000 EU-REACH-registered substances are classified as C1A/1B/2. Since the general patterns of industrial, professional and consumer use of these substances is likely to be similar in the EU-27 and the UK, it is expected that the vast majority of these substances are also relevant to the UK. It is, however, recognised that there may be some differences between the two jurisdictions that result in differences in exposure patterns, for example, due to differences in Occupational Exposure Limits (OELs), commonly used construction materials, etc.

3.3 Major uses and exposure pathways

The main exposure pathways for human carcinogens are:

- occupational exposure;
- humans via the environment (including through air, water and food); and
- consumer products.

Within each of the above categories, exposure can occur via inhalation, ingestion or dermal absorption. In addition, the presence of carcinogens in dwellings and/or the environment can have adverse impacts on terrestrial and aquatic[28] organisms.

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[25] https://www.etui.org/publications/reports/the-cost-of-occupational-cancer-in-the-eu-28
[26] https://www.hse.gov.uk/research/rrpdf/rr931.pdf
[27] Bladder, Bone, Brain, Breast, Cervix, CNS (Central nervous system), Colon & rectum, Eye, Kidney, Larynx, Leukaemia, Liver & bile duct, Lung, Lymphoma, Lymphoma and leukaemia, Malignant melanoma, Mesothelium, NHL (Non-Hodgkin lymphoma), NMSC (Nonmelanoma Skin Cancer), Oesophagus, Ovary, Pancreas, Pharynx incl. NFC (nasopharyngeal), SNC (sinonasal), Stomach, Thyroid
[28] https://www.sciencedirect.com/science/article/pii/S0160412021000155

In the past, carcinogens were widely used across a large number of economic sectors. Rushton et al (2012) highlight, for example, construction, land transport, manufacture of transport equipment, metal production, mining, repair trades, laundries and dry cleaning, etc. as sectors that substantially contribute to the current cancer burden as a result of past exposures. Rushton et al (2012) further note that workers in many industry sectors are exposed to multiple carcinogens (over 10 in many sectors).

3.4 Current regulatory controls and remaining sources of exposure

The use of many carcinogens is regulated under EU REACH, with equivalent controls also being in place in the UK. Existing regulatory measures protect both workers and consumers, as well as humans via the environment. The current regulatory approach recognises that both threshold and non-threshold carcer-inducing modes of action exist (RAC/SCOEL, 2017).[29]

Other regulatory controls apply to cosmetics, food, toys, plant protection products and biocidal products.

Although the extent of exposure to occupational carcinogens has significantly declined[30] over the past few decades, workers continue to be exposed to these substances. For example, a series of Impact Assessments on the introduction of additional EU OELs carried out by RPA between 2017 and 2021 identified large numbers of workers exposed to some carcinogenic substances.

Although many carcinogens are no longer used (e.g. asbestos) or only used to a very limited degree, exposure can still occur during the service life of legacy products and waste disposal.

3.5 Occupational exposure

3.5.1 Approach

From a methodological perspective, both Population Attributable Fractions (PAFs) and dose-response based approaches have been used for predicting the number of cases of cancer due to past and current exposure. Economic damage costs are regularly estimated with reference to direct and indirect costs (e.g. health care, informal care costs, lost working time, etc.) and Willingness to Pay (WTP) methods are used for the appraisal of non-market impacts.

Many cancer types have long latency periods, resulting in a significant lag between exposure and diagnosis. Current incidence rates thus reflect historical exposures and current exposures can be expected to result in diagnosis and treatment in many years or decades. By way of simplification, the approach taken in Rushton et al (2012)[31] is to assume that all solid tumors have a latency of 10-50 years and all haematopoietic neoplasms have a latency of 0-20 years.

Two estimates of the burden of occupational cancer are thus developed in this study:

- **an estimate of the current burden resulting from historical exposure** to carcinogenic chemicals**,** i.e. the costs associated with annual cancer registrations that can be attributed to past occupational exposure to carcinogens; and
- **an estimate of the future burden resulting from current exposure**, i.e. the costs of future (2040) cancer incidence that can be attributed to current exposure to carcinogenic chemicals.

Current burden from past exposure

[29] https://echa.europa.eu/documents/10162/13579/jtf_opinion_task_2_en.pdf/db8a9a3a-4aa7-601b-bb53-81a5eef93145

[30] RPA (2017) and other studies model the rate of decrease in exposures as 7% per annum accounting for reductions in both exposed populations and exposure levels.

[31] https://www.hse.gov.uk/research/rrpdf/rr800.pdf

With regard to the current burden resulting from historical exposures, the approach taken in this study relies on updating the overall Population Attributable Fractions (PAFs) in published literature to 2020, combining the resulting PAFs with the most recent UK cancer incidence data to derive Attributable Numbers (ANs) and monetising the ANs in accordance with the approach originally developed in RPA (2017), which is adapted to take into account the approaches proposed in HM Treasury Green Book.

An alternative approach (a detailed review of 10-15 selected carcinogens[32]) was considered by the study team but it was concluded that it is preferable to develop an estimate that encompasses the greatest possible number of carcinogenic substances to a more detailed review of a limited number of carcinogens. The advantages and disadvantages of each of the two approaches are summarised below. In addition, it should be noted that PAF approaches rely on relative risk estimates in epidemiological studies. Obtaining epidemiological evidence (especially if of high quality) is a resource intensive process (especially when it comes to endpoints with a long latency). Sole reliance on epidemiological data means that PAF approaches may not reflect recent risk levels and may omit risks for which epidemiological studies have not been carried out.

Table 3-1 Comparison of approaches to the estimation of occupational cancer burden

Approach	Advantages	Disadvantages
APPROACH 1: High-level estimate (application of PAFs to UK incidence data) **ADOPTED APPROACH**	• **Comprehensive: provides an estimate across a large number of substances and cancer sites**	• **Less robust for specific substances than Approach 2** • **Relies solely on epidemiological evidence used (quick review)** • **Typically relies on older data, so greater potential for being outdated and overestimation (this risk is minimised by use of an adjustment factor)**
APPROACH 2: Focus on 10-15 selected carcinogens DISCARDED APPROACH	• Relies on extensive evidence for each of the 10-15 carcinogen • Extensive consideration of epidemiological and toxicological evidence, including recent studies	• Less comprehensive, no more than 10-15 carcinogens would be possible within the constraints of this study • Significant potential for underestimation, data more likely to be available for carcinogens that have already been subject to regulatory action

The specific steps involved in developing the estimates under Approach 1 are:

- **Step 1:** Literature review to determine the overall PAF across all substances and cancer sites. Two studies are used: Rushton et al (2012) and RPA (2017)[33]. Rushton et al (2012) has the advantage of providing UK-specific PAFs for 42 carcinogens (IARC Category 1 and 2A) across a large number of industry sectors. However, these estimates are only available for 2004/05. On the other hand, RPA (2017) provides more recent estimates but focuses on fewer carcinogenic substances (25 carcinogens) and relies on EU-wide data to derive the PAFs. The results of these

[32] This approach would have involved extracting data from RPA OEL and SHECAN studies and/or the European Commission's IAs for OELs for 10-15 selected occupational carcinogens and adjust EU-28 estimates to the UK based on population (or extract UK-specific data from these studies where available). SHECAN studies: http://www.occupationalcancer.eu/projresults.html

[33] Rushton et al (2021) is a widely quoted study based on an extensive literature review and data analysis. It resulted in many peer-reviewed publications. RPA (2017) uses a similar approach to derive estimates at the EU-28 level based on more recent literature searches. However, only a relatively limited review/quality check of the studies used to derive the overall estimates was carried out in RPA (2017).

studies are adjusted to reflect that fact that not all risk factors considered in Rushton et al (2012) and RPA (2017) are chemical related.

- **Step 2:** Adjusting the PAFs to account for exposure trends. The PAFs in Rushton et al (2012) and RPA (2017) are updated based on an estimated 7% annual decrease in risk due to improvements in chemicals legislation. This assumption likely reflect worker safety improvements and carcinogenic chemical restrictions and is taken from past RPA work for DG Employment [34]) combined with an estimated 1% annual increase in the number of substances with a carcinogenic harmonised classification and labelling (CLH) under the CLP[35], resulting in an overall annual decrease in the PAF by 6% (7%-1%)**.** Please note that both estimates (7% and 1%) and consequently the resulting estimate of 6% are a mere approximation of the relevant trends and should be only taken as indicative of the possible order of magnitude of the relevant developments.
- **Step 3:** Deriving Attributable Numbers (ANs) by applying the updated PAFs to the most recent set of cancer incidence data for the UK (AN=PAF x overall cancer incidence).
- **Step 4:** Monetisation of the Attributable Numbers (ANs). This step relies on an adapted approach applied in RPA (2017, 2017a[36], 2021[37]) but takes into account UK-specific unit costs, including the Value of Prevented Fatality (VPF) and Statistical Life Year (SLY) used in other sections of this report.

The cost framework developed in RPA (2017, 2017a, 2021) includes direct, indirect costs and non-market effects. Direct and indirect costs include the costs of healthcare, informal care, productivity losses/lost working days and other costs to businesses-these are derived by multiplying the costs per case in the table below by the Attributable Numbers. Two methods are used for the monetisation of non-market effects: Method 1 relies on WTP values for the avoidance of a case of cancer mortality or morbidity, whilst Method 2 relies on the monetisation of the decrement in Quality Adjusted Life Years (QALYs) monetised using the value of a Statistical Life Year (SLY).

The key unit costs (updated to £2020[38]) are summarised below. These do not differentiate between specific cancer sites.

Table 3-2 Modelling inputs

Parameter	Value
Mortality rate (default value)	47%[39]

[34] See, for example, RPA (2017a): Second study on exposure to carcinogens or mutagens at work, available at https://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=8223&furtherPubs=yes and RPA (2018): Third study on exposure to carcinogens or mutagens at work, available at https://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=8224&furtherPubs=yes

[35] Based on any carcinogenic classification in Table 3 of Annex VI to the CLP Regulation as adopted by the various ATPs since the Regulation came into force. Updates over the past five years taken as a proxy. 1,098 in September 2016, 1,141 in December 2021, + 43 (4%), rounded up to 1% increase per annum. Source: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp

[36] RPA (2017a): Second study on exposure to carcinogens or mutagens at work, available at https://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=8223&furtherPubs=yes

[37] RPA (2021): Study on collecting information on substances with the view to analyse health, socio-economic and environmental impacts in connection with possible amendments of Directive 98/24/EC (Chemical Agents) and Directive 2009/148/EC (Asbestos) , available at https://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=8440&furtherPubs=yes

[38] Updated based on Department for Transport's GDP deflator. Source: https://www.gov.uk/government/publications/tag-data-book

[39] Source: RPA (2017), consistent with Cancer Research (undated). Links given in the table.

Parameter	Value
Healthcare	£5,900 per year of treatment[40]
Informal care	£2,700 per year of treatment[41]
Productivity losses	£4,600 per case[42]
Lost working days	£1,200 per case[43]
Cost to employer	£12,000 per case[44]
Disutility (QALY reduction)	0.2[45]
Value of Prevented Fatality (VPF) (includes non-market effects)	**£3,540,162 (£3.5m) per mortality case**
WTP to avoid cancer morbidity (includes non-market effects)	**£375,000[46] per morbidity case**
Value of a statistical life year (SLY)	£60,000 (HM Treasury Green Book) [47]
Sources: **Cancer Research UK (undated): Survival rate for all cancers combined, available at https://www.cancerresearchuk.org/health-professional/cancer-statistics/survival/all-cancers-combined** DG Employment (2011): BenOSH, available at: http://ec.europa.eu/social/BlobServlet?docId=7416&langId=en Huang, W. *et al.* (2018) 'Assessing health-related quality of life of patients with colorectal cancer using EQ-5D-5L: a cross-sectional study in Heilongjiang of China', *BMJ Open*, 8, p. 22711. doi: 10.1136/bmjopen-2018-022711. Hall, P. S. et al. (2015) 'Costs of cancer care for use in economic evaluation: a UK analysis of patient-level routine health system data', British Journal Of Cancer. The Author(s), 112, p. 948. Available at: https://doi.org/10.1038/bjc.2014.644. Luengo-Fernandez, R. et al (2013): Economic burden of cancer across the European Union: a population-based cost analysis; Lancet Oncology; 14: 1165–74, published online October 2014: http://dx.doi.org/10.1016/S1470-2045(13)70442-X RPA (2017): Economic cost of occupational cancer, available at https://www.etui.org/publications/reports/the-cost-of-occupational-cancer-in-the-eu-28	

For each case of cancer that is attributed to chemical pollution, the cost estimates presented in this report encompass all the costs associated with this case, including the costs that arise in the years subsequent to diagnosis (for example, treatment is expected to last for more than one year). In accordance with the HM Treasury Green Book, future costs are discounted using the social preference time rate (STPR) of 1.5% which applies to impacts involving risk to life.

Future burden from current exposure

There are very few prospective studies that estimate the overall future burden of cancer due to current occupational exposures to a range of carcinogens. Hutchings & Rushton (2011)[48] propose a method for estimating the future burden of occupational cancer that builds on the AF approach developed to estimate the current burden of occupational cancer in GB whilst taking into account past and projected trends in exposure and possible strategies to reduce the future burden. Illustrative scenarios aimed at reducing future lung cancers due to occupational exposure to respirable crystalline silica are presented that suggest that the

[40] Luengo-Fernandez (2013) but updated. Full reference given in the table.
[41] Luengo-Fernandez (2013) but updated. Full reference given in the table.
[42] Luengo-Fernandez (2013) but updated. Full reference given in the table.
[43] Luengo-Fernandez (2013) but updated. Full reference given in the table.
[44] DG Employment (2011). Full reference given in the table.
[45] Average of colorectal and breast cancer in Huang et al (2018) and Hall et al (2015). In order to account for the increasing age of the population over time, based on the results of the study by Kind et al. (1998) a utility decrement of 0.004 will be applied during each year of the model.
[46] A value of €410,000 (2012 prices) has been adopted as the willingness to pay to avoid a non-fatal case of cancer based on the EU Better Regulation Tool #31. This figure has been updated to 2020 price and rounded: €450,000, i.e. £375,000.
[47] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf
[48] https://www.hse.gov.uk/research/rrpdf/rr849.pdf

AF for lung cancer due to respirable crystalline silica could be reduced from 2.07% in 2010 to nearly zero by 2060. It is recognised that respirable crystalline silica may be a special case due to the fact that it occurs naturally and occupational exposure results from the use of building materials that contain it.

A similar method is proposed and applied to estimate the excess lifetime risk of mesothelioma for working age population asbestos exposure in Australia in Fritschi et al (2016)[49]. Note, see also respiratory effects in chapter 0.

Carey et al (2017)[50] attribute 1.4% of future cancer incidence in Australian workers to occupational exposure based on exposure patterns in 2012. This is a lower PAF than estimated in the studies that focus on the current burden due to past exposure such as Rushton et al (2010) and RPA (2017). This is not surprising given that reductions in exposed workforce and exposure concentrations (often taken as 7% per annum) have been achieved over the past few decades. On the other hand, a PAF based on current knowledge is likely to underestimate the future burden since epidemiological and toxicological research continues to identify evidence of carcinogenicity in additional substances and improve the evidence base for existing C1A/1B/2 substances. A comparable UK exercise to Carey et al (2017) has not been identified but it would be likely to suffer from similar methodological challenges resulting in the underestimation of the future burden.

The future burden from current exposure is estimated by means of adjusting the PAFs in Rushton et al (2012) and RPA (2017) to account for future trends in exposure. The resulting estimates are compared with the PAF derived for Australia by Carey et al (2017)[51].

Taking into account the latency periods estimated in Rushton et al (2012), 2040 is selected as the reference year for future estimates. Attributable Numbers are derived based on the assumption that cancer incidence in 2040 is the same as in 2019.

This approach includes the following steps:

- Step 1: Estimation of the PAF in 2040
- Step 2: Derivation of the Attributable Numbers in 2040
- Step 3: Monetisation

The resulting ANs are monetised using the same approach as above for the current burden due to past exposure.

3.5.2 Results

Current burden resulting from past exposure

Steps 1 and 2: Population Attributable Fractions (PAFs)

Rushton et al (2012) estimate UK-specific PAFs for past occupational exposure to carcinogens with International Agency for Research on Cancer (IARC) classification as group 1 (established) and 2A carcinogens (probable) and concludes that, in 2005, 5.3% (8,023) cancer deaths in the UK were attributable to occupation. The underlying data reflect historical exposures dating back to 1956 for solid tumors.

[49] https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-016-3066-1
[50] https://pubmed.ncbi.nlm.nih.gov/28081474/#:~:text=Results%3A%20The%20cohort%20of%2014.6,in%20those%20exposed%20in%202012.
[51] https://pubmed.ncbi.nlm.nih.gov/28081474/#:~:text=Results%3A%20The%20cohort%20of%2014.6,in%20those%20exposed%20in%202012.

A more recent study was completed by RPA in 2017 which uses a similar approach to estimate PAFs for 25 key occupational carcinogens. These are estimated to account for 6-12% (central estimate: 8%) of cancer incidence in 2015.

Most carcinogenic factors examined in both studies are chemical-related but they also consider non-chemical factors such as shift work, silica, wood dust, ionising radiation and solar radiation. The AFs in Rushton et al (2012) and RPA (2017) were reduced by 20%[52] to account for non-chemical carcinogens.

Adjusting the PAFs from Rushton et al (2012) and RPA (2017) for 2020 based on an assumed annual 6% decrease (the 6% comprises a 7% decrease due to better controls of known carcinogens (as mentioned earlier) minus a 1% increase in the number of known carcinogens) in exposure results in a **PAF in 2020 between 2% and 5%**[53].

Step 3: Attributable Numbers

Applying the 2020 PAF to the most recent annual cancer incidence data for the UK (390,000 per year) results in an estimated 7,000 to 21,000 annual cancer diagnoses[54] being attributable to past occupational exposure to carcinogenic chemicals.

Step 4: Monetisation

The monetary cost of annual cancer cases attributable to past occupational exposure to carcinogenic chemicals is estimated to be:

- **£3-10 billion** for 7,000 cases (of which healthcare, informal care, productivity/output-related costs account for around £0.3-0.4 billion)
- **£10-32 billion** for 21,000 cases (of which healthcare, informal care, productivity/output-related costs account for around £1 billion)

Non-market effects estimated based on WTP for the avoidance of cancer mortality or morbidity account for between 88% and 97% of the overall costs (note that some of the totals may not completely add up due to rounding).

This can be compared with RPA (2017), which estimates the monetary cost of annual registrations in the UK attributable to past occupational exposure to carcinogenic chemicals to be around £65 billion (based on an estimated share of an EU wide total). The key shortcoming of RPA (2017) is that the valuation relied on 2012 cancer incidence data primarily sourced from EUCAN whilst more recent data for the UK from other sources suggests a greater number of annual registrations (160,000 cancer registrations in RPA 2017 vs more recent data for all cancer sites suggest 390,000 new cancer diagnoses in the UK in 2019).

Jongeneel et al (2016)[55] estimate PAFs and Attributable Numbers for 42 carcinogenic substances/substance groups and 16 occupational circumstances, resulting in estimated societal costs in 2012 of €334 billion (range €242-440 billion) across Europe. When the difference between the EU and UK population is considered, the results of Jongeneel et al (2016) are broadly consistent with the results reported in this study.

Future burden due to current exposure

Step 1: Estimation of the PAF in 2040

[52] Shift work and silica account for 17% of occupational cancer mortality in Rushton et al (2012). Non-chemical factors account for at least 23% in RPA (2017).
[53] Rounded from 1.7% and 5.3%.
[54] Rounded from 6,537 and 20,731.
[55] https://www.rivm.nl/bibliotheek/rapporten/2016-0010.pdf

Adjusting the central PAF estimate (8%) in RPA (2017) by 6% per year results in a PAF of 1.5% in 2040. The PAF in Rushton et al (2012) adjusted to 2040 is 0.5%. Therefore, a range of PAFs 0.5%-1.5% is estimated. This is consistent with Carey et al (2017)[56] who attribute 1.4% of future cancer incidence in Australian workers to occupational exposure based on exposure patterns in 2012.

Step 2: Attributable Numbers in 2040

For simplicity, a hypothetical scenario is constructed in which cancer registrations remain constant between 2019 and 2040. It is estimated that between **2,000 and 6,000 cases of cancer** diagnosed in 2040 are attributable to current occupational exposure to carcinogens.

Step 3: Monetisation

The monetary cost of cancer cases diagnosed in 2040 that can be attributed to current exposure to occupational carcinogens is estimated to be:

- **£0.7-2.2 billion** for 2,000 cases (of which healthcare, informal care, productivity/output-related costs account for around £70-90 million).
- **£2.2-7 billion** 6,000 cases (of which healthcare, informal care, productivity/output-related costs account for around £240-280 million).

3.5.3 Uncertainties and limitations of the approach

The majority of the costs are associated with non-market effects. These types of costs are associated with the greatest methodological challenges. There are significant limitations to the WTP approach, recently highlighted in HSE (2020)[57]:

> *"Currently, recommended Green Book values for the VPF and the monetary value of a QALY are based on a very small sample-survey of the UK public carried out in the 1990s. The only UK study to directly elicit a VOLY is also outdated, but was carried out on larger sample. Updated values for changes in longevity derived from a broadly representative sample of the UK population would better reflect current preferences."*

It has not been possible to provide analysis at the level of individual cancer sites. This may be a significant limitation since the costs differ between cancer sites, e.g. mortality for lung cancer is 80% as opposed to the 'average' value of 47% used for modelling in this study.

It should be noted that PAF approaches rely on relative risk estimates in epidemiological studies. Obtaining epidemiological evidence (especially if of high quality) is a resource intensive process that a lot of time to complete (especially when it comes to endpoints with a long latency). Sole reliance on epidemiological data means that PAF approaches may not reflect recent risk levels and may omit risks for which epidemiological studies have not been carried out.

The modelling is based on a number of assumptions about the unit costs. For example, HSE (2016)[58] provides lower healthcare costs. The average per case lifetime treatment cost estimated in HSE study at £8,200, which is considered to reflect the top 90% of occupational cancers. Since the approach developed in RPA (2017) models a scenario whereby healthcare costs are incurred for a number of years (5 years), the

[56] https://pubmed.ncbi.nlm.nih.gov/28081474/#:~:text=Results%3A%20The%20cohort%20of%2014.6,in%20those%20exposed%20in%202012.

[57] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/903543/voly-scoping_study-report.pdf

[58] in UK HSE (2016): Costs to Britain of Work Related Cancer, Research Report 1074, available at: http://www.hse.gov.uk/research/rrhtm/rr1074.htm

healthcare costs estimated in this study are greater than those that could be estimated based on the HSE (2016) approach. However, healthcare costs are only a relatively minor component of the overall costs modelled in this study with non-market effects making up the majority of the overall cost.

With regard to the future burden, the disadvantage of the approach in this study is that it is likely to underestimate the burden since, in addition to the increasing number of carcinogens, more robust evidence of carcinogenicity emerges over time with better evidence increasing the potential for the estimation of additional cancer cases. It is, however, recognised that this assumption is highly uncertain.

In conclusion, **the costs presented in this section should be treated as order of magnitude estimates**. Despite the uncertainties, the modelling in this section clearly shows that the order of magnitude of both the current and future costs is substantial.

3.6 Humans via the environment

3.6.1 Approach

Exposure to carcinogens via the environment (air, water, food, etc.) is also a significant cause of cancer. However, there is less evidence for this exposure pathway and it is therefore harder to estimate the overall burden. In addition, the scope of the study excludes five key air pollutants (nitrogen oxides (NO_X), particulate matter (PM), sulphur dioxide (SO_2), volatile organic compounds (VOCs), and ammonia (NH_3)) which further complicates the use of published estimates. For this reason, the cancer burden from benzo(a)pyrene in air, for example, is not considered in this study as it is included in the cancer risk from PM.

Due to data limitations, the approach taken in this study is limited to a summary of the available evidence.

3.6.2 Results

Brown et al (2018)[59] provide PAFs for current incidence due to past exposures and conclude that nearly four in ten (37.7%) cancer cases in 2015 in the UK were attributable to known risk factors. Occupational exposure is estimated to account for 3.8% of cases whilst air pollution has an AF of 1% (3,591 cases). For lung cancer, the PAF for outdoor air pollution is 10%. These estimates appear to be based on exposure to all fine PM.

EP (2020)[60] estimates 168,000 to 346,000 premature deaths in the EU from exposure to outdoor air pollution in the form of fine particles ($PM_{2.5}$), accounting for 4% to 7% of all deaths. In addition to $PM_{2.5}$ being outside the scope of this study, it is not clear whether these mortality estimates only relate to cancer or include other causes. Bartlett & Trasande (2014)[61] estimate the cost of childhood cancers from environmental exposure to pollutants in the EU; their core estimate for a PAF is 5%.

Evlampidou et al (2020)[62] note that disinfectants are often not included in PAFs for water pollution. Trihalomethanes (THMs) are widespread disinfection by-products (DBPs). Evlampidou et al (2020) estimate a UK-specific PAF of 9% for bladder cancer (1,400 cases per year in the UK). EP (2020) notes that there are 342,000 sites in the EU where soil is contaminated. In Italy, an epidemiological surveillance project of 44 contaminated sites found links with 23 cancers. The cancer incidence on these contaminated sites was 9% higher for men and 7% higher for women. Tonin et al (2011)[63] investigate people's WTP for cancer risk reductions in the context of public programmes that would provide for remediation at abandoned industrial contaminated sites.

[59] https://www.nature.com/articles/s41416-018-0029-6
[60] https://www.europarl.europa.eu/meetdocs/2014_2019/plmrep/COMMITTEES/BECA/DV/2020/12-11/20201211_Background_note_hearing_EN.pdf
[61] https://pubmed.ncbi.nlm.nih.gov/23748596/
[62] https://ehp.niehs.nih.gov/doi/full/10.1289/EHP4495
[63] https://onlinelibrary.wiley.com/doi/10.1111/j.1539-6924.2011.01730.x

There are significant gaps in the available data on contaminated sites in the UK but Public Health England (2019)[64] notes that the number of determinations of contaminated land is probably 10% of the 11,000 sites investigated in detail by the Environment Agency (based on estimates from the 2005, 2009 and 2016 reports). For illustrative purposes, it is therefore assumed that there are 1,100 contaminated sites in the UK. It is not clear what proportion of these sites is contaminated with carcinogens (as opposed to other chemical pollution).

Tonin et al (2011) note that a) the estimated clean-up costs for 40 sites in Italy are estimated to be €3 billion and that the estimated clean-up costs of 57 sites in Italy are expected to total several billion euro. This amounts to £80 million per site in £2020. However, Tonin et al (2011) also note that the clean-up cost at the Marghera site, an extensive and high-profile contaminated site that is comprised of both shuttered areas and active chemical plants, was over €750 million.

If costs similar to those quoted in Tonin et al (2011) were applied to hundreds of sites in the UK, significant clean-up costs could be estimated. However, no such estimation is carried out in this study due to uncertainty about the clean-up cost estimates in Tonin et al (2011) and the number of sites in the UK that would require decontamination.

3.6.3 Uncertainties and limitations of the approach

The estimate is highly uncertain primarily due to a lack of data on contaminated sites and clean-up costs. It is not clear to what extent the relevant UK sites are contaminated with carcinogens. Moreover, clean-up costs are only a part of the overall costs associated with carcinogens in soil and water and as such do not reflect the full environmental and welfare costs associated with chemical pollution (both in terms of the impacts on the environment and the value that humans place on clean environment).

3.7 Consumer exposure

3.7.1 Approach

Limited UK-specific data are available, and this study focuses on summarising the available literature.

3.7.2 Results

Consequences of exposure via consumer articles are difficult to assess. However, despite restrictions on carcinogens in consumer uses and many articles, there are still products in use that contain carcinogens, such as products with long useful lives such as construction materials (e.g. asbestos in buildings). Also, despite limits on hazardous substances in recycled products (e.g. some POPs are carcinogens), many carcinogenic substances still find their way into new product through recycling (e.g. Turner 2019[65] found high concentrations of cadmium in recycled products).

EEA (2013)[66] highlights consumer products like waxes and polishes, building materials like formaldehyde in plywood, and flame retardants in many materials.

A number of studies focus on formaldehyde, e.g. Clean Air Day (2019)[67], with levels exceeding the WHO guideline value. Nearly half of UK homes have high indoor levels of formaldehyde and other pollutants. However, this may be more relevant to health effects other than cancer. RPA (2017a)[68] uses an exposure

[64] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/779168/factsheet_for_contaminated_land.pdf
[65] https://www.plymouth.ac.uk/news/high-levels-of-carcinogenic-chemical-found-in-everyday-consumer-products and https://www.sciencedirect.com/science/article/abs/pii/S0048969718349404?via%3Dihub
[66] https://www.eea.europa.eu/signals/signals-2013/articles/indoor-air-quality
[67] https://www.cleanairday.org.uk/files/indoor_media_release_final_3_june_19.pdf
[68] https://ec.europa.eu/social/BlobServlet?docId=21369&langId=en

risk relationship (ERR) for cancer from occupational exposure and this has a threshold for cancer above the WHO limit value.

It should be noted that, according to entries 28 and 29 in REACH Annex XVII, CLH C1A/B substances may not be placed on the market to be used by the general public. A generic concentration limit of 0.1% is applied to mixtures where substance specific concentration limits have not been established.

3.8 Summary

In terms the ***current burden of past occupational exposure***, a PAF between 2% and 5% is estimated, amounting to 7,000 to 21,000 annual cancer diagnoses being attributable to past occupational exposure to carcinogenic chemicals. The monetary cost of associated cancer cases is estimated to be between £3 billion and £32 billion. Non-market effects estimated based on WTP approaches are estimated to account for between 88% and 97% of the total costs.

With regard to the ***future burden of current occupational exposure***, the PAF in 2040 is estimated to be 0.5%-1.5%. This is consistent with Carey et al (2017)[69] who attribute 1.4% of future cancer incidence in Australian workers to occupational exposure based on exposure patterns in 2012. It is estimated that between 2,000 and 6,000 cases of cancer diagnoses in 2040 will be attributable to current occupational exposure to carcinogens. The monetary cost of cancer cases diagnosed in 2040 that can be attributed to current exposure to occupational carcinogens is estimated to be between £0.7 billion and £7 billion (£2040).

Insufficient data are available to develop similar estimates for the impact of carcinogens on *humans via the environment and consumer products.*

3.9 Future research priorities

There are data gaps for all exposure routes but particularly limited evidence is available for the impact of carcinogenic chemicals on humans via the environment and consumer products. The greatest research needs are therefore concentrated in these two areas:

- **For humans via the environment:** a literature review of the available evidence on the environmental presence of specific carcinogenic substances (including evidence generated for these substances due to other hazard classifications). This review should be as UK specific as possible or assess the transferability of the results to the UK, possibly involving the consideration of the year when the substance was phased out and the estimated half-lives of these substances in the environment where historical literature is used. Based on the outcome of this review, further research needs would be identified, possibly including the selection of specific substances for which environmental exposure scenarios could be developed or the need for further environmental analyses to determine the presence of specific substances in the environment.
- **For humans via the environment:** future research could focus on the specification of the sites in the UK that are contaminated with carcinogens (as opposed to other chemical hazards) and combining these estimates with UK specific data on clean-up costs (possibly developed by means of an industry survey). WTP values specific to environmental presence of carcinogens could also be further developed.
- **For exposure via consumer products:** in order to further assess the scale of the problem (in particular in relation to legacy products), a large scale systematic literature review of the presence of specific carcinogenic substances in consumer products could be carried out, together with an assessment of the applicability of their results to the current situation in the UK (country of origin,

[69] https://pubmed.ncbi.nlm.nih.gov/28081474/#:~:text=Results%3A%20The%20cohort%20of%2014.6,in%20those%20exposed%20in%202012.

date of publication, date of phasing out of the substance, average product lifetimes). This could be complemented with a review of the available information on the release rates from these products and the development of probabilistic scenarios for consumer exposure. In this manner, the scale of the problem could be approximated and the remaining data gaps that would require additional targeted research activities could be identified (e.g. testing of specific product groups or the potential for harmful chemicals to be transferred to new products through recycling).

- **For occupational exposure (current burden due to past exposure):** it is recommended that the available PAF approaches (Rushton et al 2012 and RPA 2017) are updated to take into account new epidemiological evidence that has emerged since their publication and to examine whether some of the epidemiological evidence used in these studies should be excluded because it is no longer relevant to the level of risk during the period under review.
- **For occupational exposure (current burden due to past exposure and future burden of current exposure):** PAF approaches that rely on epidemiological evidence could be complemented with dose-response based approaches that make use of toxicological evidence or published dose response functions, combined with estimates of the exposed workforce and exposure concentrations (based on monitoring data or approximated by means of occupational exposure limits). These approaches have the potential to generate estimates that are more up to date and more comprehensive than approaches that rely on the development of PAFs.
- **For occupational exposure (future burden due to past exposure):** Probabilistic scenarios could be constructed to model potential future developments, possibly making use of industry expert panels to update PAFs and extrapolate current data into the future.

4 Reproductive effects

4.1 Effects

Reprotoxic chemicals can be categorised as two different groups of health effects:

- Effects on sexual function and fertility (impaired fertility); and
- Effects on the development of the foetus or offspring (developmental toxicity).

Impacts on fertility include both male and female fertility, with the latter also including what may be referred to as maternal effects including links to endometriosis, still births and miscarriages. With respect to male fertility, this may be directly affected by exposures to reprotoxins or may be indirect resulting in offspring due to maternal exposures.

A wide range of potential developmental effects have been identified, with the most cited being cryptorchidism[70] and hypospadias[71] in male offspring of exposed mothers. Other endpoints include neural tube defects, spina bifida and various skeletal effects. Many of these endpoints are known to be associated with multifactorial risks related to genetic factors, lifestyles, previous illnesses, etc.

Although there is an expanding toxicological literature linking exposures to effects, there are still relatively few published data on the attributable risk (i.e. attributable fraction) linking effects to exposure to chemicals. Many of the studies that do exist are subject to high levels of uncertainty.

4.2 Substances of concern

A wide range of chemicals may give rise to such effects, with exposures taking place at the workplace, through food and food contact materials, and through consumer products containing reprotoxic substances (Amec Foster Wheeler Environment, 2017[72]). A 2019 study for the European Commission found that 194 substances registered under EU REACH were classified as being Reprotoxic Category 1A and 1B (R1A/1B) at that time (RPA et al, 2019)[73] (these would also be classified as R1A/1B under implementation of the GB CLP Regulation, assuming they are being used and will be registered in the UK[74]). A large percentage of these were also classified as Carcinogenic and Mutagenic. Exposures to these must be reduced to a minimum under Control of Substances Hazardous to health (COSHH)[75] legislation, as there is no threshold for carcinogenic effects. As a result, it was assumed that exposures to such substances would be below the threshold for reprotoxic effects. Removing those also classified as Carcinogenic 1A/1B or Mutagenic 1A/1B left 149 substances. These substances may therefore be leading to current and future burdens of fertility and developmental effects.

Historic and current burdens of such effects have been linked to substances such as phthalates; bisphenol A; borates; lead and mercury; tin compounds; trichloroethyelene; some glycol ethers; the aprotic solvents N-Methyl-2-pyrrolidone (NMP), Dimethylformamide (DMF) and Dimethylacetamide (DMAc).

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[70] Where one or both of the testicles do not descend into the scrotum while the foetus is developing
[71] A birth defect in boys in which the opening of the urethra is not located at the tip of the peni
[72] Amec Foster Wheeler et al (2017): Study on the cumulative health and environmental benefits of chemical legislation, Final Report (including Key Messages and Technical Appendix), European Commission.
[73] RPA et al (2019): Study to collect recent information relevant to modernising EU Occupational Safety and Health chemicals legislation with a particular emphasis on reprotoxic chemicals with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC and Directive 98/24/EC, Final Report, Baseline Assessment, for DG Employment.
[74] Retained CLP Regulation (EU) No. 1272/2008 as amended for Great Britain
[75] https://www.hse.gov.uk/coshh/

4.3 Major uses

The 2019 study for DG Employment (RPA et al, 2019) found that reprotoxic substances were used across 36 different industry sectors. Key sectors, i.e. those found to be linked to the broadest range of reprotoxic substances include:

- Manufacture of chemicals and chemical products
- Manufacture of plastic and rubber products
- Manufacture of pesticides and other agrochemical products
- Manufacture of paints, varnishes, coatings, printing inks and mastics
- Manufacture of soaps and detergents, and other cleaning products
- Manufacture of computer, electronic and optimal products, and
- Manufacture of fabricated metal products.

4.4 Current regulatory controls and remaining sources of exposure

The use of the key Reprotoxic 1A/1B substances has now been regulated under EU REACH, with these controls also applying in the UK. Past measures have been introduced to protect both workers and consumers, as well as humans via the environment.

Additional measures will apply under COSHH legislation to help ensure worker protection, with employers having a duty to ensure that measures are put in place to ensure the safe use of chemicals such as Reprotoxic 1A/1B substances. Unlike carcinogens and mutagens, reprotoxins are considered to have a threshold for effects; exposures below these levels should result in no fertility or reprotoxic effects.

Other regulatory controls apply in relation to cosmetics, food safety, toy safety, plant protection products and biocidal products. These are aimed at protection of the users of products placed on the market. However, not all routes of exposure will have been addressed by such legislation leaving the potential for exposures, especially for the larger set of substances not yet subject to such regulation.

4.5 Occupational exposure – fertility and maternal effects

4.5.1 Approach

Different approaches have been taken in past studies to assessment of the human health damage costs arising from occupational exposures to reprotoxins. These include derivation of estimates specific to individual chemicals and detailed exposure data, as well as more top down approaches drawing on broader exposure information.

The estimates presented here are based on the use of population level incidence and prevalence data taken from a French labour force survey. The 2010 SUMER survey[76] covered a broad range of industrial and business sectors (19 sectors) and provides data for worker exposures in terms of duration and intensity of exposures to five key reprotoxins. These data were used in combination to calculate the percentages of male and female workers potentially exposed to the substances at significant levels for extended periods.

The calculated percentages of workers potentially exposed at levels above the thresholds for effects were combined with attributable fractions for the types of health effects linked to exposures to Reprotoxic 1A/1B

[76] Vinck L & Meemi S (2015): Les expositions aux risques professionnels les produits chimiques - Enquête Sumer 2010, available from: https://dares.travail-emploi.gouv.fr/dares-etudes-et-statistiques/etudes-et-syntheses/synthese-stat-synthese-eval/article/les-expositions-aux-risques-professionnels-les-produits-chimiques

substances. Together with figures for the relevant UK worker population, this enables calculation of the potential burden of effects that could be attributed to occupational exposures above the "derived no effects level".

The analysis relies on incidence or prevalence rates in the general population. It estimates the theoretical maximum number of cases by deducting known non-occupational causes and applying the resulting incidence rates to the occupationally exposed population. This approach relies on sufficient data being available for non-occupational causes and, as a result, entails a potential for overestimation (and all of these adjustments lead to uncertainties).

Key aspects of these estimates:

- 1.1% of French workers self-reported that they were exposed to a selected group of Reprotoxic 1A/1B substances (lead, glycol ethers, phthalates NMP, DMF and DMAC);
- The self-reporting data also indicate though that only a small percentage of male and female workers are expected to be exposed for long and enough and to levels high enough to experience reprotoxic effects; and
- Within the SUMER data, however, there are significant numbers of entries which state "not declared" or missing. The reasons for these could range from ignorance to a reluctance to report. This was taken into account by assuming these entries related to exposures significantly above the threshold for effects to produce upper bound estimates.

Exposures to reprotoxins may not only occur in the workplace. As a result, the estimates presented here will not capture the full extent of reproductive effects occurring within the worker population or within their children which may arise from combined exposures. Furthermore, the SUMER survey is based on consideration of only a small number of reprotoxins (with others such as the phthalates removed from this analysis due to the reduced levels of exposure that will have occurred due to regulation). The substances covered by the survey are expected to account for the majority of workplace risks from exposure to reprotoxins. They include: 10 glycol ethers classified as Reprotoxic 1A or 1B (and a cat. 2), phthalates (including a non-Reprotoxic 1A and 1B phthalate), NMP, DMF and DMAC, and lead (including from welding).

A wide range of potential effects have been identified as being relevant to Reprotoxic 1A/1B substances, with these including impacts on male and female infertility, neo- and post-natal effects, as well as a range of congenital anomalies in newborn children. Exposures to reprotoxins are not the only risk factors for such effects, however, with other maternal and environmental factors including smoking, obesity and diabetes also acting as risk factors. As a result, in addition to data from the SUMER survey, information on the incidence and prevalence of different health effects was collated from Eurocat[77] (the European Surveillance of Congenital Anomalies) for 2012 to 2016, Euro-Peristat[78], the Office for National Statistics (ONS – for England), the UK NHS, and various other sources such as the Royal College of Obstetricians and Gynaecologists. Data were also collated from reports prepared by the European Chemicals Agency (ECHA) to support Restrictions of the phthalates in particular.

4.5.2 Results and Key Assumptions

Based on the population exposure data for France, the number of workers in England that may face workplace exposures to reprotoxic substances can be calculated for the most exposed population. The French survey identified 19 sectors of most concern, with this covering just over 20% of the female worker population and around 30% of the male worker population.

[77] https://eu-rd-platform.jrc.ec.europa.eu/eurocat_en
[78] https://www.europeristat.com/

Analysing the SUMER survey results and the self-reported levels of exposure (from very weak to very strong) and the duration of the exposure (<2 hours to >20 hours per week and ignoring the existence of protection measures), a set of worst-case estimates for the population at risk due to exposures to the five reprotoxins covered by the survey can be derived. To account for exposure to other reprotoxins, the estimated at-risk population was doubled based on consideration of the relative derived no effect levels (DNELs) of other identified reprotoxins not covered by the survey and the tonnages at which they were registered under EU REACH[79]. The resulting percentage of the population experience strong (but below the DNEL) or very strong (above the DNEL) exposures and for more than 10 hours per week were:

- Males: between 0.03% and 0.16% as the best-case to worst-case range; and
- Females: Between 0.003% and 0.039% as the best-case to worst-case range.

The higher, worst-case percentages calculated based on data from the SUMER survey are used as the basis for deriving the percentages of female (20.4% or 2.97 million) and male workers (30% or 6.17 million) as potentially exposed to reprotoxins in the workplace in England (2020 working population). Combining these figures with data on birth rates and maternities for the UK, the prevalence/incidence data per 10,000 births or pregnancies and adjustments for other risk factors (smoking, body mass index and diabetes) allows the number of cases of different fertility related outcomes to be derived under the worst-case scenario. These are given in Table 4-1 below.

As can be seen from the table, the total statistical number of cases predicted through this analysis is low at 12.5 across all effects and workers per year. The highest number of cases relates to male infertility. These estimates ignore the potential for exposures outside the workplace to contribute, as part of a combined effect, towards the incidence of reproductive effects within the worker population.

For sensitivity purposes, the same analysis is carried out to provide upper bound estimates for male infertility and potential female outcomes. **It must be noted that this analysis is more speculative for female outcomes, as there is a lack of strong scientific data providing attributable fractions for female reproductive effects and exposures to reprotoxins**. The analysis assumes that the entirety of the male and female worker populations in the key sectors (i.e. 20% of female workers and 30% of male workers) are exposed to reprotoxic substances at levels sufficient to lead to effects. No adjustments are made for the level or duration of exposures. The resulting estimates are also given in Table 4-1, in the bottom half of the table.

The estimated numbers of cases are significantly higher in this second analysis, and as indicated above must be treated with caution as it is likely to be a significant overestimate.

The next step in the assessment is to combine the two sets of predictions with human health damage cost estimates, covering direct health care costs, indirect costs and willingness to pay. Table 4-2 presents the results of this exercise. Even the lower bound estimate of cases results in per annum social damage costs of around £450,000. The more highly uncertain, second set of estimates related to male infertility alone result in per annum social damage costs of over £188 million.

[79] The decision to double the figures was based on the expert judgement of team members for the EC study. See: RPA et al (2019): Study to collect recent information relevant to modernising EU Occupational Safety and Health chemicals legislation with a particular emphasis on reprotoxic chemicals with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC and Directive 98/24/EC, Final Report, Baseline Assessment, for DG Employment.

Table 4-1 Estimated cases of effects for potentially exposed workers

	Prevalence/ Incidence per 10,000	Number of cases due to potential reprotoxin exposures
Estimated cases for number of exposed workers above threshold for effects based on SUMER survey		
Male infertility	189	8.1
Female infertility	283.5	1.4
Endometriosis	270	1.1
Ectopic pregnancy	98.5	0.4
Spontaneous abortion and miscarriages	356.4	1.5
Still births	19.5	0.1
Totals		**12.5**
Estimated cases for potentially exposed workers – unadjusted for level and duration of exposures		
Male infertility	189	**5,160**
Female infertility	283.5	**3,476**
Endometriosis	270	**2,844**
Ectopic pregnancy	98.5	**0.4**
Spontaneous abortion and miscarriages	356.4	**375**
Still births	19.5	**205**
Totals		**12,060**

The per case health care costs and productivity losses are derived from a number of sources, including NHS reference costs data, estimates developed by other researchers (e.g. ECHA, 2017[80]) and the academic literature. The intangible cost figures are based on the OECD value for a statistical life and willingness to pay surveys carried out for ECHA in 2012 (which included a sample of the UK population), and the subsequent critical review and set of recommendations for use in socio-economic analyses under REACH[81].

[80] ECHA 2017: Committee for Risk Assessment and Committee for Socio-economic Analysis Opinion on an Annex XV dossier proposing restrictions on four phthalates, ECHA/RAC/RES-O-0000001412-86-140/F. Also ECHA 2017: Annex to the background document to RAC and SEAC opinions on four phthalates. See: https://echa.europa.eu/documents/10162/e39983ad-1bf6-f402-7992-8a032b5b82aa

[81] See: https://echa.europa.eu/documents/10162/17229/seac_reference_wtp_values_en.pdf/403429a1-b45f-4122-ba34-77b71ee9f7c9 https://echa.europa.eu/documents/10162/17228/echa_review_wtp_en.pdf/dfc3f035-7aa8-4c7b-90ad-4f7d01b6e0bc

Table 4-2 Estimated per annum social damage costs due to worker exposures to reprotoxic substances (2020 prices)

Estimated cases for number of exposed workers above threshold for effects based on SUMER survey

Health endpoint	Statistical cases per annum due to exposures to R1A/1B above threshold	Total direct health care costs per statistical case	Total indirect productivity losses per statistical case	Willingness to pay or intangible costs per statistical case	Total social costs
Male infertility	8.1	£5,008	£2,496	£29,645	£302,650
Female infertility	1.4	£5,008	£2,496	£27,906	£48,033
Endometriosis	1.1	£5,008	£2,496	£29,645	£41,231
Ectopic pregnancy	0.4	£4,076	£11,575	£29,645	£15,948
Spontaneous abortion and miscarriages	1.5	£783	£0	£29,645	£4,458
Still births	0.1	£4,076	£11,575	£29,645	£3,631
			Total annual social costs		**£448,960**

Estimated cases for potentially exposed workers – unadjusted for level and duration of exposures and assumed to take into account additional exposures outside the workplace

Health endpoint	Statistical cases per annum due to exposures to R1A/1B above threshold	Total direct health care costs per statistical case	Total indirect productivity losses per statistical case	Willingness to pay or intangible costs per statistical case	Total all social costs (rounded to nearest 100)
Male infertility	5159.7	£5,008	£2,496	£29,645	£191,678,600
Female infertility	3475.6	£5,008	£2,496	£27,906	£123,072,200
Endometriosis	2843.8	£5,008	£2,496	£29,645	£105,644,000
Ectopic pregnancy	0.4	£4,076	£11,575	£29,645	£165,900
Spontaneous abortions and miscarriages	3753.8	£783	£0	£29,645	£11,422,150
Still births	205.4	£4,076	£11,575	£29,645	£9,303,100
					£441,135,950

4.5.3 Uncertainties and limitations of the approach

The top-down analysis carried out above relies on self-reported data from France. This is difficult to interpret for the UK context and to use as a robust basis for predicting the number of workers exposed to reproductive toxins in the workplace at levels sufficient to cause effects. Furthermore, it covers only a small number of reproductive toxins and takes no account of exposures outside the workplace. In contrast, the second set of estimates, covering only male infertility, is based on attributable fractions specific to chemicals exposure used in other assessments and considered to be more robust. More generally, there is a lack of good data on levels of combined exposures from occupational and non-occupational sources for a range of reproductive toxins.

There is also currently a lack of understanding of the relationship between female reproductive disorders and exposures to reprotoxins. Studies such as that by Hunt et al (2016)[82] link endometriosis and fibroids, for

[82] Hunt, P.A. et al (2016): Female reproductive disorders, diseases, and costs of exposure to endocrine disrupting chemicals in the European Union. *J Clin Endocrinol Metab.* 2016; 101: 1562-1570.

example, to exposures to phthalates but note that the evidence base is weak[83]. Indeed, the study is criticised for its selective adoption of odds-ratios from the underlying literature[84]. Similarly, an analysis of Turkish women exposed to high levels of boron also concludes that there appears to be no increased risks related to the birth weight of newborns and pregnancy outcomes.[85] Other studies have found some relationships to chemical exposures (endocrine disrupting chemicals, most of which would formally be classified as reprotoxic) but note a need for more evidence[86].

In terms of valuation of the social damage costs, some of the figures used here could be updated. For example, 2016/17 NHS costs were used due to a lack of time to collect more up to date figures. Estimates of productivity losses assumed for infertility and maternal effects should also be revisited. Of more significance to the overall costs figures is the choice of willingness to pay values, and whether to include a valuation for the loss of a child as part of the damage costs from a spontaneous abortion or still birth. Inclusion of the OECD value for a life (£3.54 million, 2020 prices) would increase total costs under the first analysis to over £7 million per annum.

4.6 Occupational exposures – developmental effects

4.6.1 Approach

Two different approaches have been adopted in order to derive estimates of the potential burden of reproductive effects arising from chemical exposures outside of the workplace.

- The first approach draws on Eurocat (the European Surveillance of Congenital Anomalies) for 2012 to 2016 to predict the number of cases of developmental effects resulting from maternal exposures to reproductive toxins.
- The second approach draws on approaches used by ECHA (2014, 2017) to support the introduction of restrictions on phthalates, where this relied in part on quantification and valuation of the impacts on offspring of maternal exposures via the environment.

Eurocat[87] provides data on foetal deaths, still births and developmental anomalies as a prevalence per 10,000 births. This includes prevalence rates, excluding known genetic factors. These act as the basis for calculating the potential attributable number of developmental effects that may be attributed to exposures to reprotoxic substances. It must be borne in mind though that many of the endpoints are known to be associated with multifactorial risks related to genetic factors, previous diseases and infections, diet, environmental exposures, etc. For example:

- Pre-term births, still births, early neonatal deaths, etc. are likely to have multifactorial causes, which may or may not include exposure to a Reprotoxic 1A/1B substances;
- Neural tube defects, anencephalus, spina bifida, and hydrocephalus have been linked to exposures to Reprotoxic 1A/1B substances together with diet in some cases (e.g. links between a lack of folic acid and spina bifida and anencephaly);

[83] Other commentators on the paper indicate a lack of statistically significant odds-ratios linking phthalates to endometriosis.
[84] Swaen, G & Otter R (2016): Letter to the Editor: Phthalates and Endometriosis, *J Clin Endocrinol Metab*. 2016; 101:L108-L109.
[85] Duydu, Y et al (2018): Birth weights of newborns and pregnancy outcomes of environmentally boron-exposed females in Turkey. Arch Toxicol. 2018; 92(8): 2475-2485.
[86] Smarr, MM et al (2016): Endocrine disrupting chemicals and endometriosis. Fertil Steril. 2016; 106(4): 959-66.
[87] EUROCAT (n.d.): What is EUROCAT? Available at: http://www.eurocat-network.eu/aboutus/whatiseurocat/whatiseurocat.
See also EUROCAT 2: Surveillance of congenital anomalies in Europe (Phase 2) (europa.eu)

- Similarly, hypospadias are linked to exposures to Reprotoxic 1A/1B substances exposures, in addition to genetic factors and the age of the mother.

Thus, although some adjustments are made in this analysis for maternal smoking, diabetes and BMI>30, accounting for the additional risk factors has not been possible. This would reduce the rates that could be attributed to chemical exposures.

4.6.2 Results and key assumptions

As a first set of estimates, Table 4-3 sets out the statistical number of cases of developmental effects that could arise within the offspring of female workers exposed above the threshold for effects, based on the same assumptions as for the previous analysis. Given the low number of births per annum that would be expected of this population (36 in total, 18 of which would be male offspring), it is not surprising that the maximum number of statistical cases is often below 1, with the exception of "small for gestational age". The associated per annum social costs are estimated at around £1.7 million. The cost figures used for these estimates are presented in Table 4-3 below, with the shading used to link a particular set of costs to specific effects.

Statistical cases and costs: offspring of highest exposed female workers

Table 4-3 Statistical cases of developmental effects in offspring born to female workers exposed above the threshold for effects (£2020 prices, based on Eurocat / Euro-peristat data up to 2016)

Reproductive toxicity effects based on Eurocat hospital birth registration data - EU incidence - and Euro-peristat	Unadjusted incidence per 10,000 excluding genetic factors	No. of cases based on adjusted EU data	Total attributed to smoking, diabetes and BMI>30	Maximum cases attributed to exposure to Repros	Valuation per statistical case	Worst case estimate
Late neoanatal death (day 7-27)	7.3	0.0	0.0	0.0	£3,540,000	83,944
Infant death	39.8	0.1	0.0	0.1	£3,540,000	457,719
Preterm birth (<32 weeks)	10.8	0.0	0.0	0.0	251,756	8,869
Preterm birth (32-36 weeks)	63.5	0.2	0.0	0.2	251,756	51,976
Low birth weight (<1,500g)	10.3	0.0	0.0	0.0	251,756	8,427
Small for gestational age	1000.0	3.6	0.3	3.3	251,756	818,913
Neural tube effects	9.3	0.0	0.0	0.0	686,043	20,798
Anencephalus and similar	3.7	0.0	0.0	0.0	686,043	8,324
Spina bifida	4.6	0.0	0.0	0.0	686,043	10,221
Hydrocephaly	4.4	0.0	0.0	0.0	251,756	3,636
Congenital heart defects	66.0	0.2	0.0	0.2	£397,661	85,398
Severe congenital heart defect	18.5	0.1	0.0	0.1	£397,661	23,930
d-transposition of great arteries	3.2	0.0	0.0	0.0	£397,661	4,165
Venticular septal defects	33.1	0.1	0.0	0.1	£397,661	42,828
Atrial septal defects	13.6	0.0	0.0	0.0	£397,661	17,644
Atrioventicular septal defects	2.0	0.0	0.0	0.0	£397,661	2,626
Tetralogy of Fallot	2.8	0.0	0.0	0.0	£397,661	3,609
Hypoplastic left heart S.	2.4	0.0	0.0	0.0	£397,661	3,092
Patent ductus arteriosus	2.7	0.0	0.0	0.0	£397,661	3,518
Coarctation of aorta	3.5	0.0	0.0	0.0	£397,661	4,463
Cleft palate	4.9	0.0	0.0	0.0	£168,600	2,704
Cleft lip, w/out palate	7.5	0.0	0.0	0.0	£168,600	4,135
Anorectal atresia and stenosis	2.8	0.0	0.0	0.0	£397,661	3,648
Cryptorchidism	76.0	0.1	0.0	0.1	£33,499	4,256
Hypospadias	17.4	0.0	0.0	0.0	£19,707	574
Testicular cancer	0.5	0.0	0.0	0.0	£397,661	332
Clubfoot- Talipes equinovarous	10.3	0.0	0.0	0.0	£168,600	5,638
Limb deficiency (defects)	4.5	0.0	0.0	0.0	£168,600	2,468
Craniosynostosis	2.4	0.0	0.0	0.0	£397,661	3,053
Gastroschisis	2.5	0.0	0.0	0.0	£397,661	3,234
Totals (*note cases are not additive*)				**£ 2020 rounded**		**£1,694,140**

Statistical cases and costs: potentially exposed female workers

Expanding the population to all potentially exposed females (2.97 million workers, as for the assessment of infertility and maternal effects) leads to calculation of a much higher incidence of adverse birth outcomes and developmental effects. These results are presented in Table 4-4. In this case, around 11,500 statistical cases of health effects are predicted, with a social damage costs valuation of over £4.3 billion. The two greatest contributors to this estimate are "infant deaths" and "small for gestational age", which may overlap with some of the other birth outcomes. It is important to note that these are the maximum attributable cases, as the incidence rates relate to all births excluding genetic factors. Only **a fraction of the total only is likely to relate to reprotoxic exposures,** with the same limitations cited above with respect to endometriosis and other maternal outcomes also applying to this analysis.

Table 4-4 Statistical cases of developmental effects to offspring born to female workers potentially exposed (£2020 prices, based on Eurocat / Euro-peristat data up to 2016)

Reproductive toxicity effects based on Eurocat hospital birth registration data - EU incidence - and Euro-peristat	Unadjusted incidence per 10,000 excluding genetic factors	Number of cases based on adjusted EU data	Total attributed to smoking, diabetes and BMI>30	Maximum cases attributed to exposure to Repro-toxins	Valuation per statistical case	Worst case estimate
Late neoanatal death (day 7-27)	7.3	66.8	6.0	60.8	£3,540,000	215,083,115
Infant death	39.8	364.1	32.8	331.3	£3,540,000	1,172,778,304
Preterm birth (<32 weeks)	10.8	99.2	8.9	90.3	251,756	22,723,908
Preterm birth (32-36 weeks)	63.5	581.3	52.3	529.0	251,756	133,175,109
Low birth weight (<1,500g)	10.3	94.2	8.5	85.8	251,756	21,590,860
Small for gestational age	1000.0	9158.7	824.3	8334.4	251,756	2,098,237,105
Neural tube effects	9.3	85.4	7.7	77.7	686,043	53,289,609
Anencephalus and similar	3.7	34.2	3.1	31.1	686,043	21,327,279
Spina bifida	4.6	41.9	3.8	38.2	686,043	26,187,383
Hydrocephaly	4.4	40.7	3.7	37.0	251,756	9,316,173
Congenital heart defects	66.0	604.7	54.4	550.2	£397,661	218,808,593
Severe congenital heart defect	18.5	169.4	15.2	154.2	£397,661	61,314,132
d-transposition of great arteries	3.2	29.5	2.7	26.8	£397,661	10,671,973
Venticular septal defects	33.1	303.2	27.3	276.0	£397,661	109,735,724
Atrial septal defects	13.6	124.9	11.2	113.7	£397,661	45,206,743
Atrioventicular septal defects	2.0	18.6	1.7	16.9	£397,661	6,727,983
Tetralogy of Fallot	2.8	25.6	2.3	23.3	£397,661	9,246,834
Hypoplastic left heart S.	2.4	21.9	2.0	19.9	£397,661	7,921,123
Patent ductus arteriosus	2.7	24.9	2.2	22.7	£397,661	9,014,834
Coarctation of aorta	3.5	31.6	2.8	28.8	£397,661	11,434,257
Cleft palate	4.9	45.2	4.1	41.1	£168,600	6,927,538
Cleft lip, w/out palate	7.5	69.1	6.2	62.8	£168,600	10,595,059
Anorectal atresia and stenosis	2.8	25.8	2.3	23.5	£397,661	9,346,262
Cryptorchidism	76.0	357.7	32.2	325.5	£33,499	10,905,157
Hypospadias	17.4	82.0	7.4	74.7	£19,707	1,471,277
Testicular cancer	0.5	2.4	0.2	2.1	£397,661	851,658
Clubfoot- Talipes equinovarous	10.3	0.0	0.0	0.0	£168,600	2,897
Limb deficiency (defects)	4.5	41.2	3.7	37.5	£168,600	6,323,311
Craniosynostosis	2.4	21.6	1.9	19.7	£397,661	7,821,695
Gastroschisis	2.5	22.9	2.1	20.8	£397,661	8,285,693
Totals (*note cases are not additive*)				11,455.6		**£ 4,326,321,600**

The damage cost valuations used in the above analysis are set out in Table 4-5. These are based on a range of sources for the direct health costs and indirect costs (productivity losses), with weighted average UK NHS health care costs used in preference to estimates for other countries. The intangible costs are based on ECHA's willingness to pay valuations, as referenced above. Where the ECHA valuations do not distinguish

between sets of the same condition, the same valuation has been applied, e.g. for low birthweight and pre-term births.

Table 4-5 Assumed damage cost valuations per statistical case (£ 2020)

	Willingness to pay /Intangible[88] [89] [90]	Direct health care costs and indirect productivity losses[91]	Total social costs
Reduced foetal growth	£249,860	£2,396	£252,260
Spina bifida		£686,040[92]	
Minor birth defect	£22,260	£1,080	£23,340
External birth defect	£167,500	£1,080	£168,600
Internal birth defect	£395,265	£2,400	£397,660
Cryptorchidism	£28,460	£5,040	£33,500
Hypospadias	£8,900	£10,800	£19,584
Premature death	£3,540,000		£3,540,000

4.7 Consumers and Humans via the Environment

4.7.1 ECHA "Restriction" Approaches: Male Fertility, Hypospadias and Cryptorchidism

Other studies have examined the potential impacts of consumer exposures or exposures of humans via the environment to reprotoxic chemicals. In particular, such assessments have been carried out in various EU REACH restriction dossiers to derive estimates of the number of cases of specific health effects that may be attributable to exposures to reprotoxic substances facing regulation. The approach adopted in those restriction proposals is repeated here for the UK for three outcomes: male infertility; hypospadias; and cryptorchidism.

Male infertility

ECHA, 2017[93] notes around 15% of couples (UK as well as EU) do not achieve conception within 1 year of trying and go on to seek medical treatment for infertility. Of these around 50% of cases are associated with male infertility due to abnormal semen quality. Around 54% of these cases may be linked to chemical exposures and other idiopathic[94] factors. The percentage of these linked to chemical exposures alone varies from a low of 25% up to 50%[95].

In 2020, there were 607,469 maternities in England. Assuming that 15% of couples were unsuccessful in conceiving, this implies that 91,120 couples suffered from infertility and failed to conceive. Applying the above percentages to this figure, suggests that between 6,151 and 12,300 of the cases of male infertility

[88] https://echa.europa.eu/documents/10162/17229/seac_reference_wtp_values_en.pdf/403429a1-b45f-4122-ba34-77b71ee9f7c9

[89] ECHA (2017): Annex to the background document to RAC and SEAC opinions on four phthalates, d6e64c7a-8529-bf51-d850-229a8c3abe61.pdf

[90] Based on OECD value of a statistical life, updated to 2020 prices

[91] NHS Reference costs 2016/17

[92] Yi Y et al. (2011): Economic burden of neural tube defects and impact of prevention with folic acid; Eur J Paediatr 2011 Nov; 170(11): 1391-1400.

[93] ECHA 2017: Annex to the background document to RAC and SEAC opinions on four phthalates, available at: d6e64c7a-8529-bf51-d850-229a8c3abe61.pdf

[94] (I.e. of unknown origin)

[95] ECHA 2017: Annex to the background document to RAC and SEAC opinions on four phthalates, available at: d6e64c7a-8529-bf51-d850-229a8c3abe61.pdf

were due to chemical exposures (which compares to the 5,160 cases calculated above for the most exposed population of male workers).

The social damage costs associated with these cases of infertility include medical fertility treatment costs, as well as the intangible costs associated with the failure to conceive for around 40% either due to no live birth following treatment or the couple not seeking treatment. The results are presented in Table 4-6 below. As can be seen from the table below, the associated damage costs are high at between £85 and £192 million per annum.

Table 4-6 Per annum social damage costs to offspring of potentially exposed women

Assumptions	Low	High
Number of infertility cases	91,120	91,120
Attributable number of infertility cases	6,151	12,301
Weighted average cost per case infertility - £2020		
Health care costs (expected value)*	£2,425	£2,425
Intangible costs (expected value)*	£11,562	£11,562
Total expected costs per case	£13,986	£13,986
Total costs	£86,024,000	£195,614,300

Note*: 40% of couples are assumed to go on and experience a live birth, 18% are assumed to be unsuccessful, while 42% do not seek treatment, based on ECHA 2017. It is assumed the same percentages apply in the UK.

Moving on to ***hypospadias,*** the EU Restriction proposal of 2017 concerning the four phthalates adopted a high estimate of the percentage of cases of hypospadias that may be attributable to chemical exposures. Its starting assumption was that there was a 3% incidence in the EU population. This higher rate is based on the view that there is significant under-reporting and a trend towards increased incidence. Both the British Association of Plastic Reconstructive and Aesthetic Surgeons (BAPRAS) and Eurocat report much lower percentages at 0.3% and 0.18% respectively. The rate quoted by BAPRAS may reflect cases more likely to require surgery and hence be associated with health care costs, while the Eurocat rate may only reflect incidence in newborns and not cases that develop later or unreported cases. The analysis presented here develops estimates for the latter two, medically derived rates.

Of these total cases, 85% are then assumed to be non-hereditary (or the full 0.18% in the case of Eurocat to be conservative), with between 100% and 30% of these requiring surgery. Due to uncertainty over the number of cases attributable to chemicals, low, mid and upper bound assumptions are made that range between 2% and 50%. This results in range for the incidence of cases due to chemical exposures of between 0.042% of cases based on BAPRAS' data and a low of 0.001% of cases based on the Eurocat data.

Based on these different incidence rates and taking the population of boys born in the UK in 2019 (329,107, latest estimate), the estimated social damage costs due to hypospadias attributable to chemical exposures range from between £70,000 to £2.7 million per annum. The most likely range is between £0.7 and £2.7 million per year, where this relates to the BAPRAS and Eurocat data on rates per 10,000 male newborns (Table 4-7).

Table 4-7 Per annum social damage costs associated with hypospadias

Assumption	BAPRAS	Eurocat
Number of male births - UK 2019	329,107	329,107
Incidence of attributable Hypospadias to chemical exposures		
Mid	0.017%	0.011%
Low	0.002%	0.001%
High	0.042%	0.027%
Number of cases of Hypospadias		
Mid	55.39	35.54
Low	5.54	3.55
High	138.47	88.86
Weighted average cost per case hypospadias - £2021		
Health care costs	€10,728	€10,728
Intangible costs	€8,857	€8,857
Weighted average cost per case*	€19,584	€19,584
Total expected annual damage costs		
Mid	£1,091,532	£700,448
Low	£109,153	£70,045
High	£2,728,830	£1,751,121
Note*: The willingness to pay costs associated with 75% of cases are assumed to equate to a minor birth defect (£3971) and the other 25% equivalent to an internal birth defect (£23,735) to derive a weighted value across different severities of effect, based on ECHA 2017		

The analysis for ***cryptorchidism in newborn males*** has been carried out in a similar manner, again taking the 2017 Restriction proposal as the starting point. In this case the starting assumption is that the incidence of cryptorchidism in males up to 1 year of age is 2.4% (other sources put the range at between 1% to 2.5% at nine months[96]). Of these, 96% are assumed to be non-hereditary (ECHA, 2017)[97], and again the fraction attributable to chemical exposures is assumed to vary between 2% and 50%, resulting in cumulative fractions ranging from 0.046% to 1.15%.

Based on these different incidence rates, the estimated number of cases of cryptorchidism that might be attributed to chemical exposures is between 152 and 3,791. The social damage costs associated with these cases range between £5 million and £126 million. The mid-point estimates, i.e. social damage costs of around £50.5 million, may provide a more robust estimate, given that the assumed 2.4% incidence of cryptorchidism in males which drives the figure of £127 million is at the upper end of the range found internationally (Table 4-8).

[96] https://www.ncbi.nlm.nih.gov/books/NBK470270/

[97] ECHA 2017: Annex to the background document to RAC and SEAC opinions on four phthalates, available at: d6e64c7a-8529-bf51-d850-229a8c3abe61.pdf

Table 4-8 Per annum social damage costs associated with cryptorchidism

Assumption	Low Estimate	Mid-Point	High estimate
Number of cases of cryptorchidism attributable to chemical exposures			
Male births England	329,107	329,107	329,107
Fraction of cases attributable to reprotoxins	0.046%	0.461%	1.152%
Number of cases attributable to reprotoxins	152	1,517	3,791
Weighted average cost per case hypospadias - £2021			
Health care costs (from ECHA 2017)	£5,041	£5,041	£5,041
Intangible costs	£28,459	£28,459	£28,459
Weighted average cost per case*	**£33,499**	**£33,499**	**£33,499**
Total expected annual damage costs			
Direct costs and indirect costs (95% of cases)	£764,427	£7,644,271	£19,110,676
Intangible costs (expected value)	£4,315,837	£43,158,365	£107,895,913
Total social damage costs	£5,080,264	£50,802,636	£127,006,590
Notes*: The intangible costs associated with 95% of cases are assumed to equate to external birth defects (£23,587) and the other 5% equivalent to an internal birth defect (£117,482)			

4.7.2 Uncertainties and limitations of the approaches

There are numerous uncertainties involved in the first approach based on Eurocat data. Firstly, the endpoints selected for the assessment carried out for DG Employment were determined by a toxicologist working together with a medical researcher. The selection was based on expert judgement rather than academic research providing odds-ratios or attributable fractions. In addition, care is required in interpreting these estimate of developmental effects linked to occupational exposures, as there will be some overlap in the various health effects for which data are presented individually within the Eurocat database.

Importantly, the associations between reprotoxins 1A/1B and effects made in this analysis were developed for a previous study for the European Commission (RPA et al 2019) and are based in part on the expert judgement of a toxicologist and a medical researcher. There is a lack of strong academic evidence for the fraction of cases stemming from maternal exposures to most reprotoxins. Extreme care is therefore warranted in the use of the estimates set out in Table 4-4, as they are likely to reflect over-estimates.

The second set of estimates draws on a range of incidence data and related statistics to estimate the fraction of fertility, hypospadias and cryptorchidism cases attributable to chemical exposures. The assumptions providing the starting point for these estimates stem from assessments developed to consider the merits of restrictions on phthalates in consumer articles across the EU. The phthalates alone were assumed to contribute to around 4% of the fraction attributable to chemical exposures. Given that action has now been taken which bans the presence of the phthalates in products placed on the market, maternal exposures to the phthalates (and other key substances) should also be reducing the extent to which this set of chemicals contributes to the burden of these health effects. This is important as all of the latter estimates are based on fractions attributable to exposure to chemicals ranging from 2% to 50%, highlighting a key uncertainty in the underlying science.

More generally, other assumptions such as the health care costs and UK incidence of disease rates could be updated, while the “intangibles” estimates are only broadly related to hypospadias and cryptorchidism.

4.8 Summary

Table 4-9 below summarises the results of the analysis carried out specific to the worker population, while Table 4-10 summarises the results carried out for the general population. The lower bound estimates for the worker population are based on those workers most likely to be exposed at levels above a threshold for

effects; note that due to uncertainties over base data, only lower bound estimates are provided for female infertility and other maternal effects. The upper bound adopts the total worker populations in the 19 sectors identified as having workers most likely to be exposed to one or more reprotoxins, in addition to having exposures outside the workplace. The robustness of this latter set of estimates is highly questionable, while the lower bound estimates take no account of exposures outside the workplace.

As noted above, the female infertility and maternal effects upper bound estimate, as well as the developmental effects upper bound estimate is highly uncertain and lack scientific credibility given that there is inadequate scientific data on the fraction of cases for the different endpoints specific to exposures to reprotoxins. The figures are therefore not included in Table 4-9 although it is worthwhile pointing out that the estimates derived for hypospadias and cryptorchidism as part of this analysis fall towards the lower end of the estimates derived based on all male births (£1.7 and £5.1 million respectively).

It is also of note that the estimate for male infertility related to the worker population in the 19 key sectors is around the same magnitude as the estimate for all male fertility assumed to due to chemical exposures.

Table 4-9 Summary of per annum social damage costs associated with potentially exposed workers (£ 2020)

	Low estimate	High estimate
Male infertility	£302,650	£191,679,000
Female infertility and maternal effects	£113,300	£249,457,000*
Developmental effects (via maternal exposures)	£1,694,100	£4,326,322,000*
Notes*: The female infertility and maternal effects, as well as higher bound estimate of developmental effects are not considered robust and should be treated with caution		

Table 4-10 Summary of per annum social damage costs associated with all exposures to reprotoxic chemicals (£ 2020 rounded)

Humans via the environment	Low Estimate	Mid-Point	High estimate
Male fertility – based on couples in England unable to conceive			
Total social damage costs	£86,024,000		£195,614,300
Hypospadias – based on number of male births per annum			
Total social damage costs	€1,751,100		€2,728,800
Cryptorchidism - based on number of male births per annum			
Total social damage costs	£5,080,300	£50,802,600	£127,006,600
Notes*: The intangible costs associated with 95% of cases are assumed to equate to external birth defects (£23,587) and the other 5% equivalent to an internal birth defect (£117,482)			

4.9 Future research priorities

The analysis carried out above suggests that the social damage costs arising from exposures to reprotoxic substances may be very large and are likely to be in the range of many tens of millions of pounds. However, there are numerous evidence gaps related to the availability of the scientific data needed to adjust incidence and prevalence data at the general population level to reflect only chemical exposures. In particular, many of the past studies focused on particular groups of substances, such as phthalates, which are already highly regulated (as are other reprotoxins acting as the focus for research). The extent to which the percentages of cases assumed in the past could still be attributed to current exposures is highly uncertain, with the potential for over estimation.

Addressing both of these gaps should act as the basis for future research priorities. Suggestions are as follows:

- A review of grandfathered substances and EU consumer product information (including publicly available information from the Nordic product registers) is carried out to identify the reprotoxic substances with the greatest level of use in the UK, where this includes both in the workplace and in consumer products (leading to combined exposures). This would also separate out substances leading to past exposures from those associated with on-going exposures.
- A systematic review is undertaken to identify potential effects, both related to fertility / maternal effects and developmental effects, for which there is the most scientific evidence.
- A meta-analysis is carried out (either as part of or as a follow-up to the systematic review) to combine data from separate studies with the aim of developing statistically robust population attributable fractions.

5 Endocrine-disrupting chemicals

Endocrine-disrupting chemicals (EDCs) are substances which can mimic or interfere with the body's endocrine system. Associated effects include Neurodevelopmental effects, Reproductive effects, and brain and immune deficiencies.[98] This chapter also provides an overview of the potential impacts on wildlife, of which there is much less evidence. A series of inter-related papers have been published since 2015 which have estimated the human health effects related to exposure to EDCs in various jurisdictions. Monetary valuations of these were also derived. These estimates are all based on an original methodology outlined in Trasande et al. (2015)[99]. This chapter will explain the methodology used in that research, the underlying assumptions associated with it, the strengths and weaknesses of both the methodological approach and the underlying evidence. It will review and discuss criticisms of the methodology and recommend how such calculations may be improved over time. This section also presents the results of UK cost estimates for 15 outcome-exposure relationships presented in the Trasande et al. (2016)[100] study. The costs are updated to 2020 prices, but not otherwise changed from that presented in the original paper.

5.1 Effects

5.1.1 Human health effects

Exposure to EDCs can create a range of human health effects due to their interference with hormone action. EDCs are known to have a range of effects including impacts on male and female reproduction, breast development and cancer, prostate cancer, neuroendocrinology, thyroid, metabolism and obesity, and cardiovascular endocrinology. Endocrine disruption in humans occurs through a variety of mechanisms including nuclear receptors, non-nuclear steroid hormone receptors, non-steroid receptors, enzymatic pathways involved in steroid biosynthesis and/or metabolism and through various other mechanisms.[101]

A series of papers published by Trasande et al. identify 15 possible exposure-outcome associations between various EDCs and human health. The effects considered are: IQ loss and intellectual disability, attention deficit disorder (ADHD), autism spectrum disorder (ASD), childhood and adult obesity, adult diabetes, cryptorchidism (undescended testicles), testicular cancer, low testosterone, male infertility, endometriosis (often painful growth of endometrium cells outside of the uterus) and fibroids (non-cancerous growths in or around the uterus).[102]

Table 5-1 outlines the human health effects associated with exposure to EDCs which are considered in the Trasande et al. (2016) analysis, the endocrine-disrupting mechanism causing the effect, the associated substances and the estimates of costs.

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[98] National Institute of Environmental Health Sciences. (n.d.) Endocrine Disruptors. https://www.niehs.nih.gov/health/topics/agents/endocrine/index.cfm

[99] Trasande, L., Zoeller, R. T., Hass, U., Kortenkamp, A., Grandjean, P., Peterson, M., DiGangi, J., Bellanger, M., Hauser, R., Legler, J., Skakkebaek, N., and Heindel, J.J. (2015). Estimating burden and disease costs of exposure to endocrine-disrupting chemicals in the European Union. doi: 10.1210/jc.2014-4324

[100] Trasande L, Zoeller RT, Hass U, Kortenkamp A, Grandjean P, Myers JP, DiGangi J, Hunt PM, Rudel R, Sathyanarayana S, Bellanger M, Hauser R, Legler J, Skakkebaek NE, Heindel JJ. Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. Andrology. 2016 Jul;4(4):565-72. doi: 10.1111/andr.12178. Epub 2016 Mar 22. PMID: 27003928; PMCID: PMC5244983.

[101] Diamanti-Kandarakis, E., Bourguignon, J. P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M., Zoeller, R. T., & Gore, A. C. (2009). Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocrine reviews*, *30*(4), 293–342. https://doi.org/10.1210/er.2009-0002

[102] Kahn, L. G., Philippat, C., Nakayama, S. F., Slama, R., & Trasande, L. (2020). Endocrine-disrupting chemicals: implications for human health. *The Lancet. Diabetes & endocrinology*, *8*(8), 703–718. https://doi.org/10.1016/S2213-8587(20)30129-7

5.1.2 Environmental effects

EDCs have also been shown to have adverse effects on wildlife, including disrupted reproductive function and development in birds, fish, amphibians and molluscs. The most widely noted example were declines in populations of birds of prey in the 1950s driven by widespread use of the organochlorine insecticide DDT which resulted in eggshell thinning and consequent reproductive failure[103]. DDT has since been banned in the UK. More recently, whilst in specific cases (e.g. endocrine disruption in fish), the evidence is strong, often the causal associations between EDCs and endocrine disruption in wildlife is unclear[104]. In most cases there is limited understanding of how endocrine disruption affects individual animals and how individual effects impact wider populations. Further research is needed to determine the extent of the risk posed.

There is very little evidence of endocrine disruption from chemicals in mammals. The focus of the literature has been on the effects in predators, with risk via biomagnification assessed[105]. There are however several studies on the impact and prevalence of endocrine disruption in wild freshwater and marine fish. The majority of observed endocrine disruption identified is associated with contamination via effluent from sewage treatment works (STW) containing steroidal oestrogen[106].

The Environment Agency assessed the feminization of male fish in English rivers and concluded that there is sufficient evidence for endocrine disruption in UK freshwater fish, although the extent of population level effects was not clear. This study uses UK and European epidemiological data to demonstrate the occurrence of intersex fish and its association with effluent discharges[107]. Jobling et al. (2006)[108] identify a significant correlation with predicted concentrations of both natural and synthetic oestrogens, suggesting that steroidal oestrogens play a major role in endocrine-disruption in freshwater fish in the UK. Nonylphenol has also been evidenced to play a role[109]. A Canadian study focussed on a lake known to be contaminated with EE2, saw evidence of a reduction in the numbers of young fish which could affect the sustainability of the population. However, this concentration was significantly higher than concentrations found in rivers receiving effluent from wastewater treatment[110].

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[103] Newton I. (2013). Organochloride pesticides and birds. Br. Birds 106, 189– 205.

[104] Jobling, S., Tyler, C. R. (2006). Introduction: The Ecological Relevance of Chemically Induced Endocrine Disruption in Wildlife. *Environmental Health Perspectives.* 114(1). https://doi.org/10.1289/ehp.8046

[105] Pelch, Katherine & Niebrugee, Bridget & Beeman, Joseph & Winkeler, Stacey & Nagel, Susan. (2010). Endocrine Disruption in Mammals.

[106] The Weybridge+15 (1996-2011) report. The impacts of endocrine disruptors on wildlife, people and their environments. https://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

[107] Gross-Sorokin, M. Y., Roast, S. D., & Brighty, G. C. (2006). Assessment of feminization of male fish in English rivers by the Environment Agency of England and Wales. *Environmental health perspectives*, *114 Suppl 1*(Suppl 1), 147–151. https://doi.org/10.1289/ehp.8068

[108] Jobling S, Williams R, Johnson A, Taylor A, Gross-Sorokin M, Nolan M, Tyler CR, van Aerle R, Santos E, Brighty G. Predicted exposures to steroid estrogens in U.K. rivers correlate with widespread sexual disruption in wild fish populations. Environ Health Perspect. 2006 Apr;114 Suppl 1(Suppl 1):32-9. doi: 10.1289/ehp.8050. PMID: 16818244; PMCID: PMC1874167.

[109] Sheahan, D. A., Brighty, G. C., Daniel, M., Kirby, S., Hurst, M. R., Kennedy, J., Morris, S., Routledge, E. J., Sumpter, J. P. and Waldock, M. J., 2002, 'Estrogenic activity measured in a sewage treatment works treating industrial inputs containing high concentrations of alkylphenolic compounds — a case study', Environmental Toxicology and Chemistry, (21) 507–514.

[110] Jobling S, Williams R, Johnson A, Taylor A, Gross-Sorokin M, Nolan M, Tyler CR, van Aerle R, Santos E, Brighty G. Predicted exposures to steroid estrogens in U.K. rivers correlate with widespread sexual disruption in wild fish populations. Environ Health Perspect. 2006 Apr;114 Suppl 1(Suppl 1):32-9. doi: 10.1289/ehp.8050. PMID: 16818244; PMCID: PMC1874167.

Table 5-1 Identified effects, associated substances and costs

Health impact category	Human health effect	Endocrine disrupting mechanism	Associated substances	Costs
Neurodevelopmental effects	IQ loss and intellectual disability, ADHD and ASD	Endocrine disruption can have adverse consequences on a developing brain through mechanisms including thyroid hormone or sex steroid actions or through other hormonal pathways.[111]	Polychlorinated biphenyls (PCBs), Polybrominated diphenyl ethers (PBDEs) and organophosphate pesticides interfere with thyroid hormone action, evidenced through human and laboratory studies. Substances including lead, methylmercury, arsenic, and pesticides have been linked to ASD and ADHD.[111]	Neurodevelopmental disabilities have been associated with IQ productivity losses and other associated health and societal costs. Trasande et al. follows the approach of previous authors[112,113,114] to estimate the cost of an IQ point lost as $19,269 (2010) in discounted lifetime costs. Other costs are estimated for intellectual disability, autism and ADHD. This is discussed further below
Obesity and metabolism effects	Childhood and adult obesity and adult diabetes	Toxicological studies have shown various endocrine-disrupting mechanisms by which EDCs contribute to obesity and diabetes. For example, phthalates affecting peroxisome proliferator-activated receptors[115] and BPA as a synthetic oestrogen.[116]	Epidemiological and toxicological evidence suggest that substances including tributyltin, organophosphate pesticides, fungicides, phthalates, environmental phenols, heavy metals. Persistent organic pollutants are associated with obesity and diabetes.	Obesity and diabetes present significant healthcare costs to society and can result in various related conditions and subsequent reductions in life expectancy. Costs considered include medical expenditures in children and adults and DALYs associated with obesity in adulthood.
Male reproductive health effects	Male reproductive health effects associated with exposure to EDCs	EDCs impact semen quality through various mechanisms, with substances affecting different parts of the endocrine system.[117]	EDCs associated with male reproductive disorders include phthalates, including dibutyl phthalate (DBP) and Di(2-Ethylhexyl) phthalate (DEHP);	There are significant individual and societal costs associated with male reproductive health problems, with costs including medical and fertility treatment. Trasande et al. used a report

[111] Bellanger et al. (2015) Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. doi: 10.1210/jc.2014-4323

[112] Attina TM, Trasande L 2013 Economic costs of childhood lead exposure in low and middle-income countries. Environ Health Perspect 121:1097-1102

[113] Trasande L, Liu Y 2011 Reducing The Staggering Costs Of Environmental Disease In Children, Estimated At $76.6 Billion In 2008. Health Affairs 30:863-870

[114] Bellanger et al. 2013 Economic benefits of methylmercury exposure control in Europe: monetary value of neurotoxicity prevention Environmental Health 12

[115] Desvergne B, Feige JN, Casals-Casas C. PPAR-mediated activity of phthalates: a link to the obesity epidemic? Mol Cell Endocrinol. 2009;304:43– 48.

[116] Alonso-Magdalena P, Morimoto S, Ripoll C, et al. The estrogenic effect of bisphenol A disrupts pancreatic -cell function in vivo and induces insulin resistance.Environ Health Perspect. 2006;114:106 – 112

[117] Rehman, S., Usman, Z., Rehman, S., AlDraihem, M., Rehman, N., Rehman, I., & Ahmad, G. (2018). Endocrine disrupting chemicals and impact on male reproductive health. *Translational andrology and urology*, *7*(3), 490–503. https://doi.org/10.21037/tau.2018.05.17

	include hypospadias, cryptorchidism, testicular cancer, prostate cancer, low testosterone and poor semen quality.		pesticides, including procymidone, vinclozolin, linuron, and prochloraz; bisphenol A (BPA); the dichlorodiphenyltrichloroethane metabolite p,p'-Dichlorodiphenyldichloroethane; and UV filters, such as octyl methoxycinnamate and 4-methylbenzylidene camphor.[118]	from the Nordic Council of Ministers to estimate the costs of cryptorchidism and testicular cancer.[119] Direct and indirect costs associated with assisted reproductive technology were estimated at €6,607 per couple from a study in Denmark.[120] The costs for mortality due to reductions in testosterone in lifetime economic productivity loss were obtained from a US source and updated to 2010 euros.[121]
Female reproductive health effects	Female reproductive health effects associated with exposure to EDCs include polycystic ovarian syndrome, endometriosis, uterine fibroids, and cancers at reproductive sites.	Whilst there is a growing body of evidence linking EDCs to female reproductive health problems, characterizing these effects presents a significant challenge, largely as a result of the inability to observe early reproductive endpoints in females without invasive procedures.	There is evidence for associations between various EDCs and impacts on the developing ovary and reproductive tract including BPA, phthalates, pesticides, and persistent organic pollutants (POPs).	Significant costs are associated with female infertility and range of other conditions, including healthcare costs, work disturbances and lost productivity.[122] Trasande et al. carried out cost estimation from a societal perspective including treatment costs and indirect costs such as productivity loss.

[118] Hauser, R., Skakkebaek, N., Hass, U., Toppari, J., Juul, A., Andersson, A. M., Kortenkamp, A., Heindel, J. J., and Trasande, L. (2015). Male Reproductive Disorders, Diseases, and Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. doi: 10.1210/jc.2014-4325

[119] Nordic Council of Ministers (lead author: Olsson IM) 2014 The Cost of Inaction : A Socioeconomic analysis of costs linked to effects of endocrine disrupting substances on male reproductive health. Available at http://norden.divaportal.org/smash/record.jsf?pid=diva2%3A763442&dswid=1666 (Accessed 24 November 2014).

[120] Christiansen T, Erb K, Rizvanovic A, Ziebe S, Mikkelsen Englund AL, Hald F, Boivin J, Schmidt L 2014 Costs of medically assisted reproduction treatment at specialized fertility clinics in the Danish public health care system: results from a 5- year follow-up cohort study. Acta Obstet Gynecol Scand 93:64-72

[121] Max W 2013 Present Value of Lifetime Earnings, 2009. Unpublished tables, Institute for Health and Aging, University of California, San Francisco.

[122] Hunt, P. A., Sathyanarayana, S., Fowler, P. A., and Trasande, L. (2016). Female Reproductive Disorders, Diseases, and Costs of Exposure to Endocrine Disrupting Chemicals in the European Union. doi: 10.1210/jc.2015-2873

There are significant gaps in the evidence on exposure to EDCs and its impact on wildlife. Whilst there is some evidence for the impact on fish populations and specific instances of impacts to other wildlife populations, in general the evidence is limited. Where laboratory evidence exists, in the majority of cases there is insufficient evidence linking this to wildlife populations in the field. Greater evidence is required to get a better picture of the impact of EDCs on wildlife populations, with more field studies and monitoring required[123].

5.2 Major uses

EDCs and potential EDCs can be found in a wide variety of products which result in human and environmental exposure, via diet, air, skin and water[124]. Products include plastic bottles, metal food cans, detergents, flame retardants, food, toys, cosmetics and pesticides[125].

5.3 Current regulatory controls and remaining sources of exposure

There are currently around 1,000 substances with suspected endocrine-acting properties[126]. EDCs are now regulated under UK REACH which categorises around 15 substances as endocrine disruptors. EU activities include[127]:

- Scientific criteria for the determination of endocrine-disrupting properties were set in 2017 and 2018 under the Plant Protection Products Regulation and the Biocidal Products Regulation. A common ECHA/EFSA guidance document has been established for the identification of endocrine disruptors for these Regulations.
- REACH, medical devices related legislation and water-related legislation all contain provisions on how to address endocrine disruptors.
- Substances of endocrine disrupting properties are considered on a case-by-case basis under the food contact materials legislation, the Cosmetic Products Regulation, the Toy Safety Directive and the occupational safety and health (OSH) legislation as they do not contain specific provisions for endocrine disruptors.

Effects of exposure persist due to lipophilic properties (which impact drug uptake and metabolism), as well as bioaccumulation in body fat, resulting in a long half-life in the body.[126] Prenatal exposure and exposure to young children can have life-long impacts on the child as well as effects that exhibit in adulthood.

5.4 Cost estimate of ongoing damage

5.4.1 Methodologies adopted in literature

[123] The Weybridge+15 (1996-2011) report. The impacts of endocrine disruptors on wildlife, people and their environments. https://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters

[124] National Insitute of Environmental Health Sciences. Endocrine Disruptors. https://www.niehs.nih.gov/health/topics/agents/endocrine/index.cfm

[125] Yang, O., Kim, H. L., Weon, J. I., & Seo, Y. R. (2015). Endocrine-disrupting Chemicals: Review of Toxicological Mechanisms Using Molecular Pathway Analysis. *Journal of cancer prevention*, *20*(1), 12–24. https://doi.org/10.15430/JCP.2015.20.1.12

[126] Yilmaz, B., Terekeci, H., Sandal, S. *et al.* Endocrine disrupting chemicals: exposure, effects on human health, mechanism of action, models for testing and strategies for prevention. *Rev Endocr Metab Disord* **21,** 127–147 (2020). https://doi.org/10.1007/s11154-019-09521-z

[127] European Commission. (2019). FITNESS CHECK of the most relevant chemicals legislation (excluding REACH), as well as related aspects of legislation applied to downstream industries. swd_2019_0199_en.pdf (europa.eu)

Trasande et al. published a series of inter-related papers since 2015, which have estimated the socio-economic costs of exposure to EDCs for the EU. Originally, four related papers were published in the *Journal of Clinical Endocrinology and Metabolism* (Trasande et al. 2015[128], Bellanger et al. 2015[129], Hauser et al. 2015[130], Legler et al. 2015[131]). These were followed by a fifth paper (Hunt et al. 2016)[132] addressing estimated costs of female reproductive disorders and diseases attributable to EDC exposure. Trasande et al. (2016) then presented an update to the original cost estimates, including estimates for individual EU countries (including the UK as a Member State at that time). The methodology used across all of these papers is outlined in Bellanger et al (2015) and evaluated below.

General approach

The general approach was to apply a "fractional contribution" of the environment to causation of illness as developed by the Institute of Medicine in the United States. This estimates the attributable disease burden and attributable costs as:

$$Attributable\ disease\ burden = Disease\ rate\ \times Attributable\ fraction\ (AF) \times Population\ size$$

$$Attributable\ costs = Disease\ rate\ \times AF \times Population\ size \times Cost\ per\ case$$

Where "cost per case" includes the direct costs of health care, rehabilitation costs, lost productivity, and is discounted over a lifetime. The attributable fraction is the product of the prevalence of a risk factor and the associated relative risk of disease:

$$AF = Prevalence_{exposure} * \left(\frac{RR - 1}{\left[1 + \left(Prevalence_{exposure} * (RR - 1)\right)\right]} \right)$$

Probability of causation

The methodology was developed by a steering committee. The Grading of Recommendations Assessment, Development and Evaluation (GRADE)[133] Working Group criteria was applied to evaluate the strength of the epidemiological evidence from very low to high based on factors such as potential bias, limitations, strength of dose-response relationships, residual confounding, and consistency. The criteria to evaluate the strength of toxicological evidence was adapted from the Danish Environmental Protection Agency which categorizes the strength of evidence as weak (*potential endocrine disruptor*), moderate (*suspected endocrine disruptor*) or strong (*endocrine disruptor*). The steering committee adopted the Intergovernmental Panel on Climate Change (IPCC) approach to assessing probability of causation, which combines the strength assessments of the epidemiological and toxicological evidence to evaluate the probability of causation. This assessment,

[128] Trasande L, Zoeller RT, Hass U, Kortenkamp A, Grandjean P, Myers JP, DiGangi J, Bellanger M, Hauser R, Legler J, Skakkebaek NE, Heindel JJ. Estimating burden and disease costs of exposure to endocrine-disrupting chemicals in the European union. J Clin Endocrinol Metab. 2015 Apr;100(4):1245-55. doi: 10.1210/jc.2014-4324. Epub 2015 Mar 5. PMID: 25742516; PMCID: PMC4399291.

[129] Bellanger, M., Barbara, D., Grandjean, P., Thomas Zoeller, R., Trasande, L. (2015). Neurobehavioural Deficits, Diseases, and Associated Costs of Exposure o Endocrine-Disrupting Chemicals in the European Union. https://doi.org/10.1210/jc.2014-4323

[130] Hauser R et al (2015) Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union. J Clin Endocrinol Metab 100(4):1267–1277. doi:10.1210/jc.2014-4325

[131] Legler J et al (2015) Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. J Clin Endocrinol Metab 100(4):1278–1288. doi:10.1210/jc.2014-4326

[132] Patricia A. Hunt, Sheela Sathyanarayana, Paul A. Fowler, Leonardo Trasande, Female Reproductive Disorders, Diseases, and Costs of Exposure to Endocrine Disrupting Chemicals in the European Union, *The Journal of Clinical Endocrinology & Metabolism*, Volume 101, Issue 4, 1 April 2016, Pages 1562–1570, https://doi.org/10.1210/jc.2015-2873

[133] https://www.gradeworkinggroup.org/

which draws on the judgement of the steering committee, has drawn some criticism outlined in Bond and Dietrich (2017) and discussed below.[134]

Quantifying attributable burden

The preferred approach of the steering committee was to use dose-response relationships from the epidemiological literature to assess the attributable burden of disease. In the absence of sufficient epidemiological evidence, toxicological data was judged suitable to provide the basis of the assessment, supported by trends in incidence above a baseline which the authors stated could suggest a causal mechanism by EDCs and data from genetic studies was then used to quantify the remaining environmental contribution.

Approach to evaluating evidence

A human capital approach was used to measure the value of resources foregone and lost output due to illness. The estimates were developed by five panels of four to eight experts, which focused on: (1) neurobehavioral deficits and diseases; (2) male reproductive disorders and diseases; (3) obesity and diabetes; (4) breast cancer; and (5) female reproductive disorders and diseases. Each panel used human epidemiology and animal toxicology to assess the probability of causation between EDCs and selected medical conditions, using a modified Delphi technique to arrive at a consensus. The Delphi technique is employed due to a preference of group judgements over those of individuals. This technique typically involves experts working anonymously and rounds of reviews to arrive at a consensus[135]. Precisely how the Delphi technique was used in this study is not clear. Monte Carlo simulations were used to produce ranges of probable costs across the exposure-outcome relationships.

Kahn et al. (2020)[136] provides an update of these exposure-outcome relationships, identifying newly available epidemiological and toxicological evidence published since the previous estimates published in Trasande et al. (2016). However, no specific updates are made to the strength of evidence or probability of causation estimates. The final column in Table 5-2 gives a brief overview of any updates to the literature since the original estimates in 2015.

Approach to economic estimation

The human capital approach estimated the value of resources foregone and output lost due to illness. Costs were split into “direct costs” which included direct costs of hospitalization expenditures, physician services, nursing home care, medical appliances and related costs, and “indirect costs” of the value of lost output of workers and of retirees suffering premature death or disability.

European data sources were used wherever possible to estimate the cost-of-illness inputs and incremental costs of a condition were favored over average cost estimates which tend to overestimate. If European data was unavailable, United States (US) estimates were used with a correction factor which represented the ratio of the per capita gross domestic product (GDP) purchasing power parity of the European country compared to the US. Ranges of probable costs were produced using a series of Monte Carlo simulations across all exposure-outcome relationships. Three sets of 1,000 simulations were performed given that the probability of causation can have a significant impact on cost estimates. For each set of simulations, ranges of burden and disease costs associated with EDCs were produced.

[134] Bond, G., and Dietrich, D. (2017). Human cost burden of exposure to endocrine disrupting chemicals. A critical review. DOI: 10.1007/s00204-017-1985-y

[135] University of Phoenix. (n.d.) Delphi Method. https://research.phoenix.edu/content/research-methodology-group/delphi-method

[136] Kahn, L., Philippat, C., Nakayama, S., Slama, R., Trasande, L. (2020). Endocrine-disrupting chemicals : implications for human health. https://doi.org/10.1016/S2213-8587(20)30129-7

Criticisms of the methodology

Whilst uncertainties in the approach were explicitly discussed, it should be noted that there has been criticism of the Trasande et al. (2015) methodology and conclusions. The series of papers based on this methodology suggest a significant disease burden from EDCs to the EU/Member States and the US in the order of billions of euros annually. Bond and Dietrich (2017) present a bluntly written, critical review of the methodology used, stating that the cost estimated were "highly speculative". The main criticisms made in this review are outlined below.

Panel selection

The steering committee and the selection of experts for the five panels has been criticized due to the alleged potential for bias. In Bond and Dietrich (2017) it is suggested that those selected "tended to favour ascribing causality from exposure to alleged EDCs and adverse health outcomes". A comparison was made with regulatory agencies in the US and EU which employ a rigorous process when they form advisory panels to ensure a balance of perspectives on an issue[137,138]. Such a process, they claim, was not employed for the selection of this committee.

Exposure-response relationships

The panels were selected to assess the probability of causation between suspected EDCs and disease outcomes through evaluating the animal toxicology and human epidemiology evidence and applying a modified Delphi technique to arrive a consensus. The fraction of disease attributable to EDC exposure and exposure-response relationships were estimated, but the authors question to extent of evidence for some of the associations, stating they were "often" based on a single epidemiology study.

Selection and evaluation of literature

The selection of studies used was also criticized, with the authors claiming this also presented a bias towards studies which support an association between exposure to EDCs and various health outcomes. The explanation of the methods employed to select the literature was similarly criticised.

Bond and Dietrich (2017) also criticize the criteria used by the Steering Committee for evaluating laboratory and animal evidence of endocrine disruption, originally proposed by the Danish Environmental Protection Agency (Danish-EPA)[139]. The GRADE Working Group criteria was adapted to evaluate human epidemiology evidence, termed "Grading of Evidence for Public Health Interventions" (GELPHI). The original GRADE methodology weighs evidence from randomized controlled trials (RCTs) more heavily and typically treats observational epidemiology evidence as of low or very low quality. If adopted, this approach is claimed to have decreased the overall probability of causation, with most estimates being placed in the lowest tiers. Furthermore, the GELPHI approach was developed to be applied to scientific evidence on indoor air pollutants which they contend is more extensive than the much smaller scientific evidence base available for EDCs. The biomonitoring data used to generate cost estimates is also very limited and single studies claimed to be "not representative of general populations" were used.

Modified Delphi technique and probability of causation

[137] EPA (2016). About the Federal Advisory Committee Act (FACA) at EPA. https://www.epa.gov/faca/about-federal-advisory-committee-act-faca-epa

[138] EU Publications Office (2017). EU Scientific committees on consumer safety (SCCS) & on health, environmental and emerging risks (SCHEER). https://op.europa.eu/en/publication-detail/-/publication/74eff770-ee72-4328-94d8-e40b2d7020cd

[139] Danish EPA (2011) Establishment of criteria for endocrine disruptors and options for regulation. http://eng.mst.dk/media/mst/Attachments/DKEDcriteria110517_finalcorr1.pdf.

Bond and Dietrich (2017) present further criticisms of the framework for evaluating probability of causation and the use of the modified Delphi technique to reach a consensus. They claim the framework for evaluating probability of causation was lacking appropriate evidence and were assigned with "sparse, weak and conflicting evidence". They state that IPCC guidance suggests a probability of causation between 33%-66% should not result in any cost estimates as this would suggest that the probability of causation is "about as likely as not". But estimates of the attributable fraction and societal costs were produced even with probability of causation estimates as low as 0-19%.

The information in Trasande et al papers indicate the process was conducted by five panels focusing on different effects, consisting of 4-8 experts each. Hsu and Sandford (2007)[140] suggest a minimum of 10 panelists are required for an "effective" Delphi technique.

5.5 Outcome-exposure evidence

Table 5-2 below summarizes the outcome-exposure exposure relationships considered in Trasande et al. (2016), the literature used to assess the probability of causation and the causation assigned. The associated costs are summarized in the results section of this chapter. It also gives a brief overview of any updates in the literature since the original estimates in 2015, as outlined in Kahn et al. (2020).

[140] Hsu, Chia-Chien and Sandford, Brian A. (2007) "The Delphi Technique: Making Sense of Consensus," Practical Assessment, Research, and Evaluation: Vol. 12 , Article 10. DOI: https://doi.org/10.7275/pdz9-th90 Available at: https://scholarworks.umass.edu/pare/vol12/iss1/1

Table 5-2 Outcome-exposure evidence behind Trasande et al. (2016)[141] results

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
Neurobehavioral deficits[143]	IQ Loss and Intellectual Disability	PBDE	Four longitudinal observational studies referenced, with three showing a consistent negative association.[144] The fourth did not measure IQ but showed substantial directionality toward cognitive and motor dysfunction at age 4.[145]	Moderate-to-high	Strong	70-100%	Additional longitudinal evidence supporting a high probability of causation.

[141] Trasande L, Zoeller RT, Hass U, Kortenkamp A, Grandjean P, Myers JP, DiGangi J, Hunt PM, Rudel R, Sathyanarayana S, Bellanger M, Hauser R, Legler J, Skakkebaek NE, Heindel JJ. Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. Andrology. 2016 Jul;4(4):565-72. doi: 10.1111/andr.12178. Epub 2016 Mar 22. PMID: 27003928; PMCID: PMC5244983.

[142] Kahn, L., Philippat, C., Nakayama, S., Slama, R., Trasande, L. (2020). Endocrine-disrupting chemicals : implications for human health. https://doi.org/10.1016/S2213-8587(20)30129-7

[143] Martine Bellanger, Barbara Demeneix, Philippe Grandjean, R. Thomas Zoeller, Leonardo Trasande, Neurobehavioral Deficits, Diseases, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union, *The Journal of Clinical Endocrinology & Metabolism*, Volume 100, Issue 4, April 2015, Pages 1256–1266, https://doi.org/10.1210/jc.2014-4323

[144] Chen A, Yolton K, Rauch SA, et al. Prenatal polybrominated di-phenyl ether exposures and neurodevelopment in U.S. children through 5 years of age: the HOME study. Environ Health Perspect. 2014;122:856 – 862.Miodovnik A, Engel SM, Zhu C, et al. Endocrine disruptors and childhood social impairment. Neurotoxicology. 2011;32:261–267

[145] Gascon M, Vrijheid M, Martínez D, et al. Effects of pre and post-natal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age. Environ Int. 2011;37:605– 611.

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
		OP pesticide	Three longitudinal observational studies identified exposure-response relationships.[146,147,148]	Moderate-to-high	Strong	70-100%	Additional longitudinal evidence supporting a high probability of causation.
	Autism spectrum disorder	Multiple exposure (phthalates and others)	Two longitudinal studies were considered which identify different EDC exposures linked to autism-associated behaviours.[149,150]	Low	Moderate	20-39%	Additional evidence for organophosphate and pyrethroid pesticides. The evidence for other exposures is more inconsistent.
	ADHD	Multiple exposures	Three longitudinal studies[151,152,153] and one cross-sectional epidemiological study[154] identified which support an association between ADHD and various EDCs including dialkyl phosphate, PBDE-47 and OPs.	Low-to-moderate	Strong	20-69%	Further associations identified in longitudinal studies for BPA, PBDEs, OPs, and pyrethroids. Note: results not uniform.

[146] Eskenazi B, Chevrier J, Rauch SA, et al. In utero and childhood polybrominated diphenyl ether (PBDE) exposures and neurodevelopment in the CHAMACOS study. Environ Health Perspect. 2013; 121:257–262

[147] Engel SM, Wetmur J, Chen J, et al. Prenatal exposure to organophosphates, paraoxonase 1, and cognitive development in childhood. Environ Health Perspect. 2011;119:1182–118

[148] Rauh VA, Garfinkel R, Perera FP, et al. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. Pediatrics. 2006;118:e1845– e1859

[149] Braun JM, Kalkbrenner AE, Just AC, et al. Gestational exposure to endocrine-disrupting chemicals and reciprocal social, repetitive, and stereotypic behaviors in 4- and 5-year-old children: the HOME study. Environ Health Perspect. 2014;122:513–520

[150] Miodovnik A, Engel SM, Zhu C, et al. Endocrine disruptors and childhood social impairment. Neurotoxicology. 2011;32:261–267.

[151] Gascon M, Vrijheid M, Martínez D, et al. Effects of pre and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age. Environ Int. 2011;37:605– 611.

[152] Chen A, Yolton K, Rauch SA, et al. Prenatal polybrominated diphenyl ether exposures and neurodevelopment in U.S. children through 5 years of age: the HOME Study. Environ Health Perspect. 2014;122(8):856 – 862

[153]Marks AR, Harley K, Bradman A, et al. Organophosphate pesticide exposure and attention in young Mexican-American children: the CHAMACOS study. Environ Health Perspect. 2010;118:1768 – 1774

[154] Wright RO, Weisskopf MG. Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. Pediatrics. 2010;125:e1270 – e1277.

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
Obesity and metabolism	Childhood obesity	DDE	Exposure-response relationships taken from a European combined analysis of longitudinal studies associating prenatal and postnatal DDE levels with early infant growth.[155] Exposure-response relationship taken from a longitudinal study associating prenatal DDE levels with early infant weight gain for sensitivity analysis.[156]	Moderate	Moderate	40-69%	Not reassessed.
		Bisphenol A	One longitudinal study used of prenatal exposure to BPA to identify increments in BMI Z score.[157]	Very low-to-low	Strong	20-69%	Measures of body fat have increased (which provide more consistent results than BMI). However, a highly variable approach to exposure assessment complicates interpretation. The pattern of sexual dimorphism is not consistent.
	Adult obesity	DEHP	One longitudinal study of phthalate exposure and obesity[158] used to extrapolate attributable weight gain and obesity in the EU.	Low	Strong	40-69%	One study supporting association.

[155] Iszatt N, et al. Prenatal and postnatal exposure to POPs and infant growth: a pooled analysis of 7 European birth cohorts. Environ Health Perspect. In press.
[156] Valvi D, Mendez MA, Martinez D, et al. Prenatal concentrations of polychlorinated biphenyls, DDE, and DDT and overweight in children: a prospective birth cohort study. Environ Health Perspect. 2012;120:451– 457.
[157] Valvi D, Casas M, Mendez MA, et al. Prenatal bisphenol a urine concentrations and early rapid growth and overweight risk in the offspring. Epidemiology. 2013;24:791–799.
[158] g Y, Hauser R, Hu FB, Franke AA, Liu S, Sun Q. Urinary concentrations of bisphenol A and phthalate metabolites and weight change: a prospective investigation in US women.Int J Obes (Lond). 2014;38:1532–1537.

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
	Adult diabetes	DDE	Meta-analysis for newly incident diabetes[159] and a long-term longitudinal study of newly incident diabetes[160] used to extrapolate burden of diabetes attributable to DDE.	Low	Moderate	20-39%	Not reassessed.
		DEHP	Odds ratio taken from one longitudinal study of phthalate exposure and diabetes.[161]	Low	Strong	40-69%	One study supporting association.
Male reproductive health	Cryptorchidism	PBDE	One small case-control study exploring the association between cryptorchidism and PBDE concentrations in breast milk and placenta. [162]	Low	Strong	40-69%	One study supporting positive association.
	Testicular cancer	PBDE	One case-control study considered which measured PBDE levels in men with testis cancer compared to control men[163]	Very low-to-low	Weak	0-19%	No new evidence.

[159] Wu H, Bertrand KA, Choi AL, et al. Persistent organic pollutants and type 2 diabetes: a prospective analysis in the nurses' health study and meta-analysis. Environ Health Perspect. 2013;121:153–161.

[160] Langenberg C, Sharp S, Forouhi NG, et al. Design and cohort description of the InterAct Project: an examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in the EPIC Study. Diabetologia. 2011;54:2272–2282.

[161] Sun Q, Cornelis MC, Townsend MK, et al. Association of urinary doi: 10.1210/jc.2014-4326 jcem.endojournals.org 1287 Downloaded from https://academic.oup.com/jcem/article/100/4/1278/2815069 by guest on 21 January 2022 concentrations of bisphenol A and phthalate metabolites with risk of type 2 diabetes: a prospective investigation in the Nurses' Health Study (NHS) and NHSII cohorts. Environ Health Perspect. 2014; 122:616 – 623.

[162] Main KM, Kiviranta H, Virtanen HE, et al. Flame retardants in placenta and breast milk and cryptorchidism in newborn boys. Environ Health Perspect. 2007;115:1519 – 1526

[163] Hardell L, Bavel B, Lindström G, Eriksson M, Carlberg M. In utero exposure to persistent organic pollutants in relation to testicular cancer risk. Int J Androl. 2006;29:228 – 234

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
	Male infertility	Benzyl and butylphthalates	Several studies considered which explore the associations between urinary concentrations of phthalate metabolites and poorer semen quality from men in infertility clinics.[164,165,166] Two studies from the general population found no association[167,168]	Low	Strong	40-69%	22 studies linking higher phthalate concentrations to lower sperm concentration, motility, or normal morphology. Three studies had increases in these measures. Three studies showed no significant association.
	Low testosterone	Phthalates	11 manuscripts considered which associate levels of urinary phthalate metabolites and serum T in adult men. Four of these were focussed on	Low	Strong	20-69%	Cross-sectional studies supporting negative association with testosterone. 12 for DEHP and MEHP and two for MiBP. Increased evidence for prenatal exposure and testosterone in children. A lack of consistent evidence for young men.

[164] Jurewicz J, Radwan M, Sobala W, et al. Human urinary phthalate metabolites level and main semen parameters, sperm chromatin structure, sperm aneuploidy and reproductive hormones. Reprod Toxicol. 2013;42:232–241.
[165] Wirth JJ, Rossano MG, Potter R, et al. A pilot study associating urinary concentrations of phthalate metabolites and semen quality. Syst Biol Reprod Med. 2008;54:143–154.
[166] Hauser R, Meeker JD, Duty S, Silva MJ, Calafat AM. Altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites. Epidemiology. 2006;17:682– 691.
[167] Joensen UN, Frederiksen H, Blomberg Jensen M, et al. Phthalate excretion pattern and testicular function: a study of 881 healthy Danish men. Environ Health Perspect. 2012;120:1397–1403.
[168] Jönsson BA, Richthoff J, Rylander L, Giwercman A, Hagmar L. Urinary phthalate metabolites and biomarkers of reproductive function in young men. Epidemiology. 2005;16:487– 493.

Health impact category	Outcome	Exposure	Literature	Strength of human evidence (2015)	Strength of toxicologic evidence (2015)	Probability of causation assigned (2015)	Updates in the literature (since 2015)[142]
			when determining the relationship.[169,170,171,172]				
Female reproductive health	Fibroids	DDE	One study was used for calculations which considered fibroids in adult women and environmental exposures.[173] Ten other studies were also considered, supported by various studies of rodents.	Low	Moderate	20-39%	Not reassessed.
	Endometriosis	DEHP	One study showed significant associations between DEHP metabolites and endometriosis in population and operative cohorts[174]	Low	Moderate	20-39%	Three studies showing a positive association. Two studies showing negative or no association.

[169] Meeker JD, Ferguson KK. Urinary phthalate metabolites are associated with decreased serum testosterone in men, women, and children from NHANES 2011–2012. J Clin Endocrinol Metab. 2014; 99:4346 – 4352.
[170] Joensen UN, Frederiksen H, Blomberg Jensen M, et al. Phthalate excretion pattern and testicular function: a study of 881 healthy Danish men. Environ Health Perspect. 2012;120:1397–1403.
[171] Jönsson BA, Richthoff J, Rylander L, Giwercman A, Hagmar L. Urinary phthalate metabolites and biomarkers of reproductive function in young men. Epidemiology. 2005;16:487– 493
[172] Han X, Cui Z, Zhou N, et al. Urinary phthalate metabolites and male reproductive function parameters in Chongqing general population, China. Int J Hyg Environ Health. 2014;217:271–278
[173] Trabert B, Chen Z, Kannan K, et al. Persistent organic pollutants (POPs) and fibroids: results from the ENDO study. J Expo Sci Environ Epidemiol. 2015;25
[174] Buck Louis GM, Peterson CM, Chen Z, et al. Bisphenol A and phthalates and endometriosis: the Endometriosis: Natural History, Diagnosis and Outcomes Study. Fertil Steril. 2013;100:162– 169.e161– e162.

5.5.1 Estimates of UK costs from EDC exposure

For illustration, costs associated with EDC exposure in the UK, taken from the Trasande et al (2016) country-specific estimates are shown below. The costs have been updated to 2020 prices and converted into sterling but are not otherwise changed from the original source. Given the significant criticism surrounding the methodology the cost estimates for EDCs should be treated with caution. A series of recommendations are made at the end of this chapter for future research activities that may support estimates in the future.

Note the direct costs include the expenditures for hospitalization, physician services, nursing home care, medical appliance, and related items. Indirect costs included the value of lost output of workers and of retirees from premature death or disability.

Table 5-3 Cost estimates for exposure to EDCs updated from Trasande et al. (2016)[175]

Exposure	Outcome	Probability of causation	UK[176] cost estimates (2020 prices)[177]
Organophosphate pesticides	IQ loss and intellectual disability	Strong	£26.0 billion
PBDE	IQ loss and intellectual disability	Strong	£1.7 billion
DEHP	Adult obesity	Strong	£1.7 billion
Phthalates	Low testosterone, resulting in increased early mortality	Strong	£864.7 million
Benzyl and butylphthalates	Male infertility, resulting in increased assisted reproductive technology	Strong	£413.8 million
Multiple exposures	ADHD	Strong	£300.0 million
Bisphenol A	Childhood obesity	Strong	£275.7 million
DEHP	Endometriosis	Moderate	£195.1 million
PBDE	Testicular cancer	Strong	£124.2 million
DDE	Adult diabetes	Moderate	£122.5 million
DEHP	Adult diabetes	Strong	£89.1 million
Multiple exposures	Autism	Moderate	£35.8 million
DDE	Fibroids	Moderate	£27.4 million
PBDE	Cryptorchidism	Weak	£23.3 million
DDE	Childhood obesity	Moderate	£4.3 million
Total (before accounting for probability of causation)			**£31.8 billion**
Total (after accounting for probability of causation)			**£27.2 billion**

[175] Trasande L, Zoeller RT, Hass U, Kortenkamp A, Grandjean P, Myers JP, DiGangi J, Hunt PM, Rudel R, Sathyanarayana S, Bellanger M, Hauser R, Legler J, Skakkebaek NE, Heindel JJ. Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. Andrology. 2016 Jul;4(4):565-72. doi: 10.1111/andr.12178. Epub 2016 Mar 22. PMID: 27003928; PMCID: PMC5244983.

[176] 2020 Prices: 2010 GDP Deflator 80.303 (2020 = 100). GDP deflators at market prices, and money GDP March 2021 (Budget) - GOV.UK (www.gov.uk)

[177] Exchange rate used: 2010 €1 = £0.8852 https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm#indicator-chart

5.6 Summary

Whilst a range of human health impacts from EDCs has been explored, evidence remains limited, resulting in challenges in estimating costs from ongoing exposure. The above results suggest very large annual costs related to EDC exposures in the UK. As highlighted above, the methodology employed to derive these estimates is associated with several uncertainties and the methodology has been criticised.

5.7 Future research priorities

There are major concerns with EDCs and their potential impact on human health and the environment due to their ability to interfere with hormonal signalling within organisms. The role of individual EDCs as potential drivers for negative health outcomes has been demonstrated in some UK studies but is hampered by a lack of direct cause and effect data indicating that stronger animal toxicological and human epidemiological evidence is required in order to confidently assess the magnitude and cost of the impact of EDCs in the UK. In particular, there is a lack of data on environmental effects, both on individual species but also potential population level impacts in both humans and wildlife. To better understand the risk posed by EDCs in the UK accurate biomonitoring data from both humans and a diverse range of wildlife is required to understand temporal and spatial trends in pollution and implications for populations and ultimately ecosystem functioning. Specific topic areas are below.

5.7.1 EDCs and fish

To date, the majority of laboratory studies on EDCs have focussed on single chemical exposures to single species. In order to better understand the potential for population level effects of EDCs in the water environment, long term studies which explore low dose chronic exposures to EDCs are required. Groups of species should be exposed in the lab to environmentally relevant concentrations of specific chemicals that frequently occur in the environment (for example mixtures could be informed by data on wastewater concentrations of chemicals). To give a better indication of the potential population level effects such studies could be extended from a single generational study to include the offspring of the first generation, who can then be exposure to the same substance from birth to maturity. The growth and reproductive success of each generation can then be observed to establish whether exposure of an EDC over multiple generations has impacts on the ability of individuals to reproduce due to abnormalities caused by the substance of concern. Whilst there are some examples of this approach in the literature, multigenerational studies considering combined mixtures which are representative to the environment is a gap. This type of multigenerational research could also be used to explore whether a lack of population effects from a chemical is due to the ability of a species to adapt to exposure over time. Again, the adaptation potential of humans and wildlife to chemicals such as EDCs is poorly understood in the UK.

5.7.2 EDCs and terrestrial effects

Compared to the various studies conducted to determine the impact of EDCs on fish, there is notable gap in evidence on effects of EDCs on terrestrial organisms. To improve the evidence base for the impacts of EDCs on non-fish species further toxicity testing using earthworms in contaminated soil for example could be used to determine the uptake and bioaccumulation of a substance and the potential for chemicals to be passed up the food chain. Historic evidence of the impact of DDT and diclofenac on higher trophic avian species (vultures) suggests that bioaccumulation of EDCs and legacy substances is a possibility, yet the risk is poorly understood and perhaps increasingly important given the sheer diversity and number of chemicals entering the environment, many of which are designed to alter biological functioning.

Some EDCs, including PFAS and PCBs, are considered legacy chemicals, which even after regulation remain a significant problem in the environment. Land and drinking water contaminated by legacy chemicals is hugely expensive to treat and remediate, emphasizing the importance of future source control. To this end, further research is required in the UK to analyse the cost and potential impact of Extended Producer Responsibility schemes for products containing EDCs such as take back schemes for pharmaceuticals. Such an EPR

approach has been explored for single use plastics in the UK and within Europe is currently under consideration for treating micropollutants. However, the feasibility of such a scheme for the UK requires further scoping and evaluation to establish the benefits to human health and the environment.

5.7.3 EDCs and human health

As with the environment, humans are exposed simultaneously to mixtures of EDCs which can cause human health effects. To assess the overall impact of EDCs to humans in the UK, research should first establish the baseline level of exposure within different population groups (age, gender, socioeconomic group etc). Currently the UK is part of the HBM4EU scheme which looks to coordinate and advance human biomonitoring in Europe. UK specific biomonitoring data should continue being gathered and the number of participants expanded to improve understanding of exposure levels to EDCs in the UK within different groups. Regional differences in exposure can be used to assess exposure effects at different locations and research should also continue to focus on the effects of EDCs to vulnerable populations, e.g. pregnant women and babies. Such additional biomonitoring data could then be used to improve the accuracy of the socio-economic cost estimates associated with the burden of disease attributable to EDC exposure. For many health impacts associated with EDCs, there is also a significant genetic component. Future research could look to disaggregate the genetic and chemical attribution of the associated disorders, to provide more accurate estimates of PAFs.

5.7.4 Methodological advances

The outcomes of this project suggest that the uncertainty associated with methodologies used to estimate costs could be improved. In part this would be reliant on obtaining greater toxicological and epidemiological data which in time would support more robust assessments of the probability of causation. In the absence of this, a cost effectiveness framework could be applied for EDCs, as per the approach taken with PBT substances, for example.

The use of the modified Delphi technique has received particular criticism and whilst the approach was adopted here in the absence of definitive empirical evidence, greater transparency in the selection and operation of such exercises may have mitigated some of the concerns raised. When estimating the probability of causation, it should be considered whether lower probabilities should result in any cost estimates at all, whether in the central estimates or – at least – in sensitivity tests. IPCC guidance suggests that where the probability of causation is between 33-66% then causation is “about as likely as not”.

6 Neurodevelopmental effects

6.1 Effects

The neurodevelopmental effects with the strongest evidence associating them with chemicals exposure are loss of intelligence quotient (IQ) points and associated increased incidence of mild mental retardation (MMR), and attention deficit hyperactivity disorder (ADHD). These effects are the focus of the assessment of impacts and costs presented in this section.

- **Intelligence quotient (IQ)** is a widely used scoring system representing human intelligence, typically determined through a series of standardised tests. The uncertainties associated with IQ scoring are discussed in Section 6.5.4. Numerous substances (discussed in Section 6.2) are linked with declines in intellectual ability which can be expressed as a **loss of IQ points**.
- While IQ loss in itself is not classed as a disease, it can result in a classification of **mild mental retardation (MMR)** where IQ scores fall below 70. This is associated with higher risk of developing mental health, behavioural and academic difficulties and of experiencing socio-economic disadvantages[178]. In childhood, MMR may not be easily identifiable, but may manifest in delayed speech[179].
- **Attention deficit hyperactivity disorder (ADHD)** is a behavioural disorder manifesting in inattentive, hyperactive and impulsive behaviours. Most cases are diagnosed between ages 3 – 7 years old[180] where it can be observed through impaired behavioural function at home and school, as well as academic performance[181]. Clinical data from between 2004 and 2013 in the UK has determined an ADHD incidence rate of 3.62% for boys aged 5 – 15 and 0.85% for girls in the same age group[182]. This compares to a global prevalence of between 2 – 7% with an average of 5% (the latter data are not split by sex). At least a further 5% of children have substantial difficulties with overactivity, inattention, and impulsivity but do not meet the full diagnostic criteria for ADHD. Estimates vary worldwide, but prevalence has been increasing over time. ADHD is still relatively under-recognised and underdiagnosed in most countries, particularly in girls and older children[183]. There is a strong genetic component to one's risk of developing the condition, but those born prematurely, with low birthweight and/or with epilepsy are at higher risk[184].

6.2 Substances of concern

6.2.1 Lead and Mercury

[178] Nouwens et al. (2017). Identifying classes of persons with mild intellectual disability or borderline intellectual functioning: a latent class analysis, BMC Psychiatry, Volume 17, 257. https://doi.org/10.1186/s12888-017-1426-8
[179] Daily et al. (2000). Identification and evaluation of mental retardation, American Family Physician, Volume 61(4), 1059-1067. https://www.aafp.org/afp/2000/0215/p1059.html
[180] NHS (2021). Overview: Attention deficit hyperactivity disorder. https://www.nhs.uk/conditions/attention-deficit-hyperactivity-disorder-adhd/
[181] Swanson et al. (1998). Attention-deficit hyperactivity disorder and hyperkinetic disorder, The Lancet, Volume 351(9100), 429-433. https://doi.org/10.1016/S0140-6736(97)11450-7
[182] Hire et al. (2015). ADHD in the United Kingdom: Regional and socioeconomic variations in incidence rates amongst children and adolescents (2004-2013), Journal of Attention Disorders, Volume 22(2), 134-142. https://doi.org/10.1177%2F1087054715613441
[183] Sayal et al. (2018). ADHD in children and young people: prevalence, care pathways, and service provision, The Lancet Psychiatry, Volume 5(2), 175-186. https://doi.org/10.1016/S2215-0366(17)30167-0
[184] https://www.nhs.uk/conditions/attention-deficit-hyperactivity-disorder-adhd/causes/#:~:text=Genetics,likely%20to%20have%20ADHD%20themselves.

Impacts of childhood lead exposure on intelligence have been extensively documented, and concerns over neurodevelopmental effects were one of the main drivers behind global phase-out of leaded petrol. The mechanisms by which lead exposure causes neurodevelopmental harm include impairment of mitochondrial function and oxygen-carrying capacity of red blood cells, increasing oxidative stress, disturbance of neurotrophic processes and alteration of gene transcription[185].

Dose-response functions have been derived linking blood lead levels (BLLs) to losses of IQ points; two dose-response functions that have been widely used in the epidemiological and valuation literature are presented in Table 6-1. These dose-response functions are expressed with an 'effect' threshold beneath which there are assumed to be no neurodevelopmental effects. At present, the impacts of very low BLLs on IQ are not fully understood, and academic sources[185] as well as the WHO[186] assert that there are no safe BLLs. A meta-analysis of 33 studies also concluded that there is a significant link association between lead exposure and ADHD[187].

Table 6-1 DRFs linking childhood lead exposure to IQ point loss

Source of DRF	Response function	'Effect' threshold
Lanphear et al. (2019)[188]	IQ point decrements associated with an increase in BLL from 2.4 to 10 µg/dL, 10 to µg/dL and 20 to 30 µg/dL of 3.8 (95% CI 2.3 – 5.3), 1.8 (95% CI 1.1 – 2.6) and 1.1 (95% CI 0.7 – 1.5) respectively.	2.4 µg/dL
Surkan et al. (2007)[189]	Children with BLL 5-10 µg/dL had 5.0 points lower IQ scores compared to children with BLLs of 1-2 µg/dL.	5 µg/dL

Devastating neurological impacts have been observed as a result of prenatal mercury exposure. In Minamata, Japan, pregnant women consuming mercury-contaminated seafood gave birth to children with a variety of neurological afflictions collectively known as Congenital Minamata Disease. The primary pathway of prenatal mercury exposure is through maternal seafood consumption[190]. As with lead, mechanisms of neurodevelopmental damage from mercury exposure are well understood and include disturbance of laminar pattern of the cerebral cortex, perturbation of cell proliferation and migration and incomplete myelination[185].

Dose-response functions have been defined by two studies; these are listed in Table 6-2. The first dose-response function is based on data on neuropsychological test from the Faroe Islands and assumes a no 'effect' threshold of 0.58 µg/g. The second was derived using data from the Faroes Island study and additional studies from the Seychelles and New Zealand. This dose-response function assumes a non-threshold relationship; this takes into account low-level lead exposure, which is of particular relevance to the UK where lead emissions have declined in recent decades as a result of legislative action.

[185] Bellinger (2018). Environmental chemical exposures and neurodevelopmental impairments in children, Pediatric Medicine, Volume 1. http://dx.doi.org/10.21037/pm.2018.11.03
[186] WHO (2021). Lead poisoning. https://www.who.int/news-room/fact-sheets/detail/lead-poisoning-and-health
[187] Goodlad et al. (2013). Lead and attention-deficit/hyperactivity disorder (ADHD) symptoms: a meta-analysis, Clinical Psychology Review, Volume 33(3), 417-425. https://doi.org/10.1016/j.cpr.2013.01.009
[188] Lanphear et al. (2019). Erratum: "Low-level environmental lead exposure and children's intellectual function: an international pooled analysis", Environmental Health Perspectives, Volume 127(9). https://doi.org/10.1289/EHP5685
[189] Surkan et al. (2007). Neuropsychological function in children with blood lead levels <10 µg/dL, Neurotoxicology, Volume 28(6), 1170-1177. https://dx.doi.org/10.1016%2Fj.neuro.2007.07.007
[190] Dubourg (2018) OECD Environment Working Papers No. 132: Economic assessments of benefits of regulating mercury: A review. https://doi.org/10.1787/77045f1a-en

Table 6-2 Dose-response functions linking childhood mercury exposure to IQ point loss

Source of dose-response functions	Response function	'Effect' threshold
Bellanger et al. (2013)[191]	0.465 IQ point reduction per 1 µg/g increase in maternal hair mercury above a cut-off level of 0.58 µg/g.	0.58 µg/g.
Axelrad et al. (2007)[192]	0.18 IQ point (95% CI 0.009 – 0.378) reduction for each part per million increase in maternal hair mercury.	No threshold.

6.2.2 Other substances

Chronic exposure to arsenic has been observed to impair neurofunction by increasing oxidative stress, reducing neurotransmitter levels, interfering with the expression of thyroid hormone receptor genes, and impairing neurogenesis in the hippocampus[193].

Pesticides are neurotoxic by design due to their intended purpose of targeting insect nervous systems. A variety of pesticides are in use, and their mechanisms of neurodevelopmental damage are known. Among the most widely used are organophosphates, which inflict damage by inhibiting the activity of acetylcholinesterase[185]. Other pesticides with adverse effects include pyrethoids and carbamates[194].

Perfluorinated compounds (PFCs) are a group of a chemicals based solely on carbon-fluorines and carbon-carbon bonds. They include substances such as perfluorooctane sulphonate (PFOS), perfluorooctanoate (PFOA) and perfluoroalkyl substances (PFASs). Studies have linked neurodevelopmental endpoints with PFAS[195] and PFOA[196], although further research is required to conclusively determine the impacts.

In addition, certain EDCs, in particular polybrominated diphenyl ethers (PBDEs) and organophosphates, are linked with alterations in thyroid receptor or oestrogen receptor regulation of neuroendocrine development and dopaminergic neuronal development, which leads to interference with important neurodevelopment processes[197, 198]. Trasande et al. (2016)[199] have estimated the cost of IQ loss in the UK through exposure to PBDEs and organophosphates at €1.5bn and €23.5 bn respectively. There are uncertainties associated with these figures which are discussed in chapter 5.

6.3 Major uses

Lead has many uses, both as a metal and in chemical compounds. The principal uses of metallic lead in the UK include batteries, cables, solders, ammunition, shielding from radiation and x-rays, electronic circuit

[191] Bellanger et al. (2013) Economic benefits of methylmercury exposure control in Europe: monetary value of neurotoxicity prevention, Environmental Health, Volume 12(3), http://www.ehjournal.net/content/12/1/3
[192] Axelrad et al. (2007) Dose-response relationship of prenatal mercury exposure and IQ: an integrative analysis of epidemiologic data, Environmental Health Perspectives, Volume 115(4), https://doi.org/10.1289/ehp.9303
[193] Bellinger (2013). Inorganic arsenic exposure and children's neurodevelopment: a review of the evidence, Toxics, Volume 1, 2-17. https://doi.org/10.3390/toxics1010002
[194] Liu & Schelar (2012) Pesticide exposure and child neurodevelopment, Workplace Health & Safety, Volume 60(5), 235-242. https://doi.org/10.1177%2F216507991206000507
[195] Liew et al. (2018) Developmental exposures to perfluoroalkyl substances (PFAS): An update of associated health outcomes, Current Environmental Health Reports, Volume 5, 1-19. https://dx.doi.org/10.1007%2Fs40572-018-0173-4
[196] Goudarzi et al. (2015) Prenatal exposure to perfluorinated chemicals and neurodevelopment in early infancy: The Hokkaido study, Science of the Total Environment, Volume 15 (541), 1002-1010. https://doi.org/10.1016/j.scitotenv.2015.10.017
[197] Ghassabian & Trasande (2018). Disruption in thyroid signalling pathway: a mechanism for the effect of endocrine-disrupting chemicals on child neurodevelopment, Frontiers in Endocrinology, Volume 9, 204. https://doi.org/10.3389/fendo.2018.00204
[198] Naughton & Terry Jr (2018). Neurotoxicity in acute and repeated organophosphate exposure, Volume 408(1), 101-112. https://www.sciencedirect.com/science/article/abs/pii/S0300483X18302646?via%3Dihub
[199] Trasande et al. (2016) Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis, Andrology, Volume 4(4), 565-572. https://onlinelibrary.wiley.com/doi/10.1111/andr.12178

boards, and optical technology. Lead compounds are used in colour pigments, enamels and ceramics, and as a plasticiser in PVC formulations, although these uses are declining[200]. The largest use of mercury in England prior to 2017 was chlor-alkali production[201]; the revised EU Mercury Regulation (EU/852/2017)[202] prohibited this use of mercury from December 2017. The Mercury Regulation has placed restrictions on use of mercury in most products, but it remains used in dental amalgam fillings (and is emitted via crematoria) and 'mercury-added products' which include fluorescent lamps, certain batteries and certain medical devices. Prior to its prohibition in 1992 (see Section 6.4), lead was used as a pigment and drying agent in paints. Changes to building regulations in 1969 discontinued lead use in water pipes, although housing from before 1970 may still have lead piping[203].

Arsenic is used in the production of a variety of electrical components, metal alloys, and certain glass and ceramic products. Arsenic is naturally present in soils and rocks, and can be disturbed and released through human activities including coal combustion, mining and smelting, and agriculture[204].

PFCs are used in a variety of applications including stain repellents in textiles and non-stick coatings in cookware[205], additives to paper products, and aqueous film-forming foams (AFFFs) used in fire extinguishers[206]. Certain PFCs, including PFOA, are used as process aids in the manufacture of fluoropolymers[207].

6.4 Current regulatory controls and remaining sources of exposure

Numerous substances with neurodevelopmental impacts were subject to restrictions under EU REACH and applied in the UK, as well as predecessor legislation including Directive 89/677/EEC[208] (restricting lead use in paints in residential settings) and Directive 88/378/EEC[209] (limiting lead bioavailability in toys). These include a restriction for lead and its compounds in articles supplied to the general public[210]; restrictions on arsenic compounds in antifouling substances, industrial water treatment substances, and wood preservation

[200] Public Health England (2016). Lead: General information. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/562435/lead_general_information.pdf

[201] Environment Agency (2019). Mercury: Sources, pathways and environmental data. https://consult.environment-agency.gov.uk/++preview++/environment-and-business/challenges-and-choices/user_uploads/mercury-pressure-rbmp-2021.pdf

[202] European Commission (2017). Regulation (EU) 2017/852 of the European Parliament and of the Council of 17 May 2017 on mercury, and repealing Regulation (EC) No 1102/2008. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32017R0852

[203] WaterSafe (n.d.) WaterSafe film highlights the dangers of lead in drinking water. https://www.watersafe.org.uk/news/latest_news/watersafe_film_highlights_dangers_of_lead/#:~:text=Lead%20dissolving%20into%20drinking%20water,likely%20to%20have%20lead%20pipes%20.

[204] Public Health England (2019). Arsenic: General information. https://www.gov.uk/government/publications/arsenic-properties-incident-management-and-toxicology/arsenic-general-information

[205] Stahl et al. (2011). Toxiciology of perfluorinated compounds, Environmental Sciences Europe, Volume 23, 38, http://www.enveurope.com/content/23/1/38

[206] Reiner et al. (2014). Chapter 3 – Analytical methodology of POPs, Environmental Forensics for Persistent Organic Pollutants, 59-139. https://doi.org/10.1016/B978-0-444-59424-2.00003-7

[207] Posner (2011). Perfluorinated compounds: Occurrence and uses in products, Perfluorinated chemicals and transformation products, 25-39. https://link.springer.com/chapter/10.1007/978-3-642-21872-9_2

[208] European Commission (1989). Council Directive 89/677/EEC of 21 December 1989 amending for the eighth time Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the member states relating to restrictions on the marketing and use of certain dangerous substances and preparations. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=celex:31989L0677

[209] European Commission (1988). Council Directive 88/378/EEC of 3 May 1988 on the approximation of the laws of the Member States concerning the safety of toys. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=celex:31988L0378

[210] ECHA (2016). Annex XVII to REACH – Conditions of restriction: Entry 63 Lead and its compounds. https://echa.europa.eu/documents/10162/851fb88e-9867-c5a0-bf15-2678ad831be6

substances[211]; restrictions on mercury use in fever thermometers and other measuring devices[212], and on mercury compounds in antifouling substances, wood preservation substances, and industrial water treatment substances[213]. After the UK's exit from the European Union, these were retained in UK law through UK REACH[214]. But currently proposed restrictions under EU REACH, such as concerning lead use in PVC, will not be automatically reflected in UK REACH. The UK Government is currently considering a ban of lead ammunition through UK REACH to protect wildlife and nature[215].

EU Directive 98/70/EC[216] relating to the quality of petrol and diesel fuels prohibited the marketing of leaded petrol in Member States from 1st January 2000; prior to this, tetraethyl-lead was commonly used as an antiknock petrol additive. The Directive was transposed into UK legislation by the Motor Fuel (Composition and Content) Regulations 1999[217].

The UK is a signatory to the 2013 Minamata Convention on Mercury which seeks to tackle mercury pollution through a legally binding agreement. The EU Mercury Regulation[202] banned mercury use in a variety of products; this was transposed into UK legislation[218] and retained after the UK's exit from the EU[219]. Dental amalgam and certain mercury-added products remain a major use of mercury, and this will include some use in the UK although the exact scale of use is not known. It is known, however, that dental amalgam fillings are the most common among fillings available on the NHS[220].

Biocidal products, including pesticides, are controlled in the UK under the GB Biocidal Products Regulation (GB BPR)[221]. The UK is also a signatory to the Stockholm Convention on Persistent Organic Pollutants (POPs) which seeks to eliminate or restrict the production of a number of chemicals, including pesticides, including aldrin, dieldrin and chlordane[222]. IED addresses emissions of heavy metals to air. IED has been applied in England and Wales through amendments to EPR 2010, implemented in the Environmental Permitting (England and Wales) (Amendment) Regulations 2013.

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[211] ECHA (n.d.). Annex XVII to REACH – Conditions of restriction: Entry 19 Arsenic and its compounds. https://echa.europa.eu/documents/10162/a798c758-371f-41e5-a38d-5f8dc9ba739d
[212] ECHA (n.d.). Annex XVII to REACH – Conditions of restriction: Entry 18a Mercury. https://echa.europa.eu/documents/10162/dbcaaec7-bd5b-4a7d-b164-23fa97950a86
[213] ECHA (n.d.). Annex XVII to REACH – Conditions of restriction: Entry 18 Mercury compounds. https://echa.europa.eu/documents/10162/5a7222b0-9d3a-4a90-9e55-258149e92b1a
[214] Legislation.gov.uk (2019). The REACH etc. (Amendment etc.) (EU Exit) Regulations 2019. https://www.legislation.gov.uk/ukdsi/2019/9780111178034
[215] Gov.uk (2021). Plans announced to phase out lead ammunition in bid to protect wildlife. https://www.gov.uk/government/news/plans-announced-to-phase-out-lead-ammunition-in-bid-to-protect-wildlife
[216] European Commission (1998). Directive 98/70/EC of the European Parliament and of the Council of 13 October 1998 relating to the quality of petrol and diesel fuels and amending Council Directive 93/12/EEC. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A31998L0070
[217] Legislation.gov.uk (1999). The Motor Fuel (Composition and Content) Regulations 1999. https://www.legislation.gov.uk/uksi/1999/3107/contents/made
[218] Legislation.gov.uk (2017) The Control of Mercury (Enforcement) Regulations 2017. https://www.legislation.gov.uk/uksi/2017/1200/contents/made
[219] Legislation.gov.uk (2020) The Control of Mercury (Amendment) (EU Exit) Regulations 2020. https://www.legislation.gov.uk/ukdsi/2020/9780348213188
[220] NHS (2021). What are NHS fillings and crowns made of? https://www.nhs.uk/common-health-questions/dental-health/what-are-nhs-fillings-and-crowns-made-of/
[221] Legislation.gov.uk (2001). The Biocidal Products Regulations 2001. https://www.legislation.gov.uk/uksi/2001/880/contents/made
[222] Stockholm Convention (2019). All POPs listed in the Stockholm Convention. http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx

6.5 Lead impacts on IQ loss and MMR

6.5.1 Approach[223]

This section uses the available evidence to structure an approach for quantifying the impacts and associated costs of lead exposure on neurodevelopment. Several established dose-response functions have been documented in academic literature linking loss of IQ points to childhood blood lead levels (BLLs), thus it has been possible to quantify impacts associated with lead exposure based on these relationships. The overall approach adopted is as follows:

- Defining the dose-response functions between BLL and loss of IQ points;
- Ascertaining the size of the childhood population potentially affected. The loss of IQ points associated with lead exposure occurs during early childhood while the brain is still developing, and is largely irreversible and thereafter, persisting throughout life. As such, impacts have been quantified for a single annual cohort to estimate the possible yearly impact of lead exposure. For the purposes of assessment, this has been assumed to be a cohort of five-year olds in 2019[224] in the UK;
- Estimating BLLs in the UK population; and
- Applying dose-response functions to those BLLs, and multiplying by the population size to estimate lost IQ points. There are uncertainties and methodological concerns associated with quantifying IQ point losses; these are detailed in Section 6.5.4.

The two dose-response functions elaborated by Lanphear et al. (2019) and Surkan et al. (2007) were used in the calculations (see Table 6-1); as an additional sensitivity test to account for the unknown effects of very low BLLs on IQ, the Lanphear et al. (2019) dose-response function (which assumes an 'effect' threshold of 2.4 µg/dL) was also applied assuming no lower threshold for observed effects. This results in a wide spread of results, as accounting for an 'effect' threshold assumes that children in the UK are largely exposed to lead levels which will not impact them. By contrast, estimating without an 'effect' threshold assumes that all children in the UK are impacted by lead exposure. Additionally, impacts were also calculated using the upper and lower 95% confidence intervals for the dose-response functions.

The latter dose-response function was applied without its effect threshold. Probabilistic simulation modelling of exposure data suggested that 0% of the population exceeded the threshold. This implies that no damage was being caused at recent estimated average exposure levels. The study population size was determined by summing the total numbers of live births for England and Wales[225], Scotland[226], and Northern Ireland[227] for the year five years previous to the assessment year (i.e. 2014). The UK under-five mortality rate for the same year, obtained from the WHO[228], was taken into account. It is important to note that in the absence of UK-specific lead biomonitoring data, BLLs were obtained from the German Environmental

[223] Note that a list of data inputs and assumptions for this chapter is in the Appendix.
[224] The latest blood lead level data are from 2019. Consequently, the assessment is focused on 2019, and all other inputs are taken for 2019.
[225] Office for National Statistics (2021). Births in England and Wales: summary tables. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/datasets/birthsummarytables
[226] National Records of Scotland (2021). Births Time Series Data. https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/births/births-time-series-data
[227] Northern Ireland Statistics and Research Agency (2020). Birth Statistics. https://www.nisra.gov.uk/publications/birth-statistics
[228] WHO (2021). Under-five mortality rate (probability of dying by age 5 per 1000 live births). https://www.who.int/data/gho/data/indicators/indicator-details/GHO/under-five-mortality-rate-(probability-of-dying-by-age-5-per-1000-live-births)

Specimen Bank[229]. This includes routine blood lead monitoring data from a sample of students (n=123 in 2019) in Munster. The implications of using this data are discussed in Section 6.5.3. As the latest year of monitoring data are from 2019, all other calculation input data have been obtained for 2019, and calculated costs and impacts are specific to 2019 as well.

Where dose-response functions with 'effect' thresholds were considered, it was necessary to determine the fraction of the population estimated to be exposed to lead beneath the assumed threshold. These children were then discounted from the calculations. Similarly, it was necessary to determine fractions of populations falling in different BLL brackets. This was done using probabilistic simulation modelling, assuming population lead exposure follows a log-normal distribution as recommended by WHO guidance[230].

In a previous assessment specifically of the impacts and costs of childhood lead exposure, Gould (2009)[231] estimated the discounted[232] total loss of lifetime earnings per IQ point loss at $17,815 (2006 prices) in the USA. This figure includes the indirect effects of lower educational achievement and workforce participation alongside the direct effect of lower hourly wages. Based on this figure, and using PPP-adjusted exchange rates[233] and UK government GDP deflators[234], lifetime loss of earnings per loss of IQ point was valued at £15,951 in 2019 prices. This figure was used to put a value on the total loss of IQ points due to lead exposure. No alternative valuation figures have been identified. Concerns around the validity of such a relationship, particularly in a UK context is discussed in section 6.5.4.

Following the calculation of lost IQ points, the number of additional cases of MMR that may result was also calculated. This involves calculating the number of people above the MMR threshold (70 IQ) who would shift into the MMR range through loss of IQ points due to lead exposure. Assuming normally distributed population IQ with a mean of 100 and standard deviation of 15[230], the percentages of the population in ranges susceptible to crossing the MMR threshold were calculated (for example, the IQ range at risk of MMR for a BLL bracket with a mean IQ loss of 1.9 is 70-71.9). For each BLL bracket, the number of MMR cases was calculated as follows:

$$MMR\ cases = \%\ population\ in\ BLL\ bracket \times \%population\ at\ risk\ of\ MMR \times study\ population$$

Total additional MMR cases were then calculated by summing MMR cases across all BLL brackets. DALYs arising from MMR in 2019 were then calculated from the cases number using a disability weight of 0.36 as suggested by Hänninen and Knol (2011)[235]. Previous valuation studies have proposed economic values for DALYs, including a willingness-to-pay figure of €126,000 (2013 prices)[236] based on French government recommendations. The present assessment adopts a figure of £60,000 as recommended by UK Government

[229] Umwelt Probenbank Des Bundes (2021). Lead: Students. https://www.umweltprobenbank.de/de/documents/investigations/results?genders=0&measurement_params=10005&sampling_areas=10104&specimen_types=10005

[230] Fewtrell et al. (2003). Environmental Burden of Disease Series, No. 2: Lead: Assessing the environmental burden of disease at national and local levels. https://apps.who.int/iris/bitstream/handle/10665/42715/9241546107.pdf?sequence=1&isAllowed=y

[231] Gould (2009). Childhood lead poisoning: Conservative estimates of the social and economic benefits of lead hazard control, Environmental Health Perspectives, Volume 117(7), 1162-1167. https://doi.org/10.1289/ehp.0800408

[232] It is not known what discount factor was applied to this figure, but it is assumed to be the standard US discount rate.

[233] OECD (2021). Purchasing power parities (PPP). https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm

[234] Gov.uk (2022). GDP deflators at market prices, and money GDP December 2021 (Quarterly National Accounts). https://www.gov.uk/government/statistics/gdp-deflators-at-market-prices-and-money-gdp-december-2021-quarterly-national-accounts

[235] Hänninen & Knol (2011). European Perspectives on Environmental Burden of Disease : Estimates for Nine Stressors in Six European Countries.

[236] Nedellec & Rabl (2016). Costs of Health Damage from Atmospheric Emissions of Toxic Metals: Part 1 – Methods and Results, Risk Analysis, March 2016, Volume 36(11), 2081-2095. https://doi.org/10.1111/risa.12599

guidance[237], based on a 2010 value of a prevented fatality (VPF) figure[238]. This is considered most applicable to the assessment of costs in the UK. This figure was adjusted for inflation[234] to a value of £70,135 in 2019. This value was applied to 2019 DALYs and discounted over a lifetime of 77.6 years[235] using declining discount rates[239] and an inflation rate of 2.0% in line with UK Government guidance[237, 240]. Additionally, for comparison, lifetime costs have been calculated without discounting, accounting only for inflation. Concerns around the validity of empirical effects from such marginal changes in IQ on wellbeing are discussed in section 6.5.4.

6.5.2 Results

Table 6-3 presents the impacts and costs associated with IQ loss and MMR cases arising from lead exposure based on the three calculations conducted. There is significant difference between figures where an 'effect' threshold is assumed, and those where it is not.

Where an 'effect' threshold is considered, less than 1% of the cohort is estimated to be exposed to lead levels above the threshold, and total lifetime IQ point loss for the 2019 cohort is calculated at **11,000**, valued at **£169m (£102-236m; £132-304 per person)** in terms of lost lifetime earnings associated with IQ loss. By contrast, calculations that do not assume an 'effect' threshold suggest a total loss of **0.9m – 2.0m IQ points**, at a cost of **£14-33bn in lost lifetime earnings (£30,000-42,000 per person)**.

Where thresholds are accounted for, **43 (25 – 64) additional cases of MMR** are calculated, corresponding to **16 (9 – 23) DALYs** and a **lifetime cost of £12-65m (£16-83 per person)**. Calculations where no thresholds are considered estimate an **additional 3,000 – 9,000 MMR cases**, equating to **1,000 – 3,000 DALYs** at a **lifetime cost of £2-9bn (£2,000-12,000 per person)**.

As mentioned in Section 6.2, there is continued uncertainty concerning impacts at very low blood lead levels, and these results highlight the importance of further consideration of effect thresholds in future scientific research and valuation work. Where established 'effect' thresholds are considered, calculated costs and impacts are comparatively low, while figures based on no assumed 'effect' thresholds are over an order of magnitude higher. The uncertainties associated with estimating and valuing IQ impacts are detailed in Section 6.5.4.

Table 6-3 IQ loss and MMR impacts and costs from lead exposure

Impact or cost	Lanphear et al. (2019) DRF	Lanphear et al. (2019) DRF, assuming no 'effect' threshold	Surkan et al. (2007) DRF, assuming no 'effect' threshold
Total IQ points lost	11,000 (6,000 – 15,000)[241]	1,500,000 (900,000 - 2,000,000)[242]	1,900,000[242]
Discounted lifetime loss of earnings from IQ loss	£169,000,000 (£102,000,000 - £236,000,000)[243]	£23,000,000,000 (£14,000,000,000 - £33,000,000,000)[244]	£31,000,000,000[244]

[237] HM Treasury (2020). The Green Book: Central Government Guidance on Appraisal and Evaluation. https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent

[238] Health and Safety Executive (2020). A scoping study on the valuation of risks to life and health: the monetary Value of a Life Year (VOLY). https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/903543/voly-scoping_study-report.pdf

[239] 3.5% for years 0-30; 3.0% for years 31-75; 2.5% for years 76-125.

[240] The DALY valuation is a willingness-to-pay value. Discounting is applied on the assumption that the willingness-to-pay value will increase over time in line with incomes. An inflation rate of 2% is used as a proxy.

[241] Rounded to the nearest 1,000.

[242] Rounded to the nearest 1,000,000

[243] Rounded to the nearest £1,000,000

[244] Rounded to the nearest £1,000,000,000

Impact or cost	Lanphear et al. (2019) DRF	Lanphear et al. (2019) DRF, assuming no 'effect' threshold	Surkan et al. (2007) DRF, assuming no 'effect' threshold
Discounted lifetime loss of earnings from IQ loss per person	£218 (£132 - £304)	£30,000 (£18,000 - £42,000)[245]	£40,000[245]
MMR cases	43 (25 – 64)	6,000 (3,000 – 9,000)[241]	8,000[241]
DALYs from MMR cases (2019)	16 (9 – 23)	2,000 (1,000 – 3,000)[241]	3,000[241]
Discounted lifetime cost of DALYs to study population	£21,000,000 (£12,000,000 - £31,000,000)[243]	£3,000,000,000 (£2,000,000,000 - £4,000,000,000)[244]	£4,000,000,000[244]
Discounted lifetime cost of DALYs per person	£28 (£16 - £40)	£4,000 (£2,000 - £6,000)[241]	£5,000[241]
Undiscounted lifetime cost of DALYs to study population	£44,000,000 (£25,000,000 - £65,000,000)[243]	£6,000,000,000 (£4,000,000,000 - £9,000,000,000)[244]	£8,000,000,000[244]
Undiscounted lifetime cost of DALYs per person	£57 (£33 - £83)	£8,000 (£5,000 - £12,000)[241]	£11,000[241]

Note: lifetime loss of earning valuation is based on a discounted figure; it is not clear what discount rate this figure was based on. All costs are presented in 2019 prices. Impacts and costs using the Lanphear et al. (2019) DRF are presented as a range based on DRF confidence intervals.

6.5.3 Key assumptions

A number of data sources were reviewed in order to determine UK blood lead levels. The UK Health Security Agency (formerly Public Health England) conducts regular monitoring of childhood blood lead levels through the Lead Exposure in Children Surveillance System (LEICSS)[246], although this is focused on cases of acute lead exposure and is not a suitable representation of general lead exposure in the UK. In the absence of any recent UK biomarker data, calculations used blood lead level measurements taken from a population of students in Munster by the German Environmental Specimen Bank in 2019. This dataset, which has been continuously collected since 1984, indicates that blood lead levels have consistently decreased over the last 35 years. Considering the similar legislation tackling lead pollution in Germany and the UK, these data were considered an adequate approximation of UK blood lead levels (see Section 6.5.4).

The approach makes use of probabilistic simulation modelling in order to determine populations at risk of impacts. This includes the assumption that population BLLs follow a log-normal distribution. While information on population BLL distribution in the UK is not available, this is a generalisation based on trends observed in previous BLL monitoring studies[247,248].

6.5.4 Uncertainties and limitations of the approach

There is potential for uncertainty in the results due to the numerous input parameters and the underlying uncertainties associated with each.

As mentioned in Section 6.5.3, no UK biomonitoring data were available to represent UK population BLLs in the calculations, and the approach has relied on biomonitoring conducted in Germany. Moreover, the

[245] Rounded to the nearest £1,000.
[246] UK Healthy Security Agency (2021). Lead exposure in children: surveillance reports (from 2021). https://www.gov.uk/government/publications/lead-exposure-in-children-surveillance-reports-from-2021
[247] Ericson et al. (2021) Blood lead levels in low-income and middle-income countries: a systematic review, The Lancet Planetary Health, Volume 5(3), E145-E153. https://doi.org/10.1016/S2542-5196(20)30278-3
[248] Rudnai (2009). Levels of lead in children's blood. https://www.euro.who.int/__data/assets/pdf_file/0003/97050/4.5.-Levels-of-lead-in-childrens-blood-EDITING_layouted.pdf

German data is based on a small sample size (n=123). Previous impact quantification and valuation work concluded that the German dataset is likely to be broadly representative of lead exposure across Europe[249], and it has been used in EU-wide assessment. Nevertheless, there is scope for further work in more accurately ascertaining general population exposure.

As outlined in Section 6.2, uncertainty persists concerning the IQ impacts at very low BLLs. Proposed dose-response functions often include BLL 'effect' thresholds beneath which there are no observed IQ impacts; these thresholds are higher than the mean BLL value used in the quantification, hence calculations accounting for thresholds suggest much smaller impacts and costs. Increasingly, there are suggestions that there may be no BLL 'effect' thresholds[185, 186], which suggests ongoing damage may be occurring to cohorts of children. To address this uncertainty, dose-response functions have also been applied assuming no safety threshold, and a range of impacts and costs is presented (Section 6.5.2).

Valuation of IQ loss is based on estimated losses in lifetime earnings associated with reduced cognitive ability. There are multiple areas of uncertainty in using these valuations. Determining individual IQ scores is difficult, partly due to the different scoring methodologies that can be applied. The uncertainty associated with an individual IQ score is likely to exceed the incremental IQ changes estimated. Once IQ scores are known, there are added uncertainties in objectively determining productivity losses associated with incremental IQ reductions and, in turn, the loss of earnings. The approach adopted in the existing methodologies assumes an empirical link between the three, which is not proven. Several factors besides IQ may account for earnings and for productivity.

Additionally, whilst the overall approach may be valid for the assessment of large, historical reductions in lead exposure associated with the phase-out of leaded petrol, the significant uncertainties raise questions over the assessment of more recent, considerably lower BLLs and the associated incremental IQ reductions. Consequently, it is necessary to understand the results in this chapter in the context of this uncertainty and to interpret them as an indicator of the level of burden, pending further assessment (see section 6.10).

Similar issues are associated with the calculation of additional MMR cases, where marginal reductions in IQ scores associated with lead exposure result in cases where IQ crosses the 70 threshold into the MMR bracket. In these instances, impacts associated with DALYs have been valued, but in practice it can be questioned whether crossing the MMR marginal differences between IQ scores of 69, 70 and 71 have a tangible impact to the individual. While this approach may be robust in assessing larger IQ shifts associated with longer-term, historical changes in lead exposure, there is significant uncertainty in applying the same method to marginal IQ changes resulting from low exposure levels. Consequently, impacts associated with MMR must similarly be interpreted with caution and as indicative of the overall burden.

6.6 Mercury impacts on IQ loss and MMR

6.6.1 Approach

Published studies have defined the relationship between levels of mercury in the hair of pregnant women and IQ loss of the subsequent child via prenatal exposure. It has been possible to quantify impacts and costs following an approach using dose-response functions similar to that above lead (Section 6.5.1). The method involves:

- Defining the dose-response functions between maternal hair mercury concentrations and loss of IQ points;
- Ascertaining the size of the childhood population. For the purposes of assessment, this has been assumed to be an annual birth cohort 2012;

[249] European Commission (2017) Study on the cumulative health and environmental benefits of chemical legislation: Final report. https://op.europa.eu/en/publication-detail/-/publication/b43d720c-9db0-11e7-b92d-01aa75ed71a1/language-en

- Determining maternal hair mercury concentrations in the study population; and
- Applying dose-response functions to maternal hair mercury, and multiplying by the population size to calculate the total number of lost IQ points.

The dose-response functions set out in Table 6-2 , defined by Bellanger et al. (2013)[191] and Axelrad et al. (2007)[192], were used in the quantification. As a sensitivity test, the dose-response function expressed by Bellanger et al. (2013), which has an 'effect' threshold of 0.58 µg/g of maternal hair mercury, was also used assuming no 'effect' threshold.

Data on total live births for 2012 for England and Wales, Scotland, and Northern Ireland were obtained from the ONS[225], National Records of Scotland[226], and the Northern Ireland Statistics and Research Agency[227], respectively. Maternal hair mercury concentrations for the UK were obtained from data collected as part of the 'Demonstration of a Study to Coordinate and Perform Human Biomonitoring on a European Scale' (DEMOCOPHES) study[250]. This study ran between 2010 and 2012, impacts and costs have been calculated for 2012 and all other input data have been obtained for 2012.

Where DRF 'effect' thresholds were accounted for in calculations, probabilistic simulation modelling was used to estimate the fraction of the population falling beneath the threshold and for whom effects could be disregarded. In line with previous studies on maternal hair mercury and IQ loss[191,199,251], population maternal hair mercury concentrations were assumed to follow a log-normal distribution.

The same discounted lifetime loss of earning figures used in quantifying costs of IQ loss from lead (Section 6.5.1) were adjusted to 2012 prices and used to put a value on IQ loss from prenatal mercury exposure. As biomonitoring data are from 2012, costs have been calculated for this year in 2012 prices.

The number of additional cases of MMR attributable to prenatal mercury exposure, as well as the associated lifetime costs expressed in 2012 prices, were calculated following the same approach used in calculating MMR impacts and costs from lead.

6.6.2 Results

Impacts and costs associated with IQ loss and MMR due to mercury exposure are displayed in Table 6-4. As with impacts and costs calculated for lead exposure (Section 6.5.2), results based on an assumption of no 'effect' threshold are considerably higher than results where a potential 'effect' threshold is accounted for.

Where an 'effect' threshold is considered, IQ loss totals **6 points**, at a cost of **£80,000 in lost lifetime earnings (this equates to less than a £1 per person)**. As such, where a threshold is considered, impacts are effectively negligible. By contrast, where 'effect' thresholds are not considered, IQ loss is estimated at **1,000 – 54,000 points**, representing a loss in lifetime earnings of **£18-761m (£22-936 per person)**.

After rounding, **0 additional MMR cases** are estimated when accounting for 'effect' thresholds. This translates to a lifetime cost of **£9,000-£18,000 (again, this equates to less than £1 per person)**. Conversely, where 'effect' thresholds are disregarded, additional MMR cases are calculated at **5 – 195**, corresponding to a lifetime cost of **£2-176m (£2-216 per person)**.

[250] Castaño et al. (2015) Fish consumption patterns and hair mercury levels in children and their mothers in 17 EU countries Appendix A. Supplementary material, Environmental Research, Volume 141, 58-68. https://doi.org/10.1016/j.envres.2014.10.029
[251] Grandjean et al. (2012) Calculation of mercury's effects on neurodevelopment, Environmental Health Perspectives, Volume 120(12), A452. http://dx.doi.org/10.1289/ehp.1206033

Table 6-4 IQ loss and MMR impacts and costs from mercury exposure

Impact or cost	Bellanger et al. (2013) DRF	Bellanger et al. (2013) DRF, assuming no 'effect' threshold	Axelrad et al. (2007) DRF
Total IQ points lost	6	19,000[252]	26,000 (1,000 – 54,000)[252]
Discounted lifetime loss of earnings from IQ loss	£80,000[253]	£268,000,000[254]	£362,000,000 (£18,000,000 - £761,000,000) [254]
Discounted lifetime loss of earnings from IQ loss per person	£0	£329	£446 (£22 - £936)
MMR cases	0	68	92 (5 – 195)
DALYs from MMR cases (2012)	0	25	33 (2 – 70)
Discounted lifetime cost of DALYs to study population	£9,000[253]	£30,000,000[254]	£40,000,000 (£2,000,000 - £85,000,000) [254]
Discounted lifetime cost of DALYs per person	£0	£37	£50 (£2 - £105)
Undiscounted lifetime cost of DALYs to study population	£18,000[253]	£62,000,000[254]	£84,000,000 (£4,000,000 - £176,000,000) [254]
Undiscounted lifetime cost of DALYs per person	£0	£76	£103 (£5 - £216)

Note: lifetime loss of earning valuation is based on a discounted figure; it is not clear what discount rate this figure was based on. All costs are presented in 2012 prices. Impacts and costs using the Axelrad et al. (2007) DRF are presented as a range based on DRF confidence intervals.

6.6.3 Key assumptions

Following a similar approach as used in assessing lead impacts, the quantification of impacts and costs from mercury on IQ included use of probabilistic simulation modelling to determine the size of the population at risk of impacts. As part of this, maternal hair mercury concentrations were assumed to follow a log-normal distribution.

6.6.4 Uncertainties and limitations of the approach

There are multiple uncertainties associated with placing an economic value on IQ and productivity loss; these are discussed in Section 6.5.4.

UK hair mercury data from the DEMOCOPHES study (2010-2012) were used to represent maternal hair mercury concentrations. The DEMOCOPHES dataset for the UK covers only a small sample (n=21), but the UK figures appear consistent with concentrations from other northern and western European countries[250]. Nonetheless, data from a study with such a small sample size present a source of further uncertainty in calculations. Furthermore, as the DEMOCOPHES study ended in 2012, the data are quite old. To avoid making questionable assumptions on trends in maternal hair mercury after 2012, projections of maternal hair mercury in more recent years were not produced; instead, impacts and costs were quantified for the year that data were collected. This highlights the need for more recent, more extensive mercury biomonitoring in the UK.

[252] Rounded to the nearest 1,000.
[253] Rounded to the nearest £1,000.
[254] Rounded to the nearest £1,000,000.

6.7 Arsenic impacts on IQ loss

6.7.1 Approach

The National Atmospheric Emissions Inventory (NAEI)[255] includes data on arsenic emissions in the UK (latest year of data 2019). The data show that emissions have declined steadily from 0.08 kt in 1970. Nedellec and Rabl (2016)[236] have estimated damage costs associating arsenic emissions with discounted lifetime earning losses[256] resulting from IQ loss. Converting these figures to 2019 costs (GBP) and multiplying by total emissions, the cost of lifetime earning losses from IQ reduction associated with 2019 arsenic emission has been estimated.

6.7.2 Results

Arsenic emissions in the UK were 0.015 kt in 2019[255]. Discounted lifetime earnings loss damage costs for arsenic emissions are estimated at £711 (2019 prices, where an 'effect' threshold is accounted for in the costs) and £885 (2019 prices, where no 'effect' threshold is accounted for). Discounted lifetime loss of earnings arising from arsenic emissions are therefore estimated at **£11-13m**.

6.7.3 Key assumptions, uncertainties and limitations of approach

There are multiple uncertainties associated with placing an economic value on IQ and productivity loss; these are discussed in Section 6.5.4. As such the values should be treated with caution. The calculations presented are based solely on UK arsenic emissions, therefore the calculated costs do not account for transboundary emissions.

6.8 Impacts of lead, perfluorinated chemicals (PFCs) and pesticides on ADHD

6.8.1 Approach

Fractions of ADHD attributable to lead, perfluorinated compounds (PFCs) and pesticides exposure have been previously estimated[257]. These are 6.6%, 23.2% and 22.7% respectively. These fractions were applied to UK 2020 birth data, along with data on UK ADHD incidence rates[258], to calculate the total number of cases of ADHD attributable to the three substances in the 2020 birth cohort. There are significant uncertainties associated with this approach which are discussed in Section 6.8.4.

Subsequently, a disability weight of 0.05, as proposed by the Institute of Health Metrics and Evaluation[259], was applied to the case numbers to calculate the number of DALYs per year attributable to ADHD. Costs were calculated using a willingness-to-pay cost per DALY figure (adjusted for inflation to 2020[234]; see Section 6.5.1). The costs of DALYs over a lifetime were then calculated assuming a duration of illness of 77.6 year[260]. A declining discount rate was applied along with a 2% inflation rate, as per UK Government Guidance[261]. In addition, undiscounted costs were also calculated for comparison, applying only the inflation rate.

6.8.2 Results

[255] National Atmospheric Emissions Inventory (2022). UK emissions data selector. https://naei.beis.gov.uk/data/data-selector-results?q=153596
[256] It is not known what discount rate was applied in calculating these figures.
[257] Trasande & Liu (2011) Reducing the staggering costs of environmental disease in children, estimated at $76.6 billion in 2008 Methodological Appendix, Health Affairs, Volume 30(5), 863-870. https://doi.org/10.1377/hlthaff.2010.1239
[258] NHS (2018) Delivering effective services for children and young people with ADHD. https://www.england.nhs.uk/north-west/wp-content/uploads/sites/48/2019/03/GM-wide-ADHD-guidance.pdf
[259] Institute of Health Metrics and Evaluation (2019) Global Burden of Disease Study 2019 (GBD) Disability Weights. http://ghdx.healthdata.org/record/ihme-data/gbd-2019-disability-weights
[260] In the absence of specific figures for ADHD, duration of illness has been assumed to be the same as for MMR.
[261] HM Treasury (2020). The Green Book: Central Government Guidance on Appraisal and Evaluation. https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent

Costs of ADHD attributable to exposure to lead, PFCs and pesticides are presented in Table 6-5. Based on ADHD incidence rates in the UK, lead exposure is estimated to result in **1,000-2,000 cases of ADHD (associated with between 61-101 DALYs)**, at a lifetime cost of **£88-302m** associated with exposure at birth, assuming a duration-of-illness of 77.6 years. Estimates for exposure to PFCs and pesticides accounted for a further **5,000-8,000 cases (213-356 DALYs)** and **5,000-8,000 cases (209-348 DALYs)** respectively. The associated lifetime costs are estimated at **£0.3-1.1bn** for PFCs and **£0.3-1.0bn** for pesticides.

Table 6-5 ADHD impacts and costs from lead, PFCs and pesticides exposure to the 2020 birth cohort

Substance	Attributable ADHD cases (2020)[262]	DALYs (2020)	Discounted lifetime cost of DALYs[263]	Undiscounted lifetime cost of DALYs
Lead (lower estimate)	1,000	61	£88,000,000	£181,000,000[263]
Lead (upper estimate)	2,000	101	£146,000,000	£302,000,000[263]
PFCs (lower estimate)	5,000	213	£309,000,000	£638,000,000[264]
PFCs (upper estimate)	8,000	356	£514,000,000	£1,100,000,000[264]
Pesticides (lower estimate)	5,000	209	£302,000,000	£624,000,000[264]
Pesticides (upper estimate)	8,000	348	£503,000,000	£1,000,000,000[264]

6.8.3 Key assumptions

NHS statistics indicate that the UK ADHD incidence rate is between 3-5%[258]. In order to account for this range, an upper and lower estimate has been calculated for impacts and costs. As noted earlier although increasing ADHD is underdiagnosed. The role of genetic predisposition alongside other factors are not fully understood.

6.8.4 Uncertainties and limitations of the approach

The method is based on environmentally attributable fractions of ADHD to lead, PFCs and pesticides elucidated by Trasande & Liu (2011)[257]. These have been calculated based on data gathered in the USA through the National Health and Nutrition Examination Survey (NHANES). In the absence of any other data specific to the UK, these fractions have been adopted, but they are not representative of UK exposure and, as such, are a further source of uncertainty. Further, where attributable fractions represent a broader basket of chemicals, as in the case of PFCs and pesticides, there is added uncertainty in applying a 'blanket' approach to such wide categorisations. Due to the lack of stronger evidence on the linkages between these substances and ADHD, scope for applying a more robust approach is limited, and the figures presented above must be understood within the context of these uncertainties. This highlights the scope for further research into the neurodevelopmental effects of poorly understood substances, detailed in Section 6.10.

[262] Rounded to the nearest 1,000.
[263] Rounded to the nearest £1,000,000.
[264] Rounded to the nearest £100,000,000.

6.9 Summary

Table 6-6 summarises the neurodevelopmental impacts and costs of chemicals pollution, and identifies the valuation methodology applied. There are significant uncertainties with these results, including between marginal changes in IQ, productivity, and earnings, and the use of attributable fractions. It is necessary to understand these results against the backdrop of these uncertainties, which are detailed in Sections 6.5.4, 6.6.4, 6.7.3 and 6.8.4.

Figures for IQ loss and MMR associated with lead and mercury, displayed in Table 6-6, vary significantly. The assessment has accounted for both the hypothesised existence and non-existence of 'effect' thresholds between lead and mercury exposure, and IQ loss. The majority of the study populations were exposed to lead and mercury levels below the threshold values, therefore by adopting these alternate assumptions a significant disparity emerges in estimated impacts and costs. In order to estimate costs with greater certainty in future and develop a more robust basis for directing chemicals policy action, research priorities are set out in Section 6.10.3.

Table 6-6 Summary of neurodevelopmental impacts and costs

Effect	Substance	Impact metric	Impact	Cost(s)[265]	Cost valuation
IQ loss	Lead	IQ points lost for a cohort of five-year olds, 2019	6,000[266] – 2,000,000[267]	£102,000,000[268] - £33,000,000,000[269]	Lifetime loss of earnings (2019)
IQ loss	Mercury	IQ points lost for an annual birth cohort, 2012	6 – 54,000[266]	£80,000[270] - £761,000,000[268]	Lifetime loss of earnings (2012)
IQ loss	Arsenic	-	-	£11,000,000 - £13,000,000[268]	Lifetime loss of earnings (2019)
MMR	Lead	DALYs per year for a cohort of five-year olds, 2019	9 – 3,000[266]	£12,000,000[268] - £4,000,000,000[269]	Lifetime cost (2019) (willingness-to-pay)
MMR	Mercury	DALYs per year for an annual birth cohort, 2012	0 – 70	£9,000[270] - £85,000,000[268]	Lifetime cost (2012) (willingness-to-pay)

[265] Lifetime costs are based on a WTP valuation, and assume a discount rate of 3.5% for years 0-30, 3.0% for years 31-75 and 2.5% for years 76-125, and a 2% annual inflation rate. Discounted lifetime losses of earnings are based on a valuation per IQ point which is already discounted over lifetime; it is not clear what discount rate was used to arrive at this figure.
[266] Rounded to the nearest 1,000.
[267] Rounded to the nearest 1,000,000.
[268] Rounded to the nearest £1,000,000.
[269] Rounded to the nearest £1,000,000,000.
[270] Rounded to the nearest £1,000.

Effect	Substance	Impact metric	Impact	Cost(s)[265]	Cost valuation
ADHD	Lead	DALYs per year for an annual birth cohort, 2020	61 – 101	£88,000,000 - £146,000,000[268]	Lifetime cost (2020) (willingness-to-pay)
ADHD	PFCs	DALYs per year for an annual birth cohort, 2020	213 – 356	£309,000,000 - £514,000,000[268]	Lifetime cost (2020) (willingness-to-pay)
ADHD	Pesticides	DALYs per year for an annual birth cohort, 2020	209 – 348	£302,000,000 - £503,000,000[268]	Lifetime cost (2020) (willingness-to-pay)

6.10 Future research priorities

6.10.1 Improved understanding of neurotoxicants

A key issue in estimating neurodevelopmental impacts and costs is the lack of information on substances of concern. This assessment has focused on six substances for which links to neurodevelopmental have been more clearly explored and defined, but there are more substances where weaker links are proposed with neurodevelopmental impacts, or where the evidence base is not yet established. Likewise, there are likely many more substances linked with neurodevelopmental impacts which have not been documented at all. An assessment in 2017 concluded that there are over 200 chemicals known to be neurotoxic in human beings with various degrees of evidence, over 1,000 substances known to be neurotoxic in animal experiments, and potentially many more as yet unidentified neurotoxicants in the wider 'chemicals universe', which numbers in the tens of thousands of substances[249].

Further research could more clearly establish the links between substances and neurodevelopmental outcomes. Initially, a detailed evidence review could be undertaken to classify substances into two categories: known neurotoxicants where impacts are not yet fully clarified (such as PFCs); and substances with suspected neurodevelopmental impacts but where the evidence base is significantly lacking. The risk potential of each substance could then be assessed based on its potential for human exposure, especially among children, as well as volumes placed on UK markets. Based on the strength of the evidence linking them to neurodevelopmental outcomes as well as their risk potential, substances could be screened to prioritise evidence collection. Additional evidence could then be gathered through commissioning further testing of substances as well as sharing of data. This could also investigate factors not presently considered in this study, such as the combined effects of certain substances, and the interactions between genetic predisposition to certain neurodevelopmental outcomes and chemicals exposure.

6.10.2 Leverage the HBM4EU programme for improved UK biomonitoring

In applying approaches using dose-response functions to quantify impacts of lead and mercury exposure, it is apparent that there is an important lack of recent biomonitoring data that can form the basis of such valuation. While some ongoing monitoring of childhood BLLs is undertaken, the approach has had to rely on data from other countries, or old data. Similarly, attributable fractions used to estimate impacts on ADHD are based on biomonitoring data from the USA. Future research could focus on better determining representative exposure levels in the UK, for example, through regular biomonitoring surveys similar to those conducted by the German Environmental Specimen Bank. This would not only form a more robust basis for future impact and cost assessments; it could also provide the data required to continuously track changes in impacts from chemicals exposure. The UK is currently a lead partner in the Human Biomonitoring for the EU (HBM4EU)[271] project; an initiative aimed at generating evidence on the exposure of citizens to chemicals. The project includes an EU human biomonitoring dashboard which presents biomonitoring data from national partners in a standardised and comparable way. At present, there are no UK data available through the dashboard. Through its involvement in the HBM4EU project, the UK can benefit from the experiences of biomonitoring in other countries to develop and expand a biomonitoring system in the UK.

6.10.3 Critical assessment of thresholds for effect and between cognition and labour market outcomes

As discussed in Section 6.2, there is uncertainty over the existence of 'effect' thresholds. This is especially an issue where exposure levels are typically low and may fall beneath suggested thresholds. The present study has sought to address this by considering impacts both with and without 'effect' thresholds, but greater certainty over impacts and costs can be achieved through a better understanding of impacts at very low

[271] HBM4EU (2022). HBM4EU: Science and policy for a healthy future. https://www.hbm4eu.eu/

exposure levels. The issue of thresholds has implications for directing further policy action, even on well-studied chemicals. Where thresholds have been accounted for, the estimated costs of exposure are comparatively low. By contrast, where no thresholds have been considered, costs are significantly higher which would suggest that these substances should be prioritised for action.

Estimated costs of MMR are based on willingness-to-pay valuation, which expresses the sum of individual preferences to accept or avoid risks. It does not consider more direct financial costs such as treatment costs, educational costs, costs to families supporting impacted individuals, etc. Data to enable valuation of impacts arising from MMR are insufficient, and further exploration of these costs would facilitate a more comprehensive assessment of costs in future.

There are particular problems with the relationship between IQ effects and economic outcomes. There is significant uncertainty in valuing lost earnings as a result of IQ reductions. There are tenuous links between IQ and productivity and, in turn, earnings, especially where incremental IQ reductions are concerned . A priority would therefore be to research the extent to which marginal IQ reductions truly translate into lost earnings, and to ascertain what the likely economic impacts are. This may reveal that the marginal IQ reductions associated with average exposure to lead and mercury in the UK do not have a tangible economic impact. Should this be the case, the focus of future valuation work could shift from average exposure across the UK (as was the focus in this study) to populations where more severe impacts (and costs) may be incurred. For example, the UK Health Security Agency conducts monitoring of acute childhood lead exposure through its LEICSS system (see Section 6.5.3). This could form the basis of more targeted valuation in future looking at populations where reductions in IQ are more significant and the economic implications more concrete.

7 Cardiovascular effects

7.1 Effects

Current evidence suggests associations between chemical pollution exposure and a number of cardiovascular effects, including increases in blood pressure, ischaemic heart disease, and cerebrovascular heart disease. This section assessed these effects.

- **Increase in blood pressure** – studies have identified causal links between exposure to certain substances and increases in blood pressure. Where systolic blood pressure[272] exceeds 140 mmHG[273] and diastolic pressure[274] exceeds 90 mmHG, **hypertension** occurs. This is associated with increased risk of heart disease, stroke, kidney disease and vascular dementia[275].
- **Ischaemic heart disease** – also known as coronary heart disease, this refers to interruption of blood supply to the heart. Ischaemic heart disease is linked to a wide variety of risk factors, including diet, alcohol consumption, physical inactivity, and hypertension[276]. In 2018, ischaemic heart disease was the leading cause of mortality among men in the UK, and the second cause of death among women[277].
- **Cerebrovascular heart disease** – this refers to a variety of diseases all linked to supply of blood to the brain. They include diseases such as stroke, carotid stenosis, vertebral stenosis, intracranial stenosis and aneurysms[278].

7.2 Substances of concern

There is a large variety of factors implicated in cardiovascular health, including diet, levels of physical activity, alcohol consumption and other lifestyle factors. Consequently, there are issues in extricating the effects of chemical pollution exposure from these other factors, and the associations are not as accurately understood as for other health outcomes. Given these issues, the present assessment is constrained to the best studied, and best regulated, substances.

Links between environmental lead exposure and cardiovascular disease have been documented, and a number of mechanisms by which lead damages the cardiovascular system have been identified. Among these are increased oxidative stress and inflammation, and interference with nitric oxide signalling[279].

Based on a review of numerous different studies, Fewtrell et al. (2003)[230] have derived dose-response functions linking increases in systolic blood pressure to increases in blood lead levels (BLLs). Separate dose-response functions exist for men and women; these are displayed in Table 7-1. The dose-response functions are expressed with an 'effect' threshold of 5 µg/dL, beneath which there are assumed to be no effects on

[272] Systolic blood pressure relates to the force with which the heart pumps blood around the body. This is the higher number in a blood pressure measurement.
[273] Blood pressure measurements are expressed in millimetres of mercury (mmHG).
[274] Diastolic blood pressure refers to the resistance to blood flow in blood vessels. This is the lower number in a blood pressure measurement.
[275] NHS (2019). Overview: High blood pressure (hypertension). https://www.nhs.uk/conditions/high-blood-pressure-hypertension/
[276] NHS (2020). Overview: Coronary heart disease. https://www.nhs.uk/conditions/coronary-heart-disease/
[277] ONS (2020). Leading causes of death, UK: 2001 to 2018. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/articles/leadingcausesofdeathuk/2001to2018
[278] Frankel Cardiovascular Center (n.d.). Cerebrovascular (carotid) disease. https://www.umcvc.org/conditions-treatments/cerebrovascular-carotid-disease#:~:text=Cerebrovascular%20disease%20refers%20to%20a,blood%20vessel%20rupture%20(hemorrhage).
[279] Vaziri (2008). Mechanisms of lead-induced hypertension and cardiovascular disease, American Journal of Physiology. Hear and Circulatory Physiology, Volume 295(2), H454-465. https://doi.org/10.1152/ajpheart.00158.2008

systolic blood pressure. It is necessary to note that, while these dose-response functions are old, no more recent evidence has been identified concerning the relationship between lead and cardiovascular impacts. There are, however, more recent suggestions that there are no 'effect' thresholds and that damage could occur at lower levels of exposure[280]. This could mean that there are continued cardiovascular impacts associated with lead exposure, despite recent policy efforts which may have been coordinated assuming a threshold for effects.

Table 7-1 Dose-response functions linking lead exposure to systolic blood pressure increase

Source of dose-response function	Response function	'Effect' threshold
Fewtrell et al. (2003)[230] based on Schwartz (1995)[281]	For males: increase of 1.25 mmHG systolic blood pressure per increase of 5 µg/dL BLL up to 20 µg/dL. Increase of 3.75 mmHG above 20 µg/dL.	5 µg/dL
Fewtrell et al. (2003)[230] based on Nawrot et al., (2002)[282]	For females: increase of 0.8 mmHG systolic blood pressure per increase of 5 µg/dL BLL up to 20 µg/dL. Increase of 2.4 mmHG above 20 µg/dL.	5 µg/dL

There is also evidence to suggest links between mercury exposure and cardiovascular disease, although the relationship has not been clearly defined and is insufficient to form the basis of a quantitative analysis[283]. The primary pathway of human mercury exposure is through fish consumption, and there are difficulties in disentangling the protective cardiovascular effects of polyunsaturated fats in fish from the detrimental impacts of mercury ingestion[236]. Nevertheless, damage costs for cardiovascular mortality in Europe have been calculated for mercury emissions[236] based on willingness-to-pay valuation of mortality.

Moreover, studies have identified causal links between a suite of other chemicals and cardiovascular disease, including PCBs, dioxins and furans, PBDEs, PFOEs, bisphenol A[284] and phthalates[285]. Further exploration of the relationships are required before impacts and costs of cardiovascular effects can be reliably estimated. Additionally, other heavy metals, specifically arsenic and cadmium, are linked to cardiovascular outcomes, although the relationships have not been conclusively resolved and the mechanisms of damage not fully characterised[286, 287]. As such, these substances have been excluded from the impact and cost assessment in this section but it is necessary to note that they may be a source of ongoing cardiovascular harm in the UK, despite regulation targeting some of them.

[280] Gambelunghe et al. (2016) Low-level exposure to lead, blood pressure, and hypertension in a population-based cohort, Environmental Research, Volume 149, 157-163. https://doi.org/10.1016/j.envres.2016.05.015
[281] Schwartz (1995) Lead, blood pressure and cardiovascular disease in men, Archives of Environmental Health, Volume 50(1), 31-37. https://doi.org/10.1080/00039896.1995.9955010
[282] Nawrot et al. (2002) An epidemiological reappraisal of the association between blood pressure and blood lead: A meta-anlysis, Journal of Human Hypertension, Volume 16(2), 123-131. https://doi.org/10.1038/sj.jhh.1001300
[283] Poulin & Gibb (2008). Environmental Burden of Disease Series, No. 16: Mercury: Assessing the environmental burden of disease at national and local levels. https://apps.who.int/iris/handle/10665/43875
[284] Zeliger (2013). Lipophilic chemical exposure as a cause of cardiovascular disease, Interdisciplinary Toxicology, Volume 6(2), 55-62. https://dx.doi.org/10.2478%2Fintox-2013-0010
[285] Mariana & Cairrao (2020). Phthalates implications in the cardiovascular system, Journal of Cardiovascular Development and Disease, 7(3), 26. https://dx.doi.org/10.3390%2Fjcdd7030026
[286] Solenkova et al. (2014) Metal pollutants and cardiovascular disease: Mechanisms and consequences of exposure, American Heart Journal, Volume 168(6), 812-822. https://doi.org/10.1016/j.ahj.2014.07.007
[287] da Cunha Martins Jr et al. (2018) Arsenic, cadmium, and mercury-induced hypertension: Mechanisms and epidemiological findings. Journal of Toxicology and Environmental Health Part B, Volume 21(2), https://doi.org/10.1080/10937404.2018.1432025

7.3 Major uses

The main uses of lead and mercury in the UK are set out in Section 6.3. Metallic lead is used in batteries, cables, solders, ammunition, radiation shielding, and electronic and optical technology. Lead compounds are used in colour pigments, enamels and ceramics, and as a plasticiser in PVC, although these uses are noted as declining[200]. Following legislative restrictions, mercury continues to be used in dental amalgam fillings and mercury-added products (MAPs).

PCBs are banned in the UK and must be disposed of unless they are covered by exemptions in certain applications, including transformers which will be included in the ban from 31st December 2025[288]. Dioxins and furans are not manufactured intentionally, but are emitted during high temperature combustion processes where chlorine is present, especially waste incineration. NAEI data indicate that emissions of dioxins and furans has declined by over 86% between 1990-2019[289]. Prior to the introduction of restrictions, PBDEs were used as flame retardants in foams, upholstery and furnishings. Production of PBDEs in the UK ceased in 1996[290]. Bisphenol A is used in the production of polycarbonate plastics, while phthalates are used as a plasticiser in PVC products.

7.4 Current regulatory controls and remaining sources of exposure

Regulatory controls on lead and mercury are detailed in Section 6.4. UK restrictions were introduced targeting lead and its compounds in articles supplied to the general public[210], mercury in fever thermometers and other measuring devices[212], and in antifouling substances, wood preservation substances and industrial water treatment substances[213]. These restrictions are now enacted through UK REACH[214].

Other legislation targeting lead includes the Motor Fuel (Composition and Content) Regulation 1999[217], which prohibited the marketing of leaded petrol from 1st January 2000.

The UK is a signatory to the 2013 Minamata Convention on Mercury which includes a legally binding agreement to tackle mercury pollution. The EU Mercury Regulation[202] banned mercury use in a variety of products; this was transposed into UK law[218] and retained after the UK's exit from the EU[219].

PCBs were banned in the UK in 1981 with the exception of certain limited uses[288]. Restrictions were introduced on placing certain PBDEs on the market through EU REACH restrictions[291], now retained in UK law through UK REACH. Additionally, seven phthalates are restricted under UK REACH (entries 51 and 52)[292].

7.5 Lead and hypertension

7.5.1 Approach[293]

As outlined in Section 7.2, dose-response functions have been defined linking increase in systolic blood pressure with BLLs. It has therefore been possible to quantify impacts using these relationships. The overall approach adopted is very similar to that used in quantifying IQ impacts associated with lead exposure (see Section 6.5.1), and involves the following steps:

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[288] Gov.uk (2021). Polychlorinated biphenyls (PCBs): registration, disposal, labelling. https://www.gov.uk/guidance/polychlorinated-biphenyls-pcbs-registration-disposal-labelling

[289] NAEI (n.d.). About Dioxins (PCDD/F). https://naei.beis.gov.uk/overview/pollutants?pollutant_id=45

[290] Environment Agency (2019). Polybrominated diphenyl ethers (PBDEs): sources, pathways and environmental data. https://consult.environment-agency.gov.uk/++preview++/environment-and-business/challenges-and-choices/user_uploads/polybrominated-diphenyl-ethers-pressure-rbmp-2021.pdf

[291] ECHA (n.d.). Annex XVII to REACH – Conditions of restriction: Entry 45 Diphenylether, octabromo derivative. https://echa.europa.eu/documents/10162/ce525a61-dbc8-4847-965f-db4f6136d5b5

[292] Health and Safety Executive (n.d.). Restrictions under REACH. https://www.hse.gov.uk/reach/restrictions.htm

[293] Note that a list of data inputs and assumptions for this chapter is in the Appendix.

- Identifying the dose-response functions linking BLLs to increases in systolic blood pressure;
- Determining the size of the affected population. As the proposed dose-response functions relate to the age range of 20-79, the population considered is the total population in this bracket. The assessment year is 2019, as this is the latest year for which BLL data are available;
- Estimating BLLs in the UK population; and
- Applying the dose-response functions to those BLLs to estimate increases in systolic blood pressure.

The dose-response functions defined by Fewtrell et al. (2003) were used in the calculations (Table 7-1). As separate dose-response functions apply to males and females, the impacts on the male and female population have been modelled separately. The dose-response functions are defined as having an 'effect' threshold of 5 µg/dl; in order to address uncertainties associated with impacts at low BLLs, the dose-response functions have also been applied assuming no 'effect' threshold.

UK population data for males and females in the 20-79 age bracket for 2019 were obtained from the ONS[294]. It is important to note that, in the absence of adequate UK-specific lead biomonitoring data, BLLs were obtained from the German Environmental Specimen Bank[229] (see Section 6.5.1 for further details on this dataset). This creates further uncertainty as discussed in Section 7.5.3.

Where dose-response functions were applied with 'effect' thresholds, the fraction of the population exposed to lead levels beneath the assumed threshold had to be estimated. This was done using probabilistic simulation modelling, assuming a log-normal distribution of population BLLs, in line with WHO guidance[230]. This fraction of the population was then discounted from the calculations.

After systolic blood pressure increases were estimated, the number of additional cases of hypertension that may result was calculated by quantifying the number of people below the hypertension threshold (140 mmHG systolic blood pressure) that would shift above this threshold[295]. Population systolic blood pressure was assumed normally distributed with a mean of 135 mmHG and a standard deviation of 15 mmHG based on previous assessment work[249]. The approach is the same as used in calculating MMR cases; please refer to Section 6.5.1 for further detail. This process was conducted separately for the male and female populations.

Total cases of hypertension were summed from male and female calculations. DALYs resulting from hypertension in 2019 were then calculated from the case numbers assuming a disability weight of 0.2[235]. Assuming a DALY cost of £70,135 in 2019 (see Section 6.5.1 for explanation of this figure), and assuming a duration of condition of 3.6 years[235] for hypertension, discounted lifetime costs were calculated using declining discount rates and adjusting for inflation (see Section 6.5.1 for further detail on discounting and inflation). Lifetime costs have also been calculated without discounting, adjusting for inflation only, for illustration.

7.5.2 Results

Table 7-2 presents the impacts and costs of hypertension among 20-79 year olds in 2019 in the UK arising from lead exposure, discounted for the duration of disease (3.6 years). Where no 'effect' threshold is assumed, estimated impacts and cost are substantially higher.

Where an 'effect' threshold is considered, an additional **3 cases** of hypertension are estimated, corresponding to a **lifetime cost of £200,000 (less than £1 per person)** to the assessed population. Conversely, where potential 'effect' thresholds are excluded from calculations, the additional cases of

[294] ONS (2021). Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland. https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland

[295] Note an evaluation of the medical significance of such marginal changes is beyond the scope of this study, but is discussed in the limitation and future research sections.

hypertension are calculated at **618,000**. This is valued at a lifetime cost of **£39-42bn (£800-900 per person)** to the study population in 2019.

As discussed in the context of neurodevelopmental impacts in Section 6.5.2, there is uncertainty regarding health impacts of low levels of lead exposure. It is not clear what effect, if any, may occur from marginal changes in hypertension risk. The wide spread of impacts and costs presented in Table 7-2 illustrate that further research into potential 'effect' thresholds is required in order to provide greater certainty in future quantification.

Table 7-2 Hypertension impacts and costs from lead exposure

Impact or cost	Fewtrell et al. (2003) dose-response function	Fewtrell et al. (2003) dose-response function, assuming no 'effect' threshold
Hypertension cases	3	618,000[296] (approximately 4% of total UK hypertension cases)[297]
DALYs from hypertension (2019)	1	124,000[296]
Discounted lifetime cost of DALYs to study population	£200,000[298]	£39,000,000,000[299]
Discounted average lifetime cost per person	>£0	£800[300]
Undiscounted lifetime cost of DALYs to study population	£200,000[298]	£42,000,000,000[299]
Undiscounted average lifetime cost per person	>£0	£900[300]

Note: all costs are presented in 2019 prices.

7.5.3 Key assumptions, uncertainties and limitations of the approach

As discussed in Section 6.5.3, insufficient data on BLLs from the UK has meant that the present quantification has used BLL data from a population of students in Munster, Germany, from 2019 to approximate UK population exposure. While previous impact assessment work determined that this dataset is likely to be broadly representative of BLLs across Europe, future biomonitoring would help to more accurately determine levels of lead exposure in the UK.

The quantification relies on probabilistic simulation modelling to determine the impacted population size, including assumptions on population BLL distribution. This is based on statistical principles which, while informed by previous observation and monitoring of population BLLs, are ultimately a generalisation (see Section 6.5.3). This introduces further uncertainty to the method.

7.6 Mercury and cardiovascular mortality

7.6.1 Approach

[296] Rounded to the nearest 1,000.
[297] Based on 2019 estimates that around 14.4 million people in the UK have high blood pressure. British Heart Foundation (2019). Four million people are living with untreated high blood pressure, new estimates show. https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2019/may/four-million-people-are-living-with-untreated-high-blood-pressure
[298] Rounded to the nearest £100,000.
[299] Rounded to the nearest £1,000,000,000.
[300] Rounded to the nearest £100.

The NAEI[301] includes data on mercury emissions in the UK covering the period 1970-2019. Over this time, emissions have steadily declined from 0.062 kt to 0.004 kt. Nedellec and Rabl (2016)[236] have estimated damage costs associating mercury emissions with cardiovascular mortality; these are willingness-to-pay costs based on stated-preference surveys. Separate costs have been calculated assuming a response 'effect' threshold, and assuming no response 'effect' threshold. In addition, Nedellec and Rabl recommend discounting costs over a ten-year period to account for the lag in mortality following exposure. These figures were converted to 2019 costs (GBP).

Costs of UK mercury emissions in terms of cardiovascular mortality have been calculated using the above data. Costs have been calculated assuming both a response 'effect' threshold, and no 'effect' threshold. Similarly, costs have been estimated both with and without an assumed ten-year lag period (in line with the approach in the Nedellec and Rabl (2016) study), and assuming declining discount rates[239] and an inflation rate of 2.0% in line with HMT Green Book guidance. Finally, costs have been calculated assuming a ten-year lag period without applying a discount rate, accounting only for inflation.

7.6.2 Results

Mercury emissions in the UK were 0.004 kt in 2019[301]. Discounted costs for mortality from mercury emissions are estimated at £16,998 (2019 prices, assuming 'effect' threshold) and £38,632 (2019 prices, assuming no 'effect' threshold). Using this data costs relating to current and future exposure from 2019 mercury exposure were estimated. Discounted costs of mortality from 2019 mercury emissions, assuming a ten-year lag period, are estimated at around **£90m**[302] where no 'effect' threshold is considered, and **£40m**[302] where a threshold is considered. Undiscounted costs from 2019 emissions, assuming no lag period, are estimated at **£127m**[302] (no 'effect' threshold') and **£56m**[302] ('effect' threshold). Where no lag period is assumed between mercury exposure and cardiovascular mortality (that is, mortality, and no discount rate is applied, costs are estimated at **£155m**[302] (no 'effect' threshold) and **£70m**[302] ('effect' threshold).

7.6.3 Key assumptions, uncertainties and limitations of the approach

Given that one of the primary pathways of mercury exposure is consumption of seafood, it is probable that exposure to mercury in the UK is also a result of emissions in other countries that reach marine ecosystems, not just emissions from sources in the UK. It is not known to what extent UK mercury exposure is a result of mercury emissions from non-UK sources, and further research in this area could enhance understanding and improve future estimations of impacts and costs.

7.7 Lead and ischaemic heart disease and stroke

7.7.1 Approach

The WHO estimates the fraction of global DALYs from stroke and ischaemic heart disease attributable to lead exposure at 5% and 4% respectively[303]. These fractions are based on comparative risk assessment methods. In addition, research into disease burdens conducted by the WHO[304] provides estimates of DALYs from stroke and ischaemic heart disease in the UK in 2019. The number of DALYs from stroke and ischaemic heart disease attributable to lead were estimated by applying lead-attributable fractions to total DALYs. A willingness-to-pay value for the cost of a DALY, recommended by the UK Government[237], was updated to 2019 costs (GBP) and subsequently applied to the number of DALYs to arrive at a cost for the UK. Information on the typical duration of illness for stroke and ischaemic heart disease was not identified in the

[301] National Atmospheric Emissions Inventory (2022). UK emissions data selector. https://naei.beis.gov.uk/data/data-selector-results?q=153879

[302] Rounded to the nearest £1,000,000,000.

[303] WHO (2016). Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks. https://www.who.int/publications/i/item/9789241565196

[304] WHO (2019). Global health estimates: Leading causes of DALYs. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/global-health-estimates-leading-causes-of-dalys

literature, therefore lifetime costs were not calculated. As such, it is necessary to recognise that these are costs for a single year and are not directly comparable with lifetime costs estimated in other sections.

7.7.2 Results

The number of DALYs in the UK from stroke and ischaemic heart disease attributable to lead was almost 30,000 and over 46,000 in 2019, respectively. Applying a willingness-to-pay cost per DALY of £117,623 (2019 prices), the cost of stroke in 2019 is calculated at **£2bn**, and the cost of ischaemic heart disease is **£3bn.** **There is significant uncertainty associated with these estimates, discussed below.**

7.7.3 Key assumptions, uncertainties and limitations of the approach

Lead-attributable fractions from the WHO applied in the quantification are representative of a global average, and are not specific to the UK. Further, there are no disaggregated fractions for different geographic regions or high/low income countries. The average is therefore not representative of the UK context, as it will account for countries where risk management is weaker, and where exposure is likely to be higher. As such, the 'true' attributable fractions for the UK are likely lower than those presented by the WHO. Further research into UK lead exposure levels through biomonitoring, as well as a better understanding of relationships between lead and ischaemic heart disease and stroke, could enable the development of UK-specific lead-attributable fractions. In addition, it is possible that there are other substances which cause ischaemic heart disease and stroke that have not yet been identified. Consequently, the impacts estimated from lead may only be a small fraction of the overall burden of ischaemic heart disease and stroke from chemicals pollution.

7.8 Summary

Table 7-3 summarises the cardiovascular impact and costs of chemicals pollution, and identified the valuation methodology applied. As detailed in Sections 7.5.3, 7.6.3 and 7.7.3, there are numerous sources of uncertainty in arriving at these values, including uncertainties over the 'real' value of marginal systolic blood pressure changes, and the application of global attributable fractions in the absence of UK-specific estimates. It is necessary that these sources of uncertainty are taken into account when interpreting figures.

Estimated costs of hypertension range from the £100,000s to the tens of billions. Section 7.5.1 explains that the assessment assumed both the existence and non-existence of an 'effect' threshold in the relationship between lead exposure and systolic blood pressure. As most of the study population is exposed to lead levels below the proposed threshold, the use of these alternate assumptions results in a significant disparity in the estimated impacts and costs. This presents a challenge in deciding which chemical pollution issues should be prioritised for further policy action. The presence of 'effect' thresholds is currently debated in the scientific literature (Section 7.2). This and other priorities for further research are set out in Section 7.9.

Table 7-3 Summary of cardiovascular impacts and costs

Human health effect	Substance	Impact metric	Impact	Cost(s)[305]	Cost valuation
Hypertension	Lead	DALYs per year for the adult population (age 20-79), 2019	1 – 124,000[306]	£200,000Error! Bookmark not defined. - £39,000,000,000Error! Bookmark not defined.	Lifetime cost (2019) (willingness-to-pay)
Cardiovascular mortality	Mercury	-	-	£40,000,000Error! Bookmark not defined. - £90,000,000Error! Bookmark not defined.	Cost (2019) (willingness-to-pay)
Ischaemic heart disease	Lead	DALYs per year for the total population, 2019	46,000[306]	-	Annual cost (2019) (willingness-to-pay)
Stroke	Lead	DALYs per year for the total population, 2019	30,000[306]	-	Annual cost (2019) (willingness-to-pay)

[305] Lifetime costs are based on a WTP valuation, and assume a discount rate of 3.5% for years 0-30, 3.0% for years 31-75 and 2.5% for years 76-125, and a 2% annual inflation rate.
[306] Rounded to the nearest 1,000.

7.9 Future research priorities

Section 7.2 identifies a number of substances linked with cardiovascular effects. While risk from a small group of substances, chiefly lead, are well understood with regard to their cardiovascular impacts, the extent to which a broader suite of chemicals pose a cardiovascular risk is not well understood. Due to the limited information on some of these links, this study only presents impacts and costs for lead and mercury. Future work should explore the risks posed by substances with known impacts as well as chemicals with suspected impacts in order to provide an evidence base for a broader impact assessment covering more substances. As set out in Section 6.10, an initial screening of substances can be undertaken to priorities chemicals for further testing and/or data acquisition.

There are also several areas of potential further research common to both neurodevelopmental and cardiovascular impacts; these are discussed in Section 6.10. Recent UK biomonitoring data are lacking, and further research could examine general exposure levels in the UK through regular biomonitoring. The UK could leverage its position as a lead partner in the HBM4EU project to develop a more comprehensive, continuous biomonitoring system. Where there is uncertainty over the existence of 'effect' thresholds, there is significant uncertainty in the socio-economic costs which has implications in decision-making in targeting policy action. Future research should explore impacts at very low exposure levels through additional substance testing and data sharing; this will provide greater certainty in estimates in any future impact and cost assessment work.

Similar to issues relating to marginal IQ loss, there are questions as to the "real" socio-economic value of marginal increases in systolic blood pressure, and the extent to which a systolic blood pressure of 140 mmHG (the threshold for hypertension) is significantly different from a measurement of 139 mmHG. For larger increases in systolic blood pressure which may traverse the hypertension threshold, the impacts may be more tangible, but for smaller increases associated with chemicals exposure the impacts are much more uncertain. Further research could explore the impacts and costs of marginal blood pressure increases. Finally, further work could determine the impact of emissions from overseas on the UK, where damage costs are used.

8 Respiratory effects

8.1 Effects

Respiratory diseases are a significant problem in the UK. They affect one in five people and represent the third largest cause of death[307]. Whilst there is extensive scientific literature on associations between air pollution and respiratory diseases, the evidence on specific chemical exposures and their effects is comparatively weak. As such, this section focusses on asthma, asbestosis, COPD and allergic rhinitis where rather more evidence is available. Taking each in turn:

- **Asthma** is a common long-term lung condition which involves recurrent attacks of breathlessness and wheezing, which can vary in severity and frequency. An attack involves the lining of the bronchial tubes swelling, resulting in narrowing of the airways and consequently the flow of air to and from the lungs[308]. Mukherjee et al. (2016)[309] estimate that the healthcare costs from asthma to the UK exceed £1.1 billion a year. Of this, 74% of the costs were associated with demands in provision of primary care, 13% to disability claims and 12% to hospital care. Chemical exposure is one of many contributing risk factors[310], however the causes of asthma are not completely understood.
- **Asbestosis** is a chronic lung disease caused by long-term exposure to asbestos fibres. Whilst use of asbestos was banned in the UK in 1999, asbestosis cases have continued to increase due to the long latency of the disease (often 20 to 30 years)[311]. Exposure to asbestos has created significant costs to society, including healthcare costs and insurance liabilities from compensation. Significant costs also relate to the removal of historical sources of asbestos in older buildings or renovations. UK deaths from asbestos-related diseases have continued to increase since the 1980s, with the burden of disease only beginning to reduce in the 2020's[312].
- **Chronic Obstructive pulmonary disease (COPD)** is the third leading cause of death globally and in the UK[313]. It is a growing problem; a 2016 study estimated annual direct healthcare costs in England attributable to COPD could rise from £1.5 billion in 2011 to £2.32 billion in 2030[314]. COPD comprises a group of lung conditions which cause breathing difficulties, including emphysema (damage to the alveoli) and chronic bronchitis (longer term inflammation of the airways). The main cause of COPD is smoking but whilst the association between COPD and chemical substances is relatively poorly understood, research suggests a likely role of occupational exposure[315].
- **Allergic rhinitis** produces cold-like symptoms including sneezing, itching and a blocked or runny nose. Allergens can result in symptoms which start soon after exposure.

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[307] NHS. Respiratory Diseases. https://www.england.nhs.uk/ourwork/clinical-policy/respiratory-disease/
[308] National Heart, Lung and Blood Institute. Asthma. https://www.nhlbi.nih.gov/health-topics/asthma
[309] Mukherjee, M., Stoddart, A., Gupta, R.P. *et al.* The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases. *BMC Med* **14,** 113 (2016). https://doi.org/10.1186/s12916-016-0657-8
[310] WHO. Asthma. https://www.who.int/news-room/fact-sheets/detail/asthma
[311] NHS. Asbestosis. https://www.nhs.uk/conditions/asbestosis/
[312] HSE. (2021). Asbestos-related disease statistics, Great Britain, 2021. Asbestosis, mesothelioma,asbestos related lung cancer and non-malignant pleural disease in Great Britain 2021 (hse.gov.uk)
[313] https://vizhub.healthdata.org/gbd-compare/
[314] McLean, S., Hoogendoorn, M., Hoogenveen, R., et al. (2016). Projecting the COPD population and costs in England and Scotland: 2011 to 2030. DOI: 10.1038/srep31893
[315] HSE. (n.d.) COPD causes – occupations and substances. https://www.hse.gov.uk/copd/causes.htm

The costs to the UK associated with asthma, asbestosis and COPD are estimated using a PAF, applied to a total number of DALYs associated with COPD. That PAF is estimated for occupational asthmagens and occupational exposure to particulate matter, gases and fumes (PMGF), respectively. Whilst occupational asthmagens is likely to include some chemical substance, only a small proportion of PMGF is likely to be attributable to chemical substances. This is discussed further below. The PAF for asbestosis is assumed to be 100% attributable to exposure to asbestos. Rhinitis is considered qualitatively, given even more limited data.

8.2 Substances of concern

There are various substances associated with an increase in risk or an exacerbation of symptoms of **asthma**. The most common substances associated with occupational asthmagens (OA) are isocyanates, Other substances include latex, reactive dyes, glutaraldehyde, metal-working fluids, bio aerosols, and azodicarbonamide.[316] Whilst all of these are considered under the PAF for occupational asthmagens, only some of them are within the scope of this study. Other substances associated with asthma are diisocyanates hexavalent chromium Cr(VI), p-phenylenediamine (p-PDA), polyaromatic hydrocarbons (PAHs) and organophosphate insecticides, Phthalates, per- and polyfluoroalkyl substances (PFAs), pyrethroid insecticides, mercury, cadmium, arsenic and lead have all been potentially associated.[317]

Asbestosis is caused by long term exposure to asbestos, which results in an accumulation of fine fibres of mineral dust in the lungs. This causes fibrosis of lungs and consequentially difficulty breathing.[318]

Known risk factors for exacerbating **COPD** include exposures to tobacco, infections by bacteria and viruses, and short term exposure to air pollutants (particulate matter, nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and ozone (O_3)). Extreme temperatures can also exacerbate COPD.[319] Some workplace exposures are also considered risk factors (substances of concern include asbestos, arsenic and styrene[320]).

Environmental factors associated with **allergic rhinitis** include tobacco smoke, indoor allergens, outdoor air pollution and pollen. Ozone (O_3) and Nickel have been linked to allergic rhinitis but there is insufficient evidence to quantify the associated impact.

8.3 Major uses

Limited data is available to attribute exposure to chemicals to increased risk which limits an assessment of where substances of concern are used. Various occupations are associated with an increased risk of asthma, particularly domestic and equipment cleaners. [321] Other occupations associated include animal health,

[316] Long Latency Health Risks Division. (2014). Occupational Asthmagens. https://www.hse.gov.uk/foi/internalops/og/og-00016.htm

[317] Mattila, T., Santonen, T., Andersen, H. R., Katsonouri, A., Szigeti, T., Uhl, M., Wąsowicz, W., Lange, R., Bocca, B., Ruggieri, F., Kolossa-Gehring, M., Sarigiannis, D. A., & Tolonen, H. (2021). Scoping Review-The Association between Asthma and Environmental Chemicals. *International journal of environmental research and public health*, *18*(3), 1323. https://doi.org/10.3390/ijerph18031323

[318] https://www.asbestos.com/asbestosis/

[319] Analysis of environmental risk factors for chronic obstructive pulmonary disease exacerbation: A case-crossover study (2004-2013) (plos.org)

[320] European Commission, Directorate-General for Environment, (2017) *Study on the cumulative health and environmental benefits of chemical legislation : final report*. Publications Office. https://data.europa.eu/doi/10.2779/070159

[321] Arif AA, Delclos GL, Whitehead LW, Tortolero SR, Lee ES. Occupational exposures associated with work-related asthma and work-related wheezing among U.S. workers. Am J Ind Med. 2003 Oct;44(4):368-76. doi: 10.1002/ajim.10291. PMID: 14502764.

cosmetology, farming and food production, healthcare, industrial, manufacturing or construction, laboratory and some office and educational work.[322]

Historically **asbestos** was used in roofing, thermal and electrical insulation, cement pipe and sheets, flooring, gaskets, friction materials, coating and compounds, plastics, textiles, paper, mastics, thread, fibre jointing and millboard.[323] Asbestos is still found in UK industrial or residential buildings built before its ban in the 1999 with potential risks associated with demolition or refurbishment.[324] Occupations known to have an increased risk of **COPD** include mining, construction, foundry, welding, steel, textiles (especially cotton) and farming.[325]

8.4 Current regulatory controls and remaining sources of exposure

UK cases of asbestosis have continued to increase despite a ban in 1999, illustrating the significant long-term costs that can occur even when regulatory action is promptly taken on an identified risk. Various action has been taken in the UK against several substances understood to be associated with respiratory (and other) burdens. Use of lead, mercury and cadmium in cosmetics has been banned since 1976 with additional waste risk management measures in place from 1978. From 1983, use was restricted in products which come into contact with food.

Integrated Pollution Prevention and Control (IPPC) under the Environmental Protection Act 1990, followed by the Industrial Emissions Directive (from 2010) (Environmental Permitting Regulations in the UK) limited emissions to the environment from industrial use in processing, whilst the REACH regulation have restricted specific uses outright. In 1972, progressive reductions of lead content in fuel began, leading to an outright ban in 2000. Limitations to mercury content in drinking water and batteries began in the early 1990s and mercury content was limited in electrical and electronic equipment from 2002. In 2008, mercury exports were banned alongside additional controls on mercury in waste.

The use of arsenic, which has been associated with COPD, was also banned in cosmetics in 1976 and industrial procession emissions reduced since 1996 via IPPC and the IED. REACH has banned various specific uses of arsenic.

Emissions limits of various VOCs have been established since 1999 through the Solvent Emission Directive and now the IED. In 2007, maximum content in paints were established, with added measures in 2011. The National Emission ceilings (NEC) directive, the Petrol Vapour Recovery Directives have both resulted in various actions and specific uses of VOCs have been prohibited through REACH. Note, this is discussed further in chapter 12. Other chemicals associated with asthma subject to regulatory control include Azodicarbonamide, glutaraldehyde and nickel.[326]

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[322] Centers for Disease Control and Prevention. (n.d.) Occupational Exposures: Asthma. https://www.cdc.gov/niosh/topics/asthma/exposures.html

[323] National Library of Medicine. Asbestos. https://webwiser.nlm.nih.gov/substance?substanceId=274&catId=24#:~:text=The%20range%20of%20applications%20in%20which%20asbestos%20has,textiles%2C%20paper%2C%20mastics%2C%20thread%2C%20fiber%20jointing%2C%20and%20millboard.

[324] https://www.hse.gov.uk/asbestos/building.htm

[325] Kraïm-Leleu M, Lesage FX, Drame M, Lebargy F, Deschamps F. Occupational Risk Factors for COPD: A Case-Control Study. PLoS One. 2016 Aug 3;11(8):e0158719. doi: 10.1371/journal.pone.0158719. PMID: 27487078; PMCID: PMC4972406.

[326] European Commission, Directorate-General for Environment, (2017) *Study on the cumulative health and environmental benefits of chemical legislation : final report*. Publications Office. https://data.europa.eu/doi/10.2779/070159

8.5 Asthma

Asthma is a significant problem across the globe, affecting more than 20% of children and 10% of adults. Its direct costs include the healthcare required to control or monitor asthma, e.g. GP and nurse consultations, prescriptions, out-patient attendances- and potentially some - ambulance services, A&E services, inpatient and day cases in hospitals, and use of intensive care units (ICUs). Indirect costs include work productivity losses, lost days in school and time or money spent on care.[327]

Risk factors of asthma

Occupational exposures, including through the use of certain chemicals (notably paints containing isocyanates), are one of multiple factors which increase the risk of developing asthma. Others include tobacco smoke, air pollution, mould and damp, pollen, animals, antibiotics and paracetamol, diet and obesity and breastfeeding alongside genetic predisposition.[328]

There is limited data available on the role of chemical exposure in developing or exacerbating asthma, partly because there is an incomplete understanding of why and how asthma itself develops. Moreover, environmental factors may have very different impacts on individuals with different genotypic susceptibilities[329]. Additional research is required on the causes of asthma, in the context of workplace practices.

Occupational asthmagens

Occupational asthma (OA) can be induced through workplace exposures either via immunological sensitization to a specific substance (sensitizer-induced OA) or via high-level exposure to an inhaled irritant (irritant-induced OA)[330]. The most common substances associated with OA are isocyanates, flour dust and wood dust. Other substances linked to OA include latex, reactive dyes, glutaraldehyde, metal-working fluids, bio aerosols, and azodicarbonamide[331]. OA is determined by a combination of environmental factors and individual genetic susceptibility. The former include the concentration and properties of the substances and the duration of exposure, as well as the conditions of exposure.

Figure 8-1 shows the trend in occupational asthma cases in Great Britain from 2002 to 2019, estimated via the number of cases reported by chest physicians to SWORD[332]. The data indicate overall decreasing trend in the number of cases since 2004, although the rate of decrease appears to have slowed since 2009 and began to rise since 2014. Whilst data from SWORD can be used as an indicator of trends, various factors may influence the number of cases reported, beyond actual changes in incidence. The number and type of participating specialists will impact the number of cases reported as not all physicians will be part of SWORD. Under reporting can occur as often only the most serious cases are reported, with milder asthma cases not being reflected in the statistics. Seasonal effects associated with the time of year can also impact the number of cases reported.

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[327] Agache, I., Jutel, M., et al. (2021). Global Atlas of Asthma 2nd Edition. European Academy of Allergy and Clinical Immunology. https://eaaci.org/documents/focusmeetings/ISAF2021/AsthmaAtlas%20II%20v1.pdf

[328] Agache, I., Jutel, M., et al. (2021). Global Atlas of Asthma 2nd Edition. European Academy of Allergy and Clinical Immunology. https://eaaci.org/documents/focusmeetings/ISAF2021/AsthmaAtlas%20II%20v1.pdf

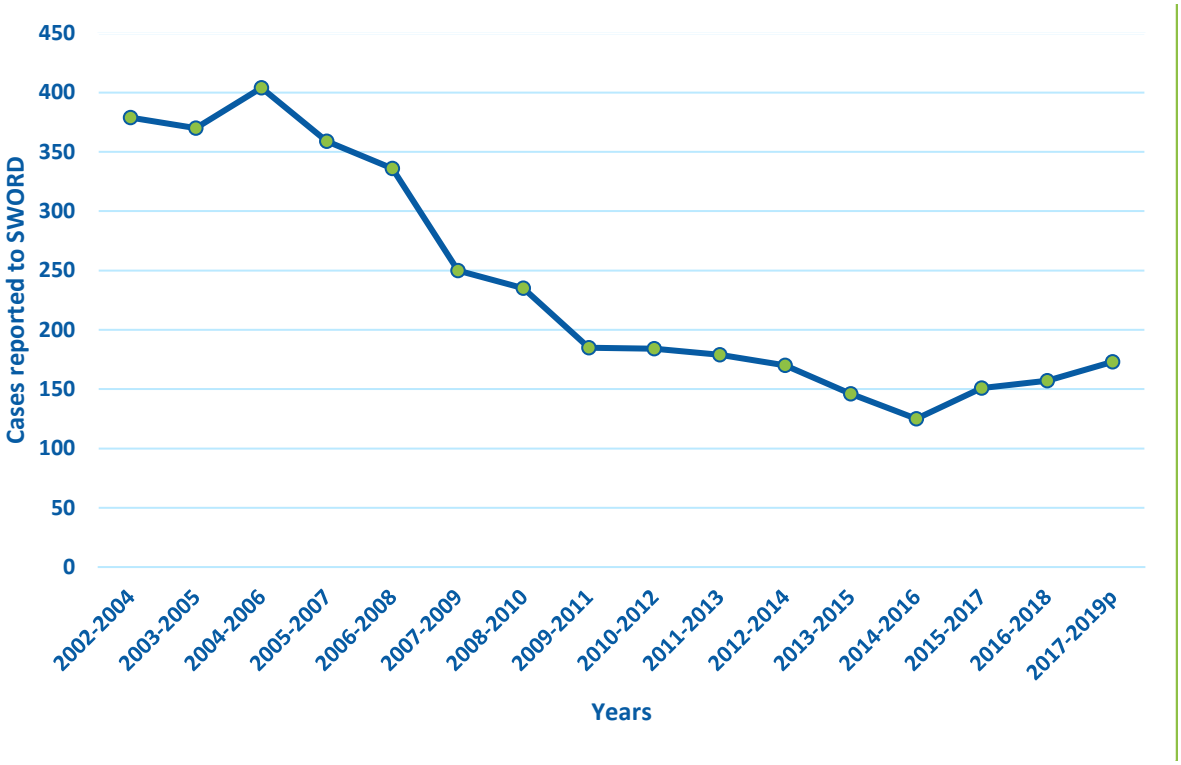
[329] Study on the cumulative health and environmental benefits of chemical legislation - Publications Office of the EU (europa.eu)

[330] Agache, I., Jutel, M., et al. (2021). Global Atlas of Asthma 2nd Edition. European Academy of Allergy and Clinical Immunology. https://eaaci.org/documents/focusmeetings/ISAF2021/AsthmaAtlas%20II%20v1.pdf

[331] Long Latency Health Risks Division. (2014). Occupational Asthmagens. https://www.hse.gov.uk/foi/internalops/og/og-00016.htm

[332] Work-related asthma statistics Great Britain, 2021. https://www.hse.gov.uk/statistics/causdis/asthma.pdf

Figure 8-1 Trend in occupational asthma cases per 100,000 workers in Great Britain (2002-2019)



Source: Work-related asthma statistics Great Britain, 2021. Note the X axis presents a rolling 3 year average. HSE https://www.hse.gov.uk/statistics/causdis/asthma.pdf

8.5.1 Approach

The approach and data for analysing the burden of occupational asthmagens is taken from the Global Burden of Disease Study (2016) [333]. IHME defines the risk of occupational asthmagens as the proportion of the population occupationally exposed to asthmagens, based on employed population distributions across nine occupational categories[334].

Analysis for the Global Burden of Disease study (2016) outlines the methodology used to estimate the global and regional burden of chronic respiratory diseases arising from "non-infectious airborne occupational exposures". This includes the burden of asthma attributable to occupational asthmagens. The associated burden was estimated using a population attributable fraction (PAF). The PAF requires information on the relative risk of asthma due to the exposure of asthmagens and the proportion of the target population exposed.

To calculate the relative risk of asthmagens, the proportion of population exposed was estimated using the proportion of the workforce in specific occupations. The ILO Labour Force database was used for data on industry of employment (based on nine categories) as well as occupation ("Background", Administration, Technical, Sales, Agriculture, Mining, Transport, Manufacturing and Services) and the proportion of the

[333] GBD 2016 Occupational Risk Factors Collaborators. (2020). Global and regional burden of chronic respiratory disease in 2016 arising from non-infectious airborne occupational exposures: a systematic analysis for the Global Burden of Disease Study 2016. Occup Environ Med. 2020 Mar; 77(3): 142–150. Published online 2020 Feb13. doi: 10.1136/oemed-2019-106013

[334] IHME. (n.d.) Occupational asthmagens – Level 3 risk. Occupational asthmagens — Level 3 risk | Institute for Health Metrics and Evaluation (healthdata.org)

population who are working.[335] In the GBD study, the RR was calculated using information from Karjalainen and Nurminen (2002) based on the Finnish population.[336] The RR for agriculture was estimated from a population-based study of occupational asthma in Europe and other high income countries by Kogevinas et al. (1999).[337] A weighted average of the separate estimates for 'farmers' and 'agricultural' workers were provided. The calculation of RR is assumed representative of the UK, as the information used is largely based on data from Finland. UK data should be produced to provide a more accurate estimate of RR.

This methodology was used as there were no suitable and valid data sources at a country or global level describing exposure to the wide range of occupational asthmagens. The counterfactual used in this analysis was people not in work and administrative workers.[338] A major limitation of this approach is due to the lack of evidence backing the RR analysis, with only one study, from 2002. This should be noted when considering the cost estimations below.

The prevalence of exposure to asthmagens was estimated using:

$$Prevalence\ of\ Exposure_{c,y,s,a} = \sum_{EA} Proportion_{occc,y} * EAP_{c,y,s}$$

Where EAP = economically active population, c = country, s = sex, OCC = occupation, y = year and a = age.

The PAF was estimated using:

$$PAF = \frac{\sum_{x=1}^{n} RR(x)P(x) - 1}{\sum_{x=1}^{n} RR(x)P(x)}$$

Where $P(x)$ is the proportion of persons exposed at level x in the relevant population and $RR(x)$ is the relative risk corresponding to exposure level x.

8.5.2 Results

Below we estimate a snapshot of costs to the UK in 2019 from asthma attributable to occupational asthmagens. Quantitative data on the role of chemical exposure in this burden is weak, and the data does not explicitly state which chemicals are included within the scope of occupational asthmagens. Potential consumer exposure is not captured. The costs are calculated via monetization of the attributable DALYs using willingness-to-pay methodology.

[335] GBD 2016 Occupational Risk Factors Collaborators. (2020). Global and regional burden of disease and injury in 2016 arising from occupational exposures: a systematic analysis for the Global Burden of Disease Study 2016. Occup Environ Med. 2020 Mar; 77(3): 133–141. Published online 2020 Feb 13. doi: 10.1136/oemed-2019-106008

[336] Karjalainen A, Kurppa K, Martikainen R, Karjalainen J, Klaukka T, Scand J. (2002). Exploration of asthma risk by occupation--extended analysis of an incidence study of the Finnish population. Work Environ Health. 2002 Feb; 28(1):49-57. DOI: 10.5271/sjweh.646

[337] Kogevinas M, Antó JM, Sunyer J, Tobias A, Kromhout H, Burney P. (1999). Occupational asthma in Europe and other industrialised areas: a population-based study. European Community Respiratory Health Survey Study Group. *Lancet; 353(9166):1750-4.*

[338] GBD 2016 Occupational Chronic Respiratory Risk Factors Collaborators. (2020). Global and regional burden of chronic respiratory disease in 2016 arising from non-infectious airborne occupational exposures: a systematic analysis for the Global Burden of Disease Study 2016. Occup Environ Med. 2020 Mar; 77(3): 142–150. Published online 2020 Feb 13. doi: 10.1136/oemed-2019-106013

Table 8-1 Asthma DALYs and costs of asthma attributable to occupational asthmagens

	DALYs and associated cost (UK, 2019)
Total asthma DALYs	Conf[339]
PAF	Conf.[340]
DALYs attributable to occupational asthmagens	Conf.
Cost per DALY	£70,135[341]
Cost of asthma cases attributable to occupational asthmagens	**Over £1 billion**

The number of DALYs from asthma in the UK in 2019 was applied to the PAF for asthma attributable to occupational asthmagens, which is assumed to include some chemicals within scope but several causes and substances which are not. The RR for occupational asthmagens is estimated using data from Finland for occupations other than agriculture, and is assumed to be representative to UK. Applying the PAF results in an estimated number of DALYs attributable to exposure to occupational asthmagens. The cost of a DALY in 2019 is estimated at £70,135 based on the UK Government's Green Book guidance[342]. The resulting cost of asthma attributable to exposure to occupational asthmagens for the UK in 2019 is estimated in the order of over **£1 billion.** Whilst some of this burden is expected to be attributable to chemical substances, it should be noted that occupational asthmagens will include other factors which are out of scope of this study.

8.5.3 Uncertainties and limitations of the approach

A major limitation of this analysis is the evidence behind the PAF calculation. There is currently a lack of evidence determining the occupational risks of asthma. The PAF used for these estimates is calculated using information on RR from a study in Finland for most occupations and a study for Europe for agriculture, which are assumed to be representative of the UK. This is a significant limitation and should be addressed in order to provide a more robust estimation of the PAF for asthma attributable to occupational asthmagens.

As mentioned above, another limitation of the approach is the use of attribution to occupational asthmagens. Occupational asthmagens will include substances which are not in the scope of 'chemicals', including dusts from flour or grain/cereal, animal feed or bedding. It is unclear as to what proportion of occupational asthmagens are attributable to in scope chemical exposure. Furthermore, another limitation of the approach is that any asthma cases attributable to chemicals outside of an occupational setting are not included within this analysis.

[339] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.
[340] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.
[341] Cost per DALY calculated based on Nedellec & Rabl (2016) and updated to 2019 prices using UK Government GDP deflators (GDP deflators at market prices, and money GDP - GOV.UK (www.gov.uk)).
Nedellec, V., and Rabl, A. (2016). Costs of Health Damage from Atmospheric Emissions of Toxic Metals: Part 1 – Methods and Results. DOI: https://doi.org/10.1111/risa.12599
[342] HM Treasury (2020). The Green Book: Central Government Guidance on Appraisal and Evaluation. https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent

Cost-of-illness analysis

Direct and indirect costs of asthma can also be calculated through considering direct costs of healthcare associated with asthma and indirect costs such as work productivity lost. Mukherjee et al. (2016)343 used national health surveys from 2010-2011 and routine administrative, health and social care datasets for 2011-12 to model the estimated direct health costs of asthma in the UK.

The costs considered are the cost of primary care consultations, hospital in-patient episodes, intensive-care unit episode and the cost of disability living allowance claims. This is estimated to cost the UK at least £1.1 billion per year, with 74% of costs for provision of primary care services (from 6.3 million consultations), 13% for disability claims (from 36,800 claims) and 12% for hospital care (from 93,000 hospital in-patient visits and 1,800 intensive care-unit episodes).

The paper notes there are significant data gaps which limit the analysis, e.g. in relation to out-patient clinic visits, presenteeism (i.e. attending work whilst unwell), and absence from work to care for children. These data gaps should be addressed to increase understanding of the scale of healthcare and societal impacts of asthma. Increased understanding of the underlying causes of asthma is needed.

Updating the costs to the UK of £1.1 billion per year (2016 prices) derived in the paper to 2019 prices , gives an annual cost of direct healthcare of £1.17 billion. The GBD (2019) gives a PAF in 2019 of 8.82% of asthma cases attributable to occupational asthmagens. Applying this suggests annual direct healthcare costs and the cost of DLA to the UK from asthma attributable to occupational asthmagens in 2019 is approximately **£100 million.**

Pavord et al. (2017)[344] estimate the total indirect cost of asthma in the UK at approximately £4.9 billion in 2011 from overall "work impairment" (from the WPAI questionnaire). This represents the total work time missed or impaired from either absenteeism or presenteeism, multiplied by the median wage figure. Updating this cost to 2019 prices (from 2016), gives an indirect cost of approximately £5.6 billion. The GBD (2019) gives a PAF in 2019 of 8.82% of asthma cases attributable to occupational asthmagens. Applying this suggests annual indirect costs related to lost productivity in the UK from asthma attributable to occupational asthmagens in 2019 are approximately **£495 million.**

8.6 Asbestosis

Exposure to asbestos fibres can result in various harmful effects including cancers such as mesothelioma and lung cancer, and other lung diseases such as asbestosis and pleural thickening. Given the delay in disease onset, current levels of asbestos-related disease reflect historic exposure. The strong relationship between asbestos exposure and the number of mesothelioma and asbestosis cases, allow a relatively simple calculation of the cost of disease attributable to asbestos. All cases of asbestosis are attributable to asbestos exposure. **Note, mesothelioma is addressed in chapter 0 on cancers.**

Asbestosis is a form of pneumoconiosis caused by the inhalation of asbestos fibres, which is characterised by scarring and inflation of the lung tissue. There is no cure, symptoms can affect normal daily activity and may

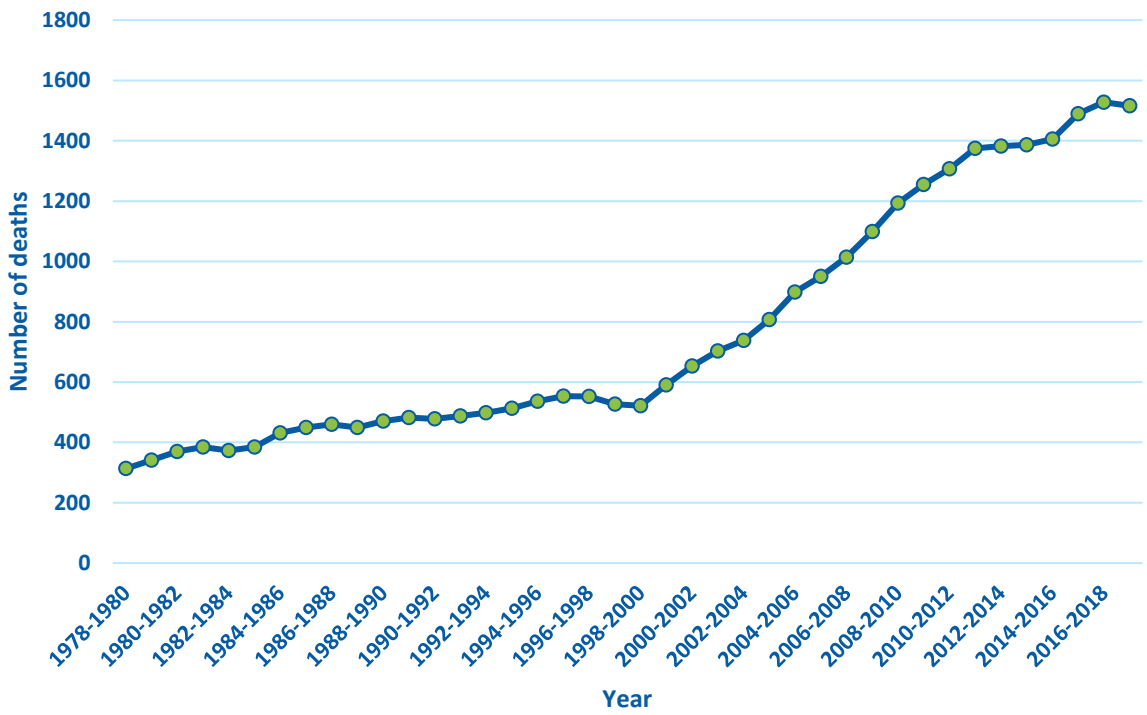
[343] Mukherjee, M., Stoddart, A., Gupta, R. P., Nwaru, B. I., Farr, A., Heaven, M., Fitzsimmons, D., Bandyopadhyay, A., Aftab, C., Simpson, C. R., Lyons, R. A., Fischbacher, C., Dibben, C., Shields, M. D., Phillips, C. J., Strachan, D. P., Davies, G. A., McKinstry, B., & Sheikh, A. (2016). The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases. *BMC medicine*, *14*(1), 113. https://doi.org/10.1186/s12916-016-0657-8

[344] Pavord, I. D., Mathieson, N., Scowcroft, A., Pedersini, R., Isherwood, G., & Price, D. (2017). The impact of poor asthma control among asthma patients treated with inhaled corticosteroids plus long-acting β_2-agonists in the United Kingdom: a cross-sectional analysis. *NPJ primary care respiratory medicine*, *27*(1), 17. https://doi.org/10.1038/s41533-017-0014-1

be fatal. In Great Britain in 2019, there were 490 deaths mentioning asbestosis on the death certificate[345] compared with around 100 per year in the late 1970s. Typically, only 2-3% of these deaths are women.

Figure 8-2 shows the trend in deaths mentioning asbestosis (excluding mesothelioma) in Great Britain since 1978[345]. The figure shows a steady increase in deaths mentioning asbestosis over the period from 1978 to 2000, followed by a large increase from 1998-2000 to 2012. Deaths appear to level off after 2012, with a signs of an initial decline from the data in 2016-2018. This strong increase in deaths following the ban of asbestos in 1999 likely reflects greater awareness and improved diagnoses, but illustrate the significant health burden, alongside the costs of removal and compensation to those affected. Compensation for a case of asbestosis also presents a significant cost burden. The value depends on the severity. Severe cases can resulting in pay-outs between £30,630 and £84,380. Milder cases seeing pay-outs typically between £12,020 and £30,630.[346]

Figure 8-2 Trend in deaths mentioning asbestosis (excl. mesothelioma) in Great Britain (1978 to 2018)



Source: Table ASIS02. Asbestos-related disease statistics, Great Britain 2021. Note the X axis presents a rolling 3 year average. https://www.hse.gov.uk/statistics/causdis/asbestos-related-disease.pdf

8.6.1 Approach to the assessment of UK costs

IHME data estimates the burden of asbestosis directly as part of the overall GBD estimates of prevalence and deaths[347]. An estimate of the number of DALYs from asbestos in the UK and associated cost per DALY were used to estimate the cost of asbestosis in the UK.

[345] HSE. (2021). Asbestos-related disease statistics, Great Britain, 2021. Asbestosis, mesothelioma,asbestos related lung cancer and non-malignant pleural disease in Great Britain 2021 (hse.gov.uk)
[346] Simpon Miller. (2019). Asbestosis Compensation Payouts Guide. Asbestosis Compensation Payouts Guide UK | Simpson Millar
[347] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.

8.6.2 Results

The table below applies an estimated number of DALYs from asbestosis in 2019 for the UK. This is all attributable to exposure to asbestos. The cost of a DALY is estimated at £70,125 in 2019 based on the value in the UK Green Book[348]. Therefore, an approximate cost to the UK is somewhere below **£300 million.**

Table 8-2 Asbestosis DALYs and costs

	DALYs and associated cost (UK, 2019)
UK DALYs attributable to exposure to asbestos	Conf[349]
Cost per DALY	£70,135[350]
Cost of UK asbestosis cases attributable to exposure to asbestos	**Below £300 million**

8.7 COPD

Chronic obstructive pulmonary disease (COPD) is a significant cause of illness and healthcare costs around the world. Known risk factors for exacerbating **COPD** include exposures to tobacco, some workplace exposure (substances of concern include asbestos, arsenic and styrene[351]), infections by bacteria and virus, and short term exposure to air pollutants (particulate matter, nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and ozone (O_3)). Extreme temperatures can also exacerbate COPD.[352] Whilst some substances in scope such as asbestos, arsenic and styrene may be included, it is likely that the vast majority of PMGF will be from air pollutants, not in the scope of this study.

8.7.1 DALYs Approach

Data for the Global burden of disease (GBD) study (2019)[353] estimates the number of COPD DALYs attributable to particulate matter, gases and fumes (PMGF). The burden for PMGF causing COPD was estimated using the PAF which was then used to estimate attributable number of DALYs. The PAF requires information on the RR of the disease due to exposure of PMGF and the proportion of the target population

[348] HM Treasury (2020). The Green Book: Central Government Guidance on Appraisal and Evaluation. https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent

[349] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.

[350] Cost per DALY calculated based on Nedellec & Rabl (2016) and updated to 2019 prices.

[351] European Commission, Directorate-General for Environment, (2017) *Study on the cumulative health and environmental benefits of chemical legislation : final report*. Publications Office. https://data.europa.eu/doi/10.2779/070159

[352] Analysis of environmental risk factors for chronic obstructive pulmonary disease exacerbation: A case-crossover study (2004-2013) (plos.org)

[353] https://vizhub.healthdata.org/gbd-compare/

exposed[354]. A limitation of this approach is that the RR estimates were based on only two studies from the United States.[355,356]

Current and historic exposures to PMGF have been shown to increase the risk of COPD. [357] The GBD study uses employment by industrial sector as the basis of exposure estimates, based on nine industry categories which also take into account historical exposure. Whilst exposure estimates were based on current industry, the proportions exposed within each industry accounted for past exposure. Estimates of proportions exposed were made for 'lower' and 'higher' levels of exposure to PMGF for high income and LMI countries. The data used to provide these estimates is limited and the expert opinion of GBD collaborators was also used to develop the estimates for the proportion of population exposed. This is a limitation of this approach and is representative of the limited research and data available linking respiratory illness to substance exposure.

A systematic review of international literature, including a meta-analysis with unpublished data, were used to estimate the RR. The reference group was persons not working and persons working in trade, finance or service industries.

The prevalence of exposure to PMGF was determined using the following equation:

$$Prevalence of Exposure_{c,y,s,a,l} = \sum_{EA} Proportion_{EAC,y} * EAP_{c,y,s} * Exposurelevelproportion_{EAl}$$

Where EAP = economically active population, c = country, s = sex, EA = economic activity, l = level of exposure, y = year and a = age.

The PAF was estimated using:

$$PAF = \frac{\sum_{x=1}^{n} RR(x)P(x) - 1}{\sum_{x=1}^{n} RR(x)P(x)}$$

Where $P(x)$ is the proportion of persons exposed at level x in the relevant population and $RR(x)$ is the relative risk corresponding to exposure level x.

8.7.2 Results

Below we estimate a snapshot of the costs to the UK in 2019 from COPD attributable to exposure to PMGF. The role of chemical exposure in this is unclear and the data does not explicitly state which chemicals are included within the scope of PMGF. Whilst some substances in scope such as asbestos, arsenic and styrene may be included, further analysis of the underlying data would be necessary to identify all of the assumptions. It is likely that the majority of the burden will be from PM. It is not possible to quantify what

[354] Occupational exposure to PGMF was estimated across nine categories (Agriculture, hunting, forestry, and fishing; mining and quarrying; manufacturing; electricity, gas and water; construction; wholesale and retail trade and restaurants and hotels; transport, storage and communication; financing, insurance, real estate and business services; and community, social and personal services), and was split into 'high' and 'low' exposure for high income and low & middle income countries.

[355] Blanc P, Iribarren C, Trupin L, et al. Occupational exposures and the risk of COPD: dusty trades revisited. Thorax 2009;64(1):6-12.

[356] Weinmann S, Vollmer W, Breen V, et al. COPD and occupational exposures: a case-control study. Journal of Occupational and Environmental Medicine 2008;50(5):561-69

[357] GBD 2016 Occupational Chronic Respiratory Risk Factors Collaborators. (2020). Global and regional burden of chronic respiratory disease in 2016 arising from non-infectious airborne occupational exposures: a systematic analysis for the Global Burden of Disease Study 2016. Occup Environ Med. 2020 Mar; 77(3): 142–150. Published online 2020 Feb 13. doi: 10.1136/oemed-2019-106013

the share of burden which cannot be explained by PM alone, a reasonable starting assumption may be in the order of <5%, but this would need to be confirmed via further research and analysis

This is a significant limitation of this analysis and a priority of future research should be an increased understanding of the role of chemical substances in causing and/or exacerbating COPD. The costs below are calculated through a monetization of DALYs from asthma attributable to exposure to PMFG.

Using estimates on the number of COPD DALYs attributable to occupational exposure to PMGF and UK costs of a DALY of £70,135[358], the estimated total cost of COPD attributable to occupational exposure to PMGF is in the order of several billion for the UK in 2019. As above, a starting assumption may be that up to 5% may be non PM component, suggesting costs somewhere below £300 million, per year. These estimates are highly uncertain and require further assessment.

Table 8-3 COPD DALYs and costs

	DALYs and associated cost (UK, 2019)
Total UK COPD DALYs	Conf [359]
PAF	Conf [360]
UK DALYs attributable to exposure to PMGF	Conf
Cost per DALY	£70,135[361]
Cost of UK COPD cases attributable to occupational exposure to PMGF	**Potentially several billion**

Cost-of-illness analysis

Alongside willingness-to-pay based assessments, direct healthcare costs and indirect productivity costs can also be assessed.

COPD represents approximately 19% of direct healthcare costs from respiratory illness in the UK. Direct costs assessed in analysis by the British Lung Foundation include secondary care were derived using the Programme Budgeting Benchmark estimates of Clinical Commissioning Group (CCG) spend for COPD. Primary care was assessed through the number of GP visits with the cost per GP visit assumed to be £37 based on published estimates. Non-governmental expenditure was also considered, it includes out-of-pocket and insurance financed private healthcare expenditure. In 2014 prices, the British Lung Foundation

[358] HM Treasury (2020). The Green Book: Central Government Guidance on Appraisal and Evaluation. https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent

[359] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.

[360] Data from IHME GBD (2019). Found: GBD Compare | IHME Viz Hub (healthdata.org). Data not permitted to be reproduced.

[361] Cost per DALY calculated based on Nedellec & Rabl (2016) and updated to 2019 prices.

estimated that COPD costs the NHS £1.9 billion in direct healthcare costs per year.[362] In 2019 prices gives estimated **direct healthcare costs to the NHS of c.£2 billion per year.**[363]

The British Lung Foundation also provides estimates for indirect costs associated with COPD where the value of lost production due to an individual's illness, injury or premature death associated with time away from labour market activities was considered. This does not include costs associated with presenteeism, non-labour market activities and informal caregiving. In 2014 prices, the British Lung Foundation estimated that COPD results in indirect costs of £61 million per year. Updating to 2019 prices gives estimated **indirect costs of COPD of £67 million per year**.

Given that the role of chemical substances in PMGF is unclear, the PAF for COPD attributable to PMGF will not be used to estimate costs attributable to chemical substances. More data is needed to determine the role of chemical pollution in COPD cases and the subsequent costs.

8.7.3 Uncertainties and limitations of the approach

These estimates have been produced using a PAF approach for COPD attributable to PMGF. It is unclear whether *any substances included in PMGF are within the scope of this report*. Whilst some occupational substances associated with COPD (such as asbestos, arsenic and styrene) are in scope, these may or may not be included in the figure above. It is likely that the vast majority of the attributable cases of COPD from PMGF are related to air pollutants. More data is required to understand the possible role of chemicals in cases of COPD and to understand the subsequent cost.

8.8 Summary

There are significant costs to the UK from respiratory diseases attributable to occupational exposure to various substances, however data availability presents a significant challenge in providing accurate estimates. Whilst asbestosis cases are 100% attributable to exposure to asbestos, the role of chemical substances in asthma and COPD is much less clear. Exposure to occupational asthmagens is used as a proxy for chemical substances for asthma. Whilst this will include some substances within scope it includes many that are not. The role of chemical substances in exposure to PMGF used to estimate the costs of COPD is even less clear. Whilst some substances in scope such as asbestos, arsenic and styrene may be included, it is likely that a significant proportion of PMGF will be from air pollutants. Improved understanding of the role of chemical substances in COPD and better data on the risks that substances pose in causing COPD is needed to improve cost estimates. The calculations for the three effects are all estimated using one source due to the limited data available, which is a significant limitation of this approach.

8.9 Future research priorities

Given that there is strong evidence that respiratory illnesses are a significant burden to the UK, future research priorities should focus on improving understanding of the environmental causes of respiratory diseases and the role of chemical exposure.

A major limitation of this analysis is in the evidence behind the RR estimates used in the calculation of PAFs for asthmagens and PMGF. These RR estimates are both based on 2 studies from high income countries which are assumed representative to the UK. Robust, UK specific studies are required to accurately determine the proportion of UK asthma and COPD attributable to chemical substances. UK epidemiological

[362] Trueman, D., Woodcock, F., and Hancock, E., (n.d.) Estimating the economic burden of respiratory illness in the UK. https://cdn.shopify.com/s/files/1/0221/4446/files/PC-1601_-_Economic_burden_report_FINAL_8cdaba2a-589a-4a49-bd14-f45d66167795.pdf?13095010944508481698_ga=2.82615569.641254879.1642171442-1388294531.1637243389

[363] Cost updated to 2019 prices using UK Government GDP deflators (GDP deflators at market prices, and money GDP - GOV.UK (www.gov.uk)).

data should be improved provide estimates specific to the UK and accurately estimate the proportion of respiratory illness associated with exposure to chemical substances.

Furthermore, greater understanding of the role of chemical exposures, particularly for COPD, would allow a more relevant PAF to be calculated as PMGF has limited relevance to the scope of this report.

Improved UK-specific biomonitoring data is required to improve understanding of exposure levels in the UK and epidemiological evidence should be improved to determine the respiratory health impacts of exposure. Currently UK PAF estimates for asthma and COPD are only available for occupational exposure, estimating the PAF for wider consumer exposure would allow for a more accurate and comprehensive cost estimate of respiratory illness attributable to chemical exposure.

9 Environmental burdens

9.1 Effects

The environment is impacted by hazardous chemicals in a range of different manners, depending on the properties of those chemicals, the sources of the emissions and the different environmental compartments affected by emissions. Effects can vary from degradation of environmental quality and hence the ecosystem services that the environment can deliver, through to the loss of particular species. The impacts can be short-term in nature or in some cases they can last for many years with lasting effects on environmental quality.

Although some of the effects will have impacts that can readily be valued in monetary terms, hazardous chemicals policy is frequently focused on addressing impacts which cannot. This can be due to a lack of information on the extent of the impacts, as well as the lack of economic markets for the environmental effects of concern. As a result, impacts frequently remain unvalued, or at best are valued in terms of the costs of remediation environmental damage or cleaning-up sites following a pollution incident.

Describing and valuing the full nature and magnitude of the impacts of chemical pollution on the UK environment is an enormous undertaking beyond the scope and time available for this study, although some attempts have been made here for the water environment.

9.2 Substances of concern

To provide illustrations of the potential magnitude of environmental impacts, we focus here on a subset of issues of concern. These include the pollution problems caused by:

- Substances of very high concern (SVHC), where these have been defined under REACH from an environmental perspective as being persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative;
- Substances that are toxic to the aquatic environment, where this includes heavy metals resulting from current and historic emissions;
- Priority hazardous substances under the Water Framework Directive, where these have an impact on quality of England's fresh and saltwater environments; and
- Land contamination, where this may be due to a wide range of different pollutants, ranging from heavy metals to solvents to other industrial chemicals, and stem from historic practices that would no longer be legal.

9.3 Major uses

The above types of substances are emitted to the environment from the range of industry sectors, with discharges including those direct to the water environment as well as from run-off and accidental releases. Emissions from wastewater treatment plants can also be a key source of some of the pollutants of concern, as a result of the substances being present in consumer goods, where this includes both goods currently being placed on the market as well as those which have long replacement times (for example, older furniture with textile coverings and foam cushions may contain poly brominated flame retardants. Cleaning of such furniture acts as one potential source of emissions to the water environment).

Other sources include historic activities, such as minerals and coal mining with abandoned sites leading to site specific contamination issues. Pollution from abandoned mines, for example, comes from point sources (drainage tunnels or mine entries), diffuse sources (mine wastes) and mine workings that are no longer pumped to control groundwater levels.

Similarly, dredging of both inland navigations and ports regularly disturbs heavy metals in sediments that relate to historic discharges. Land contamination more generally is generally linked to previous industrial uses of land and periods when there was less understanding of the hazards associated with different substances and practices.

9.4 Existing policy and remaining sources of exposure

The key pieces of environmental policy of relevance to control of such emissions include:

- River Basin Management Planning (under the Water Framework Directive) which sets out the Environment Agency's proposed approach to managing such pollution problems into the future. These, together with Environmental Quality Standards provide the framework for managing Priority and Priority Hazardous Substances as well as heavy metal pollution due to historic activities[364];
- UK REACH provides a framework for collecting data on the properties of chemicals, ensuring their safe use (i.e. placing requirements on producers and users to minimise emissions to the environment in line with "safe use" thresholds) and restricting or requiring the authorisation of future uses of SVHCs as well as other industrial chemicals of high concern; REACH can be used to address uses of chemicals that could lead to emissions to air, water and land; and
- The Environmental Protection Act 1990 (Part 2A) which sets out a risk-based approach to the identification and remediation of land where contamination poses unacceptable risks to human health and the environment.

A range of other legislation may be relevant, for example the UK Environmental Permitting Regulations[365], those related to pesticides, pharmaceutical products, cosmetic products, consumer product legislation, construction product legislation, etc. where these may also have controls on the use of substances with different properties of concern.

9.5 Metals contamination – damages caused by historic releases

9.5.1 Approach

As part of River Basin Management Planning waterbodies are assessed against several criteria to help determine the overall chemical and ecological status of the waterbody, where this may be graded from bad to good to high. Removal of chemical pressures on a waterbody may help it move from bad or poor through moderate to good status. Key pollutants of concern include arsenic, cadmium, copper, iron, manganese, nickel, lead and zinc.

In 2016 the Coal Authority reported that 1,500 km (3%) of rivers in England were affected by metal pollution from mining activities[366]. Remediation efforts are ongoing, alongside various projects (e.g. the Water and Abandoned Metal Mines (WAMM) currently operational in the North Pennines) through collaboration between the Coal Authority, DEFRA and the Environment Agency to support the Government's 25 Year Environment Plan and River Basin Management Plans[367]. In 2017, the Coal Authority was managing more than 80 mine water treatment schemes across Britain, with this involving handling and treatment of over

[364] https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&cad=rja&uact=8&ved=2ahUKEwiXzqfi39H1AhUPT8AKHYJiArEQFnoECCMQAQ&url=https%3A%2F%2Fwww.gov.uk%2Fgovernment%2Fpublications%2Flist-of-chemicals-for-water-framework-directive-assessments&usg=AOvVaw1SLG_mI2IwPgZ8dil9pRb2

[365] IED has been applied in England and Wales through amendments to EPR 2010, implemented in the Environmental Permitting (England and Wales) (Amendment) Regulations 2013.

[366] pollution-from-abandoned-mines-challenge-rbmp-2021-1.pdf (environment-agency.gov.uk)

[367] https://waterprojectsonline.com/custom_case_study/wamm-water-abandoned-metal-mines-programme/

122 billion litres of mine water per day, and improving and protecting over 350 km of rivers and several important aquifers[368]. Collectively these stop over 900 tonnes of iron (as Fe) and other pollutants each year from causing pollution, helping to protect rivers as well as drinking water supplies for approximately 500,000 people. Whilst heavy metal pollution may not always be visible, it can have serious effects on ecosystems, biodiversity and can potentially cause contamination of drinking water.[369] Protection of this 350km of rivers, however, leaves a significant on-going burden of pollution in the remaining 1,000 plus km of rivers and other water bodies.

Each mine water remediation scheme is subject to a formal cost-benefit analysis, with these making use of two different quantitative benefits assessment approaches, complemented by a qualitative ecosystem services assessment. One method relies on site specific information and applies benefit transfer techniques drawing on older valuation studies to act as the basis for the assessment. This approach continues to be used even though the studies are quite old because it allows actual site specific information to inform the likelihood and scale of indirect and direct recreational use to be taken into account. This can result in benefit estimates either lower than or higher than those derived using the NWEBs valuations, depending on location and site characteristics. In particular, NWEBs figures will tend to undervalue some rural sites, while use of the willingness-to-pay figures will better capture recreation benefits for honeypot sites. The most transferrable and readily applied methodology is the use of updated NWEBS benefits transfer values, derived from a broader WTP study used to value a change in water body status from one class to another (e.g. from poor to moderate, moderate to good). It draws on catchment level information with valuations applying per km of river affected[370].

9.5.2 **Results**

There was inadequate time within this study to develop an estimate of the overall damages being caused by historic releases of heavy metals from old mining activities. But in addition to cleaning up rivers, the above treatment schemes enhance natural capital by providing water habitats and encouraging biodiversity in the associated wetlands. A case study is provided here to illustrate the scale of the social damages that can arise from such pollution for a single site. This is based on the scheme at Saltburn Gill that has been put in place by the Coal Authority to remove iron loadings.

Saltburn Gill is a narrow stream in a wooded valley located in the East Cleveland area (some 15 km to the east of Middlesbrough). In 1999 a large, iron-rich mine water outbreak occurred which polluted Saltburn Gill and Skelton Beck, as well as discolouring a popular surfing beach. Although not harmful to people, the iron-rich water smothered the stream bed with ochre, making it hard for fish and river insects to survive, as well as affecting bathing water quality. Between this outbreak and the implementation of a treatment scheme, more than 100 tonnes of iron entered into the North Sea each year. Figure 9-1 illustrates the level of discolouration on Saltburn beach before the scheme was put in place.

[368] Coal mine water treatment - GOV.UK (www.gov.uk)

[369] pollution-from-abandoned-mines-challenge-rbmp-2021-1.pdf (environment-agency.gov.uk)

[370] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/291464/LIT_8348_42b259.pdf

Figure 9-1 Saltburn Beach, Cleveland (pre remediation)

Source: Saltburn Gill mine water treatment scheme - Case study - GOV.UK (www.gov.uk)

Using cost-benefit analysis techniques, the monetary benefits from preventing the discharge and treating the mine water were estimated at over £13.4 million (£ 2021) for a 25 year period (starting in 2012). This assessment was based on the use of a series of willingness to pay estimates, covering a range of direct and indirect uses (informal recreation, beach recreation, water-sports) of the river and beach affected and non-use values for the benefits of restoring the area to a higher quality status. The resulting estimates were then checked via the application of catchment specific valuations for the National Water Environment Benefits survey (NWEBs), which was carried out to act as the basis for assessing schemes under the Water Framework Directive.

Using the willingness-to-pay approach, the Saltburn Gill assessment found that 37% of the benefits were associated with recreational visits to the beach. The cliff at Saltburn was recorded as receiving nearly 100,00 visits a year, with good access and facilities at the beach. The remainder of the benefits were related to non-use values, capturing the benefits of protecting the environment for use by others, for future generations or to ensure its existence (in this case in a higher quality state).

Use of the NWEBs values provides a feasible methodology for deriving a national level estimate of the economic damage costs of historic metals pollution. The values can be adjusted so that they reflect metal specific impacts, e.g. discolouration, impacts on fish and invertebrates due to heavy metal pollution[371]. Central total per km values are available for England and Wales that can be updated with the GDP deflators to reflect 2021 valuations. These can then be adjusted to account for the types of benefits resulting from a scheme.

Although the present value benefits estimated for Saltburn Gill using either the willingness-to-pay or NWEBs approach appear relatively low compared to other environmental burdens, it must be remembered that they relate to just one treatment scheme; similar estimates apply to a range of schemes that have been and are being implemented by the Coal Authority (including on behalf of the Environment Agency).

[371] The full range of components being fish, other animals such as invertebrates, plant communities, clarity of water, condition of channel and flow, safety of the water for recreation contact.

The figure overleaf[372] shows the rivers in England that are polluted by at least one metal (cadmium, lead, zinc, copper, nickel, arsenic and iron, due to abandoned metal mines). Rivers are marked in the colour purple, schemes aimed at monitoring and controlling diffuse pollution are shown as green circles, while known mine water discharges are shown as a black cross inside a red circle, and black triangles show abandoned mine waste sites that are causing serious environmental harm. There will be another set of abandoned coal mines adding to these issues.

9.5.3 Uncertainties and limitations of the approach

There are several uncertainties associated with the approaches adopted as part of these assessments to value benefits from mine water remediation schemes. In part, these uncertainties are what drives the use of two different quantitative approaches to valuation, as well as the provision of a qualitative assessment of ecosystem service effects.

- The benefits transfer method that the first approach is based on draws on studies which were carried out over 20 years ago, and some were originally undertaken to address sewage discharge related quality impacts. They are therefore not wholly transferrable to the issues arising from coal or metals mine water contamination, as the impacts caused by mine water discharges vary in terms of their environmental and aesthetic impacts. In addition, the studies used approaches for eliciting the willingness-to-pay values that would no longer be considered consistent with best practice.
- The NWEBs values apply at the catchment level and do not reflect the high level of visits to the site. The NWEBs valuations are now also over 20 years old. It is unclear the extent to which they can reliably be applied as valuations at the scheme level, and whether it is appropriate to disaggregate the original values into different elements of good status as is currently done. They are also not specific to hazardous chemicals pollution, resulting in further uncertainty over their transferability.

In both cases, the greatest uncertainty relates to valuation of non-use benefits. In particular, there are questions over the population over which such benefits should be aggregated, especially as they generally account for the majority of the identified benefits.

It is understood that the Environment Agency and Defra are currently considering how some of the issues surrounding on-going use of the NWEBs values can be addressed, with this including their application to chemicals pollution issues.

[372] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/867551/Rivers_polluted_by_abandoned_metal_mines_in_England.pdf

Figure 9-2 Metal mine impacted catchments (England and Wales (2017))

Source: Coal Authority, 2020. Rivers polluted by abandoned metal mines. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/867551/Rivers_polluted_by_abandoned_metal_mines_in_England.pdf

9.6 Assessment of environmental burden to certain SVHC substances

9.6.1 Approach

Selection of SVHC for study

Substances of very high concern (SVHC) are identified under the REACH Regulation on the basis of their hazard properties according to the criteria in REACH Article 57. They include substances classified as carcinogenic, mutagenic or toxic for reproduction (CMR) category 1A or 1B, substances which are persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) or substances that cause an equivalent level of concern as CMR or PBT/vPvB substances (for example substances with endocrine disrupting properties). The list of substances that have been identified as SVHC is given in the REACH Candidate List (which was adopted under UK REACH at the time of EU Exit). The EU REACH Candidate list (as of November 2021) was used as the starting point for identification of the SVHC for this study[373].

At present, the exact number of SVHCs that are, or will be, registered for manufacture or use in the UK under UK REACH are not known precisely. The UK REACH grandfathered registration notified substance list[374] gives details of the substances for whose EU REACH registrations have been grandfathered into UK REACH. However, the details of the DUINs[375] substances were not available at the time of writing.

To select the SVHC substances that are known to be relevant to the UK, the substances on the UK grandfathered substances list (as of November 2021) were cross-checked against the substances on the EU REACH Candidate list. This identified a sub-list of the SVHC substances that had been grandfathered into UK REACH.

As a second step the sub-list of UK-relevant SVHCs was filtered to identify those that had been identified as being PBT, vPvB or having endocrine properties relevant to the environment. This resulted in the identification of twelve SVHCs of most relevance to the UK environment. Three of these substances were omitted from further study owing to uses already being restricted under EU and UK REACH. The resulting nine SVHC for further study are summarised in Table 9-1. As can be seen, the selected SVHC cover a range of SVHC-properties (namely PBT, vPvB, endocrine disruption) and also include substances classified as very toxic to aquatic life with long lasting effects, and two priority hazardous substances according to the EU Water Framework Directive (WFD)[376].

Table 9-1 SVHC substances identified for further study

Substance	SVHC properties	Other environmental hazards
Tris(4-nonylphenol, branched and linear) phosphite (EC No. 701-028-2)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment. This applies only when the 4-nonylphenol, branched and linear, content is ≥0.1% w/w.	Notified classification: H410; H400.

[373] When UK REACH came into force, all substances that were on the EU REACH candidate list were carried over onto the UK REACH candidate list. The UK REACH work programme for 2021-22 committed to assess those substances that have been added to the EU REACH candidate list since UK REACH came into force, to consider if it was appropriate to add them to the UK REACH candidate list. Defra, Policy paper 'Approach to including substances of very high concern on the UK REACH candidate list'. Published 9 December 2021

[374] https://www.hse.gov.uk/reach/grandfathering-registrations.htm

[375] Downstream Use Import Notification (DUIN). These give details of substances imported into Great Britain.

[376] Annex I to Directive 2013/39/EU

Substance	SVHC properties	Other environmental hazards
Alkanes, C_{14-17}, chloro (CAS No. 85535-85-9)	PBT/vPvB (Article 57d/57e)	Harmonised classification: H410; H400.
2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)	PBT/vPvB (Article 57d/57e)	Notified classification: H413.
4-*tert*-Butylphenol (CAS No. 98-54-4)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment.	Harmonised classification: H410.
p-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment.	Notified classification: H410.
4-Nonylphenol, branched (CAS No. 84852-15-3)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment.	Harmonised classification: H410; H400. Priority hazardous substance under the WFD.
Phenol, heptyl derivatives (CAS No. 72624-02-3)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment.	Notified classification: H410; H400.
4-*tert*-Octylphenol (CAS No. 140-66-9)	Equivalent level of concern (Article 57F) based on endocrine disrupting properties – environment.	Harmonised classification: H410; H400. Priority hazardous substance under the WFD.
Terphenyl, hydrogenated (CAS No. 61788-32-7)	vPvB (Article 57e)	Notified classification: H411

Notes: H400 – Very toxic to aquatic life.
H410 – Very toxic to aquatic life with long lasting effects.
H411 – Toxic to aquatic life with long lasting effects.
H413 – May case long lasting harmful effects to aquatic life.

Estimation of emissions of the SVHC to the UK Environment

The emissions of the SVHC to the UK environment were estimated using a relatively broad approach based on the tonnage and use (mainly use name and environmental release category, the tonnage range registered in the EU and the default release rates to the environment for the environmental release category). Where available, emission data from existing risk assessment reports relevant to the UK or EU were also taken into account. Further details of the approach in the Appendix.

EUSES Modelling and the "steady state" concept

The EUSES model[377] was used to estimate the mass of the SVHC substances that may be present in the UK environment at *steady-state*. Steady-state occurs once the rate of input of the substance into the UK environment is balanced by the rate of loss of the substance from the UK environment. In this respect, loss could occur by degradation or transport out of the UK. These processes are included in a simplified form within the EUSES model.

An adapted version of the EUSES regional model was used for the analysis. The model EUSES is set up to predict the concentration and load of substance at different spatial scales. The 'local' scale model is the area around a site where a substance is released (e.g. a manufacturing or formulation plant or a sewage treatment works); the 'region' is a theoretical country and the model assumes that the local emissions happen within that region; and 'continental', e.g. Europe, represents the concentrations that would be found remote from point sources of substance releases.

At each spatial scale, the model predicts the concentrations of the substance (at steady state) that would be found in different environmental compartments (surface water, sediment, soil etc.) The regional model was parameterised to better reflect the size and land areas of the UK (based on habitat and land use data from ONS[378]). Details of the modifications made are given in the appendix. The UK emissions for each SVHC substance as estimated above were used as an input into the regional model and the output from the model was the resulting steady-state mass of the substance in the UK environment, along with estimates of the time to reach 95% of steady-state and the half-life for loss from the UK environment following cessation of emissions. Further details of the modelling are in the appendix..

The concept of the steady-state is an important one in environmental modelling. It describes the point at which inputs (releases) are equal to outputs (losses). For substances that remain in the environment for a long time, it will take a long time for the loss from (and breakdown in) the environment to be equal to the inputs. This means that such substances will build up in the environment and remain in the environment for long periods of time. Half-life is another and related key concept, which is the time taken for half of the mass of the substance to be lost from the environment – substances that breakdown slowly in the environment will have long half-lives.

For SVHCs, the concern is that these substances can end up in the environment and remain in the environment for long periods of time and therefore the impacts of these substances can be manifest in the environment over long periods of time. The amount of substance that ends up in the environment is driven by the use volume of the substance and what fraction of that is released into the environment. What happens when that substance is in the environment is driven by the properties of that substance (i.e., how it behaves). The modelling done for this part of the study considers the volume used and how it is released and estimates how much of that substance will remain in the environment (should releases continue at their current rates). A substance that is released into the environment at high volumes but quickly breaks down in the environment, may be of less concern that one that is released at lower volumes but remains in the environment for long periods. Clearly, substances that are released into the environment in high volumes and remain in the environment for long periods are of the most concern.

[377] European Union System for the Evaluation of Substances, see https://echa.europa.eu/support/dossier-submission-tools/euses

[378] Note that sewage treatment plant (STP) assumption is it is set to 20M inhabitants. The current UK population is 68M inhabitants. The regional population defines the size of the regional STP in EUSES.

9.6.2 Results

The steady-state masses for the selected SVHC substances estimated using the modified EUSES model are summarised in Table 9-2. The estimates for the steady-state mass of the substances considered vary significantly from substance to substance, reflecting differences in the substance properties, the tonnages and uses assumed (and hence the estimated release rate to the UK environment).

Table 9-2 Steady state mass of SVHC substances based on worst case UK release estimates

Substance	Based on lower estimate from REACH data	Based on upper estimate from REACH data	Based on other published release estimates*
Tris(4-nonylphenol, branched and linear) phosphite (EC No. 701-028-2)	784,000 tonnes	7,840,000 tonnes	Not available
Alkanes, C_{14-17}, chloro (CAS No. 85535-85-9)	118,000 tonnes	1,180,000 tonnes	79,100 to 84,600
2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)	5.64 tonnes	56.4 tonnes	Not available
4-*tert*-Butylphenol (CAS No. 98-54-4)	302 tonnes	3,020 tonnes	287 kg
p-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)	55 kg	554 kg	Not available
4-Nonylphenol, branched (CAS No. 84852-15-3)	No registered uses	No registered uses	7.96 tonnes
Phenol, heptyl derivatives (CAS No. 72624-02-3)	No registered uses	No registered uses	Not available
4-*tert*-Octylphenol (CAS No. 140-66-9)	1,550 tonnes	15,500 tonnes	413 tonnes
Terphenyl, hydrogenated (CAS No. 61788-32-7)	162 tonnes	1,620 tonnes	Not available

*see appendix A1-3 for detail and references.

The corresponding times to 95% steady-state and the approximate half-life for loss from the UK environment are shown in Table 9-3. The time to 95% steady-state gives an indication of the time necessary, at a constant release rate, for the amount of substance in the UK environment to approach reaching steady-state. Once steady state is reached, no further change in the UK environmental burden would be predicted to occur unless there was a change in the release rate. This gives an indication of the time over which increasing environmental burdens of each substance may occur, after releases to the environment first occurred.

The approximate half-life for loss from the UK environment gives an indication of the time taken for the amount of substance in UK environment to decrease by 50% following cessation of emission. This provides an estimate of the timeframe over which any new risk management measures may be expected to have a significant effect. It is important to note that, in this approach, “loss” from the UK environment includes loss by degradation and also loss by other processes such as transport out of the UK environment.

Taken together, the time to 95% steady-state and half-life for loss may provide useful information for the length of time for which costs to the environment may accrue, and the length of time over which future risk management measures may be effective.

Table 9-3 Estimated time to 95% steady-state and half-life for loss from the UK environment of SVHC substances following based on worst case UK release estimates

Substance	Based on lower and upper estimates from REACH data		Based on other published release estimates	
	Time to 95% steady state (days)	Half-life for loss (days)	Time to 95% steady state (days)	Half-life for loss (days)
Tris(4-nonylphenol, branched and linear) phosphite (EC No. 701-028-2)	1,310,000 (3,589 years)	302,000 (827 years)	-[a]	-[a]
Alkanes, C_{14-17}, chloro (CAS No. 85535-85-9)	189,000 (518 years)	43,600 (119.5 years)	277,000 (759 years)	64,100 (176 years)
2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)	786	182	-[a]	-[a]
4-*tert*-Butylphenol (CAS No. 98-54-4)	55	13	37	9
p-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)	31	7	-[a]	-[a]
4-Nonylphenol, branched (CAS No. 84852-15-3)	-[a]	-[a]	68	16
Phenol, heptyl derivatives (CAS No. 72624-02-3)	-[a]	-[a]	-[a]	-[a]
4-*tert*-Octylphenol (CAS No. 140-66-9)	3,530 (9.7 years)	815	17,100 (47 years)	3,960 (10.8 years)
Terphenyl, hydrogenated (CAS No. 61788-32-7)	407	94	-[a]	-[a]

Note: a) No estimate possible.

Table 9-2 shows estimates of releases of these SVHCs into the environment. There is quite some difference in the total load of different substances that are released. If we then look at how long it would take those releases to build up to a point where the loss from the environment is equal to the releases into the environment (Table 9-3) there is a very large range (from thousands of years to one month) with similar time scales for the time it would take for that mass to reduce by half.

Since the amount and loss from the environment is influenced by the total mass that is released, we can eliminate that variable and look at the substance on an equal basis by modelling what happens if just one kilogram is released to either air or water. That way we can see how much of a substance gets into the environment and how long a substance would remain in the environment, once it is released. In this report we are concerned with substances' impacts, which are due to the potential direct damage they cause to environment receptors. How long that potential damage occurs for is relevant to that, because it tells us how long the impacts will persist. In reality this is complicated by a dynamic situation in which inputs (releases) to the environment may change over time or may stop altogether (for example if all uses of a substance are banned).

The results of the two standard scenarios (1 kg/day release to water and 1 kg/d release to air) are shown in Table 9-4 and Table 9-5. These results usefully allow a more direct comparison between substances to be undertaken as they provide estimates of the steady-state environmental burden for each substance on a standard basis.

Table 9-4 Steady state mass of SVHC substances following 1 kg/d release to waste water

Substance	Total steady state mass in UK environment (tonnes)	Time to 95% steady state (days)	Half-life for loss from UK environment (days)
Tris(4-nonylphenol, branched and linear) phosphite (EC No. 701-028-2)	839	2,520,000 (6,904 years)	581,000 (1,592 years)
Alkanes, C_{14-17}, chloro (CAS No. 85535-85-9)	122	366,000 (1,003 years)	84,600 (232 years)
2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)	0.356	1,070 (2.9 years)	247
4-*tert*-Butylphenol (CAS No. 98-54-4)	0.030	90	21
p-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)	0.020	59	14
4-Nonylphenol, branched (CAS No. 84852-15-3)	0.034	102	24
Phenol, heptyl derivatives (CAS No. 72624-02-3)	242	7,250 (19.9 years)	1,670 (4.6 years)
4-*tert*-Octylphenol (CAS No. 140-66-9)	2.62	7,850 (21.5 years)	1,810 (5 years)
Terphenyl, hydrogenated (CAS No. 61788-32-7)	0.251	753	174

Table 9-5 Steady state mass of SVHC substances following 1 kg/d release to air

Substance	Total steady state mass in UK environment (tonnes)	Time to 95% steady state (days)	Half-life for loss from UK environment (days)
Tris(4-nonylphenol, branched and linear) phosphite (EC No. 701-028-2)	30.7	92,100 (252.3 years)	21,300 (58.4 years)
Alkanes, C_{14-17}, chloro (CAS No. 85535-85-9)	6.46	19,400 (53.2 years)	4,480 (12.3 years)
2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)	0.168	503	116
4-*tert*-Butylphenol (CAS No. 98-54-4)	0.0051	15	3.6
p-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)	0.00071	2.1	0.5
4-Nonylphenol, branched (CAS No. 84852-15-3)	0.0063	19	4.3
Phenol, heptyl derivatives (CAS No. 72624-02-3)	0.014	419	97
4-*tert*-Octylphenol (CAS No. 140-66-9)	0.0018	5.3	1.2
Terphenyl, hydrogenated (CAS No. 61788-32-7)	0.01	30	6.9

As can be seen from Table 9-4 and Table 9-5, a 1 kg/day release leads to large differences in the total steady-state environmental burden times to 95% steady-state and half-life for loss between the substances. These

differences reflect the differences in the substance properties alone. Such an approach potentially allows costs accruing in the environment, and the time frame over which such costs could accrue, to be estimated on a "unit" release (e.g. kg/day) basis, allowing costs to be compared between substances on the same basis.

9.6.3 Implications and possible damage costs

At this point, however, there is no clear monetary valuation unit that could be applied to these per unit release estimates. However, this approach and assessment shows the estimated environment burden of substances based on the volume used, how they are used, and how they behave in the environment.

Furthermore, all "substances of concern" are not of equal concern if one considers the time it takes for a substance to build up in the environment to a point where the loss from the environment is equal to the releases to the environment. There are big differences between substances in terms of the residence time in the environment. The *half-life for environmental loss indicates* how long it would take for substances to be lost for the environment even if releases were stopped. This analysis shows that substances that are very persistent can have impacts (which will depend on toxicity) for very long periods of time. If the impacts can be quantified and valued, this can indicate the costs of the uses of these substances. But even where impacts cannot be valued directly, the total mass of the substance in the environment can be a surrogate for cost if one can apply the cost of removal or the cost for the abatement of those releases as a cost per unit mass.

The significance of assessing substances that are SVHC is that these substances are already subject to additional controls because of their hazardous properties. Under REACH, such substances can be subject to a socioeconomic analysis in which continued use is dependent on demonstrating that the benefits (of continued use) to society outweigh the risks. Currently, there is no specific or accepted methodology to estimate the environmental impacts of such substances, although current approaches to value impacts are based on the cost of abatement and/or removal. Nevertheless, SVHCs are released to the UK environment and may have impacts and therefore costs[379]. The assessment above indicates that for the UK there is a large variation in the mass that resides in the environment for substances of SVHC status, and a large variation in the time it would take for additional control measures or bans to take effect.

Note: section 9.7 illustrates how the type of information produced through this approach might be able to be combined with willingness to pay estimates to develop social damage costs in the future, with further improvements to the available valuations.

9.6.4 Key assumptions

The key assumptions used in the approach are discussed in more detail in the appendix. The main assumptions are summarised below.

- The UK tonnage is assumed to be 10% of the total tonnage registered in the EU in the absence of more specific information[380].

[379] For a SVHC such as a PBT within the context of REACH it is not permitted in the chemical safety assessment to compare the predicted environmental concentration (PEC) to the predicted no-effect concentration (PNEC) to determine the risk (as a risk characterisation ratio (RCR)). In an authorisation under REACH for continued use of specific uses (that are applied for), the applicant must show (in a socio-economic analysis (SEA)) that the benefits to society outweigh the 'risks' (the risks being the impacts). To date, the *impacts* have been quantified based on the costs (per unit mass) for the substance not to enter the environment (i.e. cost of abatement) or the costs (per unit mass) of removal from the environment (i.e. cost of remediation).

[380] The authors view this fraction as a reasonable assumption, based on an overview of the UK contribution to the EU chemicals market by volume.

- For the release estimates, in the absence of more specific information, the tonnage is assumed to be split equally between each different registered use[381].
- Release to the environment from each use is estimated to be at the default rate for each environmental release category (ERC)[382].
- The EU registered tonnage range is taken into account to give lower and higher release estimate.
- Where available, information from other published risk assessment reports detailing releases to the EU environment have been considered.

9.6.5 Uncertainties and limitations of the approach

The approach taken is relatively crude and subject to large uncertainties. More robust estimates require a more detailed substance-by-substance analysis of the available tonnage, use and substance property data to be undertaken; such detailed analysis is beyond the scope of the current project. The main uncertainties and limitations with the approach are summarised below.

- The available EU Registration dossiers do not give details of the tonnages that may be used in the UK or a breakdown of the substance tonnage between the different registered uses. For the analysis it has been assumed that a) the UK tonnage is 10% of the total tonnage registered in the EU and b) the tonnage is split equally between each use. This crude approach may not then reflect accurately the actual UK usage of the substance.
- Releases to the environment have been estimated based on the default release rates from the ERCs. These release rates are worst case values and, in the main, do not take into account any risk management measures that may be present for the actual use (see also the appendix). Therefore, the release estimates used as the basis of the approach may not reflect the current UK situation.
- Where available information on releases to the environment from published risk assessment reports have also been considered. These risk assessment reports, in the main, predate the identification of the substance as a SVHC and so may not take into account any subsequent risk management measures or changes in use pattern that occurred following identification of a substance as a SVHC. Therefore, the relevance of these older release estimates to the current UK situation, is unclear.
- The substance properties, particularly the rate constant for degradation in air, water, sediment and soil, are very important parameters in the regional modelling undertaken. These values were taken mainly from existing reports that identified the substance as an SVHC (see also the appendix) and were used without any further review. The amount of degradation data available varied from substance to substance and in the absence of data EUSES assigns 'default' degradation rate constants for the missing parameters. A more detailed substance-by-

[381] The uses of a substance determine how it is released to the environment. Some uses may be highly contained and not lead to a significant fraction of the substance being released, while other uses may lead to significant releases to the environment. The total release of a substance to the environment depends on how much is made and used and what those uses are; high volumes of uses that lead to high releases will lead to more of the substance ending up in the environment than low release uses. Without specific information on how much of the substances are used in each use, we assume that the total volume is split equally between each registered use.

[382] ERCs are used within the chemicals safety assessments for REACH and describe emission factors for broad processes (for example manufacture of a substance, or use of a monomer in polymerisation, or widespread use of articles with high or intended release - amongst many others). The emission factors describe the proportion (%) of the release of the substance that goes to air, water (before sewage treatment) and to soil.

substance analysis of the data available substance may reduce some of the uncertainty arising from this. However, such a detailed analysis is beyond the scope of the current project.

As indicated above, there is currently also no available approach for place a monetary value on the resulting per unit mass estimates. They would need to be combined with monitoring data on the water bodies affected by the presence of the pollutant.

9.7 Assessment of environmental burdens due to PBT Priority Substances (Substances "very toxic to aquatic life with long lasting effects")

9.7.1 Approach

As illustrated by the assessment presented in Section 9.6, PBT and vPvB substances are of particularly high concern owing to their potential to persist for long periods of time in the environment and their ability to accumulate in living organisms. These attributes, in combination with toxicity, mean that they can produce toxic effects far from any sources of emissions. Once they have entered the environment, exposures are very difficult to reverse because even a cessation of emissions will not immediately result in a significant reduction in chemical concentrations owing to the long half-lives of substances.

Even if no toxic effects can be demonstrated in laboratory tests (as is the case for vPvB substances), long-term effects are possible owing to the potentially high but unpredictable levels that may be reached in humans and/or the environment over an extended timescale and over several generations.

A core methodological difficulty for estimating (and valuing) the benefits of action to curb or cease emissions of PBTs/vPvBs (or otherwise address risks) is that 'safe' concentrations of PBT (and vPvB) substances in the environment cannot be established with reliability. Target compartments and species at risk cannot be identified with sufficient levels of accuracy and, owing to the long-term presence of these substances in the environment, secondary poisoning and multi-generational effects in wildlife cannot be readily predicted.

The inability to estimate the monetary benefits of actions to curb emissions from PBTs/vPvBs is evidenced by the lack of benefit estimations in the EU REACH restriction dossiers for PBTs/vPvBs regulated thus far under EU REACH. Few stated preference-based studies have been undertaken with the aim of developing monetary estimates of people's WTP to adopt a precautionary approach with respect to PBTs and vPvBs. As noted by ECHA (2014), the lack of information on changes in impacts makes it difficult to develop credible change scenarios which could leave survey respondents unclear as to what they are being asked to value.

The most relevant 'off the shelf' estimates are those associated with restrictions brought into force under EU REACH, expressed as costs per kg/tonne of emissions reduced/to be reduced. These are reported in ECHA's (2021) report on the *Costs and benefits of REACH restrictions proposed between 2016 to 2020*[383] but are often simply costs of switching to alternatives. Rarely, restriction dossiers have costs of clean-up in different countries (e.g. Australia with PFAS). None of the available information, then, explicitly values the impacts.

Rather than simply duplicate these kinds of values, it was decided that this study should seek to push the boundaries and, in so doing, perhaps provide a new way of assessing and valuing impacts of PBT/vPvB substances. This has drawn on earlier initial (and unpublished) work on such approaches, ideas for which were presented at the OECD Workshop *Best Practices in Assessing the Social Costs of Selected Chemicals* in Ottawa on 31 August 2017.

9.7.2 Results and Key assumptions

One of the fundamental features of PBT/vPvB substances that separates them from other substances for the purposes of risk management is their ability to build up in the environment to produce a 'stock' of pollution.

[383] https://echa.europa.eu/documents/10162/13630/costs_benefits_reach_restrictions_2020_en.pdf/a96dafc1-42bc-cb8c-8960-60af21808e2e

As illustrated in Section 9.6, the more persistent the substance, the slower it is to decay and the greater the potential for levels to build into an environmentally significant level. If the rate of emissions of a substance are greater than the rate at which those emissions decay, then the substance will build up a 'stock' of potential pollution.

The concept presented in 9.6 is built upon here but is combined with the existence of the Environmental Quality Standards that apply to PBTs that have been classed as Priority Hazardous Substances under the UK Water Environment Regulation 2017. These include the setting of EQS for a range of substances that are hazardous to the water environment, including heavy metals, industrial chemicals and pesticides. The Environment Agency monitors waterbodies for compliance with these EQS as part of ensuring achievement of good chemical status for all priority substances.

The number of waterbodies being monitored for the different substances has been increasing over time, and headline figures were provided by the Environment Agency for this study. These figures are based on 2019 monitoring data covering all priority substances. As a snapshot, the figures for the most ubiquitous PBT substances are given below, together with cypermethrin (a pesticide); these are the chemicals most responsible for failure to meet good Chemical Status:

- 100% water bodies fail the Polybrominated diphenyl ethers (PBDE) biota standard, 100% freshwater water bodies fail, 100% estuaries and 100% coastal waters
- 86.6% water bodies fail the Mercury standard, 86.1% freshwater water bodies fail, 100% estuaries and 100% coastal waters
- 25.4% water bodies fail the Perfluoro octane sulfonate (PFOS) standard, 26.3% freshwater water bodies fail, 1.9% estuaries and 0% coastal waters
- 5.9% water bodies fail the PAH standard, 5.4% freshwater water bodies fail, 24% estuaries and 16.1% coastal waters
- 3.9% water bodies fail the cypermethrin standard, 3.9% freshwater water bodies fail, 5.8% estuaries and 0% coastal waters.

The starting point for trying to place an economic valuation on the damages caused by the presence of these PBT substances in the water environment is the assumption that, e.g. 1kg of annual 'emission'[384]represents the maximum possible 'safe' level of emissions to remain within the EQS (or other 'safe/no effect level'). This implies that the 'safe level' will be reached when the stock quantity has degraded to 1kg or below. For the time period up until this point is reached, the substance will be present in the environment at levels above the EQS (or other safety value) unless there is an intervention to physically remove it (i.e. remediation).

Translating this to compliance with the EQS for the above PBT substances, means that any affected waterbodies would 'fail' to achieve good chemical status *even after mitigation of emissions has been applied and this would continue until the stock of the substance naturally reduced to a safe level, at or below the EQS*. As part of River Basin Management Planning in England, monetary values are available for improvements in waterbody status from bad to poor to moderate to good (NWEBs values). These are expressed as £'s per km per year for each level of improvement. As the exceedance of the EQS for the above PBT substances prevents improvement of water body status (from bad to poor, or from poor to moderate, or from moderate to good), the damage costs of this per km of waterbody affected can be calculated by determining the time period over which the EQS (or other safety value) could be exceeded multiplied by the

[384] Where 1 kg is used as a notional unit of mass for illustration purposes. The actual emission figure would vary by pollutant and receiving waterbody, however

NWEBs value for the relevant change in waterbody status. The result is an estimate of the value of damages to waterbodies from a given substance per km of waterbody affected by historical emissions.

The Environment Agency's 2015 update on river basin management plans[385] indicates that prior to the availability of the 2019 monitoring data presented above, only 137 out of 4,542 surface water bodies were considered to fail meeting good chemical status requirements. As indicated above, the 2019 data indicate that 100% should now be considered to fail due to PBDE concentrations and a further 26% to fail due to PFOS concentrations in freshwaters. These percentages are therefore assumed to apply to the around 170,000 km of river in England[386].

The NWEBs valuations are most often used at the catchment level, however, in 2012 figures were produced that include a national figure per km of river in England and Wales[387]. These include valuations for different changes in a waterbody's status, with valuation of partial changes in status now calculated based on the extent to which one or more of the six elements which goes into determining "good" status is affected. It is assumed here that due to the presence of PBDEs and PFOS, all waterbodies are downgraded from achieving "good" chemical status to one which is equivalent to "moderate" status, and that this is due to the toxic effects of the substances. As a result, "good" status is assumed to be failed due to the potential impacts of these substances on biota (represented by a failure of the "fish" and "invertebrates" elements which factor into the Environment Agency's overall assessment). On this basis 33% of the NWEBs national valuation per km of river is taken as an appropriate valuation. These assumptions are set out in Table 9-6.

The resulting valuation for an average UK river, in terms of society's willingness to pay to bring it up to good chemical status is £9,435 per km of river failing to meet the EQS is applied over the time period it would take for each substance to degrade to a level below the EQS, with this being 183 years for PFOS and 19 years for PBDEs. Discounting the damage costs over these periods using the Treasury's declining discount rate (from 3.5% to 2.5%), suggests damages costs for PFOS of around £14.7 billion and for PBDEs of around £22.6 billion.[388]

It is important to recognise that there is an element of double-counting in these figures. Given that 100% of waterbodies currently fail for PBDEs, then the social damage costs of £22.6 billion associated with these failures also capture 19 years of the failures also for PFOS over the same time. The waterbodies would continue to fail for PFOS beyond this point, however.

Table 9-6 Valuation of the social damages due to exceedance of the freshwater EQS for PBDEs and PFOS

NWEBs	**Moderate to good**	
2012 prices	£23 200 per km	
2021 prices	£28 304 per km	
per element (6 elements)	£4 717 per km	
fish and invertebrates = 2 elements	£9 435 per km	
Substance	**PFOS**	**PBDE**
half life	15 330	2 232
time to target (years)	183	19

[385] National_evidence_and_data_report.pdf (publishing.service.gov.uk)

[386] https://consult.environment-agency.gov.uk/++preview++/environment-and-business/challenges-and-choices/user_uploads/physical-modification-challenge-rbmp-2021.pdf

[387] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/291464/LIT_8348_42b259.pdf

[388] Due to the persistence of PBTs in the environment, an abnormally long timeframe in considered, resulting in uncertainty in the appraisal.

NWEBs	Moderate to good	
km river affected	44 200	170 000
Value - undiscounted (£million)	£76 509.4	£30 744.0
Discount factor	0.1923	0.7355
Value - discounted (£million)	£14 712	£22 612

To put these figures in context, and taking into account the extent of PFOS contamination as shown in Figure 3 from the Environment Agency's report, clean-up of individual sites affected by PFOS contamination can be high. For example, the Public Services Department of Guernsey carried out work to ensure drinking water standards were not affected by contaminated soil at Guernsey airport. The work to remove, store and dispose of the soil was estimated to cost up to £27 million in 2016[389] for this one site. Assuming this level of costs would be involved for all other sites, benefits of £14.7 billion equate to clean-up at around 545 sites.

9.7.3 Uncertainties and limitations of the approach

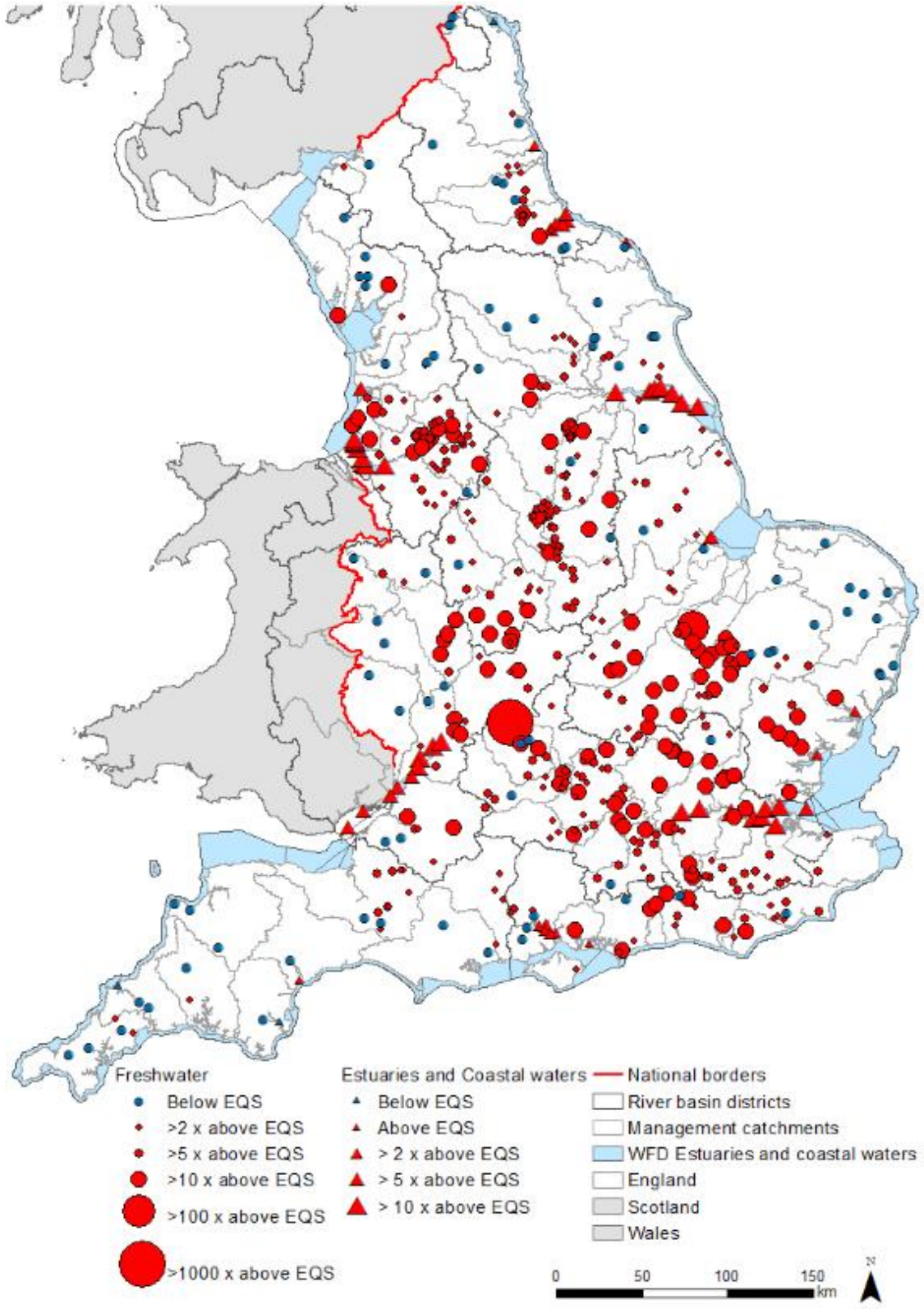
Several uncertainties surround the above approach, not least the extent to which the available NWEBs valuations can be applied in the manner adopted here. The NWEBs estimates were originally developed to provide a means of valuing changes in water body status, moving from bad to poor to moderate to good. No disaggregation of the relative importance of the different "elements" comprising good status, or of ecological versus chemical versus hydro-morphological status was made. As a result, it is unclear how valid it is to disaggregate the NWEBs valuations in the way carried out here.

A 2019 report produced by the Environment Agency[390] indicates that, of 57 freshwater sites where sampling was carried out for PFOS, around 40% failed the EQS for freshwater fish. The analysis given here may therefore be under-estimating the extent of social costs for the "fish" and invertebrates elements with respect to PFOS. However, the margins for failure between measured concentrations and the biota EQS were small except for at around 15% of those sites sampled.

A simplifying assumption also has been made that all of the water bodies fail good chemical status only due to PBDEs and PFOS. This ignores the fact that a significant percentage of waterbodies will also fail due to other chemical determinants which include ammonia concentrations, for example. However, it is also clear that PFOS will continue to be a driver of water quality failures into the future given its long half-life, based on the data shown by Figure 3 of the Environment Agency report.[391]

[389] PFOS legal case dropped by States of Guernsey at cost of £8m - BBC News
[390] https://consult.environment-agency.gov.uk/environment-and-business/challenges-and-choices/user_uploads/perfluorooctane-sulfonate-and-related-substances-pressure-rbmp-2021.pdf
[391] https://consult.environment-agency.gov.uk/environment-and-business/challenges-and-choices/user_uploads/perfluorooctane-sulfonate-and-related-substances-pressure-rbmp-2021.pdf

Figure 9-3 Sampling location and mean measured PFOS concentrations from Environment Agency monitoring compared with the water AA EQS in England, 2016 to 2018



Source: Environment Agency (2019): Perfluorooctane sulfonate (PFOS) and related substances: sources, pathways and environmental data, October 2019.

9.7.4 Future research priorities

A total of 259 substances and substance groups (covering 562 individual substances) have been considered or are being considered (consideration is pending) with respect to their PBT/vPvB status[392]. For 52 of these, the European Chemicals Agency has concluded that they are 'not PBT/vPvB'. This leaves 207 of the substances/ substance groups or 510 individual substances for which conclusions have been reached and:

- they have been identified as a PBT/vPvB/equivalent concern; or
- the results are inconclusive; or
- PBT/vPvB/equivalent concern is suspected but consideration is pending/under development.

A breakdown of these and an indication of their regulatory status is provided in the table below. This gives a simple breakdown of the substances for which conclusions have/have not been made. It highlights the large number of substances for which there remains uncertainty over their PBT status, as well as the large number of substances which are now considered to be PBT/vPvB/ or of equivalent concern.

Table 9-7 PBT/vPvB status classification

	Based on substances/groups of substances (i.e. grouping* = 259 substances)	Based on individual substances (i.e. no grouping = 562 substances)
Concluded PBT/vPvB/equivalent level of concern	65	368
Concluded negative	52	52
Inconclusive	8	8
Suspected and yet to be considered	134	134
Percent concluded on to date	45%	75%
***e.g. 'PFOS, its salts and related substances' comprises 38 individual substances**		

The importance of these figures becomes clear when one combines them with information on the extent to which the substances are already regulated or having action taken, as provided in Table 9-8.

A large number of these substances are currently unregulated but have the potential to cause significant environmental harm. The ability to identify substances of potential concern has outpaced the speed at which testing to verify their properties can be undertaken. Similarly, the identification of such substances has outpaced authorities' ability to monitor for their presence in the environment and to establish what damages if any they are causing.

The importance of these figures becomes clear when one combines them with information on the extent to which the substances are already regulated or having action taken, as provided in Table 9-8.

As set out in the section on estimations of certain SVHC substances in the environment, it is possible on the basis of UK tonnage and use data, to estimate where and how much of substances of concern end up in the environment. However, in order to estimate the cost of that burden to the UK economy it is necessary to quantify the impact (level of environmental damage) of those substances (singularly and as mixtures) on environmental receptors. There is no currently accepted methodology for that within the regulatory frameworks. Therefore, in order to robustly and consistently monetise the environmental impacts of substances (of concern) a framework needs to be developed that utilises existing information requirements in existing legalisation, that can allow impacts to be estimated and valued. Linking estimations of substance fate (modelling) with estimations of impact (based on extrapolations from ecotoxicity data based on

[392] Data collated by RPA for the purposes of this study.

(ecological) consequences of exceeding threshold values) may allow linkage to ecosystem services, which could then provide valuation of impacts. Research on how this might be applied in specific regulatory contexts (e.g. REACH or Biocides Regulations) could be tested with specific substances.

Table 9-8 Regulatory status of concluded and awaiting conclusion PBT/vPvB/equivalent concern substances at the EU level

	SVHC	Restriction	No POPs activity	Proposed POP	Ongoing POP	Recommended POP	Listed POP	Inconclusive	Pending/ Under development/ postponed	PBT	vPvB	PBT/vPvB/ equivalent concern
Based on substances/groups of substances (i.e. grouping* = 207 substances excluding 52 not identified as PBT or of concern)												
Concluded PBT/vPvB/equivalent level of concern	23	5	27	4	3	1	30	0	1	20	28	65
Inconclusive	0	0	8	0	0	0	0	8	0	0	0	0
Suspected and yet to be considered	5	0	134	0	0	0	0	0	134	0	0	0
Based on individual substances (i.e. no grouping = 510 substances total excluding 52 not identified as PBT or of concern)												
Concluded PBT/vPvB/equivalent level of concern	105	11	61	4	9	38	256	0	1	31	90	368
Inconclusive	0	0	8	0	0	0	0	8	0	0	0	0
Suspected and yet to be considered	5	0	134	0	0	0	0	0	134	0	0	0
***e.g. 'PFOS, its salts and related substances' comprises 38 individual substances**												

9.8 Contaminated land

9.8.1 Approach

It has not been possible to carry out a fully quantitative assessment of the chemical pollution associated with land contamination. The approach considered most appropriate is to provide a more qualitative assessment of the issues surrounding contaminated land, due to the limited data available on the number of contaminated land sites in the UK and the highly specific nature of contamination.

Each specific site poses almost unique risks due to the high number of influencing factors, such as soil type, water table depth, type of contamination, depth of contamination, mobility of contaminants in the soil, and organic matter content of soil. As such, it is difficult to propose a suitable method for modelling an accurate monetary value of the risks/remediation costs of contaminated land in the UK and so a more qualitative approach is deemed appropriate.

Contaminated land is defined by part 2A of the Environmental Protection Act[393] as land which is causing/has the possibility of causing significant harm or land which is causing/has the possibility to cause significant pollution of controlled waters. In this definition, harm relates to negatively impacting the health of living organisms/ecological systems and in the case of humans it can also mean harm to property[394]. It is important to recognise this definition as this indicates that 'contaminated land' will not encompass all the UK land area contaminated with harmful substances, only those land areas which have been recognised as potentially harmful/polluting. However, an area of land contaminated with hazardous substances, which was to be developed, would then transition to 'contaminated land' as a risk would be posed and remediation would need to be undertaken.

Remediation of contaminated land can be a costly and time-consuming process but is essential for the redevelopment of many brownfield sites and in areas where contaminated land may be reclaimed for agriculture. This can put the additional costs of pollution onto either the developer, the organisation who caused the contamination or the local council/state. In the majority of contaminated land cases, however, the contamination was caused historically at times when less stringent regulatory measures were in place for the control of the release of chemicals to the environment, or in cases where the negative impacts were unknown. As a result, remediation costs often fall on the landowner or onto the local authority.

In some cases, the responsibility for managing remediation efforts is passed from the local authority direct to the Environment Agency. This occurs when a contaminated land site is recognised as a special site. Special sites are designated as being one or more of the following:

- seriously affects drinking waters, surface waters or important groundwater sources;
- has been, or is being, used for certain industrial activities, such as oil refining or making explosives;
- is being or has been regulated using a permit issued under the integrated pollution control or pollution prevention and control regimes;
- has been used to get rid of waste acid tars;
- is owned or occupied by the Ministry of Defence;
- is contaminated by radioactivity;

[393] https://www.legislation.gov.uk/ukpga/1990/43/contents
[394] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/223705/pb13735cont-land-guidance.pdf

- is a nuclear site.

Between 2001 and 2019, 421 hectares of contaminated land were deemed special sites in the UK[395].

Work previously conducted in 2005 within England and Wales to try and identify the area deemed to be contaminated land, resulted in an estimate of 300,000 hectares across 325,000 sites[396]. However, these figures are likely to be an overestimate due to assumptions made in the methodology. The figures were calculated based on the assumption that each site with potential to cause contamination did cause land contamination. The figures are therefore more indicative of a worst-case scenario than a reliable estimate, as no sites were investigated for presence of contaminating substances. Additionally, the limitations mean that contamination by unrecorded activities and natural phenomena are not included in the 300,000 hectares value.

In addition to the work undertaken in the UK in 2005, the European Environment Agency (EEA) used these data as a part of a broader study to illustrate a wider scale picture of contaminated land across the EEA-39 nations. This formed part of an on-going study examining the progress made towards successful management of contaminated land in Europe. The latest updates from the study were published in 2018 by the Joint Research Council (JRC)[397]. The data presented in the JRC report, however, do little to explain the extent of contaminated land in the UK due to the data being held by local authorities and not at a national level. As such, the data presented here is reflective of those identified in 2005 (325,000 sites estimated).

The more general findings from the European-wide study illustrate that the average remediation costs for a contaminated land site in Europe ranged between €50,000 and €500,000 in 2011[398]. Additionally, the findings illustrate that these costs equate to roughly 81% of the average expenditure on a contaminated land site in Europe, with average costs of site investigation between €5,000 and €50,000. No data from the UK was used to calculate these figures, making it difficult to know if these costs are comparable to the UK context.

Between 2000 and 2013, local authorities were encouraged to report and identify areas of contaminated land throughout England as a part of the Environmental Protection Act part 2A. A report released by the Environment Agency (2016)[399] summarises the work of the local councils over this time period. It is estimated that since 2000 over 11,000 sites were investigated at a cost of over £32 million, resulting in the designation of 511 sites needing remediation activities. Of these sites, remediation started on 493 with 433 complete as of 2013. The total cost for these remedial activities was found to be in excess of £52 million[399]. Whilst Whilst this report[399] does help to provide a good overview, using more analytical techniques than the 2005 study[396], there are still major limitations to the findings. The data gathered in this study was only collected from 197 of the total 326 local authorities across England resulting in a major underestimate of the extent of the problem. In addition, the data gathered indicated at least another 10,000 sites which required more in-depth inspection before a contaminated land determination could be confirmed or rejected.

In 2021, the Campaign for the Protection of Rural England (CPRE)[400], conducted a similar survey in which 330 local authorities were contacted regarding the number of brownfield sites they had recorded within their authority. Across England, a total number of 21,566 brownfield sites were identified. Whilst this study does

[395] https://data.gov.uk/dataset/e3770885-fc05-4813-9e60-42b03ec411cf/contaminated-land-special-sites
[396] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/290711/scho0805bjmd-e-e.pdf
[397] https://esdac.jrc.ec.europa.eu/public_path/shared_folder/doc_pub/EUR29124.pdf
[398] https://www.eea.europa.eu/data-and-maps/indicators/progress-in-management-of-contaminated-sites-3/assessment
[399] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/513158/State_of_contaminated_land_report.pdf
[400] https://www.cpre.org.uk/wp-content/uploads/2021/11/Nov-2021_CPRE_Recycling-our-land_brownfields-report.pdf

benefit from the full picture of data from 330 local authorities, not all of these brownfield sites will be considered contaminated land.

Up until 2014, local authorities could apply for funding to investigate and remediate contaminated land under the 'Contaminated Land Capital Grants' scheme (CLCG)[401]. Without funding, local authorities found it difficult to justify continued contaminated land investigations, when often these would result in additional costs falling back upon themselves in cases where the polluter/current landowner could not be identified. As such work towards identifying and remediating contaminated land slowed considerably with developers taking more of a lead than local authorities. Ultimately this has led to a lack of reporting of contaminated sites in the UK and hence the difficulties with estimating the area of contaminated land, noted in the paragraphs above.

Interest in contaminated land is increasing again in recent years as the development of brownfield sites has become higher priority, as illustrated by the CPRE study. Since 2017 local authorities have been able to apply for funding under the Land Release Fund to help accelerate the development of housing on local authority owned land. A new addition to this is the Brownfield Land Release Fund (BLRF) introduced in January 2021, which is offering £75 million[402] to local authorities to release brownfield sites for redevelopment before March 2024. The purpose of this capital allocation is to address the abnormal costs arising from site viability issues, including contamination from hazardous substances. Additionally, the 2021 budget announced that a sum of £1.8bn is to be allocated to the regeneration of 1,500 hectares of brownfield sites within the UK[403]. Whilst this may not specifically deal with issues surrounding contaminated land, site evaluation and remediation are likely to be part of this investment.

A recent case study, which gives some indication of the costs of large-scale contaminated land remediation, is the Avenue Coking Works site in Chesterfield. This 98 hectare site operated between 1952-1992 to produce coke and gas but had also previously been used as a colliery and ironworks[404]. This combination of industrial activities left the site as one of the most polluted in Europe with a cocktail of hazardous substances in both the soil and nearby River Rother. The Homes and Communities Agency in partnership with the East Midlands Development Agency started work on the site in 1999, with the demolition of the structures (which had lain abandoned since 1992). Over 10 years were spent determining a suitable remediation strategy. Multiple companies (SUEZ, Deme Group, VSD Avenue) all worked from as early as 2001 to remediate both contaminated land and water to a point at which homes could safely be built on the site in 2017. The project has taken a total of 19 years and cost £179m[405] to Homes England (the public body that funds new affordable housing in England and is sponsored by the Department for Levelling Up, Housing and Communities).

9.8.2 Uncertainties and limitations of the approach

There are clearly uncertainties as to the extent of land contamination in the UK as well as to the costs that may be involved in remediating such sites. Similarly, it is unknown what impacts the existence of contamination may be having on the environment or people's health at the national level.

9.8.3 Summary

Contaminated land costs cannot be accurately calculated due to the specificity of each individual case and need for different scales and types of remediation. In addition, as noted above, there is limited data on the

[401] https://environmentanalyst.s3.amazonaws.com/downloads/MIS/insight-reports-2019/Contaminated-Land-A-Modern-Mid-Life-Crisis-2019-report-Final.pdf
[402] https://www.local.gov.uk/fund-details
[403] https://environment-analyst.com/uk/107430/sunak-commits-18bn-to-brownfield
[404] https://www.todaysconveyancer.co.uk/partner-news/avenue-coking-works-remediation-making-impossible-possible/
[405] https://www.propertyweek.com/features/contaminated-land-where-theres-muck-/5097132.article

extent of contaminated land in the UK at present. However, it is clear that the costs of such historic pollution can be high in terms of the expenditure needed to remediate such sites to a level suitable for future use and development. The Avenue Coking Works case study provides an example of a contaminated land site where remediation costs were calculated at a total of £179 million.

9.8.4 Future research priorities

A key area for future work on contaminated land would be a return to the investigation of contaminated land sites within the UK. The removal of funding for these investigations has led to a lack of understanding about the extent of contaminated land in the UK and the inaccurate estimates highlighted in the above section. To accurately determine the costs of legacy contaminated land it should be priority to first understand the extent of the problem, and additionally the main substances of concern. There may also be merit in assessing the substances leading to contamination, and establishing a regulatory profile for these to provide a better understanding of the extent to which restrictions on the manufacture and/or use of certain substances under legislation such as UK REACH may provide a means of preventing such issues in the future. A regulatory management options analysis (RMOA) study may be beneficial in determining the best regulatory approach to avoid release of specific substances of concern to land and the future costs of remediation.

Future research may be able to focus on adapting the latest information gathered as a part of the EEA monitoring programme to fit the context of the UK. By taking data such as the costs of remediation for EU Member States and comparing these against UK case studies, an assessment could be made as to the potential costs to the UK associated with contaminated land remediation.

As stated in a 2019 report by Public Health England[406] "To date, there is little conclusive evidence of serious health effects from the types and levels of land contamination found in England". Therefore, investigations on the burden of disease/environmental impacts could also be undertaken to better establish the social costs of pollutants present in contaminated land.

406 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/779168/factsheet_for_contaminated_land.pdf

10 Pesticides

10.1 Effects

Pesticides include biocidal and plant protection products. Their use has been associated with a range of impacts on both human health and the environment.

In terms of human health:

- Occupational exposures to pesticides, e.g. workers involved in pesticide spraying / application, have been identified as giving rise to a range of impacts varying from cancers to infertility to a range of chronic and acute effects (respiratory, skin, etc.).
- Consumer and bystander exposures to pesticides may also result in illness due to unintentional exposures and misuse.

In terms of environmental impacts:

- Use of pesticides may give rise to a range of environmental impacts, including impacts on non-target species (including pollinators, birds, insects), soil quality and water quality.

Pesticide poisoning in humans is difficult to identify due to a relatively large number of symptoms which may be present as a result of low-level exposure to pesticides[407]. Symptoms of acute exposure may include respiratory tract irritation, allergic sensitisation, eye/skin irritation, nausea, vomiting, diarrhoea, headaches, loss of consciousness and in extreme cases death.

There is also evidence to suggest that chronic exposure to pesticides may increase the risk of cancer, with exposure linked to brain/central nervous system (CNS), breast, colon, lung, ovarian (female spouses), pancreatic, kidney, testicular, and stomach cancers, as well as Hodgkins and non-Hodgkins lymphoma, multiple myeloma, and soft tissue sarcomas in the US[408]. Furthermore, around 40 chemicals classified as known, probably or possible human carcinogens are used in pesticides registered for use in the US.

10.2 Substances of concern

As highlighted above, a wide range of chemical pesticides may cause harm to humans/environment via exposure. As such the majority of the group of pesticide chemicals could be seen as substances of concern. The three most commonly reported substances associated with poisoning in humans were reported by the National Poisons Information Service in 2019/20[409] as follows:

- Permethrin
- Glyphosate
- Difenacoum

[407] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2718882/
[408] https://deainfo.nci.nih.gov/advisory/pcp/annualreports/pcp08-09rpt/pcp_report_08-09_508.pdf
[409] https://www.npis.org/Download/NPIS%20Report%202019-20.pdf

Between these pesticides the hazard profile to humans, listed on the ECHA website, includes skin sensitisation, reprotoxic effects and harmful/fatal if inhaled or swallowed[410] [411] [412]. These pesticides are also registered in various degrees as toxic to aquatic life.

From consultation with the Environment Agency, it was revealed that the active substance Bentazone is the most common chemical associated with groundwater contamination in the UK. Bentazone is harmful if swallowed[413] and is likely to be confirmed as 'suspected of damaging the unborn child' in the next EU CLP (Classification, Labelling and Packaging) update. Bentazone levels are therefore strictly controlled in drinking water sources. A range of other pesticides are classed as Priority Hazardous Substances and are regulated with respect to discharges to the aquatic environment.

10.3 Major uses

The active substances used for pesticides in the UK are the base constituents to mixtures sold as biocidal products and plant protection products. Biocidal products are used to protect people and animals, preserve goods, stop pests like insects or rodents and control viruses, bacteria and fungi through a chemical or biological action. Common examples are disinfectants, wood preservatives and insect repellents. These may be sold to industrial users (e.g. timber preservatives, preservatives used in coatings manufacture), professional users (e.g. treatment using preservatives of wooden windows) or consumers (e.g. treatment of sheds etc. with preservatives).

Similarly, plant protection products will be marketed for use by farmers for agricultural uses, to local authorities and others for weed maintenance along verges/in parks/on golf courses, and by consumers for horticultural use.

10.4 Current regulatory controls and remaining sources of exposure

Pesticides are currently addressed by the Biocidal Products Regulation (BPR)[414] and the Plant Protection Products (PPP) Regulation[415], both of which transitioned into the UK legislation from their EU counterparts.

Under the BPR, active substances for use in biocidal products are systematically reviewed for approval for specific end uses based on risk data. The biocidal products themselves then go through further assessment before they are authorised and can be placed on the market. This ensures the safe use and control of the most hazardous biocidal substances.

Similarly, the PPP regulation contains both an approval and authorisation process for the making available on the market of plant protection products. For users of such pesticidal products, there is a strict code of practice which sets out the training, certification, safe use and disposal requirements for users of pesticides. This is summarised in the Plant Protection Products (Sustainable Use) Regulation 2013[416]. Maximum residue levels for different pesticides also help to regulate the level of pesticide that may be present in food items, to help ensure consumer exposure is below no effect levels. Whilst these regulations help to minimise risks, pesticides exposure can still occur by accidental/deliberate misuse, overspray events and bystander exposure.

[410] https://echa.europa.eu/substance-information/-/substanceinfo/100.052.771
[411] https://echa.europa.eu/substance-information/-/substanceinfo/100.012.726
[412] https://echa.europa.eu/substance-information/-/substanceinfo/100.054.508
[413] https://echa.europa.eu/substance-information/-/substanceinfo/100.042.335
[414] https://www.legislation.gov.uk/uksi/2001/880/contents/made
[415] https://www.legislation.gov.uk/uksi/2011/2131/contents/made
[416] https://www.legislation.gov.uk/uksi/2012/1657/contents/made

10.5 Occupational burden of disease

10.5.1 Approach

Previous studies have derived estimates of the potential occupational burden of diseases associated with pesticide spraying / application in the UK. Due to limitations on the resources and time available for this study, it has not been possible to provide an updated analysis. As a result, we illustrate the potential burden of disease due to historic exposures through reference to RPA (2008)[417] in which US odds ratios were combined with UK survey data to estimate the human health impacts from exposure to active substances which were linked in particular to cancer outcomes.

10.5.2 Results

The occupational burden of pesticides mainly occurs from the chronic exposure of agricultural workers to pesticide active substances. In addition to cancer, asthma and other respiratory effects, illnesses linked to work-related pesticides exposure include Parkinson's disease, anxiety, depression, and asthma [418] [419]. Occupational exposures may also lead to risks for childhood cancers linked to parental pesticide exposure prior to conception, in utero exposures and direct exposures throughout childhood. At the time of this study, the research into chronic exposure and associated human health risks was considered to be inconclusive and further investigations were required for some of the causal links to be determined.

Pimentel (2005) conducted a US Agricultural Health Study, which provides an extensive literature on the increased risks of different cancers linked to pesticide exposures. The studies mentioned above provide odds ratios and hazard ratios that can be used to derive the population attributable fractions (PAFs)[420]. Unfortunately, it is hard to translate from these studies to the UK situation, due to factors such as differences in approved pesticides, modes of application, areas of application, frequency of application, etc.

A study carried out by RPA in 2008[421] for the Pesticide Safety Directorate drew on some of the US studies to derive cancer burden estimates from exposures to a set of plant protection products which were approved for use in the UK. US odds ratios were combined with detailed UK farm survey data to estimate the area to which the pesticides may have been applied, application method, frequency of application and number of workers exposed, in order to develop the PAFs. The study estimated that between 1% and 24% of agricultural spray operators were ever exposed to the seven case study active ingredients, with the potential human health benefits from withdrawal of the seven active ingredients estimated at between £93 to £186 million in cancer cases avoided for spray operators in England and Wales. These figures increased to £354 to £709 million in cancer cases avoided for the ever-exposed population. However, the study also noted that there was significant uncertainty in the use of the odds-ratios and that UK Committees had previously concluded at the time that the available epidemiological studies were not consistent enough or sufficient to justify regulation of the substances. The active substances were later banned from use in the UK. Other substances currently lacking in sufficient evidence for regulation may be posing a human health risk and contributing to the occupational burden of disease.

10.5.3 Key assumptions

[417] RPA, 2008, Study on the Benefits of Pesticide Regulation: Part 1, for the Pesticide Safety Directorate, July 2008, Available at: http://sciencesearch.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&Completed=0&ProjectID=15293

[418] https://researchbriefings.files.parliament.uk/documents/POST-PB-0043/POST-PB-0043.pdf

[419] https://www.pan-uk.org/health-effects-of-pesticides/

[420] See for example: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5381995/

[421] RPA, 2008, Study on the Benefits of Pesticide Regulation: Part 1, for the Pesticide Safety Directorate, July 2008.

Key assumptions within the study relate to the use of odds-ratios and hazard ratios for US farm workers and translating them to the UK context. This assumed that usage conditions and levels and durations of exposure were similar across the two populations, which may not have been the case. Similarly, as there was no data on the actual number of UK pesticide workers exposed to each of the active substances, this was derived from data on the quantities of each used in the UK, the relevant crop areas and hence the likely percentage of workers who could have been exposed.

10.5.4 Uncertainties and limitations of the approach

The uncertainties relate to the key assumptions as set out above. It is important to note that the estimates given above provide an indication of the potential historic burden of disease, which would have arisen in part due to a lack of sufficient information on the health hazards associated with some of the pesticides. The information requirements and risk assessment processes in place for the approval of active substances has improved since the 2008 study was carried out.

This type of approach could be repeated to try and develop updated figures. However, care would need to be taken in the choice of substances and in ensuring that there is sufficient data on use practices to improve the robustness of the analysis. It is of note that the study results were used in an illustrative manner to highlight the importance of the on-going regulation of pesticides on the UK market.[422]

10.6 Consumer and bystander burden of disease

A suggested approach for consumer and bystander burden of disease would be to use data from the National Poisons Information Service (NPIS) and apply monetary valuations to this based on the concept of a "restricted activity day". For example, NPIS reported only 282 cases of symptomatic accidental pesticide exposure in their 2019/20 report. Of these it is likely not all resulted in restricted activity days as symptoms to low level pesticide exposure can be mild. Additionally, the costs associated with a restricted activity day are typically less than €100[423] (roughly £83) per day and as such the overall costs determined by this approach would be likely in hundreds of thousands and not in the millions. Therefore, the selected approach is a qualitative discussion based on the existing literature.

10.6.1 Results

A study conducted by Rushton and Mann (2009)[424] gathered UK data between 2004 and 2006 to try and understand the prevalence of human health impacts relating to pesticide exposure. Participating GPs were sent a screening checklist to be filled out during consultation, alongside an information pack on pesticide related illness. Out of a total of 59,320 consultations between GPs and patients, only 20 cases were referred to as likely being related to pesticide exposure. A further 1,599 cases were deemed possibly linked to pesticides although the majority (43,210 cases) were considered unlikely to be or not at all linked to pesticide exposure. As such, the study was unable to accurately determine a direct link between reported health effects at primary care level and exposure to pesticides at industrial/professional level. The study did not include any economic valuation of effects.

[422] Defra (2009): Impact Assessment of Pesticide Regulation (Pesticides and the Environment: A strategy for the Sustainable Use of Plant Protection Products), SID5, Research Project Final Report. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwiv1eeTrtT1AhVLZcAKHbzGBhwQFnoECAIQAQ&url=http%3A%2F%2Frandd.defra.gov.uk%2FDocument.aspx%3FDocument%3DPS2536_8538_FIN.doc&usg=AOvVaw3dDmeC6YcqNQjvvvODB0NB

[423] Using data from: https://ec.europa.eu/environment/air/pdf/TSAP%20CBA.pdf and ozone/PM2.5 as aproxy.

[424] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2718882/

In contrast, in 2019/20 the National Poisons Information Service (NPIS) was consulted on 886 pesticide exposure cases[425]. Of these 80.4% were accidental acute exposures and 7.0% were attributed to accidental chronic exposure. In total, 73.3% of the total exposure cases had a low poisoning severity score (PSS) and as such only mild effects. The number of cases and impacts of pesticide poisoning are difficult to identify due to a relatively large number of symptoms which may be present as a result of low-level exposures**Error! B ookmark not defined.**. Symptoms of acute exposure may include respiratory tract irritation, allergic sensitisation, eye/skin irritation, nausea, vomiting, diarrhoea, headaches, loss of consciousness and in extreme cases death. No economic valuations are provided by the NPIS.

Note that the recent Parliamentary Office of Science and Technology (POST) report on pesticides and human health (2020) noted that: "Proving causal relationships between chronic pesticide exposure and health effects is difficult, and the research available in this area is inconclusive and of variable quality".

10.6.2 Uncertainties and limitations of the approach

The scope of this approach is limited as it does not provide any values, however, as previously mentioned the best evaluation approach is unlikely to lead to any significant contribution to the overall 'costs of pollution'.

10.7 Environmental impacts

10.7.1 Approach

A number of approaches were assessed based on adapting various studies to fit the UK. Unfortunately, the majority of methods proposed would result in high level inaccuracies in the final data. The methods set out in the available literature do not provide findings/data which could accurately be adapted to fit the present UK situation. For example, one study provides a WTP study for the impact of pesticides on farmland wildlife, however, the WTP index used and hazard index (based in part on pesticides now banned) are outdated and so could not be used to provide accurate or reliable data. One study however has been used below to illustrate the economic value of minimising the impacts of pesticides on pollinator services within the UK. In addition to this, an illustrative case study relating to the impacts of pesticide contamination of groundwater is also provided. This approach provides both a quantitative and qualitative analysis of two different environmental impacts arising from pesticide use.

10.7.2 Results

Using data from 2005, Gallai et al (2009)[426] estimated the total global value of pollinator services as €153 billion, or approximately £105 billion[427]. This value was derived by studying pollinator dependence ratios for a group of 100 different crops, grown specifically for direct human consumption. The value derived is equivalent to a present value of £142 billion (2021 prices). Using data from 2020 crop outputs for grains, cereals[428] and vegetables[429] [430], a proportion of the global agricultural crop production was attributed to the UK. For grains and cereals, this proportion was 0.36% whilst for vegetables the proportion was 0.23%. Taking the average of these two values means roughly 0.29% of the total global agricultural output can be attributed to UK production. Using this percentage and the value of £142 billion for the global economic

[425] https://researchbriefings.files.parliament.uk/documents/POST-PB-0043/POST-PB-0043.pdf
[426] https://www.sciencedirect.com/science/article/abs/pii/S0921800908002942
[427] Using a 2005 exchange rate of $1.461
[428] https://data.oecd.org/agroutput/crop-production.htm
[429] https://www.statista.com/statistics/264662/top-producers-of-fresh-vegetables-worldwide/#:~:text=Global%20vegetable%20production,billion%20metric%20tons%20in%202019.
[430] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1003935/hort-report-20jul21.pdf

benefits of pollinators indicates that the value of pollinators to the UK is estimated at approximately £435 million in 2021 (£142 billion x 0.29). Further analysis of the impacts on this value due to pollinator decline from pesticide use is not considered feasible due to limited data directly linking pollinator decline to crop yields and pesticide use. However, due to the high value of pollinator services in the UK, any decline caused by the use of pesticides may have significant economic impacts.

Further to the valuation above, a case study is provided for this section to help illustrate the potential impacts and costs arising from a pesticide contamination case, specifically on a groundwater contamination event. This event was selected as a good illustrative example as groundwater contamination from Bentazone is the most commonly occurring type of pesticide contamination event in the UK[431]. On 13 April 2017 the active ingredient Bentazone was applied to a 6.2 hectare area of land just north of the village of Upton Scudamore in Wiltshire[431]. The spray rate was 2.2 litres per hectare, resulting in the application of 5.18kg of Bentazone to the upper section of the field. This spray rate is within the acceptable limits stated on the product information (3 litres per hectare[432]) and so did not reflect a case of misuse or deliberate overspray. Following the detection of increased levels of Bentazone in groundwater, modelling found that roughly 138 grams of Bentazone had leached into the aquifer.

Bentazone is the active ingredient of the pesticide Benta 480SL (alongside other pesticides) and is an effective herbicide for protecting leguminous crops against broadleaf weeds[433]. Chemically, Bentazone is highly persistent in the environment. The chemical hazards posed by Bentazone are currently classified as follows:

- H302: Acute Tox. 4 (Harmful if swallowed)
- H319: Eye Irrit. 2
- H317: Skin Sens. 1
- H412: Aquatic Chronic 3

However, the substance was recently reviewed and the latest opinion of ECHA's Committee for Risk Assessment (RAC) recommended that H412: Aquatic Chronic be removed and H361d: Repr. 2 (Suspected of damaging the unborn child) be added[434]. Therefore, the toxicity via the oral route and suspected reproductive toxicity indicate that the presence of Bentazone in drinking water could pose a significant risk to human health, supporting the case for the 0.1µg/litre UK limit for pesticides in drinking water. In the case of the pollution at Upton Scudamore, this limit has been breached and remediation activities are required.

Since the initial detection of Bentazone in excess of the 0.1 µg/l limit, monitoring has been carried out at various boreholes in the surrounding area of the site. In 2021, each of these boreholes reported Bentazone presence in the water, however, only the borehole closest to the site reported values in excess of 0.1 µg/l. As such the operation of this borehole has been switched from pumping of water to running the borehole water to waste. This effectively acts as a system for removal of contaminated water where it can be treated/further diluted down to ensure safe levels of Bentazone.

In addition to this, the responsible authority (Wessex Water) has conducted additional sampling and groundwater modelling and has helped to support farmers in stewardship over the use of Bentazone in this area (involving the growth of a break crop). Wessex Water has also circulated the risk results of the groundwater model to other local farmers to help them understand the impacts.

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[431] Data gathered from consultation with Environment Agency (2021).
[432] https://nufarm.com/uk/product/benta/
[433] https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/bentazon
[434] https://echa.europa.eu/documents/10162/d1f83444-c719-8f3f-58fd-04a8b424a4a5#:~:text=Overall%2C%20RAC%20agrees%20to%20classify%20bentazone%20as%20Skin%20Sens.

The total costs for each of these actions are detailed below:

- Running borehole to waste: £20,000 per annum;
- Additional sampling costs: £10,000 per annum;
- Additional staffing estimate: £10,000 (to date);
- Groundwater modelling: £5,000;
- Financial support to catchment farmers for stewardship: £5,000.

Levels of Bentazone observed in the closest borehole are still roughly four times the acceptable drinking water limit: if the borehole is once again required for water supply, remediation activities will need to be undertaken. This is more likely to occur as the year progresses as demand for water goes up throughout the summer months. In the event that the contaminated borehole is required to return to pumping, then temporary granular activated carbon (GAC) remediation has been suggested. Wessex Water currently have a contingency plan to put this into operation within four weeks if required, however the cost of even a temporary GAC is estimated at roughly £150,000. If the borehole is required in the longer-term then a permanent GAC may be required which could significantly increase the cost of remediation from £150,000 to between £3 million and £5 million.

This case study provides an example of a groundwater contamination incident due to the use of pesticides in agricultural activities. In the wider context of the UK, Bentazone contamination of groundwater is the most frequently reported pesticide contamination event and so the above example could be used as a suitable proxy for other events. GAC is not the only potential remediation method for groundwater contamination however it is by far the most common. As a result, the costs of this study are likely to be widely applicable to many pesticide contamination cases in the UK, reported as 148 cases since 2001[435]. Using the costs for this study as a rough estimate and assuming a worst-case scenario in which permanent GAC remediation is required, pesticide contamination could have cost between approximately £20 million and £750 million since 2001. The true cost could be £100's millions over twenty years.

10.7.3 Key assumptions

Whilst calculating the value of pollinators for the UK assumptions were made surrounding the proportion of global agricultural production which could be attributed to the UK. This study used data for vegetable, wheat, maize, rice and soyabean outputs to calculate this figure and so the true value may be different when other crops (e.g. fruit crops) are included. A further assumption is that the proportion of UK output remains constant as the data for the global pollinator value is in 2021 whilst the UK proportion of output is based on 2020 data. For both of these assumptions, the true values are not predicted to be significantly different.

In the groundwater case study, the value of approximately £20 million to £750 million since 2001 is based on one key assumption, that is that all of the 148 reported pesticide contamination cases could be addressed in the same manner as the one case and that levels of contamination were similar to those in this example. This is highly uncertain.

10.7.4 Uncertainties and limitations of the approach

The UK value of pollinators is calculated as approximately £435 million per year and only a small proportion of this is likely to be affected by pollinator decline caused by pesticides. This number simply indicates that even if only a small proportion of this value is lost due to pesticides, it would be a significant value when compared against other costs reported in this study.

[435] https://environment.data.gov.uk/portalstg/home/item.html?id=025c69dc15784a2186c3f089c776be5c

The possible cost of pesticide contamination of groundwater supplies is highly uncertain and is a key limitation of this example. The true cost could be about £100's millions over a period of e.g. twenty years given that water companies will have been responding to this issue on an on-going basis.

10.7.5 Summary

Pesticide contamination can have impacts on both human and environmental health although these may be difficult to quantify. In human health cases, this can be due to the majority of exposures being relatively low level with minor wide ranging health impacts, making it hard to attribute them directly to pesticides. In the case of environmental health pesticides have a clearer impact although these can also be hard to value in monetary terms.

In RPA (2008), estimates of between £93 to £186 million in cancer cases avoided by regulation of seven active ingredients were found, with higher values of £354 to £709 million in cancer cases avoided for the ever-exposed population. These values however are uncertain due to the use of odds ratios for UK farm workers; it is of note that UK regulators assessed the available health data and found that it did not (at that time) justify restrictions on the use of the substances.

In terms of environmental benefits, a value of £435 million has been calculated based on research by Gallai et al (2009)[426] although this cannot be linked to directly to the impacts of pesticides on the environment. Similarly, the ground water case study illustrates that the costs of pesticide contamination of groundwater supplies may be high, with remediation of single sources potentially costing in the tens of millions.

10.7.6 Future research priorities

Given more time and resource, an up-to-date assessment of the potential occupational burden of pesticide exposure could be developed. The main difficulties with calculating human health costs of pesticides exposure are accurately attributing the symptoms to exposures to specific active substances.

Development of this attribution would be beneficial in helping to understand the true impact of pesticides on human health, especially in consumer/bystander exposure cases. To better understand this, a study similar to that of Rushton and Mann (2009)[Error! Bookmark not defined.] could be conducted. In this case, UK GPs c ould be supplied with updated information sheets regarding the impacts of pesticide exposure (potentially with a focus on those in wide circulation in the UK) and asked to record symptoms and report suspected cases of pesticide exposures. This study could help to fill in gaps in the knowledge surrounding human health impacts and scale of accidental pesticide exposure in the UK.

In terms of environmental impacts, information could be collected from the UK water companies on the levels of expenditure – on-going and expected future investments – to address pesticide contamination of groundwater supplies.

11 Skin, blood and metabolic diseases

11.1 Effects

This section uses available evidence to explore the cost of skin diseases associated with exposure to various chemical substances. Costs to the NHS, productivity losses and willingness-to-pay (WTP) data are examined. The approach follows the 2017 European Commission "CuBA" Study [436] and a 2016 RPA study on the development of system of indicators to monitor the benefits of chemical legislation [437]. These used UK data on contact dermatitis data from HSE to calculate an attributable fraction for cases attributable to chemical substances.[438] This is used to estimate the current burden to the UK from occupational skin disease associated with chemical exposure. This approach only considers occupational skin diseases, there is currently insufficient data to include an assessment on wider consumer exposure.

The following effects have been identified in the literature:

- **Skin diseases** and irritations are associated with chemicals exposure, the most common is **contact dermatitis** (inflammation of the skin resulting from the contact with a chemical or physical agent). This includes allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD), which are irreversible and cannot be cured. Therefore, exposure must be avoided. Fragrance allergies resulting in contact dermatitis will be considered to partially assess the cost of skin disorders from consumer exposure to substances.
- **Obesity** – fat accumulation that impairs health – defined at those with a body mass index above 30.[439]
- **Diabetes** - characterised by elevated levels of blood glucose, associated with potential damage to heart, blood vessels, eyes, kidneys and nerves and which can increase risk of premature death. This includes Type 1 (hereditary immune response to that destroys insulin producing cells) and type 2 (deficient production of – or non-responsiveness of the body's cells - to insulin). Some 90% of UK sufferers have Type 2.[440]
- **Anaemia –** low levels of red blood cells or levels of haemoglobin in these cells. It is caused by iron or Vitamin B9/B12 deficiency. Symptoms of anaemia include fatigue, weakness, pale or yellowish skin, irregular heartbeats, shortness of breath, dizziness, chest pain, cold hands and feet and headaches.[441]

11.2 Substances of concern

Over 14,000 substances on the EU market have been indicated to have skin sensitising properties from information in the Classification and Labelling Inventory.[442] Chemicals of concern include heavy metals (e.g.

[436] European Commission, Directorate-General for Environment, *Study on the cumulative health and environmental benefits of chemical legislation : final report*, Publications Office, 2017, https://data.europa.eu/doi/10.2779/070159
[437] European Commission, Directorate-General for Environment, *Study on the Calculation of the Benefits of Chemicals Legislation on Human Health and the Environment.* 2016. https://ec.europa.eu/environment/chemicals/reach/pdf/study_final_report.pdf
[438] HSE. Work-related skin disease statistics in Great Britain. Found at: https://www.hse.gov.uk/statistics/causdis/dermatitis/skin.pdf
[439] Centers for Disease Control and Prevention. https://www.cdc.gov/obesity/adult/defining.html
[440] NHS. Diabetes. https://www.nhs.uk/conditions/diabetes/
[441] Mayo Clinic. Anemia. https://www.mayoclinic.org/diseases-conditions/anemia/symptoms-causes/syc-20351360
[442] ECHA. Skin sensitising chemicals. https://echa.europa.eu/hot-topics/skin-sensitising-chemicals

lead), chromium VI, nickel and cobalt compounds, and formaldehyde. Other substances of concern include pharmaceuticals, dioxins, polychlorinated biphenyls (PCBs), DTT, pesticides, brominated flame retardants, perfluorinated chemicals and plasticisers[443].

11.3 Major uses

Uses are varied and include dyes in textiles, leather, synthetic leather and fur articles and additives in consumer cleaning products. Whist the severity and individual health impact of skin disorders tends to be relatively low, widespread use of substances of concern mean that skin disorders are common across the UK. Approximately 60% of people currently suffer or have suffered from some form skin disease in the UK, resulting in a significant cumulative impact[444]. Beauticians, cooks, florists, hairdressers/barbers and metal working machine operatives are at the highest risk, based on incidence rates.[445]

11.4 Current regulatory controls and remaining sources of exposure

The EU CLP regulation (EC) 1272/2008 was the legal mechanism through which the Globally Harmonized System (GHS) was applied. All EU harmonised classification and labelling in force on 31 December 2020, are retained in Great Britain as GB mandatory classification and labelling (GB MCL)[446]. A total of 1,293 are classified as skin irritants or skins sensitizers[447].

Annex XVII of EU REACH (restricted substances) classifies 12 substances for skin sensitization.[448] This includes use of chromium (VI) in cement. Use in leather products (and products containing these materials) was further restricted in 2014.[449] This legislation applies in the UK as it was in place prior to the UK's exit from EU REACH. We note further action is being considered at European level on a rage of skin sensitizers, denoting ongoing concern in other jurisdictions[450].

11.5 Skin disorders

A number of skin diseases, such as contact dermatitis, are associated with exposure to chemical or physical agents. Historic UK HSE data shows that, of occupational skin disorders recorded in the UK between 1998 and 2013, in just under 70% of cases, the primary causative factor was exposure to chemical substances[451]. The most recent data on work related skin diseases relate to Great Britain and gives data up to 2020[452]. It is

[443] European Commission, Directorate-General for Environment, *Study on the cumulative health and environmental benefits of chemical legislation : final report*, Publications Office, 2017, https://data.europa.eu/doi/10.2779/070159
[444] British Skin Foundation. https://www.britishskinfoundation.org.uk/
[445] Health and Safety Executive (HSE) Annual Statistics Work-related skins diseases statistics in Great Britain, 2020 https://www.hse.gov.uk/statistics/causdis/dermatitis/skin.pdf
[446] https://www.hse.gov.uk/chemical-classification/legal/clp-regulation.htm
[447] I.e. include Skin Sens 1, 1A,1B (H317), Skin Irrit 2 (H315) .
[448] European Commission, Directorate-General for Environment, *Study on the cumulative health and environmental benefits of chemical legislation : final report*, Publications Office, 2017, https://data.europa.eu/doi/10.2779/070159
[449] EHCA. Annex XVII to REACH – Conditions of restriction. https://echa.europa.eu/documents/10162/1f775bd4-b1b0-4847-937f-d6a37e2c0c98
[450] ECHA. (n.d.) ECHA's committees back restricting over 1000 skin sensitising chemicals used in clothing and other articles. https://echa.europa.eu/-/echa-s-committees-back-restricting-over-1-000-skin-sensitising-chemicals-used-in-clothing-and-other-articles
[451] European Commission, Directorate-General for Environment, *Study on the cumulative health and environmental benefits of chemical legislation : final report*, Publications Office, 2017, https://data.europa.eu/doi/10.2779/070159
[452] Health and Safety Executive (HSE) Annual Statistics Work-related skins diseases statistics in Great Britain, 2020 https://www.hse.gov.uk/statistics/causdis/dermatitis/skin.pdf

based on statistical collections from several sources and which focus on both incidence and prevalence. Both are relevant for estimating the costs burden. In terms of **incidence:**

- The **EPIDERM** scheme within The Health and Occupation Reporting (THOR) is based on physician diagnosed cases – likely to be more serious cases. The latest data are an average between 2017- 2019.
- These data illustrate that there were a total of 1,019 diagnoses of work related skin disease in 2019 in 1,016 individuals[453], with 87% of these cases being contact dermatitis[454]. These data cover occupational dermatitis only and is based on the estimated number of diagnoses where causative substances were identified. The most common causes are from soaps and cleaners, rubber chemicals and materials, allergic reactions to PPE, Preservatives and Nickel. It is more common amongst those under 35 and amongst women[45].
- UK data has shown a consistent decline in the overall number of cases since the late 1990's – a annual average decrease of about 7% (2010-2019). Beauticians, cooks, florists, hairdressers/barbers and metal working machine operatives are at the highest risk, based on incidence rates.
- Cases assessed for **Industrial Injuries Disablement Benefit (IIDB).** These are more serious still with 10 cases in 2019 (averaging 37 over the last 10 years)[455].

There will be a tendency to understate the disease and its cost, even that associated with occupational exposure in the UK. Not all epidemiologists are part of EPIDERM and of those that are, not all actually report cases. Many workers also fail to report cases, so there is likely to be a substantial "tail" of cases, many that are less serious, but which nevertheless may pose a significant burden on primary care and may affect presence at work to some extent for both the sufferer and potentially for partners/caregivers as well.

Moreover, as an incurable disease, the population who currently suffer from the disease compounds. So, in terms of **prevalence:**

- Labour Force Survey (LFS) data estimated 16,000 (95% confidence interval: 11,000-21,000) people working within the last year with skin problems they regard as caused or made worse by work.[456]

11.5.1 Approach to the assessment of UK costs of occupational skin sensitization

The "CuBA" study (EC, 2017) and a study on the cumulative health and environmental benefits of chemicals legislation (RPA, 2016), both developed for the European Commission, based EU estimates of the costs of skin diseases on HSE UK data, which was the extrapolated to the EU. This data was used as it was the most comprehensive and consistent time series data available. RPA (2016) reported the number of sickness absence days certified due to occupational skin diseases, at around 1% of total sickness absence days (this data no longer features in the HSE annual update). It also estimated the proportion of cases associated with chemical substances at 67%. This study applies an equivalent figure of 65% based on 2019 data[457].

The approach for this study has been to multiply the cases attributable to chemical exposure with the incidence. UK prevalence data was also added using the same attribution rate. We have monetised the impact of NHS treatment costs using the (no longer published, but still available) NHS reference costs for

[453] Data from Table THOR01.
[454] Data from Table THOR06
[455] Data from Table IIDB02.
[456] Data from Table-1 LFSILLTYP
[457] In this work we will exclude the "other substances" and the "not known" categories that were included in SK3 , including them, the equivalent like for like figure would be 66%.

diagnosis and treatment[458]. We also estimate productivity losses based on average days lost from self-reported illness caused or made worse by work[459]. These data are available from HSE for 2020. We applied the same 1% attributable fraction (AF), referenced in the RPA (2016) paper. WTP based valuation can also be added to this, based on those developed by ECHA (2016)[460]**.** These differentiate bases by severity and duration.

11.5.2 Results

Incidence data and attribution to chemical exposure

There were an estimated 886 diagnoses of occupational dermatitis reported by dermatologists to EPIDERM in which particular causative substances were identified, on average between 2017-2019 (Table 11-1).[461] Of these 886 diagnoses, 65% of cases are estimated to be attributable to chemical substances which are relevant to this study, resulting in approximately 576 cases.[462] As seen in Table 11-1, the estimated number of occupational dermatitis cases attributable to chemical substances has reduced by approximately 58% from 1998 to 2019.

The causes in red have assumed to be excluded from the scope of 'chemical substances'.

Table 11-1 Statistics on occupational dermatitis by cause, average annual estimates over 3-year and 22-year periods

Cause	*1999-2001*	*2002-2004*	*2005-2007*	*2008-2010*	*2011-2013*	*2014-2016*	2017-2019p	*1998-2019p*
Soaps and cleaners	219	306	324	322	245	320	319	292
Wet work	281	253	263	354	228	237	219	261
Rubber chemicals and materials	360	291	246	176	162	130	134	218
Personal protective equipment (PPE)	140	132	138	181	125	129	182	144
Nickel	168	214	148	120	109	88	85	136
Preservatives	91	150	122	78	81	141	132	116
Resins and acrylics	136	107	97	66	63	88	75	92
Foods and flour	100	118	128	54	56	63	59	86
Fragrances and cosmetics	75	79	64	63	84	95	73	79
Bleaches and sterilisers	43	59	97	79	95	86	92	77
Aromatic amines (PPD)	91	80	113	118	53	46	29	76
Chromium and chromates	114	118	126	41	17	36	34	73
Other biological substances	73	78	88	50	75	77	58	73
Hairdressing chemicals	78	82	85	96	51	51	37	69
Cobalt and compounds	55	105	99	47	28	46	30	60
Petroleum and products	100	83	66	34	23	19	15	51
Irritants (unspecified)	84	43	34	51	28	47	4	44
Aldehydes	58	79	47	30	28	23	13	42
Friction	63	57	50	45	33	19	21	41

[458] NHS. (2016). NHS Reference costs. https://www.gov.uk/government/collections/nhs-reference-costs
[459] HSE. (2021). Working days lost in Great Britain. https://www.hse.gov.uk/statistics/dayslost.htm
[460] ECHA. (2016). Valuing selected health impacts of chemicals https://echa.europa.eu/documents/10162/13630/echa_review_wtp_en.pdf/dfc3f035-7aa8-4c7b-90ad-4f7d01b6e0bc
[461] HSE. (2021). Work-related skin disease statistics in Great Britain, 2021. Found at: https://www.hse.gov.uk/statistics/causdis/dermatitis/skin.pdf
[462] Table THORS06. www.hse.gov.uk/statistics/tables/thors06.xlsx

Cause	*1999-2001*	*2002-2004*	*2005-2007*	*2008-2010*	*2011-2013*	*2014-2016*	2017-2019p	*1998-2019p*
Solvents and alcohols	69	58	63	26	11	25	9	40
Colophony and flux	79	46	46	30	21	9	14	36
Cutting oils and coolants	74	51	34	28	13	24	7	36
Glues and paints	30	37	28	25	18	25	16	27
Temperature and humidity	14	14	25	22	27	36	33	24
Metals and compounds	16	16	48	22	18	29	19	23
Cements, plaster and masonry	33	33	11	14	23	6	26	21
Medications	20	21	25	15	5	8	11	16
Acids and caustics	9	10	21	12	3	6	5	10
Infection	0	0	0	1	1	4	0	2
Radiation	1	1	0	1	0	0	4	1
Other substances	144	128	126	79	71	71	43	100
Other unspecified chemicals	29	17	14	1	1	2	10	12
Not known	44	45	39	35	9	31	9	33
Total number of causative substances	**2847**	**2866**	**2776**	**2281**	**1796**	**1986**	**1808**	**2378**
Total number of cases	**2012**	**1800**	**1622**	**1360**	**1102**	**1103**	**886**	**1442**
Attributable fraction (%)	**68**	**71**	**68**	**63**	**64**	**65**	**65**	**67**
Cases attributable to chemical substances	**1368**	**1278**	**1103**	**857**	**705**	**717**	**576**	**966**

Notes:
p Provisional
Figures shown in light type are based on fewer than 10 actual cases
Source: Adapted from UK HSE THORS06 statistics (www.hse.gov.uk/statistics/tables/thors06.xlsx)

NHS reference cost data

Table 11-2 shows the NHS reference cost data for 2015-2016[463] which estimates the unit cost and activity levels of treatment for various grades of skin disorders (all causes), with and without "interventions". Overall, this is estimated to cost in the order of £370 million per year. Average unit cost ranges from £642 to £8,250 per case. The majority of cases have a unit cost at the lower end of this range, with 63,564 cases having a unit cost of £642 compared to 2,994 cases with a unit cost of £8,250. To account for this, total costs of treatment was divided by total activity to get a weighted average unit cost of £1,586 per case. Updating this cost to 2018-2019 prices (i.e. the same year as the underlying data)[464] gives a weighted average unit of £1,685. The estimated cost of diagnosis, using a standard patch test[465], was £127. In 2018-2019 prices gives a cost of diagnosis of £135.

Table 11-2 NHS Reference Cost Data for Skin Disorders (2015-2016)

NHS Reference cost data 2015-2016	Activity	Unit cost	Total cost
Skin Disorders with Interventions, with CC* Score 12+	2,994	£8,250.71	£24,702,630
Skin Disorders with Interventions, with CC Score 8-11	2,893	£6,131.45	£17,738,276

[463] National Schedule of Reference Costs Year: 2015-16 – All NHS trusts and NHS foundation trusts – HRG Data. National_schedule_of_reference_costs_-_main_schedule.xlsx (live.com)
[464] UK government GDP deflators used to update costs from 2015/2016 – 2018/2019. GDP deflators at market prices, and money GDP - GOV.UK (www.gov.uk)
[465] JC45A – Standard Patch Tests, 13 years and over (NHS Reference Costs 2015/2016).

NHS Reference cost data 2015-2016	Activity	Unit cost	Total cost
Skin Disorders with Interventions, with CC Score 4-7	5,951	£3,932.96	£23,405,018
Skin Disorders with Interventions, with CC Score 0-3	22,113	£1,872.92	£41,415,921
Skin Disorders without Interventions, with CC Score 19+	1,091	£4,495.06	£4,904,116
Skin Disorders without Interventions, with CC Score 14-18	8,677	£3,171.50	£27,519,144
Skin Disorders without Interventions, with CC Score 10-13	20,252	£2,346.81	£47,527,557
Skin Disorders without Interventions, with CC Score 6-9	38,253	£1,731.68	£66,241,923
Skin Disorders without Interventions, with CC Score 2-5	65,614	£1,108.07	£72,704,735
Skin Disorders without Interventions, with CC Score 0-1	63,564	£642.61	£40,846,749
Total	**231,402**		**£367,006,069**
Total cost / total activity **£1,586**			

** CC stands for "complications or comorbidities". The score reflects the increment in complexity and treatment costs.*

Monetization of cases attributable to chemical substances

This section will provide cost estimates for occupational skin sensitization cases attributable to chemical substances in the UK. Using the data above, costs will be provided for direct healthcare costs to the NHS, the costs of productivity losses and WTP based cost estimates, using an AF based approach to attribute costs to chemical substances.

NHS costs

Self-reported data from the Labour Force Survey (LFS) estimating the prevalence of skin disorders estimated that 16,000 (95% confidence interval: 11,000-21,000) people within the last year had skin problems that were caused or made worse by work, based on data from 2018/19, 2019/20 and 2020/21.[466] Applying the previous attributable fraction of 65%, it is estimated that approximately 10,400 (7,150-13,650) cases are attributable to occupational chemical exposure.

Applying the estimated average treatment cost of skin disorders to the **prevalence** data gives an estimated annual average treatment cost of **£17.5 million** (95% confidence interval: £12.1-£23 million) for cases of occupational skin problems attributable to chemical exposure (plus £78,000 per year for diagnoses of new cases, based on incidence data).

Productivity losses

The 2019/20 data from the LFS estimates that approximately 32.5 million working days were lost from self-reported illness caused or made worse by work in the last 12 months.[467] Whilst working days lost from skin disorders is unavailable for recent years, RPA (2016) reference the no longer available HSE data from 2015 which attributes approximately 1% of total sickness absence days to occupational skin diseases. Applied to the LFS estimate above suggests 325,000 working days lost from occupational skin diseases in 2019/20.

Average annual gross value added (GVA) per head data is used to estimate productivity lost, with an estimated value of £29,599 in the UK for 2019.[468] Assuming that the average annual days worked in the UK in the UK is 230 days, this gives an average GVA per head per day of £129. Applying this to the estimated 325,000 working days lost from occupational skin diseases gives an annual productivity loss estimate of approximately **£42 million.**

[466] HSE. (2021). Work-related skin disease statistics in Great Britain, 2021. https://www.hse.gov.uk/statistics/causdis/dermatitis/skin.pdf

[467] HSE. (2021). Working days lost in Great Britain. https://www.hse.gov.uk/statistics/dayslost.htm

[468] ONS. (2021). Regional gross value added (balanced) per head and income components. https://www.ons.gov.uk/economy/grossvalueaddedgva/datasets/nominalregionalgrossvalueaddedbalancedperheadandincomecomponents

An alternative approach, as used by RPA (2016), uses average daily gross earnings to estimate productivity loss. Multiplying 325,000 lost working days by average daily gross earnings for Great Britain[469] gives estimated annual productivity losses of £35.4 million. The GVA approach will be used in final cost estimates as this is deemed a more appropriate approximation for productivity loss.

Personal valuation (willingness to pay)

ECHA (2016) provides estimates for individuals WTP to avoid skin sensitization. A range of estimates are derived in that study which depend on the nature of the skin sensitization (acute or chronic), its intensity (mild or severe), frequency of occurrence in one year, and duration (over two, five or ten years). Updating the costs from 2012 € to 2020 £ gives estimates ranging from a low of £245 for a single episode of mild acute dermatitis to £1,139 for severe chronic dermatitis. Applying these costs to the estimated 10,400 individuals over the past year who suffer from skin disorders caused or made worse by work attributable to chemical substances, gives a total cost ranging from **£2.5 million-£11.8 million[470].**

Estimated total cost

Overall, combining these three values gives an estimated cost of occupational skin disorders attributable to chemical substances in the UK of between £50-70 million per year, with an average estimate in the order of **£60 million, per year.** Cases attributable to chemical substances are theoretically avoidable and create a high number of low level, but irreversible cases, requiring treatment via the NHS.

11.5.3 Assumptions, uncertainties and limitations of the approach

As noted above, a key assumption is that the attributable fraction for occupational dermatitis is representative of all occupational skin disorders. Furthermore, uncertainty surrounds the use of 1% attributable fraction for sickness days attributable to occupational skin diseases.

As noted, the estimated cost is likely to be an underrepresentation of the total cost of skin diseases attributable to chemical substances, given that not all dermatologists are part of EPIDERM and of those that are, not all cases will be reported. There is likely to be a substantial "tail" of cases, many that are less serious, but which nevertheless may pose a significant burden on primary care and affect presence at work of both the sufferer and also to partners/caregivers.

Furthermore, this analysis only considers occupational skin disorders and the exclusion of consumer exposure will mean that the total cost of skin disorders attributable to chemical substances will likely be much greater. Better data is needed to enable any analysis of the impacts of consumer exposure.

11.6 Other effects

11.6.1 EDCs

Exposure to chemical substances, including endocrine disrupting chemicals (EDCs), is associated with metabolic diseases such as obesity and diabetes. EDCs of concern include pharmaceuticals, dioxins, polychlorinated biphenyls (PCBs), DTT and other pesticides, brominated flame retardants, perfluorinated chemicals and plasticisers[471].

[469] Average gross earnings for Jan 2020 taken from ONS data, found: https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/bulletins/averageweeklyearningsingreatbritain/latest

[470] No data on episodes is provided so it is assumed to be 10,400 episodes (1 per person)

[471] European Commission, Directorate-General for Environment, *Study on the cumulative health and environmental benefits of chemical legislation : final report*, Publications Office, 2017, https://data.europa.eu/doi/10.2779/070159

Obesity, in turn, is associated with increased risk from a range of physical and mental health problems including diabetes; coronary heart disease; breast and bowel cancers; stroke; infertility; orthopaedic problems; depression; low self-esteem and other psychological problems.

Diabetes can lead to serious damage to the heart, blood vessels, eyes, kidneys and nerves and can ultimately increase the overall risk of premature death. Data on this issue are relatively limited and it has been noted that more human epidemiological studies on the association between exposure to EDCs and obesity and diabetes were needed.[471] This is covered more extensively in Chapter 5 on EDCs.

11.6.2 **Anaemia**

The prevalence of the blood disorder anaemia has also been linked with exposure to chemical substances such as lead, especially in children. A 2003 study concluded that risk globally were still substantial, with risk concentrated in low and middle income countries in Asia and North Africa. In Western Europe (note this was based on 14 Countries which did not include the UK) the total population at risk was considered to be zero.[472]

Other studies have associated higher risk of anaemia from chronic phthalate exposure.[473,474] Zhu et al. (2018) conducted a prospective cohort study of a Chinese population to investigate the relationship between prenatal phthalates exposure and maternal hemoglobin or anaemia, for example. The study found associations between anaemia and mono-Methyl phthalate (MMP), monobutyl phthalate (MBP), mono-2-ethylhexyl phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEOHP) and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP). Exposure to MMP, MBP, MEHP, MEOHP, and MEHHP increased the risk of anaemia by 1.11-fold, 1.21-fold, 1.20-fold, 1.13-fold, and 1.16-fold, respectively. This is based on empirical data form exposure in China, not be reflective of the risks in the UK, but equivalent UK data was not identified.

11.7 Summary

This chapter focusses on the cost of occupational skin disorders attributable to chemical substances. Damage cost estimates for treatment (of existing cases), diagnoses (of new cases), productivity losses from working days lost and WTP based valuations were assessed. An attributable fraction of 65% was calculated for occupational dermatitis attributable to chemical substances. This was assumed representative of all skin disorders for the cost calculations, a limitation of the approach.

- The cost to the NHS of treatment for skin disorders (prevalence) attributable to chemical substances was estimated at £17.5 million per year with a much smaller cost (likely less than £100,000) represented by the costs for diagnoses of new cases (incidence) attributable to exposure to chemical substances.
- Annual productivity losses were calculated from working days lost attributable to skin disorders (estimated at 1%) and are estimated to amount to some £35 million per year. Another limitation of this approach is that the data used to estimate this attributable fraction is no longer available and dates back to 2014.

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[472] Fewtrell L, Kaufmann R, Prüss-Üstün A. (2003) Lead: assessing the environmental burden of disease at national and local level. Geneva, World Health Organization, 2003 (WHO Environmental Burden of Disease Series, No. 2) 73 pp.
[473]Flaws et al. (2020). Plastics, EDCs & Health. https://www.endocrine.org/-/media/endocrine/files/topics/edc_guide_2020_v1_6bhqen.pdf
[474] Zhu, Y. D., Zhu, B. B., Gao, H., Huang, K., Xu, Y. Y., Yan, S. Q., Zhou, S. S., Cai, X. X., Zhang, Q. F., Qi, J., Jin, Z. X., Sheng, J., Pan, W. J., Hao, J. H., Zhu, P., & Tao, F. B. (2018). Repeated measures of prenatal phthalate exposure and maternal hemoglobin concentration trends: The Ma'anshan birth cohort (MABC) study. *Environmental pollution (Barking, Essex : 1987)*, *242*(Pt B), 1033–1041. https://doi.org/10.1016/j.envpol.2018.07.132

- WTP based valuations found costs of skin sensitization range from £2.5-£11.8 million, per year.
- The identified costs in this chapter to the UK of occupational skin disorders attributable to chemical substances are estimated to be in the range of £50.1-£70.4 million per year. This is expected to be a small proportion of the total costs to the UK of skin disorders attributable to chemical substances, given wider consumer exposure and unreported cases.
- Other effects considered include anaemia and those from EDCs. The effects of EDCs are covered in detail in Chapter 5 of this report. There was insufficient data on levels of anaemia in the UK attributable to chemical substances (e.g. lead and phthalates) to provide accurate cost estimates.

11.8 Future research priorities

The UK provides comprehensive time series data on occupational skin disorders, but there is much more limited data available on skin disorders attributable to consumer exposure to chemical substances. Furthermore, whilst an attributable fraction could be calculated from occupational dermatitis attributable to chemical substances, data for the causative substances associated with a wider range of skin disorders would ensure that any such assessment is more representative.

Another research priority should be in improving research and data availability for other effects such as anaemia.

12 Volatile Organic Compounds (VOCs)

12.1 Effects

The United States Environmental Protection Agency (USEPA) describes VOCs as follows:

Volatile organic compounds are compounds that have a high vapor pressure and low water solubility. Many VOCs are human-made chemicals that are used and produced in the manufacture of paints, pharmaceuticals, and refrigerants. VOCs typically are industrial solvents, such as trichloroethylene; fuel oxygenates, such as methyl tert-butyl ether (MTBE); or by-products produced by chlorination in water treatment, such as chloroform. VOCs are often components of petroleum fuels, hydraulic fluids, paint thinners, and dry-cleaning agents. VOCs are common ground-water contaminants.

The following effects are considered in this section:

- Impacts of ozone generated by releases of NMVOCs (non-methane VOCs) to air on
  - Human health
    - Mortality
    - Morbidity (respiratory and cardiovascular hospital admissions)
    - Productivity
  - Materials (rubber – other materials are not considered significantly sensitive)
  - Ecosystems (via crop production, livestock production and carbon sequestration)
- Impacts arising from the effects of ozone on secondary organic and inorganic aerosols
  - Human health
    - Mortality
    - Morbidity (respiratory and cardiovascular hospital admissions, coronary heart disease, stroke, lung cancer, childhood asthma incidence, productivity)
- Cancers caused by releases of specific organics

12.2 Substances of concern

Many VOCs contribute to ozone formation in the lower atmosphere, though to varying degrees. The Defra damage cost methodology[475, 476] does not distinguish between substances but treats them collectively. The European Environment Agency (EEA)[477] also treats VOCs as a collective group for consideration of ozone impacts, including effects of ozone on atmospheric chemistry leading to impacts on the formation of

[475] Defra, 2021. Air quality appraisal: damage cost guidance, updated 26/3/2021. https://www.gov.uk/government/publications/assess-the-impact-of-air-quality/air-quality-appraisal-damage-cost-guidance.

[476] Ricardo 2020. Air Quality Damage Cost Update 2020. https://uk-air.defra.gov.uk/assets/documents/reports/cat09/2007031424_Damage_cost_update_2020_FINAL.pdf.

[477] Schucht et al, 2021. ETC/ATNI Report 04/2020: Costs of air pollution from European industrial facilities 2008–2017. For the European Environment Agency. https://www.eionet.europa.eu/etcs/etc-atni/products/etc-atni-reports/etc-atni-report-04-2020-costs-of-air-pollution-from-european-industrial-facilities-200820132017.

secondary organic and inorganic aerosols that, like ozone, are associated with health impacts. The link to the aerosols is not included in the Defra damage costs.

Damage costs are also available from the EEA for some specific organic substances of concern, covering the VOCs 1,3 butadiene, benzene and formaldehyde. Damage costs are also given for two further groups of organic chemicals, dioxins/furans and PAHs (via benzo(a)pyrene), that are not VOCs. Dioxins/furans and PAHs have been included in this assessment alongside VOCs, given that data on emissions and damage costs was available from the same sources as for VOCs.

12.3 Major uses

Data on emissions by use has been obtained from the National Atmospheric Emissions Inventory[478] (NAEI) for all years from 1970 to 2019. For this study the emissions data have been reviewed to differentiate:

- Group 1 = Uses of chemicals and incineration of chemical waste (on the basis that this addresses part of the life cycle of 'used' chemicals). Considered definitely in scope of study.
- Group 2 = Fugitive emissions from e.g., fuel distribution, some industrial releases that may be due to deliberate chemical use. Considered possibly in scope.
- Group 3 = Emissions from agriculture, fuel burning, etc. Considered out of scope of main study.

Uses include:

- VOCs
  - Agrochemicals
  - Aerosol products
  - Industrial coatings
  - Adhesives
  - Printing
  - Wood products
- 1,3 butadiene
  - Chemicals industry
- Benzene
  - No direct uses identified, but there are some fugitive emissions from oil and gas fuels
- Dioxins/furans
  - No direct uses have been identified, but there are emissions from the halogenated chemicals and pesticide industries
- PAH
  - Constituent of traditional creosote

12.4 Current regulatory controls and remaining sources of exposure

There are extensive controls on many applications of VOCs covering regulation of consumer products, vehicles and industrial installations. These controls have significantly reduced emissions of VOCs over the

[478] National Atmospheric Emission Inventory. https://naei.beis.gov.uk/.

years covered by the National Atmospheric Emissions Inventory (Table 12-1). A partial exception to this concerns PAHs. From 1990 to 2002 emissions of PAHs declined by more than 80%, though between 2002 and 2019 they have doubled. The decline is linked to legislative controls and moves away from coal burning to renewables and natural gas. The increase since 2002 is entirely a result of increased domestic combustion of wood.

Table 12-1 shows that the major sources of dioxins/furans, benzene, 1,3-butadiene and PAHs are all out of scope of this report. For NMVOCs as a group, however, uses in scope account for 36% of the inventory releases, and emissions possibly in scope for a further 26%.

Table 12-1. Maximum and minimum annual emissions of VOCs, PAHs and dioxins/furans in the UK (see Section 12.3 for definition of Groups).

		Maximum		Minimum	
	Units	**Emission**	**Year**	**Emission**	**Year**
Group 1: In scope					
Non Methane VOC	kilotonnes	827	1989	320	2019
Dioxins (PCDD/F)	g-ITEQ	6.02	1994	1.86	2017
Benzene	kilotonnes	0.07	1990	0.00	2019
1,3-butadiene	kilotonnes	0.74	1992	0.06	2015
16PAH	kilotonnes	0.11	1990	0.04	2012
Group 2: Possibly in scope					
Non Methane VOC	kilotonnes	667	1990	231	2016
Dioxins (PCDD/F)	g-ITEQ	112	1990	26.40	2018
Benzene	kilotonnes	6.09	1994	1.11	2019
1,3-butadiene	kilotonnes	0.44	1990	0.15	2019
16PAH	kilotonnes	0.00	1999	0.00	2012
Group 3: Out of scope					
Non Methane VOC	kilotonnes	1,520	1970	344	2016
Dioxins (PCDD/F)	g-ITEQ	1,218	1990	154	2019
Benzene	kilotonnes	53.02	1991	12.30	2014
1,3-butadiene	kilotonnes	9.82	1991	1.61	2014
16PAH	kilotonnes	5.28	1990	0.84	2002
Total emissions					
Non Methane VOC	kilotonnes	2,942	1990	900	2016
Dioxins (PCDD/F)	g-ITEQ	1,336	1990	182	2019
Benzene	kilotonnes	58.60	1991	13.49	2019
1,3-butadiene	kilotonnes	10.97	1991	1.85	2014
16PAH	kilotonnes	5.38	1990	0.91	2004

Current major sectors for “in scope” emissions of each substance are as follows:

- **VOCs:** Wide range of sectors contributing, none providing more than 14% of in-scope emission (aerosols for cosmetics and toiletries)
- **Dioxins/furans:** Incineration of chemical waste (covering almost the whole in-scope emission)

- **Benzene:** Incineration of chemical waste only
- **1,3 butadiene:** 'Chemistry industry – general' (the only sector considered in-scope for this substance).
- **PAH:** Creosote use (>90% of in-scope emission).

12.5 Effects of increased tropospheric ozone

12.5.1 Approach

Emissions of VOCs and some specific substances to air are reported by the UK's National Atmospheric Emissions Inventory. Emissions data are combined with the following information on damage costs.

Effects of increased tropospheric ozone:

This is made up of:

- Mortality: £3.6/t
- Respiratory hospital admissions: £18.2/t
- Cardiovascular hospital admissions: £1.6/t
- Productivity: £21.7/t
- Damage to materials (rubber): £4.9/t
- Environment £51.6/t

Environment impacts cover crop and livestock production and carbon sequestration.

Details on the calculations behind these estimates are provided by Ricardo (2020)[476] and Defra (2021)[475]. Although VOCs are recognised as a transboundary pollutant for their influence on ozone concentrations, these estimates do not account for damage caused by UK emissions in other countries[479]. For the purpose of the current analysis these damage factors have been updated to 2020 prices, **giving a damage cost of £113/t in a range of £61 to £226/tonne.**

Formation of secondary aerosols:

VOC emissions and ozone formation both influence the formation of other pollutants in the atmosphere, via chemical reactions. These are referred to as secondary organic particles and secondary inorganic particles[480]. Ozone, for example, is involved in the oxidation of sulphur dioxide and nitrogen oxides in the formation of sulphate and nitrate particles. The Defra damage costs do not account for secondary pollutant formation (beyond ozone itself). However, the effects of these secondary particles on the UK population can be modelled using data for damage cost analysis for the European Environment Agency[477, 481]. Results for the UK have been adjusted to convert to £2020, to remove the transboundary impacts, and to make the treatment of secondary aerosols consistent with Defra practice. **This gives a central estimate of £494/tonne in a range of £107 to £1,532/tonne.**

Direct effects on human health including cancer:

[479] This reflects guidance from the Treasury's Green Book (HM Treasury, 2021), though does not reflect the 'polluter pays' principle.
[480] Primary pollutants are those emitted directly into the environment. Secondary pollutants are formed through chemical reactions in the environment.
[481] EEA, 2014

Schucht et al[477] provide damage per tonne estimates for a limited number of VOCs (1,3 butadiene, benzene and formaldehyde and some non-VOC organics, dioxins/furans and PAHs). For those substances where emissions data are available from the NAEI (all of those listed except formaldehyde), impacts have been assessed using the Schucht et al damage costs adjusted to £2020 and to exclude non-UK impacts. Associated damage costs are as follows:

1,3-butadiene: £0.58/kg, range £0.1 to 0.95/kg

Benzene: £0.16/kg, range £0.03 to 0.26/kg

Dioxins/furans: £42 million/kg, range £23 million to 58 million/kg

PAH: £5,017/kg, range £915 to 8,232/kg

Note that the end-results show that the extremely high figures for dioxins/furans are mitigated by extremely low emission rates.

The following have not been considered:

- **Direct VOC impacts on ecosystems:** Response and other data necessary for the quantification of impacts of VOCs on ecosystems are unavailable so no quantification has been performed.
- **Climate change:** A more complete breakdown of the UK inventory would be needed to run the necessary calculations to quantify climate burdens.
- **Ozone layer depletion:** Controls on F-gases in response to the Montreal Protocol have largely eliminated the problem of ozone layer depletion affecting the stratosphere, such that the ozone 'hole' is now recovering. With few exceptions (some firefighting agents) ozone depletion potentials are low.
- **Flammability:** Most VOCs are flammable. There are, however, numerous regulations in place to mitigate the risks of flammability affecting the sale, use and storage of such materials.
- **Life cycle impacts of VOCs:** The production of VOCs is linked to the petrochemicals and various other industries that have a range of burdens on health and the environment. It is not possible here to characterise the life cycle burdens of the production of such a diverse group of substances, with the exception of inclusion of some emissions from the incineration of chemical waste.

12.5.2 Results

Results are summarised in Table 12-2 for Group 1 (in scope) VOC emissions.

Table 12-2. Annual damage estimates for NMVOCs as a group and for specific organic substances for uses considered in-scope

	NMVOCs	Dioxins/furans	Benzene	1,3 Butadiene	16PAH
Central estimates					
O3: Health	£8,300,000				
O3: Productivity	£7,700,000				
O3: Ecosystems	£18,000,000				
O3: Materials	£1,700,000				
PM2.5: total	£160,000,000				
Cancers		£79,000	£620	£48,000	£180,000,000
Total	**£190,000,000**	**£79,000**	**£620**	**£48,000**	**£180,000,000**

	NMVOCs	Dioxins/furans	Benzene	1,3 Butadiene	16PAH
Low estimates					
O3: Health	£980,000				
O3: Productivity	£2,400,000				
O3: Ecosystems	£14,000,000				
O3: Materials	£1,700,000				
PM2.5: total	£34,000,000				
Cancers		£43,000	£110	£8,600	£33,000,000
Total	**£53,742,058**	**£43,000**	**£110**	**£8,600**	**£33,000,000**
High estimates					
O3: Health	£23,000,000				
O3: Productivity	£25,000,000				
O3: Ecosystems	£23,000,000				
O3: Materials	£1,700,000				
PM2.5: total	£490,000,000				
Cancers		£108,703	£0	£78,475	£295,835,188
Total	**£560,000,000**	**£110,000**	**£1,000**	**£78,000**	**£300,000,000**

Results from 1,3,-butadiene, benzene, PAHs and dioxins/furans are entirely based on WTP to avoid health risks.

For VOCs, results for ozone health effects and almost all of the $PM_{2.5}$ effects are based on WTP valuation. Productivity impacts and materials damage linked to ozone are based on market costs. Ozone effects on ecosystems address costs of lost productivity in agriculture and reduced carbon sequestration. Results for NMVOCs and the other pollutants are additive.

12.5.3 Uncertainties and limitations of the approach

Key uncertainties relate to quantification of ozone, $PM_{2.5}$ effects, and carcinogenicity of VOCs as a group, and to quantification of PAH effects. For PAHs there are important uncertainties in the damage cost estimates per unit emission and possibly also in the emission factors or activity data used in the NAEI.

A clear limitation of the approach with respect to VOCs is the aggregate nature of the analysis, treating VOCs as a homogenous group. This creates difficulty in application of the results in policy analysis, as damage per unit emission will vary strongly between different VOCs depending on their efficiency for ozone and secondary aerosol generation, and their carcinogenicity.

Uncertainties for 1,3-butadiene, benzene and dioxins/furans are not so important, given the limited size of impacts relative to those for VOCs as a group and PAHs.

12.6 Summary

Combining all results for uses identified as being in-scope gives overall totals as shown in Table 12-3.

Table 12-3. Overall totals, with ranges, for emissions in-scope, possibly in-scope and out of scope.

	Central, £M/year	Low, £M/year	High, £M/year
1. In scope total	380	87	860
NMVOCs	190	54	560

	Central, £M/year	Low, £M/year	High, £M/year
Dioxins and furans	0.08	0.04	0.11
Benzene	0.0006	0.0001	0.001
1,3 butadiene	0.048	0.008	0.08
16 PAH	180	33	300
2. Possibly in scope total	150	42	430
NMVOCs	149	41	430
Dioxins and furans	1.1	0.61	1.5
Benzene	0.18	0.03	0.29
1,3 butadiene	0.09	0.02	0.15
16 PAH	0.003	0.0005	0.004
3. Out of scope total	9,100	1,700	15,000
NMVOCs	211	58	610
Dioxins and furans	6.5	3.6	8.9
Benzene	2.0	0.36	3.3
1,3 butadiene	1.0	0.19	1.7
16 PAH	8,900	1,600	15,000
Groups 1+2 total	530	130	1,300
NMVOCs	340	95	990
Dioxins and furans	1.2	0.66	1.6
Benzene	0.18	0.03	0.29
1,3 butadiene	0.14	0.02	0.22
16 PAH	180	33	296
Groups 1+2+3 total	9,600	1,800	16,000
NMVOCs	550	150	1,600
Dioxins and furans	7.7	4.2	11
Benzene	2.2	0.4	3.6
1,3 butadiene	1.2	0.2	1.9
16 PAH	9,100	1,700	15,000

The question of which emissions are considered in-scope is clearly very important to the magnitude of impacts.

12.7 Future research priorities

A general research need, not only for VOCs, is the development of an understanding of the broad range of impacts of substances, going beyond the 'targeted' effect in any policy analysis. This has the potential to highlight overlap between policy areas and for increased efficiency in policy making through greater awareness of the co-benefits and trade-offs between policies. In the case shown here, restriction of analysis to VOC effects on ground level ozone concentration (as in Defra's damage costs for VOC emissions) has potential to significantly underestimate the benefits of action.

Improved granularity of emission inventories, down to specific substances rather than VOCs as a group, would be beneficial for highlighting the different differing properties of substances. The potential for substances to cause harm by any route (by formation of ozone or secondary aerosols, via carcinogenic effects, etc.) varies substantially across the group of VOCs.

There is already further research going into the quantification of response functions linked to exposure to ground level ozone and secondary particles, formation of both of which is linked to VOC emissions as noted above. Response functions for the individual VOCs, however, could be further researched. The results here provide an indication of the importance of each pollutant, or pollutant group according to current

understanding, which can inform decisions on the priority to be given to these substances in future research relative to other research needs identified here.

13 Pharmaceuticals in water

13.1 Review of socioeconomic impacts of pharmaceuticals in the water environment (Defra, 2015)

In 2015 Defra commissioned a study which reviews the socioeconomic impacts of pharmaceuticals in the water environment. The purpose was to support Defra better take into account the associated problems and the impact of potential measures to address these issues.[482] This short section summarises key findings that that study and does not contain additional data.

The review for Defra considers the possible benefits of implementing policies which aim to reduce pharmaceuticals in the environment (PiE) and identifies data and knowledge gaps which should be addressed to inform future analysis. The report does not provide a cost of pharmaceutical pollution, but some monetary estimates are provided in terms of individuals WTP to avoid pharmaceutical pollution exposure. It notes that whilst there is a general understanding of the impacts of PiE, there is a lack of quantitative evidence linking the type and quantity of PiE and their impacts on environment and human health.

13.1.1 Exposure pathways

Humans, aquatic life and wildlife are unintentionally exposed to pharmaceutical products mainly via the sewage treatment works (STW) and the amount of pharmaceutical product entering the environment via STWs. This in turn reflects the amount of product entering the environment through patient use; diagnosis and subsequent prescription rates. But it also influenced by how much of the drug is metabolised by humans, how the substance is broken down in sewage works and how the substance partitions in the sewage treatment works. Whilst 88% of pharmaceuticals enter the environment through patient use, 10% are from medicines which are inappropriately disposed and 2% are from production waste.[483] Figure 13-1 summarise potential exposure pathways (but noticeably do not include effects from expired/unused drugs that are inappropriately disposed of).

13.1.2 Possible impact of pharmaceuticals on human health

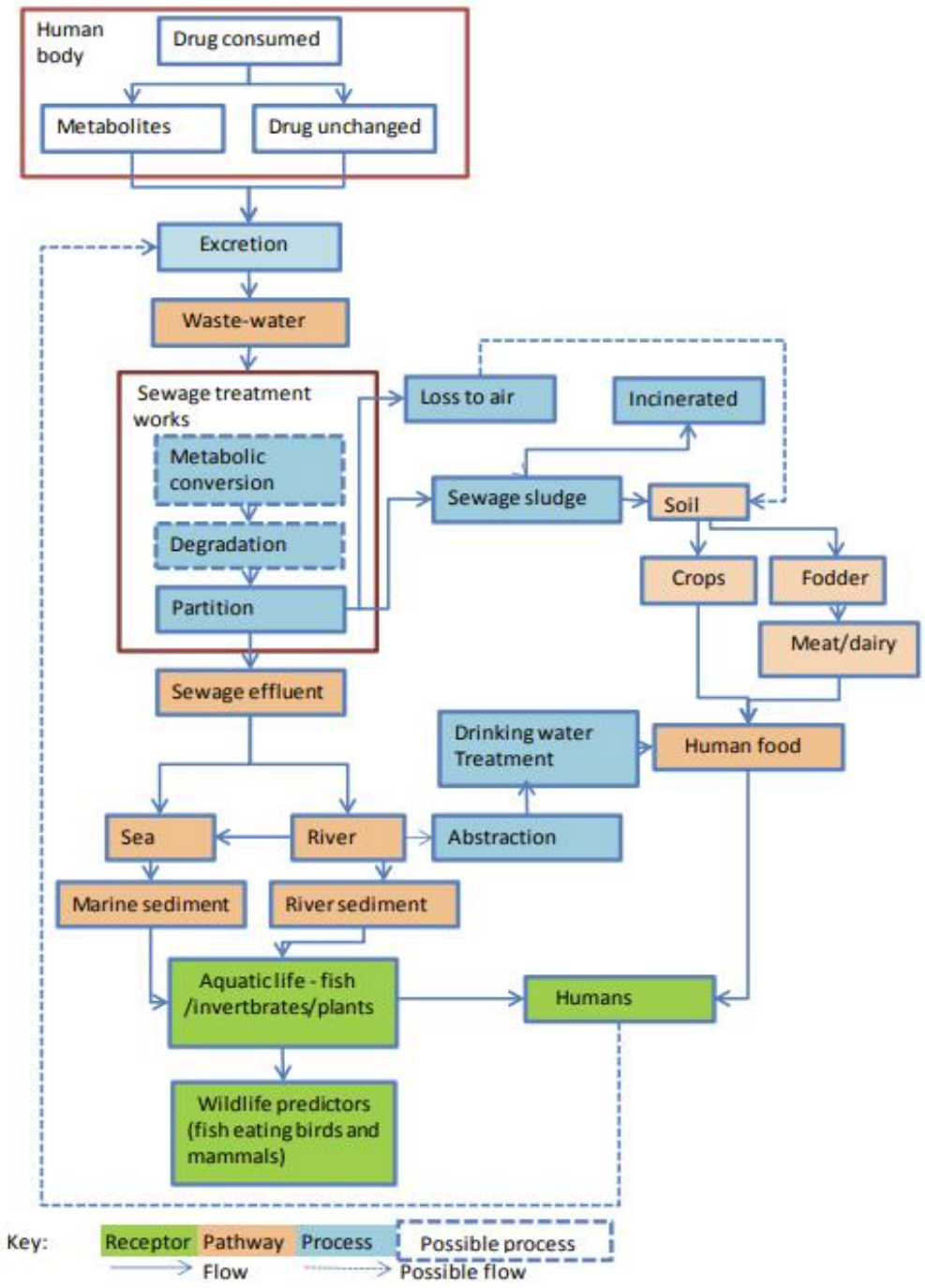
Based on available literature in the Defra (2015) report, the review suggests that current levels of drinking water purification are sufficient to remove pharmaceuticals to expected below-harmful levels. However, there are still some concerns, especially for very toxic drugs at low concentrations which are not well degraded by sewage works. A better understanding is required on the impacts that may be had on sensitive and vulnerable humans (e.g. pregnant women and unborn children).

Various risks to human health have been associated with exposure to PiE, although the evidence suggests that the overall risk to human health is low. Pharmaceuticals in drinking water may imply a widespread public health and safety risk, however, currently levels of pharmaceuticals in drinking water are thought to be below the threshold of concern. Human reproductive risks have been identified from exposures to EDCs (from EE2), although the evidence for this is relatively weak, especially concerning exposure through PiE. Antimicrobial resistance is the main concern surrounding antibiotics in the environment, as it is possible that

[482] Guiu, R., Anderson, S., Warwick, O., Mistry, R., Gianferrara, E., Koshy, A., Fowell, S., and Fisk, P. (2015). Review of socioeconomic impacts of pharmaceuticals in the water environment. *Defra*.
[483] AstraZeneca. Pharmaceuticals in the Environment. https://www.astrazeneca.com/content/dam/az/PDF/2018/A2E303_Pharmaceutical%20in%20the%20environment_A4_Final_V4.pdf

low concentrations of antibiotics in the environment allow the selection of bacteria that are resistant to antibacterial medical treatments. This presents a significant risk to global health.

Figure 13-1 Life cycle of pharmaceuticals entering the water - pathways and receptors



13.1.3 Possible costs and benefits of reducing PiE

There are various ways to reduce the impact from PiE including: reducing the amounts of prescriptions, developing more sustainable drugs which biodegrade more readily in the environment, increasing restrictions on the most harmful drugs and to more effectively remediate drugs that do enter the environment.

Table 13-1, taken from (Defra, 2015) outlines the possible environmental, economic and human health benefits from reducing the amount of PiE.

Table 13-1 Possible costs and benefits of reducing PiE

Impact	Benefits	Costs
Environment	• Improvements in water quality • Sustainability of fish populations • Avoided disposal costs (financial and environmental) of unnecessary use of pharmaceuticals	• Additional use of energy for additional water treatment
Economic	• Increase R&D in pharmaceutical industry • Increased R&D in water industry • Reduced compliance costs for other pollutants in waste water	• Additional cost of water treatment • Cost of changing pharmaceutical formulations / switching products
Human health (case study specific)	• Avoided human reproductive risks • Avoided increase in antibiotic resistance • Avoided health & safety risks of exposure	• Risk of health impacts from a restriction/ban of case study pharmaceuticals

13.1.4 Monetization of benefits from reducing PiE

The Defra review uses a valuation strategy based on WTP to reduce PiE. Scenarios for likely programmes of measures were presented to respondents who were required to rank them by preference. Estimates are provided for benefits which include general improvements to the water environment and avoided negative impacts on fish. The monetary valuations have not been included here as they are not directly attributable to reductions in PiE. More research is needed to determine the impact and subsequent benefit of removal of PiE.

13.1.5 Areas for possible future research

Currently, the data available to analyse the impact of PiE is limited and further research is required to determine the potential impact of PiE on the environment and to human health. Research is currently being undertaken, for example through the UKWIR Chemicals Investigation Programme which gives the potential for better evidence going forward. Improved data as a result of such research would allow for an assessment of the associated costs to PiE and the potential benefit of remediation.

The Defra (2015) report itself suggests areas for future research should include:

- The potential of the environment to act as a pathway for transmission of antibiotic resistance, which has large potential human health and economic consequences.
- The possible impact of combined concentrations of cancer drugs in drinking water and the potential of further treatment.
- Possible effects of cancer drugs exposed to wild mammals.

14 Appendices

A1.1 Neurodevelopmental effects

A1.1.1 Technical appendix

Input data and assumptions used in the calculation of neurodevelopment effects from lead, mercury, and pesticides and PFCs are displayed in Table 14-1, Table 14-2 and Table 14-3 respectively.

Table 14-1 Lead calculations inputs (IQ and MMR)

Input	Assumption	Source / Justification for assumption
Baseline IQ mean	100	Fewtrell et al. (2003)[230]
Baseline IQ standard deviation	15	Fewtrell et al. (2003)[230]
Total live births England and Wales (2014)	695,233	ONS (2021)[225]
Total live births Scotland (2014)	56,725	National Records of Scotland (2021)[226]
Total live births Northern Ireland (2014)	24,394	NISRA (2020)[227]
UK probability of dying by age 5 (2014)	0.5%	WHO (2021)[228]
Whole blood lead level – geometric mean	9.5 µg/L	German Environmental Specimen Bank[229]
Whole blood lead level – 95% CI for geometric mean – upper limit	10.2 µg/L	German Environmental Specimen Bank[229]
Whole blood level – sample size	123	German Environmental Specimen Bank[229]
Disability weight for MMR	0.36	Hänninen & Knol (2011)[235]
Duration of condition for MMR	77.6 years	Hänninen & Knol (2011)[235]
Willingness-to-pay value for a DALY (2019)	£70,135	HM Treasury *The Green Book* (2016)[237], adjusted for inflation

Table 14-2 Mercury calculations inputs (IQ and MMR)

Input	Assumption	Source / Justification for assumption
Baseline IQ mean	100	Fewtrell et al. (2003)[230]
Baseline IQ standard deviation	15	Fewtrell et al. (2003)[230]
Total live births England and Wales (2012)	729,674	ONS (2021)[225]
Total live births Scotland (2012)	58,027	National Records of Scotland (2021)[226]
Total live births Northern Ireland (2012)	25,269	NISRA (2020)[227]
Maternal hair mercury - geometric mean (µg/g)	0.163 µg/g	German Environmental Specimen Bank[229]
Maternal hair mercury - 95% CI for geometric mean - upper limit (µg/g)	0.192 µg/g	German Environmental Specimen Bank[229]
DEMOCOPHES UK maternal hair mercury sample size	21	German Environmental Specimen Bank[229]
Disability weight for MMR	0.36	Hänninen & Knol (2011)[235]
Duration of condition for MMR	77.6 years	Hänninen & Knol (2011)[235]
Willingness-to-pay value for a DALY (2012)	£62,227	HM Treasury *The Green Book* (2016)[237], adjusted for inflation

Table 14-3 Lead, pesticides and PFCs calculations inputs (ADHD)

Input	Assumption	Source / Justification for assumption
Total live births England and Wales (2020)	613,936	ONS (2021)[2]
Total live births Scotland (2020)	46,809	National Records of Scotland (2021)[3]
Total live births Northern Ireland (2020)	20,815	NISRA (2020)[227]

Input	Assumption	Source / Justification for assumption
UK ADHD incidence rate (upper estimate)	5%	NHS (2018)[258]
UK ADHD incidence rate (lower estimate)	3%	NHS (2018)[258]
ADHD environmentally attributable fraction for lead	6.6%	Trasande & Liu (2011) supplementary material[257]
ADHD environmentally attributable fraction for pesticides	22.7%	Trasande & Liu (2011) supplementary material[257]
ADHD environmentally attributable fraction for PFCs	23.2%	Trasande & Liu (2011) supplementary material[257]
Willingness-to-pay value for a DALY (2020)	£74,047	HM Treasury *The Green Book* (2016)[237], adjusted for inflation

A1.1 Cardiovascular effects

A1.1.1 Technical appendix

Input data and assumptions used in the calculation of cardiovascular effects from lead are displayed in Table 14-4.

Table 14-4 Lead calculations inputs (hypertension, ischaemic heart disease and stroke)

Input	Assumption	Source / Justification for assumption
Baseline mean systolic blood pressure	135 mmHG	European Commission (2017)[249]
Baseline standard deviation systolic blood pressure	15 mmHG	European Commission (2017)[249]
UK adult (20-79) male population	23,607,305	ONS (2021)[294]
UK adult (20-79) female population	24,208,954	ONS (2021)[294]
Whole blood lead level – geometric mean	9.5 µg/L	German Environmental Specimen Bank[229]
Whole blood lead level – 95% CI for geometric mean – upper limit	10.2 µg/L	German Environmental Specimen Bank[229]
Whole blood lead level – sample size	123	German Environmental Specimen Bank[229]
Disability weight for hypertension	0.2	Hänninen & Knol (2011)[235]
Duration of condition for hypertension	3.6	Hänninen & Knol (2011)[235]
Willingness-to-pay value for a DALY (2019)	£70,135	HM Treasury *The Green Book* (2016)[237], adjusted for inflation
Fraction of ischaemic heart disease DALYs attributable to lead exposure	4%	WHO (2016)[303]
Fraction of stroke DALYs attributable to lead exposure	5%	WHO (2016)[303]
2019 UK DALYs from ischaemic heart disease	1,156,677	WHO (2019)[304]
2019 UK DALYs from stroke	598,859	WHO (2019)[304]

A1.2 EUSES modelling of selected SVHCs

A1.2.1 Adaptation of EUSES regional model for the UK

The following adaptations were made to the regional model within EUSES for the purpose of estimating the UK burden of selected SVHCs.

- The regional land areas where set to match those of the whole UK.
- Data from the Office of National Statistics – UK Natural Capital Land Cover in the UK[484] were used as far as possible.

[484] https://www.ons.gov.uk/economy/environmentalaccounts/articles/uknaturalcapitallandcoverintheuk/2015-03-17

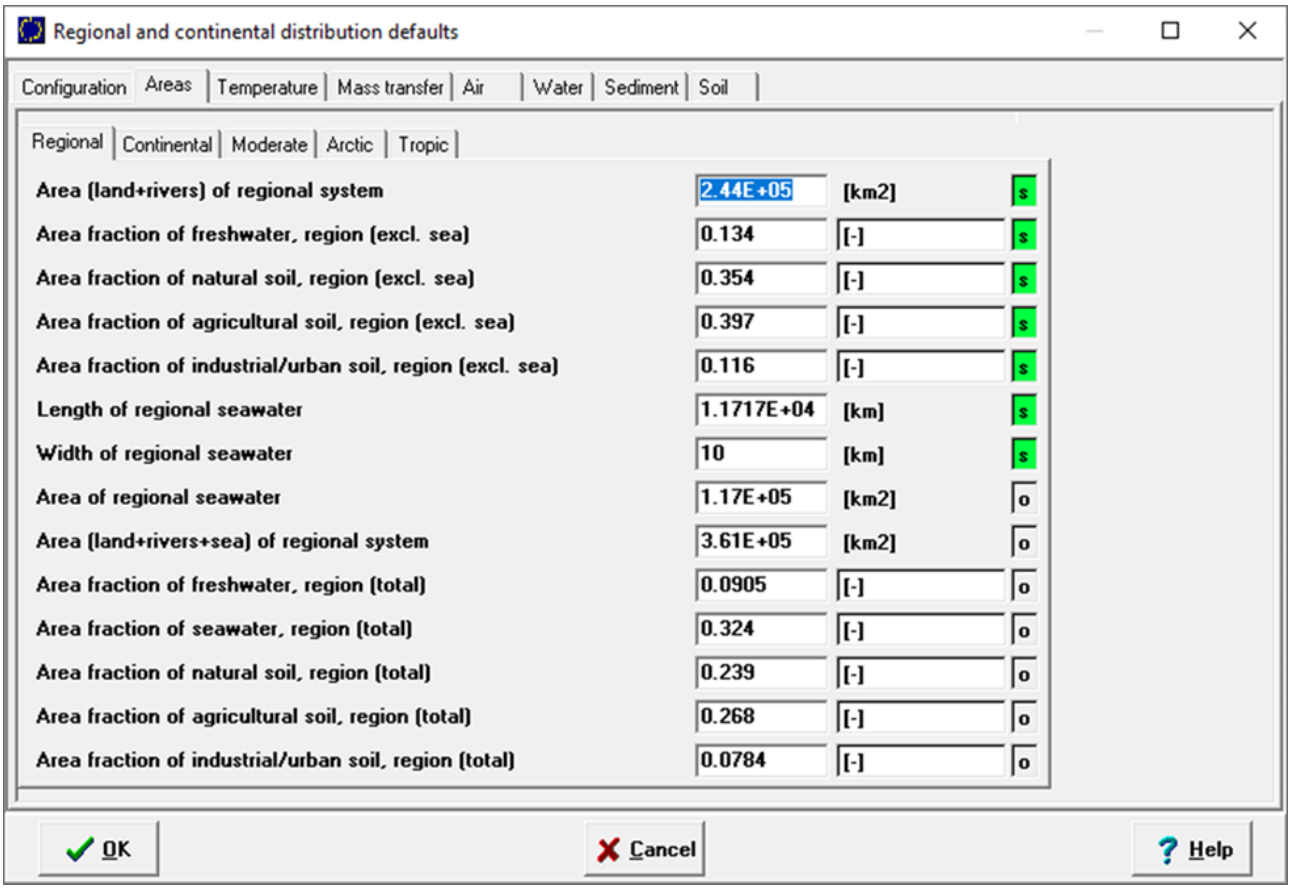
- The same source gives the area of UK territorial sea as 1.17×10^5 km^2. The standard EUSES assumptions for the width of the regional seawater compartment of 10 km; this gives the length of the regional seawater compartment of 11,717 km.
- The standard EUSES default values were used for all other aspects of the model.

These data were implemented in the EUSES regional model as outlined in Table 14-5 and Figure 14-1.

Table 14-5 Estimates of the UK release of tris(4-nonylphenol, branched and linear) phosphite

Habitat	UK area (hectares) – 2007	UK area (km^2)	Percentage of total area	Designation in EUSES
Urban and associated developed areas	2,825,000	28,250	12%	Industrial/urban
Rainfed herbaceous crops	4,275,000	42,750	18%	Agricultural
Permanent crops	52,000	520	0.2%	Agricultural
Pastures	5,363,000	53,630	22%	Agricultural
Semi-natural grassland	4,157,000	41,570	17%	Natural
Broadleaved, mixed and yew woodland	1,461,000	14,610	6%	Natural
Coniferous woodland	1,423,000	14,230	6%	Natural
Shrubland, bushland, heathland	1,312,000	13,120	5%	Natural
Barren land/sparsely vegetated areas	97,000	970	0.4%	Natural
Open wetlands	2,800,000	28,000	11%	Water
Inland water bodies	314,000	3,140	1%	Water
Coastal margins	153,000	1,530	1%	Water
Unknown	185,000	1,850	1%	Natural
Total agricultural		**96,900**	**39.7%**	**Agricultural**
Total freshwater		**32670.00**	**13.4%**	**Water**
Total natural soil		**86350.00**	**35.4%**	**Natural**
Total urban/ industrial		**28250.00**	**11.6%**	**Urban/industrial**
Overall Total		**244,170**	**100%**	

Figure 14-1 Adaptation of EUSES regional model to UK parameters



A1.2.2 Estimation of release to the UK environment

The following approach was used to estimate the releases of the SVHC substances to the UK environment based on their EU REACH Registration dossiers. It is important to note that the EU REACH Registration dossiers available via the ECHA dissemination data base only provide very limited (non-confidential) detail on tonnages and uses; mainly limited to the total overall range of the registered tonnage and the registered uses (in terms of use name and environmental release category (ERC)). This means that a crude approach has been used by necessity in order to estimate the potential releases to the UK environment. This crude approach is outlined below. The release estimates obtained therefore have a high degree of uncertainty associated with them.

- Use pattern taken from registration dossier (use name and ERC(s)).
- EU Tonnage range taken from registration dossier. This range relates to the total registered tonnage across all registrants and does not provide an indication of the tonnage used in individual uses.
- The following assumptions were used:
  - UK tonnage is assumed to be 10% of the total tonnage registered in the EU. No information was provided in the registration dossiers to allow the UK tonnage to be estimated more reliably.
  - The total tonnage is split equally between each different use. For this, different uses were identified by different use names and/or different ERCs from the registration dossier. No information was provided in the registration dossiers to allow the actual tonnage used in different applications to be estimated more reliably.

- Releases to the environment were then estimated from each use using the default release rate for each ERC[485]. The default release rates are worst case values and do not take into account any risk management measures that may be present for the actual use. In most cases no details of the actual releases to the environment, or the risk management measures that may be in place, are given in the registration dossiers used for this study. One exception to this was that for some uses the name of the use was clear that releases water or air were highly controlled; in these cases, the respective release factor was set to zero for that use.
- A tonnage range is taken into account to give a lower and higher release estimate. The tonnage range used reflected the registered tonnage range.
- Other data were considered where available included EU Risk Assessment Reports and UK Risk Assessment reports where total EU releases where given.

Based on this approach, the EUSES model was run for the following where possible. The releases were used as input to the modified EUSES model in order to estimate the steady-state environmental burden of the substances in the UK environment.

- Lower and higher release estimates using the default approach.
- Estimates based on published risk assessment reports (where available) assuming the UK release is 10% of the total EU release.
- Assuming a standard 1 kg/day release to air.
- Assuming a standard 1 kg/day release to water.

The two standard scenarios (1 kg/day release to water and 1 kg/d release to air) allow direct comparison between substances to be undertaken as they provide estimates of the steady-state environmental burden for each substance on a standard basis.

Used in this way, the adapted EUSES regional model can give estimates for the steady-state amounts of substance in the UK environment based on the assumed release rate. From these it is possible to estimate the approximate time to 95% steady-state in the UK environment (this gives an indication of the time necessary for steady-state to be approached assuming a constant release rate to the environment), and the approximate half-life for loss of the substance from the UK environment flowing cessation of emission. These estimates use an approach based on an as yet unpublished report for the UK Environment Agency (it is understood that the report is intended to be published in the near future).

A1.2.3 Tris(4-nonylphenol, branched and linear) phosphite (EC Number 701-02802)

Tris(4-nonylphenol, branched and linear) phosphite is registered under the EU REACH in the EU at a tonnage of 10,000 to 100,000 tonnes/year. There are eight active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 1,000 ('lower') -10,000 ('upper') tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-6 below. These are used as the regional release in the modified EUSES model for the UK.

[485] The default release rates are given in ECHA Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. Version 3.0, February 2016.

Table 14-6 Estimates of the UK release of tris(4-nonylphenol, branched and linear) phosphite

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)
Air	3.19×10^{5}	3.19×10^{6}
Waste water	3.20×10^{5}	3.20×10^{6}
Soil (direct release)	1.92×10^{4}	1.92×10^{5}

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2019a), supplemented as where necessary with information from the ECHA web site[486]

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-6 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-7 and show graphically in Figure 14-2 to Figure 14-5.

Table 14-7 Results of UK modelling for tris(4-nonylphenol, branched and linear) phosphite (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	2.25E+04	2.25E+05	1.52E+00	2.20E+01
Marine water (kg)	4.84E+04	4.84E+05	2.10E+01	3.13E+01
Air (kg)	3.10E+02	3.10E+03	3.49E-01	4.96E-03
Agricultural soil (kg)	7.33E+08	7.33E+09	1.54E+04	8.22E+05
Natural soil (kg)	5.70E+06	5.70E+07	6.42E+03	9.13E+01
Industrial soil (kg)	2.38E+07	2.38E+08	2.11E+03	2.99E+01
Freshwater sediment (kg)	7.47E+06	7.47E+07	5.05E+02	7.30E+03
Marine water sediment (kg)	1.44E+07	1.44E+08	6.25E+03	9.29E+03
Total	**7.84E+08**	**7.84E+09**	**3.07E+04**	**8.39E+05**

[486] https://www.echa.europa.eu/information-on-chemicals/registered-substances

Figure 14-2 Summary of steady-state masses for tris(4-nonylphenol, branched and linear) phosphite – lower estimate based on EU registered uses

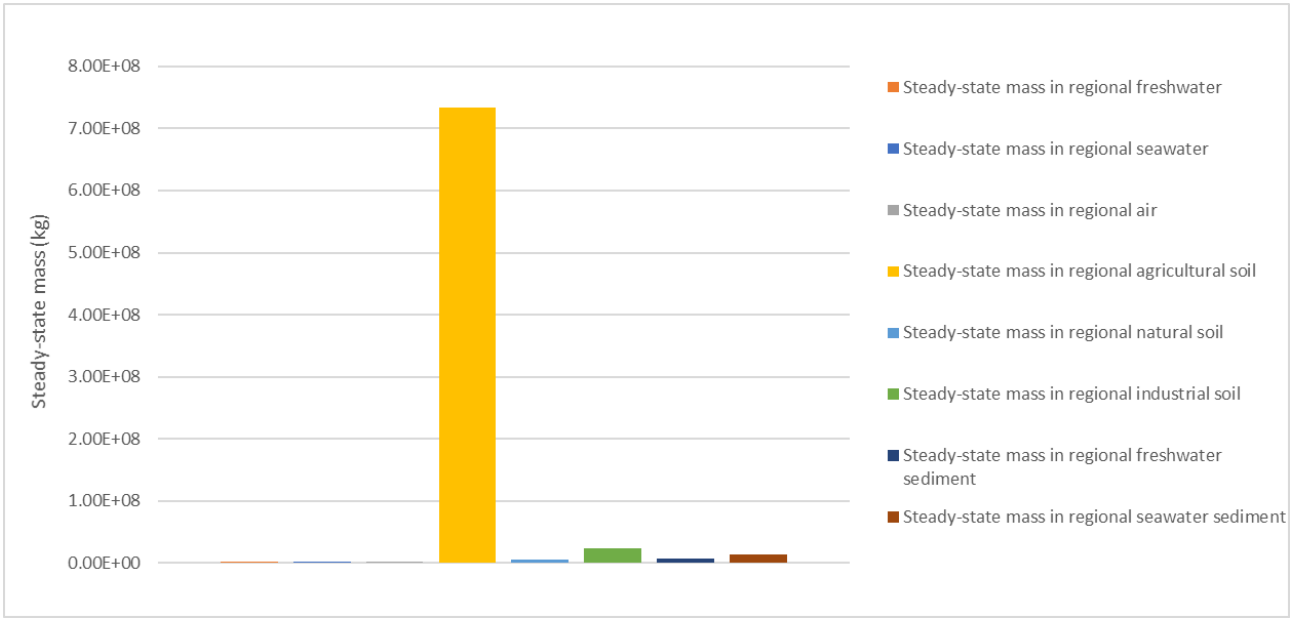


Figure 14-3 Summary of steady-state masses for tris(4-nonylphenol, branched and linear) phosphite – upper estimate based on EU registered uses

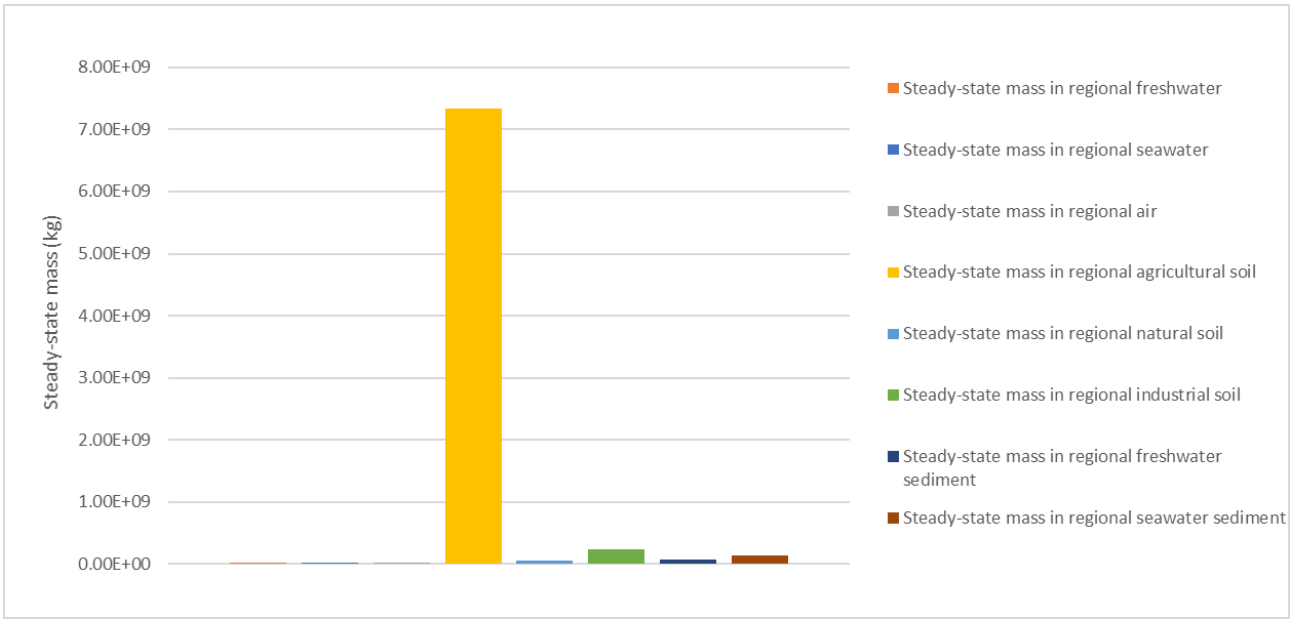


Figure 14-4 Summary of steady-state masses for tris(4-nonylphenol, branched and linear) phosphite – 1 kg/day release to air

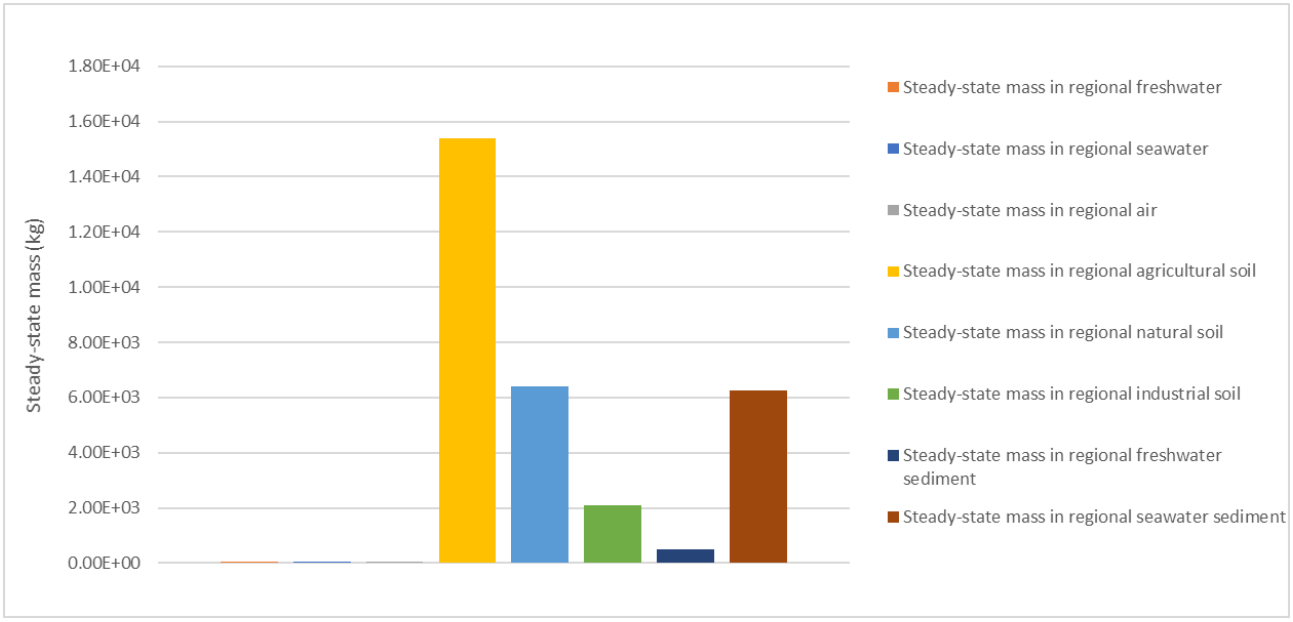
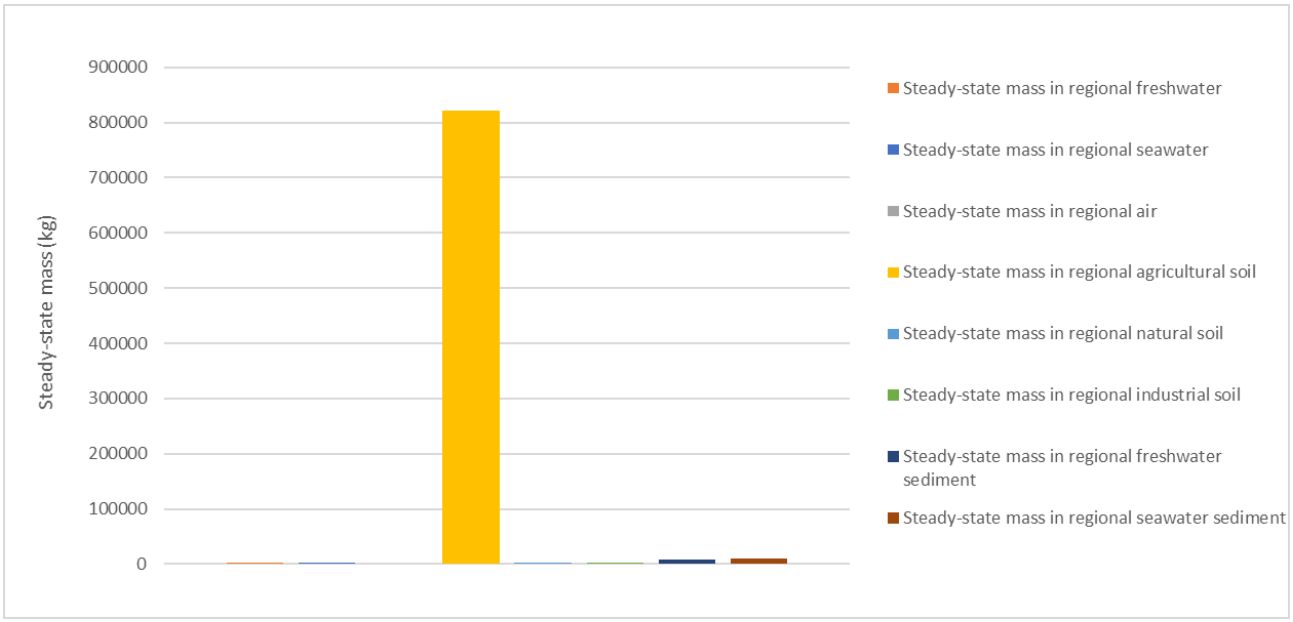


Figure 14-5 Summary of steady-state masses for tris(4-nonylphenol, branched and linear) phosphite – 1 kg/day release to waste water



A1.2.4 Alkanes, C14-17, chloro (CAS No. 85535-85-9)

Alkanes, C14-17, chloro (medium chain chlorinated paraffin or MCCP) is registered under the EU REACH in the EU at a tonnage of 10,000 to 100,000 tonnes/year. There are 11 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 1,000-10,000 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-8 below. In addition, estimates for the total EU release of alkanes, C14-17, chloro are given in the EU Risk Assessment Report (EU, 2005 and 2007). It is assumed here

that 10% of these total EU release could occur in the UK. The releases given in Table 14-8 are used as the regional release in the modified EUSES model for the UK. It is important to note that the releases given in EU (2005 and 2007) may not reflect the current releases as they pre-date the inclusion of the substance on REACH SVHC Candidate List.

Table 14-8 Estimates of the UK release of alkanes, C14-17, chloro

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)	Estimated based on EU (2005 and 2007) (kg/year)
Air	3.39×10^{5}	3.39×10^{6}	1.72×10^{4}
Waste water	3.29×10^{5}	3.29×10^{6}	2.19×10^{5}
Soil (direct release)	1.79×10^{4}	1.79×10^{5}	9.73×10^{4}

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2019b), supplemented as where necessary with information from the EU (2005 and 2007) and the Registration Dossier.

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-8 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-9 and shown graphically in Figure 14-6 to Figure 14-10.

Table 14-9 Results of UK modelling alkanes, C14-17, chloro (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Based on EU (2005 and 2007) (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	3.58E+03	3.58E+04	2.57E+03	4.61E-01	3.40E+00
Marine water (kg)	6.41E+03	6.41E+04	3.11E+03	3.44E+00	3.38E+00
Air (kg)	2.16E+03	2.16E+04	1.01E+03	1.22E+00	1.07E+00
Agricultural soil (kg)	1.13E+08	1.13E+09	7.36E+07	4.67E+03	1.20E+05
Natural soil (kg)	1.98E+06	1.98E+07	9.25E+05	1.12E+03	9.82E+02
Industrial soil (kg)	2.33E+06	2.33E+07	9.43E+06	3.66E+02	3.22E+02
Freshwater sediment (kg)	5.56E+05	5.56E+06	3.98E+05	7.16E+01	5.27E+02
Marine water sediment (kg)	4.32E+05	4.32E+06	2.10E+05	2.32E+02	2.28E+02
Total	**1.18E+08**	**1.18E+09**	**8.46E+07**	**6.46E+03**	**1.22E+05**

Figure 14-6 Summary of steady-state masses for alkanes, C14-17, chloro – lower estimate based on EU registered uses

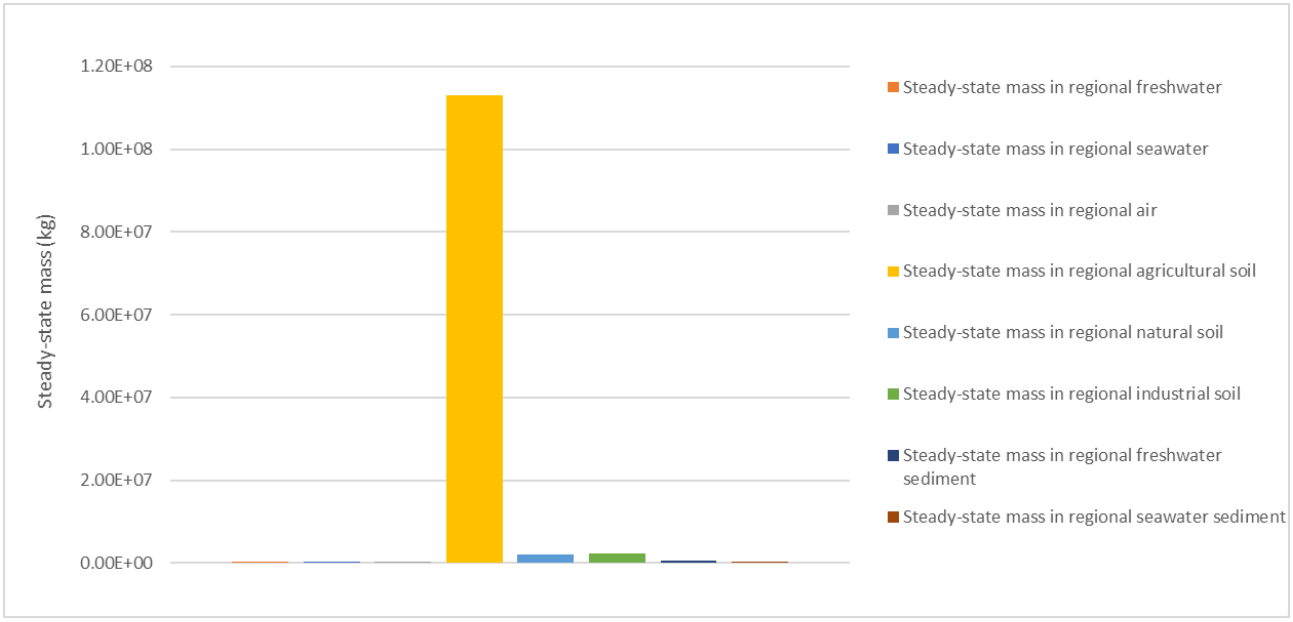


Figure 14-7 Summary of steady-state masses for alkanes, C14-17, chloro – upper estimate based on EU registered uses

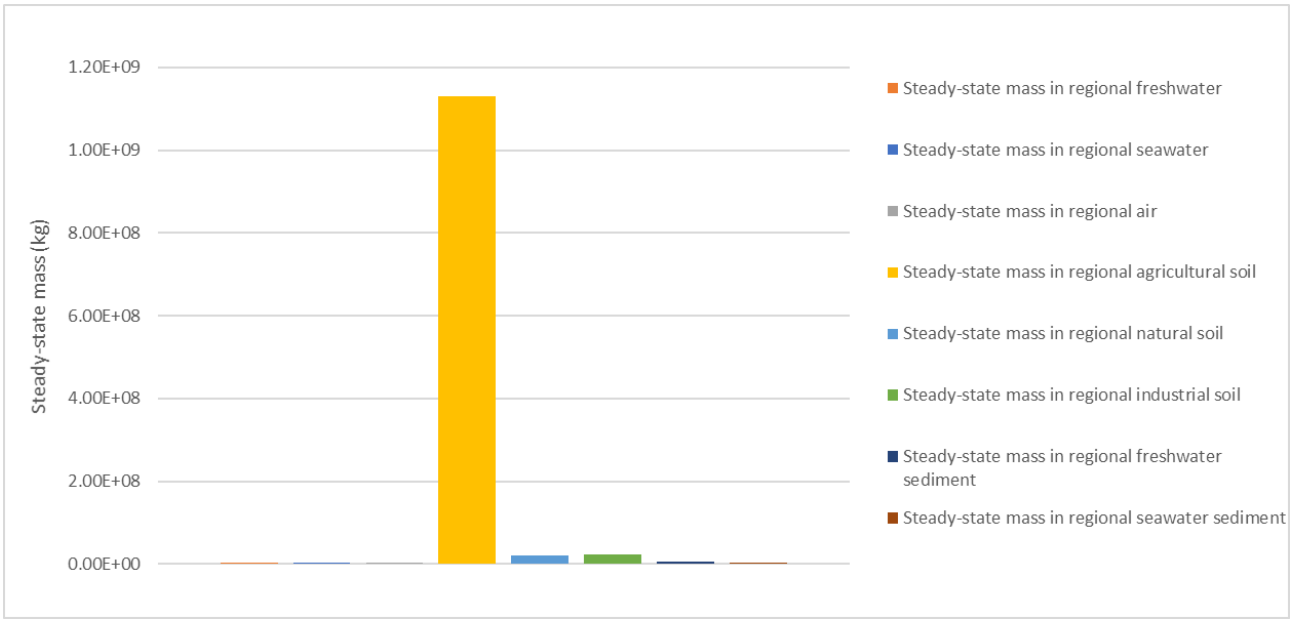


Figure 14-8 Summary of steady-state masses for alkanes, C14-17, chloro – estimate based on EU (2005 and 2007) release estimates

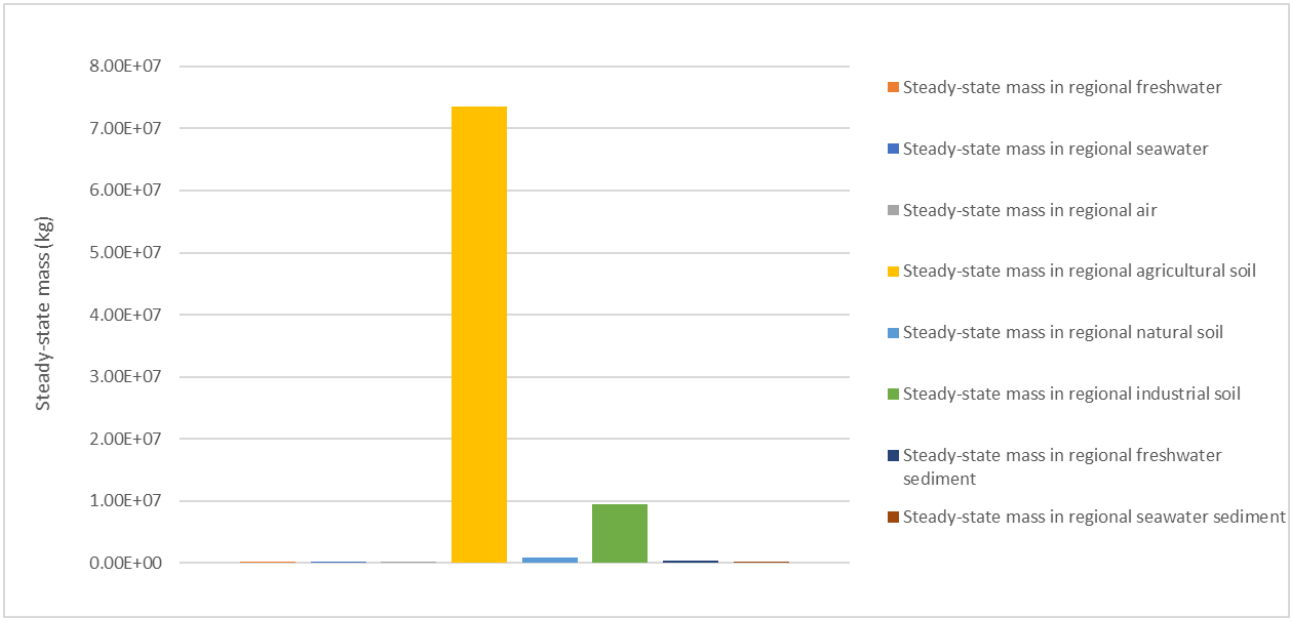


Figure 14-9 Summary of steady-state masses for alkanes, C14-17, chloro – 1 kg/day release to air

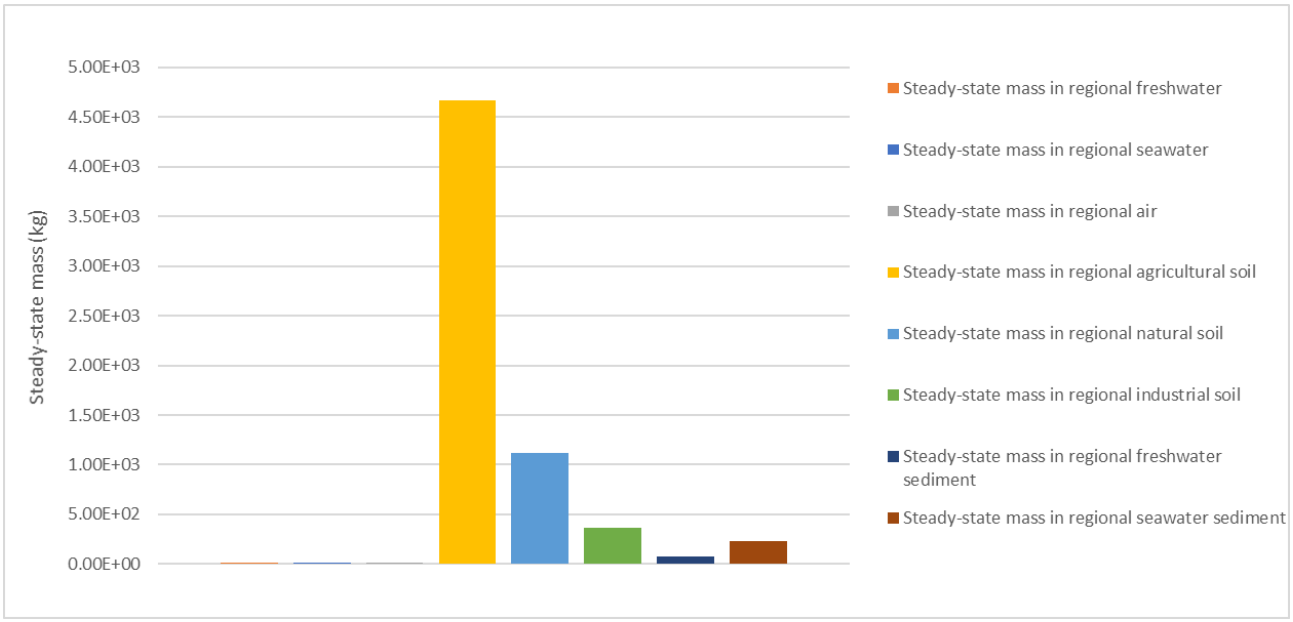
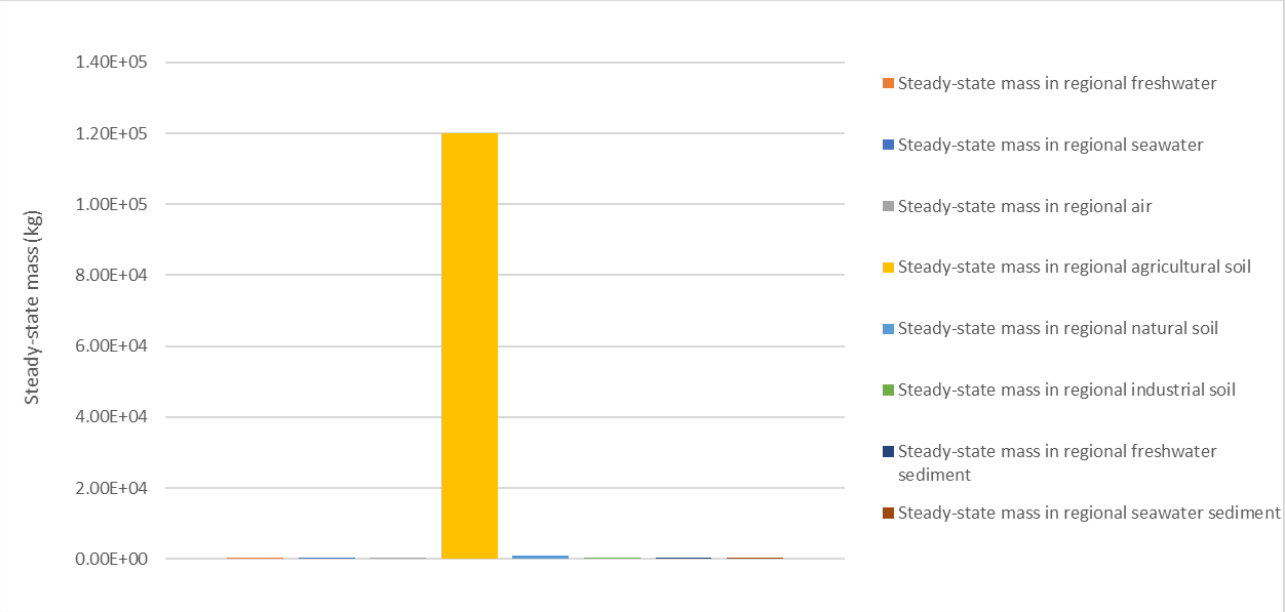


Figure 14-10 Summary of steady-state masses for alkanes, C14-17, chloro – 1 kg/day release to waste water



A1.2.5 2(2H-Benzotriazol-2-yl)-4,6-diterpentylphenol (CAS No. 25973-55-1)

2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol is registered under the EU REACH in the EU at a tonnage of 100 to 1,000 tonnes/year. There are 11 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 10-100 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-10 below. These are used as the regional release in the modified EUSES model for the UK.

Table 14-10 Estimates of the UK release of 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)
Air	3.91×10^{3}	3.91×10^{4}
Waste water	3.82×10^{3}	3.82×10^{4}
Soil (direct release)	118	1.18×10^{3}

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2014), supplemented as where necessary with information from the Registration Dossier.

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-10 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-11 and show graphically in Figure 14-11 to Figure 14-14.

Table 14-11 Results of UK modelling for 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	1.00E+01	1.00E+02	2.96E-01	6.52E-01
Marine water (kg)	5.57E+01	5.57E+02	5.03E+00	1.58E-01
Air (kg)	1.30E+01	1.30E+02	1.18E+00	2.69E-02
Agricultural soil (kg)	3.88E+03	3.88E+04	4.79E+01	3.22E+02
Natural soil (kg)	4.57E+02	4.57E+03	4.16E+01	9.45E-01
Industrial soil (kg)	2.63E+02	2.63E+03	1.36E+01	3.10E-01
Freshwater sediment (kg)	4.75E+02	4.75E+03	1.41E+01	3.10E+01
Marine water sediment (kg)	4.85E+02	4.85E+03	4.39E+01	1.38E+00
Total	**5.64E+03**	**5.64E+04**	**1.68E+02**	**3.56E+02**

Figure 14-11 Summary of steady-state masses 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol – lower estimate based on EU registered uses

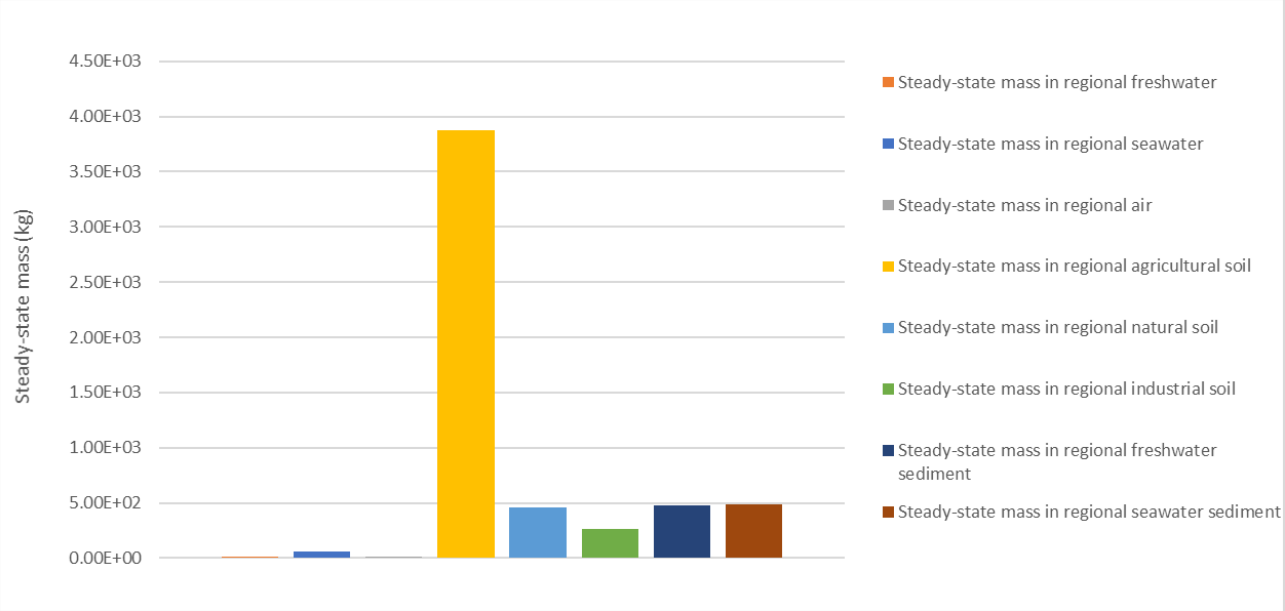


Figure 14-12 Summary of steady-state masses for 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol – upper estimate based on EU registered uses

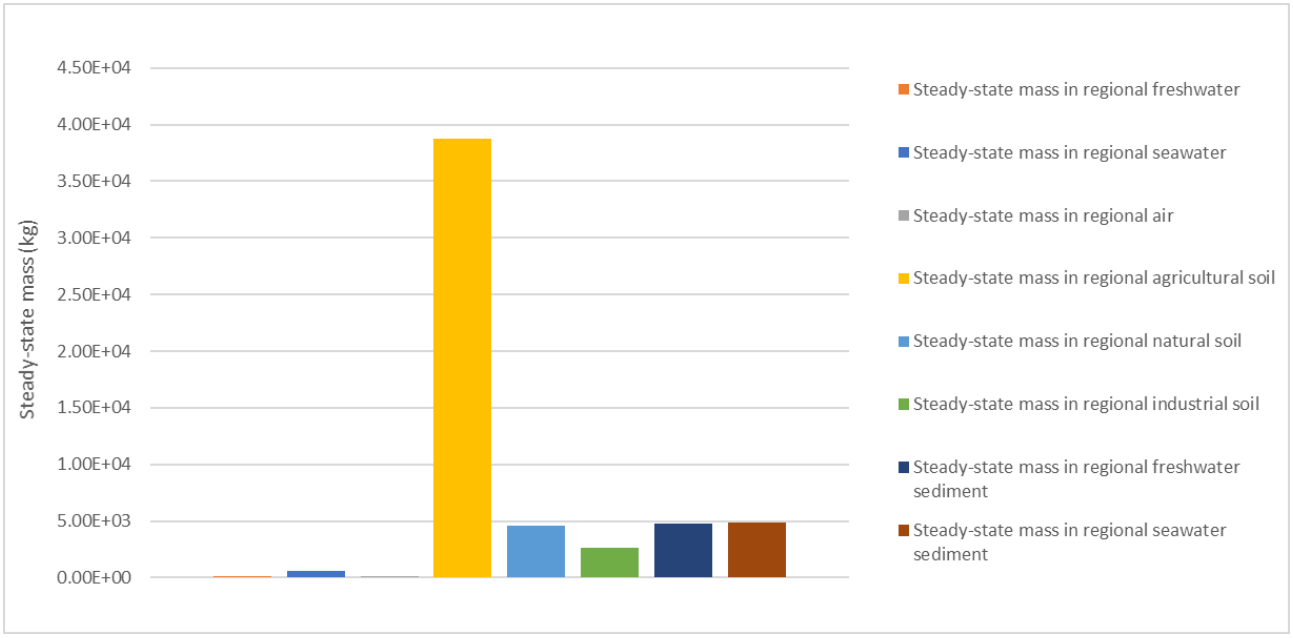


Figure 14-13 Summary of steady-state masses for 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol – 1 kg/day release to air

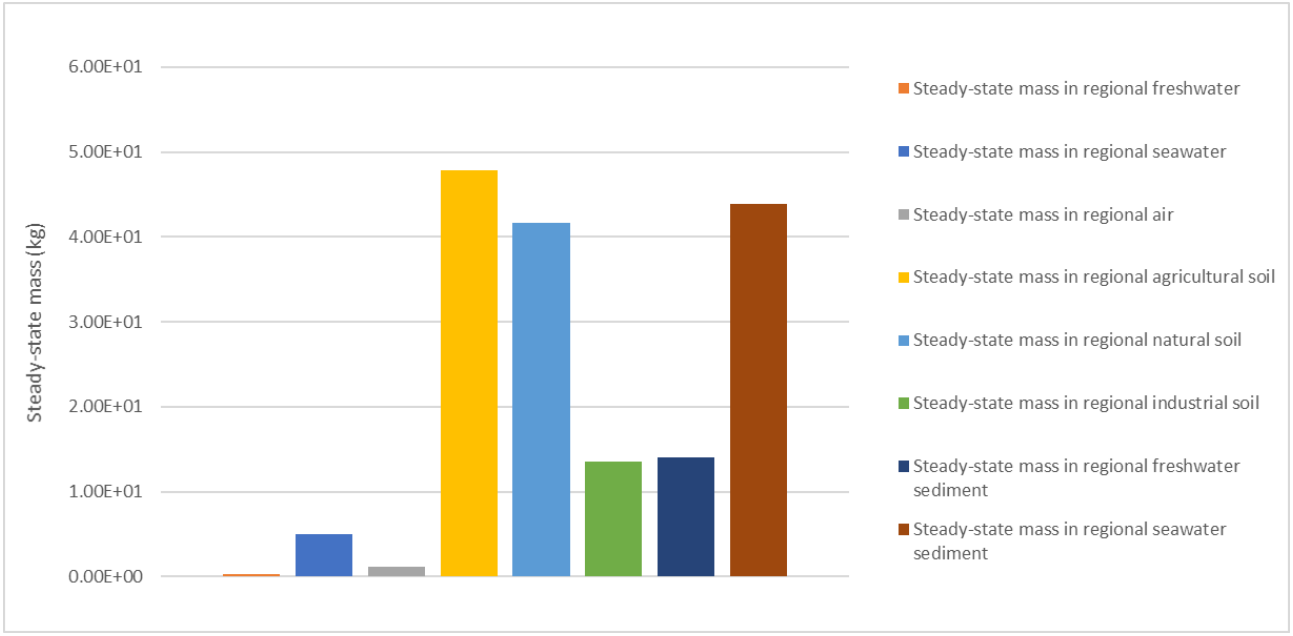
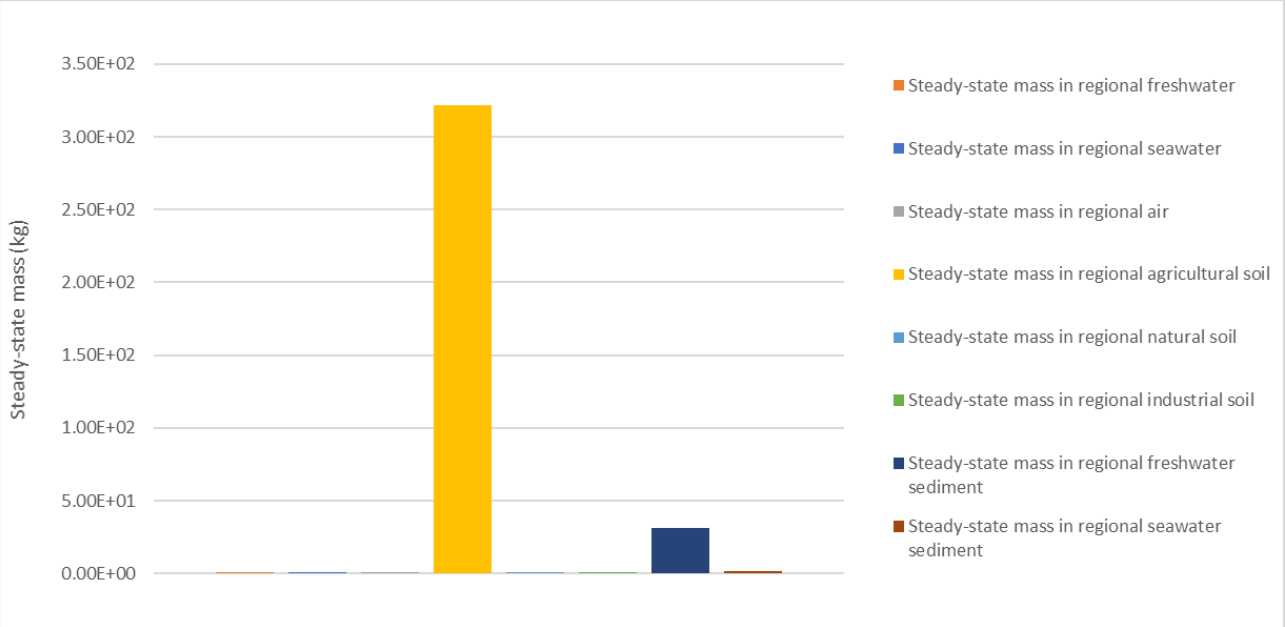


Figure 14-14 Summary of steady-state masses for 2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol – 1 kg/day release to waste water



A1.2.6 4-*tert*-Butylphenol (CAS No. 98-54-4)

4-*tert*-Butylphenol is registered under the EU REACH in the EU at a tonnage of 100,000 to 1,000,000 tonnes/year. There are 24 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 10,000-100,000 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-12 below. In addition, estimates for the total EU release of 4-*tert*-butylphenol are given in the EU Risk Assessment Report (EU, 2008). It is assumed here that 10% of these total EU release could occur in the UK. The releases given in Table 14-12 are used as the regional release in the modified EUSES model for the UK. It is important to note that the releases given in EU (2008) may not reflect the current releases as they pre-date the inclusion of the substance on REACH SVHC Candidate List.

Table 14-12 Estimates of the UK release of 4-*tert*-butylphenol

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)	Estimated based on EU (2008) (kg/year)
Air	3.23×10^{6}	3.23×10^{7}	6.02×10^{3}
Waste water	2.65×10^{6}	2.65×10^{7}	2.47×10^{3}
Soil (direct release)	1.41×10^{5}	1.41×10^{6}	No data

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2016a), supplemented as where necessary with information from the EU (2008) and the Registration Dossier.

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-12 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-13 and show graphically in Figure 14-15 to Figure 14-19.

Table 14-13 Results of UK modelling 4-*tert*-butylphenol (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Based on EU (2008) (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	1.13E+05	1.13E+06	1.07E+02	3.24E-01	1.50E+01
Marine water (kg)	6.98E+04	6.97E+05	9.31E+01	3.47E+00	5.29E+00
Air (kg)	1.57E+03	1.57E+04	2.81E+00	1.66E-01	1.24E-02
Agricultural soil (kg)	5.24E+04	5.23E+05	5.28E+01	4.83E-01	6.62E+00
Natural soil (kg)	3.32E+03	3.31E+04	5.96E+00	3.51E-01	2.63E-02
Industrial soil (kg)	3.88E+04	3.88E+05	1.95E+00	1.15E-01	8.60E-03
Freshwater sediment (kg)	2.04E+04	2.03E+05	1.93E+01	5.84E-02	2.71E+00
Marine water sediment (kg)	3.20E+03	3.20E+04	4.27E+00	1.59E-01	2.43E-01
Total	**3.02E+05**	**3.02E+06**	**3.87E+02**	**5.13E+00**	**2.99E+01**

Figure 14-15 Summary of steady-state masses for 4-*tert*-butylphenol – lower estimate based on EU registered uses

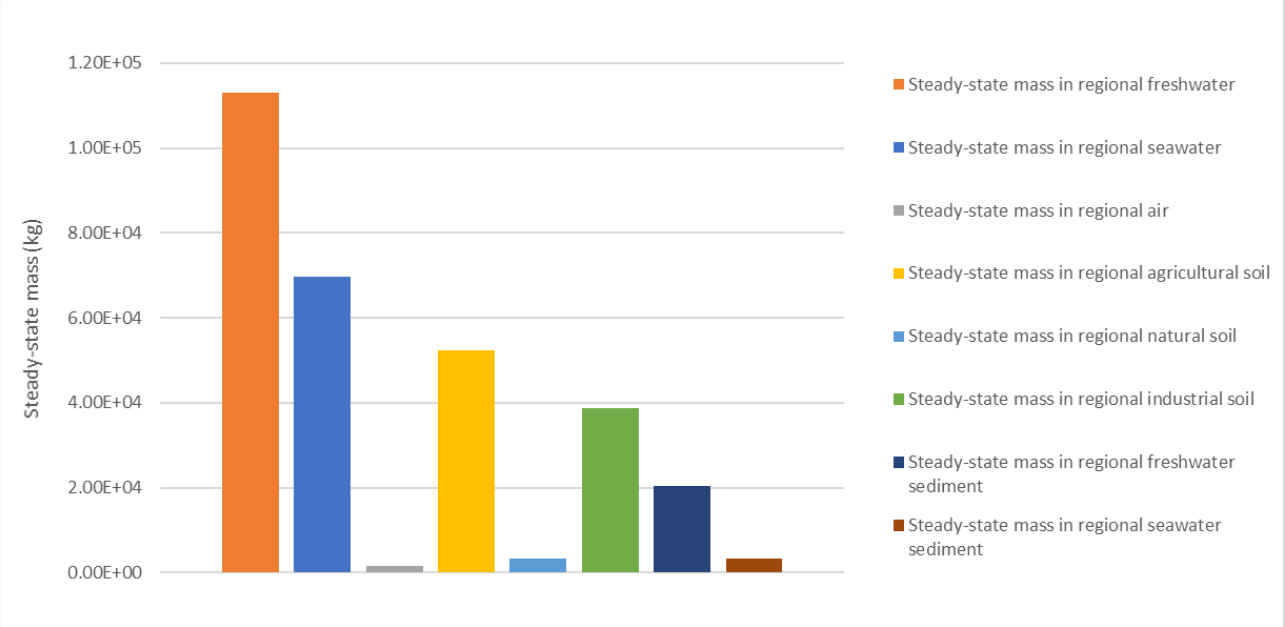


Figure 14-16 Summary of steady-state masses for 4-*tert*-butylphenol – upper estimate based on EU registered uses

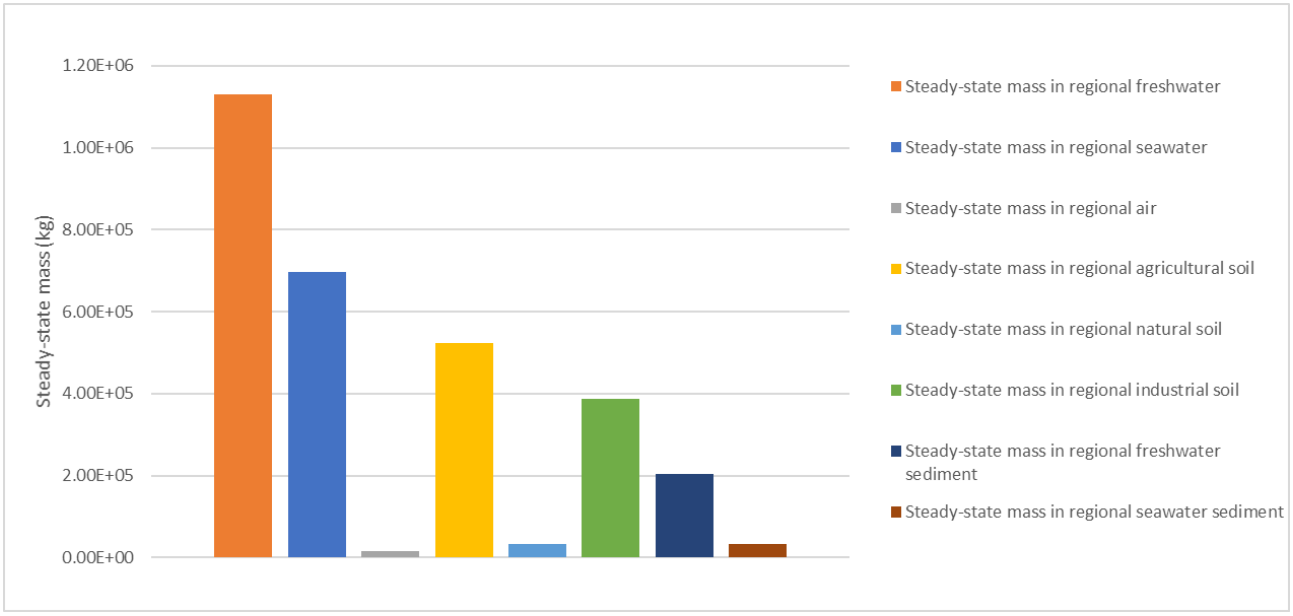


Figure 14-17 Summary of steady-state masses for 4-*tert*-butylphenol – estimate based on EU (2008) release estimates

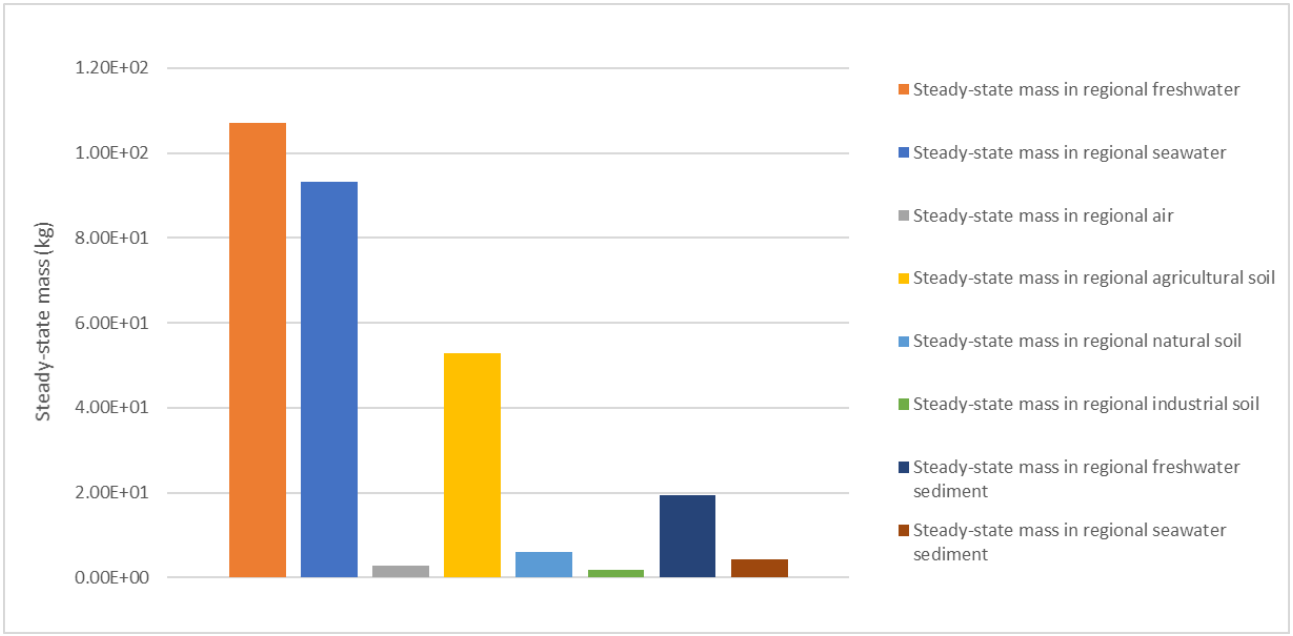


Figure 14-18 Summary of steady-state masses for 4-*tert*-butylphenol – 1 kg/day release to air

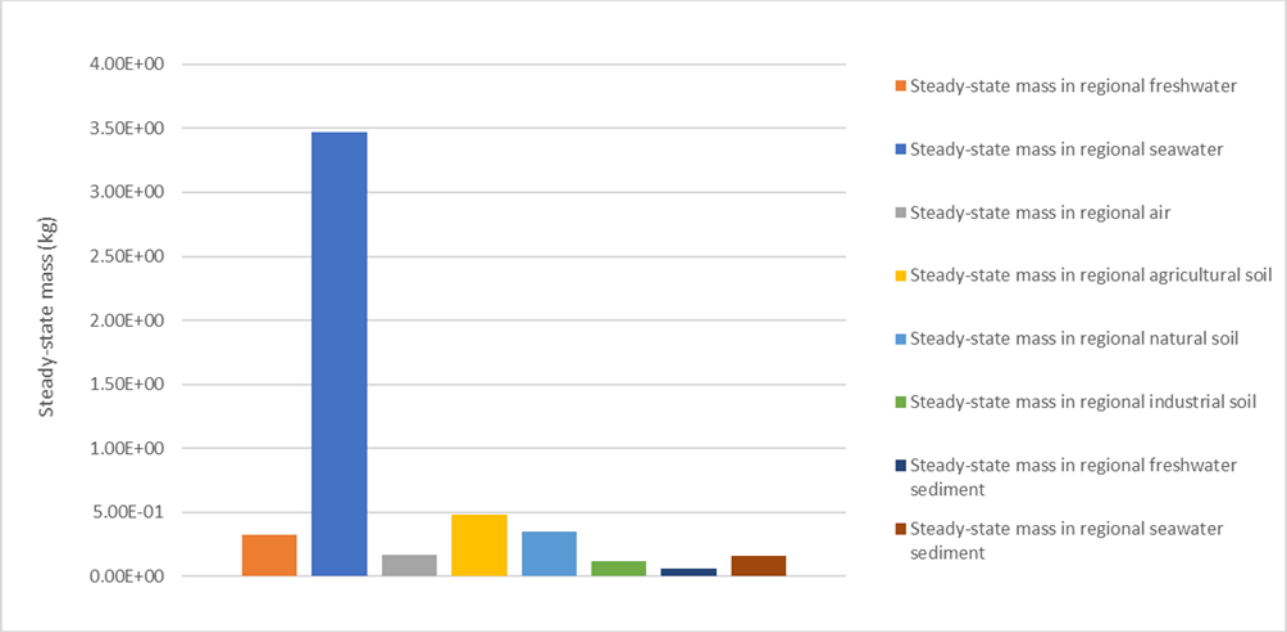
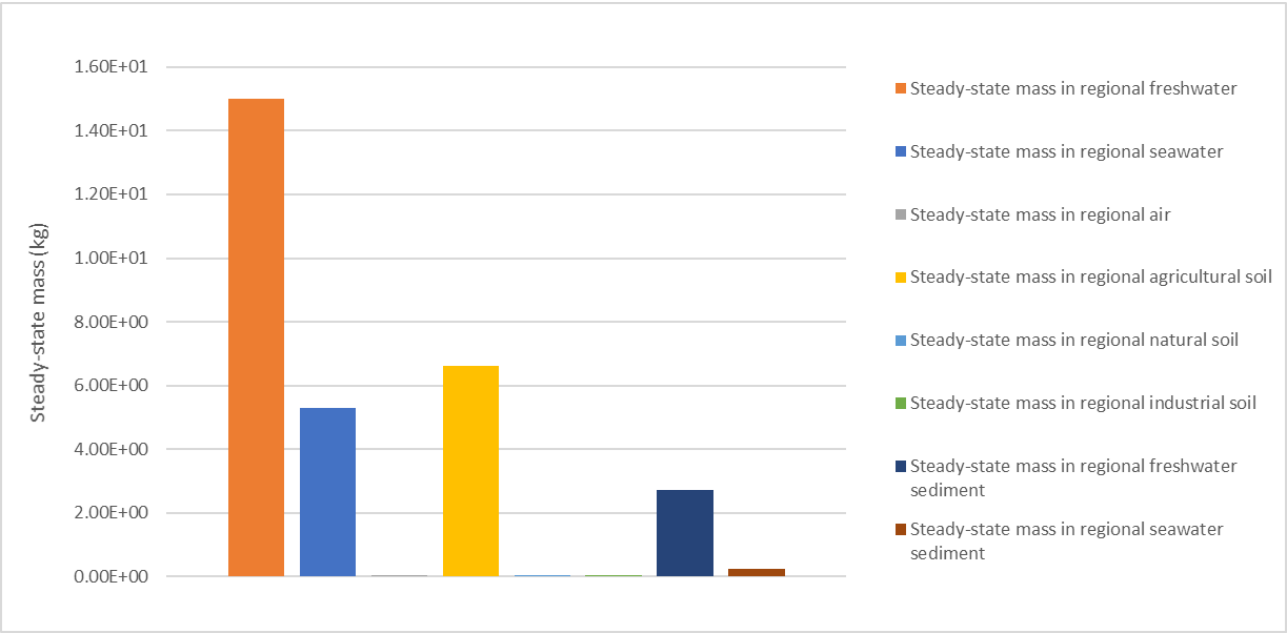


Figure 14-19 Summary of steady-state masses for 4-*tert*-butylphenol – 1 kg/day release to waste water



A1.2.7 *p*-(1,1-Dimethylpropyl)phenol (CAS No. 80-46-6)

p-(1,1-Dimethylpropyl)phenol is registered under the EU REACH in the EU at a tonnage of 100 to 1,000 tonnes/year. There are 8 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 10-100 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-14 below. A UK Risk Assessment Report (EA, 2008) is also available for this substance, however, the release estimates used in EA (2008) are confidential (and many of

the uses are stated to be confidential). The releases given in Table 14-14Table 14-6 are used as the regional release in the modified EUSES model for the UK.

Table 14-14 Estimates of the UK release of *p*-(1,1-dimethylpropyl)phenol

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)
Air	1,000	10,000
Waste water	950	9,500
Soil (direct release)	7.25	72.5

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2016b), supplemented as where necessary with information from EU (2008) and the Registration Dossier.

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-14 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-15 and show graphically in Figure 14-20 to Figure 14-23.

Table 14-15 Results of UK modelling *p*-(1,1-dimethylpropyl)phenol (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	8.40E+00	8.40E+01	3.22E-02	3.19E+00
Marine water (kg)	1.99E+00	1.99E+01	3.78E-01	3.66E-01
Air (kg)	5.66E-01	5.66E+00	1.65E-01	4.30E-02
Agricultural soil (kg)	3.82E+01	3.82E+02	3.74E-02	1.46E+01
Natural soil (kg)	8.84E-02	8.84E-01	2.58E-02	6.72E-03
Industrial soil (kg)	1.84E+00	1.84E+01	8.46E-03	2.20E-03
Freshwater sediment (kg)	4.09E+00	4.09E+01	1.57E-02	1.56E+00
Marine water sediment (kg)	2.26E-01	2.26E+00	4.28E-02	4.15E-02
Total	**5.54E+01**	**5.54E+02**	**7.05E-01**	**1.98E+01**

Figure 14-20 Summary of steady-state masses for *p*-(1,1-dimethylpropyl)phenol – lower estimate based on EU registered uses

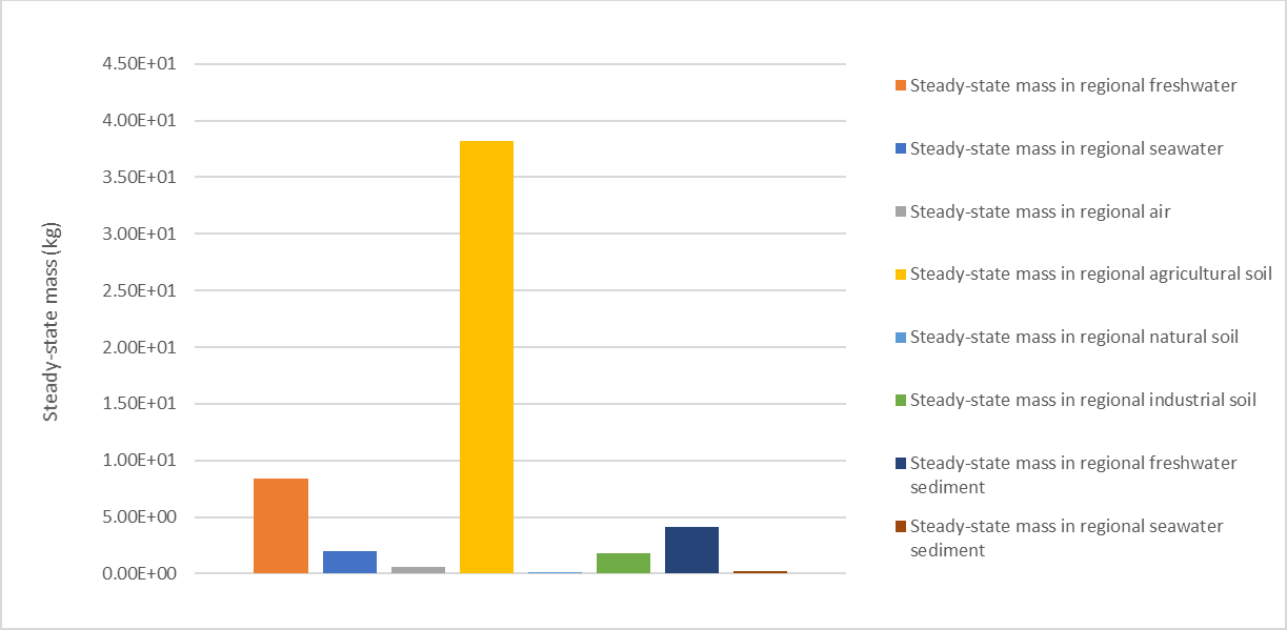


Figure 14-21 Summary of steady-state masses for *p*-(1,1-dimethylpropyl)phenol – upper estimate based on EU registered uses

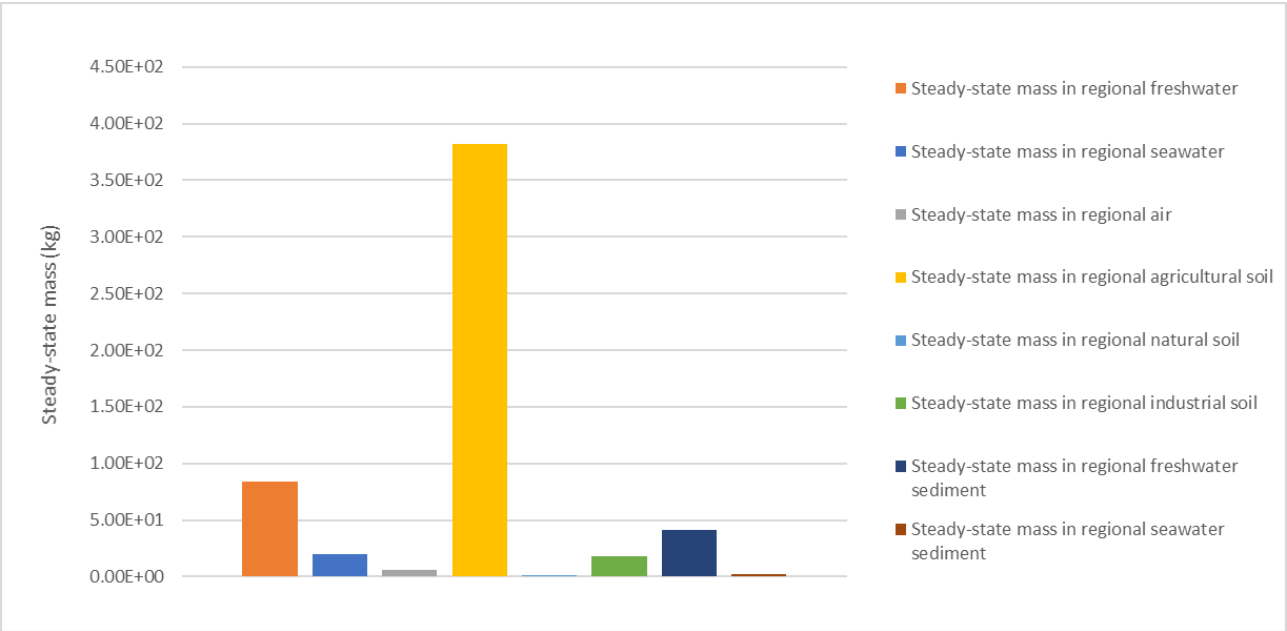


Figure 14-22 Summary of steady-state masses for *p*-(1,1-dimethylpropyl)phenol – 1 kg/day release to air

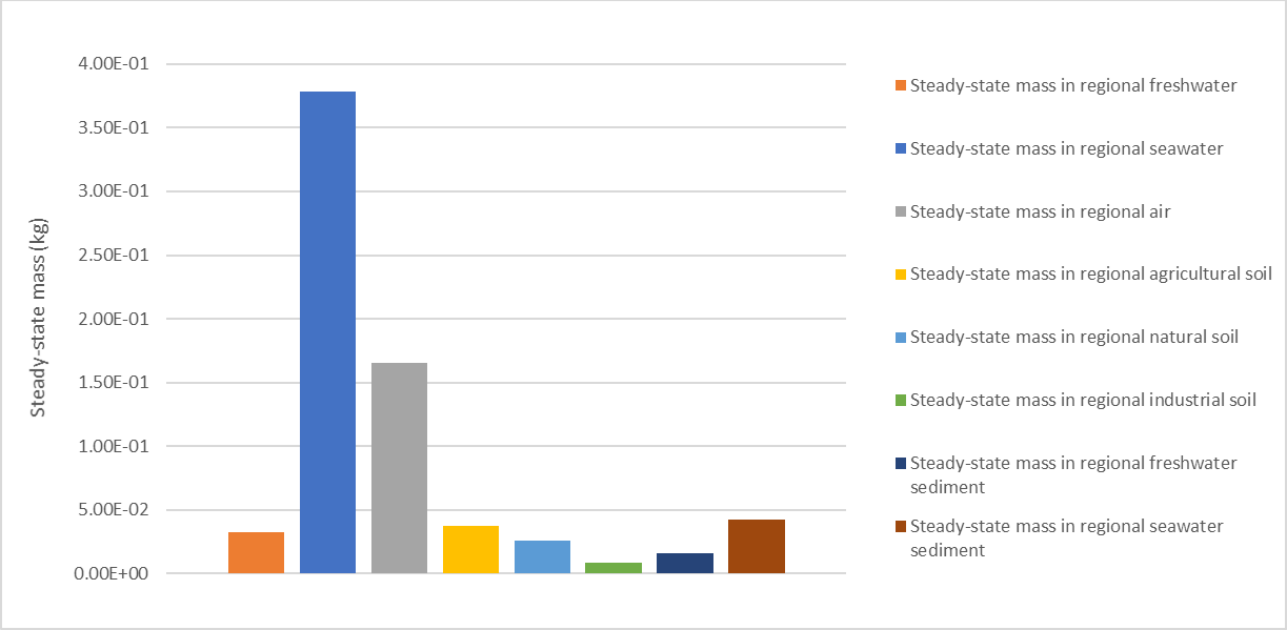
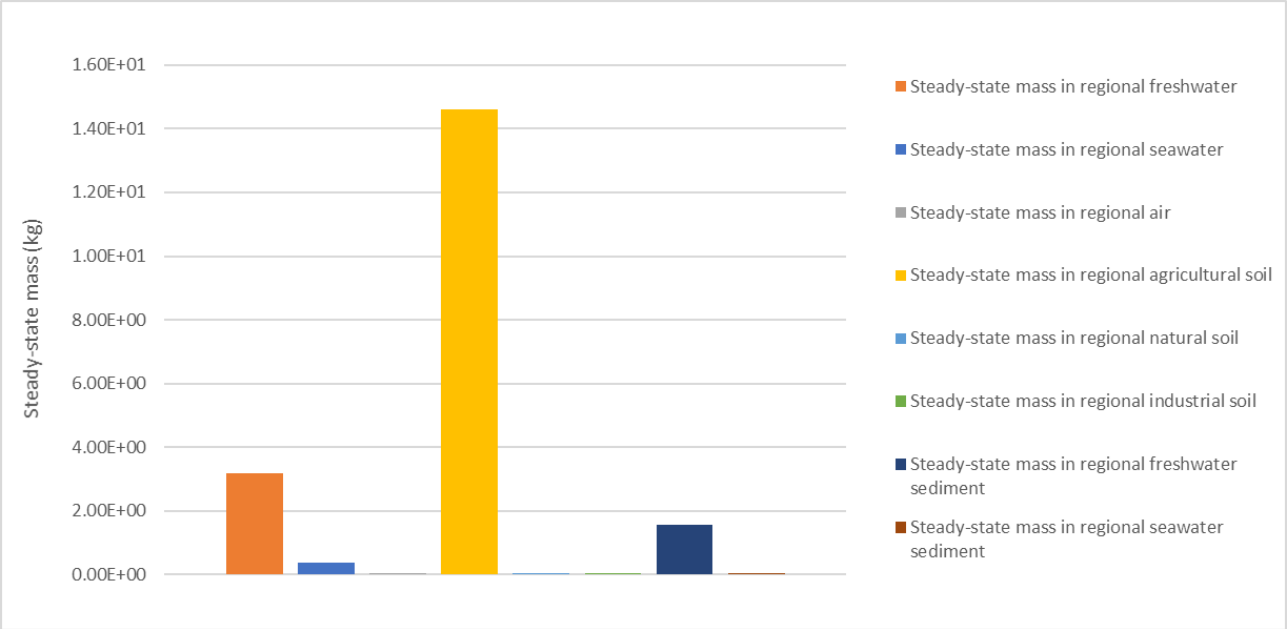


Figure 14-23 Summary of steady-state masses for *p*-(1,1-dimethylpropyl)phenol – 1 kg/day release to waste water



A1.2.8 4-Nonylphenol, branched (CAS No. 84852-15-3)

4-Nonylphenol, branched is registered under the EU REACH in the EU at a tonnage of 10,000 to 100,000 tonnes/year. There are 32 active EU registrations for the substance and there are 2 former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 1,000-10,000 tonnes /year is estimated for the analysis.

The EU REACH Registration dossier does not contain any registered uses for this substance. The dossier states that the substance is imported as monomer reacted within polymers, and the polymers contain less than 0.025% residual monomer. The polymers made from nonylphenol (presumably including nonylphenol

ethoxylates) are currently outside of the scope of registration under both EU REACH and UK REACH. Therefore, it is not possible obtain and estimate of the possible releases into the UK environment from the EU REACH Registration dossier.

The CAS Number 84852-15-3 relates to 4-nonylphenol, branched. The REACH SVHC Candidate List entry for nonylphenol covers both linear and branched nonylphenol. An EU Risk Assessment Report (EU, 2002) is available for covering 4-nonylphenol and nonylphenol (CAS No. 25154-52-3) giving estimates of the releases into the EU environment (pre-2002). It is assumed here that 10% of these total EU release could occur in the UK. The releases given in Table 14-16 are used as the regional release in the modified EUSES model for the UK. It is important to note that the releases given in EU (2002) may not reflect the current releases as they pre-date the inclusion of the substance on REACH SVHC Candidate List.

Table 14-16 Estimates of the UK release of 4-nonylphenol, branched (and nonyl phenol)

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)	Estimated based on EU (2002) (kg/year)[a]
Air	No estimate possible	No estimate possible	No estimate
Waste water	No estimate possible	No estimate possible	7.30×10^{3}
Surface water	No estimate possible	No estimate possible	1.20×10^{5}
Soil (direct release)	No estimate possible	No estimate possible	No data

Note: a) In the EU (2002) the release are given in terms of kg/day. The estimated releases for the UK are 329.8 kg/day to surface water and 20 kg/day to waste water. These have been converted here to kg/year assuming 365 days/year.

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2012), supplemented as where necessary with information from the EU (2002) and the Registration Dossier.

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-16 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-13 and show graphically in Figure 14-24 to Figure 14-26.

Table 14-17 Results of UK modelling 4-nonylphenol, branched (and nonyl phenol) (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Based on EU (2002) (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	-	-	3.19E+03	2.22E-01	5.36E+00
Marine water (kg)	-	-	1.01E+03	2.49E+00	1.69E+00
Air (kg)	-	-	6.56E+02	2.30E+00	1.24E+00
Agricultural soil (kg)	-	-	5.38E+02	4.07E-01	2.13E+01
Natural soil (kg)	-	-	9.11E+01	3.20E-01	1.72E-01
Industrial soil (kg)	-	-	2.99E+01	1.05E-01	5.65E-02
Freshwater sediment (kg)	-	-	2.34E+03	1.64E-01	3.94E+00
Marine water sediment (kg)	-	-	1.08E+02	2.67E-01	1.81E-01

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Based on EU (2002) (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Total	**No estimate possible**	**No estimate possible**	**7.96E+03**	**6.28E+00**	**3.39E+01**

Figure 14-24 Summary of steady-state masses for 4-nonylphenol, branched (and nonyl phenol) – estimate based on EU (2002) release estimates

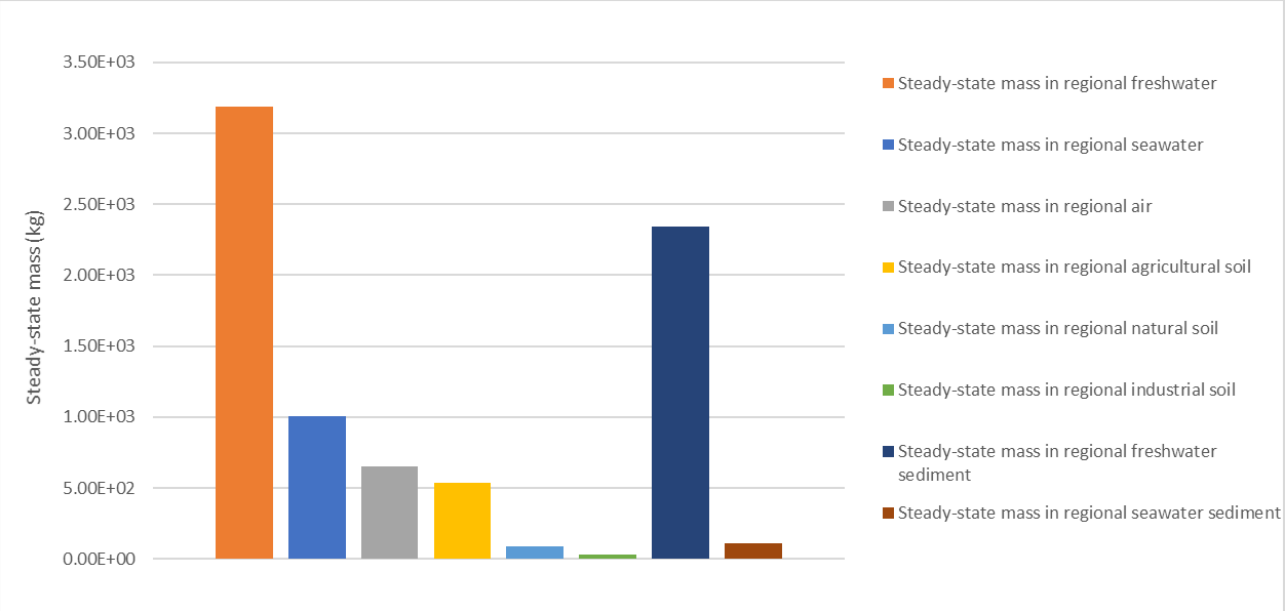


Figure 14-25 Summary of steady-state masses for 4-nonylphenol, branched (and nonyl phenol) – 1 kg/day release to air

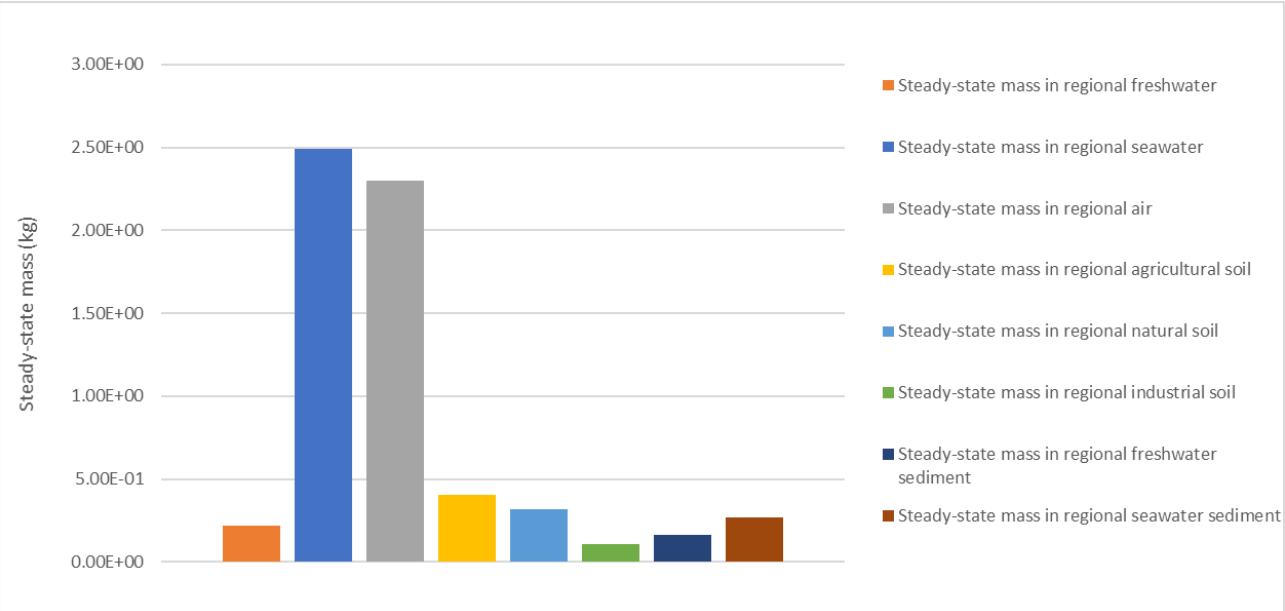
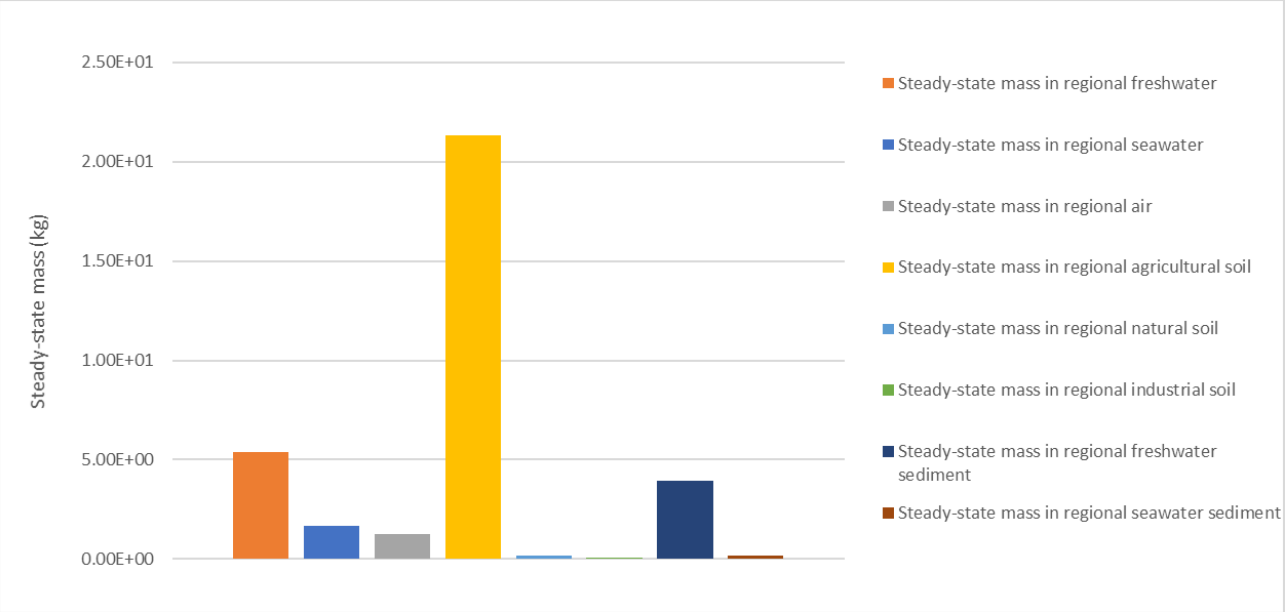


Figure 14-26 Summary of steady-state masses for 4-nonylphenol, branched (and nonyl phenol) – 1 kg/day release to waste water



A1.2.9 Phenol, heptyl derivatives (CAS No. 72624-02-3)

Phenol, heptyl derivatives is registered under the EU REACH in the EU at a tonnage of 100 to 1,000 tonnes/year. There are 5 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 10-100 tonnes /year is estimated for the analysis.

The EU REACH Registration dossier does not contain any registered uses for this substance. The dossier states that the substance is imported as monomer reacted within polymers. The polymers made from phenol, heptyl derivatives are currently outside of the scope of registration under both EU REACH and UK REACH. Therefore, it is not possible obtain and estimate of the possible releases into the UK environment from the EU REACH Registration dossier.

The substance properties used in the analysis were taken mainly from the Registration Dossier.

The resulting steady-state masses estimated in the UK environment assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-18 and show graphically in Figure 14-27 to Figure 14-28.

Table 14-18 Results of UK modelling phenol, heptyl derivatives (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	-	-	2.91E+00	3.70E+01
Marine water (kg)	-	-	3.25E+01	4.03E+01
Air (kg)	-	-	2.37E+00	2.17E+00
Agricultural soil (kg)	-	-	7.00E+01	2.27E+03
Natural soil (kg)	-	-	1.57E+01	1.44E+01
Industrial soil (kg)	-	-	5.14E+00	4.71E+00
Freshwater sediment (kg)	-	-	2.93E+00	3.73E+01

Marine water sediment (kg)	-	-	8.28E+00	1.03E+01
Total	**No estimate possible**	**No estimate possible**	**1.40E+02**	**2.42E+03**

Figure 14-27 Summary of steady-state masses for phenol, heptyl derivatives – 1 kg/day release to air

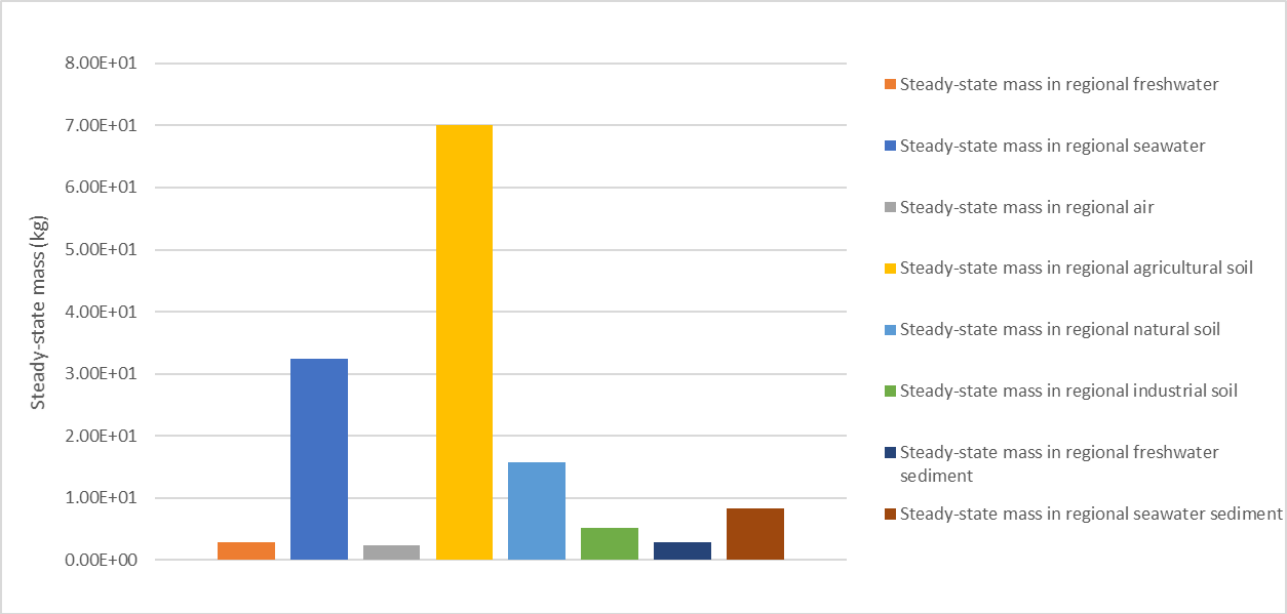
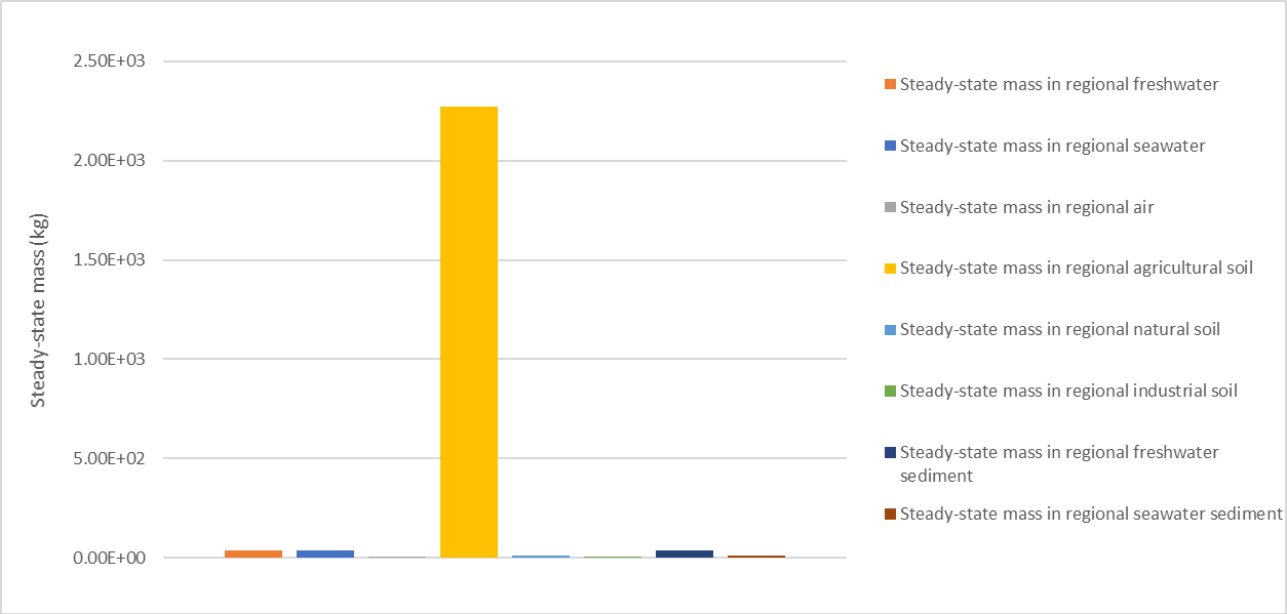


Figure 14-28 Summary of steady-state masses for phenol, heptyl derivatives – 1 kg/day release to waste water



A1.2.10 4-tert-Octylphenol (CAS No. 140-66-9)

4-*tert*-Octylphenol is registered under the EU REACH in the EU at a tonnage of 10,000 to 100,000 tonnes/year. There are 24 active EU registrations for the substance and there is one former UK registrant listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 1,000-10,000 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-19 below. Some of the entries in the EU REACH registration dossier indicate that the substance is only used as a monomer in imported polymers (presumably including octylphenol ethoxylates), however it is not possible to assess the significance of this based on the limited information in the EU Registration dossiers available on the ECHA dissemination website. In addition, estimates for the total EU release of 4-*tert*-butylphenol are given in an Environment Agency Risk Assessment Report (EA, 2005). It is assumed here that 10% of these total EU release could occur in the UK. The releases given in Table 14-19 are used as the regional release in the modified EUSES model for the UK. It is important to note that the releases given in EA (2005) may not reflect the current releases as they pre-date the inclusion of the substance on REACH SVHC Candidate List.

Table 14-19 Estimates of the UK release of 4-*tert*-octylphenol

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)	Estimated based on EA (2005) (kg/year)
Air	2.65×10^{5}	2.65×10^{6}	4.98×10^{3}
Waste water	2.13×10^{5}	2.13×10^{6}	3.21×10^{3}
Surface water	-[a]	-[a]	4.83×10^{3}
Soil (direct release)	4.36×10^{3}	4.36×10^{4}	1.34×10^{4}

Note: a) The estimates assume all releases are to waste water and enter surface water via a sewage treatment plant.

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2011).

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-19 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-20 and show graphically in Figure 14-29 to Figure 14-33.

Table 14-20 Results of UK modelling 4-*tert*-octylphenol (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Based on EA (2005) (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	4.47E+03	4.47E+04	3.15E+02	2.82E-02	7.58E+00
Marine water (kg)	7.56E+02	7.56E+03	4.79E+01	3.31E-01	8.76E-01
Air (kg)	3.90E+02	3.90E+03	1.85E+01	3.07E-01	2.83E-01
Agricultural soil (kg)	1.51E+06	1.51E+07	4.12E+05	7.47E-01	2.60E+03
Natural soil (kg)	2.13E+02	2.13E+03	1.01E+01	1.67E-01	1.54E-01
Industrial soil (kg)	3.19E+04	3.19E+05	3.30E+00	5.49E-02	5.06E-02
Freshwater sediment (kg)	5.15E+03	5.15E+04	3.63E+02	3.25E-02	8.73E+00
Marine water sediment (kg)	2.22E+02	2.22E+03	1.40E+01	9.70E-02	2.57E-01
Total	**1.55E+06**	**1.55E+07**	**4.13E+05**	**1.76E+00**	**2.62E+03**

Figure 14-29 Summary of steady-state masses for 4-*tert*-octylphenol – lower estimate based on EU registered uses

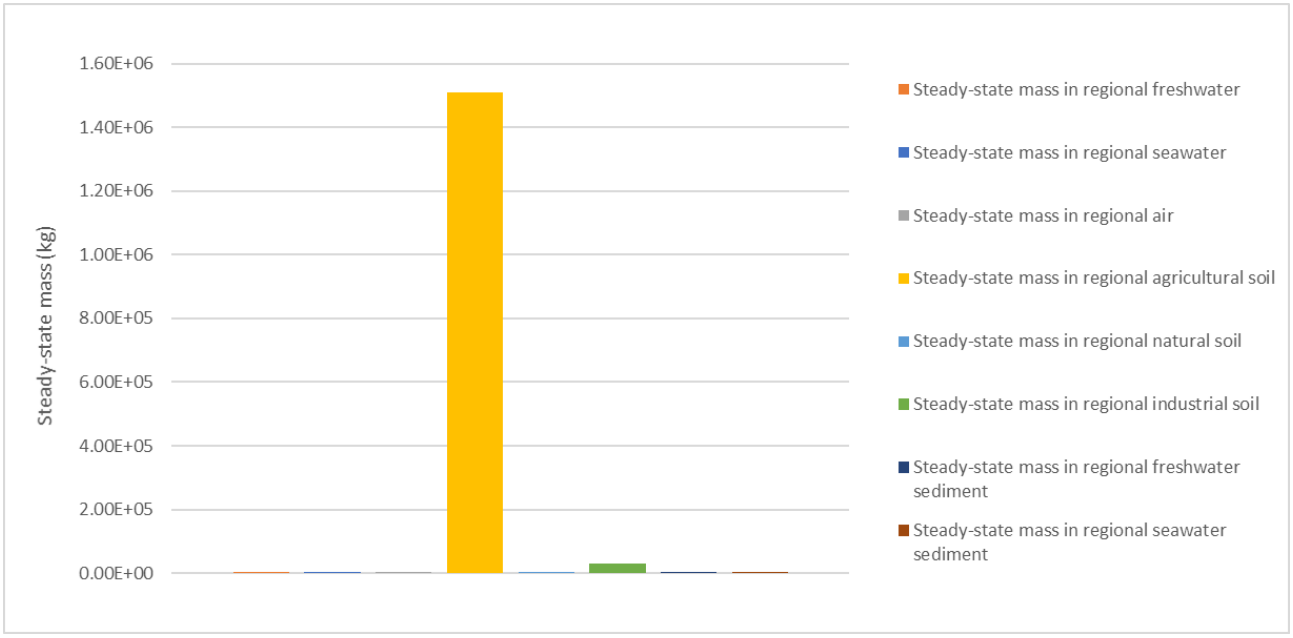


Figure 14-30 Summary of steady-state masses for 4-*tert*-octylphenol – upper estimate based on EU registered uses

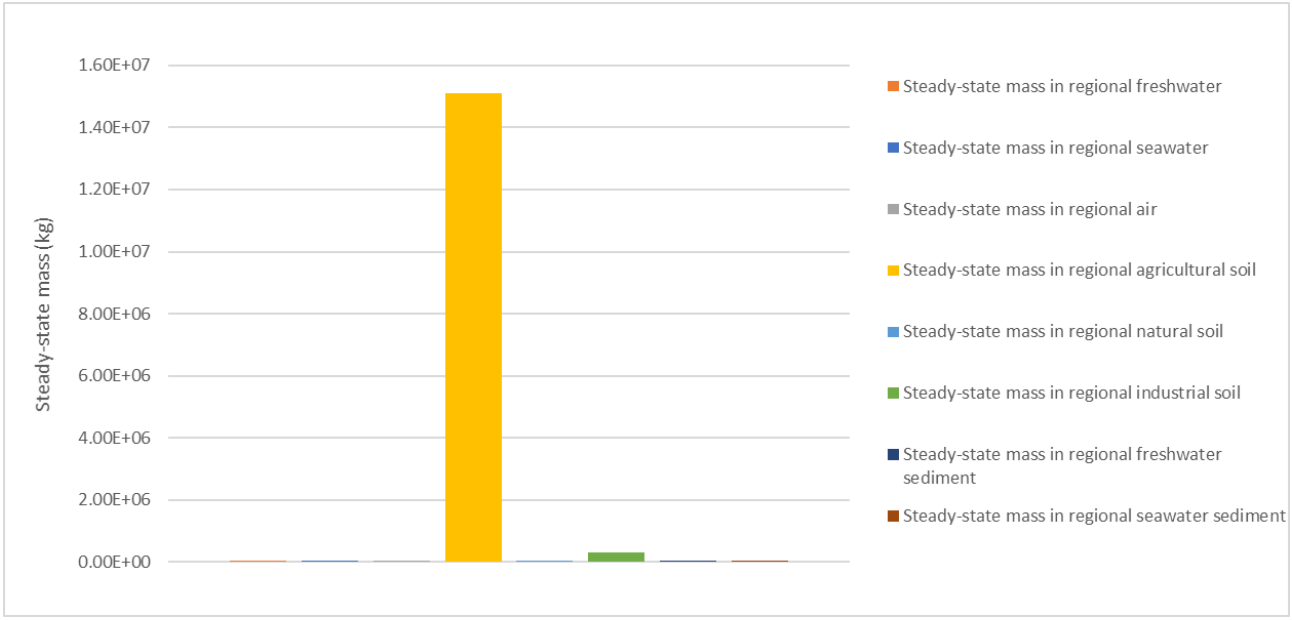


Figure 14-31 Summary of steady-state masses for 4-*tert*-octylphenol – estimate based on EA (2005) release estimates

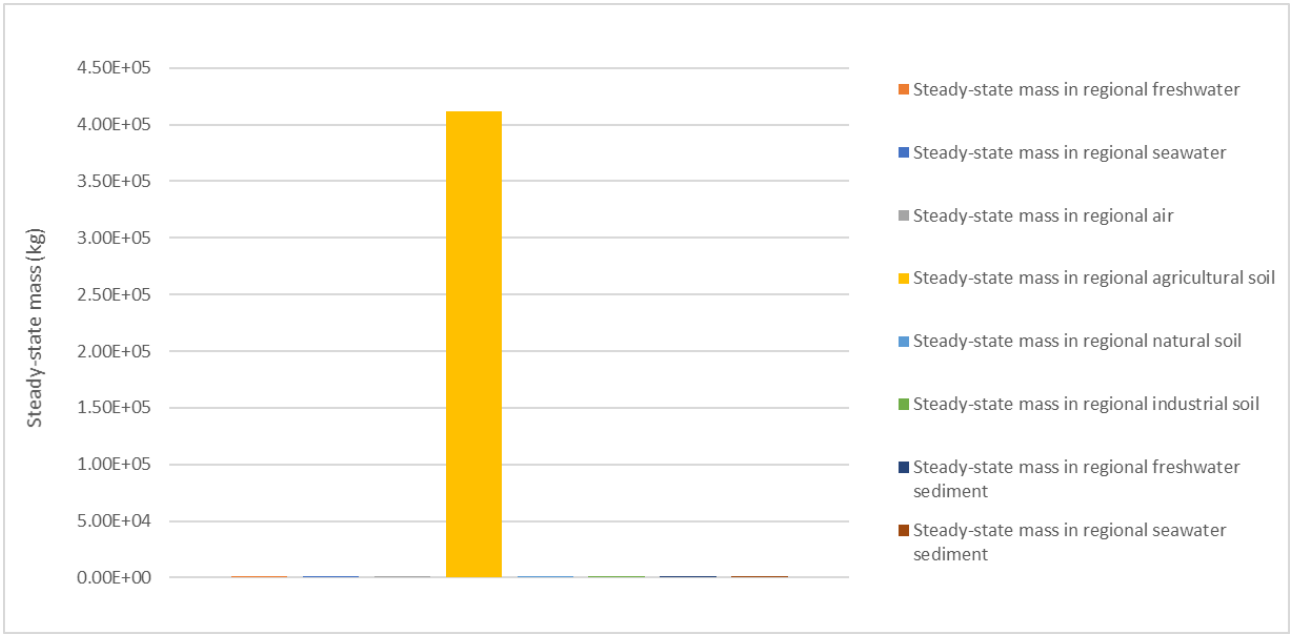


Figure 14-32 Summary of steady-state masses for 4-*tert*-octylphenol – 1 kg/day release to air

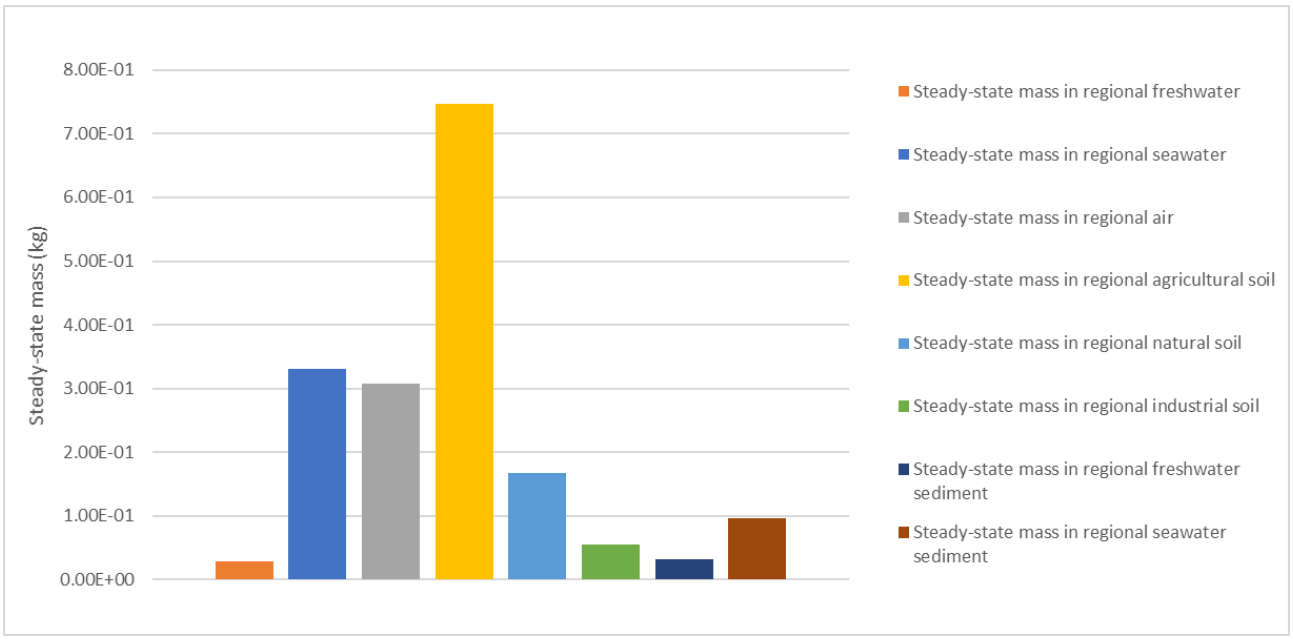
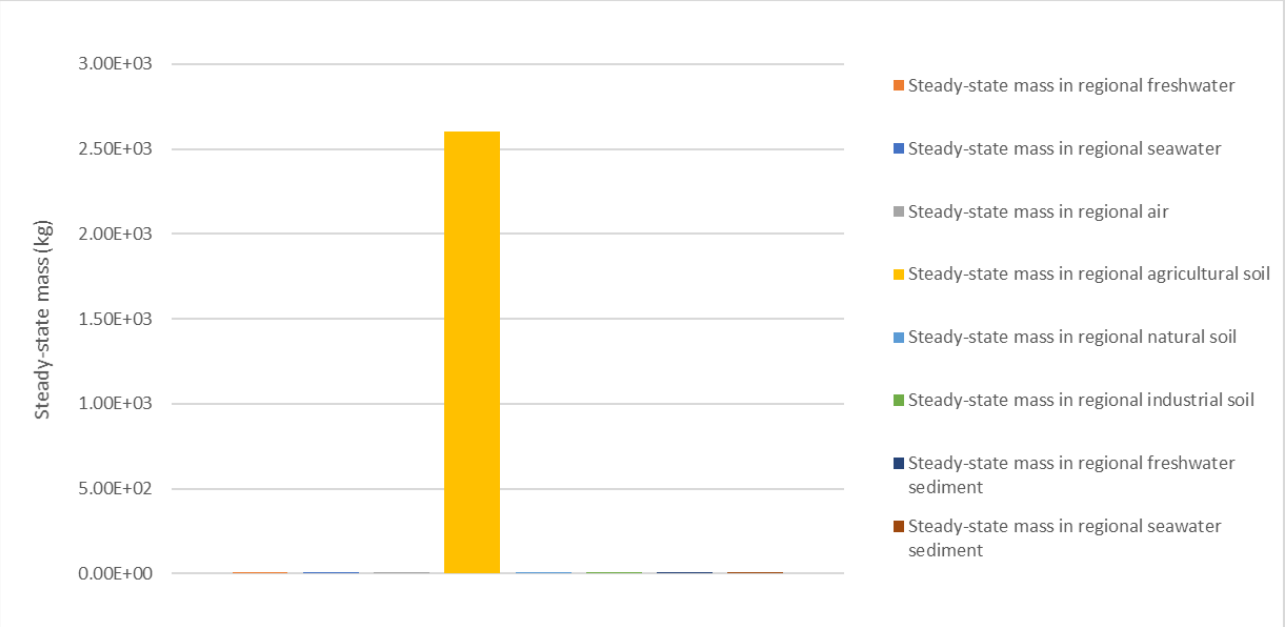


Figure 14-33 Summary of steady-state masses for 4-*tert*-octylphenol – 1 kg/day release to waste water



A1.2.11 Terphenyl, hydrogenated (CAS No. 61788-32-7)

Terphenyl, hydrogenated is registered under the EU REACH in the EU at a tonnage of 10,000 to 100,000 tonnes/year. There are 6 active EU registrations for the substance and there are no former UK registrants listed on the ECHA dissemination website. Assuming the UK usage is 10% of the total EU usage a UK tonnage of 1,000-10,000 tonnes /year is estimated for the analysis.

Using the approach outlined above, the total UK release estimated for the uses given in the EU REACH registration dossier is summarised in Table 14-21 below. The releases given in Table 14-21 are used as the regional release in the modified EUSES model for the UK.

Table 14-21 Estimates of the UK release of terphenyl, hydrogenated

Release compartment	Lower estimate based on EU registered uses (kg/year)	Upper estimate based on EU registered uses (kg/year)
Air	2.07×10^{5}	2.07×10^{6}
Waste water	2.16×10^{5}	2.16×10^{6}
Soil (direct release)	1.22×10^{4}	1.22×10^{5}

The substance properties used in the analysis were taken mainly from the ECHA Annex XV SVHC Report (ECHA, 2018).

The resulting steady-state masses estimated in the UK environment based on the release estimates outlined in Table 14-21 along with the steady-state masses assuming a standard release rate of 1 kg/day to either air or waste water, are summarised in Table 14-22 and show graphically in Figure 14-34 to Figure 14-37.

Table 14-22 Results of UK modelling terphenyl, hydrogenated (steady state masses)

Compartment	Lower estimate based on EU registered uses (kg)	Upper estimate based on EU registered uses (kg)	Assuming 1 kg/day release to air (kg)	Assuming kg/day release to waste water (kg)
Freshwater (kg)	1.99E+03	1.99E+04	8.12E-02	3.29E+00
Marine water (kg)	7.93E+02	7.93E+03	8.27E-01	5.36E-01
Air (kg)	4.59E+02	4.59E+03	5.89E-01	2.03E-01
Agricultural soil (kg)	1.23E+05	1.23E+06	2.39E+00	2.06E+02
Natural soil (kg)	1.36E+03	1.36E+04	1.74E+00	5.99E-01
Industrial soil (kg)	8.36E+03	8.36E+04	5.71E-01	1.96E-01
Freshwater sediment (kg)	2.32E+04	2.32E+05	9.47E-01	3.83E+01
Marine water sediment (kg)	2.72E+03	2.72E+04	2.84E+00	1.84E+00
Total	**1.62E+05**	**1.62E+06**	**9.99E+00**	**2.51E+02**

Figure 14-34 Summary of steady-state masses for terphenyl, hydrogenated – lower estimate based on EU registered uses

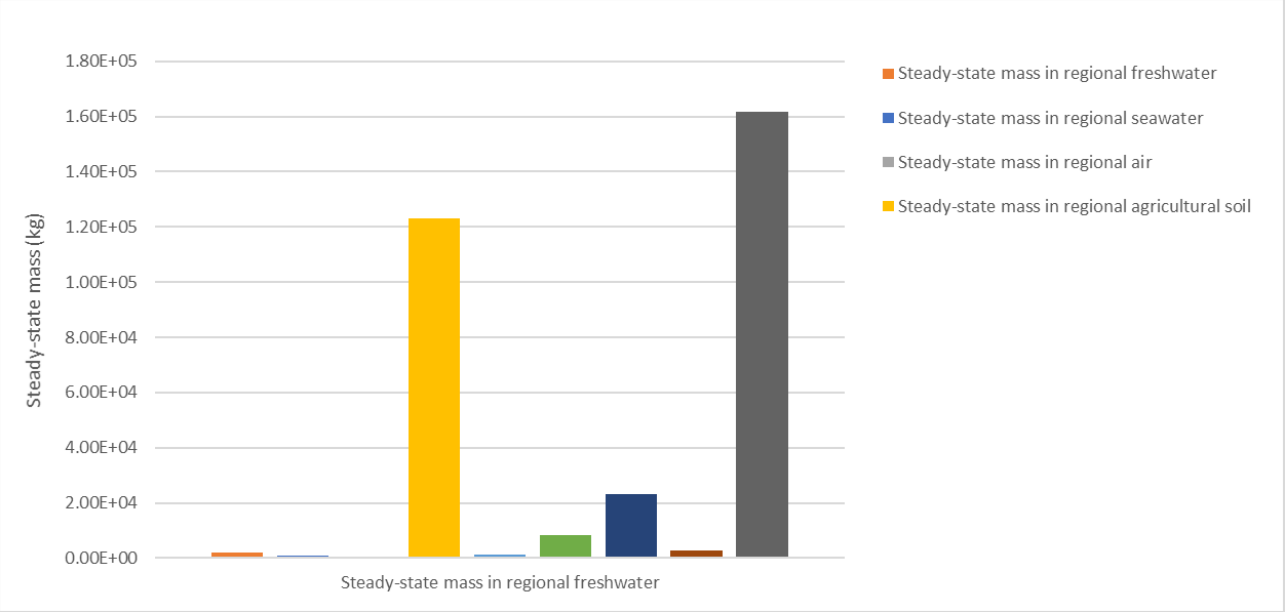


Figure 14-35 Summary of steady-state masses for terphenyl, hydrogenated – upper estimate based on EU registered uses

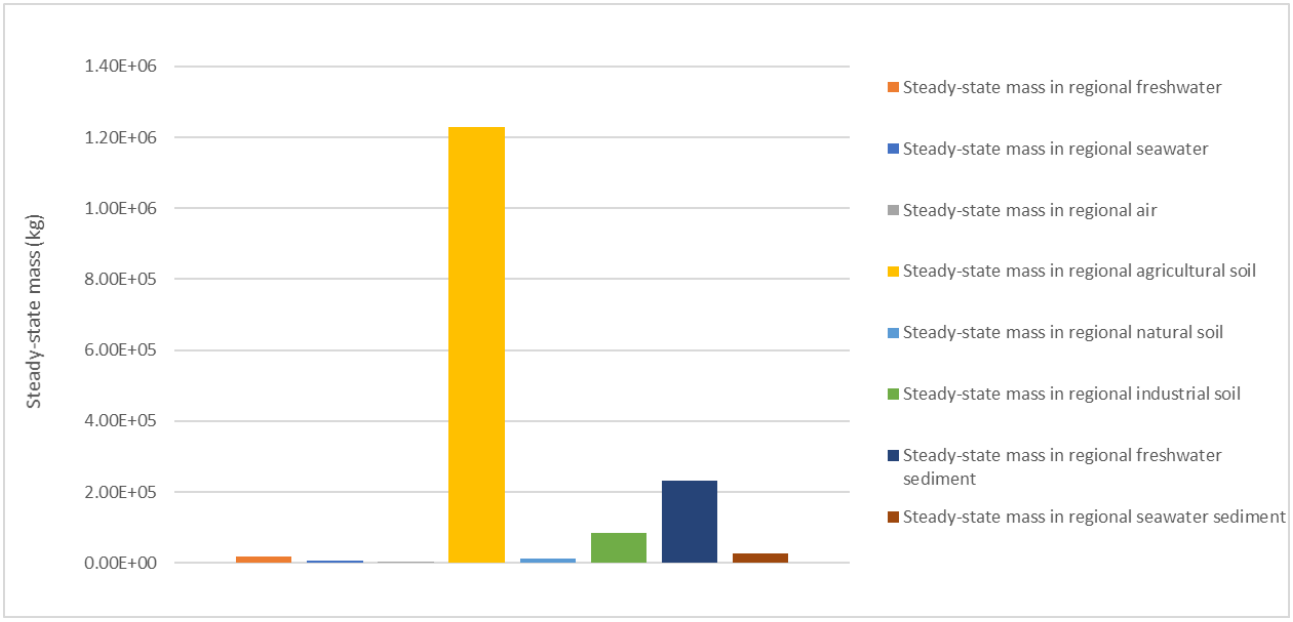


Figure 14-36 Summary of steady-state masses for terphenyl, hydrogenated – 1 kg/day release to air

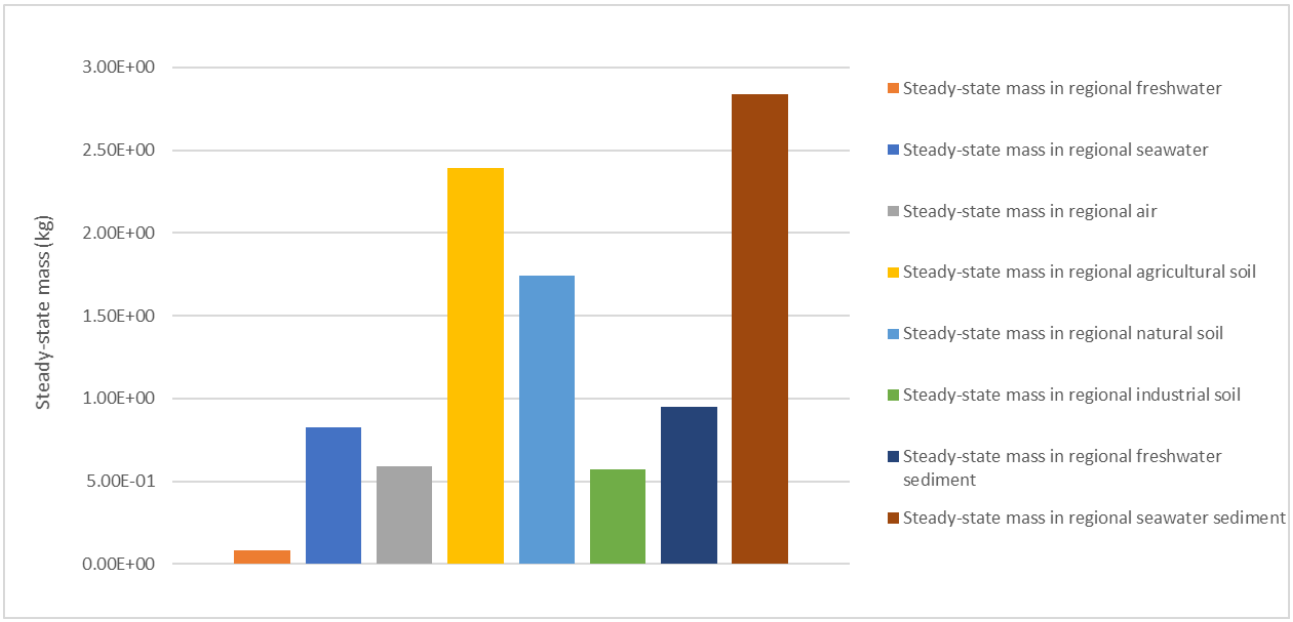
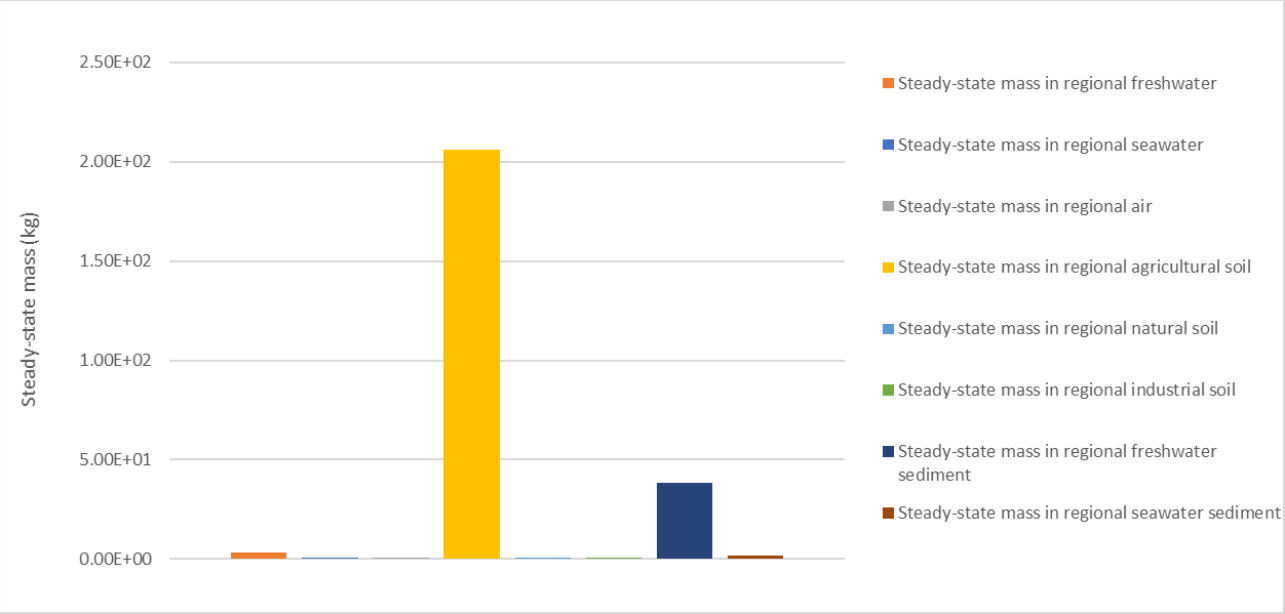


Figure 14-37 Summary of steady-state masses for terphenyl, hydrogenated – 1 kg/day release to waste water



A1.3 EUSES modelling of selected SVHCs- Further References

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