CHEMICAL ALTERNATIVES ASSESSMENT FOR SUBSTITUTION OF HAZARDOUS CHEMICALS WITH SAFER ALTERNATIVES

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I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

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ABSTRACT

CHEMICAL ALTERNATIVES ASSESSMENT FOR SUBSTITUTION OF HAZARDOUS CHEMICALS WITH SAFER ALTERNATIVES

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Consumer demand for safer chemicals has given rise to chemical alternatives assessment (CAA) to enable informed substitution of hazardous chemicals. The aim of this thesis was to evaluate alternatives for five hazardous chemicals, which are still being used in Turkey, via CAA to enable their informed substitution.

The target chemicals are: three phthalates; Bis(2-ethylhexyl) phthalate (DEHP), Dibutyl phthalate (DBP) and Benzyl butyl phthalate (BBP) used as plasticizers, and two flame retardants; Decabromodiphenyl ether (DecaBDE) and Hexabromocyclododecane (HBCD). They are all restricted or need authorization for use in Europe. A total of 13 alternative compounds were evaluated for these five target chemicals.

The CAA steps included in this study were: (i) chemical hazard assessment (CHA) with GreenScreen hazard assessment tool, (ii) environmental exposure assessment (EEA) with Equilibrium Criterion (EQC) model, and (iii) qualitative human exposure assessment (QHEA). Comparative evaluations were made among alternative and target chemicals, followed by recommendations. EEA could not be performed for six of the alternatives due to missing information or inorganic nature of chemicals. Amongst six alternatives for phthalates, Di-isononyl adipate (DINA)

showed development toxicity concern and recommended to be avoided for use, while glycerides, castor-oil-mono, hydrogenated, acetates (COMGHA) has the highest potential as a safe altenative. For HBCD, all three alternatives were safer according to CHA, two were similar according to EEA and QHEA, yet Butadiene styrene-brominated-copolymer shows the most promise owing to its least hazardous nature, as per CHA. All four selected alternatives for DecaBDE, regarding automotive applications, showed favorable CHA scoring. Although Aluminum diethylphosphinate and Polyphosphonate shows lower human exposure potential, further inquiry is required on environmental exposure of all alternatives.

Keywords: Chemical alternatives assessment, GreenScreen, Equilibrium criterion model (EQC), Phthalates, Flame retardants

ÖZET

TEHLİKELİ KİMYASALLARIN DAHA GÜVENLİ OLANLARI İLE DEĞİŞTİRİLMESİ AMACIYLA ALTERNATİF DEĞERLENDİRME ÇALIŞMASI

Rahim, Danial
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Güvenli kimyasallara yönelik tüketici talebi, tehlikeli kimyasalların bilinçli ikame edilmesini sağlamak amacıyla kimyasallar için alternatif değerlendirmesini (CAA) beraberinde getirmiştir. Bu tezin amacı, Türkiye'de halen kullanılmakta olan beş tehlikeli kimyasalın alternatiflerini CAA aracılığıyla bilinçli ikamelerini sağlamak için değerlendirmektir.

Hedef kimyasallar şunlardır: üç fitalat; plastikleştirici olarak kullanılan Bis (2-etilheksil) ftalat (DEHP), Dibutil ftalat (DBP) ve Benzil butil ftalat (BBP) ve iki alev geciktirici; Dekabromodifenil eter (DecaBDE) ve Hekzabromosiklododekan (HBCD). Kimyasalların tümünün Avrupa'da kullanımı kısıtlı veya izne tabidir. Bu beş hedef kimyasal için toplam 13 alternatif bileşik değerlendirilmiştir.

Bu çalışmada yer alan CAA adımları şunlardır: (i) GreenScreen tehlike değerlendirme aracı ile kimyasal tehlike değerlendirmesi (CHA), (ii) Denge Kriteri (EQC) modeli ile çevresel maruziyet değerlendirmesi (EEA) ve (iii) ECHA kriterleri kullanılarak nitel insan maruziyeti değerlendirmesi (QHEA). Alternatif ve hedef kimyasallar arasında karşılaştırmalı değerlendirmeler yapılmış, ardından öneriler sunulmuştur. Kimyasalların eksik bilgi veya inorganik yapısı nedeniyle altı alternatif için EQC değerlendirmesi gerçekleştirilememiştir. Fitalatlar için altı

alternatif arasında di-isononil adifat, DINA'nın, geliştirme toksisitesi endişesi gösterdiğinden kullanımdan kaçınılması tavsiye edilirken, gliseridler kastor yağı-mono hidrojene asetatlar, COMGHA'nın güvenli bir altenatif olarak en yüksek potansiyele sahip olduğu belirlenmiştir. HBCD için üç alternatifin tümünün CHA'ya göre daha güvenlir olduğu, ikisinin EEA ve QHEA'ya göre benzer olduğu, ancak Bütadien stiren-bromlu-kopolimerin CHA'ya göre en az tehlikeli yapısı nedeniyle en umut verici olanı olarak ortaya konmuştur. Otomotiv uygulamalarında kullanımıyla ilgili olarak DecaBDE için seçilen dört alternatifin tümü için olumlu CHA puanlaması belirlenmiştir. Alüminyum dietilfosfinat ve Polifosfonat daha düşük insan maruziyet potansiyeli göstermesine rağmen, tüm alternatiflerin çevresel maruziyetine ilişkin daha fazla araştırma yapılması gerekmektedir.

Anahtar Kelimeler: kimyasal alternatiflerin değerlendirilmesi, GreenScreen, Denge Kriteri modeli (EQC), fitalatlar, alev geciktiriciler

To Allah, my family and my mentor

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There was a time in my ODTU career where I genuinely thought I will not see this day where I am writing my acknowledgement chapter of the thesis but here I am and I am so happy that I am genuinely emotional to the core right now, so this is not going to be for the faint hearted. The only person responsible for me seeing this day is my adviser, my mentor Dr. Ipek İmamoğlu. I had packed my bags and was about to go back to Pakistan, but my sister just insisted upon me seeing her because she knew how much I respected her as a teacher. Thank God I did and the conversation started with her kind words ‘don’t worry we will solve everything’. She became my adviser and to this day all I have received from her is encouragement, guidance, warmth and dedication. I am indebted to her all my life. Her management style can be encapsulated by the saying ‘treat a man as he is and he will remain as he is. Treat a man as he could be and he will become he should be’. She always had her arms around my shoulder giving me advice not only about studies but life. When given the choice between being right or being kind she always chose kindness. She cared. I hope and pray for all the health and success in her way and her family.

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eternally grateful. I have heard such glowing reviews about Dr. Demirtepe that I am thankful that she is a part of such an important milestone in my life. I am genuinely humbled. May Allah bless them.

I spent more than 3 years in Turkey and I would not have survived them without my friends. I have met so many beautiful people that thanking all of them is impossible but I will name a few special ones. Erdem (Allah sent me here to find a brother from another mother and I did), Amin (my love my third musketeer, I am sure that I will be sitting around my children and grandchildren in Chitral and talking about the tales of your success), Irmak (my psychopath twin you are special and of all the warlords in ODTU I love you the most), Rayyan (your confidence inspires me and our friendship has gotten better and better with age like a fine wine), Mert (stay pretty and you are truly a friend everyone should want in their life), Yasin (good times are around the corner brother you are a superstar), Aykut (thank you and you know why), Nihan (your help was always underappreciated and your mother is right you do look like Audrey Hepburn), Dilan (that beautiful smile has always been calming), Ece (You are my sister and never forget I was the reason you are in a relationship so I am the Godfather of your kids), Berivan (you are exceptional and I like your boyfriend), Resul (I will miss our conversations about Lebron and you are a beautiful human being brother), my mother from Turkey (there was never a moment of falseness with you when I went to the canteen and met you, your love was genuine and I love you like my mother and will always pray for you). The friends I have forgotten to name, I am genuinely thankful for making me never feel like a foreigner. There will always be a special place in my heart for you all.

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Lastly, if my friends speculate that my effort and drive for the past three years was for getting a master's degree, don't believe them because every class I took, every midterm and exam I prepared for and every sleepless night I went through was about one thing, and one thing only 'reverence'. Reverence for Dr. Ipek İmamoğlu, my faculty, my department and most of all Middle East Technical University. So you don't have to wonder if I will miss ODTU, absolutely, absolutely I will.

There is a scripture reading 'I have fought the good fight, I have finished the race and I have kept the faith'. Well I fought a good fight, I finished my ODTU race and after three years it's time to go back (inshAllah☺).

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LIST OF ABBREVIATIONS

AA: Alternatives Assessment

AAF: Alternatives Assessment Framework

CAA: Chemicals Alternatives Assessment

CEPA: Canadian Environmental Protection Act

CHA: Chemical Hazard Assessment

CFC: Chlorofluorocarbon

CMR: Carcinogenic, Mutagenic and Reprotoxic

CPA: Clean Production Agency

CSCL: Chemical Substance Control List

DDT: Dichloro-diphenyl-trichloroethane

DfE: Design for Environment

ECHA: European Chemical Agency

EEA: Environmental Exposure Assessment

EPA: Environmental Protection Agency

EQC: Equilibrium Criterion

GHS: Globally Harmonised System

HCFC: Hydrochlorofluorocarbons

IARC: International Agency for Research on Cancer

IRIS: Integrated Risk Information System (USEPA)

MAK: Maximale Arbeitsplatzkonzentration (Maximum Workplace Concentration)

MFM: Multi-media Fate Modelling

NRC: National Research Council

NTP: National Toxicology Program

OECD: Organization for Economic Co-operation and Development

OSHA: Occupational Safety and Health Administration

PBT: Persistent, bioaccumulative and toxic

PBDE: Polybrominated diphenyl ether

POPs: Persistent organic pollutants

QHEA: Qualitative Human Exposure Assessment

REACH: Registration, Evaluation, Authorization and Restriction of Chemicals

RoHS: Restriction of Hazardous Substances Directive

RSL: Regional Screening Level

SVHC: Substance of very High Concern

TURI: Toxic Use Reduction Institute

TBBPA: Tetrabromobisphenol A

UNEP: United Nations Environmental Programme

UNESCO: United Nations Educational, Scientific and Cultural Organization

USCDC: United States Center of Disease Control

USDHHS: United States Department of Health and Human Serivices

USNIH: United States National Institute of Health

USEPA: United States Environmental Protection Agency

vPvB: Very Persistent very Bioaccumulative

WHO: World Health Organisation

CHAPTER 1

1 INTRODUCTION

Release of hazardous chemicals during production, use or disposal in the past decades has been a cause of concern in the scientific, government and public domains. The harmful impact, such as the neurotoxicity of lead or carcinogenicity of vinyl chloride or more recently, bisphenol A which has shown a wide range of potential harmful health impacts have been brought to light by scientific discoveries (Jacobs et al., 2016). The print and social media has rightfully exacerbated the public concern about the commercially used toxic chemicals. This awareness has led to a sense of responsibility towards the human health and ecosystem.

The most effective way to prevent the harmful impact of a toxic chemical as a result of exposure is to reduce or completely eliminate the use of the chemical of concern. New regulations, particularly in the EU and at the state level in the US, as well as supplier, manufacturer, and consumer demand for safer chemicals have been key drivers for chemicals with hazard potential to be restricted or substituted. The debate and actions have gotten to the point where policy makers are trying to address even the presence of chemicals in products which have not been studied in detail for their health and environmental effects. But 'regrettable substitution' in the absence of a proper evaluation of substitutes can happen (Jacobs et al., 2016). Many recent examples have been an evidence of this mishap where a substitute/alternative of a toxic chemical has shown to have toxic properties itself. For example, in the late 1990s, methylene chloride and trichloroethylene which had known carcinogenic properties were substituted by 1-bromopropane (N-propyl

bromide) as a drop-in replacement (USDHHS , 1992; IARC, 2014). After a few months, cases of severe neurotoxicity started to emerge amongst the workers (Ichihara et al., 2012; Majersik, 2007). 1-bromopropane is not only highly neurotoxic but the National Toxicology Program (NTP) also designated it as an 'anticipated to be human carcinogen' (NTP, 2016). Such bad examples show that it has become paramount to ensure before use that the alternative chemical selected has reduced health and environmental risk when compared to the original chemical.

Chemical Alternatives Assessment (CAA) or alternatives assessment is a process for identifying, comparing, and selecting safer alternatives to chemicals of concern (including those used in materials, processes, or technologies) on the basis of their hazards, comparative exposure, performance, and economic viability (NRC, 2014). Other terms are used for alternatives assessment, including chemicals alternatives assessment, alternatives analysis, or substitution assessment (Jacobs et al., 2016). Organisation for Economic Co-operation and Development (OECD) in their review noted that the most common focus of all these terms is the reduction of hazard and substitution of chemicals of concern with safer alternatives (OECD, 2013). In this study, comparative hazard assessment was carried out. Additionally, comparative exposure assessment and qualitative human exposure assessment were also carried out to help in decision making process. Economic feasibility and technical performance assessment were beyond the scope of this study.

Hazardous chemicals which are deemed 'priority' or 'very high concern' require alternative assessments for safer alternative chemicals in the chemicals management regulations in the EU. This is a regulatory requirement under Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), as part of authorization in the EU (EC1907/2006) and in states such as Washington and California in the US (Jacobs et al., 2016). The alternative assessment for safer chemicals has also become an active policy approach for leading product manufacturers and retailers (Lavoie et al., 2010a; NRC, 2014)

When the Turkish chemical inventory list is filtered, 67 chemicals are found to be manufactured or imported into Turkey which are either in the Restriction or Authorization list of EU REACH. The Ministry of Environment and Urbanization (MoEU) in Turkey published TURKREACH KKDIK regulation, which came into force on 23rd December, 2017 (TURKREACH, 2017), in the footsteps of EU REACH to manage, regulate and evaluate the chemicals on the Turkish market.Therefore it is important to carry out alternatives assessment for chemicals, which are still being used in Turkey, that are restricted or need authorization so that informed substitution can be made for such chemicals.

Chemicals currently being manufactured or imported in Turkey which are listed in the restricted and authorized chemicals of concern in EU are identified for the purposes of this study. Subsequently, five chemicals are selected, namely, DecaBDE, HBCD, and three phthalates (DEHP, DBP, BBP). DecaBDE and HBCD are flame retardants which are in the Turkish inventory (1-1000 tons/year), with evidence for use in Turkish industry (Demirtepe & Imamoglu, 2019). In addition, the main phthalates DEHP (>1000 tons/year), DBP (1-1000tons/year) and BBP (1-1000 tons/year) are also present in the Turkish inventory, with evidence for human exposure in Turkish population (Durmaz et al., 2010). Phthalates are used as plasticizers in PVC and although the main functional use of PVC in Turkey is not known, in this thesis the CAA assessment was done for the functional use of toys.

The overall aim of this study is to conduct alternative chemical assessments for the aforementioned chemicals in order to propose safer alternatives to substitute them. The novelty of this study stems from bringing together tools for hazard assessement, environmental and human exposure assessment in a CAA framework so that it can be used as a screening method for comparing alternative chemicals.

Specifically, the study aims to:

1. Identify alternatives from the already existing alternative assessments previously conducted for the chemical of concern and narrow them down for the function they are being used for in Turkey.

2. Conduct comparative hazard assessment for the selected chemicals and their alternatives using GreenScreen hazard assessment tool.
3. Evaluate the fate of selected chemicals and their alternatives according to their relative environmental distribution in air, water, soil and sediment in an evaluative environment via the Equilibrium Criterion (EQC) multimedia model.
4. Evaluate human exposure potential via a comparative qualitative exposure assessment of the selected chemicals and their alternatives, for the routes and patterns of exposure that might be relevant during use and disposal.
5. Recommend comparatively safer alternatives to the selected chemicals; identify limitations of study together with potential data gaps so that future research priorities can be set to strengthen the field of chemical alternatives assessment.

CHAPTER 2

2 LITERATURE REVIEW

2.1 Growing Chemical Dependence

Dr. Bruce Hammock, a National Academy Member for his work in environmental toxicology, once said "***citizens fail to acknowledge that, it is not the chemicals themselves that are evil, but rather their overuse that is harmful.***" We have become dependent on chemicals more and more as years have gone by because the performance and appearance in all the manufactured products is enhanced by the very same chemicals. Figure 2.1 shows that the global chemical production rate has already overtaken the global population growth rate and by the year 2050, it is estimated that it will be 4 folds greater than the global population growth rate.

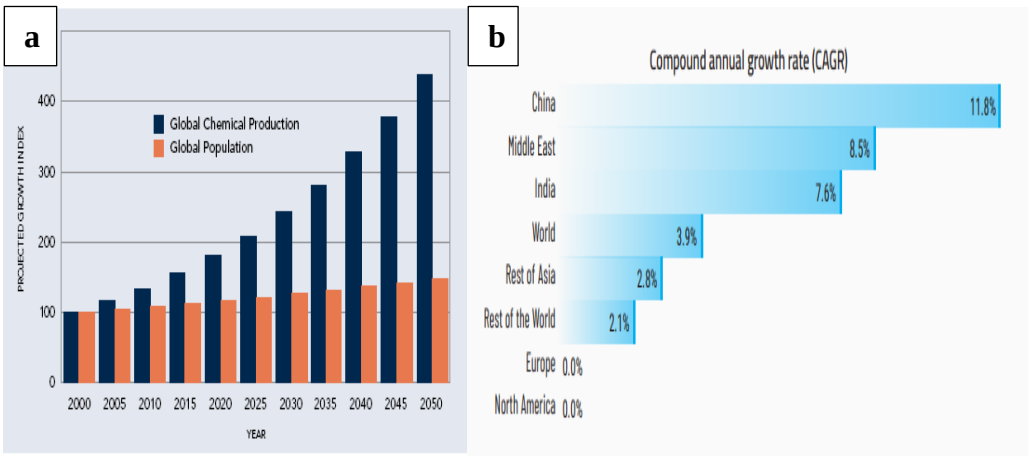

Figure 2.1. (a) Growth of global chemical production vs. global population growth (Goldenman et al., 2017) (b) Growth in production volumes, 2000-2017 (UNEP, 2019b).

In 2017, the total global sales revenue generated by the chemical industry was estimated to be $5.68 trillion (UNEP, 2019b), which makes the chemical industry

the second largest manufacturing industry in the world (ILO , 2018) and is supporting 120 million jobs worldwide (UNEP, 2019b). By 2060, the estimated global sales revenue from the chemical industry is estimated to reach $ 22 trillion (OECD, 2011).

Figure 2.1.(b) shows that the growth in production volume from 2000 to 2017 in Europe and North America has stagnated whereas China, Middle East and India have taken over the chemical manufacturing industry and have experienced growth at a compound annual growth rate of 11.8, 8.5 and 7.6%, respectively (UNEP, 2019b). 48% of the output of the chemical industry is directly used by other manufacturing industries, making it a cornerstone for the progress of other industries (Dickson et al., 2017). These statistics and facts allude to our growing dependence on the chemical industry to create livelihood opportunities, stabilize economies and make our lives easier by their application in the different daily products we use. ***But the most important thing is the urge for prudent use.***

2.1.1 Global Concerns Regarding Chemicals

Chemicals have become an indispensable part of our lives but it has been reported that out of the millions of industrial chemicals on the market, only 5% have been properly evaluated for their health and environmental effects (Schaafsma et al., 2009). Adverse effects of some of the chemicals on human health and environment have been proven by numerous studies. For example, some chemicals can cause endocrine disruption or negatively affect human immune system (Prüss-Ustün et al., 2011). Some chemicals can be carcinogenic or cause reproductive toxicity or development toxicity or can be a cause of brain impairment (Fredslund & Bonefeld-Jørgensen, 2012). With research it has become more evident that many chemicals which were considered safe at negligible doses, are proven to have biological effects, so the safety barometer of the chemicals is in question now (Vandenberg et al., 2012). Subtle harm has also been caused by the long term exposure by the chemicals at low doses (Birnbaum, 2012). Another problem which

has caused a stir in the research community is the effect of mixtures of thousands of chemicals from innumerable sources, because chemicals when combined may have different safe levels than the individual safe levels of the chemicals (Sarigiannis & Hansen, 2012).

It was estimated in 2016, around 1.6 million lives were lost due to the diseases caused by chemicals which is equivalent to 2.7% of total global deaths (UNEP, 2019b). Landrigan et al., (2018) indicated data gaps for many chemicals in use which is a cause of underestimation for the disease burden caused by the chemicals.

According to the UNESCO report, without adequate treatment greater than 80% of the industrial and municipal wastewater which contains hazardous chemicals is released into the environment which is causing ecosystem and wildlife degradation (UNESCO, 2015). Due to ineffective treatment, pharmaceutical wastewater has been a cause of river and groundwater pollution (Larsson, 2014). Domestic and commercial products in the sewage contain heavy metals such as cadmium, lead and mercury as well as a number of persistent organic pollutants (POPs), causing hazard to the environment (UNEP, 2019b).

Two of the chosen chemicals for in this study, namely, DecaBDE and HBCD, are amongst the persistent organic pollutants (POPs) in Annex A by the Stockholm Convention. The Water Framework Directive also identified them as priority substances (Demirtepe & Imamoglu, 2019). The phthalates (DEHP, DBP and BBP) chosen to be evaluated in this study have also been identified as toxic for reproduction category 1B and have been restricted to be used in the EU after 7th July, 2020 (ECHA, 2018).

2.1.2 Chemical Legislations and Regulations

The knowledge of chemicals, being an important part of our daily lives and the concerns they propose makes people wary and anxious that is why the first thought

that cross peoples mind when they hear the word chemical is toxic. So what can be done to make people less afraid of chemicals? Joseph P. Bradley once said **"*Society cannot exist without law. Law is the bond of society: that which makes it, that which preserves it and keeps it together. It is, in fact, the essence of civil society.*"** But when did the world realize that chemicals need to be legislated or regulated? Scientific knowledge regarding the persistent, bioaccumulative and toxic (PBT) chemicals existed before Rachel Carson's book the Silent Spring (1962) but Carson's book caught mass attention like nothing had ever before and made people aware about the devastation pesticides caused to the environment (Matthies et al., 2016). The book shook the world and the New York Times captured the public sentiment with the headline ***'Silent spring is now noisy summer'.***

Rachel Carson's work gave rise to a national debate amongst the masses and the scientists alike and became an inspiration to the modern environmental movement and the generation of activists. Her work inspired the U.S Congress into action and they passed the National Environmental Policy Act (NEPA) in 1969 and led to the establishment of U.S Environmental Protection Agency (USEPA), a federal regulatory agency established in 1970. The first achievement by USEPA was to ban DDT and some other pesticides (Whitney, 2012). Over 150 signatories joined forces to tackle the problem of 12 key POPs, by reducing or eliminating their use, production and release under the banner of Stockholm Convention in 2001. Figure 2.2 below shows the timeline of international regulations and legislations regarding POPs and PBT chemicals through the decades as major achievements. Figure 2.2 shows the international regulation compiled in Matthies et al., (2016) study till 2012 which have been updated till 2021 in this thesis. Early international agreements between Canada and US were driven to safeguard the Great Lakes ecosystem and water quality. Fifty years of progress has brought everyone to the same conclusion that without regulating and maintaining chemical inventories, humans and environment will always be at risk against known and unknown PBT chemicals.

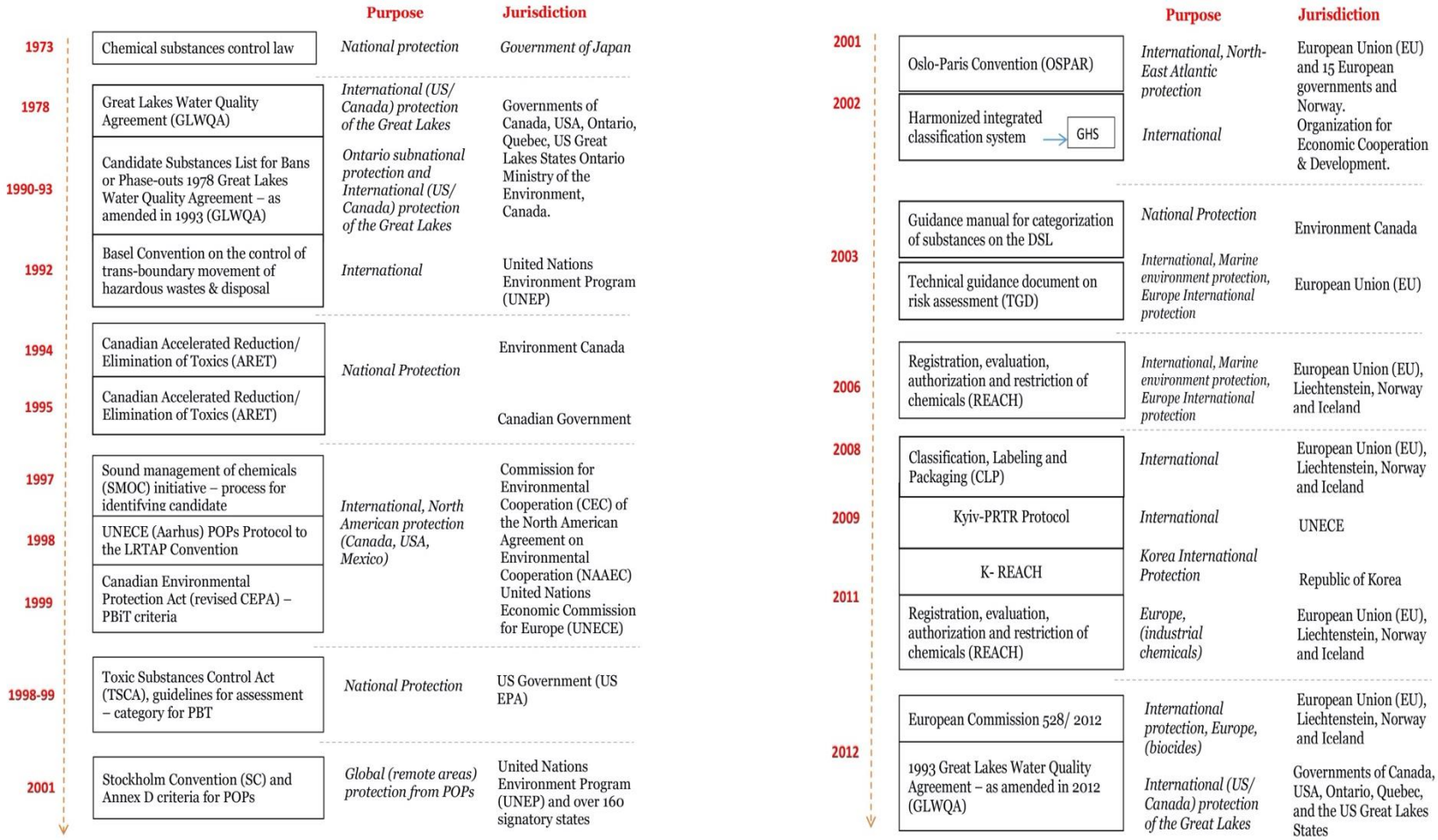

Figure 2.2. Timeline of selected international regulations and legislations regarding POPs and PBT chemicals (Matthies et al., 2016).

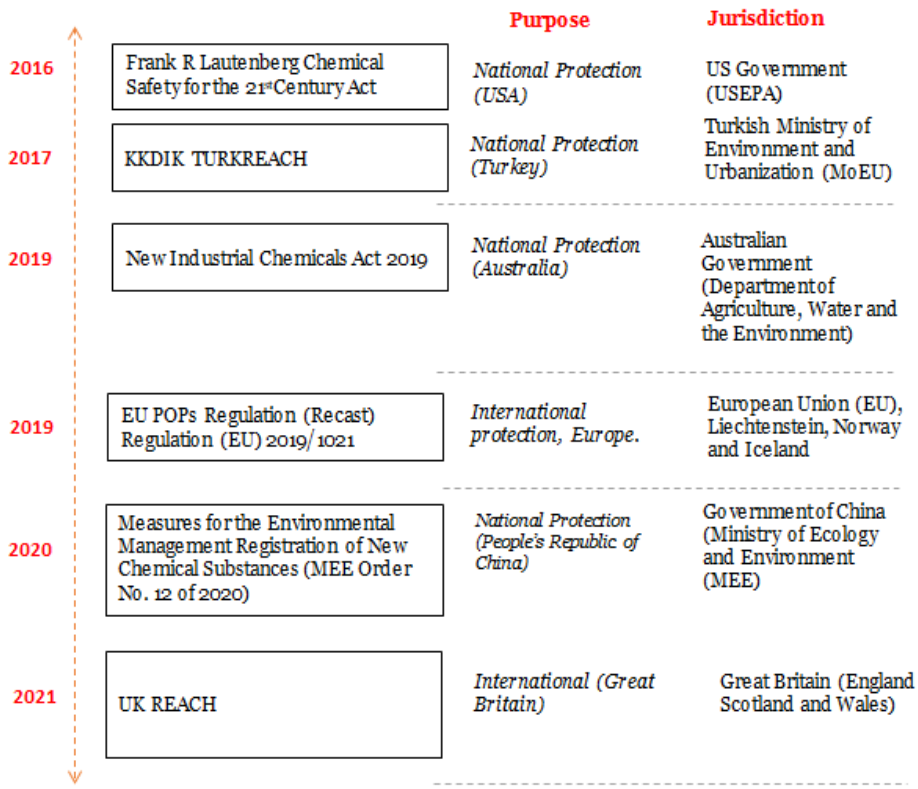

Figure 2.2. (cont'd): Timeline of selected international regulations and legislations regarding POPs and PBT chemicals (Matthies et al., 2016).

A list of national legislation can be seen in Table 2.1. Furthermore, Table 2.2 provides a brief summary of national and global regulations and protocols which lists chemicals as restricted, banned or of great concern to the environment or human health.

Table 2.1. Turkish legislation on POPs and PBT chemicals.

Name of Legislation	Official Gazette No	Date
Law on the Approval of Ratification of the Basel Convention Controlling Trans-boundary Movements of Hazardous Wastes and their Disposal	21804	30.12.1993
Law on the Approval of Ratification of the Stockholm Convention on Persistent Organic Pollutants	27200	14.04.2009
By-law on Classification, Packaging and Labeling of Dangerous Substances and Preparations	28848	11.12.2013
By- Law on Registration, Evaluation, Authorization and Restriction of Chemicals	30105	23.06.2017
Regulation on Persistent Organic Pollutants	30595	14.11.2018

Table 2.2. Restriction and substances of high concern list around the globe.

Lists	Jurisdiction	Salient Features
REACH Substance of Very High Concern (SVHC[1]) List	European Union (except Switzerland)	Substances fulfilling one or more criteria of the Article 57 of the EU REACH Regulation. There are 211 substances on the SVHC List (last updated on 19th January, 2021).
REACH Restricted Substance List	European Union (except Switzerland)	Annex XVII is the restriction list in the EU REACH Regulation of substances, mixtures or articles to be used or placed in the European market. There are 69 entries in Annex XVII as of 5th January, 2021. An entry can be a substance, a group of substances or a mixture.

Lists	Jurisdiction	Salient Features
REACH Authorization List	European Union (except Switzerland)	Annex XIV is the authorization list in the EU REACH Regulation for which substances, mixtures or articles in the annex require authorization to be used and placed in the European market. 54 entries are on the Authorization List (EC 2020/171) (last updated 7th February, 2020).
Swiss Chemical Risk Reduction Ordinance	National regulation in Switzerland	The substances, mixtures or articles prohibited or restricted for use or placing on market according to this ordinance in Switzerland. This ordinance is a combined version of REACH Restriction, Authorization list and EU RoHS.
China RoHS [2]	National regulation in People's Republic of China	Six hazardous substances are on the restriction list to be used in the electrical and electronic equipment which came into force on 1st July, 2016.
EU RoHS/RoHS[2]	European Union except Switzerland	Certain hazardous substances are restricted for use in the electrical and electronic equipment according to the (EU Directive 2011/65/EU). 10 substances are currently in the restricted list. 6 substances are the same in China RoHS 2 with 4 phthalates included.
Canada CEPA[3] Priority Substances List	National regulation in Canada	As per section 76, CEPA (1999), a priority substance list (PSL) should be compiled by the minister of environment and health where the chemicals on the list should be evaluated on priority basis. There are 69 chemicals on the list (last updated January, 2015).
California proposition 65 List	State legislation in California	It contains the chemicals in the state of California which are deemed to cause cancer or reproductive toxicity. California Proposition 65 List doesn't ban or restrict any chemical and it is only concerned with the safe exposure levels of the chemicals present on the list. There are currently more than 950 substances on the list which is updated annually.

Lists	Jurisdiction	Salient Features
Japan CSCL Class I Specified Substances	National regulation in Japan	This list contains the substances which are evaluated to be persistent, highly bioaccumulative or toxic to human. 33 substances are on the list (last updated April, 2018). Some chemicals require authorization for import or manufacture and some chemicals are permanently banned as per this list to be used in products.
K-REACH Restricted Substance List	Republic of Korea	The list was released in 2017 and contains 12 chemicals which are restricted to be used in products in Republic of Korea.
Persistent Organic Pollutants (POPs)	Stockholm Convention. More than 140 countries have ratified it	Adopted in 22nd May, 2001 and entered into force on 17th May, 2004. There are over 30 chemicals on the POPs list in the Stockholm convention three annexes. The Annex A contains the chemicals which should be eliminated. Annex B contains the restricted chemicals and Annex C contains the chemicals for which measures should be taken for unintentional releases.
Ozone Depleting Substances	Montreal Protocol (a protocol to the Vienna Convention for the Protection of the Ozone Layer)	Montreal Protocol agreed on September 16, 1987 and entered into force on January 1st, 1989 was designed to phase out chemicals which have ozone depleting potential. Chlorofluoro carbons (CFCs) have already been phased out by 2015 and parties have agreed to freeze consumption and production of HCFCs by 2013 and goal of HCFC phase out is planned by 2030.
Mercury and its compounds	Minamata Convention. 128 signatories and ratification by 125 countries	Minamata Convention on mercury was agreed on 19th January, 2013 under which ban has been imposed on new mercury mines as well as phasing out of the products which contains mercury and its compounds by 2020.

[1] Substance of Very High Concern

[2] Restriction of Hazardous Substances

[3] Canadian Environmental Protection Act.

2.1.3 How REACH Regulation Became a Trendsetter for Chemical Management

REACH stands for Registration, Evaluation, Authorization and Restriction of Chemicals. The aim of REACH (EC1907/2006) is to protect the human health and environment from the risks that are posed by the chemicals around us. REACH was approved on the 18th of December, 2006. The implementation and administration of REACH in Europe is the responsibility of European Chemical Agency (ECHA) which is a European Union (EU) regulatory agency for chemicals.

Key Principles and Provisions of REACH:

In the literature, REACH is termed as the 'paradigmatic shift' for chemical policy (Führ & Bizer, 2007). It is also termed as a 'unique policy' and 'a truly revolutionary chemical policy' (Fuchs, 2009). Some of the key provisions and principles of the regulation are as follows:

1. To eradicate toxic ignorance, the REACH follows the concept of 'no data no market' which means that without providing reliable information about the chemical, access to the European market will not be granted to the manufacturer or importer of the substance.
2. The chemical industry is responsible for providing burden of proof for the substance to ensure the safety of the chemical.
3. Hazard based approach of REACH makes it necessary for the industry to provide hazard information of chemicals.
4. The Regulation covers all the chemicals in the market whether they are already existing or new. Article 2 of the REACH states the exempted substances which are covered by other regulations in the EU.
5. Registration has to be done for each chemical manufactured or imported above 1 tons/year by submitting a registration dossier fulfilling necessary requirements to complete the information required by the agency. For 10 tons/ year and above, a chemical safety report with exposure scenarios documented should be part of the registration dossier.
6. Evaluation of the registration dossier is done by ECHA by random checks for its completeness and testing proposals. A substance of concern can be

prioritized for evaluation if it is placed on the Community Rolling Action Plan (CoRAP) by ECHA. Member states evaluate the substances in the CoRAP within three years to clarify the concern that the substance could pose a risk to human health or environment.

7. Management of chemical risks is ensured by the Restriction and Authorization processes in the REACH. SVHC list contain the chemicals which are mainly Carcinogenic, Mutagenic or Reprotoxic (CMR), PBT or vPvB or substances with equivalent level of concern. Once on the SVHC list, the chemical can be put into authorization list (Annex XIV) after which the chemical can only be placed on the market or used in articles after authorization from the commission**.** The main aim is to encourage substitution of the chemical of concern or control the hazard of the chemical. Restriction is proposed by the Member State or ECHA itself when it is demonstrated that the chemical poses unacceptable risk to the human health or the environment. In such case, a chemical cannot be placed on the market or be used in an article or as a mixture unless it complies with specific requirements for its use.

The Ministry of Environment and Urbanization (MoEU) in Turkey, published TURKREACH KKDIK regulation on 23rd June, 2017 which came into force on 23rd December, 2017 (TURKREACH, 2017). Under this regulation, substances above 1 tons/year have to be registered before the deadline 31st December, 2023. The KKDIK Authorization List (Annex XIV) and Restriction List (Annex XVII) will have the same entries as the EU REACH list.

2.1.4 Green Chemistry and Hazardous Chemicals

Green Chemistry is defined as the ***''design of chemical products and processes to reduce or eliminate the use and generation of hazardous substances''*** (Anastas & Breen, 1997)**.** Nearly 30 years ago, in the early1990s, Green Chemistry definition and philosophy was first used (Collins, 2017). It has been universally adopted ever since and opened avenues for countless research programs and initiatives by governmental agencies on Green Chemistry around the globe. The initial global leaders on Green Chemistry were the U.S, United Kingdom and Italy, with a considerable role in the field of sustainable design (McDonough et al.,

2003). The torch bearing programs were the U.S Presidential Green Chemistry Challenge Awards established in 1995, the creation of Green Chemistry Institute in 1997 and the first volume publication of the now famous Green Chemistry journal of the Royal Society of Chemistry in 1999 (Clark, 1999).

The three main points about the Green Chemistry framework were summarized by Anastas & Eghbali, (2010):

- Across all stages of a life-cycle of a chemical, Green Chemistry design should be followed.
- The Green Chemistry design aims to reduce the intrinsic hazard of the chemical products and processes.
- Green Chemistry works as a cohesive system of principles or design criteria.

The sustainable design framework's guidelines or design protocols are 'The Twelve Principles of Green Chemistry', to design safer chemicals and chemical transformations (Anastas & Eghbali, 2010). Chemistry has always been imagined as a dangerous science with 'chemical' perceived and associated with 'toxic' by the general masses. Protective gears are an example of safety precaution can lessen the risk but in case of failure of safety precautions, risk increases. Risk is a function of hazard and exposure and if exposure control fails and hazard is high, fatal consequences can be faced (McDonough et al., 2003). That is why the focus has shifted in recent times from exposure control to minimizing the hazard portion of the equation, because even in case of undesired accidents, risk can be minimal when the chemical is safe. Designing safer sustainable chemicals is fruitless when the intrinsic hazard of the chemical is not reduced to a minimum and therefore reducing the risk of accident and damage (Anastas & Breen, 1997).

Green Chemistry advocates that reduction of hazard across all life-cycle stages is economically profitable. The adverse effect caused by the chemical to the humans or the environment is termed as hazard. Intrinsic hazard (as either toxicity or physical hazard such as explosivity, flammability, or global hazard potential such as depletion of stratospheric ozone) should be minimized at every level of a process

in a safe chemical design. A safe and careful design with integration of cohesive set of Twelve Principles will decrease or eradicate intrinsic hazards within chemicals and processes (Anastas & Eghbali, 2010). These 12 principles are given in Figure 2.3.

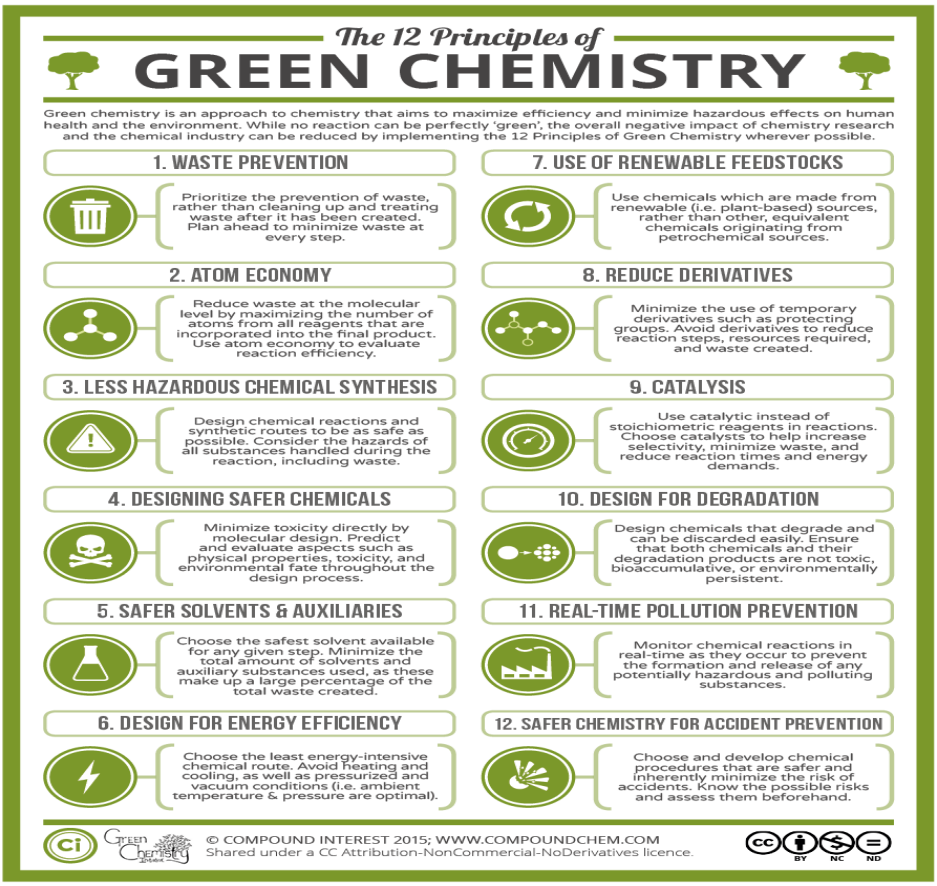

Figure 2.3. The 12 Principles of Green Chemistry (CompoundChem, 2015).

The Concept of Designing Safer Chemicals and Design for Degradation

Designing safe chemicals entails "***The employment of structure - activity relationships (SAR) and molecular manipulation to achieve the optimum relationship between toxicological effects and the efficacy of intended use***" (Garrett, 1996). Achieving zero toxicity and maximum level of efficacy at the same time is often impossible that is why **'optimum'** is the magic word in the

above definition because optimum combination of the two aspects is achievable (Garrett, 1996). Hence to synthesize a "safe chemical", as the result of safe design, its effect on human health and environment should be the central point of interest.

Figure 2.4 shows the application of this philosophy to structural redesigning of an existing chemical as well as the structural designing of a new chemical.

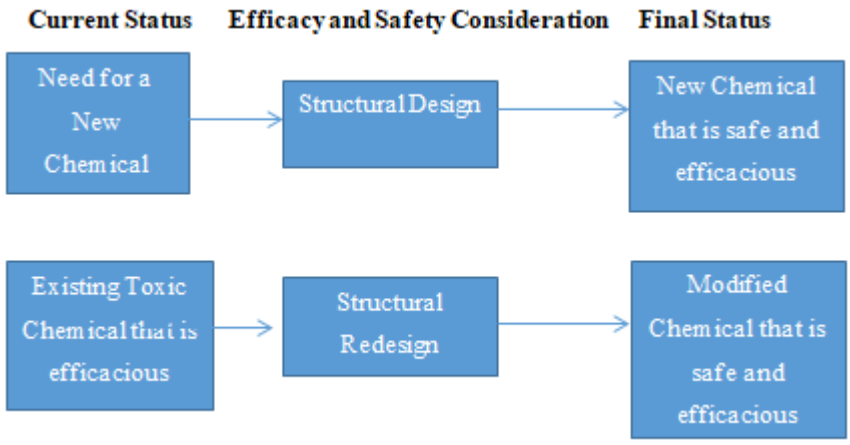

Figure 2.4. Philosophy of designing safer chemicals (Garrett, 1996).

Designing safer chemicals concept is incomplete if we don't cater for the safe and complete degradation of the chemical. If a chemical designed is safe from toxicity point of view but it's gravely persistent in the environment then that is a danger in itself. That is why we are seeing our oceans getting polluted; even the Arctic is showing trans-boundary chemicals through long range transport. Therefore, designing chemicals which are only safe from human toxicity perspective is not enough and degradation products and complete degradation should be thoroughly investigated when a new chemical is being designed or an already existing chemical is being redesigned.

The 'Twelve Principles of Green Chemistry' have become a building block for achieving sustainability goals, that is why the entire industrial sector is trying to

adopt the principles of green chemistry from aerospace to agriculture; pharmaceutical to electronics, energy to automobile. This has led to economically innovative green technologies in all of the industrial sectors (Zhao, 2018). Now everyone is conscious of the role they need to play to make this planet sustainable and in doing so what choices they have to make so that the next generation products they use are made by the chemists which are advantageous for human health and the environment. This change of mindset and enthusiasm in the general public, has extrapolated teaching initiatives, extra funding and Green Chemistry Research Centers in the last three decades (Linthorst, 2010).

The chemical alternatives assessment concept also follows the two principles of green chemistry, i.e., designing safer chemicals and design for degradation to assess the chemical hazard and fate of the chemical in the environment to propose safer alternatives and make informed substitution for the chemical of concern (USEPA, 2005; 2014b).

2.2 Chemical Alternatives Assessment (CAA)

CAA or alternative assessment is defined as the identification, comparison and selection of safer alternatives to chemicals of concern on the basis of their hazard, comparative exposure, performance and economic viability (NRC, 2014). Other terms are used for alternatives assessment, including chemicals alternatives assessment, alternatives analysis, or substitution assessment (Jacobs et al., 2016). Organisation for Economic Co-operation and Development (OECD) in their review noted that the most common focus of all these terms is the reduction of hazard and substitution of chemicals of concern with safer alternatives (OECD, 2013). The major focus of alternative assessment is to select alternatives for a specific function for which the chemical of concern is being used. The chemical of concern can be substituted by chemical or non-chemical alternatives, or by process design change or by innovative technology with which the need for the chemical is completely eradicated. With the help of properly conducted alternatives assessment, a

systematic image can be drawn so that informed and well researched safer alternatives can be proposed where the aspect of anomaly is absent and regrettable substitutions are avoided. It may seem straightforward but in order to make alternative assessment fruitful it has to be kept in mind that it is an interdisciplinary science policy approach and the true essence of alternatives assessment is in the combination of different sectors working together robustly to achieve the same goal of proposing an informed substitution for the chemical of concern (Tickner et al., 2019b). It is important because in the past shoe-in or drop-in replacements for a chemical of concern without proper research has given rise to problems. This caused dissolution of trust between the general consumer market and the corporate sector as well as the regulatory authorities which are there to remove the concerns of the masses. For example, Bisphenol A (BPA) was replaced by Bisphenol S (BPS) and Bisphenol F (BPF) as a drop-in replacement in baby bottles by constant pressure by the consumer market. 32 studies were conducted and after extensive review, it became apparent that the two alternative chemicals had the same estrogenic effects as BPA (Rochester & Bolden, 2015). Sometimes regulatory pressures to replace a chemical with a drop-in replacement can also create mishaps like in the case of suspected carcinogenic solvents methylene chloride and trichloroethylene which were replaced by a drop-in replacement of 1-bromopropane (N-propyl bromide) (Majersik et al., 2007;Ichihara et al., 2012). Severe neurotoxic effects were observed in the workers who were exposed to the chemical (Jacobs et al., 2016). After extensive studies conducted, 1- bromopropane was also classified as ‘anticipated to be human carcinogen’ by the NTP (NTP, 2016). This shows that the drop-in replacement which was supposed to eradicate toxicity due to inhalation, forced the workers to come face to face with a different hazard.

The shortcoming of restriction policies and drop-in replacements were pointed out by Tickner et al., (2013) as follows:

- If policies by governmental agencies of a particular population are adopted to restrict a chemical of concern keeping in view a particular population or media, then there is a chance that the risk is shifted to some other population or media, at a different lifecycle of the product.
- Restriction policies don't cater for the process and technology change that may arise due to adopting a new chemical due to which the exposure patterns and work practices may change.
- If the policies are only adopted to eliminate a chemical of concern and due diligence is not provided to understand the 'functional use' of the chemical, then uninformed substitution can become a reality. By understanding the function of the chemical in the product, technological innovation or product design change might be enough to eradicate the chemical of concern.
- The restriction policies adopted by the regulatory authorities mostly focus on generating authoritative lists. Given the lack of data regarding hazard endpoints especially for carcinogenic properties which require extensive research, the authoritative lists may be missing key hazard parameters and the manufacturers may develop false hope that if the chemical is not on these lists, then it is safe to be used.

The above shortcomings clearly enlighten that restriction policies for the sake of restriction should not be the motto. The aim of restriction policies should be to develop guidelines for transition to safer chemicals with proper knowledge and research. That is why alternative assessment policies should go hand in hand with the restriction policies for regulatory authorities to promote safer identification of alternative chemicals for the chemicals of concern.

2.2.1 Development of Alternatives Assessment Philosophy around the Globe

Figure 2.5 below shows the timeline in United States and Europe of major developmental achievements for the alternative assessment policy in regulatory

frameworks and some other historical benchmarks in the field of CAA, as mentioned in Tickner et al (2013).The first mention of alternatives assessment was in NEPA of the US in 1970, as depicted in the figure. Then from 1989 onwards, starting with substitution of ozone depleting chemicals, the term and hence the philosophy has found wider acceptance and application.

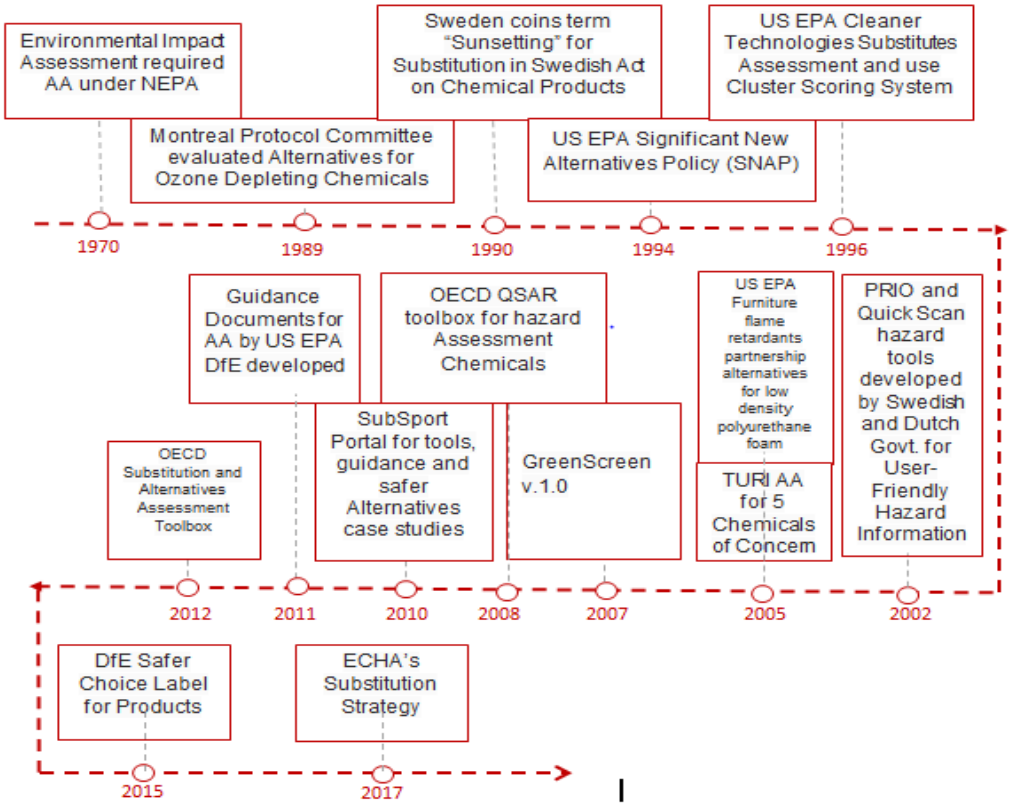

Figure 2.5. Major developmental achievements for the alternative assessment policy in United States and Europe through the years.

2.2.2 Components of CAA

The method or criteria by which assessment of the alternatives to a chemical (or material or product) of concern should be done, is the basic conundrum which every alternative assessment framework tries to solve.

Figure 2.6 enlists the nine alternative assessment frameworks (AAF) which were identified by OECD in their metareview. All the frameworks have a number of commonalities (OECD, 2013): (1) Intrinsic properties: hazard, fate, physico-chemical properties, (2) Functional use approach, (3) Technical feasibility, (4) Product performance. The attributes in each framework and the level of detail creates the variation amongst them. Table 2.3 shows a comparison of the different attributes in the nine AAFs identified by OECD (OECD, 2013).

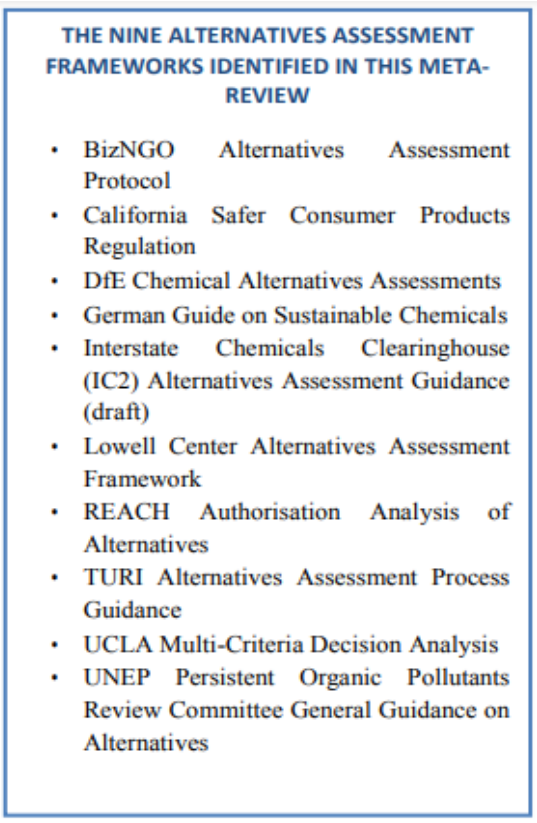

Figure 2.6. The nine AA frameworks identified in the OECD metareview (OECD, 2013).

Table 2.3. Comparison of the attributes in different alternative assessment frameworks (OECD, 2013).

Attributes / Framework	Use-Based Exposure/ Risk	Cost & Availability	Other Life-cycle Impacts	Social Impacts	Stakeholders	Includes Comparison of Materials and/or Processes
BizNGO Alternatives Assessment Protocol [35]	As needed	Yes	As needed	Not mentioned	Not mentioned	Yes
California Safer Consumer Products Regulation [36]	Yes	Yes	Yes	Yes	Yes	Yes
DfE Chemical Alternatives Assessment Steps [22]	As needed	As needed	As needed	As needed	Yes	Can be added
German Guide on Sustainable Chemicals [33]	Yes	Yes	Yes	Yes	Not mentioned	No
Interstate Chemicals Clearinghouse (IC2) Alternatives Assessment Guidance (draft) [30]	Yes	Yes	As needed	As needed	As needed	As needed
Lowell Center Alternatives Assessment Framework [37]	Not mentioned	Yes	Not mentioned	Yes	Yes	Yes
UNEP Persistent Organic Pollutants Review Committee General Guidance on Alternatives [38]	Yes	Yes	As needed	Yes	As needed	As needed
REACH Authorisation Analysis of Alternatives [7]	Yes	Yes	As needed	Yes (but in the Socio-Economic Analysis)	Yes	Yes
TURI Alternatives Assessment Process Guidance (also referred to as "Five Chemicals Guidance") [32]	Yes	Yes	Yes	Yes	Yes	Yes
UCLA Multi-Criteria Decision Analysis [39]	Yes	Yes	Yes	Not mentioned	Can be added	Can be added

Tickner et al. (2019b) combines the frameworks in the literature and relevant regulations to provide a general layout containing all the elements of an Alternative Assessment which can be seen in Table 2.4 below.

In this study, comparative hazard assessment was carried out. Additionaly, comparative exposure assessment and qualitative human exposure assessment were also carried out to help in decision making process. Economic feasibility and detailed technical performance assessment and other life cycle considerations were beyond the scope of this study. Components of the CAA methodology adopted in this study is presented in Figure 3.1. in Chapter 3 (Materials & Methods).

Table 2.4. Elements of alternative assessment (Tickner et al., 2019b).

	Component	What it involves
Assessment	Scoping, problem formulation	– Establishes the scope and plan for the assessment – Identifies stakeholders to engage and the decision rules that will guide the assessment – Gathers data on the chemical of concern, its function and application
	Identify alternatives	– Identifies alternatives to be considered based on the functional needs in the application currently being performed by the chemical of concern
	Hazard assessment	– Evaluates the human health and ecological hazards for each alternative compared to the chemical of concern
	Exposure characterization	– Evaluates the intrinsic exposure potential for each alternative on the basis of boundaries established in the problem formulation step
	Technical feasibility assessment	– Assesses the performance of alternatives against the requirements established during the problem formulation step
	Comparative economic feasibility assessment	– Assesses the economic feasibility of alternatives against the requirements established during the problem formulation step
	Other life cycle considerations	– Addresses additional factors critical for characterizing effects to human health and the environment beyond those included in the hazard and exposure assessment component to avoid risk trade-offs (e.g., energy, climate change effects, etc.)
	Decision making	– Identifies acceptable alternatives on the basis of information compiled in previous steps – Addresses situations in which no alternatives are currently viable by initiating research and development to generate new alternatives or improve existing options – Establishes an implementation plan
Action	*Adoption*	– Implementation of the safer, feasible alternative and identification of any potential trade-offs and continuous improvement opportunities
	Link to safer chemistry and/or technology research and development	– When no safer, feasible alternative is identified, research and development should be initiated

Source: Expands on the NRC (2014) framework by including additional details on technical, economic assessment and decision making that is inclusive of other AA frameworks, such as the Interstate Chemicals Clearinghouse Alternatives Assessment Guidance, V. 1.1 (IC2 2017).

Table 2.5 contains selected pertinent review papers and reports which have discussed in detail the CAA frameworks used. Whittaker& Heine (2013) comprehensively discussed the numerous tools used for chemical hazard assessment (CHA). The regulations which played a pivotal role in making CAA an important part of chemical policy development are elaborated in Tickner et al. (2013). In Jacobs et al. (2016), the differences and variations in the elements of the 20 AAFs are reviewed comprehensively and the methodological gaps in the frameworks are identified. In Tickner et al. (2019b), a blueprint is provided to conduct the CAA in an easier and correct way by reviewing existing frameworks and associated gaps. This paper provides an input on the priorities identified for the researchers and funding agency to exhaust the resources towards making AAFs refined and easier to conduct.

2.3 Chemical Hazard Assessment (CHA)

Canadian Centre of Occupational Health and safety defines hazard as the **'potential source of harm or adverse heath effect on a person or persons'**.

Table 2.5. Major review articles and reports on CAA.

Aim of the Study	Key Attributes	Reference
The report reviews 9 methods and tools of hazard assessment developed by government or private sector in US and Europe.	The report reviews the tools and methods of hazard assessment under the detailed evaluative display method in which decision making is done by the user and the screening method for quick information for the general public in which chemical hazard information and recommendations are provided by the tool for the user .	(Edwards & Rossi, 2005)
The aim of the paper was to describe the CAA that has been used by the USEPA.	The paper elaborated on the USEPA CAA steps in detail and where the stakeholders input is necessary to be part of the decision making process to make informed substitution.	(Lavoie et al., 2010b)
The aim was to focus on chemicals of concern in the consumer products and the tools, methods by which assessment is done for the chosen alternatives.	The study provides information regarding regulations on toxic chemicals and alternative assessment approaches in the regulations. Comparison of the different AAF and the tools that can be used to make informed substitutions.	(Kuczenski & Geyer, 2011)
A review of the landscape of the alternative assessment in practice.	Comparison of the elements of the different AAF's and the different tools used for hazard assessment.	(OECD, 2013)
Review and comparison of the CAA to evaluate human health and environmental impacts of potential alternatives.	Comprehensive review of the hazard assessment tools and the comparison of the criterion used in them.	(Whittaker & Heine, 2013)

Aim of the Study	Key Attributes	Reference
This review article aims to justify the adoption of AA as a tool for rational chemical policies for informed substitution.	Explains the rationale for informed substitution and the evolution of AA elements in government chemicals reduction policies.	(Tickner et al., 2013)
Reviews the USEPA (DfE) CAA in detail. The case studies carried out by USEPA are discussed.	Reviews the evolution of CAA in USEPA (DfE). The CAA methodology and case studies are discussed. The safer product labeling program is also elaborated upon.	(Davies et al., 2013)
Reviews the achievements of ChemSec (NGO) which is influencing safer substitutes in EU after the enforcement of REACH regulation in EU.	ChemSec has established the SIN List to inform people about the toxic chemicals in EU. SUBSPORT, a substitution support portal helps the EU companies in substituting the chemicals which have been deemed toxic for health and environment.	(Ligthart, 2013)
A 13 step framework to guide the decision makers for informed substitution for chemicals of concern.	A systematic elaboration of how the different elements in the assessment should be done and where are the data gaps in the knowledge of AAF steps.	(NRC, 2014)
A CAA blueprint structured around three steps: (1) Scope, (2) Assessment, (3) Selection & Implementation.	Specific tasks and tools are identified for each of these three steps.	(Geiser, 2015)

Aim of the Study	Key Attributes	Reference
Elaborates on how to take fundamental steps to improve CAA.	The challenges faced in the current methodology of substitution of hazardous chemicals and phasing out of the toxic chemicals. Recommendations are made to make the CAA fundamental and transparent and to overcome the challenges faced right now.	(Fantke et al., 2015)
This detailed review article aims to establish the differences and similarities in the different steps in the AAF's used and in doing so the research gaps for future prospective funding and collaborative research is identified.	Twenty frameworks were reviewed. The differences and similarities were identified and the methodological gaps to improve were elaborated for the different components of the AAF.	(Jacobs et al., 2016)
This review focuses on the small and medium size enterprises. The adoption of 6 alternative assessment frameworks which might cause regrettable substitution in the enterprises because of the different components in the AAFs.	Reviews the differences in the components of the six alternative assessment frameworks which may result in different outcomes. A special focus is also given to life cycle assessment in the paper.	(Oguzcan et al., 2017)
This report investigates the substitution principle currently adopted in the European Chemical Legislation and the challenges faced by the chemical manufacturers in the European market.	Regrettable substitutions were investigated as a result of regulatory processes and how grouping of chemicals can help in avoiding that. Recommendations are made via literature review and existing CAA frameworks adopted to make informed substitution in the future.	(Goldenman et al., 2017)

Aim of the Study	Key Attributes	Reference
The article aims to provide an assessment of the current field of CAA, the policies and practices that are being undertaken in the global landscape and the global lessons learned from the substitution cases.	Roles and actions for government agencies, private sector and academic community are defined. Policies regarding the CAA are reviewed and regrettable substitution examples are discussed. AAFs and tools used for the different assessment steps are reviewed and data gaps are mentioned.	(Tickner et al, 2019a)
Reviews the developments in methodology of AAF. The gaps are also identified in the methods and application of the AAF.	Comprehensive input was provided in the study to researchers, funding agencies, the authorities and market forces to prioritize the research areas that need strengthening for better and comprehensive alternative assessments.	(Tickner et al., 2019b)
The aim of the article is to demonstrate the nexus of CAA and green chemistry.	The article elaborated on the green chemistry principle of designing safer chemicals which will provide innovation driven developments and strengthen the CAA to adopt safer chemicals and avoid regrettable tradeoffs.	(Tickner et al, 2021)

CHA or comparative chemical hazard assessment is the method by which the intrinsic hazard properties of the chemicals are compared to make informed substitution (Heine & Franjevic, 2013). CHA philosophy is based on the risk paradigm where risk is a function of hazard and exposure and the aim behind the premise of green chemistry is that risks can be managed by the reduction of hazard. On the other hand exposure controls can always fail due to technical problems or the products can always be used in ways they were not supposed to (Heine & Franjevic, 2013). CHA is a paramount for any chemical assessment without it the chemical alternative assessment is incomplete and with the help of which the impact of the chemical's intrinsic properties on the human health and environment is known. The major goal of CHA is to gather complete information about the hazard endpoints of the chemical of concern and its alternatives and comparatively characterize it. CPA (2018) defines hazard endpoint as a specific type of adverse health outcome or physical property that can cause harm. There are 18 hazard endpoints in GreenScreen version 1.4 which include carcinogenicity, acute aquatic toxicity and flammability.

Use of CHA will advocate the selection of safer alternatives and an informed substitution which is a term coined by the USEPA can be made instead of transitioning to a chemical which might have intrinsic properties which are detrimental to the human health or environment from some other hazard endpoint. This systematic approach will guide the decision makers in justifying their decisions and will minimize subjectivity in hazard classification since a structured approach is used to assign hazards (Whittaker & Heine, 2013). Information for over 100 tools has been collected by the Toxics Use Reduction Institute (TURI) at the University of Massachusetts for comparative hazard assessment and a report has been compiled as detail guidance on the methods and tools which are practical and recommended to be followed (Edwards et al., 2011)

Amongst all the tools and methods for chemical hazard assessment, GreenScreen for Safer Chemicals was developed as the first fully transparent, freely and publicly

accessible method to assess, evaluate and compare chemicals based on inherent hazard (Heine & Franjevic, 2013).

2.3.1 Origins of GreenScreen for Safer Chemicals

Clean Production Action (CPA), a nonprofit research and education organization developed the GreenScreen with the aim of advancing green chemistry and sustainable management. The confluence of the two initiatives – the USEPA Design for Environment (DfE) Program and the initiatives of the state regulators seeking to ban certain flame retardants from being used in the USA gave rise to the emergence of GreenScreen version 1.0 (Heine & Franjevic, 2013). DfE hosts Alternatives Assessment Partnerships with relevant stakeholders to identify and evaluate alternatives to chemicals of concern. Pentabromodiphenyl ether (PentaBDE) used in polyurethane foam in furniture and tetrabromobisphenol-A (TBBPA) used in printed circuit boards were the first two partnerships (USEPA, 2005; 2008)

A comprehensive set of hazard endpoints were addressed by each DfE CAA like carcinogenicity, mutagenicity, reproductive and developmental toxicity, neurotoxicity, acute and chronic mammalian toxicity, sensitization, irritation/corrosion and environmental toxicity, persistence and bioaccumulation Based on measured data, estimation or expert judgment, a hazard classification was given for each endpoint (e.g. high, medium or low) for each chemical whether existing as a pure substance or in a mixture (USEPA, 2005). A hazard table was then compiled which is easy to understand, transparent and in a meaningful template containing the necessary knowledge about the chemical (USEPA, 2005).

The DfE comparative hazard information provided a general hazard score for each hazard endpoint, but did not recommend which alternative chemical to use or prefer. This created confusion amongst the participants (Heine & Franjevic, 2013). Around the same time, certain US States were planning to ban DecaBDE as a flame

retardant. CPA independently evaluated and compared DecaBDE and three alternatives for the inherent hazard properties. CPA did this by making modifications to the hazard assessment and classification approach of the DfE Alternative Assessment Partnerships. The results were published in a report which became the GreenScreen version 1.0 (Rossi & Heine, 2007).

Unlike the USEPA DfE assessment, the addition of benchmarks added a utility to the decision maker to make logical decisions to the hazard classifications. The benchmarks were developed based on the principles underlying regulations in the USA, Canada and Europe (Heine & Franjevic, 2013). For example, Benchmark 1 chemicals (Figure 3.2 in Chapter 3 Materials and Methods) are the chemicals of concern with attributes consistent with the definition of SVHC under REACH**.** Benchmark 2 and 3 are the chemicals with lesser degree of hazard than Benchmark 1, while Benchmark 4 chemicals are the preferred chemicals with inherently low or no hazard.

Table 2.6 contains the major review papers which have discussed CHA in detail as well as the major tools used for CHA. Table 2.6 also contains the studies which have used GreenScreen hazard assessment tool for hazard assessment. The studies are presented in chronological order in Table 2.6.

In the study by Gauthier et al., (2015), the tools for CHA were evaluated and given scores as per the criteria developed in the study. The evaluation criteria were developed using the NSF/GCI/ANSI (National Sanitation Foundation International/Green Chemistry Institute/American National Standards Institute) 355 Greener Chemicals and Processes Information standard and professional judgment.

Table 2.6. The major studies, reports and review articles for CHA and studies that have used GreenScreen hazard assessment tool.

Aim of the Study	Key Attributes	References
The report reviews 9 methods and tools of hazard assessment developed by government or private sector in US and Europe.	The report reviews the tools and methods of hazard assessment under the detailed evaluative display method in which decision making is done by the user and the screening method for quick information for the general public in which chemical hazard information and recommendations are provided by the tool for the user .	(Edwards & Rossi, 2005)
This report was prepared to assess the chemicals of concern in consumer products and the methods, tools and standards used to compare the alternatives.	The report discusses the regulatory frameworks that are pertinent to the alternative assessments. Special focus on the existing tools and methods to evaluate the hazardous impact of chemicals on human health and environment.	(Kuczenski & Geyer, 2011)
A compendium prepared by Lowell Center for Sustainable Production of methods and tools to examine the ecological and human health impacts of chemical based products.	The tools and methods are divided into 3 types: 1) Screen and identify hazardous chemicals, 2) To compare alternatives, 3) To identify preferred and already existing safe chemicals and products.	(Edwards et al., 2011)
Review and comparison of the chemical alternative assessments (CAA) to evaluate human health and environmental impacts of potential alternatives.	Comprehensive review of the hazard assessment tools and comparison of the criteria used among them.	(Whittaker & Heine, 2013)

Aim of the Study	Key Attributes	References
The aim of the study is to discuss the importance of CHA with a special focus on GreenScreen hazard assessment tool.	The study describes the origins of GreenScreen hazard assessment tool and elaborates the process of applying the method. It also describes the success stories as in the case of informed substitution by Hewlett-Packard, Staples, Royal DSM and the Wercs. The GreenScreen future developments are also underscored.	(Heine & Franjevic, 2013)
Hewlett-Packard's use of the GreenScreen hazard assessment tool in an integrated alternatives assessment protocol for safer chemicals	This study describes the protocol used by Hewlett Packard and how they have incorporated GreenScreen hazard assessment tool as the central figure of the hazard assessment whereas RSL screening as well as R Phrase screening against eco-label criteria are also done simultaneously.	(Wray, 2013)
The study focuses on the alternative assessment for toxic plasticizers in PVC and non-PVC wire and cable applications.	The study elaborates the chemical alternative assessment steps as well as the lessons learned by involving the multi-disciplinarian stakeholders. Initial hazard assessment screening of the alternatives was done with QCAT whereas detailed hazard assessment was done with GreenScreen hazard assessment tool.	(Morose & Becker, 2013)
The clarification and simplification of the decision making in chemical alternatives assessment by the single score system is elaborated in this research by accounting the uncertainty factor.	This study uses GreenScreen hazard assessment tool as a guide and develops a scoring system incorporating uncertainty quantitatively in the final score and successfully identifies tradeoffs between alternatives, showing finer resolution than GreenScreen Benchmark system.	(Faludi et al., 2016)

Aim of the Study	Key Attributes	References
This study uses a modified GreenScreen tool to conduct a screening-level comparative hazard assessment of conventional silver and two forms of nano-silver.	It was recommended in the study that existing GreenScreen hazard assessment tool can be used with minor adjustments for nanomaterials but more research is needed to identify data gaps for some hazard profiles.	(Sass et al., 2016)
CAA of different flame retardants – A case study including multi-walled carbon nanotubes as synergist.	In this study the REACH guidance, the criteria of USEPA Design for Environment (DfE) and the GreenScreen hazard assessment tools were used and compared for intrinsic hazard properties of the alternatives.	(Aschberger et al., 2017)
The study focuses on the data source selection role in CHA with organic photovoltaic case study.	The organic substances used in the photovoltaic are assessed with GreenScreen hazard assessment tool. The data gaps are being minimized by utilizing seven data sources which allow for complete assessments for the chemicals of concern in the study. Recommendation is made to have a standardized and comprehensive data source because the type of data source used has a direct effect on the CHA outcomes.	(He et al., 2019)
An approach for shared information infrastructure for CAA by the Data Commons—now a part of the related Pharos Project—which includes an online portal providing access to different information sources for the user.	The table of hazard assessment information for each chemical in the Pharos Project website is based on the GreenScreen assessment and it also includes the List Translator for easy screening of chemicals of concern because of their inclusion in different authoritative and screening lists.	(Kokai et al., 2020a)

Aim of the Study	Key Attributes	References
The study investigates three Green Design Tools to select safer materials for green building case study.	The GreenScreen for Safer Chemicals, Pharos, and the Health Product Declaration tools are examined for selecting safer chemicals for building materials.	(Kokai et al., 2020b)

Amongst the hazard assessment tools in which a user can modify the criteria, GreenSuite and GreenWercs scored high. However, neither of these hazard tools are free and annual registration charges are required for their use. Amongst the fixed criteria hazard assessment tools, following tools ranked high based on high score in the analysis;

- Design for the Environment (DfE) by USEPA,
- GreenScreen,
- iSUSTAIN

The presence of a Benchmark score gives an added advantage to GreenScreen when compared to USEPA DfE method. With Benchmark score, it is easier to compare the alternatives, whereas USEPA DfE comparative hazard method does not recommend which alternative is preferable or should be used. The iSUSTAIN green chemistry index is an internet based tool which had four levels of success and on free public access level only one process evaluation could be saved. The iSUSTAIN tool has ended its business and the domain (https://www.isustain.com/) is no longer functional.

In this study, GreenScreen hazard assessment tool was chosen because it was transparent, publicly accessible with no free and in the review by Gauthier et al. (2015), it was recommended amongst the high ranking fixed criteria based hazard assessment tools.

2.4 Exposure Assessment

The use of comparative exposure assessment as a distinct element of Alternative Assessment Framework (AAF) was recommended by the 2014 National Research Council's in the report 'A Framework to Guide Selection of Chemical Alternatives' (NRC, 2014). Previously, frameworks deliberated mostly on intrinsic hazard assessment and the exposure assessment was minimally considered (Jacobs et al., 2016).

The NRC (2014) framework recommended that the exposure assessment between alternatives should be compared with the help of four categories of attributes: physicochemical properties, use characteristics, environmental release, and fate & transport.

The NRC framework describes these as intrinsic exposure properties (NRC, 2014). Exposure assessment should be a distinct element of reason for choosing safer alternatives because considerations should be made that is **"focused on the intrinsic potential for exposure without physical or administrative controls"** (NRC, 2014). The NRC (2014) framework, states that exposure assessment is different from risk assessment. Exposure assessment can be done with existing exposure models or physicochemical properties as the aim is to understand the potential trade-offs and prioritizing of alternatives whereas risk assessments are done in greater detail for a single chemical at a time (NRC, 2014).Tickner et al (2019b) stressed on the importance of developing a comparative exposure evaluation method even for those chemicals which are not persistent, bioaccumulative and toxic, but are constantly released in the environment and are in constant contact with the humans and the environment. This will help selection amongst alternatives. Justification and recommendations can also be made in case of requirement of more detailed quantitative exposure evaluation (Tickner et al.,2019b).

2.4.1 Human Exposure

It is strongly recommended in NRC (2014) that exposure potential should be a part of comparative toxicity information because any routes, levels and patterns of exposure change should be catered for to get a complete image of the hazard assessment (NRC, 2014). The alternatives chosen for the chemical of concern are assumed to be causing the same exposure or substantially equivalent in most of the frameworks that is why concerns about reducing toxicity and hazard is the main focus (Jacobs et al., 2016). This approach can work if the alternatives used have the

same functional groups and physicochemical properties. As this is not true hence the assumption of same exposure doesn't hold true (NRC, 2014).

In NRC (2014) it is also stated that in most of the frameworks, the role of exposure is different for human and environment. The inherent properties of the chemicals shape the environmental component of the alternative assessment like degradation, bioaccumulation, persistence and other processes which help in the identification of the fate and transport of the chemical in the environment. However, the effect of these inherent exposure related properties are absent from the human exposure point of view (NRC, 2014).

The comparative human exposure assessment can be done with two approaches according to the NRC (2014), as illustrated in Figure 2.7.

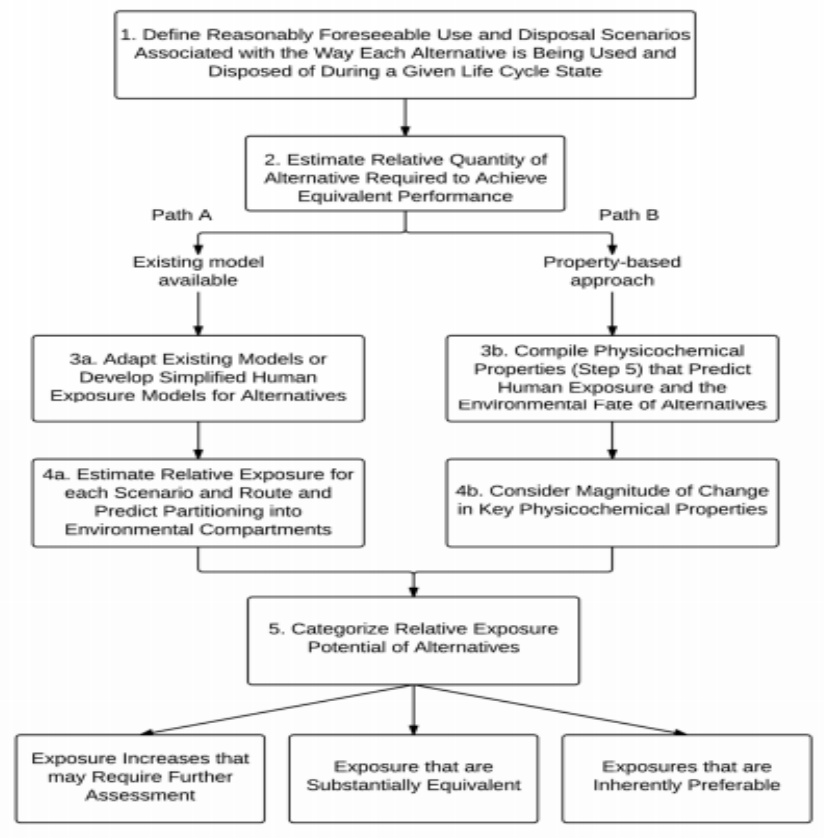

Figure 2.7. An approach to comparative exposure assessment recommended by (NRC, 2014).

Path A is the quantitative approach in which existing models or new models are developed for use and disposal scenarios for a product containing the chemical of concern and its alternatives. Arnold et al. (2017) demonstrated a method in which information by quantitative exposure is integrated with risk-based screening methodology for alternative assessment. Path B is property based qualitative approach where physical and chemical properties are compared to predict human exposure. The studies by Mason et al. (2018) and Greggs et al. (2019) have developed approaches for qualitative exposure assessment, which can be included in alternative assessments and can provide information to help prioritize alternatives.

2.4.2 Environmental Fate and Transport

Key role is played by the physicochemical properties of a chemical in determining the partitioning of the chemical into the environmental compartment(s). Properties like melting point, boiling point and vapor pressure predict the physical state of a chemical and indicate the environmental compartments into which the chemical will partition-air, water, soil, sediment and biota. For example, highly volatile chemicals escape to air from soil and water compartment whereas the chemicals which have more sorption capacity tend to remain in soil or sediment phase or move into biota respectively. Multimedia fate models (MFM) are used for risk assessment, management, optimization of testing and monitoring methods and chemical ranking studies. MFMs based on the principle of mass balance are useful in determining the transport and transformation mechanisms in several compartments. These models can be used to evaluate the relative environmental concentration in various media by the assumed emission rates. Overall persistence Pov and long range transport potential LRTP can also be obtained by the help of these models (Valsaraj & Thibodeaux, 2010).

In the past 25 years, major developments in the chemical property estimation, emission data, and environmental media addition, different temporal and spatial

scales have improved the MFM immensely. Still when it comes to polar and ionisable chemicals the partitioning coefficient prediction becomes a challenge and to adapt it to the real ecosystem and defining it as per the bioavailability term is still difficult to implement (Di Guardo et al., 2018).

The EQC Model

The EQC model is a fugacity based evaluative model. Donald Mackay in 1979 introduced the fugacity concept in environmental systems as a likely behavior indicator of a toxic compound (Mackay, 1979). The general characteristics of a chemicals behavior such as the likely partitioning compartment, the primary loss mechanism and the persistence of the chemical are evaluated by the EQC model. That is why this model can be an important screening level tool for the authorities to decide whether a chemical of concern should be further evaluated in detail. It is an evaluative model and it does not simulate the fate and transport of a chemical in a real environment (Mackay, 1996a).

EQC model was used by Palm et al. (2002) to investigate the fate and research needs of PBDEs by utilizing a six stage methodology. In the study, the EQC model was used to compare the PBDEs fate with the experimental data inputs and the EPI Suite predicted inputs. The main transport mechanism and the effect of mode of entry were evaluated on the mass distribution between air and water phase for methyl tert-butyl ether (Achten et al., 2002). EQC models have also been adopted as a physicochemical review tools as well as the impact of the different emission rates and try to compare it with the monitoring studies and data (Cousins et al., 2002).

The multimedia fate evaluation is done by Level I, Level II and Level III in the EQC model in a generic environment with air, water, soil and sediment as the compartments with predetermined dimensions (Mackay, 1996b). Level I is evaluation under steady state and equilibrium without degradation, degradation and advection are included in Level II and in Level III intermedia transfer is incorporated under non-equilibrium and steady state conditions (Mackay, 1996b).

Figure 2.8. shows the block diagram depicting the levels and type of chemicals evaluated by the EQC model.

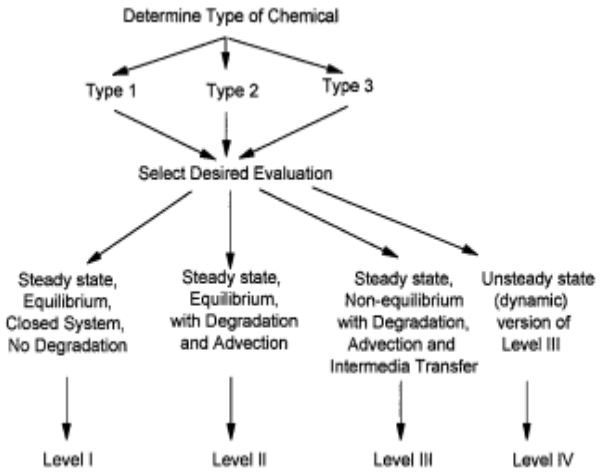

Figure 2.8. Block diagram indicating the different simulations possible with the EQC program (Mackay, 1996a).

Table 2.7 contains the qualitative and quantitative exposure assessment studies. It also contains the major review papers which discuss in detail the different exposure assessment methods which are being used in the different alternative assessments.

Table 2.7. Exposure characterization studies in the literature.

Aim of the Study	Key Attributes	Comments	References
A history of the multimedia fate models. How they are used? Why they are used? And how have they become a part of the assessment of the fate and transport of the chemicals as well as exposure to the humans.	Multimedia contaminant fate and multi-pathway exposure models are differentiated and their use is explained.	The fugacity based models are used for the fate and transport of the chemical in the environment but for human exposure multi-pathway exposure models like CALTOX are used which links the environmental media to the exposure media in the model to assess the effect on human.	(McKone & MacLeod, 2003)
A 13 step framework to guide the decision makers for informed substitution for chemicals of concern.	A systematic elaboration of how the different elements in the assessment should be done and where are the data gaps in the knowledge of AAF steps.	Fugacity based models are recommended to be used for fate and transport of the chemical. Exposure of the humans from the environmental compartment in multimedia fate models are compiled in list form. Environmental exposure assessment is also discussed and fugacity models are enlisted.	(NRC, 2014)

Aim of the Study	Key Attributes	Comments	References
The study reviews the differences and similarities in the different steps in the AAF are used.	Twenty frameworks were reviewed and in doing so the research gaps for future prospective funding and collaborative research is identified.	Different methods of exposure assessment done in different frameworks. Data requirement in different frameworks are shown in a table for easy comprehension.	(Jacobs et al., 2016)
This study aims to design a quantitative exposure assessment in which the exposure pathways are evaluated along a product life cycle by a flexible mass balance based on near field, far field and human intake compartments.	The study develops a user friendly framework for human exposure scenarios in which near field, far field and human intake compartments are coupled to understand the individual contribution of each compartment on the overall exposure to humans.	Quantitative exposure assessment. This is a model which seems very appropriate for human exposure because it compartmentalizes the near field and far field environment and assesses the exposure to humans but it is based on dynamic phenomenon. Two examples are also given in the paper.	(Fantke et al, 2016)

Aim of the Study	Key Attributes	Comments	References
This article proposes to incorporate quantitative based exposure study steps to improve alternatives assessment evaluation and decision making.	The criteria, methods and considerations that need to be incorporated to exposure models are explained with case studies. Human health scenario in one case study and the environmental impact in the second case study	Quantitative based exposure study. Case studies focusing on human health and environmental impact were separately discussed.	(Arnold et al., 2017)
A tiered approach for screening ingredients of a product by incorporating exposure as well as hazard information.	Qualitative approach for human exposure assessment as a screening tool with publically available data.	A detailed assessment can be recommended for such chemicals with authority which fail the screening tier.	(Mason et al., 2018)
In this article the data gaps and the methods and tools that need to be adopted in the 5 critical areas including the comparative exposure characterization in the AAFs are elaborated with input from over 40 experts.	Comprehensive input was provided in the study to researchers, funding agencies, and practitioners to outline the priorities for research in the field of Alternative assessment.	The qualitative and quantitative based exposure studies are referenced here.	(Tickner et al., 2019a)

Aim of the Study	Key Attributes	Comments	References
This paper aims to incorporate an approach for exposure assessment module into the alternatives assessment decision making process to make informed substitution for the chemical of concern.	Qualitative exposure evaluation approach for chemical ingredient and product related exposure with focus on relevance of the data adopted and the quality of data obtained. The case studies and supplementary information provide the general outline of the method adopted to make it easier to follow for the user.	A stepwise qualitative approach for exposure characterization and has two case studies for understanding. It is from the same 'Advances in Methods and Practice of Alternatives Assessment' series and the input is provided by all the stakeholders including the major researchers in the field of alternatives assessment.	(Greggs et al., 2019)

CHAPTER 3

3 MATERIALS AND METHODS

This study aims to conduct a chemical alternatives assessment (CAA) of phthalates (DEHP, DBP, BBP), HBCD and DecaBDE which are known to be used in Turkey and also restricted or need authorization under the REACH regulation in Europe. In order to select the chemicals to be used in this study, first of all, the Turkish chemicals inventory was downloaded from turkreach.com.tr. Then it was filtered and a list was compiled of the chemicals which are in the REACH Restriction and Authorization Lists. Out of this list, the aforementioned chemicals were selected and potential alternatives for each were identified, taking into account relevant commercial uses. After that, CHA was conducted using GreenScreen hazard assessment tool. Secondly, environmental exposure assessment (EEA) with EQC model for fate and transport of the chemical in the environment was conducted. Lastly, a comparative qualitative human exposure assessment (QHEA) was carried out. The study is finalized with recommendations for informed decision making regarding substitution of the chemicals of concern with assessed alternatives. The outline of the methodology adopted in this study is shown in Figure 3.1.

3.1 Selection of Chemicals for the Study

In this study, five chemicals were selected, three of them are phthalates, which are used as plasticizers and two of them are flame retardants. The usage and the current status of the target chemicals will be discussed in detail in Chapter 4 (Results and Discussion). The selected target chemicals and the proposed alternatives are shown in Table 3.1.

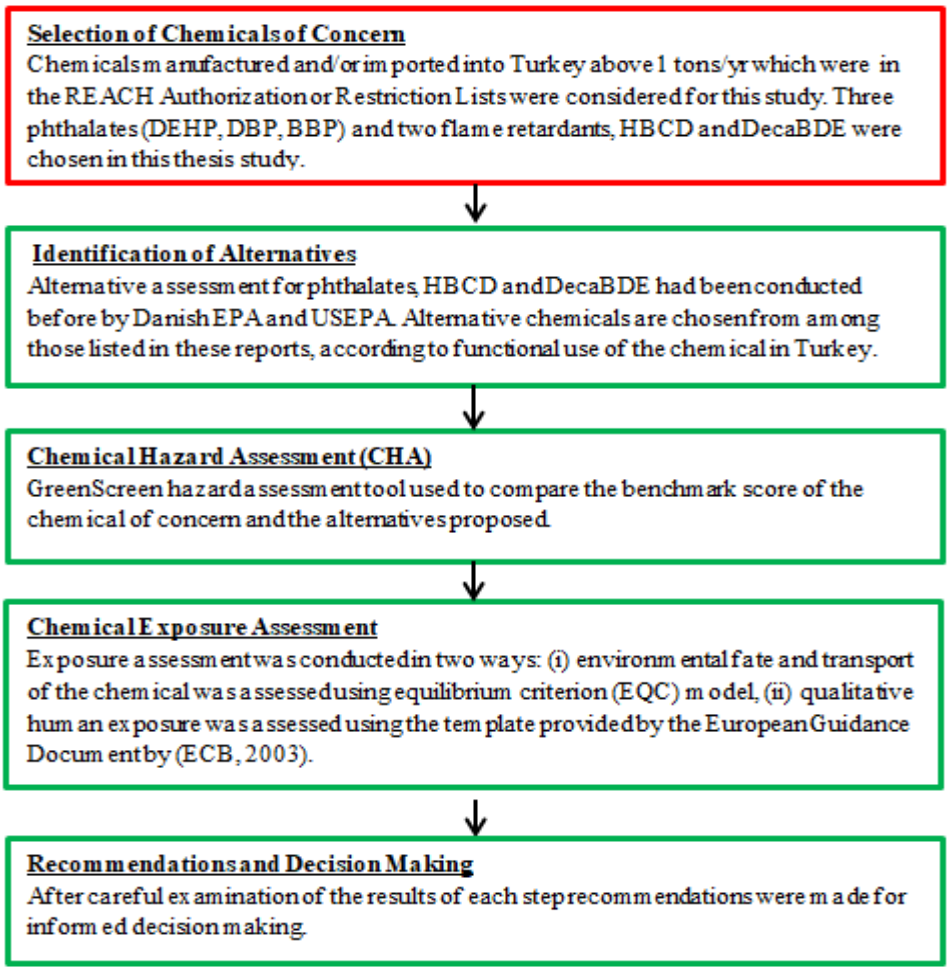

Figure 3.1. CAA methodology adopted in this study.

3.2 GreenScreen Hazard Assessment Tool

The GreenScreen Hazard Assessment v1.4 (January 2018) method downloaded from https://www.greenscreenchemicals.org/learn/guidance-and-method-documents-downloads was used in this study.

3.2.1 Data Collection for Hazard End Points

In this study, the primary source of experimental (measured) data was the alternative chemical assessment reports from authoritative sources like USEPA(DecaBDE, HBCD) and Danish EPA (phthalates).

Table 3.1. Selected target chemicals and their proposed alternatives.

Target Chemicals	Proposed Alternatives
Phthalates Bis (2-ethylhexyl) phthalate (DEHP) Dibutyl phthalate (DBP) Benzyl butyl phthalate (BBP)	• Sulfonic acids, C10-C21-alkane, phenylester(ASE), • Acetyl tributyl citrate (ATBC), • Glycerides, castor-oil mono-hydrogenated, acetates (COMGHA), • Di-ethylhexylterephthalate (DEHT), • Di-isononyl adipate (DINA), • Di-isononylcyclohexane-1,2-Dicarboxylate (DINCH).
1,2,5,6,9,10-Hexabromocyclododecane, Hexabromocyclododecane (HBCD)	• Tetrabromobisphenol A (TBBPA)-bis brominated ether derivative, • TBBPA bis(2,3-dibromopropyl) ether, • Butadiene styrene brominated copolymer
Decabromodiphenyl ether, bis(pentabromophenyl) ether (DecaBDE)	• Aluminum diethylphosphinate, • Ammonium polyphosphate, • Magnesium hydroxide, • Polyphosphonate.

In addition, in order to incorporate the most recent data, ECHA registration dossiers for the chemicals were explored to check for missing hazard endpoint information or any new reliable data that has been included which could change the hazard scores of the previously conducted alternative assessments (i.e., by USEPA or Danish EPA).

The hazard end point data, source of data and the confidence in the data is comprehensively described in Annex B. If a chemical evaluated in this study was present in any authoritative or screening list for a specific hazard endpoint, this information was recorded in Annex B. Each list is briefly described below:

Authoritative Lists: The government regulatory processes by recognized experts identify the chemicals for associated hazards that's why the confidence in the data and the score is high. Some examples for this type of lists are: US NIH (National

Institute of Health) - Report on Carcinogens is an Authoritative A list for carcinogenicity hazard endpoint. Similarly, IARC (International Agency for Research on Cancer) is also an Authoritative A list for carcinogenicity hazard end point.

Screening Lists: The confidence in the score is low because a screening list score is developed using less comprehensive review or compiled by an organization which is not considered authoritative, or by using estimated data or a score is provided to identify the chemical to further review the chemical for hazard endpoint and score e.g. GHS Japan for all the hazard endpoints is termed as screening A list.

A and B Sublists: There are also Authoritative A or Authoritative B sublists. Similarly there are Screening A and Screening B sublists. Sublists A include data which are clear and focused hazard levels e.g., one hazard endpoint with only one possible hazard score (e.g., a US CDC occupational carcinogen can only lead to the score "H-High" for Carcinogenicity), Sublist B includes data which cannot be in a single hazard endpoint or assigned a single hazard score. Below the first case shows a chemical is in the B sublist and the proposed score is in range for Moderate to Very High. In the second case, two hazard endpoints are combined and not separately scored:

- The neurotoxic chemicals are in the G&L list but the potency levels are not identified that is why a range of score can be assigned from Moderate to Very High.
- More than one hazard endpoint might be combined to assign a score. For example GHS classification combines reproductive and development toxicity into a single hazard endpoint and does not separate them.

Pharos online tool (pharosproject.net), a project of Healthy Building Network was used to check whether a chemical was on any GreenScreen specified list for any hazard endpoints. By entering the CAS number of a chemical in the search bar, the presence of the chemical on the GreenScreen specified lists can be seen. All target and alternative chemicals evaluated were checked for their presence on the Authoritative and Screening lists and the information was compiled for each chemical (please see Annex B).

In case of "professional judgment" or "estimated data using structural activity relationship (SAR) methods", the guidance in the alternative assessment reports of USEPA, Danish EPA or the ECHA registration dossiers was followed:

- In case of a chemical having missing information for a specific hazard endpoint, the studies conducted for the structural analog (similar chemical structure) were used to assign a hazard score for the chemical, as per professional judgment in the USEPA reports, Danish EPA or the ECHA registration dossiers. For example, the reproductive toxicity data of DINA (one of the alternative chemicals proposed instead of phthalates) was not available. The score was assigned based on the structural analog bis(2-ethylhexyl) adipate, also known as DEHA, in the Danish EPA study on phthalate alternatives (Nielsen & Larsen, 2014).
- Scores were also provided by professional judgment based on structural considerations e.g. for chemicals with MW>1000 'L-low' score was assigned for bioaccumulation potential for butadiene styrene brominated copolymer in (USEPA, 2014a).

3.2.2 Hazard Classification/Scoring

The classification of the hazard level for the chemical of concern was evaluated with the GreenScreen Chemical Hazard Criteria from the GreenScreen Guidance document version 1.4 (CPA, 2018). This guidance document was downloaded from https://www.greenscreenchemicals.org/learn/guidance-and-method-documents-downloads (Access Date: 4th August, 2020).

Table 3.2 indicates the GreenScreen v1.4 criteria for Group I human hazard endpoints. Table 3.3 indicates the GreenScreen v1.4 criteria for Group II and II* human hazard endpoints. Table 3.4 indicates the GreenScreen v1.4 criteria for single hazard endpoints.

The hazards which cause chronic or life threatening effects caused at low doses and are transferable between generations. These hazard endpoints are of high concern. National and international criteria are developed for them to identify the chemicals with these hazardous properties. These hazard endpoints are under Group I Human Health endpoints.

Group II and II* can be mitigated. Group II are single exposure with (vH, H, M and L score), whereas Group II* contain hazard endpoints which are based on repeat exposure with (H, M and L score). The hazard data was narrowed down from different sources but the score was alotted as per the GreenScreen criteria scores (Table 3.2, 3.3 and 3.4 below).

Table 3.2. GreenScreen criteria (Group I Human).

Score / **Hazard Endpoint**	**High (H)**	**Moderate (M)**	**Low (L)**
Carcinogenicity	GHS Category 1A (Known) or 1B (Presumed) for any route of exposure	GHS Category 2 (Suspected) for any route of exposure or limited or marginal evidence of carcinogenicity in animals	Adequate data available, and negative studies, no structural alerts, and GHS not classified.
Mutagenicity/Genotoxicity	GHS Category 1A (Known) or 1B (Presumed) for any route of exposure. AND Evidence of mutagenicity supported by positive results in in vitro AND in vivo somatic cells and/or germ cells of humans or animals.	GHS Category 2 (Suspected) for any route of exposure or limited or marginal evidence in animals.	Adequate data available and negative studies for chromosomal aberrations and gene mutations, no structural alerts, and GHS not classified.
Reproductive Toxicity **NOAEL (mg/kg bw/day)** **LOAEL (mg/kg bw/day)**	GHS Category 1A (Known) or 1B (Presumed) for any route of exposure NOAEL≤50 LOAEL≤250	GHS Category 2 (Suspected) for any route of exposure or limited or marginal evidence in animals NOAEL>50-1000 LOAEL >250-1000	Adequate data available, and negative studies, no structural alerts, and GHS not classified. NOAEL >1000 LOAEL >1000
Development Toxicity **NOAEL (mg/kg bw/day)** **LOAEL (mg/kg bw/day)**	GHS Category 1A (Known) or 1B (Presumed) for any route of exposure NOAEL≤50 LOAEL≤250	GHS Category 2 (Suspected) for any route of exposure or limited or marginal evidence in animals NOAEL>50-1000 LOAEL >250-1000	Adequate data available, and negative studies, no structural alerts, and GHS not classified. NOAEL >1000 LOAEL >1000
Endocrine Activity	Evidence of endocrine activity and related human health effect.	Evidence of endocrine activity.	Adequate data available and negative studies, no structural alerts.

Table 3.3. GreenScreen criteria (Group II and Group II* Human).

Score / Hazard Endpoint	Very High (VH)	High (H)	Moderate (M)	Low (L)
Acute Mammalian Toxicity **Oral (mg/kg)** **Dermal (mg/kg)** **Inhalation (mg/L)**	Oral LD50 ≤50 Dermal LD50 ≤200 Inhalation LC50 ≤2 Inhalation (Dust/Mist/Fumes) ≤0.5	>50 – 300 >200 – 1000 >2-10 >0.5 – 1.0	>300 – 2000 >1000 – 2000 >10-20 >1 – 5	>2000 >2000 >20 >5
Systemic Toxicity/Organ Effects (Single Exposure) **(NOAEL Oral and Dermal mg/kg bw)** **(Inhalation mg/L)**	Oral LD50 ≤300 Dermal LD50 ≤1000 Inhalation (Gas/Vapor)LC50 ≤10 Inhalation (Dust/Mist/Fumes)≤1	>300 – 2000 >1000 – 2000 >10-20 >1.0 – 5.0	Not Applicable	>2000 >2000 >20 >5
Systemic Toxicity/Organ Effects (Repeat Exposure *) **(NOAEL Oral and Dermal mg/kg bw/day)** **(Inhalation mg/L)**	Not Applicable	Oral LD50 ≤10 Dermal LD50 ≤20 Inhalation (Gas/Vapor)LC50 (mg/L) ≤0.2 Inhalation (Dust/Mist/Fumes) ≤0.02	>10 – 100 >20 – 200 >0.2-1.0 >0.02 – 0.2	>100 >200 >1.0 > 0.2
Neurotoxicity (Single Exposure) **(NOAEL Oral and Dermal mg/kg bw)** **(Inhalation mg/L)**	Oral LD50 ≤300 Dermal LD50 ≤1000 Inhalation (Gas/Vapor)LC50 (mg/L) ≤10 Inhalation (Dust/Mist/Fumes) ≤1	>300 – 2000 >1000 – 2000 >10-20 >1.0 – 5.0	Not Applicable	>2000 >2000 >20 >5
Neurotoxicity (Repeat Exposure *) **(NOAEL Oral and Dermal mg/kg bw/day)** **(Inhalation mg/L)**	Not Applicable	Oral LD50(mg/kg) ≤10 Dermal LD50 (mg/kg) ≤20 Inhalation (Gas/Vapor)LC50 (mg/L) ≤0.2 Inhalation (Dust/Mist/Fumes) ≤0.02	>10 – 100 >20 – 200 >0.2-1.0 >0.02 – 0.2	>100 >200 >1.0 > 0.2
Skin Sensitization*	Not Applicable	GHS Category 1A (high frequency of occurrence)	GHS Category 1B (low to moderate frequency of occurrence)	• Adequate data available and negative studies; and • GHS not classified
Respiratory Sensitization*	Not Applicable	GHS Category 1A (high frequency of occurrence)	GHS Category 1B (low to moderate frequency of occurrence)	• Adequate data available and negative studies; and • GHS not classified
Skin Irritation	GHS Category 1 (Corrosive)	GHS Category 2 (Irritant)	GHS Category 3 (Mild irritant)	Adequate data available and negative studies; and • GHS not classified
Eye Irritation	GHS Category 1 (Irreversible)	GHS Category 2A (Irritating)	GHS Category 2B (Mildly irritating)	• Adequate data available and negative studies; and • GHS not classified

Table 3.4. GreenScreen criteria (Single Hazard endpoints).

Score / Hazard Endpoint	Very High (VH)	High (H)	Moderate (M)	Low (L)	Very Low (VL)
Acute Aquatic Toxicity (LC50/EC50)(mg/L)	≤1	>1 to 10	> 10 to 100	>100	Not applicable
Chronic Aquatic Toxicity (mg/L)	≤0.1	>0.1-1	> 1-10	>10	Not applicable
Persistence **Soil or Sediment (1/2 Life Days)** **Water (1/2 Life Days)** **Air (1/2 Life Days)**	>180 or recalcitrant. >60 or recalcitrant >5 or recalcitrant	>60-180 >40-60 >2-5	>16-60 >16-40	<16 or GHS 'Rapid Degradability' <16 or GHS 'Rapid Degradability' <2	Meets 10-day window in "Ready Biodegradation Test" Meets 10-day window in "Ready Biodegradation Test"
Bioaccumulation Potential (BAF/BCF) **Log Kow** **Monitoring Data**	> 5000 >5.0	> 1000 to 5000 >4.5-5 Evidence	> 500 to 1000 >4.0-4.5 Suggestive Evidence	> 100 to 500 -	≤ 100 ≤ 4

Apart from the hazard endpoints mentioned above, two more hazard endpoints are included which are:

> Reactivity: A chemical is scored for reactivity based on explosivity, self-reactivity and oxidation potential properties. The whole table and the criteria used to assign score is elaborated in detail in (CPA, 2018).
>
> Flammability: A chemical is scored for flammability based on flammable properties as in gas liquid or solid state. The whole table and the criteria used to assign score is elaborated in detail in (CPA, 2018).

The GreenScreen guidance document contains the criteria as well as all the other authoritative and screening lists and guidance in detail for all the hazard endpoints (CPA, 2018). Score was assigned for each hazard end point as per GreenScreen criteria mentioned in the tables above (CPA, 2018) for chemical of concern and the proposed alternatives in a comparative table format (Table 3.5).

3.2.3 Assigning Confidence Level for each Hazard Endpoint

Data sources, data quality and expert judgment were considered while assigning the level of confidence on the endpoint data. Rationale is provided below for the assigned level of confidence for each hazard point:

Authoritative A lists are preferred over Authoritative B or Screening A or B lists. When lists conflict, the most conservative of the authoritative results were used (CPA, 2018), such that:

1. Valid measured data were generally preferred over hazard lists or estimated values (e.g., suitable analogs or QSAR models). For example HBCD is in the TEDX-Potential Endocrine Disruptor (Sceening B List) with a score of (*H-M).* In the USEPA report, HBCD was termed as an endocrine disruptor and showed evidence of adverse effects on thyroid and related human health effect. Thus in this study, the measured data of USEPA report held more weight than Screening B List TEDX-Potential Endocrine Disruption score and a high confidence score of 'H-High' was assigned (CPA, 2018).
2. Authoritative A lists were preferred over Authoritative B or Screening A or B lists. For example, in the DEHP GreenScreen Assessment for carcinogenicity, DEHP is in Authoritative A list (CA EPA Prop 65) as a carcinogen which makes its score as **H** with higher confidence**.** However, it is also included in the Screening A list (GHS Japan), as a category 2 carcinogen, which makes its score *M* with lower confidence. Authoritative A lists are preferred, so the score of DEHP in the carcinogenicity hazard endpoint was marked as **H,** indicating High-with high confidence).

Note that, in USEPA assessment reports and GreenScreen template, bold capital letters were used to indicate hazard levels of high confidence (e.g. **H** for High). *Italic* capital letters were used to indicate hazard level of low confidence (e.g. *H* for *High*).

3.2.4 Handling Missing Information

In CHA, ideally all the hazard endpoints should be covered with the available data but in reality insufficient data is always a problem. So user is faced with the task of finding information to be able to assign a score to all hazard endpoints, or if there

really is no recent or other information, then assign “DG – Data Gap”. In this study, if a chemical was assigned a data gap for a specific hazard end point in the USEPA and Danish EPA alternative assessments reports, then ECHA registration dossiers were consulted to explore whether new information regarding the hazard endpoint had been included or not. If no new information could be obtained, then for that particular end point a hazard score cannot be assigned, instead “DG-Data Gap” was used.

3.2.5 Documenting Detailed Hazard Levels

Annex B attached at the end of the study contains the supporting documents and the reason for the hazard score. The supporting document contains:

1) Hazard score/level
2) Rationale for hazard level
3) Confidence level
4) Rationale for confidence level

3.2.6 Filling the GreenScreen Hazard Summary Table

GreenScreen Hazard summary table for target chemical and its alternatives is shown in Table 3.5.

Some differences between USEPA Hazard Assessment template and GreenScreen template exists, which are listed below:

- Endocrine activity in U.S EPA DfE Alternative Assessment is not designated a Hazard Score. A qualitative assessment of available data was prepared in the USEPA report.
- USEPA DfE Alternative Assessment template does not use Single dose for systemic toxicity as a separate hazard endpoint, it uses Specific Target Organ Toxicity Repeated Exposure (STOT-RE) (USEPA, 2011), while GreenScreen has separate hazard endpoints for single and repeated dose. The data of single dose systemic toxicity is gotten from necropsy or gross pathology studies from acute mammalian toxicity studies. For systemic toxicity repeat dose, necropsy or gross pathology studies from chronic

exposure studies oral, dermal and inhalation routes are used to assign hazard score.

- USEPA DfE Alternative Assessment template does not use Single dose for neurotoxicity as a separate hazard endpoint, it uses Specific Target Organ Toxicity Repeated Exposure (STOT-RE) (USEPA, 2011), while GreenScreen has separate hazard endpoints for single and repeated dose. The data of single dose neurotoxicity is gotten from cage behavior and neurofunction studies from acute mammalian toxicity studies. For neurotoxicity repeat dose, cage behavior and neurofunction studies from chronic exposure studies oral, dermal and inhalation routes are used to assign hazard score.
- USEPA DfE Alternative Assessment template doesn't have reactivity and flammability hazard point.
- In case of Systemic toxicity/ Organ effects and neurotoxicity endpoints, results for repeated exposure are mandatory otherwise a data gap was assigned. If single exposure data was missing but repeated exposure data was provided, then as per GreenScreen criteria, the single exposure sub-endpoint cell was shaded the same color as the repeat dose score and it did not result in a data gap, instead a '- ' is used. (CPA, 2018).

A general template of the GreenScreen hazard summary table (Table 3.5) for target chemical and proposed alternatives is shown below.

3.2.7 Preliminary Benchmark Score

The preliminary benchmark criteria for organic and inorganic chemicals are found in Annexes 3 and 4 of the GreenScreen guidance document v1.4, respectively (CPA, 2018). Figure 3.2 and 3.3 show the four Benchmark levels for organic and inorganic chemicals, respectively. For each benchmark level there are criterion statements. While analyzing a chemical, if any of the criterion statements is **'TRUE'** then that Benchmark score was assigned to the chemical in the preliminary stage. This score is assigned according to preset criteria given in section 3.2.8 (CPA, 2018). If the chemical satisfies criterion statement for Benchmark 1, then that score is assigned, if not, the evaluator proceeds to Benchmark 2. Similarly, if all the criterion statement of Benchmark 2 for the chemical being evaluated is false, then evaluator proceeds to Benchmark 3, etc.

Table 3.5. Sample GreenScreen hazard summary table for target chemical and alternatives.

	GreenScreen Hazard Summary Table for Target Chemical and Alternatives																				
	Group I Human					Group II and II* Human								Ecotox		Fate		Physical		
CHEMICALS	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability	BENCHMARK SCORE
							single	repeat*	single	repeat*	*	*									
CHEMICAL OF CONCERN (Target Chemical)																					
Target Chemical	*M*	**L**	***H***	**H** [a]	**H**	**L**	*M*	**M**	**DG**	*M*	**L**	**DG**	**L**	**L**	**VH**	**VH**	**H** [a]	**VH** [a]	*L*	*L*	**BM-1a**
ALTERNATIVES																					
Alternative A	*M* [c]	*M*	*M*	*M*	*M*	*L*	-	*M*	-	*L*	*L*	**DG**	*L*	*L*	*L*	*L*	*H*	*H*	*L*	*L*	**BM-2a**
Alternative B	*L*	**L**	**L**	**L**	*L*	**L**	-	**L**	-	*L*	**L**	**DG**	**L**	**M** [b]	*L*	*L*	*VH*	*L*	*L*	*L*	**BM-2c**

Note to Table:

[a, b, c] The superscripts with the hazard score indicates the reference for the hazard score such that **a**: Authoritative A; **b**: Screening A; **c**: ECHA registration dossier of the specific chemical.

Dash '-' used in case of missing single or repeat Systemic toxicity or neurotoxicty hazard end point. Missing Single exposure when repeat exposure is available is not considered a Data Gap on its own.

- E.g. **H**[a] (a: Authoritative A) which means the chemical was present in the authoritative A list for the specific hazard endpoint. Similarly superscripts were provided and the references were mentioned as a footnote.
- For a hazard score without any superscript, it means that the source of the hazard score is the USEPAreport for HBCD alternatives (2014a),USEPAreport for DecaBDE alternatives (2014b) or Danish EPA report for phthalate alternatives (Nielsen & Larsen, 2014).

Bold score indicates high confidence data while *italic* score indicates low confidence data.

Group II Human Health endpoints have four hazard scores (i.e., VH, H, M, and L) and Group II* Human Health endpoints have three hazard scores (i.e., H, M, and L), and are based on single exposures instead of repeated exposures.

Persistence and Bioaccumulation have five hazard scores (i.e., VH, H, M, L and VL).

The legend for the scores is indicated below

	Hazard Score	Acronym Used
	Very High	VH
	High	H
	Moderate	M
	Low	L
	Very Low	VL
	Data Gap	DG

Inorganic chemicals are recalcitrant in nature, that is why persistence for inorganic chemicals is not necessarily considered a negative characteristic-especially for minerals and metal oxides. Due to this reason, benchmark criteria for inorganic chemicals (Figure 3.3) are different from benchmark criteria for organic chemicals (Figure 3.2) (CPA, 2018). For inorganic chemicals, persistence is only considered in combination with chronic hazards (CPA, 2018). Inorganic chemicals which are assigned 'L-low' hazard score for all the hazard endpoints except persistence are Benchmark-4 (Preferred-Safer Chemicals). Figure 3.2 and Figure 3.3 show the Benchmark criteria for organic and inorganic chemicals respectively.

3.2.8 Final Benchmark Score

The final benchmark score was assigned to a chemical after conducting a data gap analysis as per Annex 5 of the GreenScreen guidance document v1.4 (CPA, 2018). If a chemical is determined to be Benchmark-3 due to preliminary benchmark score, but it didn't fulfill the data requirement for Benchmark-3, then it is assigned a final benchmark score of Benchmark-2 (a worse score) and is written with a subscript DG (Benchmark-2 DG). The data requirements for Benchmark-1, Benchmark-2 and Benchmark-3 are specified in Figures 3.4, 3.5 and 3.6, respectively (CPA, 2018).

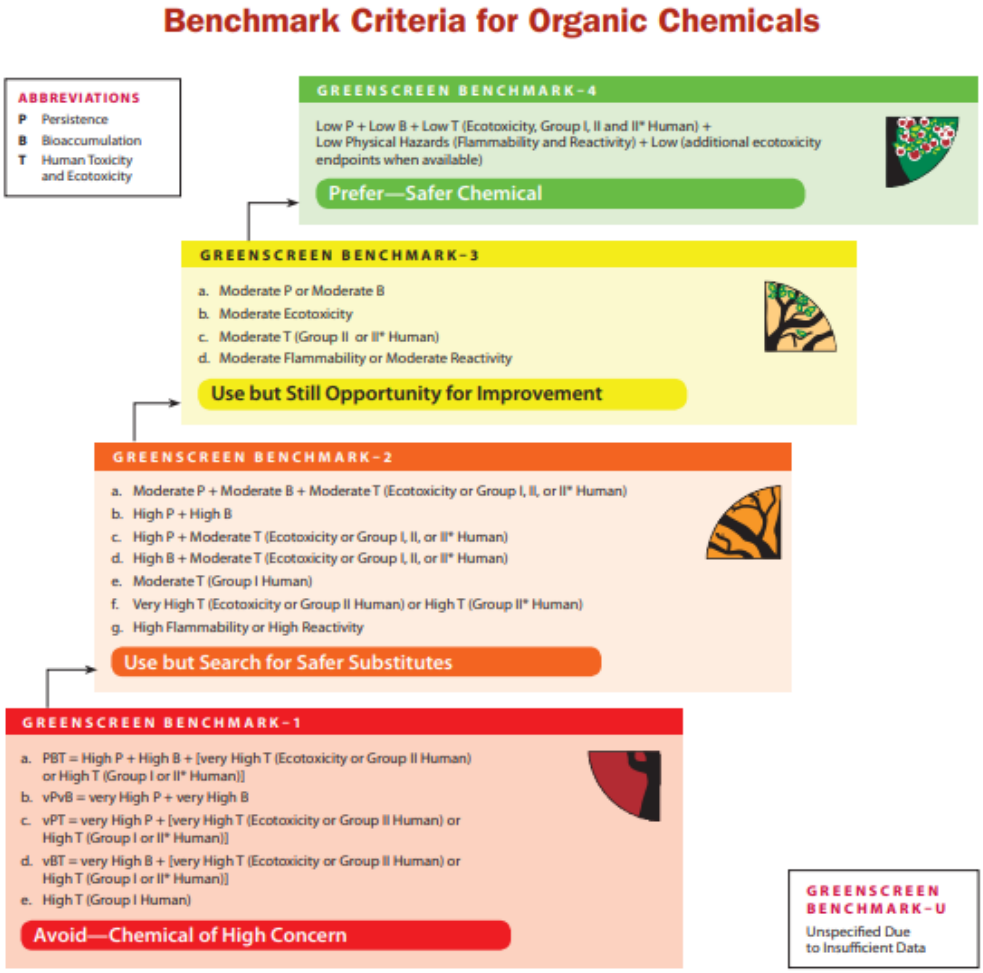

Figure 3.2. GreenScreen benchmark criteria for organic chemicals (CPA, 2018).

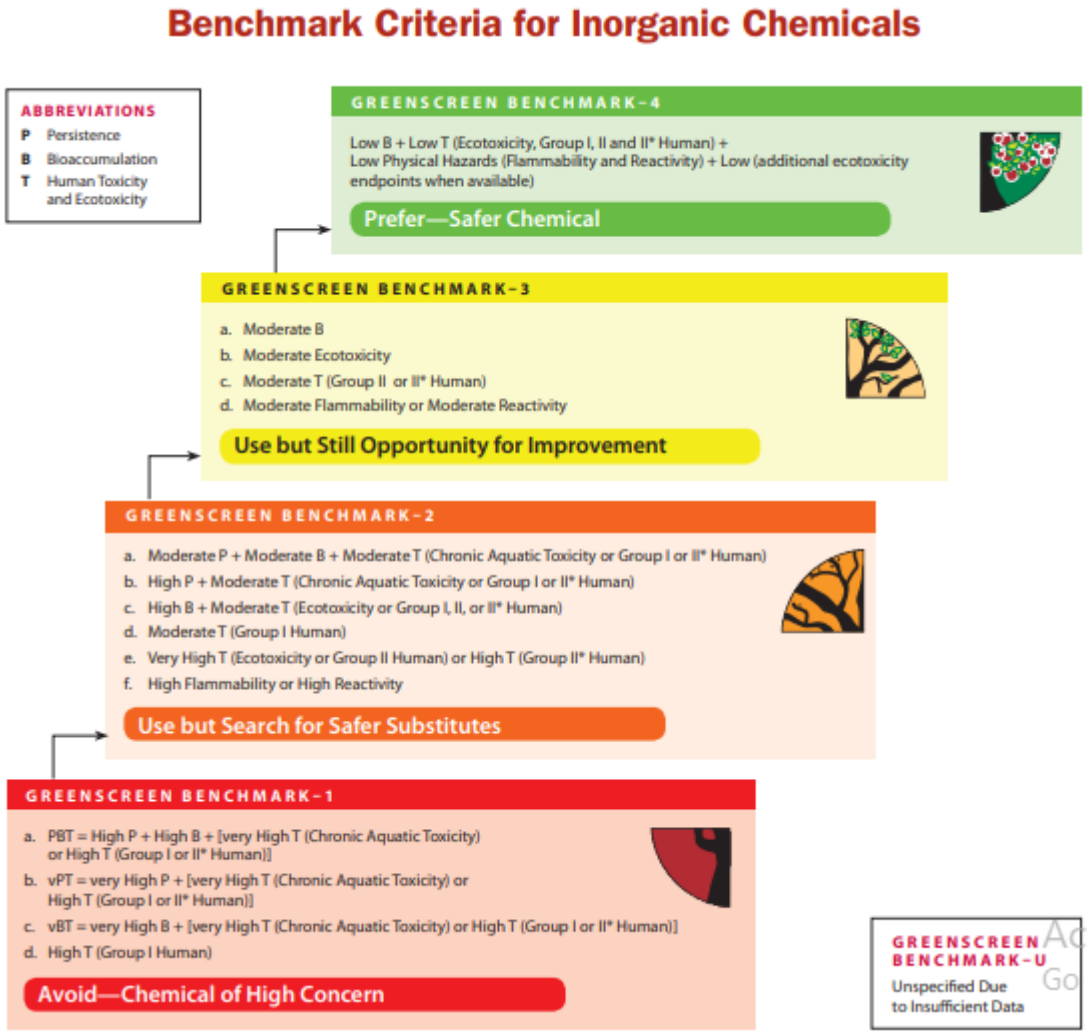

Figure 3.3. GreenScreen benchmark criteria for inorganic chemicals (CPA, 2018).

Benchmark Score	Data Requirements and Permissible Data Gaps by Hazard Endpoint Category
Benchmark-1	A chemical may be assigned Benchmark-1 with data on as few as one endpoint. For example, if a chemical is definitively classified as a GHS Category 1 (High in GreenScreen) for the Group I endpoint Carcinogenicity, it would be assigned Benchmark-1 even if other endpoints had data gaps. If a chemical is not classified as Benchmark-1 based on hazard, then it must meet the data requirements for Benchmark-2.

Figure 3.4. Benchmark-1 Data gap analysis and data requirement (CPA, 2018).

Benchmark Score	Data Requirements and Permissible Data Gaps by Hazard Endpoint Category			
Benchmark- 2	Group I Human	Group II and II* Human	Ecotoxicity& Fate	Physical Properties
	Data required for 3 out of 5 endpoints. Permissible data gaps include: 1. Endocrine Activity 2. Reproductive or Developmental Toxicity	Data required for 4 out of 7 endpoints. Permissible data gaps include: 1. Skin OR Respiratory Sensitization 2, Skin OR Eye Irritation 3. One other hazard endpoint	Data required for 3 out of 4 endpoints. Permissible data gaps include: 1. Acute OR Chronic Aquatic Toxicity	Data required for both endpoints.[1]

Figure 3.5. Benchmark-2 Data gap analysis and data requirement (CPA, 2018).

Benchmark Score	Data Requirements and Permissible Data Gaps by Hazard Endpoint Category			
Benchmark-3	Group I Human	Group II and II* Human	Ecotoxicity & Fate	Physical Properties
	Data required for 4 out of 5 endpoints (max 1 data gap). Permissible data gap is: Endocrine Activity	Data required for 5 out of 7 endpoints (max 2 data gaps). Permissible data gaps include: 1. Skin OR Respiratory Sensitization 2. One other hazard endpoint	Data required for all 4 endpoints (max zero data gaps).	Data required for both endpoints (max zero data gaps).[2]

Figure 3.6. Benchmark-3 Data gap analysis and data requirement (CPA, 2018).

3.3 Exposure Assessment

Most published alternatives assessments are mainly hazard based and a comparative exposure assessment is not included. This results in ignoring potential human exposure or environmental fate of the alternatives. In this study, exposure assessment is included as an additional tool in the decision making process to more comprehensively compare the alternatives.

To compare the environmental fate and transport of chemicals in different compartments of the environment, the EQC model is used (Mackay, 1996a). Furthermore, to incorporate human exposure, comparative qualitative human exposure assessment (QHEA) was carried out by narrowing down the exposure routes for the target chemicals and most relevant exposure parameters in accordance with the technical guidance document on risk assessment (ECB, 2003).

3.3.1 The EQC Model

The EQC model was preferred because it was able to serve as a relatively simple yet useful tool with a comparative evaluative environment having relatively low input data requirement. Output to be obtained from the model was in line with the requirements of the task in this study. Mackay and colleagues (1996b) proposed a five stage process to assess the fate of chemicals in which classification of chemicals was the first step. Classifying the chemical and hence collection of the physicochemical data are the most important steps for getting correct results in modeling studies. In this study EQC Version 4.00 was used which was downloaded from the webpage of Trent University Chemical Properties Research Group (https://tuspace.ca/~mparnis/Models.html). The EQC model consists of Level I, Level II and Level III with increasing level of complexity. The results of each level were discussed briefly for all the chemicals evaluated in this study.

The EQC levels are as follows (Mackay, 1996a):

- **Level I:** steady-state, equilibrium, closed system, no degradation.
- **Level II:** steady-state, equilibrium with degradation and advection.
- **Level III:** steady-state, non-equilibrium with degradation, advection and intermedia transfer.

Input data to the model is composed of (1) physicochemical properties of the chemicals being assessed, (2) environmental properties of the evaluative environment, and (3) the emission scenarios (i.e. mode-of-entry of chemical into the system which can be air, water, soil or any combination of the three) the user wants to assess and evaluate. How each input is prepared is explained briefly under the relevant sub-heading.

Physicochemical Properties:

The physicochemical properties which are required for a chemical to be used in the EQC model are the molar mass, melting point, vapor pressure, solubility in water, Henry's law constant (K_H), logarithm of octanol-water partition coefficient ($\log K_{ow}$), organic carbon water partition coefficient (K_{oc}) and reaction half-lives in

air, water, soil, and sediment. Figure 3.7 shows a screenshot of the input screen for chemical properties of the EQC model.

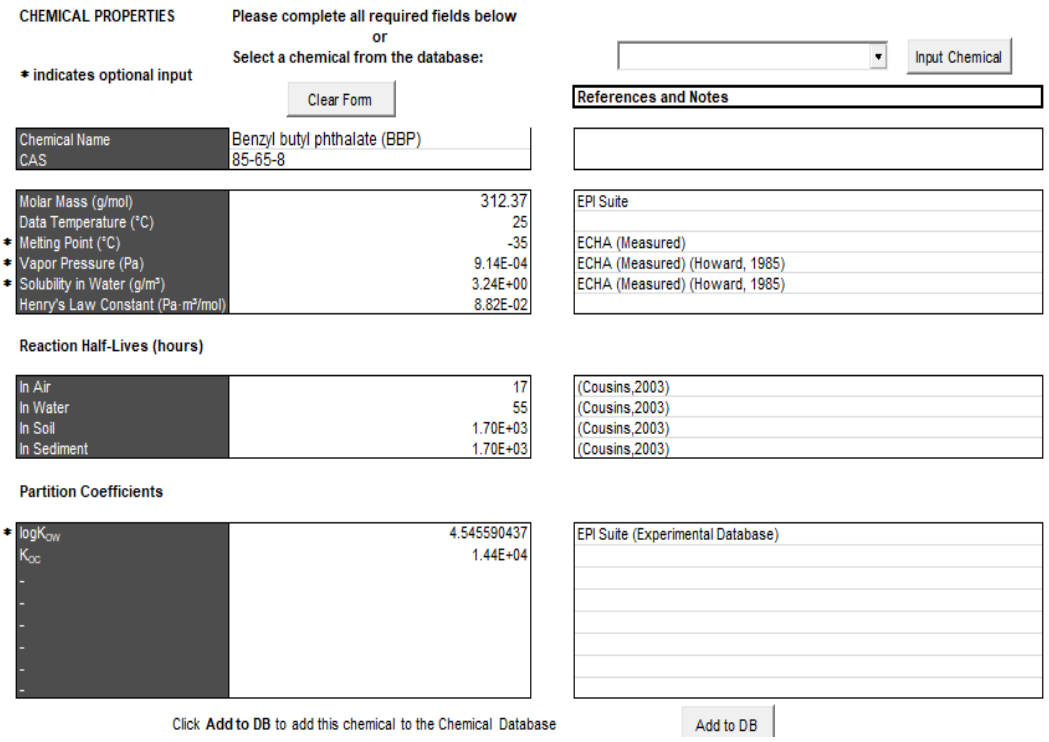

Figure 3.7. Example EQC input screen table (BBP)

The data was compiled for each chemical using literature information. Experimental data was preferred as much as possible. Usually there are more than one experiment conducted for a property and multiple values are listed. For example melting point of HBCD has been indicated as 180-195°C as per the secondary sources reported in (USEPA, 2014a). The melting point of 185.9 °C was reported in ECHA registration dossier, based on OECD Guideline 102 and EU Method A.1 under Good Laboratory Practices (GLP) and it was chosen. The experimental values for physicochemical property of each studied target and alternative chemical are presented in Annex C. The source of data and all necessary information are presented therein.

OECD has developed the echemportal (https://www.echemportal.org/echemportal/) in collaboration with other stakeholders and ECHA to enable public access to all

chemical properties. In the substance search by inserting the CAS number, all reliable databanks containing properties of the chemical can be reached. The data obtained from reliable databanks like ECHA (REACH) or USEPA(ACToR) was preferred because comment regarding the reliability of the data is mentioned. For example, the melting point of BBP was chosen as -35˚C, because in ECHA registration dossier it was stated that the data was obtained from reliable peer-reviewed handbook and is supported by the value cited in the peer-reviewed International Chemical Safety Card for BBP. All necessary information regarding the source of data and Guideline tests for physicochemical properties are presented in Annex C.

The major challenge in this study was in finding information on alternative chemicals. Alternative chemicals proposed in this study are new and for many, experimental data on their physicochemical properties is unavailable. In that case, properties are estimated using EPI Suite v4.11 (June 2017) at 25ºC. The software was downloaded from https://www.epa.gov/tsca-screening-tools/download-episuitetm-estimation-program-interface-v411. The CAS numbers and the Smiles notation are usually required for the prediction of physicochemical properties by EPI Suite, and they were obtained from PubChem webpage https://pubchem.ncbi.nlm.nih.gov/. Annex C contains details of all the physicochemical data used in this study and references from which the data was obtained

EPI Suite's MPBPWIN v1.44 was used to estimate the melting point and vapor pressure. For the melting point, mean or weighted value of the adapted Joback group contribution method (Joback, 1984) and Gold & Ogle prediction (Lyman, 1985) was taken, and for the vapor pressure Modified Grain method was preferred (Lyman, 1985). WATERNT v1.01 and KOWWIN v1.68 were used to estimate the water solubility and logKow values. Atom/fragment contribution method is the basis of both of the subprograms where multiplication of each fragment is done after a chemical is converted into several fragments and the coefficient is summed (William, 1992). The Henry's constant (K_H) was estimated by HENRYWIN v3.20 bond method (Hine & Mookerjee, 1975) where a compound is separated into

individual bonds excluding some functional groups and then Henry's constant is obtained by multiplying each bond with a unique variable in a linear equation. BIOWIN 3 was used to obtain the half-life in water which is based on experts' survey (Boethling et al., 1994)**.** EPI Suite converts the BIOWIN 3 results to half-life in water medium. To obtain the half-life in soil and sediment, the value obtained from the half-life in water was multiplied by two and nine, respectively, as was adopted by (Fenner et al., 2009). AOPWIN is used for estimation of half-life in air. Koc values were simply calculated using Kow, according to the equation in the EQC model (0.41*10^logK_{OW}).

Thermodynamic Consistency Check of Physicochemical Properties Input Into the EQC Model:

An important last step before input of physicochemical properties into the EQC model is the thermodynamic consistency check and subsequent adjustment of physicochemical properties. Modeling of environmental fate of chemicals depends very much on the quality of the physicochemical property data. Beyer et al (2002) argue that physicochemical properties are interrelated such that there should be an internal consistency or thermodynamic consistency amongst them. For this purpose, the method of Schenker et al. (2005) was used to get thermodynamically consistent data for the solubility and partitioning properties for the chemicals of concern and the alternatives proposed in the study. This was performed on both EPI Suite predicted and experimentally obtained physicochemical properties from the literature. The data selected as input which are known as literature derived values (LDVs) and the final derived values (FDVs) which were achieved after adjustments by applying the thermodynamic consistency check are presented in Annex C2. Least squares adjustment of properties according to Schenker et al., (2005) method which was used in this study is also comprehensively explained in this Annex C2.

Lastly, handling of the EQC model depends on the general classification of compounds, as listed in Table 3.6. Some of the proposed alternatives could not be evaluated in the EEA because of limitations. Butadiene styrene brominated copolymer (HBCD alternative), Ammonium polyphosphate and Polyphosphonate

(DecaBDE alternatives) could not be included in the fate evaluation due to the unavailability of important information on environmental degradation half-lives. Typically, EPI Suite is used for estimation of physicochemical parameters as well as environmental degradation half-lives. The chemicals mentioned above are polymers and have molecular weight greater than 1000g/mole which is not amenable to SMILES notation; therefore it was not possible to estimate LogKow and environmental half-lives via EPI Suite. SMILES notation for COMGHA (phthalate alternative) was also unavailable due to COMGHA being a mixture of two ingredients. Aluminum diethylphosphinate (DecaBDE alternative) is an organophosphorus salt and unfortunately is not amenable to the fugacity based model (USEPA, 2014b). Magnesium hydroxide (DecaBDE alternative) dissociates in the environment into Mg^{2+} and OH^- ion. The heavy metals and trace metals are recalcitrant. The distribution and fate of such metal ions are usually modeled with Mackay aquivalence approach without involving the degradation parameter (Chang & Li, 2020). This study was focused on the comparative evaluation of the persistence of target chemical and proposed alternatives hence magnesium hydroxide was also not evaluated. Table 3.6 contains the type of chemicals and the data required as EQC input.

Environmental Inputs

The environmental parameters which must be defined by the user are the sub-compartment volume fractions and densities, media depth and area, organic carbon content and intermedia transport velocities for different processes.

The EQC developers have suggested default values for each of these, and they were directly used in all the runs in this study. Figure 3.8 shows a screenshot of the input screen for environmental properties of EQC model.

Table 3.6. Type of chemicals and their classification ((Mackay et al., 1996a).

Chemical category	Z values	Partitioning data required	Examples	Equilibrium criterion
Type 1	Measurable in all phases	Water and fat or lipid solubility, vapor pressure, Henry's law constant, and octanol–water partition coefficient	Most organic chemicals, e.g., chlorobenzene, hexachlorobenzene, PCBs, etc.	Fugacity
Type 2	Zero or near zero in air, measurable in all other phases	Partition coefficients to solid surfaces and to organic carbon, solubility in water and fat	Cations, anions, and involatile organic chemicals	Aquivalence
Type 3	Zero or near zero in water, measurable in all other phases	Partition coefficient to solids from air or from a pure phase	Very hydrophobic compounds, e.g., long-chain hydrocarbons, silicones, and polymers	Fugacity
Type 4	Zero or near zero in air and water	Sorptive properties from a pure phase to various solids	Large molecular weight substances, polymers, many elemental metals, and inorganic substances such as minerals	Models may not be useful
Type 5	Relevant Z values required for all species in all phases	Partitioning data for all species	Organo-metals, phenols of low pKa	Probably aquivalence

ENVIRONMENTAL PROPERTIES

Please complete all fields or select an environment from the database:

Environment Name	EQC

Volume Fractions

Aerosol in Air	2.00E-11
Susp. Particles in Water	5.00E-06
Fish in Water	1.00E-06
Air in Soil	0.2
Water in Soil	0.3
Solids in Soil	0.5
Water in Sediment	0.8
Solids in Sediment	0.2

Depth (m) (Level I & Level II)

Air	1000
Water	20
Soil	0.1
Sediment	0.01

Depth (m) (Level III)

Air	1000
Water	20
Soil	0.2
Sediment	0.05

Densities for subcompartments (kg/m³)

Vapour phase of Air	1.21
Aerosol in Air	2000
Liquid phase of Water	1000
Sup. Particles in Water	1500
Fish in Water	1000
Air in Soil	1.21
Water in Soil	1000
Solid in Soil	2400
Water in Sediment	1000
Solid in Sediment	2400

Area (m²)

Air	1.00E+11
Water	1.00E+10
Soil	9.00E+10
Sediment	1.00E+10

Advective Flow Residence Times (h)

Air	100
Water	1000
Soil	0
Sediment (burial)	50000

Organic Carbon (g/g)

Susp. Particles	0.2
Fish Lipid	0.05
Soil	0.02
Sediment	0.04

Transport velocities (m/h)

Air side air-water MTC	5.00E+00
Water side air-water MTC	5.00E-02
Rain rate	1.00E-04
Aerosol deposition velocity	6.00E-10
Soil-air phase diffusion MTC	2.00E-02
Soil-water phase diffusion MTC	1.00E-05
Soil-air boundary layer MTC	5.00E+00
Sediment-water diffusion MTC	1.00E-04
Sediment deposition velocity	5.00E-07
Sediment resuspension velocity	2.00E-07
Soil-water runoff rate	5.00E-05
Soil-solids runoff rate	1.00E-08

Figure 3.8. Environmental properties screen table in EQC model for this study.

Mode of Entry

Selection of both the emission amount and into which type of media (i.e. soil, air, water), also known as "mode of entry", is another necessary input of the EQC model. The mode of entry has an impact on the output of only Level III, as those

are non-equilibrium steady-state calculations. The default value of 100,000 kg was selected for the Level I case and 1000 kg/h was selected for Levels II and III. In this study, actual environmental concentrations or masses of chemicals are not sought after, instead, the aim is to compare target and alternative chemicals in terms of their fate and transport, persistence in the environment. Hence, use of default input amounts was preferred.

Four scenarios were tested for each chemical during evaluation of fate and transport of the chemicals: emission into air, soil and water media, individually at 1000 kg/h and in the fourth simulation, emission was done simultaneously to air, water and soil at 1000 kg/h each.

Sensitivity Analysis

Sensitivity analysis was carried out for all the chemicals by increasing and decreasing the physiochemical properties one by one and the percent difference impact on persistence was evaluated

0.1%, 1%, 10% and 100% incremental change was tested and for +100% and -100% the most observable change was attained that is why the sensitivity analysis was carried out by increasing or decreasing the physicochemical properties by 100%. The mode of entry for the analysis was taken as the chemical entering simultaneously air, water and soil at 1000 kg/h.

3.3.2 Comparative Qualitative Human Exposure Assessment

Comparative qualitative human exposure assessment (QHEA) was done for target chemicals (phthalates, HBCD and decaBDE) and the proposed alternatives for the functional use selected in the study. The likely exposure routes were selected through which humans can come into contact with the target chemical. After narrowing down the main exposure routes, most relevant exposure parameters, from the technical guidance document on risk assessment ECB (2003), were recognized for inhalation, dermal absorption and ingestion routes. The parameters were evaluated as per the criteria defined in the ECB (2003) indicated in the below

tables. Namely, Table 3.7, 3.8,3.9 and Table 3.10 show the main exposure parameters for inhalation, oral ingestion, dermal absorption routes and bioaccumulation in adipose tissues, respectively (ECB, 2003).

Table 3.7. Parameters used for inhalation exposure route (obtained from Table 1 in ECB (2003)).

Vapor Pressure	Highly volatile substances are those with a vapor pressure greater than 25 KPa (or a boiling point below 50°C). Substances with low volatility have a vapor pressure of less than 0.5 KPa (or a boiling point above 150°C)
Particle Size	Indicates the presence of inhalable/respirable particles. As a rough guide, particles with aerodynamic diameters below 100 µm have the potential to be inhaled. Particles with aerodynamic diameters of above 1- 5 µm have the greatest probability of settling in the nasopharyngeal region whereas particles with aerodynamic diameters below 1- 5 µm are most likely to settle in the tracheobronchial or pulmonary regions. (<5µm has been taken as red shade)
Log K_{ow}	Log K_{ow} values above 0 indicate the potential for absorption directly across the respiratory tract epithelium.
Solubility	1-100 mg/L (Slightly Soluble) <0.1 mg/L (Negligible Solubility) (Greggs et al., 2019) **This is from European Document** Very hydrophilic substances may be retained within the mucus or for low molecular weight substances (MW<200) could be absorbed through aqueous pores. Very low water solubility (1 mg/l or less) and small particle size (below 1 µm) indicates the potential for accumulation.
Oral Toxicity Data	If signs of systemic toxicity are present in an oral toxicity study or there are other data to indicate the potential for absorption following ingestion it is likely the substance will also be absorbed if it is inhaled. The systemic toxicity data was taken from the CHA.

Table 3.8. Parameters used for oral ingestion route (obtained from Table 2 in ECB (2003)).

Molecular Weight	Molecular weights below 500 g/mole are favorable for absorption; molecular weights in the 1000's g/mole do not favor absorption.
Solubility	1-100 mg/L (Slightly Soluble) <0.1 mg/L (Negligible Solubility) (Greggs et al., 2019) **This is from European Document** Absorption of very hydrophilic substances by passive diffusion may be limited by the rate at which the substance partitions out of the gastrointestinal fluid. However, if the molecular weight is low (less than 200) the substance may pass through aqueous pores or be carried through the epithelial barrier by the bulk passage of water.
Log K_{ow}	Moderate log K_{ow} values (between 0 – 4) are favorable for absorption by passive diffusion. Any lipophilic compound may be taken up by micellular solubilization but this mechanism may be of particular importance for highly lipophilic compounds (log K_{ow} >4), particularly those that are poorly soluble in water (1 mg/l or less) that would otherwise be poorly absorbed.
Oral Toxicity Data	Systemic Toxicity (Single and Repeated Dose). The chemical having Moderate or High score as per CHA presented in this thesis study are colored Red.

Table 3.9. Parameters used for dermal absorption route (obtained from Table 3 in ECB (2003)).

Molecular Weight	Less than 100 g/mole favors dermal uptake. Above 500 g/mole the molecule may be too large.
Solubility	If water solubility is below 1 mg/L, dermal uptake is likely to be low. Between 1-100 mg/l absorption is anticipated to be low to moderate and between 100-10,000 mg/l moderate to high. However, if water solubility is above 10,000 mg/l and the log K_{ow} value below 0 the substance may be too hydrophilic to cross the lipid rich environment of the stratum corneum. Dermal uptake for these substances will be low.
Log K_{ow}	For substances with log K_{ow} values below 0, poor lipophilicity will limit penetration into the stratum corneum and hence dermal absorption. log K_{ow} values between 1 and 4 favor dermal absorption (values between 2 and 3 are optimal) particularly if water solubility is high. Above 4, the rate of penetration may be limited by the rate of transfer between the stratum corneum and the epidermis, but uptake into the stratum corneum will be high. Above 6, the rate of transfer between the stratum corneum and the epidermis will be slow and will limit absorption across the skin. Uptake into the stratum corneum itself may be slow.
Vapor Pressure	Vapors of substances with vapor pressures below 100 Pa are likely to be well absorbed and the amount absorbed dermally may be more than 10% of the amount that would be absorbed by inhalation.
Skin Irritation and Skin Sensitization	The chemical having Moderate or High score as per CHA presented in this thesis study for skin irritation or skin sensitization are colored Red.

Table 3.10. Parameter used for bioaccumulation in adipose tissues (obtained from Table 5 in ECB (2003)).

Log K_{ow}	If the interval between exposures is less than 4 times the whole body half-life of the substance, then there is the potential for the substance to accumulate. It is generally the case that substances with high log K_{ow} values have long biological half-lives. On this basis, daily exposure to a substance with a log Kow value of around 4 or higher could result in a build-up of that substance within the body.

The steps followed during QHEA were as follows: Firstly, for each target chemical (phthalates, HBCD, DecaBDE) and proposed alternatives, the potential exposure routes were narrowed down. The chemicals were evaluated as per the criteria defined in the above tables (Table 3.7, 3.8, 3.9 and 3.10) for the respective exposure route parameters. Apart from the exposure routes, ingredient concentration in the product and extraction potential of the chemical from the product were also compared. Both these parameters were added because they cause significant impact on human exposure. A chemical was shaded red for a parameter if it fulfilled the criterion. It meant the predicted exposure from the parameter would be harmful. A chemical was shaded green for a parameter if it did not fulfill a criterion. It meant the predicted exposure from the parameter would be safe. A comparative summary table for QHEA was compiled at the end which compared

the overall score from the selected exposure routes and ingredient concentration and extraction potential were added. The overall scores of the highest scoring target chemical-phthalate (DEHP) or HBCD or DecaBDE were compared with the proposed alternatives. If the overall score of the proposed alternative was the same as the target chemical, cell was shaded blue. If the overall score was less, cell was shaded red which showed more predicted qualitative exposure potential of the proposed alternative in comparison to the target chemical (DEHP used for phthalates, HBCD or DecaBDE). This meant that the proposed alternative performed worse than target chemical in terms of QHEA. If the overall score was more, then cell was shaded green which showed less predicted qualitative exposure potential of the proposed alternative in comparison to the target chemical. This meant that the proposed alternative was safer than target chemical in terms of QHEA.

3.4 Limitations of the study

3.4.1 Chemical Hazard Assessment

Any impurity present at greater than or equal to 100 ppm (0.01%) should be assessed as per GreenScreen criteria (CPA, 2018). In this study, the chemicals evaluated were considered as pure and no impurity information was available.

For the polymer substance, with average molecular weight between 1000 - 10,000 Da, the hazard classification of the oligomer should also be included, if oligomer<500 Da are present at higher than or equal to 10%, or if oligomer <1000 Da are present at higher than or equal to 25%. None of the polymers in this study had the recommended percentage of oligomers as per the available information, so the CHA only included the polymer substance itself.

No information regarding stabilizers or impurities was available for the polymers evaluated in this study that is why they were not included in the hazard assessment. Transformation products of the chemicals were not evaluated in the hazard assessment.

As this study is CAA and not detailed risk assessment, the GreenScreen CHA was done for the chemical and not product. Subsequently, the concentration and/or dosage of chemical was not included in the scope of the hazard assessment.

3.4.2 Environmental Exposure Assessment

The environmental exposure assessment was done for the chemical and not the product, that is why neither the exact concentration nor the amount of the chemical in the product was included in the EQC calculations.

3.4.3 Qualitative Human Exposure Assessment

The QHEA score is scenario dependent. If a different scenario is adopted for a given chemical, then the route of exposure changes so the QHEA score would change.

CHAPTER 4

4 RESULTS AND DISCUSSION

4.1 Selection of Chemicals for the Study

In this study, five chemicals were selected, three of them are phthalates, which are used as plasticizers and two of them are flame retardants. In order to make the selection, the Turkish inventory of chemicals which contains the information of the chemicals, imported/manufactured at more than 1tons/yr was obtained. The Turkish chemicals inventory data was downloaded from (turkreach.com.tr). Although the current Turkish regulation mandates listing of these chemicals by the ministry periodically, at the time of this study, the most current and only list was for November 2011. Therefore, due to lack of a more current list, this one was used. The list was filtered to identify chemicals listed in the REACH restriction or/and authorization lists.

As per the data, 2886 substances are manufactured or imported into Turkey (1 tons/year to 1000 tons/year) and 597 substances are manufactured or imported above 1000 tons/year. 29 chemicals in the list are also on the REACH Authorization List (Annex XIV). The list is attached, at the end of the study; in Annex A (Table A4). Authorization needs to be taken from ECHA by the manufacturer or supplier to manufacture or to place it on the EU market or to use it in an article or mixture. 38 chemicals in the Turkish inventory list are also on the REACH Restriction List (Annex XVII). The list is attached, at the end of the study; in Annex A (Table A3).

After identification of the potential chemicals to be studied, the next elimination step is related to components of CAA. A major component of CAA is the hazard assessment step. The hazard assessment depends on the quality of the data that can be obtained regarding the different hazard endpoints. To be able to reach relevant hazard information on chemicals, alternative assessment studies that have been

carried out previously were evaluated. This way, the chemicals to be studied could be short listed.

The GreenScreen hazard assessment v1.4 method was selected comprising of 18 hazard endpoints. The methodology of completing GreenScreen is discussed in Section 3.2 (Materials & Methods). Scores for hazard endpoints are determined after examining toxicological data from primary literature sources or peer reviewed authoritative secondary sources like governmental risk assessments and authoritative toxicological databases. That is why first literature search was conducted for the chemicals for which alternative CHA was already done so that reliable authorized hazard endpoints data could be obtained. Table 4.1, 4.2 and 4.3 contain the alternative assessments which are done by the USEPA, Danish EPA and TURI (2006), respectively. The updated versions of the reports are referenced in the tables. In the tables, evaluations are shown in colored fonts such that: Green color font indicates major advantageous points of the alternative assessment; the orange color font indicates information which can be helpful in this study whereas the red color font indicates a limitation or disadvantageous for the assessment with respect to this study.

Table 4.1. Alternatives assessments by USEPA (DfE)*.

Report Title	Chemicals	Turkish Inventory	Comment	Reference
1. DfE Alternatives Assessment for Nonylphenol Ethoxylates.	Nonylphenol (NP) and Nonylphenol Ethoxylates (NPE) as a surfactant.	Nonylphenol, ethoxylated **(EC 500-024-6).** Nonylphenol, branched, ethoxylated **(EC 500-209-1).** 4-Nonylphenol, branched, ethoxylated **(EC 500-315-8).** 26-(nonylphenoxy)-3,6,9,12,15,18,21,24-octaoxahexacosan-1-ol **(EC 247-816-5)** are all present: >1000tons/yr	The CHA is only done for environmental fate and toxicity but human health hazard endpoints are not evaluated. (Partnership kicked off in 2012)	(USEPA, 2012)
2. Flame Retardant Alternatives for Hexabromocyclodecane (HBCD).	HBCD as a FR in expanded and extruded polystyrene foam in building insulation. **EC:247-148-4**	Present: 1to1000tons/yr.	CHA is comprehensive and technical assessment is based upon stakeholder assessment and the alternatives are proposed for a specific function. 3 alternatives were proposed which were also brominated flame retardants. (Partnership kicked off in 2011)	(USEPA, 2014a)
3. An Alternative Assessment for the Flame Retardant (FR) DecaBDE.	Decabromodiphenyl Ether (DecaBDE) **EC:214-604-9**	Present: 1to1000tons/yr	CHA is comprehensive and technical assessment is also done for alternatives in a tabular format in which alternatives are proposed for end user applications and sector. (Partnership kicked off in 2010)	(USEPA, 2014b)
4. FR used in Polyurethane Foam: An Alternative Assessment Update.	Pentabromodiphenyl ether (PentaBDE). **EC:251-084-2**	Not present in Turkish inventory	This is an updated work by the USEPA. The previous report was updated and the Hazard assessment is comprehensive. They included the FR used in automobile and aircraft seating. (Partnership kicked off in 2005)	(USEPA, 2015a)
5. Bisphenol A Alternatives in Thermal Paper.	Bisphenol A**.** EC: 201-245-8	Present: >1000tons/yr	CHA is comprehensive, technical assessment based upon stakeholders where alternatives are proposed for bisphenol A in thermal paper. 19 potential alternatives were proposed. (Partnership kicked off in	(USEPA, 2015b)

Report Title	Chemicals	Turkish Inventory	Comment	Reference
			2010)	
6. Flame Retardants in Printed Circuits.	Tetrabromobisphenol A (TBBPA). EC: 201-236-9.	Present: 1to1000tons/yr	CHA is comprehensive. 10 alternatives are proposed. Technical assessment and testing was done to understand combustion products. (Partnership kicked off in 2008).	(USEPA, 2015c)

*Green: major advantage, Orange: helpful information, Red: limitation or disadvantage.

Table 4.2. Alternatives assessments by Danish EPA*.

Report Title	Chemicals	Turkish Inventory	Comment	Reference
1.Identification and assessment of alternatives to selected phthalates (used in toys and childcare.	DEHP(EC: 204-211-0),BBP(EC: 201-622-7),DBP EC: 201-557-4)	DEHP: >1000tons/yr, BBP: 1 to 1000tons/yr, DBP: 1 to 1000 tons/yr	Hazard assessment template is complex but the hazard endpoints data is comprehensive to swap it into GreenScreen. The technical assessment is also comprehensive with stakeholder output and alternative chemicals already used in market and comprehensive data provided.	(Maag et al., 2010)
2.Bisphenol A (BPA) alternatives and alternative technologies in thermal receipt.	Bisphenol A EC: 201-245-8	Present: >1000tons/yr	Hazard assessment is based on USEPA report on BPA in thermal paper mostly. Migration potential of the alternatives is discussed. Alternative technologies are discussed in detail which serves the same purpose as thermal paper receipts.	(Møller Christensen et al., 2014)

Report Title	Chemicals	Turkish Inventory	Comment	Reference
3.Alternatives to classified phthalates in medical devices.	DEHP (EC: 204-211-0), BBP (EC: 201-622-7), DBP (EC: 201-557-4), DIBP (EC: 201-553-2)**.**	Present: DEHP: >1000tons/yr, BBP: 1 to 1000tons/yr, DBP: 1 to 1000 tons/yr, DIBP>1000 tons/yr.	10 alternatives were proposed. Hazard Assessment has been done and the alternatives were shortlisted by stakeholders and Danish EPA but no comprehensive technical assessment was done.	(Nielsen & Larsen, 2014)
4.Alternatives to perfluoroalkyl and polyfluoroalkyl substances (PFAS) in textiles.	PFAS	Not present in Turkish inventory	The hazard assessment is not comprehensive and no extensive literature review is done like USEPA and there is no set template thus a lot of data gaps but the technical and functional assessment is based on stakeholder output and is comprehensive.	(Lassen et al., 2015)
5.Phosphorus flame retardant alternatives to halogenated flame retardants.	The Flame Retardants are the same as US EPA. (EC:204-112-2), (EC: 425-220-8), (EC: 273-066-3), (EC: 269-789-9)	DecaBDE: 1to1000tons/yr, TBBPA: 1to1000tons/yr, HBCD: 1to1000tons/yr	Comprehensive hazard assessment is done by adopting USEPA data into GreenScreen. GreenScreen was used with only data sources used in Europe with some adjustments to few hazard classification limits (i.e. bioaccumulation and removal of physical hazards).	(Mikkelsen , 2016)

*Green: major advantage, Orange: helpful information, Red: limitation or disadvantage.

Table 4.3. Alternative assessments by TURI (2006)*.

Report Title	Chemicals	Turkish Inventory	Comment	References
Five Chemicals Alternatives Assessment Study	1. Lead and lead compounds, 2.Formaldehyde, 3.Perchloroethylene, 4.Hexavalent Chromium. 5. DEHP.	All are present in Turkish Inventory above 1000 tons/year.	Very detailed report where alternatives are selected as per different functional criteria in the state of Massachusetts. Hazard assessment is comprehensive and technical assessment is in detail with respect to alternatives. Financial assessment is also part of the report.	(TURI, 2006)
Assessment of Alternatives to Perchloroethylene for the Dry Cleaning Industry	Perchloroethylene (EC: 204-825-9)	Present in Turkish Inventory >1000tons/yr	The alternatives were chosen by dry cleaning stakeholders who are already using alternatives. Performance assessment as well as financial assessment was a part of the report for each alternative. The hazard assessment is done but is not as elaborate as the USEPA.	(TURI, 2012)

*Green: major advantage , Orange: helpful information, Red: limitation or disadvantage.

Table 4.4 shows the chemicals that were selected for the CAA in this study. Phthalates (DEHP, DBP and BBP), HBCD and DecaBDE were selected in this thesis, mainly because they were known to be used in Turkey; also toxicological hazard detail was available for them. All the other details are written as comments in Table 4.4. The selected phthalates (DEHP, DBP and BBP) are in the REACH Restriction Annex XVII and Authorization Annex XIV. HBCD is in the REACH Authorization Annex XIV. HBCD is also in the Stockholm Convention Annex A. DecaBDE was removed from the REACH Restriction Annex XVII on 16th December, 2020 due to its inclusion in the Stockholm Convention Annex A.

Table 4.4. Chemicals selected for this study.

Chemical & Functional Use	**CAA compiled by**	**Comment**
DEHP, DBP and BBP (Phthalates) in toys.	Danish EPA (Maag et al., 2010) (Nielsen & Larsen, 2014)	The CHA template of Danish EPA was complex, and in this thesis study hazard assessment was compiled with GreenScreen template. Danish EPA has compiled two alternative assessment reports regarding the use of phthalates in toys and medical devices so the hazard endpoint information was gathered and compared from both reports. Common alternatives were selected. ECHA registration dossiers and GreenScreen specified lists were searched for new hazard information. Exposure Assessment was missing which was carried out in this thesis study.
HBCD as a flame retardant in expanded and extruded polystyrene foam in building insulation.	(USEPA, 2014a)	Comprehensive CHA was done in the USEPA template; this was compiled with GreenScreen template in this study. Also, ECHA registration dossiers and GreenScreen Specified lists were searched for new hazard information. In the USEPA report, general information regarding the exposure of HBCD was summarized. In this thesis study, exposure assessment was done considering fate and transport of the chemical in the environment, and qualitative assessment of the chemical exposure on human was also done.
DecaBDE as a flame-retardant in Automobiles **(the end user application of automobiles is considered in this study).**	(USEPA, 2014b)	Comprehensive CHA was done in the USEPA template and the same information had been compiled by Danish EPA in the GreenScreen template. Yet, ECHA registration dossiers and GreenScreen Specified Lists were assessed to seek updated information and studies regarding hazard endpoints which can change the hazard score from these USEPA report. In the USEPA report, general exposure and lifecycle information was summarized whereas in this thesis study, exposure assessment was done in detail with respect to fate and transport of the chemical in the environment as well as qualitative human exposure assessment.

4.2 Phthalates

Phthalate esters like DEHP, DBP and BBP are used to impart flexibility as primary plasticizers in polyvinyl chloride (PVC). PVC is widely used in consumer products such as toys, medical devices, flooring, water piping, cosmetics and food packaging, hence making it world's 3rd most widely used synthetic plastic polymer (Greggs et al., 2019). Children have a tendency to put toys in their mouth. They can get exposed through ingestion, dermal absorption and inhalation because phthalates are not chemically bound to PVC and have a migration potential (Little et al., 2012). Similarly in the use in medical devices, plasticizer migration can be a cause of concern for consumer exposure (Nielsen & Larsen, 2014).

DEHP, DBP and BBP are in GHS toxic for reproduction category 1B (EC, 2017). They were prohibited to be used in children toys in 1999, and were permanently banned in 2005 in childcare articles as per EU Directive (2005/84/EC). They are also included in the REACH Restriction List and have been banned from placement on the market in articles after 7th July, 2020. Alternative chemicals and substances have been used in the market in toys and childcare articles. Danish EPA has compiled two reports where alternatives for phthalates are proposed in toys (Maag et al., 2010) and medical devices (Nielsen & Larsen, 2014).

In this study, a chemical alternatives assessment for three phthalates, namely, DEHP, DBP and BBP, in toys and childcare articles was conducted.

4.2.1 Selection of Alternatives

In the two Danish EPA reports, 10 chemicals were assessed on phthalates alternatives each in toys (Maag et al., 2010) and medical devices (Nielsen & Larsen, 2014). In this thesis study, six common alternatives were selected from these reports and the market experience of the alternatives is described in Table 4.1. For hazard information, the Nielsen & Larsen study (2014) was mostly preferred due to updated hazard data. DEHP, DBP and BBP are being manufactured/imported into Turkey as per the Turkish inventory (Annex A) but the

articles in which they are being used are not exactly known. Table 4.5. gives an overview of the market experience i.e., usage of the alternatives for the traditional uses as well as in toys and medical devices instead of the phthalates.

4.2.2 Chemical Hazard Assessment

The GreenScreen summary table (Table 4.6.) shows comparison of the hazard endpoint scores for the phthalates and the proposed alternatives. The complete GreenScreen hazard assessment for each chemical is presented in Annex B, summary descriptions are provided in the next subsection CHA Result Discussion.

A) Group I Human Hazard Endpoints

Carcinogenicity:

DEHP is on the Authoritative A list, USEPA IRIS Carcinogens in Group B2 probable human carcinogen, and assigned a score of 'H-high'. On the other hand, BBP is in Group C- possible human carcinogen.

DBP is in MAK Carcinogen Group 3B-Evidence of carcinogenic effects but not sufficient for assigning a 'H-High' score, that is why both DBP and BBP are assigned a score of 'M-moderate'.

All the alternatives have 'L-low' score for carcinogenicity. A 2-year carcinogenicity study was conducted for ATBC, DINCH and DEHT that is why the confidence in the data is high, whereas no study was conducted for COMGHA but a weight of evidence approach was used to give it a hazard score of low as per Danish EPA report (Nielsen & Larsen, 2014). The weight of evidence approach was also used to assign ASE a low score for carcinogenicity in the ECHA registration dossier. A carcinogenicity study was not conducted for ASE that is why the confidence in the data is low. DINA was assigned 'L-low' score based on two year carcinogenicity study on Di (2-ethylhexyl) adipate, a structural analog. It is highly recommended for ASE, DINA and COMGHA two year carcinogenicity studies should be conducted. Table 4.6 shows CHA table.

Table 4.5. Identified alternatives in the study.

Chemical	**CASRN**	**Market Experience***	**REACH registration (Tonnage band)(tons/year)** **
ASE (Sulfonic acids, C10-C21-alkane, phenylester)	91082- 17-6	Significant market experience for most traditional DEHP, DBP and BBP uses.	10,000 to 100,000
ATBC (Acetyl tributyl citrate)	77-90-7	Significant market experience for DEHP and DBP applications. In medical devices it is used as an effective alternative to DEHP.	10,000 to 100,000
COMGHA (Glycerides, castor-oil mono-, hydrogenated, acetates)	736150- 63-3	Relative moderate market experience for traditional DEHP, DBP uses.	1000 to 10,000
DEHT (Di-ethylhexylterephthalate)	6422- 86-2	Significant market experience for traditional DEHP and some BBP uses.	100,000 to 1,000,000
DINA (Diisononyl adipate)	33703- 08-1	Frequently used alternative in toys, according to surveys and has mostly been used for low temperature PVC applications. Already used in market for specific group of medical devices.	100 to 1000
DINCH (Di-isononylcyclohexane-1,2-Dicarboxylate)	166412- 78-8	Most used alternative in PVC applications for DEHP. Most abundant alternative found in toys and childcare articles on the Dutch market. Already used in market for specific group of medical devices. Significant market experience.	10,000 to 100,000

* Source: Danish EPA Reports (Maag et al., 2010; Nielsen & Larsen, 2014)
**Source: ECHA Registration Dossiers and Danish EPA Reports (Nielsen & Larsen, 2014).

Table 4.6. GreenScreen hazard summary table for phthalates and alternatives.

	GreenScreen Hazard Summary Table for Phthalates and Alternatives																				
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical		
CHEMICALS	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability	BENCHMARK SCORE
							single	repeat*	single	repeat*	*	*									
CHEMICALS OF CONCERN (PHTHALATES)																					
DEHP	H[a]	L[c]	H[a]	H[a]	H[a]	L[c]	H[c]	M[c]	L[c]	L[c]	L[c]	*L[c]*	L[c]	L[c]	L[c]	L[c]	VL[c]	M[c]	*L[c]*	L[c]	BM-1e
DBP	M[a]	*L[c]*	H[a]	H[a]	H[a]	L[c]	*M[b]*	*H[b]*	-	L[c]	*H[b]*	DG	L[c]	L[c]	VH[a]	H[c]	VL[c]	*L[c]*	*L[c]*	L[c]	BM-1e
BBP	M[a]	L[c]	*H[a]*	H[a]	H[a]	L[c]	-	*M[b]*	-	L[c]	L[c]	DG	L[c]	*L[c]*	VH[a]	H[c]	VL[c]	L[c]	*L[c]*	L[c]	BM-1e
ALTERNATIVES																					
ASE	*L[c]*	*L*	*M*	*L*	DG	L	-	L	-	L[c]	L	DG	L	L	L	L	*M*	L	*L[c]*	L[c]	BM-2e
ATBC	L	L	*L[c]*	*M*	DG	L	-	L	DG	DG	*L*	DG	L	L	L	M	M	*VL*	*L[c]*	L[c]	BM-2e
COMGHA	*L*	L	L	L	L	L	-	L	-	L	L	DG	L	L	L	*L[c]*	VL	M	*L[c]*	L[c]	BM-3a
DEHT	L	L	*M*	*L*	DG	L	L[c]	L	L[c]	DG	L	*L[c]*	L	L	L	L	VL	L	*L[c]*	L[c]	BM-2e

	GreenScreen Hazard Summary Table for Phthalates and Alternatives																				
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical		
CHEMICALS	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability	BENCHMARK SCORE
							single	repeat*	single	repeat*	*	*									
DINA	*L*	*L*	*M*	*H*	DG	L	*L*[c]	*M*	DG	DG	L	DG	L	L	L	*L*	VL	*VL*	*L*[c]	L[c]	BM-1e
DINCH	L	L	L	L	M	L	L [c]	*M*	L[c]	L[c]	L	*L*[c]	M	L	L	L	*M* [c]	L	*L*[c]	L[c]	BM-2e

Note to Table:

[a, b, c] The superscripts with the hazard score indicates the reference for the hazard score such that **a**: Authoritative List; **b**: Screening List; **c**: ECHA registration dossier of the specific chemical.

- E.g. **H**[a] (a: Authoritative A) which means the chemical was present in the authoritative A list for the specific hazard endpoint. Similarly superscripts were provided and the references were mentioned as a footnote.
- For a hazard score without any superscript, it means that the source of the hazard score is the Danish EPA (Nielsen & Larsen, 2014).
- Dash '-' used in case of missing single or repeat Systemic toxicity or neurotoxicty hazard end point. Missing Single exposure when repeat exposure is available is not considered a Data Gap on its own.

Bold score indicates high confidence data while *italic* score indicates low confidence data.

Group II Human Health endpoints have four hazard scores (i.e., VH, H, M, and L) and Group II* Human Health endpoints have three hazard scores (i.e., H, M, and L), and are based on single exposures instead of repeated exposures.

Persistence and Bioaccumulation have five hazard scores (i.e., VH, H, M, L and VL).

The legend for the scores is indicated below

	Hazard Score	Acronym Used
	Very High	VH
	High	H
	Moderate	M
	Low	L
	Very Low	VL
	Data Gap	DG

Mutagenicity:

DEHP, DBP and BBP were not present on any authoritative or screening lists, also the information on the ECHA registration dossiers of the chemicals showed that they are not mutagenic.

For none of the alternatives, mutagenic behavior was stated in the Danish EPA report (Maag et al., 2010; Nielsen & Larsen, 2014). That is why 'L-low' hazard score was assigned. For ASE, only *in vitro* studies were available that showed low mutagenicity that is why a low confidence score was assigned. DINA was assigned 'L-low' score based on structural analog study. For all the other chemicals, *in vitro* and *in vivo* studies were available in Danish EPA report to make a high confidence score.

Reproductive Toxicity:

DEHP, DBP and BBP are present on the EU - Annex VI CMRs (Reproductive Toxicity - Category 1B) due to which 'H-high' hazard score was assigned. They are present on many other authoritative and screening lists which are written in the Annex B attached at the end of this study.

The two generation reproductive toxicity study (TG OECD 416) was available for only COMGHA, DEHT and DINCH in the Danish EPA report. Recently, TG OECD 416 guideline study was added for ATBC, which was used to score ATBC in this study. For ASE and DINA, only one generation reproductive toxicity test (OECD 415) results were available that is why the confidence in the score is low. For DINA, the test was performed with a structural analog bis (2-ethylhexyl) adipate and the score 'M-moderate' was assigned in the Danish EPA because of NOAEL value of 170 mg/kg bw/day for parental toxicity. For DEHT, the NOAEL value for parental toxicity was 133-478 mg/kg bw/day for male and female rats which is in the 'M-moderate' range as per the criteria of GreenScreen (50-1000 mg/kg bw/day) (CPA, 2018).

Developmental Toxicity:

DEHP, DBP and BBP were scored ‘H-high’ as development toxicant due to their presence on Authoritative A list like CA EPA – Prop 65 (Development Toxicity) and as reproductive 1B EU GHS (H360FD/H360Df). All the other authoritative and screening lists on which they were present are detailed in the attached Annex B.

The studies for development toxicity for the alternatives did not warrant high development toxicity score except DINA which showed high score due to NOAEL value of 28 mg/kg-bw/day. For any chemical to be ‘H-high’ development toxicant the NOAEL value should be less than 50 mg/kg-bw/day and for ‘M-moderate’ score this value should be between 50 to 1000 mg/kg-bw/day (CPA, 2018). The confidence in the data is low because the result was read-across from bis (2-ethylhexyl) adipate, a structural analog of DINA. ATBC was scored ‘M-moderate’ due to NOAEL value of 50 mg/kg bw/ day for maternal toxicity and was assigned moderate effect score in Danish EPA report as well (Nielsen & Larsen, 2014). This was not a guideline study and was given a Klimisch score of 2 that is why this is a low confidence score. It is highly recommended that guideline development toxicity study for DINA and ATBC should be carried out in the future for high confidence data.

Endocrine Disruption:

DEHP, DBP and BBP were scored high as endocrine disruptors due to the presence on Authoritative A list EU – SVHC Authorization List (Equivalent Concern – Candidate List: endocrine disrupting properties cause probable serious effects to the environment or human health).

Except COMGHA and DINCH, complete studies for alternatives were not available to score them for endocrine disruption in the Danish EPA report as well as ECHA registration Dossiers. That is why a ‘data gap’ score was assigned. ToxServices (2016a) carried out a GreenScreen assessment for DINCH and stated moderate effects on thyroid could be seen as well as anti-androgenic effects

because of DINCH that is why it was scored ‘M-moderate’ as per their assessment. The ‘M-moderate’ score has been assigned for DINCH in this study as well.

B) Group II and Group II* Human Hazard Endpoints

Acute Mammalian Toxicity:

The phthalates as well as all the alternatives scored low for acute toxicity hazard endpoint. All the evaluated chemicals were assigned ‘L-low’ hazard score for acute mammalian toxicity because the acute toxicity values were greater than 2000 mg/kg for oral dose which makes it in ‘L-low’ score range as per the GreenScreen criteria (CPA, 2018).

Systemic Toxicity (Single Dose):

DEHP is found as harmful to human target organs and is found in GHS New Zealand and Japan and as per guideline study found in ECHA registration dossier it can cause liver weight changes and lesions that is why ‘H-high’ score was assigned. DBP was given ‘M-moderate’ hazard score due to its presence on GHS Japan as a category 3 toxicant.

DEHT, DINA and DINCH showed no signs of systemic toxicity after gross pathology and necropsy studies, hence ‘L-low’ score was assigned. No necropsy and gross pathology studies were found for ASE, ATBC and COMGHA, that is why no hazard score could be assigned

Systemic Toxicity (Repeat Dose):

DEHP is found to be systemic toxicant for repeated exposure and is present as a category 2 chemical in GHS Japan and as per guideline study found in ECHA registration dossier it can cause liver damage at NOAEL 28.9 mg/kg bw/day that is why it was scored ‘M-moderate’ with high confidence. DBP and BBP were scored “H-high’ and ‘M-moderate’ respectively due to the presence on Screening A GHS Japan as category 1 and category 2, inhalation toxicants with H372 and H373 hazard statement codes respectively.

All the chemicals scored ‘L-low’ for the hazard endpoint except DINA and DINCH. DINCH was scored ‘M-moderate’ for the systemic toxicity repeated dosage in the Danish EPA report based on NOAEL 107.1 mg/kg bw/day for kidney weight changes, 40 mg/kg bw/day liver weight changes and 200 mg/kg bw/day for thyroid changes. For this study, ‘M-moderate’ score was assigned as well because a chemical to be moderately toxicant for systemic toxicity/ organ effects (repeated dosage) the NOAEL has to lie between 10-100 mg/kg bw/day as per GreenScreen criteria (CPA, 2018). The confidence in the data is low because a GreenScreen hazard assessment by ToxServices (2016a) scored it low for systemic toxicity citing the problems arising from previous studies were not because of DINCH. DINA was also assigned ‘M-moderate’ score due to a low confidence read across guideline study of DEHA, a structural analog, in the Danish EPA report (Nielsen & Larsen, 2014).

Neurotoxicity (Single and repeated dose):

Most of the chemicals lacked data for single dose neurotoxicity except DEHP, DEHT and DINCH. The three chemicals stated were assigned ‘L-low’ hazard score for single dose neurotoxicity.

Neurotoxicity is studied by observing neural functions and cage behavior of the target species and is incorporated in the guideline studies for other hazard endpoints like carcinogenicity, reproductive toxicity or acute and chronic dosage studies. ‘L-low’ score was assigned for all the chemicals which had available repeated dosage neurotoxicity studies available in ECHA registration dossiers. ATBC, DEHT and DINA were assigned a ‘DG-data gap’ due to absence of pertinent studies.

Skin Sensitization:

Out of all the chemicals evaluated in this study only DBP had ‘H-high’ score as skin sensitizer due to its presence on the GHS Japan Skin sensitizer category 1 (H317). All the other chemicals were deemed not to be skin sensitizers and assigned ‘L-low’ hazard score.

Respiratory Sensitization:

Most of the chemicals were missing data regarding the respiratory sensitization hazard endpoint that is why 'DG-data gap' was assigned. Data for DEHP, DEHT and DINCH from registration dossiers showed that they are not respiratory sensitizers due to absence of respiratory sensitizing functional groups.

Skin Irritation:

Apart from DINCH, all the chemicals evaluated showed no sign of being a skin irritant that is why 'L-low' score was assigned. DINCH was classified as category 3 skin irritant as per GHS criteria due to persistent erythema for 48 hours in rabbits and given a 'M-moderate' hazard score as per GreenScreen criteria (CPA, 2018).

Eye Irritation:

None of the chemicals were classified as eye irritants and 'L-low' score was assigned for all of them.

C) Ecotoxicity

Acute Aquatic Toxicity:

DBP and BBP were assigned 'VH-very high' score due to presence on EU-GHS (H Statements) as very toxic to aquatic life (H400) and all other chemicals were scored low for acute aquatic toxicity. Most of them were assigned 'L-low' score based on no effects expected at saturation level due to low solubility of the chemicals as per Danish EPA report (Nielsen & Larsen, 2014).

Chronic Aquatic Toxicity:

DBP and BBP were assigned 'H-high' hazard score based on the presence on studies reported in ECHA registration dossiers. The NOEC for chronic toxicity lied in the range of 0.1-10 mg/L for both chemicals which is in the 'H-High' range as per GreenScreen criteria (CPA, 2018).

ATBC was assigned a 'M-moderate' score as per the study in Danish EPA report which states a no observed effect concentration (NOEC) value of 1.11 mg/L in Daphnia magna (Nielsen & Larsen, 2014). As per the GreenScreen criteria

moderate score is assigned when (NOEC) value is >1-10 mg/L (CPA, 2018). Other alternatives were assigned 'L-low' score for chronic toxicity due to no effect expected at saturation level.

D) Fate

Persistence:

A chemical is termed 'readily biodegradable', if in any of the six methods permitted for the screening of ready biodegradability, the pass levels are reached within 10 days window in the OECD 301 test. The pass levels are 70% DOC removal, 60% ThOD or ThCO2 production for respirometric methods (OECD, 1992). Except ASE, ATBC and DINCH, all the chemicals were scored 'VL-very low' for persistence because of passing ready biodegradability test in the 10 day window. DINCH was deemed inherently biodegradable as per the Danish EPA report (Nielsen & Larsen, 2014). 'M-moderate' score was assigned because the half-life of the chemical was between 16 and 60 days in the soil or sediment compartment based on the extensive biodegradation studies carried out in (ToxServices, 2016a). ATBC was assigned 'M-moderate', because it was termed inherently biodegradable in the Danish EPA report (Nielsen & Larsen, 2014). 60% degradation of ASE was achieved after 47 days. It was assigned 'M-moderate' score as per the GreenScreen criteria (CPA, 2018).

Bioaccumulation Potential:

The bioaccumulation potential was comparatively evaluated by bioconcentration factor (BCF) values. DEHP was assigned a 'M-moderate' score due to BCF value of 614 L/kg-ww in a guideline study in the ECHA registration dossier. This is because as per GreenScreen criteria, if the BCF value is between 500 and 1000, the chemical is deemed bioaccumulative (CPA, 2018). All the alternatives except COMGHA scored 'L-low' for bioaccumulation potential due to BCF score being lower than 500. COMGHA scored 'M-moderate' for bioaccumulative potential due to BCF=981 L/kg-ww in OECD guideline 305 study in Danish EPA.

E) Physical Hazards

Reactivity:

None of the chemicals contained functional groups that could be oxidized or had any explosive characteristics and none of them were GHS classified for reactivity.The confidence in the score was low due to absence of experimental data as it was based on expert judgment.

Flammability:

All the chemicals had a flashpoint above 93°C which is a cut-off point for liquids to be flammable that is why a low score was designated to all the chemicals.

Benchmark Scores

The benchmark scores were assigned as per the 'Benchmark score criteria for organic chemical' provided in Figure 3.2 in Chapter 3. A summary of the benchmark scores assigned for each chemical is provided below. Despite presence of data gaps, all chemicals could be assigned a benchmark score. Results from single and repeated exposures are not considered as separate endpoints but rather sub-endpoints, therefore, a benchmark score was also assigned to ATBC and DINA by not counting 2 data gaps for neurotoxicity (single and repeated) as separate, as per the GreenScreen criteria (CPA, 2018).

Chemicals of Concern:

DEHP: Benchmark 1e: High toxicity (Group I Human)

DBP: Benchmark 1e: High toxicity (Group I Human)

BBP: Benchmark 1e: High toxicity (Group I Human)

Alternatives:

ASE: Benchmark 2e: Moderate toxicity (Group I Human)

ATBC: Benchmark 2e: Moderate toxicity (Group I Human)

COMGHA: Benchmark 3a: Moderate bioaccumulation

DEHT: Benchmark 2e: Moderate toxicity (Group I Human)

DINA: Benchmark 1e: High toxicity (Group I Human)

DINCH: Benchmark 2e: Moderate toxicity (Group I Human)

4.2.3 Exposure Assessment

4.2.3.1 Environmental Exposure Assessment using the EQC Model

Environmental fate of phthalates (DEHP, DBE and BBP) and the alternative chemicals which are proposed to replace them are comparatively evaluated in a generic environment of the EQC model. This evaluation will provide insight into the fate and transport of the chemicals involved. The results of this will help in determining the persistency of the chemicals, environmental compartments of concern and what should be the focus of efforts in eradicating the concern. COMGHA could not be included in the fate evaluation due to unavailability of required information like environmental degradation half-lives. Table 4.7 shows the final adjusted values (as per thermodynamic consistency check) of physicochemical properties of the chemicals. Please see Annex C for a complete list of sources for each property in the table and the least square method followed for thermodynamic consistency check of physicochemical input properties used in the EQC model.

In the study of Cousins et al. (2003), half-lives for DEHP, DBP and BBP were assigned by using a semi-decade logarithmic scale to take into account the large uncertainty in measured biodegradation half-lives. Although DEHP, DBP and BBP readily passed the biodegradability tests and were assigned a ‘VL-very low’ score in CHA conducted in this study, in environmental exposure assessment the picture was different due to conservative half-lives for water, soil and sediment compartment.

Table 4.7. Physicochemical properties of the phthalates and their alternatives used in EQC model.

Chemical Name	**Melting Point (°C)**	**Vapor Pressure (Pa)**	**Solubility (g/m3)**	**Henrys law Constant (Pa-m^3/mol)**	**log Kow**	**Koc**	**Environmental Half Lives (h)**			
							Air	**Water**	**Soil**	**Sediment**
DEHP	-55	2.68E-05	2.01E-01	5.21E-02	7.3	8.2E+06	17.0	550	5500	5500
DBP	-35	3.94E-03	7.62E+00	1.44E-01	4.45	1.1E+04	55	170	1700	5500
BBP	-35	9.14E-04	3.24E+00	8.82E-02	4.54	1.4E+04	17	55	1700	1700
ASE	-150	3.66E-04	1.80E+00	7.48E-02	7.7	2.0E+07	6.23	360	720	3240
ATBC	-80	1.44E-04	6.65E+00	8.73E-03	5.1	5.1E+04	17.8	209	416	1870
DEHT	-55	2.40E-05	2.13E-01	4.40E-02	7.4	9.6E+06	11.7	360	720	3240
DINA	-68	3.39E-07	1.89E-03	7.16E-02	9.1	5.6E+08	9.58	360	720	3240
DINCH	-54	3.69E-05	1.10E-02	1.42E+00	9.6	1.6E+09	8.36	900	1800	8100

For example, Cousins et al., (2003) argues that the conservative approach in assigning half-lives is appropriate and necessary because experimental biodegradation tests are carried out at 25˚C, whereas environmental temperatures are much lower and the use of acclimated inoculum can also alter the results from un-acclimated ones. Some studies can also not differentiate the degradation losses from partitioning into the sediments or volatilization.

Keeping in view of the argument, the EEA in this study will show a different picture to the one in persistence hazard endpoint of CHA. The CHA scores were based on ready biodegradability or inherent biodegradability tests, whereas the EEA in this study tried to give a more complete picture, an overall evaluation via investigating the effect of mode of entry of the chemicals into the different compartments. The sensitivity analysis underlines the effect of physicochemical data and the impact it has on the overall persistence (P_{ov}) of the chemical in the modeling studies by incremental change of the data.

Each chemical was run through the EQC model separately (Mackay et al., 1996b), then results are evaluated comparatively. In addition, results for each level of the EQC model, i.e. Levels I, II and III are discussed separately in the following subsection.

Level I:

Table 4.8 indicates the partitioning of chemicals into different compartments at equilibrium condition and steady state. All chemicals are predicted to partition into the soil compartment by 94-98%. This high partitioning into the soil phase can be explained by the relatively high log K_{OW} and K_{OC} values associated with the chemicals. DBP and BBP can partition into the water compartment (i.e., 4% and 3%, respectively) due to their comparatively lower K_{OW} values than the other evaluated chemicals. Amongst the proposed alternative chemicals, only ATBC can partition into the water compartment (0.9%). All the chemicals of concern and alternatives at equilibrium condition partition into the sediment compartment to about 2-2.2 %. Only DBP partitions into the air compartment (0.1%).

Level II:

Level II results show the same chemical partitioning percentages as those of Level I, but degrading reactions are included. Accordingly, reaction in soil is the dominating loss process for all chemicals. In DBP and BBP, it's 64% and 46%, respectively, other than that in DEHP its 97.4%. Amongst the proposed alternatives, the reaction in soil is the primary loss mechanism and is nearly 99.5% in all apart from ATBC, which is 97%. DBP and BBP can also be lost via advection in water by 6.2% and 3.6%. Advection in air is a loss mechanism in DBP (1.8%) and BBP (0.6%) which can be a cause of concern. Due to very low vapor pressure and greater affinity to soil, the proposed alternatives don't have a long range transport potential (LRTP).

Table 4.8. Percentage distribution and persistence at Level I and II of EQC model.

Compartment	DEHP	DBP	BBP	ASE	ATBC	DEHT	DINA	DINCH
Percentage distribution at Level I and Level II								
Air	0	0.1	0	0	0	0	0	0
Water	0	4	3	0	0.9	0	0	0
Soil	98	94	95	97.8	97	97.8	97.8	97.8
Sediment	2	2	2	2.2	2.1	2.2	2.2	2.2
Suspended Solid	0	0	0	0	0	0	0	0
Fish	0	0	0	0	0	0	0	0
Level II Percentage Loss by								
Advection in air	0	1.8	0.6	0	0	0	0	0
Reaction in air	0	2.3	2.6	0	0	0	0	0
Reaction in soil	97.4	64	46	99.5	97.2	99.5	99.5	99.4
Adv. in water	0	6.2	3.6	0	0.5	0	0	0
Reaction in water	0	25	46	0	1.7	0	0	0
Adv. in sediment	0.34	0	0	0	0	0	0	0.1
React.in sediment	2.1	0.4	1	0.5	0.5	0.5	0.5	0.5
Persistence (Days)								
Overall	329	69	50	44	25	44	44	110
Reaction	331	76	52	44	25	44	44	110
Advection	84,100	858	1,148	90,700	4,492	85,830	95,700	95,670

At equilibrium condition, the P_{ov} of DEHP, DBP and BBP are 329, 69 and 50 days respectively. All the proposed alternatives have persistence less than the phthalates, apart from DINCH which has a P_{ov} of 110 days. The high environmental persistence in DINCH can be of concern due to its partitioning into the soil compartment majorly because there will be a year to year carry over. On the other hand, that does not necessarily mean high exposure to human and wildlife as the

chemical will be largely soil bound. It may not be expected to enter the food chain due to relatively low bioavailability which can also be evidenced by the low bioaccumulation score in the CHA Table 4.6. Table 4.8 shows a detailed summary of the results obtained from level I and II calculations. The P_{ov} is closer to the reaction persistence due to the presence of the chemicals abundantly in the soil phase and the advection losses playing a negligible role.

Level III:

Due to the inclusion of intermedia transport processes and non-equilibrium steady state condition, level III results are regarded as the most relevant (Palm et al., 2002). As shown in Table 4.9, the chemical partitioning into the compartments is different from level I and II due to the inclusion of intermedia transport processes and that there is no longer equilibrium.

The mode of entry, that is the media into which the chemical is introduced, plays an important role in the P_{ov} and the compartment into which the chemical resides most. In order to comparatively evaluate level III calculations, 1000 kg/h of chemical was emitted individually into air, water and soil compartment. In the last simulation the chemical was emitted into air, water and soil compartment simultaneously at 1000 kg/h. Table 4.9 shows the environmental mass distribution of the chemicals in the different compartments, the total mass and the P_{ov}.

Mode of Entry

In the study of Cousins et al (2003), it was concluded that the majority of the phthalates are released to the atmospheric environment from product end use. In the study of Greggs et al (2019), the ecological exposure for the phthalates used in toys and childcare articles was deemed as disposal in landfill and incineration.

In this study, fate and P_{ov} were evaluated by simulating the entry of the chemicals into atmosphere (air), soil, water separately. In addition to these scenarios, simultaneous emissions of 1000 kg/h to the air, water and soil compartment was also carried out to comparatively evaluate the phthalates and the proposed alternatives.

Table 4.9. EQC model Level III results.

Chemical	Emission Medium	In air (kg)	In air (%)	In water (kg)	In water (%)	In soil (kg)	In soil (%)	In sediment (kg)	In sed. (%)	Total Amount (kg)	Persistence (d)
DEHP	Air	1.31E+04	0.5	5.74E+03	0.22	2.38E+06	93.4	1.49E+05	5.8	2.5E+06	106
	Water	0	0	1.65E+05	3.7	0	0	4.29E+06	96.3	4.5E+06	186
	Soil	0	0	0	0	7.93E+06	100	0	0	7.9E+06	331
	All three	0	0	1.71E+05	1.2	1.03E+07	69	4.46E+06	29.7	1.5E+07	207
DBP	Air	3.88E+04	13.8	5.58E+03	2	2.34E+05	83.2	2.90E+03	1	2.8E+05	12
	Water	0	0	1.94E+05	65.7	6.40E+02	0.2	1.00E+05	34.1	2.9E+05	12
	Soil	0	0	0	0	2.45E+06	100	0	0	2.5E+06	102
	All three	3.89E+04	1.3	2.00E+05	6.60	2.68E+06	88.7	1.04E+05	3.4	3.0E+06	42
BBP	Air	1.74E+04	6.8	1.33E+03	0.5	2.39E+05	92.6	3.23E+02	0.1	2.6E+06	11
	Water	0	0	7.29E+04	80.3	1.51E+02	0.2	1.77E+04	19.5	9.1E+04	4
	Soil	0	0	0	0	2.45E+06	100	0	0	2.5E+06	102
	All three	1.74E+04	0.6	7.44E+04	2.66	2.7E+06	96.1	1.81E+04	0.6	2.8E+06	39
ASE	Air	7.35E+03	7.1	1.42E+03	1.37	6.98E+04	67.3	2.52E+04	24.3	1.0E+05	4
	Water	0	0	1.42E+05	5.35	0	0	2.50E+06	94.6	2.6E+06	110
	Soil	0	0	0	0	1.04E+06	100	0	0	1.0E+06	43
	All three	7.35E+03	0.2	1.43E+05	3.8	1.11E+06	29.3	2.53E+06	66.8	3.8E+06	53
ATBC	Air	1.27E+04	5.4	8.69E+03	3.7	2.06E+05	87.8	7.62E+03	3.2	2.4E+05	10
	Water	0	0	2.15E+05	53.3	0	0	1.88E+05	46.7	4.0E+05	17
	Soil	0	0	0	0	6.0E+05	100	0	0	6.0E+05	25
	All three	1.27E+04	1	2.23E+05	18	8.07E+05	65.1	1.96E+05	15.8	1.2E+06	17
DEHT	Air	1.07E+04	3.1	4.13E+03	1.20	2.59E+05	75.3	7.04E+04	20.4	3.5E+05	14
	Water	0	0	1.45E+05	5.5	0	0	2.47E+06	94.5	2.6E+06	109
	Soil	0	0	0	0	1.04E+06	100	0	0	1.0E+06	43
	All three	1.07E+04	0.3	1.49E+05	3.7	1.30E+06	32.5	2.54E+06	63.5	4.0E+06	55
DINA	Air	9.16E+03	2.70	3.81E+03	1.1	2.56E+05	75.6	6.97E+04	20.6	3.4E+05	14
	Water	0	0	1.39E+05	5.2	0	0	2.54E+06	94.8	2.7E+06	111
	Soil	0	0	0	0	1.04E+06	100	0	0	1.0E+06	43
	All three	9.16E+03	0.2	1.43E+05	3.5	1.30E+06	32	2.6E+06	64.3	4.0E+06	56
DINCH	Air	8.35E+03	1.4	3.6E+03	0.6	4.5E+05	75.8	1.3E+05	22.2	5.9E+05	25
	Water	0	0	1.8E+05	2.6	0	0	6.5E+06	97.4	6.7E+06	278
	Soil	0	0	0	0	2.60E+06	100	0	0	2.6E+06	108
	All three	0	0	1.80E+05	1.8	3.05E+06	30.8	6.64E+06	67.3	9.9E+06	137

The results show that the fate and the P_{ov} of the chemicals depend highly on the mode of entry. That is why it is pertinent to discuss the effect of the mode of entry separately. Detailed EQC model outputs are presented in Annex D.

Air Compartment:

When a chemical is emitted into the air compartment only, it can be clearly seen that all the chemicals are predicted to be deposited into the soil compartment from air at a much larger percentage. This is due to the large K_{oc} and K_{ow} values as well as long half-lives in soil.

The higher persistence of DEHP is evident from Figure 4.1(a) which clearly shows that much larger mass (2.38E+06 kg) is predicted to reside in the soil compartment. All the alternatives are partitioned into the air compartment albeit at a lower quantity than soil compartment. ASE and ATBC contain 7.1 % (7.35E+03kg) and 5.4% (1.27E+04 kg) in the air compartment whereas DEHT, DINA and DINCH are 3.1%, 2.7% and 1.4% respectively partitioned into the air compartment. DEHT, DINA and DINCH also partition into the sediment compartment 20.4%, 20.6% and 22.2% respectively. It can be seen by comparing the physicochemical properties that DEHP and DEHT have similar K_{oc} and K_{ow} values but larger soil half-life value that is why DEHP has a very larger P_{ov} than DEHT. Figure 4.1(b) shows the P_{ov} of the chemicals when the mode of entry is air and DEHP show the largest P_{ov}. Amongst the alternatives, DINCH has largest P_{ov}. This can be explained because DINCH has the largest $K_{ow,}$ K_{oc} as well as the largest soil and sedimentation half-lives amongst the alternatives.

The primary loss mechanisms in all the chemicals evaluated was reaction in air. Reaction in soil was the secondary loss mechanism for DEHP, ATBC, DEHT, DINA and DINCH. From air, the chemicals were mainly deposited in the soil compartment. In case of DEHP, DEHT, DINA and DINCH, the intermedia transfer from water to sediment compartment was also of importance.

Advection in air was the secondary loss mechanism for DBP, BBP and ASE accounting for 39%, 17.4% and 7.4% of the total losses. Amongst the alternatives, the lowest overall persistence belongs to ASE and ATBC, with P_{ov} values of 4 and 10 days respectively.

Overall, if all chemicals are emitted in the air compartment, it can be said that all alternatives have an overall persistence significantly lower than that of DEHP, yet, only alternatives ASE and ATBC have P_{ov} smaller than DBP and BBP. The rest of the alternatives all have comparable or even higher overall persistence (i.e., DINCH) when compared to those of DBP and BBP. In the study by Cousins et al., (2003), P_{ov} values of 100, 12 and 5.4 days were obtained in the EQC model when the mode of entry was air only. In this study, closer P_{ov} values of 106, 12 and 11 days were seen for DEHP, DBP and BBP respectively to the values seen in (Cousins et al., 2003).

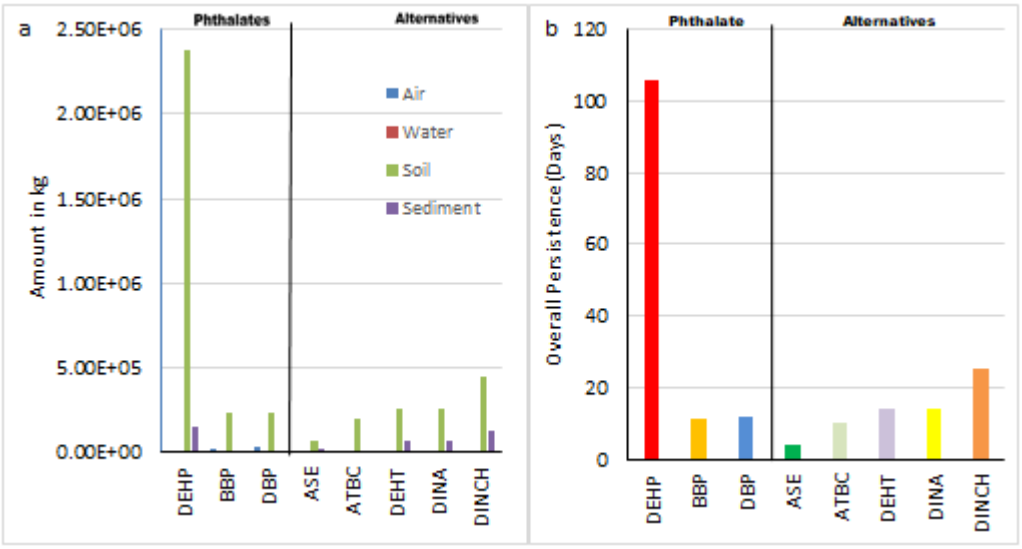

Figure 4.1. (a) Amount (kg) of each chemical in different environment compartments when mode of entry is air only. (b) P_{ov} (days) when mode of entry is air only.

Water Compartment Only:

It can be deduced from Figure 4.2(a) that when the chemicals are emitted in the water compartment, all the alternatives, except ATBC end up accumulating in the sediment. A similar behavior is observed for DEHP among the phthalates. As the half-lives in sediment are typically large, this partitioning ends up increasing the persistence of these alternatives. For example, the highest overall persistence is for DINCH with 278 days (Figure 4.2(b)), owing to it having the largest K_{ow}, K_{oc} as

well as the sediment half-life. It can be seen that discharging the above mentioned chemicals into the water compartment can be dangerous because they persist in the benthic sediment compartment for a very long duration.

ATBC, DBP and BBP show much lower P_{ov} due to smaller K_{ow}, K_{oc} values. The major loss mechanism for DBP, BBP and ATBC were the reaction in water followed by advection in water and the transfer to the sediment compartment was negligible. For all the other chemicals evaluated the reaction in sediment was the primary loss mechanism and the intermedia transfer from water to sediment compartment played a major role in abundance of the chemicals in the benthic sediment compartment.

In the study by Cousins et al., (2003), P_{ov} values of 190, 11 and 4 days were obtained in the EQC model, when the mode of entry was water only. In this study, closer P_{ov} values of 186, 12 and 4 days were seen for DEHP, DBP and BBP, respectively, which are very similar to the ones of Cousins et al. (2003).

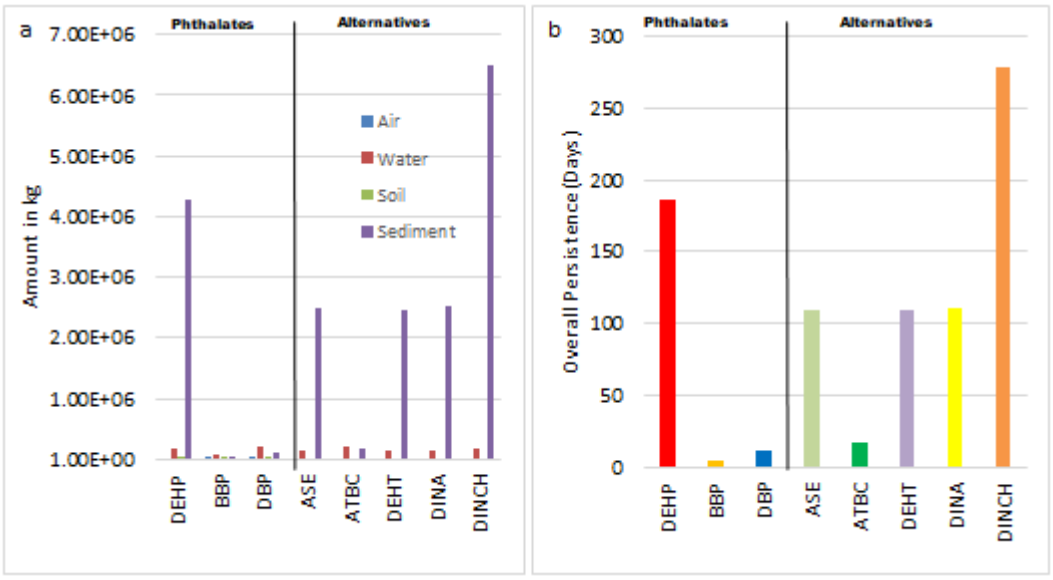

Figure 4.2. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is water only. (b) P_{ov} (days) when mode of entry is water compartment only.

Soil Compartment Only:

When a chemical is emitted totally into soil, this compartment ends up being the one in which all chemicals reside. It can be clearly seen from Figure 4.3(a) that DEHP emission into soil causes a much higher abundance of DEHP in soil (7.93E+06 kg), when compared to other chemicals due to the highest soil half-life when compared to all others (i.e. 5500 h when compared to 720-1800 h for all others, as given in Table 4.7. DBP and BBP also show P_{ov} of 102 days when emitted to soil only, which is a cause of concern (Figure 4.3(b)).

The persistence of all alternatives, except DINCH, are much less than the phthalates. This can be explained by lower soil half-lives of these alternatives.

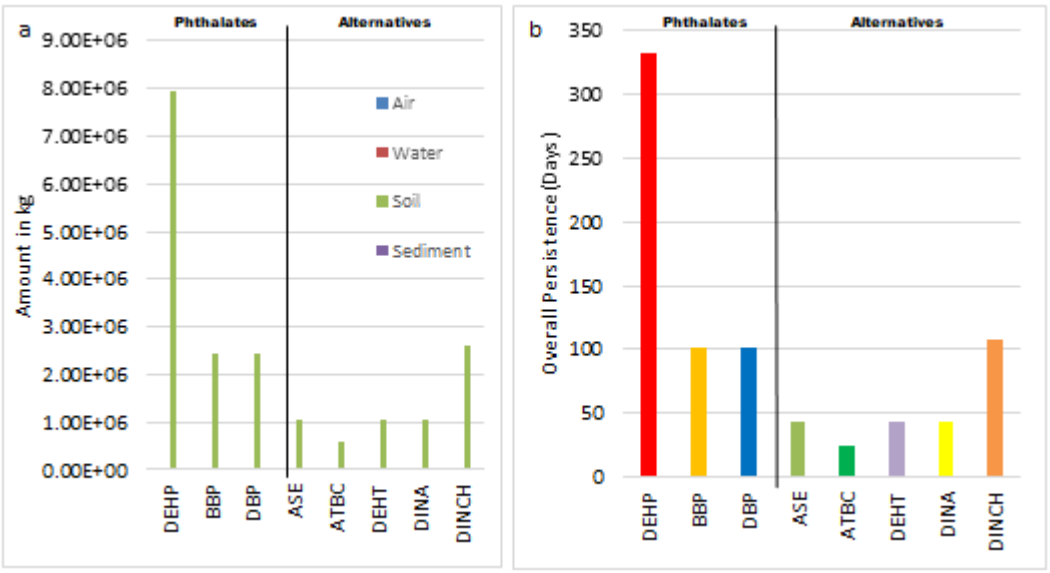

Figure 4.3. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is soil only. (b) P_{ov} (days) when mode of entry is soil compartment only.

Although BBP and DBP have less K_{oc} values than all the alternatives, the soil half-life (1700 h) is more than double the half-life values of all the alternatives except DINCH which has soil half-life of 1800 h and shows persistence values similar to BBP and DBP. This shows that the soil half-life is the governing parameter when it comes to the evaluated chemicals discharged into the soil compartment only.

The primary loss mechanism for all the chemicals evaluated was reaction in soil and no transfer of chemical into any other medium occurred due to strong tendency of sorption to soil and no migration potential. In the study by Cousins et al., (2003), P_{ov} values of 330, 100 and 100 days were obtained in the EQC model when the mode of entry was soil only. In this study, closer P_{ov} values of 331, 102 and 102 days were obtained for DEHP, DBP and BBP, respectively, which are very similar to the ones of Cousins et al. (2003).

All three compartments equally:

Figure 4.4(a) shows the amount (kg) of the chemical in different environmental compartments while Figure 4.4(b) shows the P_{ov} of the phthalates and the proposed alternatives. As can be seen from the figure, when chemicals are emitted into all three compartments at equal rate of 1000 kg/h, soil is the major compartment into which the phthalates reside.

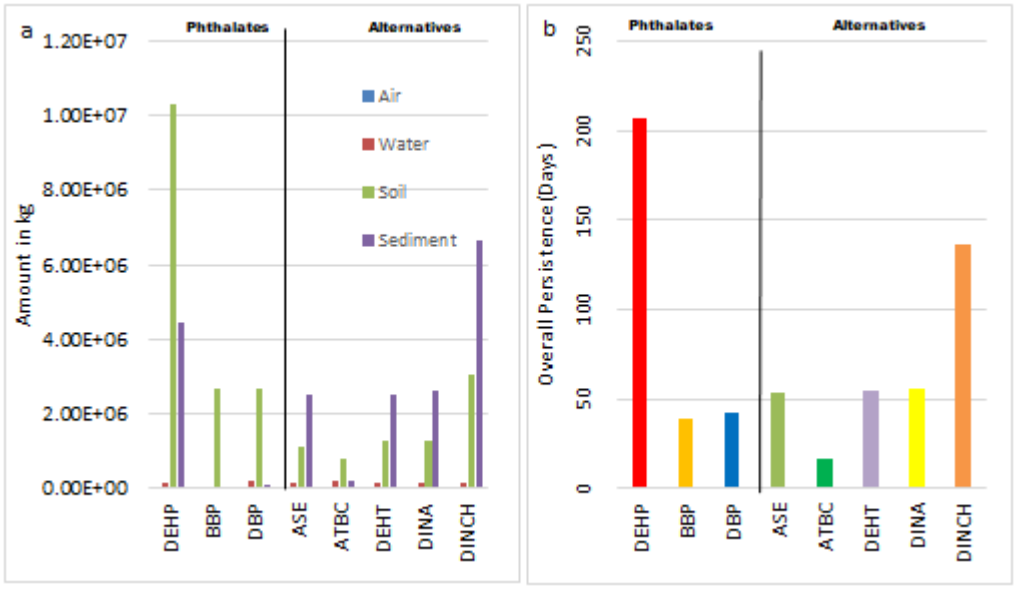

Figure 4.4. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is air, water and soil compartment simultaneously at 1000 kg/h (b) P_{ov} (days) when mode of entry is air, water and soil compartments simultaneously at 1000 kg/h.

The largest amount can be seen in the case of DEHP (1.03E+07 kg) which is almost an order of magnitude larger than all the chemicals evaluated. DEHP has also shown the propensity to be deposited from air to soil compartment mainly.

In case of alternatives, it can be seen from Figure 4.4(a), for ASE, DEHT, DINA and DINCH the major compartment of concern is the sediment compartment where the chemicals reside 67, 63.5, 64 and 67% respectively. This can be explained from the large K_{ow}, K_{oc} values as well as large sediment half-life values. DINCH having the largest sediment half-life shows the largest P_{ov}.

Although DEHP has larger sediment half-life than DEHT and DINA, its larger soil half-life plays a bigger role resulting in a much larger P_{ov} for DEHP. ASE, DEHT and DINA show similar P_{ov} which can be explained by same soil and sediment half-lives. The comparative P_{ov} of all the chemicals can be seen from Figure 4.4(b).

The primary loss mechanism for DBP, BBP and ATBC was the reaction in soil followed by the reaction in water. From air, the above mentioned chemicals were mainly deposited into the soil phase. The intermedia transfer from water to sediment compartment was small.

For DEHP, reaction in soil was primary loss mechanism (43%) followed by reaction in sediment (19%) of the total losses. Reaction in air accounted for 18% of the total losses for DEHP. For ASE, DEHT, DINA and DINCH reaction in soil was the primary loss mechanism followed by reaction in air. Reaction in sediment also accounted for 18-20 % of all losses. The major deposition occurred from the water to the sediment compartment for these chemicals and in case of DINCH it was maximum (834 kg/h). No intermedia transfer of the chemicals occurred from soil compartment.

Overall, when introduced into three compartments simultaneously, only ATBC seems to perform better as a potential alternative to the phthalates. Although DEHP is definitely the most persistent among all, the persistence of alternatives – except perhaps ATBC- are not necessarily much smaller when compared to DBP or BBP.

In the study by Cousins et al., (2003), P_{ov} values of 210, 42 and 37 days were obtained in the EQC model when the mode of entry was air, water and soil

simultaneously. In this study, very similar P_{ov} values 207, 42 and 39 days were seen for DEHP, DBP and BBP, respectively.

Sensitivity Analysis:

During sensitivity analysis, the mode of entry for the analysis was taken as the chemical entering simultaneously air, water and soil at 1000 kg/h. As it can be seen from the Table 4.10 below, DEHP, DBP and BBP, the P_{ov} is majorly affected by soil half-life which makes it the most sensitive parameter. For DEHP half-life in sediment is also a sensitive parameter. It can be seen from Table 4.10 that by doubling the log K_{ow} the P_{ov} of DBP increases by 98% whereas in BBP it only increases by 20%. This can be explained by the relatively more DBP in the water compartment as well as the sediment compartment than BBP due to larger water and sediment half-life than BBP. Thus by increasing K_{ow} more DBP will move into the sediment phase and hence the P_{ov} will be more than BBP.

Amongst the alternatives, for ASE and ATBC, all the half-life values of the different compartments are sensitive. ASE, DEHT, DINA and DINCH have a propensity to be deposited in the sediment which can be explained by the sensitivity of half-life of sediment compartment and log K_{ow} on the persistence on these chemicals. By decreasing the sediment half-life the persistence of the above mentioned chemicals decreases. Interestingly by increasing the log K_{ow} of the above mentioned chemicals we can see no major change in the P_{ov}. This can be explained by the already very large K_{ow}. It can be observed that the chemicals having log K_{ow} values greater than 7 showed very little or no effect when log K_{ow} was increased. But when the log K_{ow} value was halved then the P_{ov} of the chemicals was greatly reduced. This phenomenon can also be explained for DBP, BBP and ATBC which had lower log K_{ow} values (4.45, 4.54 and 5.1 respectively). When the log K_{ow} was increased for these chemicals the persistence value increased much more in comparison to what was observed in DEHP, ASE, DEHT, DINA and DINCH.

Table 4.10. Sensitivity analysis results (% difference impact on persistence upon 100% change in physicochemical properties).

Modified Input	DEHP		DBP		BBP		ASE		ATBC		DEHT		DINA		DINCH	
	100%	-100%	100%	-100%	100%	-100%	100%	-100%	100%	-100%	100%	-100%	100%	-100%	100%	-100%
Melting Point	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vapor Pressure	-1	1	-1	2	-2	3	-1	1	0	0	-1	0	0	0	-1	1
Solubility	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Henrys Law Cont.	0	0	-2	4	-2	3	0	1	-3	5	0	0	0	0	0	0
Half Life (Air)	6	-6	3	-3	5	-4	2	-1	6	-6	4	-3	4	-3	3	-3
Half Life (Water)	4	-5	7	-4	3	-2	11	-15	19	-14	11	-15	11	-14	5	-8
Half Life (Soil)	69	-35	88	-44	96	-48	29	-15	65	-33	33	-16	32	-16	31	-15
Half Life (Sediment)	21	-13	2	-1	1	0	53	-31	13	-8	50	-30	52	-30	42	-29
Log K_{ow}	1	-31	98	-25	20	-24	1	-61	84	-16	2	-58	0	-56	0	-56

But when the log K_{ow} values of DBP, BBP and ATBC was halved the persistence value decreased but this decrease was almost half in effect to what was observed for ASE, DINA and DINCH. K_{ow} values for the chemicals used in this study are all from reliable experimental work except ASE which was estimated by EPI Suite. Although informative, the sensitivity analysis for logKow is not realistic since values are reliable and not expected to change much. For ASE, there is a possibility for change in log K_{ow} value and hence a change in the P_{ov} because log K_{ow} is estimated.

One purpose of sensitivity check is to identify the most critical parameters for persistence and fate evaluations. It is obvious from all EQC model outputs (at all levels) that soil is an important compartment for which phthalates and their alternatives partition in. Subsequently, half-life in soil is the most influential parameter on persistence. Use of realistic, reliable, experimental rather than predicted half-life information in soil (and in sediment, for especially the alternatives) would enable more realistic and accurate evaluations to be made.

EEA Summary:

In the study of Cousins et al (2003), it was concluded that the majority of the phthalates are released to the atmospheric environment from product end use. In the study of Greggs et al (2019), the ecological exposure for the phthalates used in toys and childcare articles was deemed as disposal in landfill and incineration. The EEA summary (Table 4.11) below compares the highest scoring phthalate i.e. BBP with the proposed alternatives when the mode of entry is atmosphere and soil. The overall score (last row) indicates the overall assessment after both the mode of entries (air and soil) are assessed. DBP was provided an overall score of blue because its P_{ov} in air is only 1 day more than BBP whereas its P_{ov} in soil is equal to BBP.

The comparative summary matrix shows that amongst the phthalates, BBP was the highest scoring phthalate as per P_{ov} in relevant mode of entries in air and soil. As can be seen from the table, DEHP was the worst performing phthalate. Amongst the proposed alternatives, ASE and ATBC showed less persistence in

comparison to BBP in air and soil mode of entries. DEHT and DINA showed more persistence when emitted in air, but their soil persistence is lower than BBP. DINCH showed more persistence than BBP in both air and soil mode of entries.

Table 4.11. EEA Summary (according to Pov for only relevant modes of entry).

	BBP	DEHP	DBP	ASE	ATBC	DEHT	DINA	DINCH
Air	11	106	12	4	10	14	14	25
Soil	102	331	102	43	25	43	43	108
Overall Score								

EEA Colour Indicator	
	Worse than the highest scoring phthalate (BBP)
	Better in one mode of entry & worse in one mode of entry than BBP
	Better than the highest scoring phthalate (BBP)

4.2.3.2 Qualitative Human Exposure Assessment:

The second type of exposure assessment used in this study, as a component of CAA, is QHEA. A qualitative human exposure was done for phthalates for the functional use in childrens' toys. Phthalates have a potential to migrate from PVC and can be a cause of concern because children have a tendency to put toys in their mouth (Greggs et al., 2019). Children can get exposed through ingestion, dermal absorption and inhalation because the chemicals are not bound to PVC (Little et al., 2012).

Similar to the study by Greggs et al. (2019), ingestion and dermal contact were assumed to be the most relevant exposure pathways for children playing with toys containing phthalates or alternatives in this study, and accordingly QHEA was carried out. Deductions in QHEA were made based on values of physicochemical parameters listed in Table 4.12, based on ECB (2003) guideline criteria presented in Material and Methods, Chapter 3. Physicochemical properties are taken directly from the literature, unlike the FDV used in the EQC model during EEA.

Table 4.12. Physicochemical properties of the chemicals evaluated as part of QHEA.

	DEHP	**DBP**	**BBP**	**ASE**	**ATBC**	**COMGHA**	**DEHT**	**DINA**	**DINCH**
Molecular Weight (g/mol)	390.56	278.3	312.37	368.58	402.49	943	390.57	398.63	424.67
Solubility (mg/L)	2.7E-01	1.1E+01	2.69	2.2	5	0.33	2.7E-01	0.0032	0.02
Log K_{OW}	7.6	4.5	4.7	8.2	4.9	6.4	7.6	9.6	10
Vapor Pressure (Pa)	2E-05	2.7E-03	1.1E-03	3E-04	6.07E-04	1.09E-07	1.9E-05	2.0E-07	2.2E-05
Extraction Potential (%)*	0.01	0.25	0.07	0.03	0.09	Much less than DEHP but value not given.	0.01	0.14	3 to 10 times lower than DEHP
Ingredient concentration in product**	1	1	1	DG	1	1	1.03	0.98	DG

* Data from Danish EPA report (Maag et al., 2010).

**Base concentration is DEHP. Data from Danish EPA report (Maag et al., 2010).

Table 4.13 gives the qualitative evaluation for oral ingestion exposure pathway as part of QHEA, while Table 4.14 gives that of dermal absorption.

Evaluation is based on the criteria of ECB (2003) guidelines such that physicochemical property of each chemical is compared with the ECB, (2003) recommended criteria, and assigned one of two colors: red if physicochemical property indicates higher exposure and green if it indicates lower exposure.

Table 4.13. Qualitative evaluation for oral ingestion exposure pathway as part of QHEA.

	DEHP	DBP	BBP	ASE	ATBC	COMGHA	DEHT	DINA	DINCH
Molecular Weight									
Solubility									
Log K_{OW}									
Systemic Toxicity									
Overall Score	**1/4**	**1/4**	**1/4**	**2/4**	**2/4**	**3/4**	**2/4**	**1/4**	**1/4**

	More exposure as per criteria
	Less exposure as per criteria

Table 4.14. Qualitative evaluation for dermal absorption exposure pathway as part of QHEA.

	DEHP	DBP	BBP	ASE	ATBC	COMGHA	DEHT	DINA	DINCH
Molecular Weight									
Solubility									
Log K_{OW}									
Vapor Pressure									
Skin Sensitization/Skin Irritation									
Overall Score	**4/5**	**1/5**	**2/5**	**3/5**	**2/5**	**4/5**	**4/5**	**4/5**	**3/5**

	More exposure as per criteria
	Less exposure as per criteria

Apart from criteria related to exposure pathways, three more parameters are also considered in this study as part of QHEA. These are: (i) Bioaccumulation, which is

an important indicator for human exposure regardless of the intake route, (ii) Extraction potential, which is used by Greggs et al. (2019) as an indicator affecting exposure, and (iii) Ingredient concentration in product, which is a parameter that has a direct impact exposure.

Accordingly, Table 4.15 gives a combined overall summary for the QHEA for comparison of phthalates with the alternative chemicals from the perspective of human exposure. In the summary matrix (Table 4.15), this time alternatives are evaluated compared to the "highest scoring phthalate" in terms of human exposure, which was DEHP in this case.

Table 4.15. Comparative summary matrix for QHEA.

Pathway/Criteria	DEHP	DBP	BBP	ASE	ATBC	COMGHA	DEHT	DINA	DINCH
Oral Ingestion	1/4	1/4	1/4	2/4	2/4	3/4	2/4	1/4	1/4
Dermal Absorption	4/5	1/5	2/5	3/5	2/5	4/5	4/5	4/5	3/5
Bioaccumulation	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
Extraction Potential	1/1	0/1	0/1	0/1	0/1	1/1	1/1	0/1	1/1
Ingredient concentration in product	1/1	DG	DG	DG	1/1	1/1	0/1	1/1	DG
Overall Score	**7/12**	**2/12**	**3/12**	**5/12**	**5/12**	**9/12**	**7/12**	**6/12**	**5/12**

QHEA Colour Indicator	
	Exposure equal to the highest scoring phthalate (DEHP)
	Exposure less than the highest scoring phthalate (DEHP)
	Exposure more than the highest scoring phthalate (DEHP)

Overall score from oral ingestion (Table 4.13) and dermal absorption (Table 4.14) for each of the chemicals are carried over to this overall summary table as the first and second rows. In addition, the three aforementioned indicators of exposure are added as extra rows. Lastly, the total summed score for each chemical is compared with that of DEHP. A lower score indicates worse standing in terms of human exposure, i.e., the chemical shows a higher potential for human exposure. Those having a higher score means they are safer chemicals showing lower human exposure potential. The summary matrix shows that all the alternatives perform

better when compared to DBP and BBP, however, only two chemicals perform equal or better than DEHP in QHEA. In comparison to DEHP, COMGHA and DEHT shows promise in terms of having a lower human exposure potential.

4.2.4 Conclusion

In this section, evaluation for alternatives of three phthalates is presented on the basis of hazard, environmental exposure and human exposure assessments. The chemicals hazard assessment adopts benchmark criteria (as presented in Section 4.1.2 and assigns colors from red to green in order of preferability. The same coloring scheme chosen for the comparative EEA summary matrix (Table 4.11) and comparative QHEA summary matrix (Table 4.15) will be used for the conclusion table, i.e., Table 4.16. As can be seen from these tables and the above discussions under each subsection, some of the properties of alternatives that are disadvantageous for environmental exposure (such as high logKow leading to partitioning into soil which has much higher degradation half-lives) leading to high persistence for chemical may be advantageous for human exposure (a logKow higher than a certain level would disable dermal absorption). In a number of instances, a chemical preferable for EEA may not be as preferable for QHEA (e.g. ATBC preferable for EEA but not as much for QHEA in comparison to DEHP, similarly, DINCH not preferable for EEA but preferable for QHEA in comparison to DBP and BBP). It is therefore both not possible in this study and not the intention of this study to propose one single chemical alternative to all three phthalates. The main purpose is to evaluate each alternative from a number of different perspectives to provide the necessary information to the user for informed chemical substitution. A summary below (Table 4.16) shows the benchmark scores and comments of the different CAA components carried out for phthalates and the proposed alternatives.

Table 4.16. Conclusion summary for chemical alternative assessment for phthalates.

Chemical	CHA		Exposure Assessment				Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
DEHP	**BM-1**	Chemicals of concern. Should be avoided. EU – Annex VI CMRs (Reproductive Toxicity – Category 1B)		Worst performing phthalate with higher persistence in both relevant modes of entries.		Highest scorer amongst target phthalates.	Use should be avoided.
DBP	**BM-1**	Chemicals of concern. Should be avoided. EU – Annex VI CMRs (Reproductive Toxicity – Category 1B)		Closer persistence values to BBP that is why shown with similar performance indicator color.		Performs even worse than DEHP.	Use should be avoided.
BBP	**BM-1**	Chemicals of concern. Should be avoided. EU – Annex VI CMRs (Reproductive Toxicity – Category 1B)		Highest scoring amongst target phthalates.		Performs even worse than DEHP.	Use should be avoided.
Alternatives							
ASE	BM-2	Moderate reproductive toxicity score. The confidence in the score is low due to one generation study. OECD TG 416 two		Shows less P_{ov} for atmospheric and soil mode of entries than the highest scoring phthalate- BBP.		More exposure potential than the highest scoring phthalate i.e. DEHP.	ASE is a safer alternative than phthalates in terms of CHA, EEA. But QHEA shows more

Chemical	CHA		Exposure Assessment				Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
		generation reproductive toxicity test is recommended.					exposure potential than DEHP.
ATBC	BM-2	Moderate development toxicity score. Conflicting score in ECHA registration dossier study from a structural analogue and Danish EPA reported non-guideline study. Extensive guideline study is recommended.		Shows less P_{ov} for atmospheric and soil mode of entries than the highest scoring phthalate- BBP.		More exposure potential than DEHP.	ATBC is safer than phthalates in terms of CHA and EEA. It has more exposure potential than the highest scoring phthalate DEHP as per QHEA.
COMGHA	BM-3	Moderate bioaccumulation potential. No other hazards found.		Missing physicochemical data. Environmental half-lives are not available.		Shows less exposure potential than DEHP, DBP and BBP.	COMGHA is the safest alternative as per CHA and QHEA. EEA was not conducted due to missing information.
DEHT	BM-2	Moderate reproductive toxicity. The confidence in the study is low		Performs worse than the highest scoring phthalate-BBP when		Same exposure potential as the highest scoring	Suitable alternative because safer

Chemical	CHA		Exposure Assessment				Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
		because of conflicting score between ToxServices (2016b) GreenScreen Assessment and Danish EPA report.		emitted to atmosphere and performs better than BBP when emitted to soil.		phthalate DEHP.	alternative than the phthalates as per CHA. Same exposure potential as per QHEA and EEA (in soil) to the highest scoring phthalate. If emitted properly in atmosphere, then can be recommended as a better alternative than the phthalates.
DINA	BM-1	Should be avoided because of high development toxicity score. The study was based on read across data from structural analog that is why an extensive development		Performs worse than the highest scoring phthalate-BBP when emitted to atmosphere and performs better than BBP when emitted to soil.		More exposure potential than the highest scoring phthalate DEHP but less exposure potential than DBP and BBP.	This alternative should be avoided due to BM-1 score in CHA.

Chemical	CHA		Exposure Assessment				Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
		toxicity study for DINA itself is recommended.					
DINCH	BM-2	Moderate endocrine disruption (thyroid) score.		More persistent than the highest scoring phthalate-BBP in both mode of entries (atmosphere and soil).		More exposure potential than the highest scoring phthalate DEHP.	Safer than phthalates as per CHA but its use is not recommended if it is not disposed safely, because it has potential to be persistent in the environment. Similarly, quantitative risk analysis should be done for its use because it shows more exposure potential than DEHP as per QHEA.

EEA Legend:

	Better in one mode of entry & worse in one mode of entry than BBP
	Better than the highest scoring phthalate (BBP)
	Worse than the highest scoring phthalate (BBP)

QHEA Legend:

	Exposure equal to the highest scoring phthalate (DEHP)
	Exposure less than the highest scoring phthalate (DEHP)
	Exposure more than the highest scoring phthalate (DEHP)

4.3 Hexabromocyclododecane (HBCD)

HBCD is a brominated flame retardant. The most common application of HBCD as a flame retardant is in building thermal insulation in extruded (XPS) and expanded (EPS) polystyrene foam (USEPA, 2014a). As per the USEPA (2014a) report, HBCD was also being used in minor amounts as a flame retardant for textile back coating and high-impact polystyrene (HIPS) used in electronic housing but 96% was being used in the applications of EPS and XPS in EU.

EPS and XPS are used as building insulation due to their unique characteristics such as energy efficiency, durability, and better performance against moisture. It is also resistant against microbial growth and degradation. Due to its cost effectiveness it is being widely used all over the world (USEPA, 2014a).

HBCD due to its persistent, bioaccumulative and toxic (PBT) properties was added to the SVHC list of REACH in 2008 and in 2011 it was added to the authorization list; which meant that apart from the use which is authorized by ECHA it will be phased out (UBA, 2017). EU had planned to phase it out by 2016 under REACH. Stockholm Convention on Persistent Organic Pollutants voted to ban the use of HBCD globally in 2013 by adding it to Annex A with specific exemptions in its use in XPS and EPS (UNEP, 2011). The plan by the convention was to phase out HBCD completely in 6 years. Authorization for the use of HBCD is mostly granted for EPS and XPS. As per ECHA registration dossier, five major companies have ceased manufacture/import of HBCD from 2016-2020 but three companies are still seeking authorization for its use. HBCD is registered in the 1000-10,000 tons/year registration band.

As per the Stockholm convention website, Turkey had an exemption for HBCD use in XPS and EPS in buildings which expired on 26th November, 2019. As per the last available Turkish inventory (2011), attached in Annex A, it was still being manufactured/imported 1-1000 tons/year.

4.3.1 Selection of Alternatives

As per the technical function and existing manufacturing processes, three alternatives were identified by the stakeholders from industrial, academic, governmental and non-governmental organizations (NGOs), engaged by the USEPA DfE in a multistakeholder partnership for the selection and evaluation of alternatives for HBCD, in XPS and EPS thermal foam insulation (USEPA, 2014a). Table 4.17 indicates the market experience and registration tonnage bands (ECHA) of the proposed alternatives. None of the alternatives are presently imported/manufactured in Turkey as per the Turkish inventory.

Table 4.17. Identified alternatives in the study.

Chemical	**CASRN**	**Market Experience***	**REACH registration (Tonnage band)(tons/year)****
Tetrabromobisphenol A (TBBPA)-bis brominated ether derivative	97416-84-7	Pyroguard SR 130 and AP 1300 SF are commercially available and mostly used in EPS. Pyroguard SR 130 is also being used in XPS.	1000 to 10,000
TBBPA bis(2,3-dibromopropyl) ether	21850-44-2	It is already an alternative to HBCD for XPS commercially. FR -720 a product of ICL-Industrial Products is available commercially.	1000 to 10,000
Butadiene styrene brominated copolymer	1195978-93-8	Commercially available from 2012 as Emerald Innovation 3000 by Great Lakes Solutions Chemtura Business. ICL Industrial Products have been producing the FR-122p also known as PolyFR. Albemarle also has a commercial product named GreenCrest.	Not registered in ECHA.

*****Source: Van Dijk & Reichenecher, 2019 ******Source: ECHA Website

4.3.2 Chemical Hazard Assessment

The GreenScreen summary (Table 4.18), below shows a comparison of the hazard endpoint scores for HBCD and the proposed alternatives. Most of the hazard data was obtained from USEPA report on flame retardant alternatives for HBCD (USEPA, 2014a). The ECHA registration dossiers were investigated to include any updated hazard studies, if available. The authoritative and screening lists were also searched and included in the assessment if a chemical was included on any list after the USEPA report. The complete GreenScreen hazard assessment for each chemical is presented in Annex B, summary descriptions are provided in the next subsection. Tetrabromobisphenol A (TBBPA)-bis brominated ether derivative was shortly referred to as TBBPA ether derivative in this study. TBBPA bis(2,3-dibromopropyl) ether was referred to as TBBPA ether and Butadiene styrene brominated copolymer was shortly referred to as Butadiene-Brp in this study.

CHA Result Discussion

A) Group I Human Hazard Endpoints

Carcinogenicity:

HBCD was assigned ‘M-moderate’ score, due to tumor incidences in lab rats (USEPA, 2014a). The results were not enough to classify HBCD as a carcinogen that is why a low confidence score was assigned.

Butadiene-Brp was assigned ‘L-low’ score for carcinogenicity based on USEPA (2014a) professional judgment, as no carcinogenicity studies have been conducted. TBBPA ether and TBBPA ether derivative were assigned ‘M-moderate’ score for carcinogenicity based on USEPA (2014a) professional judgment which indicates potential for alkylation.

Table 4.18. GreenScreen hazard summary table for HBCD and alternatives.

	GreenScreen Hazard Summary Table for HBCD and Alternatives																				
	Group I Human					Group II and II* Human								Ecotox		Fate		Physical		
CHEMICALS	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability	BENCHMARK SCORE
							single	repeat*	single	repeat*	*	*									
CHEMICAL OF CONCERN (HBCD)																					
HBCD	*M*	**L**	***H***	**H** [a]	**H**	**L**	*M* [b]	**M**	**-**	*M*	**L**	**DG**	**L**	**L**	**VH**	**VH**	**H**	**VH** [a]	*L*	*L*	**BM-1a**
ALTERNATIVES																					
TBBPA ether derivative	*M*	*M*	*M*	*M*	*M*	*L*	**-**	*M*	-	*L*	**L** [c]	**DG**	**L** [c]	**L** [c]	**L**	*L*	*H*	*H*	*L*	*L*	**BM-2a**
TBBPA ether	*M*	**M**	*M*	**M**	*M*	**L**	**-**	*M*	**-**	*L*	**L**	**DG**	**L**	**L**	**L**	*L*	**VH**	*H*	*L*	*L*	**BM-2a**
Butadiene-Brp	*L*	**L**	**L**	**L**	*L*	**L**	**-**	**L**	**-**	*L*	**L**	**DG**	**L**	**M**	*L*	*L*	*VH*	*L*	*L*	*L*	**BM-2c**

Note to Table:

[a, b, c] The superscripts with the hazard score indicates the reference for the hazard score such that **a**: Authoritative A; **b**: Screening A; **c**: ECHA registration dossier of the specific chemical.

- E.g. **H**[a] (a: Authoritative A) which means the chemical was present in the authoritative A list for the specific hazard endpoint. Similarly superscripts were provided and the references were mentioned as a footnote.
- For a hazard score without any superscript, it means that the source of the hazard score is the USEPA report for HBCD alternatives (2014a).
- Dash '-' used in case of missing single or repeat Systemic toxicity or neurotoxicty hazard end point. Missing Single exposure when repeat exposure is available is not considered a Data Gap on its own.

Bold score indicates high confidence data while *italic* score indicates low confidence data.

Group II Human Health endpoints have four hazard scores (i.e., VH, H, M, and L) and Group II* Human Health endpoints have three hazard scores (i.e., H, M, and L), and are based on single exposures instead of repeated exposures.

Persistence and Bioaccumulation have five hazard scores (i.e., VH, H, M, L and VL).

The legend for the scores is indicated below

	Hazard Score	Acronym Used
	Very High	VH
	High	H
	Moderate	M
	Low	L
	Very Low	VL
	Data Gap	DG

Mutagenicity:

HBCD was assigned a high confidence 'L-low' score as per the multiple *in vitro* tests in the USEPA (2014a) report which classified HBCD as non-mutagenic and non-genotoxic.

Butadiene-Brp was assigned 'L-low' score as per no mutagenic activity reported in *in vitro* studies in the USEPA (2014a) report. The polymer has a MW>1000, which makes its bioavailability limited to cause mutagenicity and genotoxicity.

Most of the *in vitro* and *in vivo* tests indicated negative potential for mutagenicity but in one assay TBBPA ether was mutagenic to *Salmonella typhimurium* (USEPA, 2014a). USEPA (2014a) report professional judgment also stated potential mutagenicity due to the potential of alkylation by TBBPA ether. TBBPA ether and TBBPA ether were assigned 'M-moderate' score for mutagenicity (USEPA, 2014a), similarly 'M-moderate' score was assigned in this study.

Reproductive Toxicity:

HBCD is in the GHS Japan under category 1B, as toxic to reproduction (H360) and it should be assigned high hazard score. Moderate hazard score was assigned in the USEPA (2014a), based on conservative approach stating uncertainty in reproductive effects occurring between NOAEL and LOAEL doses. In the study, reported in USEPA (2014a), NOAEL was 14.3 mg/kg-bw/day and LOAEL was identified as 138 mg/kg bw/day. In this study 'H-High' score is assigned based on the inclusion in the GHS Japan Screening A list and the NOAEL of 14.3 based on GreenScreen criteria (CPA, 2018). The confidence in the score was assigned low due to conflicting score between USEPA (2014a) and this study.

Butadiene-Brp was assigned 'L-low' score as per OECD guideline reproductive toxicity study, reporting an NOAEL >1000 mg/kg bw/day (USEPA, 2014a). TBBPA ether and TBBPA ether derivative were assigned 'M-moderate' score, based on the professional judgment of USEPA (2014a), based on potential of alkylation. In ECHA registration dossier, TBBPA ether reproductive toxicity study has been waivered based on the negative result in development toxicity test. In this thesis study, development toxicity and reproductive toxicity have been considered

as separate hazard endpoints as per GreenScreen criteria. ‘M-moderate’ hazard score has been assigned in this study, for reproductive toxicity based on USEPA (2014a) professional judgment (CPA, 2018).

Developmental Toxicity:

HBCD was assigned ‘H-high’ score for developmental toxicity due to its presence in the authoritative A list (EU GHS), as a chemical which may cause harm to breast-fed children (H362). In a development toxicity study, reported in USEPA, (2014a), an NOAEL of 0.9 mg/kg-bw/day was reported due to which it was assigned a ‘H-high’ score.

Butadiene-Brp was assigned ‘L-low’ score as per OECD guideline development toxicity study, reporting an NOAEL >1000 mg/kg bw/day in the USEPA (2014a) report. TBBPA ether and TBBPA ether derivative were assigned ‘M-moderate’ score for development toxicity based on professional judgment which indicates potential for alkylation (USEPA, 2014a). For TBBPA ether, guideline study for development toxicity was reported in ECHA registration dossier, having maternal toxicity NOAEL = 300 mg/kg bw/day which also comes in the moderate range as per GreenScreen criteria (CPA, 2018).

Endocrine Disruption:

HBCD was assigned ‘H-high’ score due to thyroid effect at NOAEL 14 mg/kg-bw/day in *in vivo* tests reported in (USEPA, 2014a). Many *in vivo* and *in vitro* tests, in the USEPA, (2014a) report, also showed HBCD exhibited antiandrogenic, antiprogesteronic.

Butadiene-Brp was assigned ‘L-low’ hazard score for endocrine activity based on professional judgment in USEPA (2014a) report, which indicated that due to the MW being greater than 1000 there is limited bioavailability and inability of the chemical to be metabolized readily. TBBPA ether and TBBPA ether derivative were assigned ‘M-moderate’ score in this study, because two *in vitro* tests showed endocrine activity (USEPA, 2014a). No *in vivo* studies were located to further clarify endocrine activity concern on the organism level (ECHA, 2016). They are also under assessment as potential endocrine disruptors by ECHA due to the above

mentioned *in vitro* tests (ECHA, 2016). In ECHA (2016), testing proposals for further *in vivo* tests have been recommended to understand the effect better.

B) Group II and Group II* Human Hazard Endpoints

Acute Mammalian Toxicity:

Acute oral LD_{50} was greater than 2000 mg/kg for HBCD. It was assigned 'L-low' hazard score as per the GreenScreen criteria (CPA, 2018). Acute oral LD_{50} was greater than 2000 mg/kg for all the proposed alternatives that is why they were similarly assigned 'L-low' score for acute mammalian toxicity based on GreenScreen criteria (CPA, 2018).

Systemic Toxicity (Single and Repeat Dose):

HBCD was assigned 'M-moderate' score for systemic toxicity single dose due to the presence in Category 3 GHS Japan as (H335 or H336). For systemic toxicity repeated exposure, HBCD was assigned 'M-moderate' score due to development study (USEPA, 2014a); in which lowest dose tested was 14.8 mg/kg-bw/day, which caused thyroid mass to increase. As per the GreenScreen criteria, a chemical is assigned moderate hazard score for systemic toxicity repeat dose if NOAEL > 10-100 mg/kg-bw/day (CPA, 2018).

For Butadiene-Brp, USEPA (2014a) report indicated that in a 28 day OECD guideline systemic toxicity repeated dose study an NOAEL of >1000 mg/kg bw/day was observed. Butadiene-Brp was assigned 'L-low' hazard score as per the GreenScreen criteria for systemic toxicity repeat dose because NOAEL > 100 mg/kg bw/day (CPA, 2018). For TBBPA ether and TBBPA ether derivative, 'M-moderate' score was assigned based on professional judgment because brominated compounds usually cause liver problems and poly-halogenated aromatic hydrocarbons have been a source of potential immunotoxicity. One study was available in the USEPA (2014a) for TBBPA ether derivative and TBBPA ether which stated an NOAEL >1000 mg/kg bw/day, but the study was not reliable and didn't follow GLP guidelines, that is why in this study the 'M-moderate' score of USEPA (2014a) is adopted.

Neurotoxicity (Single and repeated dose):

HBCD was assigned 'M-moderate' score, as per the professional judgment of USEPA (2014a). Neurotoxic behavior due to presence of cyclic halogenated aliphatic hydrocarbons was indicated in the USEPA, (2014a), which is a structural alert for neurotoxicity repeated dose.

In the reproductive/development toxicity, OECD guideline study reported in USEPA (2014a), no neurotoxic effects were observed because of Butadiene-Brp that is why 'L-low' hazard score was assigned. TBBPA ether and TBBPA ether derivative were assigned 'L-low' score based on professional judgment, in (USEPA, 2014a).

Skin Sensitization:

HBCD was assigned 'L-low' score based on negative skin sensitization results in guinea pig and human volunteers reported in (USEPA, 2014a). Butadiene-Brp and TBBPA ether were assigned 'L-low' score based on studies reported in USEPA (2014a), which showed no sensitization effect in guinea pigs. TBBPA ether derivative showed no skin sensitization in a study reported in ECHA registration dossier.

Respiratory Sensitization:

HBCD and all the alternatives were assigned a 'DG-Data Gap' due to no information available regarding respiratory sensitization.

Skin Irritation:

HBCD was not found to be a skin irritant in the tests on guinea pig reported in (USEPA, 2014a). 'L-low' score was hence assigned for skin irritation.

In a dermal irritation study, reported in USEPA (2014a) report, Butadiene-Brp caused slight skin irritation which cleared within 24 hours. 'L-low score was assigned based on the GreenScreen criteria (CPA, 2018). TBBPA ether was assigned 'L-low' score based on a study reported in USEPA (2014a), which

showed no skin irritation in rabbits. TBBPA ether derivative was assigned 'L-low' score based on guideline study reported in ECHA registration dossier.

Eye Irritation:

HBCD was not found to be an eye irritant in the tests on rabbits (USEPA, 2014a). 'L-low' score was hence assigned for eye irritation.

As per GreenScreen criteria, 'M-moderate' score was assigned to Butadiene-Brp based on the study in USEPA (2014a) in which mild irritation in rabbits was observed, which cleared within 72 hours. TBBPA ether was assigned 'L-low' score based on a study in USEPA (2014a), where slight irritation was observed in rabbits which reversed in 24-48 hours. TBBPA ether derivative was assigned 'L-low' score based on guideline study reported in ECHA registration dossier.

C) Ecotoxicity

Acute Aquatic Toxicity:

HBCD was assigned 'VH-very high' acute toxicity hazard score due to presence on GHS Japan as hazardous to the aquatic environment Category 1 (H400). USEPA reported an EC50 of 0.027 mg/L in algae. As per GreenScreen, a 'VH-very high' score is designated if EC50 < 1 mg/L (CPA, 2018).

Butadiene-Brp was assigned 'L-low' score for acute aquatic toxicity based on USEPA (2014a) which state that the MW >1000 and solubility is low, so the concentration will never reach the level which can cause acute toxicity. TBBPA ether and TBBPA ether derivative were assigned 'L-low' score based on experimental and estimated ECOSAR data reported in USEPA (2014a), stated no adverse effects expected at saturation.

Chronic Aquatic Toxicity:

HBCD was assigned 'VH-very high' hazard score based on study in USEPA (2014a), reported where the NOEC was 0.0031 mg/L in *Daphnia magna*. As per GreenScreen criteria, a chemical is designated a 'VH-very high' score if the NOEC<0.1 mg/L (CPA, 2018).

Butadiene-Brp was assigned ‘L-low’ score for chronic aquatic toxicity based on professional judgment in USEPA (2014a), which indicated the MW >1000 and solubility is low, so the concentration will never reach the level which can cause acute toxicity. TBBPA ether and TBBPA ether derivative were assigned ‘L-low’ score based on estimated ECOSAR data reported in USEPA (2014a), which stated no adverse effects expected at saturation.

D) Fate

Persistence:

HBCD was assigned ‘H-high’ score because it did not pass the ready biodegradability test. USEPA (2014a) also stated that in the monitoring studies it has been found in sediments from the 1960s and 1970s. It has also been found in Arctic region, that is why United Nations Economic Commission for Europe (UNECE) considered HBCD to meet the persistent organic pollutants (POPs) criteria (Arnot et al., 2009)

Butadiene-Brp was assigned a ‘VH-very high’ score for persistence based on USEPA professional judgment. Butadiene-Brp has MW>1000, minimal solubility and vapor pressure and limited bioavailability for microbial degradation. In OECD anaerobic biodegradability test, no biodegradation was observed after 62 days. TBBPA ether was assigned ‘VH-very high’ score. TBBPA ether was not readily biodegradable based on OECD 301C ready biodegradability test, reported in USEPA (2014a) and showed only 1% degradation after 28 days. Soil and sediment biodegradation tests reported in USEPA (2014a) also stated that 0% degradation of the chemical occurred in soil and sediments in OECD TG 307 and OECD TG 308 tests respectively. TBBPA ether derivative was not readily biodegradable as per OECD 301B ready biodegradability test but no other detail was provided and based on aerobic biodegradation modeling studies reported in USEPA (2014a), high persistence is expected that is why ‘H-high’ score of USEPA (2014a) is assigned in this study as well.

Bioaccumulation Potential:

HBCD was assigned 'VH-very high' score for bioaccumulation potential based on measured BCF of 8974. In the USEPA (2014a), it is also stated that monitoring data indicate highly bioaccumulative properties of HBCD in trophic level organisms.

Butadiene-Brp was assigned 'L-low' score as the MW>1000 which makes it low bioaccumulation potential chemical as per professional judgment in USEPA, (2014a). TBBPA ether was assigned 'H-High' score in USEPA (2014a) as well as in this study based on TBBPA ether detection in Great Lakes Herring gull eggs. The measured fish BCF was 3.4 to 43 for 15µg concentration, and <17 to 130 for 1.5µg concentration, in studies for TBBPA ether (USEPA, 2014a). These ranges indicate low bioaccumulation potential as per the GreenScreen criteria; nevertheless, based on their very high log Kow and presence in Great Lakes Herring gull eggs, it is assigned 'H-High' score in this study as per USEPA (2014a). TBBPA ether derivative was assigned 'H-high' score, based on USEPA (2014a) high score due to estimated BAF of 1,600 as per GreenScreen criteria (CPA, 2018).

E) Physical Hazards

Reactivity:

HBCD and the proposed alternatives are not expected to be form mixtures which are explosive in air (USEPA, 2014a).

Flammability:

HBCD and the proposed alternatives are not expected to be flammable due to their flame retardant properties (USEPA, 2014a).

Benchmark Scores

The benchmark scores were assigned as per the 'Benchmark score criteria for organic chemical' presented in Figure 3.4 in the Materials and Methods, Chapter 3.

Chemical of Concern:

HBCD: Benchmark 1a (PBT): High P + High B + High T (Group I Human)

Alternatives:

Tetrabromobisphenol A (TBBPA)-bis brominated ether derivative: Benchmark 2a: High P + High B + Moderate T (GroupI)

Tetrabromobisphenol A (TBBPA)-bis brominated ether: Benchmark 2a: Very High P + High B + Moderate T (Group I)

Butadiene styrene brominated copolymer: Benchmark 2c: High P + Moderate Toxicity (Group II Human Eye Irritation)

Despite the data gaps all the chemicals meet the above mentioned preliminary benchmark scores.

TBBPA ether and TBBPA ether derivative are included in the CoRAP. They already fulfill the REACH screening criteria of persistence and bioaccumulation. If the *in vivo* tests prove TBBPA ether and TBBPA ether derivative to be endocrine disruptors, they will be considered to be moved into SVHC list which will lead to authorization and restriction of the chemicals in the future (ECHA, 2016).

4.3.3 Exposure Assessment

4.3.3.1 Environmental Exposure Assessment using the EQC Model

Environmental fate of HBCD and the proposed alternative are comparatively evaluated in a generic environment of the EQC model. This evaluation will provide insight into the fate and transport of the chemicals involved. The results of this will help in determining the environmental compartments of concern and what should be the focus of efforts in eradicating the concern. Butadiene-Brp could not be included in the fate evaluation due to the unavailability of important information on environmental degradation half-lives. Typically, EPI Suite is used for estimation of physicochemical parameters as well as degradation half-lives but because this chemical is a polymer and has a molecular weight greater than 1000g/mole which

is not amenable to SMILES notation, therefore it was not possible to estimate logKow via EPI Suite. Annex C presents a complete list of sources for each physicochemical property in the table as well as the least square method followed for thermodynamic consistency check. The chemicals were run through the EQC model (Mackay et al., 1996a) and the results discussed separately for each level. Table 4.19 shows the finally adjusted (FAV) physicochemical data of the chemicals after the thermodynamic consistency check, which were then used as input in the EQC model.

Level I:

Table 4.20 indicates the partitioning of chemicals into different compartments at equilibrium condition and steady state. All chemicals are predicted to partition into the soil compartment by almost 98%. HBCD and the alternatives at equilibrium condition partition into the sediment compartment (2.2 %).

Only TBBPA ether partitions into air compartment (0.2%) amongst all the chemicals evaluated due to much higher vapor pressure than the other two chemicals.

Level II:

Level II results show the same chemical partitioning percentages as the level I results but degrading reactions are included. The reaction in soil is the dominating loss process in all the chemicals. In HBCD and TBBPA ether derivative, the reaction in soil accounts for 93.8% and 99% of the total loss. Reaction in soil (46%) is the primary loss mechanism for TBBPA ether as well. Due to the higher vapor pressure and very high Henry's Law constant of TBBPA ether, reaction in air accounts for 40% of the losses, followed by advection in air which accounts for 13.8%. Advection in air can be a cause of concern for LRT potential of the chemical.

At equilibrium condition, the P_{ov} of HBCD, TBBPA ether derivative and TBBPA ether are 118, 526 and 245 days respectively. In Arnot et al., (2009), similar P_{ov} of 118 days was obtained in RAIDAR model for HBCD.

Table 4.19. Physicochemical properties of HBCD its alternatives used in EQC model.

Chemical Name	Melting Point (°C)	Vapor Pressure (Pa)	Solubility (g/m3)	Henrys law Constant (Pa-m^3/mol)	log Kow	Koc	Environmental Half Lives (h)			
							Air	Water	Soil	Sediment
HBCD	190	5.94E-07	3.50E-03	1.09E-01	5.8	2.7E+05	31	2,040	2,040	840
TBBPA ether derivative	110	9.49E-04	9.27E-03	9.94E+01	11.6	1.7E+11	17	4,320	8,640	38,900
TBBPA ether	117	5.17E-02	7.95E-05	6.14E+05	10.8	2.4E+10	24	4,320	8,640	38,900

All the proposed alternatives have larger P_{ov} than HBCD. The high environmental persistence of alternatives is due to almost exclusive partitioning of the alternatives into the soil compartment.The amount of HBCD at equilibrium in the soil compartment is 2.8E+06 kg, whereas in case of TBBPA ether it is 5.7E+06 kg and for TBBPA ether derivative it is 1.23E+07 kg. Overwhelming partitioning into soil is in line with the much larger log Kow value of the alternatives, when compared to HBCD. Subsequently, P_{ov} of the chemicals vary with varying amount of chemicals found in the soil compartment. Table 4.20 shows a detailed summary of the results obtained from level I and II calculations.

Table 4.20. Percentage distribution and persistence at Level I and II of EQC model.

Compartment	**HBCD**	**TBBA Ether Derivative**	**TBBPA Ether**
Percentage distribution at Level I and Level II			
Air	0	0	0.2
Water	0.2	0	0
Soil	97.6	97.8	97.6
Sediment	2.2	2.2	2.2
Suspended Solid	0	0	0
Fish	0	0	0
Level II Percentage Loss by			
Advection in air	0.1	0	13.8
Reaction in air	0.2	0	40
Reaction in soil	93.8	99	46
Adv. in water	0.5	0	0
Reaction in water	0.2	0	0
Adv. in sediment	0.1	0.5	0.3
React.in sediment	5.0	0.5	0.3
Persistence (Days)			
Overall	118	526	245
Reaction	119	529	285
Advection	16,750	95,780	1,746

TBBPA ether derivative and TBBPA ether getting deposited in the soil compartment can be of great concern because there will be a year to year carry over

and as the CHA assessment (Table 4.18) indicates, both the chemicals have 'H-high' bioaccumulation potential score.

In case of TBBPA ether, advection persistence is less than the other chemicals, because advection losses play a larger role among total loss mechanisms due to the higher vapor pressure and higher Henry's Law constant when compared to those of the other two.

All the chemicals mostly reside in the soil compartment that is why advective persistence is very high compared to reaction persistence as chemicals residing in soil compartment are mostly degraded by reaction losses and no advective losses are included in soil.

Level III:

Due to the inclusion of intermedia transport processes and non-equilibrium steady state condition, Level III results are regarded as the most relevant (Palm et al., 2002). As shown in Table 4.21, the chemical partitioning into the compartments is different from level I and II; due to the inclusion of intermedia transport processes and that there is no longer equilibrium. The mode of entry plays an important role in the P_{ov} and the compartment into which the chemical resides. In order to comparatively evaluate level III calculations, 1000 kg/h of chemical was emitted individually into air, water and soil compartment. In the last simulation the chemical was emitted into air, water and soil compartment simultaneously at 1000 kg/h each. Table 4.21 shows the environmental mass distribution of chemicals in different compartments, the total mass and the P_{ov}.

Mode of Entry:

HBCD is used in EPS and XPS insulations, the end of life application mostly occurs when a building is demolished which can cause the release of HBCD to the atmosphere in dust (European Commission, 2008). Most of the debris waste of the construction and demolition would be disposed of in landfills in the U.S (USEPA, 2014a)

Table 4.21. EQC Model Level III Results.

Chemical	Emission Medium	In air (kg)	In air (%)	In water (kg)	In water (%)	In soil (kg)	In soil (%)	In sediment (kg)	In sed. (%)	Total Amount (kg)	Persistence (d)
HBCD	Air	0	0	5.51E+05	42	7.67E+05	58	0	0	1.3E+06	55
	Water	0	0	7.45E+05	99.9	0	0	1.1E+03	0.1	7.5E+05	31
	Soil	0	0	5.3E+05	38.4	8.52E+05	61.6	0	0	1.4+06	58
	All three	0	0	1.83E+06	53	1.62E+06	47	0	0	3.5E+06	48
TBBPA Ether Derivative	Air	1.91E+04	9.8	6.96E+02	0.4	1.20E+05	61.3	5.57E+04	28.5	1.9E+05	8
	Water	0	0	2.39E+05	1.2	0	0	1.91E+07	98.8	1.9E+07	806
	Soil	0	0	0	0	1.3E+07	100	0	0	1.3E+07	520
	All three	0	0	2.40E+05	0.75	1.26E+07	39.3	1.92E+07	60	3.2E+07	445
TBBPA Ether	Air	2.57E+04	74.8	0	0	8.20E+03	24	4.46E+02	1.3	3.4E+04	1.4
	Water	0	0	2.39E+05	1.2	0	0	1.90E+07	98.8	1.9E+07	806
	Soil	0	0	0	0	1.3E+07	100	0	0	1.3E+07	520
	All three	0	0	2.39E+05	0.8	1.25E+07	39	1.91E+07	60	3.2E+07	442

Apart from that, HBCD may be released to air, water or soil during manufacture, transport, improper handling and storage, transportation or disposal of the products containing HBCD (Environmental Canada, 2011).

In this study, fate and P_{ov} were evaluated by simulating the entry of the chemicals into atmosphere (air), soil, water separately and then simultaneously.

The results show that the fate and the P_{ov} of the chemicals depend highly on the mode of entry. That is why it is pertinent to discuss the effect of the mode of entry separately.

The worst case P_{ov} obtained for HBCD were in the range (12-1200: 120 days) obtained in the study by Arnot et al. (2009), for the three HBCD degradation scenarios (lower bound –higher bound: median) when emission was into 100% soil compartment. Whereas when HBCD is emitted into water 100%, the range of P_{ov} obtained was (12-970: 120 days) and for 100% air, it was (1.3-320: 20 days) (Arnot et al. ,2009).

These results indicate that mode of entry plays a pivotal role in the persistence value and amount of chemical in the respective compartment into which the chemical is emitted.

Air Compartment:

When HBCD is emitted into the air compartment only, it is predicted to be deposited into the soil compartment from air at a faster rate of 900 kg/h, than the water compartment where it is deposited at a rate of 100 kg/h.. The higher persistence of HBCD is evident from Figure 4.5(a), which clearly shows that much larger mass (7.67E+05 kg) is predicted to reside in the soil compartment, than the two alternatives. HBCD which resides in the water compartment is mostly lost by advection. The primary loss mechanism for HBCD is thus advective losses in water, accounting for 55%, followed by reaction in soil (26%). The intermedia transfer from soil to water compartment (639 kg/h), in the form of surface runoff, plays an important role in deposition of HBCD from soil to water compartment.

Due to the much larger vapor pressure and Henry's Law constant of TBBPA ether, 74.8% of it resides in the air compartment. That is why the reaction in air is the major loss mechanism accounting for 74% of the total losses, followed by advection in air which accounts for 26% of the losses. The TBBPA ether found in the soil compartment only amounts to 8.20E+03 kg, and that is why the P_{ov} is only 1.4 days. Figure 4.5(b) shows the P_{ov} of HBCD and the alternatives.

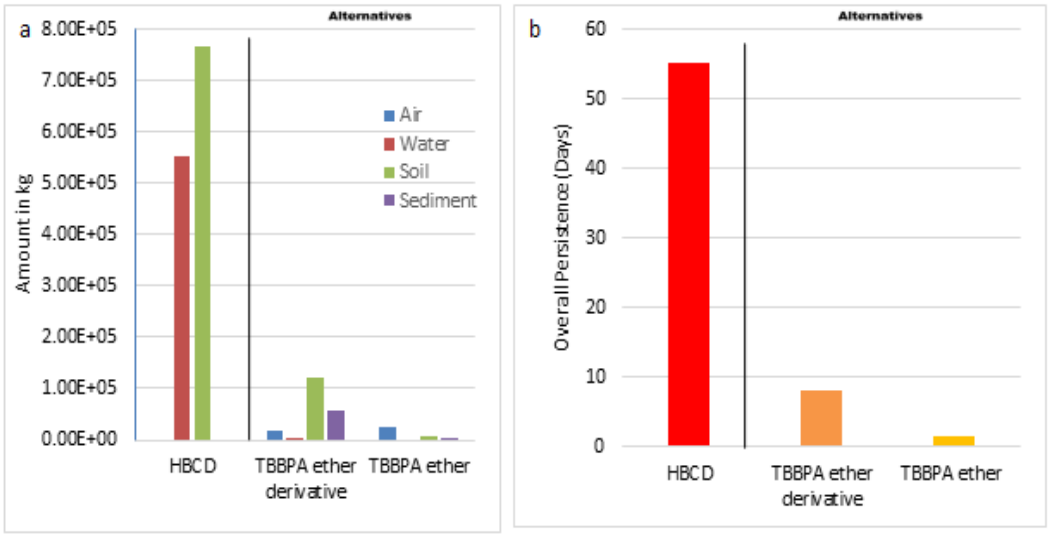

Figure 4.5. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is air only. (b) P_{ov} (days) when mode of entry is air only.

TBBPA ether derivative has larger vapor pressure and Henry's Law constant than HBCD but much lower than TBBPA ether. The Henry's Constant is almost 4 magnitudes lower than TBBPA ether that is why only 9.8% is predicted to reside in the air compartment. Due to very large K_{ow} and K_{oc}, 61% resides in the soil compartment and the remaining 28.5% finds its way to the benthic sediment compartment. The reaction in air is the primary loss mechanism followed by advection in air. Although the degradation half-life in soil and sediment of TBBPA ether derivative is much larger than HBCD, P_{ov} is only 8 days. The amount partitioning into soil compartment (1.20E+05) and sediment compartment (5.6E+04 kg), in comparison to HBCD (7.67E+05 kg in soil) is small and explains the P_{ov} for HBCD being almost 7 times more than TBBPA ether derivative. It can

be clearly seen from Figure 4.5(b) that if the alternatives are emitted into air, the P_{ov} is much less than HBCD.

Water Compartment Only:

It can be deduced from Figure 4.6(a) that when HBCD is discharged into the water compartment almost 100% stays in the water compartment and doesn't move into the sediment compartment due to smaller K_{ow} and K_{oc} value. The advection in water accounts for 75% of the losses that is the reason why the P_{ov} of HBCD is only 31 days.

When the model is run without advective losses, the P_{ov} of HBCD is 122 days which is significantly higher when advective losses are included in the model.

In comparison to HBCD, 98.8% of TBBPA ether derivative and TBBPA ether move into the sediment compartment. This can be explained because of very high K_{ow} and K_{oc} values (Table 4.19).

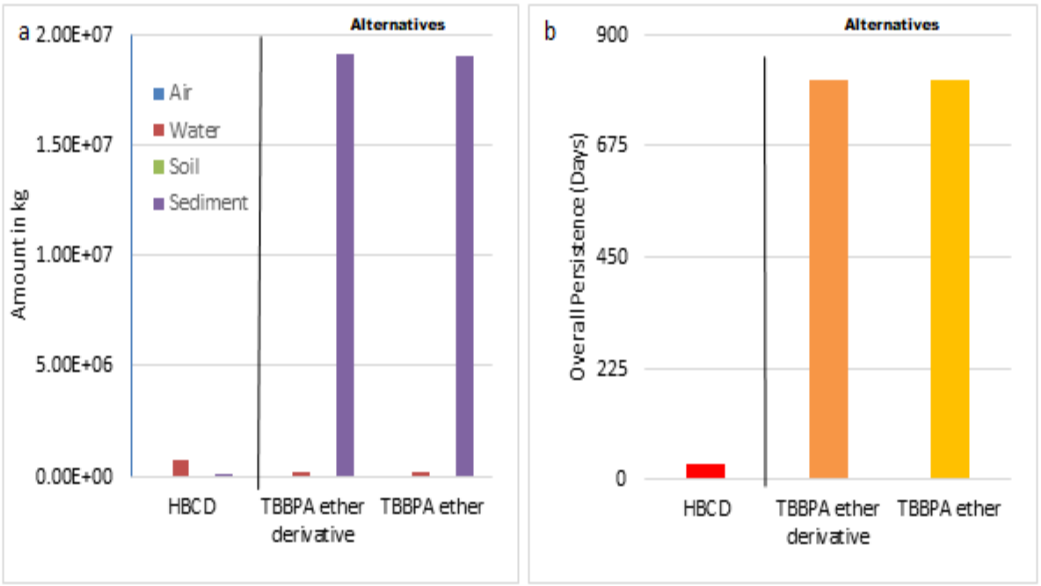

Figure 4.6. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is water only. (b) P_{ov} (days) when mode of entry is water only.

The sediment half-lives of both alternatives are very high and the reaction losses in sediment compartment being negligible, results in the P_{ov} to be very high. Figure 4.6(b) shows the overall persistence of the alternatives in comparison to HBCD.

Soil Compartment Only:

In the scenario where chemical is emitted into the soil compartment only, soil is the compartment in which both alternatives reside. It can be clearly seen from Table 4.21 as well as Figure 4.7(a) that when alternatives are emitted into soil, 100 % resides in soil (1.3E+07 kg).

Both alternatives have P_{ov} values of 520 days due to similar K_{ow} and K_{oc} values. They also have the same soil half-life of 8640 h which explains the same P_{ov}. In comparison, when HBCD is emitted only into the soil compartment, only 62% (8.52E+05 kg) stays in the soil compartment. The remaining amount is transferred into the water compartment at a rate of 710 kg/h. From Figure 4.7(a), it can be seen that in comparison to the proposed alternatives, the amount of HBCD in the soil compartment is almost two orders of magnitude less, that is why the P_{ov} is less in comparison to the alternatives as well. Figure 4.7(b) shows the comparison of P_{ov} of HBCD and the proposed alternatives.

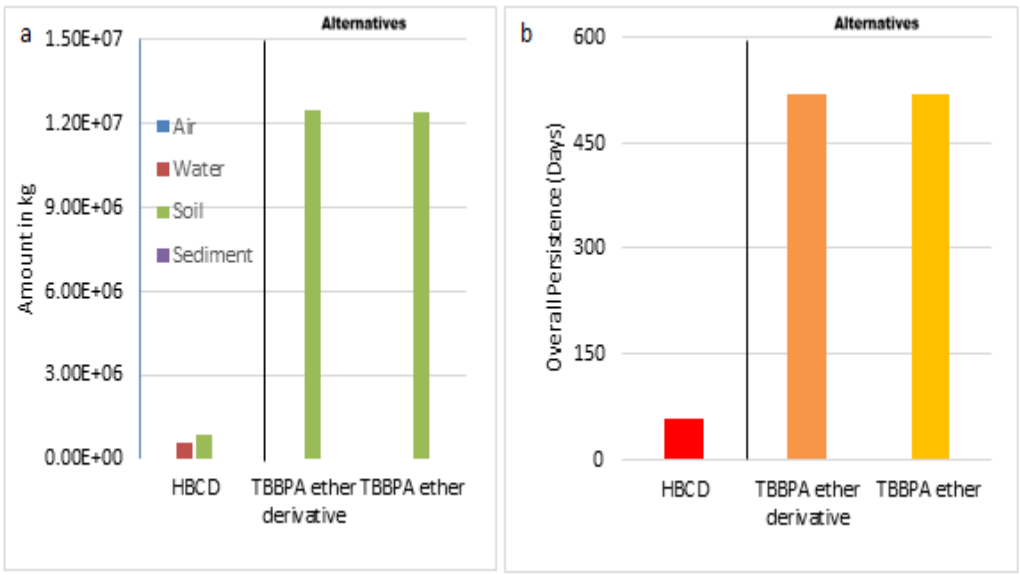

Figure 4.7. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is soil only. (b) P_{ov} (days) when mode of entry is soil only.

The less amount of HBCD in the soil compartment can be explained by small K_{ow} and K_{oc} values in comparison to the proposed alternatives. The advection in water is the primary loss mechanism and the smaller K_{ow} and K_{oc} values don't facilitate the movement of HBCD into the benthic environment. Unfortunately, all the alternatives show persistence much larger than that of HBCD.

The higher persistence can be explained by higher soil half-lives of alternatives when compared to that of HBCD, and two orders of magnitude higher amount moving into the soil compartment in comparison to HBCD.

The sole loss mechanism for the alternatives evaluated was reaction in soil. Advection losses in water (53%) were the primary loss mechanism for HBCD followed by reaction in soil (29%)

All three compartments equally:

As can be seen from Figure 4.8(a), when proposed alternatives TBBPA ether and TBBPA ether derivative are emitted into all three compartments equally, sediment (60%) is the major compartment into which both chemicals reside. The second compartment is soil with 39%. This can be explained by the very large K_{ow} and K_{oc} values. Figure 4.8(b) indicates the P_{ov} which is very high as compared to HBCD due to the very large amount residing in the benthic sediment. The large K_{ow} and K_{oc} values expedite intermedia transport to the sediment compartment and the very large sediment half-life for both chemicals (38,900 h) is predicted to cause the large $P_{ov.}$ Sediment re-suspension is also a major concern for both alternatives. The reaction in sediment only accounts for 11% of the total loss mechanisms due to which the chemical stays in the sediment compartment for a long time and can be a cause of concern for LRT. For the alternatives, reaction in soil is the primary loss mechanism (33%) and the reaction in air accounts for 25-27% of the total losses. In case of HBCD, 53% is found in the water compartment and 47% resides in the soil compartment. From the water compartment, HBCD doesn't move into the sediment compartment and advection in water accounts for 61% of the total losses that is why the P_{ov} for HBCD is lower when compared to the alternatives. Reaction in water accounts for 21% of the losses whereas reaction in soil accounts for 18% of

the total losses. The intermedia transport processes from soil to water (1350 kg/h) is very high as compared to the HBCD deposition from air to soil (900 kg/h) or air to water (100 kg/h) compartment.

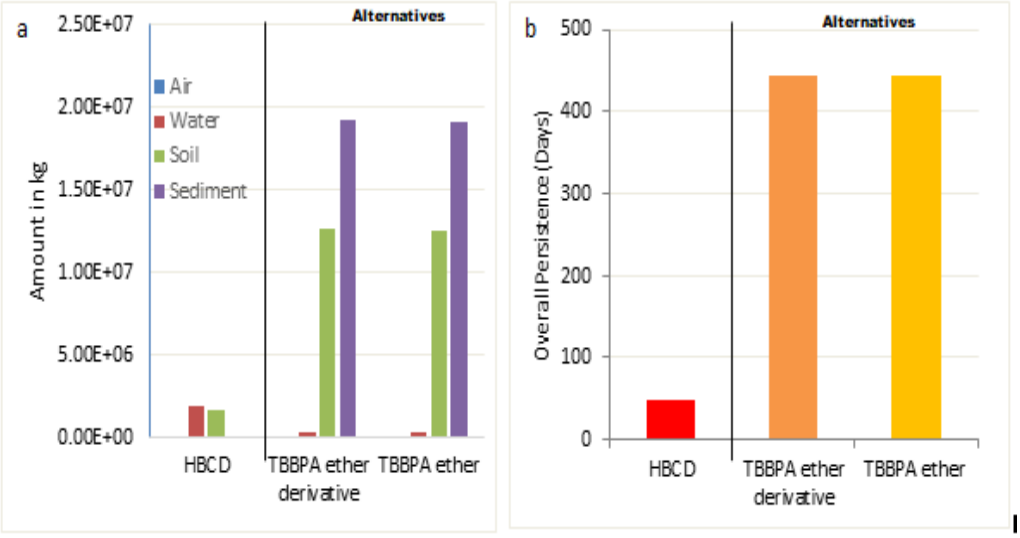

Figure 4.8. (a) Amount (kg) of each chemical in different environment compartment when mode of entry is all three media at equal rate (b) P_{ov} (Days) when mode of entry is air, soil and water simultaneously at 1000 kg/h.

Sensitivity Analysis:

The mode of entry for the analysis was taken as the chemical entering simultaneously air, water and soil at 1000 kg/h. As it can be seen from Table 4.22 below, for HBCD and the proposed alternatives, the P_{ov} is majorly affected by soil half-life which makes it a sensitive parameter. For both the alternatives half-life in sediment is also a sensitive parameter. It can be seen from Table 4.22 that by doubling the log K_{ow}, the P_{ov} of the alternatives does not change. This can be explained by the already greater K_{ow} value for both the alternatives. When the K_{ow} is halved, P_{ov} value is greatly reduced in case of TBBPA ether (-89%) and TBBPA ether derivative (-38%). TBBPA ether log K_{ow} is 10.8 which is reduced to 5.4 and the amount of TBBPA ether in the benthic sediment compartment is 2.94E+06 kg whereas in the case of TBBPA ether derivative the log K_{ow} is 11.6 and is reduced to 5.8 and the amount of TBBPA ether derivative in the benthic sediment compartment is 6.87E+06 kg.

This shows that only a small amount of change of log K_{ow} can have a pronounced effect on the P_{ov} but this effect is dependent on other factors as well. Usually the pronounced effect of log K_{ow} on the P_{ov} is seen between the ranges of 4.5-8.

Table 4.22. Sensitivity Analysis (Percent difference impact on persistence upon 100% change in physicochemical properties).

Modified Input	HBCD		TBBPA Ether Derivative		TBBPA Ether	
	100%	-100%	100%	-100%	100%	-100%
Melting Point	0	0	0	0	0	0
Vapor Pressure	0	0	0	0	0	0
Solubility	0	0	0	0	0	0
Henry's Law Constant	0	0	0	0	0	0
Half Life (Air)	0	0	0	0	0	0
Half Life (Water)	8	-11	1	-2	1	-2
Half Life (Soil)	13	-17	39	-20	39	-20
Half Life (Sediment)	0	0	16	-18	16	-18
Log K_{ow}	0	0	0	-38	0	-89

The logK_{ow} values of both the alternatives are derived from EPI Suite estimation software so they are prone to errors. It can be seen that reduction of logK_{ow} values makes a difference in the persistence of the alternatives. It is recommended that logK_{ow} values are experimentally derived to enhance the accuracy of evaluations such as those attempted here. The complete picture of the sensitivity analysis can be seen from Table 4.22.

EEA Summary:

HBCD is used in EPS and XPS insulations, the end of life application mostly occurs when a building is demolished which can cause the release of HBCD to the atmosphere in dust (European Commission, 2008). Most of the debris waste of the construction and demolition would be disposed of in landfills in the US (USEPA, 2014a). The comparative EEA summary matrix (Table 4.23) below shows

performance of proposed alternatives in comparison to HBCD for these relevant mode of entries (atmosphere and soil). The comparative EEA summary table shows that TBBA ether and TBBPA ether derivative performed much better than HBCD when emitted in the air, which means when a building is demolished, the tendency for the alternatives to be persistent in atmosphere is much less than HBCD. But when the debris is moved into the landfill, the proposed alternatives have a tendency to stay in soil for a much longer duration than HBCD.

Table 4.23. EEA Summary (according to Pov for relevant mode of entries).

	HBCD	**TBBA ether derivative**	**TBBA ether**
Air	55	8	1.4
Soil	58	520	520
Overall Score			

EEA Color Indicator	
	Worse than HBCD.
	Better than HBCD.
	Performs better in one mode of entry and worse in one mode of entry

That is why an overall score of blue is assigned because the proposed alternatives show better result for air mode of entry and worse result than HBCD for soil mode of entry.

4.3.3.2 Qualitative Human Exposure Assessment:

The second type of exposure assessment used in this study, as a component of CAA, is QHEA. Comparative qualitative exposure assessment was done for HBCD and the proposed alternatives for the functional use in EPS and XPS thermal insulation boards used in buildings. In the risk assessment of the European Commission (2008), the consumer exposure for XPS insulation boards was also assessed. Dust inhalation from indoor air because of exposure from XPS construction boards was determined to be the most relevant exposure pathways for human (European Commission, 2008). Dermal contact was excluded because the XPS boards are usually covered (European Commission, 2008). In this study,

qualitative exposure assessment was done based on the scenario of debris removal by the worker after the building has been demolished. Dermal absorption was included. Deductions in QHEA were made based on values of physicochemical parameters listed in Table 4.24.

Table 4.24. Physicochemical properties of the chemicals evaluated as part of QHEA.

Physicochemical Property	**HBCD**	**Butadiene-BRP**	**TBBPA ether derivative**	**TBBPA ether**
Molecular Weight (g/mol)	641.7	>1000	971.68	943.62
Solubility (mg/L)	3E-03	<10^-3	2E-02	1.40E-04
Log K_{OW}	5.6	DG	12.4	11.52
Vapor Pressure (Pa)	5.6E-07	<1.3E-06	4.4E-04	2.9E-02
Particle Size (μm)*	<10 (3%)	DG	8 (no % given)	12.5 (10%)
Concentration in product**	(0.7% EPS) (1.5% XPS) Br Content (74%)	20% (Br Content 64%)	18% (Br Content 65%)	12% (Br Content 68%)

* % indicates the amount present in the mixture as per ECHA Registration Dossier.

**Butadiene ingredient concentration data was taken from(Amec Environmental, 2014). The TBBPA ether and TBBPA ether derivative concentrations were estimated from bromine content %. Less bromine content means more concentration needed.

Most relevant exposure parameters, from the technical guidance document on risk assessment ECB (2003), were recognized for inhalation and dermal absorption route in Table 4.25 and Table 4.26.

Table 4.25 gives the qualitative evaluation for inhalation exposure as part of QHEA, while Table 4.26 gives that of dermal absorption. Evaluation is based on the criteria of ECB (2003), such that physicochemical property of each chemical is compared with the ECB (2003) recommended criteria, and assigned one of two colors: red if physicochemical property indicates higher exposure and green if it indicates lower exposure according to the criteria Tables (3.7 and 3.9) presented in the Material and Methods, Chapter 3.

Apart from criteria related to exposure pathways, three more parameters are also considered in this study as part of QHEA. These are: (i) Bioaccumulation, which is an important indicator for human exposure regardless of the intake route, (ii) Extraction potential, which can indicate the amount of exposure based on separation potential of the chemicals from the EPS/XPS insulation board, and (iii) Ingredient concentration in product, which is a parameter that has a direct impact on exposure.

Table 4.25. Qualitative evaluation for inhalation exposure pathway as part of QHEA.

	HBCD	TBBPA ether derivative	TBBPA ether	Butadiene Copolymer
Vapor Pressure				
Particle Size				DG
Log K_{OW}				DG
Solubility				
Systemic Toxicity				
Overall	**3/5**	**3/5**	**3/5**	**3/5**

	More exposure as per criteria
	Less exposure as per criteria

Table 4.26. Qualitative evaluation for dermal absorption exposure pathway as part of QHEA.

	HBCD	TBBPA ether derivative	TBBPA ether	Butadiene Copolymer
Molecular Weight				
Solubility				
Log K_{OW}				DG
Vapor Pressure				
Skin Sensitization/Irritation				
Overall	**3/5**	**4/5**	**4/5**	**3/5**

	More exposure as per criteria
	Less exposure as per criteria

Accordingly, Table 4.27 gives a combined overall summary for the QHEA for comparison of HBCD with the alternative chemicals from the perspective of human exposure. Overall score from inhalation (Table 4.25) and dermal absorption (Table

4.26) for each of the chemicals are carried over to this overall summary table as the first and second rows.

In addition, the three aforementioned indicators of exposure are added as extra rows. Lastly, the total summed score for each chemical is compared with that of HBCD. A lower score indicates worse standing in terms of human exposure, i.e., the chemical shows a higher potential for human exposure.

Those having a higher score means they are safer chemicals showing lower human exposure potential. The summary matrix shows that two alternatives (TBBPA ether and TBBPA ether derivative) perform similar when compared to HBCD, however, Butadiene-Brp performed worse than HBCD in QHEA.

Table 4.27. Comparative Summary Matrix for QHEA.

Pathway/Criteria	**HBCD**	**TBBPA ether derivative**	**TBBPA ether**	**Butadiene Copolymer**
Inhalation	3/5	3/5	3/5	3/5
Dermal Absorption	3/5	4/5	4/5	3/5
Bioaccumulation	0/1	0/1	0/1	DG
Extraction Potential	DG	DG	DG	DG
Ingredient Concentration in Product	1/1	0/1	0/1	0/1
Overall Score	**7/13**	**7/13**	**7/13**	**6/13**

QHEA Colour Indicator	
	Exposure equal to HBCD
	Exposure less than HBCD
	Exposure more than HBCD

4.3.4 Conclusion

In this section, evaluation for alternatives of HBCD and the proposed alternatives is presented on the basis of hazard, environmental exposure and human exposure assessments. The chemicals hazard assessment adopts benchmark criteria (as presented in Section 4.3.2) and assigns colors from red to green in order of preferability. The coloring scheme chosen for the comparative EEA summary

matrix (Table 4.23) and comparative QHEA summary matrix (Table 4.27) will be used in the conclusion Table 4.28 so that an overall conclusion can be put forth by comparing all assessments for target and alternative chemicals.

As can be seen from these tables and the above discussions under each subsection, some of the properties of alternatives that are disadvantageous for environmental exposure (such as high logKow leading to partitioning into soil which has much higher degradation half-lives) leading to high persistence for chemical may be advantageous for human exposure (a logKow higher than a certain level would disable dermal absorption). In a number of instances, a chemical preferable for CHA may not be as preferable for QHEA (e.g. Butadiene-Brp preferable for CHA but not as much for QHEA in comparison to HBCD, similarly, TBBPA ether and TBBPA ether derivative not preferable for soil mode of entry but preferable as per CHA and similar performance to HBCD in QHEA). Data gaps and missing information also plays a crucial role in QHEA where one missing data reduces the score without knowing the effect it will have in reality.

It is therefore both not possible in this study and not the intention of this study to propose one single chemical alternative to HBCD. The main purpose is to evaluate each alternative from a number of different perspectives to provide the necessary information to the user for informed chemical substitution.

Hence, Table 4.28 below shows the benchmark scores and comments of the different CAA components carried out for HBCD and the proposed alternatives.

Table 4.28. Conclusion summary for chemical alternative assessment for HBCD.

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
HBCD	**BM-1**	Chemicals of concern. Should be avoided due to presence on EU-GHS as developmental toxicant Category 1B. Included in the REACH SVHC and Authorization list as PBT chemical.		HBCD is a PBT chemical as per ECHA status and is included in the Authorization list and SVHC list. EEA results support this classification with relatively high overall persistence.		Systemic chronic toxicity shows potential of adverse effect but as per the risk assessment by EC (2008), the exposure is insignificant when it is used in XPS/EPS insulation.	Use should be avoided.
Alternatives							
TBBA ether derivative	BM-2	Moderate hazard score in all the Human Group 1 hazard endpoints due to the potential of alkylation and included in CoRAP by ECHA to be studied for potential endocrine disruption.		TBBPA ether derivative shows lower persistence than HBCD when emitted in the atmosphere whereas it has longer persistence when emitted into soil.		TBBPA ether derivative shows similar exposure potential as HBCD.	TBBPA ether derivative is a safer alternative as per CHA. QHEA shows same performance as HBCD. CoRAP endocrine

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							activity review has asked for more tests for its potential endocrine activity. It has to be disposed safely because any emission into soil would result in higher persistence than HBCD.
TBBPA ether	BM-2	Moderate hazard score in all the Human Group 1 hazard endpoints due to the potential of alkylation and included in CoRAP by ECHA to be studied for potential endocrine disruption.		TBBPA ether shows lower persistence than HBCD when emitted in the atmosphere whereas it has longer persistence when emitted into soil.		TBBPA ether shows similar exposure potential as HBCD.	TBBPA ether is a safer alternative as per CHA. QHEA show similar performance as HBCD. CoRAP endocrine activity review has asked for more tests for its

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							potential endocrine activity. It has to be disposed safely because any emission into soil would result in higher persistence than HBCD.
Butadiene copolymer	BM-2	It shows no effect in terms of Group I hazard endpoint. It is marked BM-2 due to moderate eye irritation. CHA determines it to be a much safer alternative than HBCD and the two alternatives studied in this study.		Missing physicochemical data. Environmental half-lives are not available. But this is termed persistent based on biodegradation lab studies and looking at the MW>1000 it could be persistent in the environment.		Due to missing information Butadiene-Brp showed more qualitative human exposure potential. It didn't show any systemic toxicity in the CHA and hence a detailed quantitative assessment is required for a better comparison	Safest alternative as per CHA. Missing information is needed to carry out the EEA. QHEA indicates more exposure potential than HBCD because of missing physicochemical properties. Detailed risk

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
						with HBCD.	analysis has to be carried out for its use in articles.

EEA Legend

	Exposure equal to HBCD.
	Exposure less than HBCD.
	Exposure more than HBCD.

QHEA Legend

	Performs better in one mode of entry and worse in one mode of entry than HBCD.
	Better than HBCD in both of entries.
	Worse than HBCD in both of entries.

4.4 Decabromodiphenyl ether (DecaBDE)

DecaBDE is a brominated flame retardant which belongs to the polybrominated diphenyl ether (PBDE) group. It is mainly used as an additive flame retardant. It is combined with the material to inhibit ignition or slow down the spread of flames in case the material catches fire. Its wide range applicability in the US was investigated by USEPA (2014b); it was stated that out of the total mass of produced DecaBDE, 26% was used in textile industry, 26% in automotive and transportation industry, 26% in building and construction, 13% in electronic and electrical equipment and the remaining 9% for other uses. Due to its persistence in the environment and highly bioaccumulative nature, the plastic and textile industry in Germany declared a voluntary phase-out of DecaBDE in 1986 (Lassen et al., 2006). Under the European Union Restriction of Hazardous Substances Directive (RoHS), DecaBDE was supposed to be phased out in EU by 2006 in electrical and electronic equipment, but exemption was granted for 2005-2010. After a successful legal battle against the exemption in the European Court of Justice, it was ordered that DecaBDE must be phased out by July 1st, 2008.

DecaBDE was included in the SVHC list by ECHA in 2012 and a restriction proposal was submitted in 2014. On the 10th February, 2017, EU published Regulation (EU) 2017/227 and included DecaBDE in the restriction list (Annex XVII) (European Commission, 2017). In 2019, DecaBDE was added to the Stockholm Convention Annex A to restrict its use globally. Exemptions in some aviation and automotive applications has been granted till 2036 (UNEP, 2019a). Due to the addition into the Stockholm Convention, DecaBDE has been removed from the REACH restriction list (Annex XVII) on 16th December, 2020. It has not been added to the authorization list till now but it will be added in the future like HBCD, as it is also in Stockholm Convention Annex A. DecaBDE is present in the inventory of chemicals used in Turkey, within 1 to 1000tons/yr (see Annex A).

4.4.1 Selection of Alternatives

In the USEPA (2014b) report, alternative assessment for DecaBDE was comprehensively conducted, in which 29 alternatives were identified as viable in various polymer applications in a variety of industries. In this thesis study, a screening was performed on the 29 alternatives, such that only those alternatives which were used in the automotive end user application were kept, because this application was the most relevant for Turkey.

Table 4.29 shows the polymer application for which DecaBDE is used as a flame retardant in the automotive industry and Table 4.30 shows the narrowed down alternatives. Four alternatives were chosen for comprehensive assessment in this thesis study because a comprehensive GreenScreen assessment was previously done for them and they showed a BM-3 score. Out of the alternatives, magnesium hydroxide is being manufactured/imported (>1000tons/year) and Ammonium polyphosphate is being manufactured/imported (1-1000tons/year) in Turkey, as per the Turkish chemicals inventory. The other two alternatives are not present in the Turkish inventory.

Table 4.29. DecaBDE polymer application in automotive end use application.

Flame Retardant Chemical	**Polymer Applications**
Decabromodiphenyl ether, DecaBDE	Elastomers
	Engineering Thermoplastic
	Polyethylene (PE)
	Polypropylene (PP)

Table 4.30 indicates the alternatives which are already being used as additive flame retardants in the polymer applications in the automotive industry. They show significant market experience already as a DecaBDE alternative for the polymer applications mentioned (USEPA, 2014b)**.**

Elastomers are rubber like materials which are a special type of polymer widely used owing to their elastic properties. Thermoplastic elastomers are type of elastomers which can be easily molded like natural thermoplastics (polyethylene,

polypropylene) whereas the elastic property of elastomers can also be attained (Spontak & Patel, 2000).

Table 4.30. Alternative chemicals for DecaBDE to be investigated in this study.

Chemical	**CASRN**	**Market Experience***	**REACH registration (Tonnage band) (tons/year)****
Aluminum diethylphosphinate	225789-38-8	Elastomers	Under pre-registration process
Ammonium polyphosphate	68333-79-9	Polypropylene (PP)	10,000-100,000
Magnesium hydroxide	1309-42-8	Elastomers, Polyethylene (PE) and Polypropylene (PP).	100,000-1,000,000
Polyphosphonate	68664-06-2	Elastomers and Engineering thermoplastics.	No information on ECHA website. Not registered.

***(USEPA, 2014b) ****ECHA Website

Polypropylene has been used as an excellent car seat cover because of its strength, stain-resistant and fade-resistant advantages. Thermoplastic and thermoplastic elastomers have wide range of application in the automotive industry especially when it comes to seat covers and interior car structures. Due to its luxurious feel and soft touch, car manufacturers are moving away from conventional materials to thermoplastic elastomers and engineering thermoplastics. The proposed alternatives (Table 4.30) are additive flame retardants which are incorporated into the polymer applications mentioned above via physical mixing and are not chemically bound to the polymer. The additive flame retardants can be incorporated into the product until the final manufacturing stages, that is why, they are being widely used nowadays instead of reactive flame retardants (USEPA, 2014b). The additive flame retardants like PBDEs are not chemically bound to the matrix and have been found in dust in households and in cars and have been a cause of human exposure (Fowles, 2013).

4.4.2 Chemical Hazard Assessment

The GreenScreen summary Table 4.31 below shows a comparison of the hazard endpoint scores for DecaBDE and the proposed alternatives. GreenScreen assessments for Aluminum diethylphosphinate was prepared by ToxServices (2019). GreenScreen assessment for Ammonium polyphosphate was prepared by Rosenblum Environmental (2016a). GreenScreen assessment for Magnesium hydroxide was prepared by Rosenblum Environmental (2019). GreenScreen assessment for Polyphosphonate was also prepared by Rosenblum Environmental (2016b). The hazard assessment data used in this GreenScreen assessment was mostly taken from the DecaBDE USEPA alternative assessment report (USEPA, 2014b). In the summary description, it has been reported whether there was any difference which was reported between the GreenScreen assessments and the USEPA (2014b).

The GreenScreen assessment of BM-3 chemicals is updated after every five years for assessments done after January, 2019. The assessments which were updated before January, 2019 have a validity period of three years. Ammonium polyphosphate and Polyphosphonate assessments expired on in February, 2019 and have not been updated yet, whereas Aluminum diethylphosphinate and Magnesium hydroxide were updated in 2019. The most recent source available at the time of this thesis study was used.

CHA Result Discussion

A) Group I Human Hazard Endpoints

Carcinogenicity:

DecaBDE was assigned ‘M-moderate’ score based on National Toxicology Program (NTP) study providing evidence of carcinogenicity in male mice in a study reported in (USEPA, 2014b). The presence on Authoritative B list IRIS has classified DecaBDE as ‘Suggestive evidence of carcinogenic potential’. As per GreenScreen criteria, DecaBDE is assigned ‘M-moderate’ hazard score for carcinogenicity (CPA, 2018).

Table 4.31. GreenScreen hazard summary table for DecaBDE and alternatives.

GreenScreen Hazard Summary Table for DecaBDE and Alternatives																					
	Group I Human					Group II and II* Human								Ecotox		Fate		Physical		
CHEMICALS	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability	BENCHMARK SCORE
							single	repeat*	single	repeat*	*	*									
CHEMICAL OF CONCERN (DecaBDE)																					
DecaBDE	M	L	M	H	*M*[a]	L	L	M	-	*L*	L	DG	*M*[b]	L	*L*	*L*	VH	*H*	*L*	L	BM-1a
ALTERNATIVES																					
Aluminum Diethyl phosphinate	*L*	L	*L*	*L*[d]	DG	L	-	L[d]	-	L[d]	L	*L*	L	L	L[d]	L[d]	*vH*	*vL*	*L*[d]	L[d]	BM-3a
Ammonium Polyphosphate	*L*	*L*[d]	*L*[d]	*L*[d]	*L*	L	L[d]	*L*	-	*L*	L	DG	*M*	L	*L*	*L*	*vH*	*vL*	*L*[d]	L[d]	BM-3c
Magnesium Hydroxide	L	*L*	L	*L*	DG	L	-	L	-	*L*	*L*	DG	*L*	M	L	*L*	*vH*	*vL*	*L*[d]	L[d]	BM-3c
Polyphosphonate	*L*	*L*	*L*	*L*	*L*	L	-	*L*	-	*L*	*L*	DG	*L*	*L*	*L*	*L*	*vH*	*vL*	*L*[d]	L[d]	BM-3a

Note to Table:

The superscripts with the hazard score indicates the reference for the hazard score (a, b, c sources of information)

a: Authoritative A,B; **b**: Screening A; **c**: ECHA registration dossier of the specific chemical; **d:** Hazard studies from recent GreenScreen assessments.

- E.g. **H**[a] (a: Authoritative A) which means the chemical was present in the authoritative A list for the specific hazard endpoint. Similarly superscripts were provided and the references were mentioned as a footnote.
- For a hazard score without any superscript it means that the source of the hazard score is the USEPA report (2014b) or the aforementioned GreenScreen assessments.
- Dash '-' used in case of missing single or repeat Systemic toxicity or neurotoxicty hazard end point. Missing Single exposure when repeat exposure is available is not considered a Data Gap on its own.

Bold score indicates high confidence data while italic score indicates low confidence data.

Group II Human Health endpoints have four hazard scores (i.e., VH, H, M, and L) and Group II* Human Health endpoints have three hazard scores (i.e., H, M, and L), and are based on single exposures instead of repeated exposures.

Persistence and Bioaccumulation have five hazard scores (i.e., VH, H, M, L and VL).

The legend for the scores is indicated by the table below

	Hazard Score	Acronym Used
	Very High	VH
	High	H
	Moderate	M
	Low	L
	Very Low	VL
	Data Gap	DG

Aluminum diethylphosphinate was assigned ‘L-low’ score based on estimation and modeling studies (USEPA, 2014b). Ammonium polyphosphate and Polyphosphonate were assigned ‘L-low’ score based on professional judgment by USEPA (2014b), as no experimental studies were present. Magnesium hydroxide was assigned ‘L-low’ score based on non-carcinogenic behavior in experimental studies reported (USEPA, 2014b).

Mutagenicity:

DecaBDE was assigned a high confidence ‘L-low’ score, as per the multiple *in vitro* tests and *in vivo* tests in the USEPA, (2014b), which classified DecaBDE as non-mutagenic and non-genotoxic.

Aluminum diethylphosphinate was assigned ‘L-low’ score based on negative results reported in *in vitro* and *in vivo* studies (USEPA, 2014b). Ammonium polyphosphate was assigned ‘L-low’ score based on professional judgment by USEPA (2014b), which was substantiated by non-mutagenic results obtained in OECD TG 476 study on ammonium dihydrogenorthophosphate, a structural analog to ammonium polyphosphate reported by Rosenblum Environmental (2016a). Magnesium hydroxide was also shown to be non-mutagenic by USEPA (2014b) *in vitro* studies. It is recommended that *in vivo* studies should also be carried out to achieve a high confidence score. Polyphosphonate was assigned ‘L-low’ score based on USEPA (2014b) professional judgment, as MW>1000 and limited bioavailability, so non-mutagenic as a result of it.

Reproductive Toxicity:

DecaBDE was assigned ‘M-moderate’ score in this study. Reproductive toxicity study reported in USEPA (2014b) indicated NOAEL=100 mg/kg bw/day and LOAEL=500 mg/kg bw day on sperm. USEPA (2014b) assigned a low score based on the information but as there was no dose between 100 and 500 mg/kg bw/day, it is very much possible that LOAEL can be lower than 500 mg/kg bw/ day. In this study, a conservative approach is adopted and moderate score is assigned because as per GreenScreen NOAEL>50-1000 mg/kg bw/day and LOAEL>250-1000 mg/kg bw/day comes in moderate range (CPA, 2018). A GreenScreen assessment

for Decabromodiphenyl ethane used the same study for reproductive toxicity hazard endpoint of DecaBDE, and assigned a moderate hazard score for reproductive toxicity for Decabromodiphenyl ethane (NSF, 2016).

Aluminum diethylphosphinate was assigned 'L-low' score based on one generational OECD-421 study reported in USEPA (2014b), in which NOAEL > 1000 mg/kg bw/day was indicated which makes it in the region of low hazard score as per GreenScreen criteria (CPA, 2018). Ammonium polyphosphate was assigned 'L-low' score based on professional judgment in USEPA (2014b), which was substantiated by no reproductive toxicity effects observed at NOAEL=1500 mg/kg bw/day in OECD TG 402 study on Polyphosphoric acids, ammonium salts a structural analog to ammonium polyphosphate reported by Rosenblum Environmental (2016a). Magnesium Hydroxide also showed no reproductive toxicity as per study reported in USEPA (2014b), as well as more recent study reported by Rosenblum Environmental (2019). The NOAEL was greater than 1000 mg/kg bw/day in both studies and that is why 'L-low' score was assigned as per GreenScreen criteria (CPA, 2018). Polyphosphonate was assigned 'L-low' score based on USEPA (2014b) professional judgment, which stated as the MW>1000 and the bioavailability will be limited to cause any adverse effect.

Developmental Toxicity:

DecaBDE was assigned 'H-High' score based on LOAEL as low as 6 mg/kg bw/day (USEPA, 2014b). Many studies reported in USEPA (2014b) indicated LOAEL less than 10 mg/kg bw/day, which is in the high score range as per USEPA and GreenScreen criteria (CPA, 2018).

Aluminum diethylphosphinate was assigned 'L-low' score based on NOAEL>1000 mg/kg bw/day in the OECD Guideline 421 (USEPA, 2014b). Recent OECD Guideline 414 study reported by Toxservices (2019) also showed no development toxicity at NOAEL >1000 mg/kg bw/day. The confidence in the data was low due to missing neurotoxic data, that is why USEPA (2014b) and Toxservices (2019) recommended additional neurotoxic studies included in the development toxicity studies. Ammonium polyphosphate was assigned 'L-low' score based on

professional judgment in USEPA (2014b), which was substantiated by no development toxicity effects observed at NOAEL=1500 mg/kg bw/day in OECD TG 422 study on Polyphosphoric acids, ammonium salts a structural analog to ammonium polyphosphate reported (Rosenblum Environmental, 2016a). Magnesium hydroxide was assigned 'L-low' score, based on structural analog development study reported in USEPA (2014b), which indicated NOAEL>1000 mg/kg bw/day. Polyphosphonate was assigned 'L-low' score based on professional judgment (USEPA, 2014b), which indicated MW>1000 and limited bioavailability to cause any adverse effect.

Endocrine Disruption:

DecaBDE was assigned 'M-moderate' score based on its presence on Authoritative B list OSPAR-Endocrine Disruptor - Chemical for Priority Action. It is highly recommended to carry out more studies because very limited studies were available in USEPA report and presence on authoritative B list is a low confidence score.

Aluminum diethylphosphinate and Magnesium hydroxide were assigned 'DG-Data Gap' based on not enough studies reported to assign a hazard score (USEPA, 2014b). Ammonium polyphosphate and Polyphosphonate were assigned 'L-low' score based on USEPA report professional judgment, which indicated MW>1000 and the bioavailability will be limited to cause any adverse effect.

B) Group II and Group II* Human Hazard Endpoints

Acute Mammalian Toxicity:

Acute oral LD_{50} was greater than 5000 mg/kg for DecaBDE (USEPA, 2014b). It was assigned 'L-low' hazard score as per the GreenScreen criteria (CPA, 2018). Acute oral LD_{50} was greater than 2000 mg/kg, for all the proposed alternatives (USEPA, 2014b), that is why they were assigned 'L-low' score for acute mammalian toxicity based on GreenScreen criteria (CPA, 2018).

Systemic Toxicity (Single and Repeat Dose):

DecaBDE was assigned 'M-moderate' score for systemic toxicity repeat dose due to LOAEL= 80 mg/kg bw/day causing adverse thyroid and liver effects in a

systemic toxicity repeated dose study reported (USEPA, 2014b). As per the GreenScreen criteria, a chemical is assigned moderate hazard score for systemic toxicity repeat dose if NOAEL > 10-100 mg/kg bw/day (CPA, 2018).

Aluminum diethylphosphinate was assigned a moderate score by USEPA, (2014b), based on professional judgment which indicated there will be presence of Aluminum which has shown moderate hazard for immunotoxicity. Yet, experimental study OECD TG 407 indicated NOAEL>1000 mg/kg bw/day (ToxServices, 2019). That is why in this study 'L-low' score was assigned because no neurotoxic effects were seen in repeated dose studies and lack of bioavailability of Aluminum seen in the experimental studies (ToxServices, 2019).

Magnesium hydroxide was assigned 'L-low' score based on experimental studies reported (USEPA, 2014b), whereas Ammonium polyphosphate and Polyphosphonate were assigned 'L-low' score based on USEPA (2014b) professional judgment, which stated MW>1000 and the limited bioavailability will be reason not to see any adverse effect.

Neurotoxicity (Single and repeated dose):

DecaBDE was assigned 'L-low' score as per the professional judgment of USEPA (2014b), score due to absence of any structural alert associated with neurotoxicity. Aluminum diethylphosphinate was assigned a moderate score in (USEPA, 2014b), based on professional judgment which indicated there will be presence of Aluminum which has shown moderate hazard for immunotoxicity, but experimental study OECD TG 407 indicated NOAEL>1000 mg/kg bw/day (ToxServices, 2019). In this study 'L-low' score was assigned because no neurotoxic effects were seen in repeated dose studies and lack of bioavailability of Aluminum reported in the experimental studies. All the other three alternatives were assigned 'L-low' hazard score for neurotoxicity based on professional judgment based on USEPA (2014b). For all the alternatives, 'DG-Data Gap' was assigned based on lack of studies available for neurotoxicity single dose.

Skin Sensitization:

DecaBDE was assigned ‘L-low’ score based on no skin sensitization effect observed in guinea pigs and human volunteers (USEPA, 2014b). Aluminum diethylphosphinate and Ammonium polyphosphate were assigned ‘L-low’ score based on negative skin sensitization studies (USEPA, 2014b). Magnesium hydroxide and Polyphosphonate were assigned ‘L-low’ score based on professional judgment (USEPA, 2014b).

Respiratory Sensitization:

DecaBDE and all the alternatives were assigned a ‘DG-Data Gap’, because no information could be located regarding respiratory sensitization apart from Aluminum diethylphosphinate which showed lack of any structural alerts for respiratory sensitization (ToxServices, 2019).

Skin Irritation:

DecaBDE was assigned ‘M-moderate’ score based on its presence on screening A list ‘GHS Japan as Category 3 chemical (Skin corrosion / irritation (H316)). The study in USEPA (2014b) also indicated slight skin irritation in human volunteers. Aluminum diethylphosphinate and Polyphosphonate were assigned ‘L-low’ score based on professional judgment (USEPA, 2014b). Ammonium polyphosphate was assigned ‘M-moderate’ score based on experiment indicating mild irritation equivalent to GHS Category 3as per GreenScreen criteria (CPA, 2018). Magnesium hydroxide was assigned ‘L-low’ score based on experimental study, which indicated no skin irritation on rabbit skin (USEPA, 2014b).

Eye Irritation:

DecaBDE was assigned ‘L-low’ score based on eye irritation study (USEPA, 2014b). Mild irritation was observed which cleared after 48 hours that is why no GHS classification was assigned and as per GreenScreen criteria, low score was assigned (CPA, 2018).

Aluminum diethylphosphinate and Ammonium polyphosphate were assigned ‘L-low’ score based on negative eye irritation studies (USEPA, 2014b).

Polyphosphonate was assigned ‘L-low’ score based on professional judgment as no experimental studies were available (USEPA, 2014b). Magnesium hydroxide was assigned ‘M-moderate’ score based on moderate score assigned in (USEPA, 2014b).

C) Ecotoxicity

Acute Aquatic Toxicity:

DecaBDE was assigned ‘L-low’ score based on professional judgment by USEPA (2014b), which states that DecaBDE has Log K_{ow} = 9.97 and as per ECOSAR cutoff value, a chemical having Log K_{ow} > 5 no effect at saturation are predicted.

Aluminum diethylphosphinate and Magnesium hydroxide were assigned ‘L-low’ score based on LC50/EC50 >100 mg/L reported in (USEPA, 2014b). As per GreenScreen criteria, chemical having acute aquatic toxicity LC50 or EC50 >100 mg/L is scored low (CPA, 2018). Ammonium polyphosphate and Polyphosphonate were assigned ‘L-low’ score based on professional judgment in USEPA (2014b), which stated MW>1000 and low solubility due to which the adverse effect won’t be seen at saturation.

Chronic Aquatic Toxicity:

DecaBDE was assigned ‘L-low’ score based on estimated values for fish, daphnia and algae that exceed the water solubility and as such it is predicted that no effect will be observed at saturation level. Aluminum diethylphosphinate and Magnesium hydroxide were assigned ‘L-low’ score based on NOEC >10 mg/L reported in USEPA report. As per GreenScreen criteria, chemical having chronic aquatic toxicity NOEC >10 mg/L is scored low (CPA, 2018). Ammonium polyphosphate and Polyphosphonate were assigned ‘L-low’ score based on USEPA professional judgment based on MW>1000 and low solubility due to which the adverse effect won’t be seen at the saturation level.

D) Fate

Persistence:

DecaBDE was assigned ‘VH-very high’ score based on experimental biodegradation studies reported by USEPA (2014b), which indicate very high persistence of DecaBDE in the environment. Magnesium hydroxide were assigned ‘VH-very high’ score based on professional judgment and experimental studies, which state the chemicals to be inorganic and recalcitrant in nature (USEPA, 2014b). Aluminum diethylphosphinate was assigned ‘VH-very high’ score based on aluminum moiety which is recalcitrant and inorganic in nature (ToxServices, 2019). Ammonium polyphosphate and Polyphosphonate were assigned ‘VH-very high’ score based on professional judgment which state that MW>1000 and limited solubility and poor bioavailability of the chemicals will cause the chemicals to be highly persistent in the environment (USEPA, 2014b).

Bioaccumulation Potential:

DecaBDE was assigned ‘H-high’ score for bioaccumulation potential based on estimated BAF and monitoring data indicating highly bioaccumulative properties of DecaBDE in organisms at various trophic levels (USEPA, 2014b). Aluminum diethylphosphinate was assigned ‘VL-very low’ score based on estimated BCF<100 (USEPA, 2014b). As per GreenScreen criteria, BCF<100 is in very low range for bioaccumulation potential (CPA, 2018). Magnesium hydroxide was not expected to bioaccumulate as per USEPA (2014b), that is why it was assigned ‘VL-very low’ score. Ammonium polyphosphate and Polyphosphonate were assigned ‘VL-very low’ score based on professional judgment as MW>1000 and poor solubility makes it poorly bioavailable (USEPA, 2014b).

E) Physical Hazards

Reactivity:

DecaBDE and Aluminum diethylphosphinate were assigned ‘L-low’ because they are not assigned GHS criteria for reactivity (ToxServices, 2019). Magnesium hydroxide, Ammonium polyphosphate and Polyphosphonate were assigned ‘L-

low' score based on professional judgment (USEPA, 2014b). The confidence in the data was low because of lack of experimental data.

Flammability:

DecaBDE and all the alternatives were assigned 'L-low' score for flammability because none of them are flammable under GHS criteria.

Benchmark Scores

Inorganic chemicals are recalcitrant in nature that is why persistence for inorganic chemicals is not necessarily considered a negative characteristic-especially for minerals and metal oxides. Due to this reason, benchmark criteria for inorganic chemicals (Figure 3.3 in Chapter 3 Materials and Methods) are modified from benchmark criteria for organic chemicals (Figure 3.2 in Chapter 3 Materials and Methods) (CPA, 2018). For inorganic chemicals, persistence is only considered in combination with chronic hazards (CPA, 2018). Inorganic chemicals which are assigned 'L-low' hazard score for all the hazard endpoints except persistence are Benchmark-4 (i.e., Preferred-Safer Chemicals).

For inorganic chemicals, persistence is not considered in combination with group II toxicity endpoints as per the GreenScreen criteria Section 12.6 (CPA, 2018). Ammonium polyphosphate and Magnesium hydroxide are inorganic chemicals and benchmark scores were assigned based on Figure 3.3 in Chapter 3 (benchmark criteria for inorganic chemicals). Polyphosphonate is an organic polymer and Aluminum diethylphosphinate is an organophosphorus salt and were assigned benchmark scores based on Figure 3.2 in Chapter 3 (benchmark criteria for organic chemicals).

Chemical of Concern:

DecaBDE: Benchmark 1a (PBT): Very High P + High B + High T (Group I Human)

Alternatives:

Aluminum Diethylphosphinate: Benchmark 3a: VH-Very High Persistence P

Ammonium Polyphosphate: Benchmark 3c: Moderate T (Group II Human Skin Irritation)

Magnesium Hydroxide: Benchmark 3c: Moderate T (Group II Human Eye Irritation)

Polyphosphonate: Benchmark 3a: VH-Very High Persistence

4.4.3 Exposure Assessment

4.4.3.1 Environmental Exposure Assessment using (EQC Model)

Environmental fate of DecaBDE is evaluated in a generic environment of the EQC model. This evaluation will provide insight into the fate and transport of DecaBDE. The results of this will help in determining the persistency of DecaBDE, environmental compartments of concern and what should be the focus of efforts in eradicating the concern. Aluminum diethylphosphinate is an organophosphorus salt and unfortunately is not amenable to the fugacity based model (USEPA, 2014b). Ammonium polyphosphate and Polyphosphonate could not be included in the fate evaluation due to the unavailability of important information on environmental degradation half-lives. Typically, EPI Suite is used for estimation of physicochemical parameters as well as degradation half-lives, but because both of these chemicals are polymers and have molecular weight greater than 1000g/mole, the SMILES notation could not be written. Therefore, it was not possible to estimate logKow and environmental half-lives via EPI Suite. Magnesium Hydroxide dissociates in the environment into Mg^{2+} and OH^- ion. The distribution and fate of heavy metal ions are usually modeled with Mackay aquivalence approach without involving the degradation parameter of the ions involved (Chang & Li, 2020). Since Mg^{2+} could not degrade in the environment, and only environmental distribution would not present a good basis for comparison of this alternative with the target chemical, DecaBDE, Magnesium Hydroxide was also not evaluated with EQC. Table 4.32 shows the FAV physicochemical properties of DecaBDE evaluated after thermodynamic consistency check. Please see Annex C for a complete list of sources for each property in the table and the least square

method followed for thermodynamic consistency check for the physicochemical input properties used in the EQC model.

DecaBDE was run through the EQC model (Mackay et al., 1996a). In addition, results for each level of the EQC model, i.e. Levels I, II and III are discussed separately in the following subsection. However, no comparison with alternative chemicals could be presented.

Level I:

Table 4.33 indicates partitioning of the chemicals into different compartments at equilibrium condition and steady state. 97.8% DecaBDE is predicted to partition into the soil compartment because of the high K_{ow} and K_{oc} value. Remaining 2.2% of DecaBDE is predicted to partition into the sediment compartment.

Level II:

Level II results show the same chemical partitioning percentages as the Level I results but degrading reactions are included. The reaction in soil is the dominant loss process for DecaBDE accounting for 99.2% of the total loss. At equilibrium, the P_{ov} of DecaBDE is predicted to be 220 days. The high environmental persistence of DecaBDE is due to much larger amount of the chemicals (5.2E+06 kg) partitioning into the soil compartment. The soil degradation half-life of DecaBDE is 3600 h due to which it stays in the soil for larger duration. Table 4.33 shows the persistence for Level I and II and the Level II dominant loss mechanisms for DecaBDE.

Level III:

Due to the inclusion of intermedia transport processes and non-equilibrium steady state condition, the Level III results are regarded as the most relevant (Palm et al., 2002).

Table 4.32. Physicochemical Properties of DecaBDE used in EQC model.

Chemical Name	Melting Point (°C)	Vapor Pressure (Pa)	Solubility (g/m3)	Henrys law Constant (Pa-m³/mol)	log Kow	Koc	Environmental Half Lives (h)			
							Air	Water	Soil	Sediment
DecaBDE	300	3.95E-10	2.13E-04	1.78E-03	10.1	5.0E+09	7,620	3,600	3,600	14,400

Table 4.33. Percentage distribution and persistence at Level I and II of EQC model.

Compartment	DecaBDE
Percentage distribution at Level I and Level II	
Air	0
Water	0
Soil	97.8
Sediment	2.2
Suspended Solid	0
Fish	0
Level II Percentage Loss by	
Advection in air	0
Reaction in air	0
Reaction in soil	99.2
Adv. in water	0
Reaction in water	0
Adv. in sediment	0.2
React.in sediment	0.6
Persistence (Days)	
Overall	220
Reaction	220
Advection	9.59E+04

As shown in Table 4.34, the chemical partitioning into the compartments is different from level I and II due to the inclusion of intermedia transport processes and that there is no longer equilibrium.

The mode of entry plays an important role in the P_{ov} and the compartment into which the chemical resides. In order to comparatively evaluate Level III calculations, 1000 kg/h of chemical was emitted individually into air, water and soil compartment. In the last simulation, the chemical was emitted into air, water and soil compartment simultaneously at 1000 kg/h. Table 4.34 shows the environmental mass distribution of the chemicals in the different compartments, the total mass and the P_{ov}.

Mode of Entry:

The end-of-life application of DecaBDE used in automotive industry mostly occurs when a car is scrapped of completely in a car scrap yard where it can be released to the atmosphere. Nowadays shredding of the cars is done and recycling of the metal content in the car is carried out. In many developed countries, recycling of plastics and glass can be done by machines in a recycling plant and the shredder residue is placed into the landfill. That is why the fate and transport of DecaBDE in soil and atmosphere is of primary concern.

Table 4.34 indicates the effect of mode of entry on the overall persistence of DecaBDE as well as the major compartment into which DecaBDE resides.

In Turkey, Demirtepe & Imamoglu's (2019) study shows that high concentrations of DecaBDE could be found in wastewater treatment plant sludges, which indicate that DecaBDE can find its way to the aquatic environment as well.

That is why in this study, the fate and transport of DecaBDE was evaluated in all the mode of entries.In this study, fate and P_{ov} were evaluated by simulating the entry of the chemicals into atmosphere (air), soil, water separately. In addition to these scenarios, simultaneous emissions of 1000 kg/h to the air, water and soil compartment was also carried out to evaluate DecaBDE. The results show that the fate and the P_{ov} of the chemicals depend highly on the mode of entry. That is why it is pertinent to discuss the effect of the mode of entry separately.

Table 4.34. EQC Model Level III Results.

Chemical	Emission Medium	In air (kg)	In air (%)	In water (kg)	In water (%)	In soil (kg)	In soil (%)	In sediment (kg)	In sed. (%)	Total Amount (kg)	Persistence (d)
DecaBDE	Air	2.48E+04	0.6	1.58E+04	0.4	3.5E+06	80.1	8.29E+05	19.1	4.4E+06	182
	Water	0	0	2.1E+05	2	0	0	1.1E+07	98	1.1E+07	467
	Soil	0	0	0	0	5.2E+06	99.9	5.7E+03	0.1	5.2E+06	217
	All three	2.48E+04	0.1	2.3E+05	1	8.7E+06	42	1.2E+07	57	2.1E+07	289

Air Compartment:

When DecaBDE is emitted into the air compartment only, it is predicted to be deposited into the soil compartment from air, at a rate of 675 kg/h whereas water deposition occurs at 75 kg/h. The higher persistence of DecaBDE is evident from Figure 4.9(a) which clearly shows that much larger mass (3.5E+06 kg) is predicted to reside in the soil compartment.

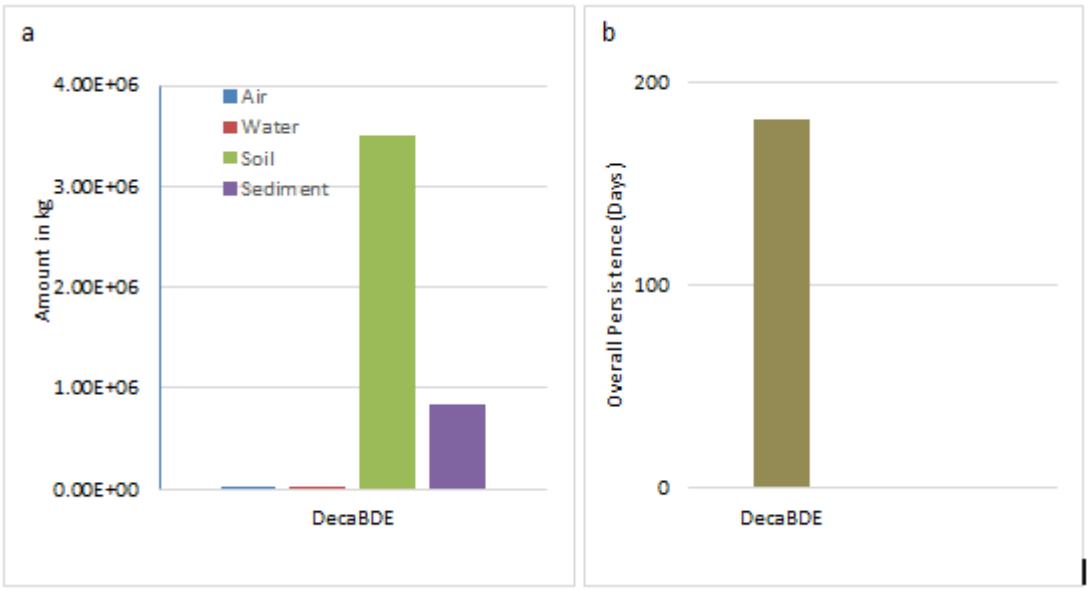

Figure 4.9. (a) Amount (kg) of DecaBDE in different environment compartment when mode of entry is air only. (b) Overall Persistence of DecaBDE (P_{ov}).

The DecaBDE which deposits in the water compartment mostly transfers to the benthic sediment compartment due to the large K_{ow} and K_{oc} values.

The primary loss mechanism for DecaBDE is reaction in soil (67.4%) followed by advection in air (25%). The intermedia transfer from water to sediment compartment occurs at a rate of 73 kg/h. The P_{ov} when DecaBDE is emitted into the air compartment only is predicted to be 182 days. In the study by Palm et al. (2002), the same value of 182 days was reported for overall persistence of BDE 209. Figure 4.9(a) shows the distribution of DecaBDE in the different compartments. Figure 4.9(b) shows the P_{ov} of DecaBDE.

Water Compartment Only:

It can be deduced from Figure 4.10(a), that when DecaBDE is discharged into the water compartment, 98.1% is deposited into the benthic sediment compartment due to large K_{ow} and K_{oc} values.

DecaBDE has a sediment degradation half-life of 600 days which makes it highly persistent once it moves into the benthic sediment. It can be seen from Figure 4.10(b), the P_{ov} of 467 days. That is why it is highly advisable not to discharge DecaBDE into water.

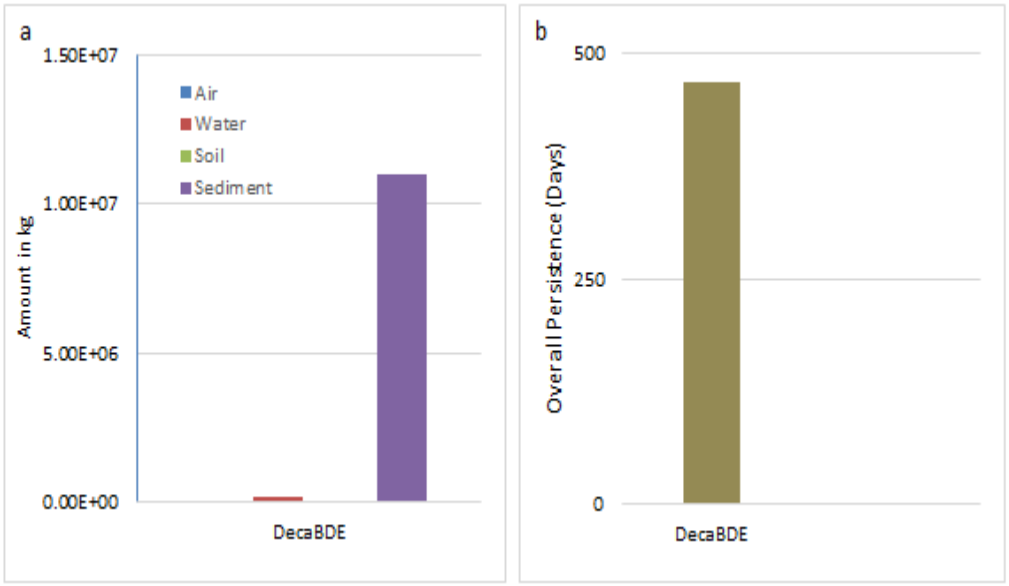

Figure 4.10. (a) Amount (kg) of DecaBDE in different environment compartment when mode of entry is water only. (b) Overall Persistence of DecaBDE (P_{ov}).

The same P_{ov} of 467 days, was predicted for DecaBDE in the study of Palm et al. (2002), when DecaBDE was discharged solely into the water compartment.

This propensity of the alternatives to move into the sediment compartment and the very high P_{ov} indicates potential for long range transport (Palm et al., 2002). Reaction in sediment accounts for 53% of the total losses, whereas advection in sediment accounts for 22% of the total losses for DecaBDE.

Soil Compartment Only:

In the scenario where DecaBDE is emitted into the soil compartment only, soil is the compartment in which almost 100% of DecaBDE resides.

DecaBDE has P_{ov} of 217 days due to very large K_{ow} and K_{oc} values. DecaBDE also has large soil half-life value of 150 days which explains such a large P_{ov} value. In the study by Palm et al., (2002), the same P_{ov} of 217 days was reported for BDE 209. Figure 4.11(b) shows the P_{ov} of DecaBDE.

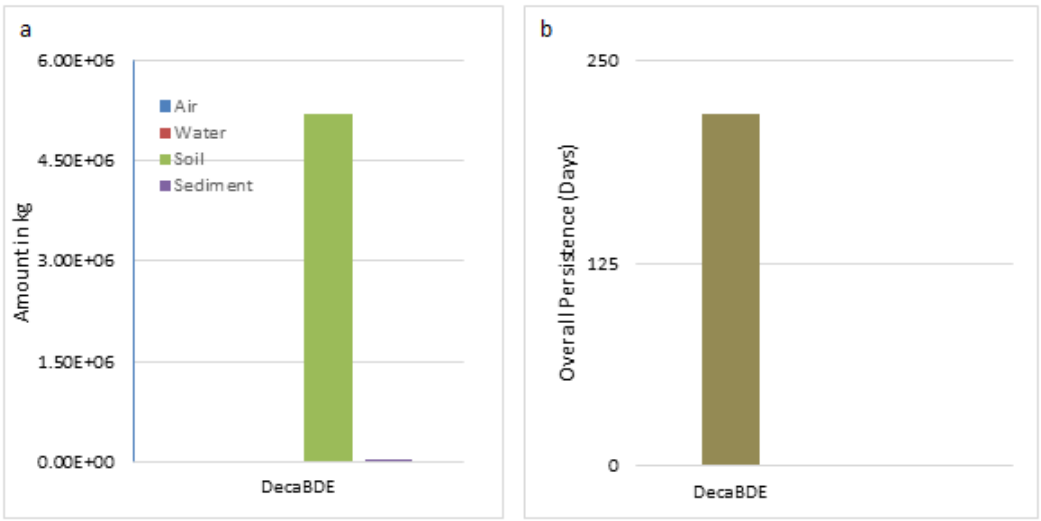

Figure 4.11. (a) Amount (kg) of DecaBDE in different environment compartments when mode of entry is soil only. (b) Overall Persistence of DecaBDE (P_{ov}).

All three compartments equally:

As can be clearly seen from Figure 4.12(a), when DecaBDE is emitted into all three compartments, at equal rate of 1000 kg/h, sediment compartment (57%) is the major compartment into which DecaBDE resides and remaining amount resides in the soil compartment (42%).

This can be explained by larger K_{ow} and K_{oc} values. Due to very large soil and sediment half-lives, the P_{ov} is 289 days. Reaction in soil is the primary loss mechanism accounting for 56% of the total losses and reaction in sediment account

for 19% of the total losses. In the study by Palm et al. (2002), the same P_{ov} value of 289 days was reported for BDE 209.

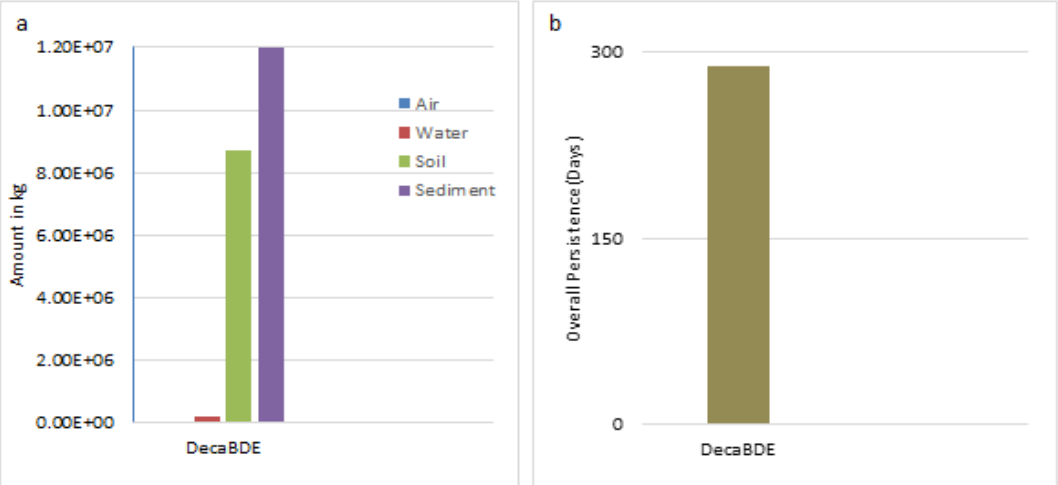

Figure 4.12. (a) Amount (kg) of DecaBDE in different environment compartments when mode of entry is all three media at equal rate (b) Overall Persistence of DecaBDE (P_{ov}).

Sensitivity Analysis:

The mode of entry for the sensitivity analysis was taken as the chemical entering simultaneously into air, water and soil at 1000 kg/h. As it can be seen from the Table 4.35 below, for DecaBDE, the P_{ov} is majorly affected by soil half-life which makes it a sensitive parameter. The complete picture of the sensitivity analysis can be seen from the Table 4.35. DecaBDE, due to large K_{ow} and K_{oc} values finds its way into the sediment compartment that is why the sediment half-life is a sensitive perimeter. The log K_{ow} of DecaBDE is 10.1, when doubled, doesn't increase the persistence because it is already very high, yet when it is halved the P_{ov} is reduced by 42%.

Table 4.35. Sensitivity Analysis (Percent difference impact on persistence upon 100% change in physicochemical properties).

Modified Input	DecaBDE	
	100%	-100%
Melting Point	4	0
Vapor Pressure	0	0
Solubility	0	0
Henrys Law Constant	0	0
Half Life (Air)	0	0
Half Life (Water)	1	-2
Half Life (Soil)	42	-21
Half Life (Sediment)	29	-23
Log K_{ow}	0	-42

EEA Summary:

The mode of entries pertinent to the release of DecaBDE to the environment when it is used in the automotive applications are atmosphere and soil (landfill). However, in Turkey, Demirtepe & Imamoglu's (2019) study shows that high concentrations of DecaBDE could also be found in wastewater treatment plant sludges, that is why water compartment is also added in the table. Table 4.36 shows the overall persistence of DecaBDE when the mode of entry is air, water and soil separately. DecaBDE exposure in the environment is of great concern due to the very high persistence in the environment.

Table 4.36. EEA Summary (according to Pov on all modes of entry).

	DecaBDE
Air	182
Water	467
Soil	217

4.4.3.2 Qualitative Human Exposure Assessment

DecaBDE is added to plastics and polyurethane foams in car seats as a flame retardant. They have been found in the house dust and studies show that they have

been found in the dust in the cars as well (Fowles, 2013). In the study by Fowles (2013), risk assessment for the oral, inhalation and dermal exposures to polybrominated diphenyl ethers (PBDEs), was carried out for an infant, while sitting in a car seat. The direct dermal absorption from the seat itself was not included in the study due to missing information, but it was stated that it was not a major contributor to the exposure assessment overall (Fowles, 2013).

In this study, comparative qualitative exposure assessment was done for DecaBDE and the proposed alternatives for the functional use as a flame retardant in car seat/cover. In this qualitative assessment, oral ingestion of the car dust containing flame retardants, inhalation of the car dust and direct dermal absorption as a result of the infant's skin coming in contact with the seat/cover were included. Table 4.37 contains the physicochemical properties used to evaluate the chemicals for qualitative exposure assessment.

Table 4.37. Physicochemical properties used to fill the exposure pathway tables.

Parameter	**DecaBDE**	**Aluminum Diethyl-phosphinate**	**Ammonium Polyphosphate**	**Magnesium Hydroxide**	**Poly-phospho nate**
Molecular Weight (g/mol)	959.2	390.27	>10,000	58.32	>10,000
Solubility (mg/L)	1xE-04	2500	5000	1.78	<1E-03
Log K_{OW}	9.97	-0.44	DG	1.65	DG
Vapor Pressure (Pa)	5.2E-10	<1.33E-06	<1.33E-06	<1.33E-06	<1.33E-06
Extraction Potential (%)*	DG	DG	DG	DG	DG
Ingredient concentration in product**	DG	DG	DG	DG	DG

Most relevant exposure parameters, from the technical guidance document on risk assessment by ECB (2003) were recognized for oral ingestion, inhalation and dermal absorption route in Table 4.38, Table 4.39 and Table 4.40 respectively. The parameters were shaded (i.e., physicochemical property of each chemical is evaluated and assigned one of two colors: red if physicochemical property indicates

higher exposure, and green if it indicates lower exposure when compared to DecaBDE) as per the criteria defined in the ECB (2003) and given in Table 3.7, 3.8, 3.9 and 3.10 in Chapter 3 (Materials and Methods).

Table 4.41 is the comparative summary matrix where all the scores of exposure routes are added up to give a clear picture. Table 4.41 gives a combined overall summary for the QHEA for comparison of DecaBDE with the alternative chemicals from the perspective of human exposure. In the summary matrix, the alternatives are evaluated compared to DecaBDE.

Table 4.38. Oral ingestion exposure pathway.

Parameter/ Criteria	**DecaBDE**	**Aluminum Diethyl-phosphinate**	**Ammonium Polyphosphate**	**Magnesium Hydroxide**	**Poly-phosphonate**
Molecular Weight					
Solubility					
Log K_{OW}			DG		DG
Systemic Toxicity					
Overall Score	**2/4**	**2/4**	**2/4**	**1/4**	**3/4**

	More exposure as per criteria
	Less exposure as per criteria

Table 4.39. Inhalation exposure route.

Parameter/ Criteria	**DecaBDE**	**Aluminum Diethyl-phosphinate**	**Ammonium Polyphosphate**	**Magnesium Hydroxide**	**Poly-phosphonate**
Vapor Pressure					
Particle Size	DG	DG	DG	DG	DG
Log K_{OW}			DG		DG
Solubility					
Systemic Toxicity					
Overall Score	**2/5**	**3/5**	**2/5**	**2/5**	**3/5**

	More exposure as per criteria
	Less exposure as per criteria

Table 4.40. Dermal absorption exposure pathway.

Parameter/ Criteria	**DecaBDE**	**Aluminum Diethyl-phosphinate**	**Ammonium Polyphosphate**	**Magnesium Hydroxide**	**Poly-phosphonate**
Molecular Weight					
Solubility					
Log K_{OW}			DG		DG
Vapor Pressure					
Skin Sensitization/ Skin Irritation					
Overall Score	**3/5**	**3/5**	**1/5**	**1/5**	**3/5**

	More exposure as per criteria
	Less exposure as per criteria

Overall score from oral ingestion (Table 4.38), inhalation exposure (Table 4.39) and dermal absorption (Table 4.40) for each of the chemicals are carried over to this overall summary Table 4.41 below as the first, second and third rows.

In addition, the extra indicators (i.e., bioaccumulation, extraction potential and ingredient concentration in product) for exposure were added to the summary template as extra rows. However, information on extraction potential and ingredient concentration could not be obtained; hence DG (data gap) is assigned for those. Lastly, the total summed score for each chemical is compared with that of DecaBDE. A lower score indicates worse standing in terms of human exposure, i.e., the chemical shows a higher potential for human exposure. Those having a higher score means they are safer chemicals showing lower human exposure potential. The summary matrix shows that two alternatives (i.e., aluminum diethylphosphinate and polyphosphonate) perform better, while two others (i.e., ammonium polyphosphate and magnesium hydroxide) perform worse when compared to DecaBDE in QHEA.

The comparative summary shows that Aluminum diethylphosphinate and Polyphosphonate performed better in the QHEA and showed no skin

sensitization/irritation or systemic toxicity which makes them a good alternative when exposed to infants sitting in car seats.

Table 4.41. Comparative QHEA summary matrix.

Pathway/ Criteria	**DecaBDE**	**Aluminum Diethyl-phosphinate**	**Ammonium Poly-phosphate**	**Magnesium Hydroxide**	**Poly-phosphonate**
Oral Ingestion	2/4	2/4	2/4	1/4	3/4
Inhalation	2/5	3/5	2/5	2/5	3/5
Dermal Absorption	3/5	3/5	1/5	1/5	3/5
Bioaccumulation	0/1	1/1	DG	1/1	DG
Extraction Potential	DG	DG	DG	DG	DG
Ingredient conc. in product	DG	DG	DG	DG	DG
Overall Score	**7/17**	**9/17**	**5/17**	**5/17**	**9/17**

QHEA Colour Indicator	
	Exposure equal to DecaBDE
	Exposure less than DecaBDE
	Exposure more than DecaBDE

None of the alternatives showed systemic toxicity and only Ammonium polyphosphate showed moderate skin irritation. Ammonium polyphosphate and Magnesium hydroxide showed more qualitative exposure potential in comparison to DecaBDE.

4.4.4 Conclusion:

As can be seen from these tables and the above discussions under each subsection, some of the properties of alternatives that are disadvantageous for environmental exposure (such as high $\log K_{ow}$ leading to partitioning into soil which has much higher degradation half-lives) leading to high persistence for chemical may be advantageous for human exposure (a $\log K_{ow}$ higher than a certain level would decrease dermal absorption). In a number of instances, a chemical preferable for

CHA may not be as preferable for QHEA (e.g. Ammonium Polyphosphate and Magnesium hydroxide for CHA but not as much for QHEA in comparison to DecaBDE). Data gaps and missing information also play a crucial role in QHEA where one missing data reduces the score without knowing the effect it will have in reality.

It is therefore both not possible in this study and not the intention of this study to propose one single chemical alternative to DecaBDE. The main purpose is to evaluate each alternative from a number of different perspectives to provide the necessary information to the user for informed chemical substitution. A summary Table 4.42 below shows the benchmark scores and comments of the different CAA components carried out for DecaBDE and the proposed alternatives.

Table 4.42. Conclusion summary for chemical alternative assessment for DecaBDE.

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
DecaBDE	**BM-1**	Chemicals of concern. Should be avoided due to persistence, bioaccumulation and toxic (PBT) properties. Based on LOAEL value as low as 6 mg/kg bw/day, DecaBDE is a development toxicant.		DecaBDE is PBT as well as persistent organic pollutant and is in the Stockholm Convention Annex A.		As per risk characterization in the study by Fowles (2013), infants and toddlers sitting in a car seat were not at risk in New Zealand from DecaBDE and other PBDEs for neurodevelopment toxicity. But body burden from food and direct dermal contact exposure from the seat surface were not considered.	Use should be avoided.
Alternatives							
Aluminum Diethylphosphinate	BM-3	It's a much safer alternative than DecaBDE and did not show any Group I, II or II* toxicity.		Aluminum diethylphosphinate is an organophosphorus salt and is not amenable to the fugacity based model.		Showed better performance than DecaBDE in QHEA.	It is much safer as per CHA and shows less exposure potential in

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							QHEA. EEA could not be carried out due to missing information.
Ammonium Polyphosphate	BM-3	It's a much safer alternative than DecaBDE and showed only moderate skin irritation in the CHA.		EEA could not be carried due to important missing information.		Showed more exposure potential than DecaBDE. Showed worse dermal absorption performance based on skin irritation.	It is much safer as per CHA but shows more exposure potential in QHEA. Due to important missing information EEA could not be carried out. QHEA shows more exposure potential than DecaBDE so before of the alternative, detailed risk assessment is

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							recommended. It is recommended that comprehensive environmental fate studies should be carried out to understand any environmental impact.
Magnesium Hydroxide	BM-3	It's a much safer alternative than DecaBDE and showed only moderate eye irritation in the CHA.		EEA could not be carried due to being inorganic chemical which dissociates into Mg^{2+} ion in the environment. The Mg^{2+} ion is recalcitrant and is not amenable to the EQC model used in this study where degradation of the chemical is of prime concern.		The summary matrix shows that the predicted exposure will be more than DecaBDE due to more oral, dermal and inhalation absorption as a result of preferable $\log K_{ow}$ value.	Much safer as per CHA. QHEA shows more exposure potential than DecaBDE. It is recommended that detailed risk assessment is carried out for human

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							exposure potential and EEA for magnesium hydroxide should be carried out before its use.
Polyphosphonate	BM-3	It's a much safer alternative than DecaBDE and did not show any Group I, II or II* toxicity.		EEA could not be carried due to missing important information.		Showed less exposure potential than DecaBDE in QHEA.	Much safer than DecaBDE as per CHA and QHEA. Can be a preferable alternative to DecaBDE but it is recommended that comprehensive environmental fate studies should be carried out to

Chemical	CHA		Exposure Assessment				Overall Conclusion
			Environmental Exposure Assessment		Qualitative Human Exposure Assessment		
	Score	Comment	Score	Comment	Score	Comment	
							understand any environmental impact.

EEA Legend:

	Performs better in one mode of entry and worse in one mode of entry than DecaBDE
	Worse than DecaBDE in both mode of entries.
	Better than DecaBDE in both mode of entries.

QHEA Legend:

	Exposure equal to DecaBDE
	Exposure less than DecaBDE
	Exposure more than DecaBDE

CHAPTER 5

5 CONCLUSIONS

The template of CAA followed in this study can be adopted as a screening method to filter a large number of alternatives available for a chemical of concern. Few alternatives can be narrowed down via this method so that they can be evaluated in depth. It should however be emphasized that the assessment is highly dependent on the availability and reliability of data, therefore new toxicological and physicochemical data availability could change the results and conclusions. Uncertainty in the assessment also depends on presence of any missing hazard data which was assigned 'DG-data gap' in this study. Due to unavailability of the pertinent environmental degradation half-life data, environmental exposure could not be assessed for some chemicals. The GreenScreen persistence score gives an idea about the biodegradation of the chemicals but availability of environmental data would give a detailed picture of the effect of mode of entry of the chemical in the environment. The uncertainty in the exposure assessment (EEA and QHEA) can also arise from differences in concentration and quantity of the alternative when compared to the target chemical in a given product. The toxicology information obtained from the ECHA registration dossiers are the responsibility of the registrant and the results drawn from those are therefore referenced in this evaluation.

In line with the aims of this study, alternatives for three phthalates (DEHP, DBP and BBP), HBCD and DecaBDE are evaluated within the aforementioned CAA steps. For the phthalates (DEHP, DBP and BBP), as per CHA, all alternatives evaluated are safer than the phthalates, except DINA. The reproductive and development toxicity evaluation of DINA was done with a structural analogue DEHA, which showed development toxicity capability because of an NOAEL value of 28 mg/kg bw/day. Keeping in mind, DEHA has been included in the CoRAP list due to reproductive toxicity concerns, due to structural similarity with

DEHP, which makes DINA a prime candidate to be included in the CoRAP in the future as well. Two generation reproduction guideline (OECD TG 416) study should be conducted to evaluate the adipate group of chemicals in detail. COMGHA was evaluated to be the safest option as an alternative based on Benchmark-3 score with all the major toxicology data available. EEA assessment could not be carried out due to missing data and it is highly recommended to evaluate the environmental impact of COMGHA to have a complete set of results. DEHT is also a viable option based on the results obtained in this study.

For HBCD used in XPS and EPS building insulation, although all alternative chemicals were Benchmark-2, Butadiene styrene brominated copolymer was the safest because it did not show any hazardous qualities in the Group I human hazard endpoints, whereas TBBPA ether and TBBPA ether derivative showed moderate hazard concerns. EEA for Butadiene styrene brominated copolymer could not be carried out due to missing information, but based on the functional use of the chemical it should be highly persistent in the environment and steps should be taken for its safe release into the environment. TBBPA ether and TBBPA ether derivative are already in the CoRAP list due to their persistence, bioaccumulative properties and potential endocrine disruption capabilities. More *in vivo* tests will determine the fate of these chemicals because if proved to be endocrine disruptors, they could be added to the SVHC list. This would in turn be most probably followed by addition into Authorization or Restriction annexes.

For DecaBDE used in the automobile industry, all the alternatives showed promise. All of them were Benchmark-3 chemicals. Aluminum diethylphosphinate and Polyphosphonate also showed less exposure capability than DecaBDE in QHEA. All proposed alternatives were persistent in the environment due to the nature of the chemicals and the functional use it is required for. Steps should be taken to regulate the safe discharge of these chemicals to the environment which will help in eradication of the environmental concerns posed by these highly persistent chemicals.

CHAPTER 6

6 RECOMMENDATIONS

- For future studies, the chemical structure of target and alternative chemicals, their function in a product and CAA could be studied together in a multidisciplinary approach to expand from replacing single chemical to a group of similar structured hazardous chemicals used for a specific function.
- Software and tools could be developed which can flag structurally similar chemicals of a hazardous chemical which has been included in SVHC, Authorization or Restriction annex to expedite the fate of such similar structured chemicals from the databanks instead of waiting for years.
- Environmental exposure assessment can be expanded by incorporating regional or local evaluation models.
- Quantitative fugacity based models could be incorporated in CAA to quantify exposure of humans from the various environmental compartments.
- Uncertainty analysis could be done for GreenScreen hazard assessment tool to prioritize the specific hazard endpoints which are deemed more prevalent and problematic in the chemicals for a specific function in a product.
- The transformation products of the alternatives could be included in the CHA and exposure assessment to get a more complete picture.
- Risk assessment could be done for the chemicals having the same Benchmark scores to come to a definitive conclusion.

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APPENDICES

Appendix A: Chemicals which are in Turkish Inventory as well as REACH SVHC, Authorization and Restriction List

Table A1. Chemicals selected in the study with S. Nos found in Turkish Inventory (Dec 14th, 2011)

The chemicals selected in this study.
DBP (S.No 158)
BBP (S.No 163)
DEHP (S.No 474)
HBCD (S.No 1064, 1779)
DecaBDE (S. No 824)

Table A2: Chemicals which are in the ECHA (SVHC) List (May, 2020) and are still being imported into Turkey as of December 14, 2011 Inventory. The Sira No indicates the S.No in the Turkish inventory in Table A1 above.

S.No	Sira.No	EC No	Chemical Name	Date of Inclusion
1	57	200-679-5	N,N-dimethylformamide	19/12/2012
2	87	200-879-2	Propylene oxide; 1,2-epoxypropane; Methyloxirane	19/12/2012
3	99	201-058-1	Dimethyl sulphate	19/12/2012
4	122	201-167-4	Trichloroethylene	18/06/2010
5	123	201-173-7	Acrylamide	30/03/2010
6	135	201-245-8	4,4'-isopropylidenediphenol	12/1/2017
7	141	201-280-9	p-(1,1-dimetilpropil)fenol	12/1/2017
8	155	201-545-9	dicyclohexyl phthalate	27/06/2018
9	157	201-553-2	Diisobutyl phthalate	13/01/2010
10	158	201-557-4	dibutyl phthalate	28/10/2008
11	159	201-604-9	cyclohexane-1,2-dicarboxylic anhydride	19/12/2012
12	163	201-622-7	benzyl butyl phthalate	28/10/2008
13	200	202-318-7	butyl 4-hydroxybenzoate	25/6/2020
14	217	202-506-9	imidazolidine-2-thione	16/12/2013
15	237	202-679-0	4-tert-butylphenol	16/07/2019
16	245	202-716-0	nitrobenzene	17/12/2015
17	267	202-974-4	4,4'-diaminodiphenylmethane; 4,4'-methylenedianiline	28/10/2008
18	325	203-458-1	1,2-dichloroethane	19/12/2011
19	327	203-468-6	ethylenediamine	27/06/2018

20	372	203-713-7	2-methoxyethanol	15/12/2010
21	396	203-804-1	2-ethoxyethanol	15/12/2010
22	406	203-839-2	2-ethoxyethyl acetate	20/06/2011
23	428	203-924-4	bis(2-methoxyethyl) ether	19/12/2011
24	468	204-118-5	tris(2-chloroethyl) phosphate	13/01/2010
25	474	204-211-0	bis(2-ethylhexyl) phthalate	28/10/2008
26	521	204-650-8	C,C'-azodi(formamide)	19/12/2012
27	551	204-826-4	N,N-dimethylacetamide	19/12/2011
28	601	205-426-2	4-(1,1,3,3-tetramethylbutyl)phenol	19/12/2011
29	659	206-114-9	hydrazine	20/06/2011
30	681	208-169-4	cobalt carbonate	15/12/2010
31	700	208-762-8	dodecamethylcyclohexasiloxane	27/06/2018
32	701	208-764-9	decamethylcyclopentasiloxane	27/06/2018
33	712	209-008-0	benzene-1,2,4-tricarboxylic acid 1,2-anhydride	27/06/2018
34	717	209-136-7	octamethylcyclotetrasiloxane	27/06/2018
35	792	212-828-1	1-methyl-2-pyrrolidone	20/06/2011
36	824	214-604-9	bis(pentabromophenyl) ether	19/12/2012
37	838	215-125-8	diboron trioxide	18/06/2012
38	842	215-146-2	cadmium oxide (non-pyrophoric)	20/06/2013
39	864	215-235-6	orange lead	19/12/2012
40	869	215-267-0	lead monoxide	19/12/2012
41	894	215-540-4	disodium tetraborate, anhydrous	18/06/2010
42	902	215-607-8	chromium trioxide	15/12/2010
43	920	215-693-7	lead sulfochromate yellow	13/01/2010
44	1004	219-514-3	1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione; TGIC	18/06/2012
45	1064	221-695-9	1,2,5,6,9,10-hexabromocyclododecane	28/10/2008
46	1100	223-383-8	2,4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol	17/12/2015
47	1243	230-770-5	2-[2-[2-[2-(4-nonylphenoxy) ethoxy]ethoxy]ethoxy]ethanol	20/06/2013
48	1252	231-100-4	lead	27/06/2018
49	1295	231-556-4	Sodium peroxometaborate	16/06/2014
50	1345	231-846-0	lead chromate	13/01/2010
51	1375	232-142-6	strontium chromate	20/06/2011
52	1483	233-139-2	boric acid	18/06/2010
53	1489	233-245-9	lead dinitrate	19/12/2012
54	1497	233-334-2	cobalt sulphate	15/12/2010
55	1521	234-190-3	sodium dichromate	28/10/2008
56	1528	234-343-4	Boric acid	18/06/2010
57	1530	234-390-0	Perboric acid, sodium salt	16/06/2014
58	1547	235-252-2	trilead dioxide phosphonate	19/12/2012
59	1551	235-380-9	tetralead trioxide sulphate	19/12/2012
60	1573	235-702-8	dioxobis(stearato)trilead	19/12/2012

61	1575	235-759-9	lead chromate molybdate sulfate red	13/01/2010
62	1649	239-622-4	2-ethylhexyl 10-ethyl-4,4-dioctyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate	17/12/2014
63	1747	246-356-2	Dichromium tris(chromate),Chromium III chromate,Chromic chromate	19/12/2011
64	1757	246-672-0	nonylphenol	19/12/2012
65	1772	247-094-1	hexahydromethylphthalic anhydride	19/12/2012
66	1779	247-148-4	hexabromocyclododecane	28/10/2008
67	1785	247-384-8	2-(2H-benzotriazol-2-yl)-4,6-ditertpentylphenol	17/12/2014
68	1799	247-759-6	tris(nonylphenyl) phosphite	16/07/2019
69	1802	247-816-5	26-(nonylphenoxy)-3,6,9,12,15,18,21,24-octaoxahexacosan-1-ol	20/06/2013
70	1936	256-418-0	pentazinc chromate octahydroxide	19/12/2011
71	1882	251-823-9	tetrahydro-4-methylphthalic anhydride	19/12/2012
72	2127	266-028-2	Pitch, coal tar, high-temp.	13/01/2010
73	2517	284-325-5	Phenol, 4-nonyl-, branched	19/12/2012
74	2726	400-600-6	2-methyl-1-(4-methylthiophenyl)-2-morpholinopropan-1-one	16/01/2020
75	2804	500-024-6	Nonylphenol, ethoxylated	20/06/2013
76	2849	500-209-1	Nonylphenol, branched, ethoxylated	20/06/2013
77	2868	500-315-8	4-Nonylphenol, branched, ethoxylated	20/06/2013

Table A3: Substances in the Turkish Inventory and in REACH Restriction List (Annex XVII) (May, 2020) (The Sira No indicates the S.No in the Turkish Inventory of chemicals Table A1)

S.No	Sıra No*	EC No	Chemical Name	Restriction Starting Date
1	49	200-659-6	Methanol	9-May-19
2	52	200-663-8	chloroform	
3	67	200-753-7	Benzene	
4	76	200-831-0	Chloroethylene	
5	79	200-838-9	Dichloromethane	
6	123	201-173-7	Acrylamide	5-Nov-12
7	135	201-245-8	4,4'-isopropylidenediphenol	2-Jan-20
8	157	201-553-2	Diisobutyl phthalate	7-Jul-20
9	158	201-557-4	dibutyl phthalate	7-Jul-20
10	163	201-622-7	benzyl butyl phthalate	7-Jul-20
11	265	202-966-0	4,4'-methylenediphenyl diisocyanate	27-Dec-10
12	317	203-400-5	1,4-dichlorobenzene	
13	360	203-625-9	toluene	
14	397	203-806-2	cyclohexane	27-Jun-10

15	423	203-906-6	2-(2-methoxyethoxy)ethanol	27-Jun-10
16	438	203-961-6	2-(2-butoxyethoxy)ethanol	27-Jun-10
17	474	204-211-0	bis(2-ethylhexyl) phthalate	
18	475	204-214-7	dioctyl phthalate	
19	701	208-764-9	decamethylcyclopentasiloxane	31-Jan-20
20	717	209-136-7	octamethylcyclotetrasiloxane	31-Jan-20
21	728	209-544-5	4-methyl-m-phenylene diisocyanate	24-Aug-23
22	792	212-828-1	1-methyl-2-pyrrolidone	9-May-20
23	842	215-146-2	cadmium oxide (non-pyrophoric)	
24	1185	227-534-9	o-(p-isocyanatobenzyl)phenyl isocyanate; Diphenylmethane-4,4'-diisocyanate	27-Dec-10
25	1213	229-347-8	ammonium nitrate	27-Jun-10
26	1252	231-100-4	lead	9-Oct-13
27	1256	231-111-4	nickel	
28	1262	231-148-6	arsenic	
29	1519	233-954-3	cadmium dioleate	
30	1757	246-672-0	nonylphenol	
31	1797	247-714-0	methylenediphenyl diisocyanate	27-Dec-10
32	1807	247-977-1	di-"isodecyl" phthalate	
33	1838	249-079-5	di-"isononyl" phthalate	
34	2299	271-090-9	1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	
35	2300	271-091-4	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	
36	2804	500-024-6	Nonylphenol, ethoxylated	3-Feb-21
37	2849	500-209-1	Nonylphenol, branched, ethoxylated	3-Feb-21
38	2868	500-315-8	4-Nonylphenol, branched, ethoxylated	3-Feb-21

*There are some chemicals for which restriction enforcement date has not been specified because they were already restricted under other historical legislations in the E.U before REACH regulation was approved. That is why such chemicals have just been included in the Restriction Annex XVII without specifying the restriction enforcement date. After REACH regulation entered into force on 1st June 2007, the chemicals which been restricted have been specified a restriction enforcement date, mentioned in the table above.

Table A4: Substances in the Turkish Inventory and in REACH Authorization List (Annex XIV) (May,2020) (Sira No indicates the S.No in Turkish inventory of chemicals in Table A1)

S.No	Sıra No*	EC No	Chemical Name	Application Date	Sunset Date
1	122	201-167-4	Trichloroethylene	21/10/2014	21/04/2016
2	157	201-553-2	Diisobutyl phthalate	21/08/2013	21/02/2015
3	158	201-557-4	dibutyl phthalate	21/08/2013	21/02/2015
4	163	201-622-7	benzyl butyl phthalate	21/08/2013	21/02/2015
5	267	202-974-4	4,4'-diaminodiphenylmethane; 4,4'-methylenedianiline	21/02/2013	21/08/2014

6	325	203-458-1	1,2-dichloroethane	22/05/2016	22/11/2017
7	428	203-924-4	bis(2-methoxyethyl) ether	22/02/2016	22/08/2017
8	468	204-118-5	tris(2-chloroethyl) phosphate	21/02/2014	21/08/2015
9	474	204-211-0	bis(2-ethylhexyl) phthalate	21/08/2013	21/02/2015
10	902	215-607-8	chromium trioxide	21/03/2016	21/09/2017
11	920	215-693-7	lead sulfochromate yellow	21/11/2013	21/05/2015
12	1064	221-695-9	1,2,5,6,9,10-hexabromocyclododecane	21/02/2014	21/08/2015
13	1100	223-383-8	2,4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol	27/05/2022	27/11/2023
14	1243	230-770-5	2-[2-[2-[2-(4-nonylphenoxy) ethoxy]ethoxy]ethoxy]ethanol	4/7/2019	4/1/2021
15	1295	231-556-4	Sodium peroxometaborate	27/11/2021	27/05/2023
16	1345	231-846-0	lead chromate	21/11/2013	21/05/2015
17	1375	232-142-6	strontium chromate	22/07/2017	22/01/2019
18	1521	234-190-3	sodium dichromate	21/03/2016	21/09/2017
19	1530	234-390-0	Perboric acid, sodium salt	27/11/2021	27/05/2023
20	1575	235-759-9	lead chromate molybdate sulfate red	21/11/2013	21/05/2015
21	1747	246-356-2	Dichromium tris(chromate),Chromium III chromate,Chromic chromate	22/07/2017	22/01/2019
22	1779	247-148-4	hexabromocyclododecane	21/02/2014	21/08/2015
23	1785	247-384-8	2-(2H-benzotriazol-2-yl)-4,6-ditertpentylphenol	27/05/2022	27/11/2023
24	1802	247-816-5	26-(nonylphenoxy)-3,6,9,12,15,18,21,24-octaoxahexacosan-1-ol	4/7/2019	4/1/2021
25	1936	256-418-0	pentazinc chromate octahydroxide	22/07/2017	22/01/2019
26	2127	266-028-2	Pitch, coal tar, high-temp.	4/4/2019	4/10/2020
27	2804	500-024-6	Nonylphenol, ethoxylated	4/7/2019	4/1/2021
28	2849	500-209-1	Nonylphenol, branched, ethoxylated	4/7/2019	4/1/2021
29	2868	500-315-8	4-Nonylphenol, branched, ethoxylated	4/7/2019	4/1/2021

Appendix B: GreenScreen Hazard Assessment for Each Target Chemical

Chemical: Bis (2-ethylhexyl) phthalate (DEHP) (CAS# 117-81-7) (EC: 204-211-0) Hazard Assessment.

DEHP is present >1000tons in Turkish Inventory.

	GreenScreen and DfE Hazard Summary Table for DEHP																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	H	L	H	H	H	L	H	M	L	L	L	*L*	L	L	L	L	vL	M	*L*	L

Hazard Endpoints Detailed Evaluation Summary

Carcinogenicity			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
Authoritative A: CA EPA - Prop 65	**Screening A:** GHS - Australia (H350	Slight Effect observed as per Danish	**HIGH:** As per the Authoritative A

(Carcinogen) **(H).** **Authoritative A:** US CDC - Occupational Carcinogens (Occupational Carcinogen). **(H).** **Authoritative A:** USEPA - IRIS Carcinogens ((1986) Group B2 - Probable human Carcinogen) **(H).** **Authoritative A:** US NIH - Report on Carcinogens (Reasonably Anticipated to be Human Carcinogen) **(H).** **Authoritative A:** IARC (Group 2B - Possibly carcinogenic to humans) **(M).** **Authoritative A:** MAK (Carcinogen Group 4 - Non-genotoxic carcinogen with low risk under MAK/BAT levels) **(M).**	- May cause cancer) (*H*). **Screening A:** GHS - Japan (Carcinogenicity - Category 2 [H351]) (*M*).	EPA classification.	and Screening A List high score is designated. The confidence in the data is high.
Mutagenicity (M)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		No adverse effect observed (negative) as per Danish EPA Report.	**LOW:** As per the ECHA Registration dossier the possible genotoxic effect of DEHP has been thoroughly investigated in several different short-term tests. Most of the studies are performed according to GLP principles and are comparable to guideline studies. **No adverse effect observed (negative) as per Danish EPA Report.** The confidence in the data is high due to experimental data.

Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
Authoritative A: CA EPA - Prop 65 (Reproductive Toxicity – Male) **(H).** **Authoritative A:** US NIH - Reproductive & Developmental Monographs (Clear Evidence of Adverse Effects - Reproductive Toxicity) **(H).** **Authoritative B:** EU - Annex VI CMRs (Reproductive Toxicity - Category 1B) (*H*). **Authoritative B:** EU - SVHC Authorization List (Toxic to reproduction - Banned unless Authorized) (*H).*	**Screening A:** GHS - Japan (Toxic to reproduction - Category 1B [H360]) (*H*). **Screening A:** GHS - Korea (Reproductive toxicity - Category 1 [H360 - May damage fertility or the unborn child]) (*H*). **Screening A:** GHS - New Zealand (6.8A - Known or presumed human reproductive or developmental toxicants) (*H*).	Clear effect (GHS Classified).	**HIGH:** As per the Authoritative A and Screening A List high score is designated. The confidence in the data is high.
Development Toxicity (D)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
Authoritative A: CA EPA – Prop 65 (Developmental toxicity) **(H).** **Authoritative A:** US NIH – Reproductive & Developmental Monographs (Clear Evidence of Adverse Effects – Developmental Toxicity) **(H).** **Authoritative A:** EU – GHS (H-Statements) (H360FD – May damage fertility. May damage the unborn child) (H). **Authoritative B:** MAK (Pregnancy Risk Group C) (*M-L*). **Authoritative B:** EU – REACH Annex XVII CMRs (Toxic to	**Screening A:** GHS – Malaysia (H360Fd – May damage fertility. Suspected of damaging the unborn child) (*H-M*). (Check for Neurotoxicity). **Screening A:** GHS – Australia (H360FD – May damage fertility. May damage the unborn child) (*H*).	Clear effect (GHS Classified).	**HIGH:** As per the Authoritative A and Screening A List high score is designated. The confidence in the data is high.

Reproduction Category 2 – Substances which should be regarded as if they impair fertility or cause Developmental Toxicity in humans) (*H*).			
Endocrine Activity (E)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
Authoritative A: EU - SVHC Authorization List (Equivalent Concern - Candidate List) **(H).** **Authoritative A:** EU - SVHC Authorization List (Equivalent Concern - Candidate List: endocrine disrupting properties cause probable serious effects to the environment or human health) **(H).**	**Screening B:** EU - Priority Endocrine Disruptors (Category 1 - In vivo evidence of Endocrine Disruption Activity) *(H-M).* **Screening B:** OSPAR - Priority PBTs & EDs & equivalent concern (Endocrine Disruptor - Chemical for Priority Action) *(H-M).* **Screening B:** TEDX - Potential Endocrine Disruptors (Potential Endocrine Disruptor) (*H-M*).	Clear effect (GHS Classified).	**HIGH:** As per the Authoritative A and Screening A List high score is designated. The confidence in the data is high.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		No effect observed.	**LOW:** As per ECHA Registration Dossier the LD50 values are greater than 2000 mg/kg. Confidence in the score is high based on experimental data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
	Screening A: GHS – New Zealand		**HIGH:** As per the Screening A List

	(6.9B (oral) – Harmful to human target organs or systems (Cat. 2)) (*H*). **Screening A:** GHS – Japan (Specific target organs/systems toxicity following single exposure – Category 3 [H335 or H336]) (*M*).		high score is designated. In the ToxServices database GreenScreen study for DEHP it is stated that at 1500 mg/kg bw/day liver weight was increased that is why a high score was provided because GHS category 2 single dose toxicants lie between 300 and 2000 mg/kg (CPA, 2018). The confidence in the data is high due to experimental data.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
	Screening A: GHS – Japan (Specific target organs/systemic toxicity following repeated exposure – Category 2 [H373]) (*M*).	Clear Effect observed.	**MODERATE:** As per the Screening A List moderate score is designated. The confidence in the data is low. A study in the registration dossier showed NOAEL of 28.9 mg/kg bw/day less than 50 mg/kg bw/ day was based on hepatotoxicity (liver) observed in chronic oral toxicity study in rat which comes in the moderate range (10-100 mg/ kg bw/day (CPA, 2018). The confidence in the data is high due to experimental data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
			LOW: As per ECHA Registration Dossier study no adverse neural effects were observed in the single dose study (5000 mg/kg bw). The confidence in the data is high due to experimental data.

Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
	Screening B: Boyes - Neurotoxicant (Neurotoxic) (*vH-L*).		**LOW:** As per ECHA Registration Dossier No sign of neurofunction impairment was noted in any of the various parameters of the Water Maze Test, the Functional Observation Battery, and the Motor Activity Assessment. (NOAEL 1500 mg/kg bw/day). The confidence in the data is high due to experimental data.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		No effect observed.	**LOW:** As per ECHA Registration Dossier DEHP is not a skin sensitizer. The confidence in the data is high due to experimental data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
			LOW: No respiratory sensitizing functional group present. The score assigned is low confidence score due to expert judgment.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		No effect observed.	**LOW:** As per ECHA Registration Dossier DEHP is slightly irritating but still it was classified as low because GHS classifies a chemical as dermal irritant when mean erythema and edema scores are greater than 1.5 but in registration dossier the score is

			1.11. The confidence in the data is high due to experimental data.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
	Screening A: GHS - Japan (Serious eye damage / eye irritation - Category 2B [H319]) (*M*).	No effect observed.	**LOW:** Although it is in Screening A list as moderate but in ECHA Registration dossier studies DEHP is not eye irritant as per reported study. **Danish EPA also reported it as no effects observed.** The confidence in the data is high due to experimental data.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
	Screening A: GHS - Japan (Hazardous to the aquatic environment (acute) - Category 1 [H400]) (*vH*). **Screening A:** GHS - Korea (Hazardous to the aquatic environment (acute) - Category 1 [H400 - Very toxic to aquatic life]) (*vH*).	EC50: >0.003 mg/L LC50: >0.16 mg/L* Not ecotoxic.	**LOW:** As per ECHA Registration Dossier the reliable acute toxicity studies indicate low acute toxicity for DEHP. The reasoning behind it is if the aquatic toxicity is greater than water solubility than no adverse effects are expected on aquatic biota at saturation. The confidence in the data is high due to experimental data.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		NOEC: 5000 µg/L* (Fish) Not ecotoxic	**LOW:** Based on ECHA Registration Dossier it is not toxic. The confidence in the data is high due to experimental data.
Persistence (P)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		Readily biodegradable.	**VERY LOW:** As per ECHA

			Registration Dossier as it met 10 day window in an OECD 301B ready biodegradability test. The confidence in the data is high. The confidence in the data is high due to experimental data.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
		The substance is not PBT / vPvB.	**MODERATE:** As per ECHA Registration Dossier **Value used for CSA and PBT-assessment:** BCF: 614 dimensionless (L/kg ww or dimensionless). This value comes in the moderate range as per GreenScreen criteria (CPA, 2018). The confidence in the data is high due to experimental data.
Reactivity (R)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
			LOW: In the registration dossier no oxidizing potential due to the absence of oxidizing functional groups. The flash point is 200C which indicates that the liquid is not flammable because it is above 93C cutoff criteria to make it a flammable liquid. The confidence in the data is lower due to absence of experimental data.
Flammability (F)			
Authoritative List	**Screening List**	**DANISH EPA**	**Final Decision**
			LOW: The flash point is 200C which indicates that the liquid is not flammable because it is above 93C

			cutoff criteria to make it a flammable liquid. The confidence in the data is high due to presence of experimental data.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

Nielsen, B. S., & Larsen, P. B. (2014). *Alternatives to classified phthalates in medical devices*. Retrieved from https://www2.mst.dk/Udgiv/publications/2014/03/978-87-93178-27-4.pdf

Pharos. (2021). 'Di (2-ethylhexyl) phthalate (DEHP) (CAS# 117-81-7)' Retrieved from https://pharosproject.net/chemicals/2007650#hazards-panel

ECHA Registration Dossier:

ECHA (2021). Registered Substances Dossier for Bis (2-ethylhexyl) phthalate (DEHP) (CAS# 117-81-7). European Chemicals Agency. Last Revised 6th March, 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15358/1/1

ToxServices (2021). Registered Substances Dossier for Bis (2-ethylhexyl) phthalate (DEHP) (CAS# 117-81-7). Viewed on 20th December, 2020. https://database.toxservices.com/FMD/User/Greenscreen/Greenscreen?id=260

Chemical: Dibutyl Phthalate (DBP) (CAS# 84-74-2) (EC: 201-557-4) Hazard Assessment

DBP is present in 1 to 1000tons/year in Turkish Inventory

	GreenScreen and DfE Hazard Summary Table for DBP																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	**M**	*L*	**H**	**H**	**H**	**L**	*M*	*H*		**L**	*H*	**DG**	**L**	**L**	**VH**	**H**	**vL**	*L*	*L*	**L**

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Carcinogenicity		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: MAK (Carcinogen Group 3B – Evidence of carcinogenic effects but not sufficient for		**MODERATE:** As per Authoritative A list Moderate hazard score. The confidence in the

classification) **(M).** **Authoritative B:** USEPA – IRIS Carcinogens ((1986) Group D – Not classifiable as to human carcinogenicity) (*H-L*).		data is high.
Mutagenicity (M)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: *In vitro* gene mutation study in bacteria (key study with Klimisch score 2 without guideline) negative genotoxicity was observed. The *in vivo* study reported was missing crucial data and results that is why it is not considered in this study. The data is gotten from ECHA Registration dossier. Confidence in data is low due to only *in-vitro* studies.
Reproductive Toxicity		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: CA EPA – Prop 65 (Reproductive Toxicity – Female) **(H).** **Authoritative A:** CA EPA – Prop 65 (Reproductive Toxicity – Male) **(H).** **Authoritative A:** US NIH – Reproductive & Developmental Monographs (Clear Evidence of Adverse Effects – Reproductive Toxicity) **(H).** **Authoritative B:** EU – Annex VI CMRs (Reproductive Toxicity – Category 1B) (*H*). **Authoritative B:** EU – SVHC Authorization List (Toxic to reproduction – Banned unless Authorized) (*H*).	**Screening A:** GHS – Japan (Toxic to reproduction – Category 1B [H360]) (*H*). **Screening A:** GHS – Korea (Reproductive toxicity – Category 1 [H360 – May damage fertility or the unborn child]) (*H*). **Screening A:** GHS – New Zealand (6.8A – Known or presumed human reproductive or developmental toxicants) (*H*).	**HIGH:** Based on the presence in Authoritative A List with a HIGH designated score. The confidence in the data is high.
Development Toxicity (D)		

Authoritative List	Screening List	Final Decision
Authoritative A: CA EPA – Prop 65 (Development Toxicity) **(H).** **Authoritative A:** US NIH – Reproductive & Developmental Monographs (Clear Evidence of Adverse Effects – Developmental Toxicity) **(H).** **Authoritative A:** EU – GHS (H-Statements)(H360Df – May damage the unborn child. Suspected of damaging fertility) **(H-M).** **Authoritative B:** EU – REACH Annex XVII CMRs (Toxic to Reproduction Category 2 – Substances which should be regarded as if they impair fertility or cause Developmental Toxicity in humans) (*H*).	**Screening A:** GHS – Australia (H360Df – May damage the unborn child. Suspected of damaging fertility) *(H-M).* **Screening A:** GHS – Malaysia (H360Df – May damage the unborn child. Suspected of damaging fertility) *(H-M).*	**HIGH:** Based on the presence in Authoritative A List with a HIGH designated score. The confidence in the data is high.
Endocrine Activity		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: EU – SVHC Authorization List (Equivalent Concern – Candidate List: endocrine disrupting properties cause probable serious effects to the environment or human health) **(H).**	**Screening B:** EU – Priority Endocrine Disruptors (Category 1 – In vivo evidence of Endocrine Disruption Activity). *(H-M).* **Screening B:** OSPAR – Priority PBTs & Eds & equivalent concern (Endocrine Disruptor – Chemical for Priority Action) *(H-M).* **Screening B:** TEDX – Potential Endocrine Disruptors (Potential Endocrine Disruptor) *(H-M).*	**HIGH:** Based on the presence in Authoritative A List with a HIGH designated score. The confidence in the data is high.
Acute Mammalian Toxicity (AT)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS – New Zealand (6.1E (oral) – Acutely toxic) (*L*)	**LOW:** As per the screening A list low score is designated. In the ECHA Registration Dossier The oral LD50 value for the rat is ≥6,300 mg/kg bw for dibutyl phthalate; the dermal LD50 is >20,000 mg/kg bw for the

		rabbit. Higher confidence in data due to experimental data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS – Japan (Specific target organs/systemic toxicity following single exposure – Category 3 [H335 or H336]) (*M*).	**MODERATE:** As per the screening A list MODERATE score is designated. The confidence in the data is low. No gross pathology data in acute toxicity study in ECHA registration dossier located that is why Screening A list low confidence score is adopted.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS – Japan (Specific target organs/systemic toxicity following repeated exposure – Category 1 [H372]) (*H*).	**HIGH:** As per the screening A list HIGH score is designated. The confidence in the data is low. But H372 is for inhalation. But the experimental measurement in the registration dossiers show that in OECD Guideline study (Klimisch 1) the NOAEL is 152 mg/kg bw/ day for oral which makes it a hazard score low and this score is assigned in this study but H372 is for inhalation that is why it is scored H.
Neurotoxicity-Single Exposure (N)		
Authoritative List	**Screening List**	**Final Decision**
		DG: No pertinent study located.
Neurotoxicity-Repeat Exposure (N)		
Authoritative List	**Screening List**	**Final Decision**

	Screening B: G&L – Neurotoxic Chemicals (Neurotoxic) (*vH-M*)	**LOW:** AS per Registration Dossier OECD 408 Guideline study neural behavior regarding neural function was part of the test and no neural effect was observed. The confidence in the data is high due to experimental data.
Skin Sensitization (SnS)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS – Japan (Skin sensitizer – Category 1 [H317]) (*H*)	**HIGH:** As per the screening A list HIGH score is designated. The confidence in the data is low. In the Registration Dossier there are conflicting studies although it says not skin sensitizing but it has discarded previous studies which showed sensitization effects in humans that is why a definite conclusion could not be drawn and the Screening A score is preferred in this study.
Respiratory Sensitization (SnR)		
Authoritative List	**Screening List**	**Final Decision**
		DG: No pertinent data located.
Skin Irritation/Corrosivity (IrS)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: As per the ECHA Registration Dossier it is not skin irritating. Key study Klimisch score 1.
Eye Irritation/Corrosivity (IrE)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS - New Zealand (6.4A - Irritating to the eye (Cat. 2A)) (*H*)	**LOW:** As per the screening A list HIGH score is designated. The confidence in the data is low.

		As per ECHA Registration Dossier (Klimisch Score 1) Guideline study it is not eye irritant. High confidence score that is why low score is assigned in this study.
Acute Aquatic Toxicity (AA)		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: EU - GHS (H-Statements) (H400 - Very toxic to aquatic life) **(vH).**	**Screening A:** GHS - Australia (H400 - Very toxic to aquatic life) (*vH*). **Screening A:** GHS - Japan (Hazardous to the aquatic environment (acute) - Category 1 [H400]). *(vH).* **Screening A:** GHS - Korea (Hazardous to the aquatic environment (acute) - Category 1 [H400 - Very toxic to aquatic life]) *(vH).* **Screening A:** GHS - Malaysia (H400 - Very toxic to aquatic life) *(vH).*	**VERY HIGH:** As per the Authoritative A list Very High score is designated. The confidence in the data is high.
Chronic Aquatic Toxicity (CA)		
Authoritative List	**Screening List**	**Final Decision**
		HIGH: EC10, LC10 or NOEC for freshwater fish: 100 µg/L as per ECHA Registration Dossier. Higher confidence in data due to experimental data. It is less than the solubility of DBP that's why as per GreenScreen criteria High score is assigned. The lowest NOEC was observed in a 99-day test (60 days post hatch) with *Oncorhynchus mykiss.* A measured value of 100 µg/l was established based on growth as the most sensitive endpoint. As per GreenScreen

		criteria (0.1-1 mg/L) comes in High score.
Persistence (P)		
Authoritative List	**Screening List**	**Final Decision**
		VERY LOW: In biodegradation tests DBP can be considered as readily biodegradable as per ECHA Registration Dossier. The confidence in the data is high due to reliable experimental data.
Bioaccumulation (B)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: BCF=432.6 L/kg ww as per EPI Suite estimation. The confidence in the data is low due to estimation data. Based on measurements for the highest exposure concentration in water and fish a BCF value of 1.8 L/kg was found. No Klimisch score provided that is why the estimated BCF value is used to be conservative.
Reactivity (R)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: Based on expert judgment because lack of oxidizing functional group and no experimental data set was available that's why the confidence in the data is low.
Flammability (F)		
Authoritative List	**Screening List**	**Final Decision**

		LOW: The flash point is 186.5C which is above the cutoff criteria 93C for flammable liquid. Based on experimental data that is why the confidence in the data is high.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

Nielsen, B. S., & Larsen, P. B. (2014). *Alternatives to classified phthalates in medical devices*. Retrieved from https://www2.mst.dk/Udgiv/publications/2014/03/978-87-93178-27-4.pdf

Pharos. (2021). 'Dibutyl Phthalate (DBP) (CAS# 84-74-2) ' Retrieved from https://pharosproject.net/chemicals/2007694#hazards-panel

ECHA Registration Dossier:

ECHA (2021). Registered Substances Dossier for Dibutyl Phthalate (DBP) (CAS# 84-74-2). European Chemicals Agency. Last Revised 23rd March, 2016. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14862/1/1

Chemical: Benzyl butyl phthalate (BBP) (CAS# 85-68-7) (EC: 201-622-7) Hazard Assessment

BBP present in 1 to 1000tons in Turkish Inventory.

	GreenScreen and DfE Hazard Summary Table for BBP																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	**M**	**L**	*H*	**H**	**H**	**L**	-	*M*	-	**L**	**L**	**DG**	**L**	*L*	**VH**	**H**	**VL**	**L**	*L*	**L**

Hazard Endpoints Detailed Evaluation Summary

Carcinogenicity (C)		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: USEPA - IRIS Carcinogens ((1986) Group C - Possible human Carcinogen) **(M).**		**MODERATE:** As per the Authoritative A List Moderate score is designated. The confidence in the data is high.

Authoritative B: IARC Group 3 - Agent is not classifiable as to its carcinogenicity to humans. (*H-L)*		
Mutagenicity (M)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: As per ECHA Registration Dossier no adverse effect was observed as per reliable guideline study *in vivo and in vitro.* The confidence in the data is high due to experimental data.
Reproductive Toxicity		
Authoritative List	**Screening List**	**Final Decision**
Authoritative B: US NIH – Reproductive & Developmental Monographs (Some Evidence of Adverse Effects – Reproductive Toxicity) (*H-M*) **Authoritative B:** EU – Annex VI CMRs (Reproductive Toxicity – Category 1B) (*H*). **Authoritative B:** EU – SVHC Authorization List (Toxic to reproduction – Banned unless Authorized) (H)	**Screening A:** GHS Japan (Toxic to reproduction – Category 1B [H360]) (*H*). **Screening A:** GHS Korea (Reproductive toxicity – Category 1 [H360 – May damage fertility or the unborn child]) (*H).*	**HIGH:** As per the Authoritative B and Screening A List high score is designated. The confidence in the data is low.
Development Toxicity (D)		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: CA EPA – Prop 65 (Developmental toxicity) **(H).** **Authoritative A:** US NIH – Reproductive & Developmental Monographs (Clear Evidence of Adverse Effects – Developmental Toxicity) **(H)** **Authoritative A:** EU – GHS (H-Statements)(H360Df – May damage the unborn child. Suspected of damaging fertility) **(H-M).** **Authoritative B:** EU – REACH Annex XVII CMRs (Toxic to Reproduction Category 2 – Substances which should be	**Screening A:** GHS – Australia (H360Df – May damage the unborn child. Suspected of damaging fertility) *(H-M)*	**HIGH:** As per the Authoritative A List High score is designated. The confidence in the data is high.

regarded as if they impair fertility or cause Developmental Toxicity in humans) (*H).* **Authoritative B:** MAK (Pregnancy Risk Group C) (*M-L*)		
Endocrine Activity		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: EU – SVHC Authorization List (Equivalent Concern – Candidate List: endocrine disrupting properties cause probable serious effects to the environment or human health) (**H).**	**Screening B:** EU – Priority Endocrine Disruptors (Category 1 – In vivo evidence of Endocrine Disruption Activity) (*H-M*). **Screening B:** OSPAR – Priority PBTs & EDs & equivalent concern (Endocrine Disruptor – Substance of Possible Concern) (*H-M*). **Screening B**: TEDX – Potential Endocrine Disruptors (Potential Endocrine Disruptor) (*H-M*).	**HIGH:** As per the Authoritative A List High score is designated. The confidence in the data is high.
Acute Mammalian Toxicity (AT)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS – New Zealand (6.1E (oral) – Acutely toxic) (*L).*	**LOW:** As per the screening A list low score is designated. In the ECHA Registration Dossier The LD50 value was estimated to be 2330 mg/kg bw for rats (of both sexes), 6160 mg/kg bw for male mice and 4170 mg/kg bw for female mice. LD50 was greater than 10,000 mg/kg bw. The confidence in the data is high due to measured data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)		
Authoritative List	**Screening List**	**Final Decision**
		DG: No pertinent data could be located.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)		

Authoritative List	Screening List	Final Decision
	Screening A: GHS - Japan (Specific target organs/systemic toxicity following repeated exposure - Category 2 [H373])(*M*)	**MODERATE:** As per the screening A list moderate score is designated. In the ECHA Registration Dossier a number of GLP compliant studies have been referenced from 14 days to 2 years and the lowest NOAEL is 151 mg/kg bw/day which makes it a hazard score of Low as per GreenScreen criteria for oral toxicity (CPA, 2018). H373 is for inhalation that is why it is scored moderate. The confidence in the data is low due to screening list.
Neurotoxicity-Single Exposure (N)		
Authoritative List	**Screening List**	**Final Decision**
		DG: No pertinent data could be located.
Neurotoxicity-Repeat Exposure (N)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: As per ECHA Registration Dossier reliable studies no neurological effects were observed and the NOAEL is 1500 mg/kg bw/day. The confidence in the data is high.
Skin Sensitization (SnS)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: No skin sensitization was reported as per ECHA Registration Dossier.
Respiratory Sensitization (SnR)		
Authoritative List	**Screening List**	**Final Decision**
		DG: No pertinent data could be located.
Skin Irritation/Corrosivity (IrS)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: GHS - New Zealand (6.3B - Mildly irritating to the	**LOW:** As per the screening A list moderate score is designated. The confidence in the data is low.

	skin) (*M).*	In the ECHA Registration dossier with (Klimisch score 1) studies BBP is termed as non-irritant after human testing. The confidence in the data is high that is why the low score is designated.
Eye Irritation/Corrosivity (IrE)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: No eye irritation was reported as per ECHA Registration Dossier study. The confidence in the study is low as Klimisch score is not provided.
Acute Aquatic Toxicity (AA)		
Authoritative List	**Screening List**	**Final Decision**
Authoritative A: EU - GHS (H-Statements)(H400)-Very toxic to aquatic life) **(vH)**	**Screening A:** GHS - Japan (Hazardous to the aquatic environment (acute) - Category 1 [H400]) (*vH*). **Screening A:** GHS - Korea (Hazardous to the aquatic environment (acute) - Category 1 [H400 - Very toxic to aquatic life]) *(vH).*	**VERY HIGH:** As per the Authoritative A and Screening A List very high score is designated. The confidence in the data is high.
Chronic Aquatic Toxicity (CA)		
Authoritative List	**Screening List**	**Final Decision**
		HIGH: As per ECHA Registration Dossier chronic toxicity test for up to 0.20 mg/L no adverse effect were shown on fishes. More dose studies are requiring so the confidence in the data is low. The NOEC, based upon mortality and reproduction of the daphnids was 0.28 mg/L (the LOEC was 1.4 mg/L) performed a 21 day flow-through test. The two-generation

		42 day flows through test. The NOEC, based upon mortality and reproduction of the daphnids was 0.26 mg/L. Effects were seen at the 0.76 mg/L level. The confidence in the score is high. As per GreenScreen 0.1-1 mg/L is High score (CPA, 2018).
Persistence (P)		
Authoritative List	**Screening List**	**Final Decision**
		VERY LOW: Data is available from multiple studies in the Registration Dossier ECHA. All indicate that BBP is readily biodegradable.
Bioaccumulation (B)		
Authoritative List	**Screening List**	**Final Decision**
	Screening A: EC - CEPA DSL (Bioaccumulative) (*vH*).	**LOW:** As per the Screening A List very high score is designated. The confidence in the score is low. Monsanto (1979), tested for bioaccumulation of the test substance in *Lepomis macrochirus* in a near-guideline (ASTM Proposed Standard Practice for Conducting Bioconcentration Tests with Fishes and Saltwater Bivalve Molluscs Draft No. 9) test. The whole-body BCF was 188. This study is acceptable for use as a key study. Even in the ECHA support document for BBP as SVHC it is stated that the experimental BCF of 449 l/kg using 14C-labelled BBP is therefore used for estimating secondary poisoning. 100-500 BCF comes in the low range and that is why this high confidence measured data is adopted.
Reactivity (R)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: Based on expert judgment because lack of oxidizing functional group and no experimental data set was available that's why the confidence in the data is low.

Flammability (F)		
Authoritative List	**Screening List**	**Final Decision**
		LOW: The flash point is 198C which is above the cutoff criteria 93C for flammable liquid. Based on experimental data that is why the confidence in the data is high.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

Nielsen, B. S., & Larsen, P. B. (2014). *Alternatives to classified phthalates in medical devices*. Retrieved from https://www2.mst.dk/Udgiv/publications/2014/03/978-87-93178-27-4.pdf

Pharos. (2021). 'Benzyl butyl phthalate (BBP) (CAS# 85-68-7)' Retrieved from https://pharosproject.net/chemicals/2006945#hazards-panel

ECHA Registration Dossier:

ECHA (2021). Registered Substances Dossier for Benzyl butyl phthalate (BBP) (CAS# 85-68-7). European Chemicals Agency. Last Revised 14th May, 2018. https://echa.europa.eu/registration-dossier/-/registered-dossier/12721/1/1

Chemical: Sulfonic acids, C10-C21-alkane, phenylester (ASE) (CAS# 91082-17-6) Hazard Assessment

	GreenScreen and DfE Hazard Summary Table for ASE																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	*L*	*L*	*M*	*L*	**DG**	**L**	**-**	**L**	**-**	**L**	**L**	**DG**	**L**	**L**	**L**	**L**	*M*	**L**	*L*	**L**

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		No data (Nielsen & Larsen, 2014).	**LOW:** In the ECHA registration dossier the data has been updated as per weight of evidence approach

			which says on the absence of a genotoxic potential in multiple in vitro assays similar to current guidelines and no observation of pre-neoplastic lesions in a comprehensive sub-chronic study no carcinogenic potential can be seen. The confidence in the data is low.
Mutagenicity (M)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		Negative in the V79 -HPRT Forward Mutation Assay (+/- metabolic activation) (No guideline) - Klimisch score 2 (key study) Negative in the vitro Mammalian Chromosome Aberration Test (+/- metabolic activation) (OECD Guideline 473) - Klimisch score 2 (key study) Negative in the bacterial reverse mutation assay (No guideline) - Klimisch score 2 (key study). **No effect as per Danish EPA.**	**LOW:** Only *in vitro* Studies and the Danish EPA reports the data is not very substantial due to missing *in vivo* studies. Lower confidence in data. **No effect as per Danish EPA.**
Reproductive Toxicity			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		Reproductive toxicity – one generation reproduction (OECD 415): NOAEL (parental toxicity) 600 ppm (68 mg/kg bw/day*), LOAEL 3000 ppm (liver/kidney weight) NOAEL (reproduction) 600 ppm (68 mg/kg bw/day*), LOAEL 3000 ppm (fetal weight/development – balano separation), LOAEL 15000 ppm (vaginal opening) Klimisch score 1	**MODERATE:** Lower confidence in data because reproductive toxicity studies over two generations is not done. **Moderate effect as per Danish EPA.** 50-1000 comes under the moderate score as per GreenScreen criteria. As the NOAEL is 68 mg/kg bw/day and LOAEL is 340 mg/kg bw/day

		(key study). **Moderate effect as per Danish EPA.**	that is why it can lie in the moderate range (CPA, 2018)
Development Toxicity (D)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		Developmental toxicity (OECD 414): NOAEL (maternal toxicity) 300 mg/kg bw/day; LOAEL 1000 mg/kg bw/day (body weight gain) NOAEL (developmental toxicity) = 1000 mg/kg bw/day (highest dose level) Klimisch score 1 (key study).	**LOW:** Based on Danish EPA study indicating NOAEL 300mg/kg bw/day. **NOAEL 300mg/kg bw/day and LOAEL= 1000 mg/kg bw/day which comes under the criteria of Moderate score as per this study criteria based on NOAEL but LOAEL is 1000 mg/kg bw/day that is why a low score is assigned but confidence in the data is low.**
Endocrine Activity (E)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		No data.	**DG:** No complete data set to assign a score.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		LD50 (oral) > 15 mL/kg bw – (>2000 mg/kg bw/ day) Klimisch score 2 (key study) LD50 (dermal) > 1055 mg/kg bw - Klimisch score 2 (key study). **No effect observed as per the Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per the Danish EPA.**
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			DG: No necropsy studies available

			for single dose.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		NOAEL 3000 ppm (90 day - OECD 408) (males: 228.0 mg/kg bw./day; females: 282.6 mg/kg bw./day) LOAEL =12000 ppm (Kidney weight and increased tromboplastin-time) (males: 985.2 mg/kg bw./day; females: 1488.5 mg/kg bw./day) Klimisch score 1 (key study). **Slight Effect is indicated in Danish EPA assessment.**	**LOW:** Slight Effect is indicated in Danish EPA assessment. But NOAEL value against the criteria set by USEPA and GreenScreen the hazard score is LOW (CPA, 2018). The confidence in the data is high.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			DG: No neurobehavioral studies located for single dose toxicity.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			LOW: High Confidence. GLP compliant OECD 408 Repeated toxicity test indicates no behavior changes in the ECHA registration dossier. The confidence in the data is high due to experimental work.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		No skin sensitization (Guinea Pig Maximization Test -OECD 406) Klimisch score: 1 (key). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Respiratory Sensitization (SnR)			

Authoritative List	Screening List	DANISH EPA	Comment
			DG: No data located.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		No skin irritation (rabbit - no guideline) - Klimisch score 2 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		No eye irritation (rabbit - no guideline) - Klimisch score 2 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		Fish: LC50 (Danio rerio, 96 hours): >=2 mg/L (EU Method C.1 (Acute Toxicity for Fish)) Klimisch score: 1. Algae: EC0 (Desmodesmus subspicatus, 72 hours): >=2 mg/L (EU Method C.3 (Algal Inhibition test)) Klimisch score: 1 Crustaceans: EC0 (Daphnia magna, 48 hours): >=100 mg/L* (EU Method C.2 (Acute Toxicity for Daphnia)) Klimisch score: 1.	**LOW:** Based on the available data in Danish EPA report which indicates no acute toxicity. Therefore, ASE is assigned a Low hazard score for acute aquatic toxicity. The confidence in the score is high due to experimental data.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			LOW: ASE has a reported water

			solubility of 2.2 mg/L (ECHA Measured). Based on the available data, no effects are expected at saturation levels for ASE. Therefore, ASE is assigned a Low hazard score for chronic aquatic toxicity. The confidence in the score is high due to experimental data.
Persistence (P)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		Inherently biodegradable as the pass level of 60 % degradation (BOD) was achieved after 47 days (EU Method C.4-D) (OECD 301F).	**Moderate:** Moderate hazard for persistence when the half-life of a chemical is between 16 and 60 days and the major partitioning compartment is soil or sediment. Confidence in the data is low due to less experimental details. In the ECHA registration dossier it is stated that there is evidence, supported by the degradation of the hexadecane sulfonic acid phenyl ester, that degradation takes places just starting after a lag phase of approximately one week. Therefore, the substance can be scored as almost biodegradable. That is why a low confidence moderate score is assigned.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
		BCF: 212 with a reliable Klimisch score of 1.	**LOW:** The score is low when the BCF is between 100 and 500 as per GreenScreen criteria. The confidence in the data is high

			due to experimental work and Klimisch score 1.
Reactivity (R)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			LOW: In the registration dossier the substance does not contain a chemical moiety suggesting an oxidizing potential. The flash point is above 200 which indicate that the substance is not reactive. The confidence in the data is lower because of lack of experimental data.
Flammability (F)			
Authoritative List	**Screening List**	**DANISH EPA**	**Comment**
			LOW: In the registration dossier the flash point is above 200 which indicate that the substance is not flammable. The confidence in the data is high.
• EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment.			

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

Nielsen, B. S., & Larsen, P. B. (2014). *Alternatives to classified phthalates in medical devices*. Retrieved from https://www2.mst.dk/Udgiv/publications/2014/03/978-87-93178-27-4.pdf

Pharos. (2021). 'CAS# 91082-17-6 Alkane (C10-C21) sulfonic acid phenyl esters' Retrieved from https://pharosproject.net/chemicals/2013983#hazards-panel.

ECHA Registration Dossier: (The C10-C21 ASE studies are all in this registration dossier because C14-C17 alkanes has C10-C21 Mesamoll as structural analogue)

ECHA (2021). Registered Substances Dossier for C14-17 alkanes, sec-mono- and disulfonic acids, phenyl esters. European Chemicals Agency. Last Revised 29th May, 2019. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/153

Chemical: tributyl O-acetylcitrate (ATBC) (CAS: 77-90-7) (EC: 201-067-0) Hazard Assessment

	GreenScreen and DfE Hazard Summary Table for ATBC																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	L	L	*L*	*M*	DG	L	-	L	DG	DG	L	DG	L	L	L	M	M	*VL*	*L*	L

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		NOEL 1000 mg/kg bw/day (no neoplastic lesions in male/female) (104 wk. In diet - combined repeated dose and carcinogenicity study - 875/318/EEC; 83/571/EEC; 91/507/EEC guideline - comparable to OECD 452) Klimisch score 1 (Key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. High Confidence in data. **No effect observed as per Danish EPA.**
Mutagenicity (M)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Negative in Bacterial Reverse Mutation Assay (+/- metabolic activation) (OECD 471) - Klimisch score 2 (key study) Negative in mammalian cell gene mutation assay (+/- metabolic activation) (OECD 476) - Klimisch score 2 (supporting study) Negative in in vivo chromosome aberration assay (rat) (OECD Guideline 475) - Klimisch score 1 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. High Confidence in data. **No effect observed as per Danish EPA.**
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**

		No data.	**LOW:** In OECD two generation TG 416 Reproductive toxicity test (Klimisch score 1), NOAEL of 1000 mg/kg bw/ day was observed in the ECHA registration dossier. The confidence in the score is low due to some anomalies which were detected in the kidney and liver in the control and the dose group but the registrant termed it as not applicable to the study. The other repeated dose toxicity tests like OECD 408 and 452 for (Specific Target organ Test- Repeated exposure) show kidney and liver problems at 1000 and 300 mg/kg-bw/day respectively. That is why additional studies are required.
Development Toxicity (D)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Not guideline study NOEL (maternal toxicity) 50 mg/kg bw/day LOAEL (maternal toxicity) 250 mg/kg bw/day (body weight increase, length of the progeny and placental weight) NOEL (developmental toxicity) 250 mg/kg bw/day (highest dose level) (no effects to male sexual cells, no embryotoxic effects and no impact on the development in offspring) - Klimisch score 2 (key studies). **Moderate effect observed as per Danish EPA but not a guideline**	**MODERATE:** Moderate effect observed as per Danish EPA but not a guideline study. **In the registration dossier GLP study from read across supporting substance Klimisch score 1 in the maternal Wistar rats and fetuses the NOAEL is 1000 mg/kg bw/day. A moderate score is provided due to Danish EPA score based on experimental work NOAEL 50 mg/kg bw/day and LOAEL 250 mg/kg bw/ day.** The confidence in

		study.	the data is low due to conflicting score and Klimisch score 2 study and not guideline study so the confidence in the data is low.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No data.	**DG:** No complete data set to assign a score.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		LD50 (oral) > 30 mL/kg (ca. 31500 mg/kg) - Klimisch score 2 (key study) LD50 (dermal) > 1000 mg/kg bw - Klimisch score 2 (key study).	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			DG: No necropsy studies were performed.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		NOAEL 1000 mg/kg bw/day (male/female) (90 day in diet - OECD 408) (highest dose level - slightly increased liver weights accompanied by minimal hepatocellular hypertrophy) - Klimisch score 1 (key study) NOAEL 300 mg/kg bw/day (male/female) (52 weeks in diet - comparable to OECD 452), LOAEL 1000 mg/kg bw/day (increased liver	**LOW:** Sufficient data set. Higher Confidence in data. **Slight effect as per Danish EPA assessment.** But as per the criteria of USEPA and GreenScreen >100 mg/kg-bw/day for repeated dose is termed as LOW score as the NOAEL and LOAEL are above 100 mg/kg bw/day.

		weight and centrilobular hypertrophy) - Klimisch score 1 (key study).	
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			DG: No pertinent studies could be located.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			DG: No pertinent studies could be located.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No skin-sensitization potential (guinea pigs-OECD 406) - Klimisch score 4 (only summary - WOE) No skin-sensitization or irritation potential (human - patch test) - Klimisch score 4 (only summary - WOE). **No effect observed as per Danish EPA.**	**LOW:** Lower Confidence in data because it is from read across data. **No effect observed as per Danish EPA.**
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			DG: No pertinent studies could be located.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No skin irritation (rabbit-no guideline) - Klimisch score 2 (key	**LOW:** Sufficient data set. Higher Confidence in data.

		study).	**No effect observed.**
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Slightly eye irritation (rabbit) - Klimisch score 2 (key study).	**LOW:** Sufficient data set. Higher Confidence in data. **Slight effect observed as per Danish EPA.** As per GreenScreen and USEPA if the clearing is in 24hrs and then it is designated as LOW hazard score.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Algae: EC50 (Desmodesmus subspicatus, 72 hours): 74.4 mg/L* (OECD Guideline 201) Klimisch score: 1. Fish: LC50 (Lepomis macrochirus, 96 hours): >38 and <60 mg/L. (OECD Guideline 203) Klimisch score: 2.	**LOW:** As per USEPA and GreenScreen the EC50 and LC50>10 to 100 is designated as Moderate hazard score whereas the water solubility of ATBC is 4.49 mg/L in Danish EPA report that is why lack of effect will be observed at the water solubility limit. The confidence in the data is high.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
	Screening B: German FEA - Substances Hazardous to Waters (Class 2- Hazard to waters). (U) **Screening B:** GHS New Zealand (9.1B (crustacean) - ecotoxic in the aquatic environment. (U)		**Moderate**: NOEC is 1.11 mg/L in daphnia magna as per guideline study and as per GreenScreen criteria >1-10 mg/L comes in moderate score. The confidence in the data is high due to experimental data.
Persistence (P)			

Authoritative List	Screening List	Danish EPA	Comment
		As per Danish EPA assessment inherently biodegradable in water. But in the soil compartment it is readily biodegradable.	**Moderate:** Classified as a Moderate hazard for persistence when the half-life of a chemical is between 16 and 60 days and the major partitioning compartment is water. The test item proved to be inherently biodegradable under the test conditions employed (82% biodegradation after 28 d). The functional control reached the pass level >60% after 14 d. The confidence in the data is high due to experimental data.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		BCF: 31.57 L/Kg As per EPI Suite estimation (EPIWIN)	**VERY LOW:** As per the USEPA and GreenScreen Criteria the BCF < 100 is score as very Low. The confidence in the data is low due to estimated data,
Reactivity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: In the registration dossier it does not contain oxygen or halogen atoms that are why it is not an oxidizing chemical and the flash point is 217.9C to make it a flammable liquid. The confidence in the data is low

			due to lack of experimental data.
Flammability (F)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: In the registration dossier according to ASTM D 93-02, EPA OPPTS 830.6315 (Flammability), and EU Method A.9 (Flash-Point) the flash point is 217.9C which is above the 93C cutoff criteria to be classified as a flammable liquid. The confidence is high due to the experimental data.
EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment. Positive Lists: • Cosmetic Ingredient Review (CIR): Safe as Used • Inventory of Existing Cosmetic Ingredients in China (IECIC 2015): Cosmetic Ingredients • TCO Certified Accepted Substance List: Benchmark-3 Accepted Substance			

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Chemical: bis (2-ethylhexyl) terephthalate (CAS#6422-86-2) (DEHT) Hazard Assessment

	GreenScreen and DfE Hazard Summary Table for DEHT																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	**L**	**L**	*M*	*L*	**DG**	**L**	**L**	**L**	*L*	**DG**	**L**	*L*	**L**	**L**	**L**	**L**	**VL**	**L**	*L*	**L**

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		A GLP compliant 104 week carcinogenicity study in rat using dose levels of 1500 ppm (79/102 mg/kg/day - M/F), 6000 ppm (324/418 mg/kg/day - M/F) and 12000 ppm (666/901 mg/kg/day - M/F) (EPA OPPTS 870.4200) NOEL	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**

		12000 ppm (666/901 mg/kg/day - M/F – no neoplastic changes) Klimisch score 1 (key study). **No effect observed as per Danish EPA.**	
Mutagenicity (M)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Negative in *in vitro* Mammalian Chromosome Aberration Test (+/- metabolic activation) (OECD 473) - Klimisch score 1 (key study). Negative *in vitro* in Bacterial Reverse Mutation Assay (+/- metabolic activation) (OECD 471) - Klimisch score 1 (key study). Negative in vitro in mammalian cell gene mutation assay (+/- metabolic activation) (OECD 476) - Klimisch score 1 (key study). Urine samples from rats given 2000 mg/kg bw/day for 15 days were negative in Bacterial Reverse Mutation Assay (+/- metabolic activation) (OECD 471). Klimisch score 2 (supporting study). **No effect as per Danish EPA.**	**LOW:** Only in Vitro Studies and the Danish EPA says the data is not very substantial. (ToxServices, 2016b) reports higher confidence data as it has already done GreenScreen assessment for the chemical and has assigned low hazard score (ToxServices, 2016b) **No effect as per Danish EPA.**
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		A GLP compliant Reproductive toxicity (OECD 416, EPA OPPTS 870.3800 - two generation reproduction): NOAEL (parental toxicity) 3000 ppm (F0: 133-478 mg/kg bw/day for male-female, respectively) (F1: 159-516 mg/kg bw/day for male-female, respectively). LOAEL (parental toxicity) 6000 ppm (reduced body weight gain in parent/offspring) (F0: 265-940 mg/kg bw/day for male-female, respectively) (F1: 320-1036 mg/kg bw/day for male-female, respectively) NOAEL (reproduction) = 10000 ppm (447-1349 mg/kg bw/day for male-female, respectively) Klimisch score 1 (key study). **Slight effect observed as per Danish EPA.**	**MODERATE:** The confidence in the data is low due to conflicting hazard score in Danish EPA and ToxServices (2016a) GreenScreen Assessment. **Slight effect observed as per Danish EPA.** As per the criteria designation in this study NOAEL 50-1000 mg/kg bw/day comes under Moderate hazard score and LOAEL >250-1000 mg/kg bw/day comes under Moderate score. ToxServices, (2016a) has given it a low hazard score because they consider the weight loss to be not because of the chemical dose but Danish EPA and ECHA registration dossiers have quoted the NOAEL and LOAEL is the range of moderate hazard score.

			That's why the confidence in the data is low.
Development Toxicity (D)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Developmental toxicity - rat (Prenatal developmental toxicity - OECD 414, EPA OPPTS 870.3700): NOAEL (maternal toxicity) 6000 ppm (458 mg/kg bw/day) LOAEL (maternal toxicity) 10000 ppm (747 mg/kg bw/day - higher liver weights, reduced body weight/body weight gain) NOAEL (developmental toxicity) 10000 ppm (747 mg/kg bw/day) Klimisch score 1 (key study) Developmental toxicity - mice (Prenatal developmental toxicity OECD 414, EPA OPPTS 870.3700): NOEL (maternal toxicity) 1000 ppm (197 mg/kg bw/day) LOAEL (maternal toxicity) 3000 ppm (592 mg/kg bw/day - (increased liver weight) NOEL (developmental toxicity) 7000 ppm in diet (1382 mg/kg bw/day). Klimisch score 1 (key study). **Slight effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. The change in liver weights was addressed as per ToxServices, (2016b) in the Systemic Toxicity Organ Effects for which NOAEL>100 mg/kg bw/day comes in the low hazard score as per GreenScreen criteria. NOAEL of >700 mg/kg bw/day was derived for development toxicity by ToxServices, (2016b) and Low score was specified. The NOAEL and LOAEL do come in the Moderate range but the conflicting result with ToxServices, (2016b) that's why it is a low confidence score. **Slight effect observed as per Danish EPA so Low score is assigned in this study aswell.**
Endocrine Activity (E)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Uterotrophic Assay (no guideline followed): Immature female Sprague-Dawley rats dosed by gavage once daily from postnatal days 19 through 21 at dose levels of 0, 20, 200 and 2000 mg/kg bw/day. No test substance related differences in mean uterine weights (wet or blotted) or luminal fluid weights. No biological activity consistent with agonism of natural oestrogens at dose levels up to 2000 mg/kg bw/day. Klimisch score 2 (key study) Pregnant rats were exposed to 0.75 g/kg bw/day (oral gavage) from gestation day 14 to postnatal day 3 in a modified developmental toxicity study (no guideline followed – OECD 414 normally start dosing at gestation day 6 or 7): Offspring	**DG:** *In Vitro* and *In vivo* studies. Higher Confidence in data. **No effect as per Danish EPA.** **It is not termed as complete data because thyroid effect is not studied which is very important that is why a data gap is assigned as per ToxServices GreenScreen assessment.**

		were sacrificed at 4-7 months of age, body and selected organ weights were measured, and animals were examined for abnormalities. This study did not investigate many of the endpoints normally measured in standard (Guideline) developmental/teratology studies; instead, endpoints specific to androgen disruption (reduced anogenital distance, retained nipples, cleft phallus, hypospadias, undescended testes, blind vaginal pouch, epididymal agenesis, underdeveloped accessory sex glands, and histological alterations in the testes) were investigated. No effect in male offspring on the endpoints specific to androgen disruption and sexual differentiation. Klimisch score 1 (supporting study) Pregnant Sprague-Dawley rats were exposed from gestation day 12 through gestation day 19 to 500 mg/kg bw/day (no guideline followed): Anogenital distance was not significantly altered in male foetuses and none of the genes representing major gene pathways that allow for normal male reproductive tract development were altered. Klimisch score 1 (supporting study). **No effect observed as per Danish EPA.**	
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		LD50 (oral, rat) > 5000 mg/kg bw/day (other guideline comparable to OECD) Klimisch score 1 (key study) LD50 (dermal, guinea pigs) > 20000 mg/kg bw) (No guideline) Klimisch score 2 (key study) LC50 (inhalation): No data. **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: In the ECHA Registration Dossier Sufficient data set. Higher Confidence in data. GLP-compliant acute toxicity study performed according to TSCA FHSA regulations (1979). All

			animals gained weight and there was no treatment related change upon gross necropsy (ToxServices,2016b)
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		NOEL 0.5% in diet (277 mg/kg bw/day (male) and 309 mg/kg bw/day (female)) LOAEL 1% (561 mg/kg bw/day (male) and 617 mg/kg bw/day (female) - minor effects on red blood cell formation and enlargement of the liver) (90 days-EPA guideline 799.9310 TSCA) - Klimisch score 1 (key study) NOEL 1500 ppm (79/102 mg/kg/day - M/F) LOEL 6000 ppm (324/418 mg/kg/day – M/F, reduced body weight gain, food conversion efficiency, minor haematological effects, suspected ocular changes) NOEL 12000 ppm (666/901 mg/kg/day - M/F) -testes NOEL 12000 ppm (666/901 mg/kg/day - M/F) - liver (Chronic toxicity-EPA OPPTS 870.4200) - Klimisch score 1 (key study). **Slight effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **Slight effect observed as per Danish EPA.** As per the Green Screen and USEPA hazard criteria designation >100 mg/kg bw/day comes under low hazard score for 90 day test. The EPA OPPTS toxicity test is chronic test which is even more so the values are in low range. A score of Low for systemic toxicity (repeated dose) based on oral NOAELs > 100 mg/kg/day in sub-chronic and chronic studies.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Low for neurotoxicity (single dose) based on lack of clinical signs of neurotoxicity in acute toxicity studies via the oral, dermal and inhalation routes but the confidence in the data was low. Based on ToxServices, (2016b) new data.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			DG: No pertinent data located.
Skin Sensitization (SnS)			
Authoritative	**Screening List**	**Danish EPA**	**Comment**

List			
		No skin-sensitization potential (Human patch test -modified Draize procedure) Klimisch score 1 (key study) No skin-sensitization potential (guinea pigs - topical application - no guideline) Klimisch score 2 (supporting study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: was assigned a score of Low for respiratory sensitization based on lack of structural alerts for respiratory sensitization and negative skin sensitization data following a human repeat patch test and a guinea pig sensitization study. Confidence in the data is low due to absence of experimental data for respiratory sensitization.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No skin irritation (rabbit-OECD 404) - Klimisch score 1 (key study) No skin irritation (human patch test - semi-occlusion) - Klimisch score 1 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Mildly eye irritating but not classified under GHS (rabbit-OECD 405) - Klimisch score 1 (key study). **Mild effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **Mild effect observed as per Danish EPA.** As per USEPA and GHS criteria mildly irritating clearing in 48 hours is designated as LOW score.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**

		Algae EC50 (Selenastrum capricornutum, 72 hours): >0.86 mg/L* (OECD Guideline 201) Klimisch score: 1 Crustaceans EC50 (Daphnia magna, 48 hours): >1.4 µg/L* (OECD Guideline 202) Klimisch score: 1 LC50 (Pimephales promelas, 96 hours): >984 mg/L* (OECD Guideline 203) Klimisch score: 2	**LOW:** Based on experimental data that is why the confidence in the data is high. DEHT has a reported water solubility of 0.4 µg/L (ToxServices, 2016b). Based on the available data, no effects are expected at saturation levels for DEHT. Therefore, DEHT is assigned a Low hazard score for acute aquatic toxicity.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		NOEC (Oncorhynchus mykiss, 60 days): >=0.28 mg/L* (ASTM. 1983. Proposed New Standard Practice for Conducting Fish Early Life Stages Toxicity Tests. Draft No. 7.) Klimisch score: 1.	**LOW:** Based on experimental data that is why the confidence in the data is high. In ToxServices, (2016a) NOEC of ≥ 0.28 mg/L was established in Oncorhynchus mykiss (fathead minnow, 60- day). NOEC of ≥ 0.86 mg/L was established in Pseudokirchnerella subcapitata (green algae, 72-hour) Based on the available data; no effects are expected at saturation levels for DEHT. Therefore, DEHT is assigned a Low hazard score for chronic aquatic toxicity.
Persistence (P)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Readily biodegradable (OECD Guideline 301 B).	**VERY LOW:** As per the Danish EPA readily biodegradable. Higher confidence in data due to experimental data.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: DEHT has a measured BCF of 393 in Crassotrea virginica following EPA OPPTS 850.1710 (Oyster Bioconcentration Test). Following GreenScreen® criteria, chemicals with a BCF < 500 are considered to have low potential for

			bioaccumulation (ToxServices, 2016b). Higher confidence in data due to experimental data.
Reactivity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on expert judgment that is why the confidence in the data is low. DEHT was assigned a score of Low for reactivity based on an HMIS reactivity rating of 0 and expert judgment (ToxServices, 2016b).
Flammability (F)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on experimental data that is why the confidence in the data is high. Assigned a score of Low for flammability based on not being classified as a GHS Flammable Liquid. DEHT has a flash point of 212°C, which is above the 93°C cut-off criteria to be classified as flammable as a liquid by GHS (ToxServices, 2016b).

Positive Lists:

- TCO Certified Accepted Substance List: Benchmark-3 Accepted Substance
- German FEA - Substances Hazardous to Waters: Non-Hazardous to Water (Water Hazard Class 0 NWG)

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Chemical: Diisononyl adipate DINA (CAS# 33703-08-1) Hazard Assessment

	GreenScreen and DfE Hazard Summary Table for DINA																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	*L*	*L*	*M*	*H*	DG	L	*L*	*M*	DG	DG	*L*	DG	L	L	L	*L*	VL	*L*	*L*	L

Hazard Endpoints Detailed Evaluation Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		LOAEL 12000 ppm (1715 mg/kg bw/day - male/female mice) - (103 weeks OECD 451) (Read-across from bis(2-ethylhexyl) adipate –	**LOW:** Sufficient data set. Lower confidence in data due to data from structural analog.

		(CAS nr 103-23-1)) Di(2-ethylhexyl)adipate was carcinogenic for female mice, causing increased incidences of hepatocellular carcinomas and was probably carcinogenic for male mice, causing hepatocellular adenomas - Klimisch score 2 (key study) NOAEL 25000 ppm (600 mg/kg bw/day - male/female rats) - (103 weeks OECD 451) (Read-across from bis(2-ethylhexyl) adipate – (CAS nr 103-23-1)). Di(2-ethylhexyl)adipate was not carcinogenic (no tumour incidence) for rats at 25000 ppm in diet (considered to be equivalent to 600 mg/kg bw.) Klimisch score 2 (key study). **No effect observed as per Danish EPA.**	**No effect observed as per Danish EPA.**
Mutagenicity (M)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		Negative in *in vitro* Mammalian Cell Micronucleus Test (+/- metabolic activation) (OECD 487) - Klimisch score 1 (key study) Negative in Bacterial Reverse Mutation Assay (+/- metabolic activation) (OECD 471) - Klimisch score 2 (key study) Negative in mammalian cell gene mutation assay (+/- metabolic activation) (OECD 476) - Klimisch score 1 (key study). Negative in *in vivo* mammalian chromosome aberration test (OECD 474) Klimisch score 2 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Data from an analog. So lower confidence. **No effect observed as per Danish EPA.**
Reproductive Toxicity			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		Reproductive toxicity (OECD 415-one generation) (Read-across from bis(2-ethylhexyl) adipate – (CAS nr 103-23-1)): NOAEL (parental toxicity) 170 mg/kg bw/day (nominal) LOAEL (parental toxicity) 1080 mg/kg bw/day (increased liver weight, decreased body weight gain) NOAEL (reproduction) 170 mg/kg bw/day LOAEL (reproduction) 1080 mg/kg bw/day (reduced mean pup weight gain and total litter weight) - Klimisch score 1 (key study).	**MODERATE**: Data from analog. The reproductive toxicity study has not been done over two generations so the confidence on the data is low. **Moderate effect as per Danish EPA.** As per the GreenScreen hazard criteria designation 50-1000 mg/kg bw/day comes under Moderate hazard score as well. As there is too much of a gap between NOAEL (170 mg/kg bw/day) and LOAEL (1080 mg/kg bw/day) that is why a conservative

			approach is adopted and moderate score is assigned because the LOAEL can lie in the moderate range (CPA, 2018).
Development Toxicity (D)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		Developmental toxicity (OECD 414) (Read-across from bis(2-ethylhexyl) adipate – (CASRN 103-23-1)): NOAEL (maternal toxicity) 170 mg/kg bw/day (nominal) LOAEL (maternal toxicity) 1080 mg/kg (minimal foetotoxicity (reduced bodyweight gain, feed intake) - Klimisch score 1 (key study) NOEL (developmental toxicity) 28 mg/kg bw/day LOAEL (developmental toxicity) 170 mg/kg (reduced ossification, increase in the incidence of visceral variants) - Klimisch score 1 (key study). **Moderate effect as per Danish EPA.**	**HIGH**: Data from analog. Confidence in the data is low due to read across data For development toxicity the NOAEL is 28 mg/kg bw/ day for foetotoxicity. **Moderate effect as per Danish EPA.** As per the GreenScreen hazard criteria designation less than 50 mg/kg bw/day comes under High hazard score. As there is a gap between NOAEL (28 mg/kg bw/day) and LOAEL (170 mg/kg bw/day) and the actual value of LOAEL can lie in the HIGH range for development toxicity that is why a conservative approach is adopted and high score is assigned (CPA, 2018).
Endocrine Activity			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		No data	**DG:** No complete data set to assign a score.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		LD50 (oral) > 5000 mg/kg bw (male/female) (OECD 401) - Klimisch score 2(key study) LD50 (dermal): no data LC50 (inhalation): 5.7 mg/L air (male/female) (OECD 403) - Klimisch score 1 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**

			LOW: As per ECHA registration dossier based on structural analog DEHA, acute toxicity oral (comparable to OECD 401) and inhalation (OECD 403) test no adverse effect was observed to be termed as systemic toxicant for 5000 mg/kg bw/ day at gross pathology observation. The confidence in the data is low due to read across data.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		NOAEL 200 mg/kg bw/day (male) (nominal) (28 days-OECD 407) (Read-across from bis(2-ethylhexyl) adipate CAS nr 103-23-1); LOAEL 1000 mg/kg bw/day (Increased kidney weight/histopathological changes, increased liver weight) Klimisch score 2 (key study) NOAEL 200 mg/kg bw/day (male/female) (nominal) (90 days-OECD 408) (Read-across from bis(2-ethylhexyl) adipate (CAS nr 103-23-1)) LOAEL 400 mg/kg bw/day (male/female) (decreased bodyweight gain) Klimisch score 2 (key study) NOAEL 595 mg/kg bw/day (male) (nominal) (90 days-OECD 408) (Read-across from bis(2-ethylhexyl) adipate – (CAS nr 103-23-1)) LOAEL 595 mg/kg bw/day. (decreased bodyweight gain) Klimisch score 2 (key study). **Slight effect observed in Danish EPA.**	**MODERATE:** Data from analog. **Slight effect observed in Danish EPA.** As per the GreenScreen hazard criteria designation 30-300 mg/kg bw/day comes under Moderate hazard score for 28 day test. **As the NOAEL (200 mg/kg bw/day and LOAEL (1000 mg/kg bw day) has a gap and LOAEL can lie in moderate range. A conservative moderate score is provided as Danish EPA also reported slight effect observed.** But for the 90 day study >100 mg/kg bw/day comes under Low hazard score so to be conservative Moderate score is given.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
			DG: No pertinent data located.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
			DG: No pertinent data located.
Skin Sensitization (SnS)			
Authoritative	**Screening**	**U.S EPA**	**Final Decision**

List	**List**		
		No skin-sensitization potential (QSAR prediction) - Klimisch score 2 (WOE) No skin-sensitization potential (guinea pig maximization test - no guideline) (read-across from supporting substance: bis(2-ethylhexyl adipate) - Klimisch score 2 (WOE). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Confidence in the data is low due to read across data. **No effect observed as per Danish EPA.**
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
			DG: No pertinent data located.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		No skin irritation (rabbit-OECD 404) - Klimisch score 1 (key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		No eye irritation (rabbit-OECD 405) - Klimisch score 1 (key study).	**LOW:** Sufficient data set. Higher Confidence in data. **No effect observed as per Danish EPA.**
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		Algae: EC50 (Scenedesmus subspicatus, 72 hours): >100 mg/L* (OECD Guideline 201) Klimisch score: 2 Crustaceans :EC50 (Daphnia magna, 48 hours): >100 mg/L* (OECD Guideline 202) Klimisch score: 2 Fish LC50 (Leuciscus idus, 96 hours): >500 mg/L* (OECD Guideline 203) Klimisch score: 2.	**LOW:** As per USEPA and GreenScreen the EC50 and LC50>100 is designated as LOW hazard score. No effects on fish, aquatic invertebrates or algae were observed up to the limit of water solubility (0.0032 mg/L). Confidence in the data is high due to experimental data.
Chronic Aquatic Toxicity (CA)			
Authoritative	**Screening**	**Danish EPA**	**Final Decision**

List	List		
		NOEC (Daphnia magna, 21 days): >=0.77 mg/L* (OECD Guideline 211) (Read-across) Klimisch score: 2.	**LOW:** The confidence in the score is low due to read across. No effects on Daphnia magna at solubility range (0.0032 mg/L).
Persistence (P)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		Readily biodegradable (OECD Guideline 301 F).	**VERY LOW:** As per the Danish EPA readily biodegradable. The confidence in the data is high.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
		BCF: 27 with experiment of a read across analog study.	**LOW:** Read across data that is why the confidence in the data is low. As per the USEPA and GreenScreen Criteria the BCF > 100 to 500 is scored as Low.
Reactivity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
			LOW: In the registration dossier no oxidizing potential due to the absence of oxidizing functional groups. The flash point is 210C which indicates that the liquid is not flammable because it is above 93C cutoff criteria to make it a flammable liquid. The confidence in the data is lower due to absence of experimental data.
Flammability (F)			
Authoritative List	**Screening List**	**Danish EPA**	**Final Decision**
			LOW: In the registration dossier the flash point is 210C which indicates that the liquid is not flammable because it is above 93C cutoff criteria to

			make it a flammable liquid. The confidence in the data is higher due to reliable sources

- EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment.

Positive Lists:

- Cosmetic Ingredient Review (CIR): Safe as Used
- TCO Certified Accepted Substance List: Benchmark-2 Accepted Substance

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

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Pharos. (2021). 'Diisononyl adipate DINA (CAS# 33703-08-1)' Retrieved from https://pharosproject.net/chemicals/2008609#hazards-panel

ECHA Registration Dossier:

ECHA (2021). Registered Substances Dossier for Diisononyl adipate (CAS#33703-08-1). European Chemicals Agency. Last Revised 11th June, 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13808/1/2

Chemical: DINCH (CAS#166412-78-8) Hazard Assessment

	GreenScreen and DfE Hazard Summary Table for DINCH

	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	**L**	**L**	**L**	**L**	**M**	**L**	**L**	*M*	**L**	**L**	**L**	*L*	**M**	**L**	**L**	**L**	*M*	**L**	*L*	**L**

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		2 year chronic toxicity and carcinogenicity OECD 453 study in which only thyroid abnormality was observed but it has been proven in previous studies that the thyroid abnormality in rats has no relevance to the humans. No treatment related mortality or increases in malignant neoplasia up to the highest dose of 1,000 mg/kg were observed (ToxServices, 2016a).	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **Slight effect observed as per Danish EPA. The recent GreenScreen assessment by** (ToxServices, 2016a) **shows that NOAEL >1000 mg/L so low score is designated.**

Mutagenicity (M)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		(OEDC 471) - No Klimisch score (Key study) Negative in mammalian cell gene mutation assay. (OECD 476) - No Klimisch score (Key study) Negative in vitro mammalian chromosome aberration test. (OECD 473) - No Klimisch score (Key study) Negative in vivo mammalian micronucleus test. **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		A GLP-compliant Two Generation Reproductive Toxicity study (OECD 416) using Wistar rats. 1000 mg/kg bw/day NOAEL for reproductive toxicity. **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**
Development Toxicity (D)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		A GLP-compliant pre-/postnatal developmental study performed according to OECD 414/TG 415 The maternal NOAEL was determined to be 1,000 mg/kg/day based on the lack of treatment-related effects at the highest dose tested and a fetal LOAEL of 1,000 mg/kg/day. **No effect observed as per Danish EPA.**	**LOW:** As per the USEPA hazard criteria designation >1000 mg/kg bw/day comes under low hazard score. Higher confidence in data due to experimental data.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Based on 2 year chronic toxicity and carcinogenicity OECD 453 study effects (thyroid and anti-androgenic effects, and possibly steroidogenesis). **Slight effect observed as per Danish EPA.**	**MODERATE:** In Vitro and In vivo studies**.** **Slight effect observed as per Danish EPA.** Recent GreenScreen assessment by ToxServices, (2016a), has assigned a moderate score so that is adopted in this study. Higher confidence in data due to experimental data.

Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		LD50 (oral) > 5000 mg/kg bw (male/female) (OECD 423) – no Klimisch score (Key study) LD50 (dermal) > 2000 mg/kg bw (male/female) (OECD 402) – no Klimisch score (Key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Sufficient data set. Higher Confidence in data due to experimental data. Based on GLP compliant OECD 423 acute oral toxicity on Witsar Rats no effects observed for 5000 mg/kg oral dose for gross pathology. Similarly based on GLP compliant OECD 403 acute oral toxicity on Witsar Rats no effects observed for 2000 mg/kg dermal dose.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		NOAEL 107.1-389.4 mg/kg bw/day (male-female) based on kidney weight changes (male/female) and degenerated epithelial cells (2μ-microglobulin) in the urine of males (90-day, diet – according to 408) No Klimisch score (Key study)* NOAEL 40 mg/kg bw/day (males) and 200 mg/kg bw/day (females) based on liver weight changes (both sexes) and kidney weight changes (males). Dose- related follicular cell hyperplasia and increased number of follicular adenomas were observed in the thyroid glands of male rats administered ≥ 200 mg/kg bw/day and females at 1000 mg/kg bw/day. However, thyroid effects in rats are probably secondary effects of liver enzyme induction and therefore of limited relevance to humans. (chronic toxicity according to OECD 453) - No Klimisch score (Key study). **Moderate effect as**	**MODERATE:** Sufficient data set. **Moderate effect as per Danish EPA.** As per the GreenScreen and USEPA hazard criteria designation 30-300 mg/kg bw/day comes under Moderate hazard score for 28 day test. But for the 90 day study >100 mg/kg bw/day comes under Low hazard score so to be on the safe side Moderate score is given. Danish EPA due to kidney weight changes and thyroid effects has been taken into account. **Moderate score is assigned because ToxServices (2016a) GreenScreen Assessment has given it a**

		per Danish EPA.	**low score but has written LOAEL = 40 mg/kg bw/day for thyroid change in OECD 453 test which should make it in moderate range. The confidence in the data is low due to conflicting score with ToxServices GreenScreen assessment.**
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on sufficient data and high confidence data set due to experimental data. GLP compliant OECD 402 and 423 no neurotoxicity was observed for an oral dose of 5000 mg/kg or dermal dose of 2000 mg/kg (ToxServices, 2016a)
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on sufficient data and high confidence due to experimental data. Based on GLP compliant OECD 408 no neurotoxicity was observed for dose up to 1311.8 mg/kg (ToxServices, 2016a).
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No skin-sensitization potential (guinea pig) – (according to OECD 406) No Klimisch scores (Key study).	**LOW:** Sufficient data set. Higher confidence in data due to experimental data. **No effect observed as per Danish EPA.**
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on expert judgment and lack of experimental data the confidence in the data was

			low. Based on skin sensitization study and it lacks structural alerts to be a respiratory sensitizer.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Based on reversible, but well defined erythema that persisted for 48 hours in rabbits, which results in categorization of the test substance as a GHS Category 3 dermal irritant. **Slight effect observed as per Danish EPA.**	**MODERATE:** Sufficient data set. Higher Confidence in data due to experimental data. Based on reversible, but well defined erythema that persisted for 48 hours in rabbits, which results in categorization of the test substance as a GHS Category 3 dermal irritant. **Slight effect observed as per Danish EPA.**
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		No eye irritation (rabbit) – (according to OECD 405) No Klimisch scores (Key study). **No effect observed as per Danish EPA.**	**LOW:** Sufficient data set. Higher Confidence in data due to experimental work. **No effect observed as per Danish EPA.**
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
	Screening B: German FEA-Substances Hazardous to waters Class 1 Low Hazard to waters.	Algae EC50 (Scenedesmus subspicatus, 72 hours): >100 mg/L* (-) Klimisch score: - Crustaceans EC50 (Daphnia magna, 48 hours): >100 mg/L* Klimisch score: - Fish LC50 (Brachydanio rerio, 96 hours): >100 mg/L* Klimisch score: -	**LOW:** As per USEPA and GreenScreen the EC50 and LC50>100mg/L is designated as LOW hazard score. Higher confidence in data due to experimental data.
Chronic Aquatic Toxicity (CA)			
Authoritative	**Screening**	**Danish EPA**	**Comment**

List	List		
	Screening B: German FEA-Substances Hazardous to waters Class 1 Low Hazard to waters.	OECD TG 211 Daphnia magna reproduction test. NOEC value of >0.021 mg/L and is not expected to have any adverse effects to aquatic biota at water solubility limits.	**LOW:** Sufficient data set. Higher Confidence in data due to experimental data.
Persistence (P)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
		Inherently biodegradable. Not readily biodegradable (41% in 28 d) Moderate for persistence based on half-lives ranging from 32 days to 60.9 days in soil	**MODERATE:** Due to limited details on soil degradation studies. The confidence in the data is low.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Sufficient data set. Higher Confidence in data due to experimental data. A GLP-compliant bioconcentration test (OECD 305). A bioconcentration factor (BCF) of 189.3 was obtained (ToxServices, 2016a)
Reactivity (R)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Based on expert judgment and no experimental data set was available that's why the confidence in the data is low. Low for reactivity based on a lack of functional

			groups indicating reactivity.
Flammability (F)			
Authoritative List	**Screening List**	**Danish EPA**	**Comment**
			LOW: Sufficient data set. Higher confidence in data due to experimental work. Low for flammability based on a flash point of 224°C, which indicates the chemical is not classifiable as being flammable.
EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment. **Positive List:** TCO Certified Accepted Substance List: Benchmark-2 Accepted Substance			

ToxServices. (2016). DIISONONYL CYCLOHEXANEDICARBOXYLATE (DINCH) (CAS #474919-59-0, 166412-78-8) GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT *2015 © ToxServices and Clean Production Action*. (October 2014). Retrieved from http://www.greenchemistryandcommerce.org/documents/Hexamoll-DINCHGS5.28.13.pdf

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

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ECHA Registration Dossier:

ECHA (2021). Registered Substances Dossier for 1,2-Cyclohexanedicarboxylic acid, 1,2-diisononyl ester CAS#166412-78-8. European Chemicals Agency. Last Revised 10th February, 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/16022/1/2

Chemical: Hexabromocyclododecane, 1,2,5,6,9,10-Hexabromocyclododecane (HBCD) Hazard Assessment.

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014a)

	GreenScreen and DfE Hazard Summary Table for HBCD				
	Group I Human	Group II and II* Human	Ecotox	Fate	Physical

	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*M*	L	H	H	H	L	*M*	M	DG	*M*	L	DG	L	L	VH	VH	H	VH	*L*	*L*
USEPA DfE Assessment [2]	*M*	L	M	H	-	L	-	M	-	*M*	L	DG	VL	VL	VH	VH	H	VH	-	-

1 GreenScreen hazard assessment conducted in this thesis study,

2 Chemical hazard assessment by USEPA (DfE) for HBCD (USEPA, 2014a)

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: This study is not adequate to determine a hazard designation for the carcinogenicity endpoint due to high tumor incidence in control males. Carcinogenic potential cannot be ruled out therefore an estimated	**MODERATE:** HBCD is not in any screening or authoritative list so the USEPA hazard designation of **MODERATE** has been adopted.

		Moderate hazard is designated.	The confidence on the data is lower due to estimation.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on negative results for gene mutations in bacterial cells, a lack of chromosomal aberrations in human peripheral blood lymphocyte cells in vitro, and negative results in recombination and mouse micronucleus tests.	**LOW:** HBCD is not in any screening or authoritative list so the USEPA hazard designation of **LOW** has been adopted. The confidence in the data is high as it is based on measured data.
Reproductive Toxicity			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
Authoritative A: EU GHS (Suspected of damaging fertility or the unborn child – Category 2[H361]) **(M)** **Authoritative B:** EU – Annex VI CMRs (Reproductive Toxicity – Category 2) (*M)*	**Screening A:** GHS Japan (Toxic to reproduction – Category 1B [H360]) (*H)* **Screening A:** GHS – Australia (H361 – Suspected of damaging fertility or the unborn child) (*M)*	**MODERATE:** Based on a LOAEL of 138 mg/kg-day for reduced number of primordial follicles in F1 females in a two-generation dietary study in rats. There is uncertainty in that reproductive effects may occur at doses between the identified NOAEL (14.3 mg/kg-day) and the LOAEL (138 mg/kg-day).Using a conservative approach, a MODERATE hazard is designated. There were no treatment-related effects on the fertility index, sperm parameters, estrous cyclicity, reproductive organ weights or histopathology in F0 or F1 adults.	**HIGH:** In the Screening A List HIGH designation is allotted but due to availability of measured data in USEPA assessment which is higher confidence data a designation of **MODERATE** is adopted for reproductive toxicity. In the Authoritative B List EU – Annex VI CMRs (Reproductive Toxicity – Category 2) **MODERATE** designation is given for this hazard point as well. As per the criteria defined in Materials and Methods Chapter 3 (the LOAEL and NOAEL are in the high score range but as per EU it is Category 2 which comes in MODERATE score range but as per GHS Japan and low value of NOAEL and LOAEL HIGH score is adopted in this study.

			The confidence in the data is low due to conflicting assessment.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
Authoritative A: EU – GHS (H-Statements)- (H362 – May cause harm to breast-fed children)) **(H).**	**Screening A:** GHS – Australia (H362 – May cause harm to breast-fed children) (*H).*	HIGH: Based on a LOAEL of 13.5 mg/kg-day (NOAEL = 0.9 mg/kg) in mice for reduced habituation, decreased locomotion, and decreased rearing in neonatal male mice exposed to HBCD on postnatal day (PND) 10.	**HIGH** score is given to the development toxicity hazard point based on HIGH score on Authoritative A and Screening A lists as well as based on the measured data in the USEPA assessment. The confidence in the data is high.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening B: TEDX - Potential Endocrine Disruptors (Potential Endocrine Disruptor) (*H-M).*	In Vivo and vitro studies endocrine activity was shown and thyroid effects.	**HIGH:** Due to presence in Screening B List and experimental data in USEPA assessment. The confidence in the data is high.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on acute oral and dermal LD50 values >2,000 mg/kg in rats and rabbits and an acute inhalation LC50 >200 mg/L in rats.	**LOW** score is given based on the measured data from USEPA assessment. The confidence in the data is high.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening A: GHS - Japan (Specific target organs/systemic toxicity following single exposure - Category 3 [H335 or H336]) (*M)*		**MODERATE** score is given based on the presence in the Screening A list. The confidence in the data is low.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**

		Moderate: In a developmental study in rat dams exposed from gestation day (GD) 10 until postnatal day (PND) 20, increased thyroid weights and increased incidence of thyroid follicular cell hypertrophy were observed at 146.3 mg/kg-day (NOAEL= 14.8 mg/kg-day). Repeat dose studies reported liver effects including increased liver weights in conjunction with histopathological findings in a 90-day gavage study in rats administered 100 mg/kg-day (lowest dose tested) and increased liver weights in a 28-day gavage study in rats at a dose of 940 mg/kg-day (lowest dose tested). There is potential for nephrotoxicity based on a structural alert for halogenated aliphatic hydrocarbons.	**MODERATE** score is given based on the measured data from USEPA assessment. The confidence in the data is high. The NOAEL=14.8 for thyroid weight increase which comes in the range of MODERATE (10-100 mg/kg bw/day) as per GreenScreen criteria (CPA, 2018).
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			DG: No data located.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated to have potential for neurotoxicity based on structural alert for cyclic halogenated aliphatic hydrocarbons and professional judgment.	**MODERATE** score is given based on the professional judgment from USEPA assessment. The confidence in the data is low.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on negative results for skin sensitization in human volunteers and guinea pigs.	**LOW** score is given based on the measured data from USEPA assessment. The confidence in the data is high.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			DG: No data located.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		VERY LOW: HBCD is not a dermal irritant in rabbits or	**LOW** score is given based on the

		guinea pigs.	measured data from USEPA assessment. The confidence in the data is high. The low score is designated because as per GreenScreen criteria there is no very low designation (CPA, 2018).
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		VERY LOW: HBCD is not an eye irritant in rabbits.	**LOW** score is given based on the measured data from USEPA assessment. The confidence in the data is high. The low score is designated because as per GreenScreen criteria there is no very low designation (CPA, 2018).
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening A: GHS – Japan (Hazardous to the aquatic environment (acute) – Category 1 [H400]) (*vH)*	**VERY HIGH:** Based on an EC50 of 0.027 mg/L in algae. NES is expected based on physical-chemical properties and other experimental and estimated values for fish, daphnia and algae; however, there is some indication of toxicity to algae at concentrations that are within the range of water solubility.	**VERY HIGH** score is given based on the measured data from USEPA assessment as well as presence on Screening A list as Very High designation. The confidence in the data is high. The EC50 is in the VERY HIGH range of GreenScreen criteria (CPA, 2018).
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		VERY HIGH: Based on experimental 21-day LOEC = 0.0056 mg/L and NOEC = 0.0031 mg/L for γ-HBCD in Daphnia magna.	**VERY HIGH** score is given based on the measured data from USEPA assessment. The confidence in the data is high. The NOEC is in the VERY HIGH range of GreenScreen criteria (CPA, 2018)
Persistence (P)			

Authoritative List	Screening List	USEPA	Final Decision
	Screening B: EC-CEPA DSL (Persistent). (v*H-H).* **Screening A:** ChemSec SIN List (PBT). (v*H).*	HIGH: The persistence designation for HBCD is high. HBCD was considered by the Executive Body of the United Nations Economic Commission for Europe (UNECE) Convention on Long-Range Trans-boundary Air Pollution (LRTAP) to meet the criteria for persistent organic pollutants (POPs) as defined under the POPs protocol. HBCD is persistent in the air, and as such, has been detected in remote regions including the Arctic, and in sediment layers from the 1960s and 1970s through core sampling studies. HBCD is not expected to appreciably degrade under aerobic conditions. Degradation through debromination may occur under anaerobic conditions. Experimental studies indicate no degradation after 28 days in a ready biodegradation test. Aerobic biodegradation data obtained in soil also suggest high persistence.	**HIGH** score is given based on the measured data from USEPA assessment and monitored data as well as meeting UNECE POPs criteria. The confidence in the data is high.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening A: EC-CEPA DSL (Bioaccumulative). (v*H).* **Screening A:** ChemSec SIN List (PBT). (v*H).*	VERY HIGH: The bioaccumulation designation for HBCD is based on measured BCF values. Available monitoring data demonstrate HBCD being detected in a range of organisms, including higher trophic level organisms. BCF measured 8974	**VERY HIGH** based on the measured data from USEPA assessment as well as monitoring data from range of organisms. The confidence in the data is high.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Not explosive (Estimated).	**LOW:** Based on estimation in USEPA assessment. The confidence in the data is low.
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Not flammable (Estimated).	**LOW:** Based on estimation in USEPA assessment. The confidence in the data is low.

HBCD is in the EU SVHC Authorization List (Authoritative A List) as PBT that is why it needs authorization in EU.

USEPA. (2014a). Flame Retardant Alternatives for HBCD. https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf. *[Žiūrėta: 2017-05-11]*, (June), 230. Retrieved from https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf

6.1.1.1.1 Pharos. (2021). *'1,2,5,6,9,10-Hexabromocyclododecane'* Retrieved from https://pharosproject.net/chemicals/2004475#hazards-panel

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

Chemical: TBBPA-bis brominated ether derivative (CAS# 97416-84-7) Hazard Assessment.

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014a)

	GreenScreen and DfE Hazard Summary Table for Butadiene-Brp				
	Group I Human	Group II and II* Human	Ecotox	Fate	Physical

	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment[1]	*M*	*M*	*M*	*M*	*H*	*L*	-	*M*	-	*L*	**L**	**DG**	**L**	**L**	**L**	*L*	*H*	*H*	*L*	*L*
USEPA DfE Assessment[2]	*M*	*M*	*M*	*M*	**NI**	*L*	**NI**	*M*	**NI**	*L*	*L*	**DG**	*L*	*L*	*L*	*L*	*H*	*H*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,
2 Chemical hazard assessment by USEPA (DfE) for HBCD (USEPA, 2014a)

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: No data located. Estimated to have potential for carcinogenicity based on the potential for alkylation and professional judgment.	**MODERATE:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists.

			The confidence in the data is low.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. The analog TBBPA bis(2,3-dibromopropyl) ether was mutagenic to Salmonella typhimurium but did not cause chromosomal aberrations in Chinese hamster ovary (CHO) cells (in vitro), was negative in an in vivo micronucleus assay in mice and did not produce unscheduled DNA synthesis in rats.	**MODERATE:** Based on USEPA analog study. The confidence in the data is low.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated based on a mechanistic consideration of its potential to act as an alkylating agent using professional judgment.	**MODERATE:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. In the ECHA registration dossier two generation toxicity study of a surrogate is reported which is not Guideline study (Klimisch score 2) (reliable with restriction) which stated NOAEL>1000 mg/kg bw/day. As the study was of low confidence professional judgment of USEPA is adopted in this study. The confidence in the data is low.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated based on a mechanistic consideration of its potential to act as an alkylating agent using professional judgment.	**MODERATE:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. The confidence in the data is low. In ECHA registration dossier (Klimisch score 2) non guideline study is reported for a structural analogue with NOAL>2500 mg/kg bw/day. Due to non-guideline nature low confidence score the

			professional judgment of USEPA is adopted in this study.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening B: TEDX - Potential Endocrine Disruptors (Potential Endocrine Disruptor) (*H-M).*	Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. Based on four in vitro assays, the analog TBBPA bis(2,3-dibromopropyl) ether can interact with the endocrine system. The analog TBBPA bis(2,3-dibromopropyl) ether may have potential estrogenic and transthyretin-binding effects; it appears to inhibit sulfation of estradiol (E2), but does not exhibit estrogenic activity via interference with estrogen receptors (ER); it does not appear to interfere with aryl hydrocarbon receptor (AhR)-mediated, androgenic or progestagenic pathways. The analog TBBPA bis(2,3-dibromopropyl) ether competed with thyroid hormone precursor thyroxine (T4) for binding to human transthyretin (TTR), but did not exhibit thyroid hormone (T3) mimicking activity.	**HIGH:** Based on analog study from USEPA assessment and presence in Screening B List TEDX Potential Endocrine Disruptor of the analog TBBPA bis(2,3-dibromopropyl) ether. The confidence in the data is low. It is also included in CoRAP by ECHA for potential endocrine Disruption to further evaluate endocrine disruption potential. Based on absence of *in-vivo* studies low confidence moderate score is assigned. Campioli and Papadapolous also acknowledge that in vitro findings may not translate *in vivo* (USEPA, 2014a).
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. Available experimental oral and dermal LD50 values for the analog TBBPA bis(2,3-dibromopropyl) ether are >2,000 mg/kg and an inhalation LC50 value for the analog is >20 mg/L.	**LOW:** Based on USEPA analog estimation study. The confidence in the data is low.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			Not present in any list and USEPA has no single exposure systemic toxicity hazard assessment.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated based on analogy to a confidential analog.	**MODERATE:** Based on USEPA analog estimation

		There is also potential for liver toxicity as TBBPA-bis brominated ether derivative is a highly brominated compound.	study. The confidence in the data is low. The ECHA registration dossier has showed no systemic toxicity at necropsy examination for another structural analogue of TBBPA ether derivative but MODERATE score of USEPA is adopted in this study because it's a brominated compound and professional judgment of USEPA is adopted conservatively.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			Not present in any list and USEPA has no single exposure neurotoxicity hazard assessment.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Low potential for neurotoxicity estimated based on expert judgment. No data located.	**LOW:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. The confidence in the data is low.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: No data located. Estimated to have low potential for skin sensitization based a closely related confidential analog and professional judgment. There is some potential for skin sensitization based on a mechanistic consideration of the potential for alkylation.	**LOW:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. In the ECHA registration dossier it is termed as not skin sensitizing as per experimental data with reliable Klimisch score 1. The confidence in the data is high.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		No data located.	
Skin Irritation/Corrosivity (IrS)			

Authoritative List	Screening List	USEPA	Final Decision
		LOW: Estimated not to cause dermal irritation based on expert judgment. No experimental located.	**LOW:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. In the ECHA registration dossier, Klimisch 1 (reliable without restriction) is present conducted in 2015 which shows it is not skin irritant. The confidence in the data is high.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Estimated not to cause eye irritation based on expert judgment. No experimental data located.	**LOW:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. In the ECHA registration dossier, Klimisch 1 (reliable without restriction) is present conducted in 2015 which shows it is not eye irritant. The confidence in the data is high.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on estimated acute toxicity values for fish, Daphnids, and green algae that suggest no effects at saturation (NES).	**LOW:** Based on USEPA estimated study as no experimental data is found and it is not present on nay Authoritative or Screening Lists. No toxic effect at the limit of saturation as per tests in the ECHA registration dossier. The confidence in the data is high.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on estimated chronic toxicity values for fish, Daphnia,	**LOW:** Based on USEPA estimated study as no

		and green algae that suggest NES.	experimental data is found and it is not present on nay Authoritative or Screening Lists. Data waivered as per ECHA registration dossier. The confidence in the data is low.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		HIGH: High persistence of TBBPA-bis brominated ether derivative is expected. Aerobic biodegradation is not expected to be an important removal process, based on analog data. Although anaerobic biodegradation (by dehalogenation) may occur, the rate is likely to be low, and any such transformation will only lead to intermediate products that have essentially the same environmental properties. In other words, if emission to the environment occurs at any rate greater than negligible, this substance will accumulate. TBBPA-bis brominated ether derivative will exist primarily in the particulate phase in the atmosphere and is not expected to undergo removal by gas-phase oxidation reactions; however due to its properties, it is not expected to be released or transported to the atmosphere to a significant degree. TBBPA-bis brominated ether derivative is not anticipated to undergo removal by hydrolysis, since it does not contain hydrolysable functional groups.	**HIGH:** Based on USEPA analog study. The confidence in the data is low. Not readily biodegradable as per ECHA registration dossier 301B test. No other detail is provided. Because of lack of Klimisch score and any detail low confidence.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		HIGH: High potential for bioaccumulation based on an estimated BAF of 1,600.	**HIGH:** Based on estimation of BAF in USEPA assessment. The confidence in the data is low. The estimated BAF reported in the ECHA registration dossier of 1589 (structural analogue) in ECHA registration dossier. The confidence in the data is low.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Not expected to form explosive mixtures with air (Estimated).	**LOW:** As per professional judgment in USEPA

			assessment. The confidence in the data is low.
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Nonflammable (Estimated).	**LOW:** As per professional judgment in USEPA assessment. The confidence in the data is low.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

USEPA. (2014a). Flame Retardant Alternatives for HBCD. https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf. *[Žiūrėta: 2017-05-11]*, (June), 230. Retrieved from https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf

Pharos. (2021). '*CAS# 97416-84-7 Pyroguard SR-130, SR-130*' Retrieved from https://pharosproject.net/chemicals/2036911#hazards-panel

ECHA Registration Dossier: ECHA. (2021). 'Registration Dossier: *CAS# 97416-84-7 1,1'-(isopropylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]*' Accessed: https://echa.europa.eu/registration-dossier/-/registered-dossier/15903/5/3/2

Chemical: TBBPA bis(2,3-dibromopropyl) ether (CAS# 21850-44-2) Hazard Assessment.

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014a)

	GreenScreen and DfE Hazard Summary Table for TBBPA ether

	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*M*	**M**	*M*	**M**	*M*	**L**	**-**	*M*	**-**	*L*	**L**	**DG**	**L**	**L**	**L**	*L*	**VH**	*H*	*L*	*L*
USEPA DfE Assessment [2]	*M*	**M**	*M*	*M*	**NI**	**L**	**NI**	*M*	**NI**	*L*	**L**	**DG**	**L**	**L**	**L**	*L*	**VH**	*H*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,
2 Chemical hazard assessment by USEPA (DfE) for HBCD (USEPA, 2014a)

Hazard Endpoints Detailed Evaluation Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: No data located. Estimated to have	**MODERATE:** Based on USEPA professional judgment as no

		potential for carcinogenicity based on the potential for alkylation and professional judgment.	experimental data is found and it is not present on nay Authoritative or Screening Lists. The confidence in the data is low.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: TBBPA bis(2,3-dibromopropyl) ether was mutagenic to Salmonella typhimurium in one assay, while it was negative in other assays in S. Typhimurium and E. coli. This substance was also negative for mutagenicity in mouse lymphoma cells. TBBPA bis(2,3-dibromopropyl) ether is also estimated to have potential for genotoxicity based on the potential for alkylation. TBBPA bis(2,3-dibromopropyl) ether did not cause chromosomal aberrations or sister chromatid exchanges in Chinese hamster ovary (CHO) cells (*in vitro*), was negative in an *in vivo* micronucleus assay in mice and did not produce unscheduled DNA synthesis in rats	**MODERATE:** Based on experimental data in USEPA assessment. The confidence in the data is high due to experimental data.
Reproductive Toxicity			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated to have potential for reproductive effects based on the potential for alkylation and professional judgment.	**MODERATE:** Based on USEPA professional judgment. The confidence in the data is low due to absence of experimental data. In ECHA registration dossier the reproductive toxicity data has been waivered based on presence of development toxicity data. But in this study the score of USEPA is adopted.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: Estimated to have potential for developmental effects based on the potential for alkylation and professional judgment.	**MODERATE:** Based on USEPA professional judgment as no experimental data is found and it is not present on any Authoritative or Screening Lists. In the ECHA Registration Dossier development toxicity study (Klimisch score 1) OECD 414 guideline study, maternal

			NOAEL was 300 mg/kg bw/day which was in the moderate range as per GreenScreen criteria. Fetal NOAEL was 1000 mg/kg bw/day. The confidence in the data is high.
Endocrine Activity			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
	Screening B: TEDX - Potential Endocrine Disruptors (Potential Endocrine Disruptor) (*H-M)*	Based on 4 in vitro assays, TBBPA bis(2,3-dibromopropyl) ether can interact with the endocrine system. TBBPA bis(2,3-dibromopropyl) ether may have potential estrogenic and transthyretin-binding effects. TBBPA bis(2,3-dibromopropyl) ether appears to inhibit sulfation of estradiol (E2), but does not exhibit estrogenic activity via interference with estrogen receptors (ER). TBBPA bis(2,3-dibromopropyl) ether also does not appear to interfere with AhR-mediated, androgenic or progestagenic pathways. TBBPA bis(2,3- dibromopropyl) ether competed with thyroid hormone precursor thyroxine (T4) for binding to human transthyretin (TTR), but did not exhibit thyroid hormone (T3) mimicking activity.	**Moderate:** Based on *in vitro* studies from USEPA report and presence in Screening B List TEDX Potential Endocrine Disruptor. The confidence in the data is low. It is also included in CoRAP by ECHA for potential endocrine Disruption to further evaluate endocrine disruption potential. Based on absence of *in-vivo* studies low confidence moderate score is assigned. Campioli and Papadapolous also acknowledge that in vitro findings may not translate *in vivo* (USEPA, 2014a).
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on oral and dermal LD50 values >2, 000 mg/kg and an inhalation LC50 value >20 mg/L.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			DG: Not present in any list and USEPA has no single exposure systemic toxicity hazard assessment.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: There is potential for liver toxicity because TBBPA bis(2,3-dibromopropyl) ether is a highly	**MODERATE:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay

		brominated compound and potential for immunotoxicity associated with polyhalogenated aromatic hydrocarbon structure. Located data were insufficient.	Authoritative or Screening Lists. The studies in the ECHA Registration Dossier have been recognized by USEPA report and have been deemed insufficient to make high confidence judgment. The confidence in the data is low due to absence of experimental data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			Not present in any list and USEPA has no single exposure neurotoxicity hazard assessment.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Estimated not to have potential for neurotoxicity based on expert judgment; no data located.	**LOW:** Based on professional judgment in USEPA assessment. The confidence in the data is low.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Not a skin sensitizer in guinea pigs. There is potential for skin sensitization based on the potential for alkylation.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		No data located.	**DG: No pertinent data located.**
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Not a skin irritant in rabbits	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**

		LOW: Minimal eye irritation in rabbits clearing within 48 hours.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on experimental and estimated acute toxicity values for fish, daphnia, and algae that suggest no effects at saturation (NES).	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on estimated chronic toxicity values for fish, daphnia and green algae that suggest NES.	**LOW:** Based on estimated data in USEPA assessment. The confidence in the data is low.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
Authoritative A: OSPAR - Priority PBTs & EDs & equivalent concern (But no score is provided). Every Brominated Flame Retardant is automatically included in this list.		**VERY HIGH:** High persistence of TBBPA bis(2,3-dibromopropyl) ether is expected as a result of located biodegradation studies and the absence of other expected likely removal processes under environmental conditions. In the course of a 28-day Japanese Ministry of International Trade and Industry (MITI) test, only 1% of TBBPA bis(2,3-dibromopropyl) ether was degraded. TBBPA bis(2,3-dibromopropyl) ether will exist primarily in the particulate phase in the atmosphere and is not expected to undergo removal by gas phase oxidation reactions. It is also not anticipated to undergo removal by hydrolysis.	**VERY HIGH:** Based on measured data in USEPA assessment. The confidence in the data is high.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**

		HIGH: Based on an estimated BAF of 12,000 and its detection in Great Lakes Herring gull eggs, potential for bioaccumulation is high.	**HIGH:** Based on estimated data in USEPA assessment. The confidence in the data is low. Although it comes in Very High range as per GreenScreen and USEPA criteria but the USEPA has assigned HIGH score. In this study USEPA score is adopted.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Some secondary sources are used.	**LOW:** As per USEPA report not reactive and doesn't contain oxidative functional group. The confidence in the data is low due to absence of experimental data.
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		Some secondary sources are quoted for non-flammability.	**LOW:** As per USEPA and usage as a flame retardant. The confidence in the data is low.

References:

USEPA. (2014a). Flame Retardant Alternatives for HBCD. https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf. *[Žiūrėta: 2017-05-11]*, (June), 230. Retrieved from https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf

Pharos (2020), Tetrabromobisphenol A bis(2,3-dibromopropyl ether). Retrieve from https://pharosproject.net/chemicals/2006727#hazards-panel.

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

ECHA Registration Dossier: ECHA. (2021). 'Registration Dossier: *CAS# 97416-84-7 1,1'-(isopropylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]'* Accessed: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13876/7/6/1

Chemical: Butadiene styrene brominated copolymer (Butadiene-Brp) (CAS#1195978-93-8) Hazard Assessment.

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014a)

	GreenScreen and DfE Hazard Summary Table for Butadiene-Brp																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*L*	**L**	**L**	**L**	*L*	**L**	-	**L**	-	*L*	**L**	**DG**	**L**	**M**	*L*	*L*	*VH*	*L*	*L*	*L*
U.S EPA DfE Assessment [2]	*L*	**L**	**L**	**L**	**NI**	**L**	**NI**	**L**	**NI**	*L*	**L**	**DG**	**L**	**M**	*L*	*L*	*VH*	*L*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,
2 Chemical hazard assessment by USEPA (DfE) for HBCD (USEPA, 2014a)

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**

		LOW: This polymer is large, with a MW >1,000. It is expected to have few to no residual monomers. Additionally, it is not expected to have crosslinking, swellability, dispersability, reactive functional groups, and potential for inhalation or hindered amine groups. This chemical therefore has a low potential for carcinogenicity. No experimental data located.	**LOW:** Based on USEPA professional judgment as no experimental data is found and it is not present on nay Authoritative or Screening Lists. The confidence in the data is low due to absence of experimental data.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: This compound did not induce gene mutations in bacteria or cause chromosomal aberrations in mammalian cells in vitro. In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for genotoxicity.	**LOW:** Based on *in vitro* studies and professional judgment in USEPA assessment. The confidence in the data is high.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Available experimental data (NOAEL >1000 mg/kg bw/day) indicate a Low hazard designation. In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for reproductive effects.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high due to presence of experimental data. As per the GreenScreen criteria the score assigned is low (CPA, 2018).
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Available experimental data also indicate a Low hazard designation (NOAEL >1000 mg/kg bw/day). In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for developmental effects.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high. As per the GreenScreen criteria the score assigned is low (CPA, 2018).
Endocrine Activity			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: This polymer is large, with a MW >1,000. It is not	**LOW:** Based on professional judgment and lack of

		expected to have endocrine activity due to its limited bioavailability and inability to be readily metabolized in the body	experimental data. The confidence in the data is low.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on experimental LD50 values >2,000 mg/kg. This polymer is also expected to have limited bioavailability and is therefore of low potential for acute mammalian toxicity.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			Not present in any list and USEPA has no single exposure systemic toxicity hazard assessment.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: Based on an experimental NOAEL >1,000 mg/kg-day in rats exposed via gavage for 28 days. This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; however, because the number average molecular weight (MW) is >10,000, there is the possibility of lung overloading in dust forming conditions.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high due to experimental data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
			Not present in any list and USEPA has no single exposure neurotoxicity hazard assessment.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for neurotoxicity. There were no neurological effects reported in a 28-day repeated dose toxicity study in rats at doses as high as 1,000	**LOW:** Based on professional judgment in USEPA assessment. The confidence in the data is low as no experimental measured data was found.

		mg/kg-day.	
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: This polymer did not cause skin sensitization in a guideline study.	**LOW:** Based on measured data in USEPA assessment. The confidence in the data is high due to experimental data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		No data located.	DG: No data
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		LOW: This polymer is slightly irritating to the skin of rabbits.	**LOW:** Based on measured data in USEPA assessment. The slight irritation reversed within 24 hours. The confidence in the data is high.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Final Decision**
		MODERATE: This polymer is mildly irritating to rabbit eyes, with effects clearing within 72 hours post instillation.	**MODERATE:** Based on experimental data in USEPA assessment. The confidence in the data is high due to experimental data.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
		LOW: Non-ionic polymers with MWs >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to display no effects at saturation (NES). These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic	**LOW:** Based on estimated data in USEPA assessment and professional judgment. The confidence in the data is low.

		toxicity hazard results in a Low hazard designation for those materials that display NES. Experimental data for Daphnia magna indicate NES with EC50 values > 1,000 mg/L; these reported values exceed the compound's water solubility by several orders of magnitude.	
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
		LOW: Non-ionic polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to display NES. These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic toxicity hazard results in a low hazard categorization for those materials that display NES.	**LOW:** Based on estimated data in USEPA assessment and professional judgment. The confidence in the data is low. In the ECHA registration dossier it is stated that scientific study not necessary.
Persistence (P)			
Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
Authoritative A: OSPAR - Priority PBTs & EDs & equivalent concern (But no score is provided). Every Brominated Flame Retardant is automatically included in this list.		**VERY HIGH:** This polymer is large, with a MW >1,000. It has negligible water solubility and is expected to have poor bioavailability to microorganisms, indicating that neither biodegradation nor hydrolysis are expected to be important removal processes in the environment. Additionally, experimental guideline studies did not detect anaerobic biodegradation of this polymer after 62 days or degradation by hydrolysis after five days at pH 1.2 to 9. Although debromination by photodegradation of polybrominated benzenes has been observed, this process is not anticipated to lead to ultimate degradation of the material; also, limited debromination is not likely to significantly alter the environmental properties of this material. As a result, a half-life for this high MW polymer of >180 days leads to a potential for Very High persistence.	**VERY HIGH:** Based on estimated data from models in USEPA assessment and professional judgment. The confidence in the data is low.
Bioaccumulation (B)			

Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
		LOW: Due to the large size and limited bioavailability of the high MW brominated polymer, it is of low potential for bioconcentration or bioaccumulation.	**LOW:** Based on professional judgment in USEPA assessment. The confidence in the data is low.
Reactivity (R)			
Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
		Not expected to form explosive mixtures with air (Estimated).	**LOW:** As per professional judgment in USEPA assessment. The confidence in the data is low.
Flammability (F)			
Authoritative List	**Screening List**	**U.S EPA**	**Final Decision**
		Nonflammable (Estimated).	**LOW:** As per professional judgment in USEPA assessment. The confidence in the data is low.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

USEPA. (2014a). Flame Retardant Alternatives for HBCD. https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf. *[Žiūrėta: 2017-05-11]*, (June), 230. Retrieved from https://www.epa.gov/sites/production/files/2014-06/documents/hbcd_report.pdf

Pharos. (2021). '*CAS#1195978-93-8 benzene, ethenyl-, polymer with 1,3- butadiene, brominated'* Retrieved from https://pharosproject.net/chemicals/2036887#hazards-panel

Chemical: Decabromodiphenyl ether (DecaBDE) Hazard Assessment

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014b)

	GreenScreen and DfE Hazard Summary Table for DecaBDE																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	**M**	**L**	**M**	**H**	*M*[a]	**L**	**L**	**M**	**-**	*L*	**L**	**DG**	*M*[b]	**L**	*L*	*L*	**VH**	*H*	**L**	**L**
U.S EPA DfE Assessment [2]	**M**	**L**	**L**	**H**	**-**	**L**	**-**	**M**	**-**	*L*	**L**	**DG**	**L**	**L**	*L*	*L*	**VH**	*H*	**-**	**-**

1 GreenScreen hazard assessment conducted in this thesis study,
2 Chemical hazard assessment by USEPA (DfE) for DecaBDE (USEPA 2014b)

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
Authoritative B: USEPA - IRIS Carcinogens - (2005) Suggestive evidence of Carcinogenic potential *(H-L).* **Authoritative B:** IARC - Group 3 - Agent is not classifiable as to its carcinogenicity to humans *(H-L).*		**MODERATE:** National Toxicology Program (NTP) study showed equivocal evidence of carcinogenicity in male mice.	**MODERATE:** Based on NTP study and 'Suggestive evidence of Carcinogenic Potential' by IRIS. The confidence in the score is high based on measured data.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening A: GHS - Japan Germ cell mutagenicity - Category 2 [H341] *(M).*	**LOW:** Based on negative results for gene mutations in bacterial and mammalian cells and lack of chromosomal aberrations in Chinese hamster ovary (CHO) cells in vitro.	**LOW:** Based on negative results obtained in *in-vitro* and *in-vivo* tests. The confidence in the data is high based on measured data.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on EPA IRIS NOAEL 100 mg/kg bw/day and LOAEL was 500 mg/kg bw/day in mice for adverse effect on sperm.	**MODERATE:** Based on NOAEL=100 mg/kg bw/day and LOAEL=500 values because the value can be 250 mg/kg bw/day that is why due to the gap between and NOAEL and LOAEL that is why moderate score is assigned. The confidence in the data is high due to measured data.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening B List: G&L Neurotoxic	**HIGH:** Based on LOAEL<10 mg/kg bw/ day in a number of development toxicity tests.	**HIGH:** Based on measured data indicating LOAEL as low as 6 mg/kg

	Chemicals (Developmental Neurotoxicant) *(H-M).*		bw/ day which is in the HIGH score range for development toxicity. The confidence in the data is high due to measured data.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
Authoritative B List: OSPAR - Priority PBTs & EDs & equivalent concern - Endocrine Disruptor - Chemical for Priority Action	**Screening B Lists:** EU - Priority Endocrine Disrupters - Category 1 - *In vitro* evidence of Endocrine Disruption Activity *(H-M).* ChemSec - SIN List - Endocrine Disruption TEDX - Potential *(H-M).* Endocrine Disruptors - Potential Endocrine Disruptor (*H-M)*	Some metabolites of decaBDE are known to produce estrogenic effects.	**MODERATE:** Based on the presence in Screening B lists and showing some estrogenic effects in USEPA report. The confidence in the data is low.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Acute oral LD_{50} was greater than 5000 mg/kg for DecaBDE.	**LOW:** Acute oral LD_{50} was greater than 5000 mg/kg for DecaBDE. It was assigned 'L-low' hazard score as per the GreenScreen criteria (CPA, 2018). The confidence in the data is high because of experimental measured data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Based on lack of any systemic effect observed at high dosage in acute mammalian toxicity studies.

Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening A List: GHS Japan Specific target organs/ systemic toxicity following repeated exposure-Category 2 [H373] *(M).*	**MODERATE:** Based on a LOAEL of 80 mg/kg-day for adverse liver and thyroid effects following a 30-day oral exposure in rats.	**MODERATE:** Based on LOAEL= 80 mg/kg bw/day reported in USEPA report. As per the GreenScreen criteria a chemical is assigned moderate hazard score for systemic toxicity repeat dose if NOAEL > 10-100 mg/kg bw/day (CPA, 2018). The confidence in the data is high due to measured experimental data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening B List: G&L-Neurotoxic Chemicals *(vH-M).*	**LOW:** Based on professional judgment indicating no structural alerts causing neurotoxicity.	**LOW:** Based on professional judgment indicating no structural alerts causing neurotoxicity. The confidence in the data is low because of lack of experimental data.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on negative results in guinea pigs and human volunteers.	**LOW:** Based on negative results in guinea pigs and human volunteers. The confidence in the data is high due to experimental data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		DATA GAP	**DATA GAP**
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening A: GHS - Japan (Skin corrosion /	**LOW:** Based on no skin irritation in rabbit but in human volunteers slight skin irritant.	**MODERATE:** As per Screening A list and slight irritation in human

	irritation - Category 3 [H316]) *(M).*		volunteers' moderate score is assigned. The confidence in the data is low because of screening list.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening A: GHS - Japan (Eye irritation - Category 2B [H319]) *(M).*	**LOW:** Mild irritation which is reversible in 48 hours.	**LOW:** Although present in GHS Japan but any irritation which clear within 48 hours, as per GreenScreen criteria low score. The confidence in the data is high because of experimental data.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: The log Kow of the compound (9.97) exceeds the ECOSAR cutoff value of 5.0 for acute endpoints and therefore, no effects at saturation (NES) are predicted. Although experimental studies were located for fish and green algae, they were considered to be inadequate due to deviations from standard protocols and resulting toxicity values that exceed the compound's water solubility.	**LOW:** Based on professional judgment in USEPA which indicates that Log Kow> 5 for acute toxicity**.** The confidence in the data is low due to absence of guideline experimental data.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on estimated values for fish, daphnia and algae that exceed the water solubility and are therefore predicted to have NES.	**LOW:** Based on USEPA estimation. The confidence in the score is low based on estimated data.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		VERY HIGH: DecaBDE was assigned 'VH-very high' score based on experimental biodegradation studies reported in USEPA report which indicate very high persistence of DecaBDE in the environment.	**VERY HIGH:** DecaBDE was assigned 'VH-very high' score based on experimental biodegradation studies reported in USEPA report which indicate very high persistence of DecaBDE in the environment. The confidence in the data is high

			because of monitoring data.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		HIGH: Based on estimated BAF values suggesting that the potential for bioaccumulation is high and located monitoring data indicating that decaBDE has been detected in higher trophic level organisms.	**HIGH:** The score is based on USEPA report and the confidence in the data is low because it is based on estimated data.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: DecaBDE was assigned a score of LOW for instability based on NFPA score of 0. The confidence in the score is high.
Flammability (F)			
Authoritative List	**Screening List**	**U.S EPA**	**Comment**
			LOW: DecaBDE was assigned a score of LOW for flammability based on NFPA score of 0. The confidence in the score is high.

References:

CPA. (2018). The GreenScreen for Safer Chemicals Guidance v1.4. *Version4*. Retrieved from http://www.cleanproduction.org/Greenscreen.php

USEPA. (2014). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Pharos. (2021). '*Decabromodiphenyl ether'* Retrieved from https://pharosproject.net/chemicals/2007598#hazards-panel

Chemical: Aluminum Diethylphosphinate (CAS# 225789-38-8) Hazard Assessment

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014b).

	GreenScreen and DfE Hazard Summary Table for Aluminum diethylphosphinate																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*L*	**L**	*L*	*L*	**DG**	**L**	**-**	**L**	**-**	**L**	**L**	*L*	**L**	**L**	**L**	**L**	*vH*	*vL*	*L*	**L**
U.S EPA DfE Assessment [2]	*L*	**L**	**vL**	*M*	**DG**	**L**	**NI**	*M*	**NI**	*M*	**L**	**DG**	**vL**	**L**	**M**	**M**	*H*	*L*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,

2 Chemical hazard assessment by USEPA (DfE) for DecaBDE (USEPA, 2014b).

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: According to the U.S EPA professional judgment and modeling Aluminum diethylphosphinate was designated a Low score for carcinogenicity	**LOW:** According to USEPA report low score is designated. The confidence in the score is low as it is not based on authoritative lists or measured data.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: According to *in-vivo* and *in-vitro* tests negative result for genotoxicity and mutagenicity.	**LOW:** Low score is designated because of measured data. The confidence in the data is high.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		VERY LOW: Aluminum diethylphosphinate was assigned a score of Low for reproductive toxicity based on the lack of reproductive toxicity observed in an OECD 421 reproductive/developmental toxicity screening test in rats. A reproductive NOAEL of 1,000 mg/kg/day was identified.	**LOW:** Low score was designated because of NOAEL of 1000 mg/kg/day in the screening OECD 421 test in USEPA report. The confidence in the score is low due to screening level test.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		MODERATE: There were no developmental effects reported in a reproduction/developmental toxicity screen in rats at doses up to 1,000 mg/kg-day. There is moderate hazard for aluminum diethylphosphinate given exposure may result in neurodevelopmental effects based on the presence of a phosphinate; there were no experimental studies specifically designed to evaluate the neurodevelopmental endpoint located. The	**LOW:** According to OECD Guideline studies 421 in the USEPA report NOAEL of 1,000 mg/kg/day for development toxicity which is low hazard score. The confidence in the score is low because of limited neurotoxicity endpoints assessed in the studies. The weight of evidence approach was taken because in ToxServices (2019) OECD 414 and other studies showed NOAEL >1000 mg/kg bw/ day but the confidence in the data

		potential for neurodevelopmental effects cannot be ruled out.	is low because more neurotoxic studies are recommended.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: More studies are recommended for endocrine activity so a data gap is assigned.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Aluminum diethylphosphinate was assigned a score of Low for acute toxicity based on oral and dermal LD50 values greater than 2,000 mg/kg.	**LOW:** Low score was designated due to measured data of oral and dermal LD50 greater than 2,000 mg/kg in the USEPA Report and the confidence in the score is high due to measured data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Aluminum diethylphosphinate was assigned a score of Data Gap for systemic toxicity (single dose) based on the lack of data identified for this endpoint.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		MODERATE: Aluminum diethylphosphinate is estimated to be of moderate hazard for immunotoxicity, due to the presence of a bioavailable metal species (Aluminum) and based on comparison to analogous metal salts and professional judgment.	**LOW:** The designated score is low as per the studies in the NICNAS 2005 report in the OECD TG 407 study with NOAEL of 1,000 mg/kg bw/day and the confidence in the score is high due to presence of measured data. ToxServices (2019) indicates that aluminum won't be available based on new experimental *in vivo* data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Aluminum diethylphosphinate was assigned a score of Data Gap for neurotoxicity (single dose) based on the lack of

			data identified for this endpoint.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		MODERATE: Aluminum diethylphosphinate is expected to have a moderate hazard potential for neurotoxicity as the results of bioavailable (inhalation and oral, but not dermal) aluminum in the compound.	**LOW:** Aluminum diethylphosphinate was assigned a score of Low for neurotoxicity (repeated dose) based on lack of neurotoxicity in a 28-day repeated-dose toxicity OECD 407 study with a NOAEL of 1,000 mg/kg and expected lack of bioavailability for aluminum from aluminum diethylphosphinate (ToxServices, 2019). The confidence in the score is high due to presence of measured data
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Negative for skin sensitization in guinea pigs	**LOW:** Aluminum diethylphosphinate was assigned a score of Low for skin sensitization based on the lack of dermal sensitization reactions observed in a guinea pig maximization OECD 406 (ToxServices, 2019). The confidence in the score is high due to measured data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: No structural alerts as per the (ToxServices, 2019). The confidence in the data is low due to absence of experimental data.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		VERY LOW: Aluminum diethylphosphinate is not irritating to rabbit skin.	LOW: It was assigned a score of Low for skin irritation/Corrosivity based on the lack of dermal irritation observed in a rabbit study. The confidence in the data is high due to measured data.
Eye Irritation/Corrosivity (IrE)			

Authoritative List	Screening List	USEPA	Comment
		LOW: Aluminum diethylphosphinate was assigned a score of Low for eye irritation/Corrosivity based on lack of significant effects observed in multiple studies. The transient and slight irritation observed was attributed to mechanical effects.	**LOW:** USEPA report reported it as score of low designation as per studies reported in **USEPA Report.** the confidence in the score is high due to presence of measured data
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		MODERATE: The measured green algae EC50 is between 10 and 100 mg/L. For fish and Daphnia, adequate toxicity values have not been determined; reported values are not LC50 but the highest dose tested.	**LOW:** EC50 as well as NOEC were determined to be > 180 mg/L for this study. 48 hour LC50 and 96 hour LC50 studies show greater than 100 mg/L which makes it a designation of low score (ToxServices, 2019). The confidence in the score is high due to presence of measured data (ToxServices, 2019). The inhibition of algal growth observed in the GLP-compliant algae study was attributed to the test compound's impact on pH in USEPA (2014b).
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		MODERATE: An experimental value of 1.8 mg/L was reported for green algae, while measured toxicity values for fish and Daphnia are >10 mg/L.	**LOW:** The studies in the ToxServices, (2019), indicate 21-day LC50 (D. magna) = 22.3 mg/L (test substance: commercial preparation containing 100% a.i.) 21-day NOEC (D. magna) = 10 mg/L (test substance: commercial preparation containing 100% a.i.) and the **USEPA studies** also show low hazard for chronic aquatic toxicity. The confidence in the score is high. In the OECD Guideline 201 study, OECD notes that recent scientific developments have led to a recommendation of replacing the concept of NOEC with regression-based point estimates ECx. Although a value for x has not been established for the test, a range of 10% to 20% appears to be appropriate (ToxServices, 2019)

Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		HIGH: For the organic counter-ion, estimates indicate that the half-life for ultimate aerobic biodegradation in water is less than 60 days, which converts to moderate potential for persistence. However, the metal ion is recalcitrant to biodegradation or other typical environmental removal processes.	**VERY HIGH:** The confidence in the score is low due to expert judgment. Aluminum diethylphosphinate was assigned a score of Very High for persistence based on the expert judgment that aluminum moiety being inorganic and recalcitrant and on the nature of its flame retardant function as well as not inherently biodegradable as per OECD 302C test and not readily biodegradable OECD 301F test (ToxServices, 2019).
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Aluminum diethylphosphinate was assigned a score of Very Low for bioaccumulation based on a BCF estimated to be less than 100.	**VERY LOW:** As per USEPA report designation of low score is given. The confidence in the score is low as it is based on estimated data.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Aluminum diethylphosphinate was assigned a score of Low for reactivity based on ToxServices, (2019) not classifying it as a reactive chemical under GHS criteria. The confidence in the score is low due to absence of measured data.
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		Not readily combustible measured according to guideline 96/69/EEC test A. 10. No self-ignition below 402ºC (measured).	**LOW:** Aluminum diethylphosphinate was assigned a score of Low for flammability based on ToxServices, (2019) not classifying it as a flammable chemical under GHS criteria. The confidence in the score is high due to presence of experimental study.

TCO Certified Accepted Substance List: Benchmark-3 Accepted Substance (Pharos, 2021).

ToxServices. (2019). *Aluminum Diethylphosphinate (CAS #225789-38-8) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment*. (October 2014). Retrieved from https://database.toxservices.com/

USEPA. (2014b). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Pharos. (2021). 'CAS#225789-38-8 Aluminum diethylphosphinate' Retrieved from https://pharosproject.net/chemicals/2036887#hazards-panel

Chemical: Ammonium polyphosphate (CAS#68333-79-9) Hazard Assessment

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014b).

	GreenScreen and DfE Hazard Summary Table for Ammonium Polyphosphate																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*L*	*L*	*L*	*L*	*L*	**L**	**L**	*L*	**-**	*L*	**L**	**DG**	*M*	**L**	*L*	*L*	*vH*	*vL*	*L*	**L**
U.S EPA DfE Assessment [2]	*L*	*L*	*L*	*L*	**NI**	**L**	**NI**	*L*	**NI**	*L*	**L**	**DG**	**L**	**vL**	*L*	*L*	*vH*	*L*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,

2 Chemical hazard assessment by USEPA (DfE) for DecaBDE (USEPA, 2014b).

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Ammonium polyphosphate was assigned a score of LOW for Carcinogenicity based on professional judgment because it is a large polymer with >1000 MW.	**LOW:** Hazard score of low is designated as per USEPA report. The confidence in the score is low due to expert judgment.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Ammonium polyphosphate was assigned a score of LOW for Mutagenicity due to professional judgment that the MW>1000. It is expected to have limited bioavailability and therefore has low potential for genotoxicity	**LOW:** In a study performed to a valid guideline (OECD TG 476, adopted 21 July 1997) and conducted under GLP conditions reports that ammonium dihydrogenorthophosphate which is a structural analog to ammonium polyphosphonate is not mutagenic in the TK mutation test system under the experimental conditions in (Rosenblum Environmental 2016a). The confidence in the score is low due to structural analog study.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Low score was based on professional judgment due to the size of the molecule and the limited bioavailability.	**LOW:** A NOAEL of 1500 mg/kg/day (highest dose tested) is reported based on no reproductive effects noted during the study in the OECD TG 402 for structural analog Polyphosphoric acids, ammonium salts in (Rosenblum Environmental 2016a). The confidence in the score is low due to structural analog study.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for developmental effects based on professional judgment and SF polymer assessment guidance.	**LOW:** The NOAEL for both maternal and fetal toxicity is > 128 mg/kg bw for the structural analog Polyphosphoric acids, ammonium salts which was the lowest dose. NOAEL of 1500 mg/kg/day (highest dose tested) in the guideline study OECD TG 422; Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity

			Screening Test (Rosenblum Environmental 2016a). The confidence in the data is low due to structural analog.
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is not expected to have endocrine activity due to its poor bioavailability and inability to be readily metabolized in the body based on professional judgment.	**LOW:** The score is designated as per the USEPA report professional judgment. The confidence in the score is low.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Low hazard designation is also supported by a rat oral median lethal dose (LD50) of >2,000 mg/kg, a rat dermal LD50 of >2,000 mg/kg and a 4-hour rat median lethal concentration (LC50) of >5.09 mg/L.	**LOW:** The designation is based on USEPA Report. The confidence in the score is high based on measured data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: No abnormalities were noted at necropsy of animals orally dosed at concentrations of 2000 mg/kg and animals appeared normal after inhalation doses of 4.85 mg/L. All transient effects reported following both oral and inhalation exposures are considered of minor toxicological significance and do not support classification (Rosenblum Environmental 2016a). The confidence in the score is high due to presence on measured data.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; however, because the MW is >10,000, there is the possibility	**LOW:** The low hazard score is designated as per the USEPA report professional judgment. The confidence in the score is low due to absence of measured data.

		of lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations. The score is designated as per professional judgment.	
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Ammonium polyphosphate was assigned a score of DATA GAP for single exposure Neurotoxicity.
Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on professional judgment due to the size of the molecule and the limited bioavailability.	**LOW:** The low score is designated as per USEPA Report professional judgment. The confidence in the score is low due to absence of measured data.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This conclusion was based on information reported in chemical data sheet and adequate study details provided.	**LOW:** The low score is designated as per the USEPA Report analysis. The confidence in the score is high due to presence of measured data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		DG: Ammonium polyphosphate was assigned a score of DATA GAP for respiratory sensitization.	**DG:** Ammonium polyphosphate was assigned a score of DATA GAP for respiratory sensitization.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Slightly irritating in rabbit 24-hour occlusive patch test. This fulfills the guidance of a category 3 Skin Irritation/Corrosivity under GHS	**MODERATE:** As per the USEPA reported study slightly irritating which makes it a hazard score of moderate but the confidence in the score is low due to poorly reported empirical data from USEPA (Rosenblum Environmental 2016a).

Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		VERY LOW: Mixtures containing primarily ammonium polyphosphate were not irritating to rabbit eyes.	**LOW:** The score is based on the USEPA report and the confidence in the score is high.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	German FEA - Substances Hazardous to Waters - Class 1 - Low Hazard to Waters.	**LOW:** Water insoluble polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to have no effects at saturation (NES). These polymers have NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed.	**LOW:** The low hazard score is designated based on the USEPA report professional judgment. The confidence in the score is low.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Water insoluble polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to have NES. These polymers have NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed.	**LOW:** The low hazard score is designated based on the USEPA report professional judgment. The confidence in the score is low.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	EC - CEPA	**VERY HIGH:** This polymer is large, with a MW >1,000. It is expected to have negligible water	**VERY HIGH:** Due to the presence on the screening list and expert judgment in the USEPA report a score of very high is designated. The

	DSL – Persistent	solubility and poor bioavailability to microorganisms indicating that biodegradation is not expected to be an important removal process in the environment.	confidence in the score is low.
Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This ionic polymer is large, with a MW >1,000. It is expected to have negligible water solubility and poor bioavailability indicating that it will have low potential for bioaccumulation based on professional judgment.	**LOW:** The low score is designated as per the USEPA professional judgment and the confidence in the score is low due to absence of measured data.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Based upon identification by the EU that ammonium polyphosphate is appropriate for food applications and professional judgment, reactivity was assigned as low. The confidence in the score is low (Rosenblum Environmental 2016a).
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		Ammonium polyphosphate was assigned a score of LOW for Flammability based on a not flammable description.	**LOW:** Ammonium polyphosphate was assigned a score of LOW for Flammability based on a not flammable description within the USEPA report. The confidence in the score is high (Rosenblum Environmental 2016a).
TCO Certified Accepted Substance List: Benchmark-3 Accepted Substance (Pharos, 2021).			

References:

Rosenblum Environmental. (2016). *GreenScreen® Assessment for [Ammonium Polyphosphate (CAS#68333-79-9)]*. (October 2014). Retrieved from https://store.greenscreenchemicals.org/gs-assessments/assessment/ammonium-polyphosphate-cas68333-79-9

USEPA. (2014b). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Pharos. (2021). ‘ CAS# 68333-79-9 Polyphosphoric acids, ammonium salts' Retrieved from https://pharosproject.net/chemicals/2012709#hazards-panel

Chemical: Magnesium Hydroxide (CAS#1309-42-8) Hazard Assessment

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014b).

	GreenScreen and DfE Hazard Summary Table for Magnesium Hydroxide																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	**L**	*L*	**L**	*L*	**DG**	**L**	**-**	**L**	**-**	*L*	*L*	**DG**	*L*	**M**	**L**	*L*	*vH*	*vL*	*L*	*L*
U.S EPA DfE Assessment [2]	**L**	**L**	**L**	*L*	**NI**	**L**	**NI**	**L**	**NI**	*L*	*L*	**DG**	**L**	**M**	*L*	*L*	*H*	*L*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,

2 Chemical hazard assessment by USEPA (DfE) for DecaBDE (USEPA, 2014b).

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Experimental studies indicate that magnesium hydroxide is of low concern for carcinogenicity.	**LOW:** The score is designated as per the USEPA report and the confidence is high due to presence of experimental studies.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Experimental studies indicate magnesium hydroxide is not mutagenic to bacteria or mammalian cells in vitro and does not cause chromosomal aberrations in human lymphocytes in vitro.	**LOW:** The low score is designated as per the USEPA report and the confidence in the score is low due to *in-vitro* studies. No *in vivo* studies located that is why confidence in the data low.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: There were no reproductive effects observed in rats in a repeated dose toxicity study with the reproduction/developmental toxicity screen at doses of magnesium hydroxide as high as 1,000 mg/kg-day.	**LOW:** As per the USEPA report as well as the Rosenblum Environmental (2019) reported study in which no reproductive toxicity was observed. The confidence in the score is high because of presence of measured data.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Magnesium hydroxide is expected to be of low concern for developmental effects based on a non-standard experimental study indicating magnesium chloride produces no adverse effects on developmental outcomes at levels up to 96 mg/kg/day of Mg2+ ion and an experimental study from a secondary source showing no effect on human newborns. In addition, there were no developmental effects observed in rats in a repeated dose toxicity study with the reproduction/developmental toxicity screen at doses	**LOW:** The low score is designated as per the USEPA report study of analog chemical and the confidence in the score is low due to absence of measured data for the chemical itself.

		as high as 1,000 mg/kg/day.	
Endocrine Activity (E)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Magnesium hydroxide was assigned a score of DATA GAP for Endocrine Activity based on no data reported
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Acute lethality values suggest that magnesium hydroxide is of low concern for acute toxicity for oral exposure. There were no data located regarding acute dermal and inhalation exposure.	**LOW:** The low score is designated as per the experimental data in the USEPA report and the confidence in the data is high due to presence of measured data.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Magnesium hydroxide was assigned a score of DATA GAP for single dose systemic toxicity/organ effects based on lack of sufficient available necropsy studies in acute mammalian toxicity studies.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: The score was based on experimental data which indicated LOAELs all significantly above 1000 mg/kg-bw. In addition, magnesium hydroxide is expected to have a low immunotoxicity hazard based on expert judgment	**LOW:** The score is designated as per the USEPA report and the confidence in the score is high due to measured data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Magnesium hydroxide was assigned a score of DATA GAP for single dose neurotoxicity effects based on no data reported

Neurotoxicity-Repeat Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Magnesium hydroxide is expected to be of low hazard for neurotoxicity based on expert judgment.	**LOW:** The low score is designated as per the USEPA Report and the confidence in the score is low due to expert judgment.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Magnesium hydroxide was assigned a score of LOW for Skin Sensitization. This conclusion was made based on expert judgment with no additional information provided.	**LOW:** The low score is designated as per the USEPA report and the confidence is low due to professional judgment. Rosenblum Environmental (2019) also showed no skin sensitization based on analog study.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		DG: Magnesium hydroxide was assigned a score of DATA GAP for Respiratory Sensitization based on no data reported	DG: Magnesium hydroxide was assigned a score of DATA GAP for Respiratory Sensitization based on no data reported
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: An experimental study indicates that magnesium hydroxide is not an irritant to rabbit skin.	**LOW:** A preliminary skin irritation study (mice) on magnesium sulfate (in propylene glycol) was performed prior to the skin sensitization study. Skin irritation of the ears was not observed in any of the animals tested with 50% anhydrous magnesium sulfate. Additionally, there was no evidence of macroscopic abnormalities of the surrounding area. The confidence in the score is low as it is based on analog study.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	New	**MODERATE:** Based on irritation and damage to the corneal	**MODERATE:** The score is designated as per the

	Zealand - GHS - 6.4A - Irritating to the eye (Cat. 2A) *(H)*	epithelium in rabbits that cleared within 2-3 days.	presence in screening list as well as experimental data in the USEPA report. The confidence in the score is high. Rosenblum Environmental (2019) also assigned MODERATE eye irritation.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Estimated LC50 values for all of the species in the standard toxicity profile are greater than 100 mg/L. LC50 values are much greater than the anticipated water solubility, suggesting no effects at saturation (NES).	**LOW:** The score is designated as per the USEPA report and the confidence in the score is high due to measured data.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Estimated chronic values (ChV) are all >10 mg/L. ChVs are much greater than the anticipated water solubility, suggesting NES.	**LOW:** The study reports a 21 days EC10 of 82 mg Mg/L (which is a structural analog) for the effect of MgCl2 on the reproduction of Daphnia magna (or 321 mg of MgCl2 /L). The confidence in the score is low due to estimated data as well as structural analog experimental study.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
	Screening B: EC - CEPA DSL – Persistent (vH-H)	**HIGH:** As an inorganic compound, magnesium hydroxide is not expected to biodegrade, oxidize in air, or undergo hydrolysis under environmental conditions. Magnesium hydroxide does not absorb light at environmentally relevant wavelengths and is not expected to photolyze. Magnesium hydroxide is recalcitrant and it is expected to be found in the environment >180 days after release.	**VERY HIGH:** The classification is based on the expert judgment provided by the USEPA report but as per GreenScreen assessment the score should be very high. The confidence in the data is low due to expert judgment.

Bioaccumulation (B)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Magnesium hydroxide is not expected to bioaccumulate based on professional judgment.	**VERY LOW:** The designation low in USEPA report is equivalent to very low in GreenScreen Assessment. The confidence in the score is low due to expert judgment.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Magnesium hydroxide was assigned a score of LOW for Reactivity based on professional judgment and supporting information from industry. The confidence in the data is low due to absence of concrete experimental work (Rosenblum Environmental 2019).
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		Magnesium hydroxide is not flammable.	**LOW:** Magnesium hydroxide was assigned a score of LOW for flammability based on a not flammable description in the USEPA Report. The confidence in the data is high (Rosenblum Environmental 2019)..

Positive Lists:

- Cosmetic Ingredient Review (CIR): Safe with Qualifications
- Inventory of Existing Cosmetic Ingredients in China (IECIC 2015): Cosmetic Ingredients
- TCO Certified Accepted Substance List: Benchmark-3 Accepted Substance
- German FEA - Substances Hazardous to Waters: Non-Hazardous to Water (Water Hazard Class 0 NWG)
- USEPA - DfE SCIL: Green Circle - Verified Low Concern

Environmental, R. (2019). *GreenScreen ® Chemical Assessment Magnesium Hydroxide (CAS#1309-42-8)*. 1–19. Retrieved from

https://store.greenscreenchemicals.org/gs-assessments/assessment/magnesium-hydroxide-cas1309-42-8

USEPA. (2014b). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Pharos. (2021). 'CAS#1309-42-8 Magnesium Hydroxide' Retrieved from https://pharosproject.net/chemicals/2008981#hazards-panel

Chemical: Polyphosphonate (CAS#68664-06-2) Hazard Assessment

Comparison of chemical hazard assessment conducted in this study with that of USEPA (2014b).

	GreenScreen and DfE Hazard Summary Table for Polyphosphonate																			
	Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
	Carcinogenicity	Genotoxicity/Mutagenicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
							single	repeat*	single	repeat*	*	*								
GreenScreen Assessment [1]	*L*	*L*	*L*	*L*	*L*	**L**	**DG**	*L*	**DG**	*L*	*L*	**DG**	*L*	*L*	*L*	*L*	*vH*	*vL*	*L*	**L**
U.S EPA DfE Assessment [2]	*L*	*L*	*L*	*L*	**NI**	*L*	**NI**	*L*	**NI**	*L*	*L*	**DG**	*L*	*L*	*L*	*L*	*vH*	*L*	**NI**	**NI**

1 GreenScreen hazard assessment conducted in this thesis study,

2 Chemical hazard assessment by USEPA (DfE) for DecaBDE (USEPA, 2014b).

Hazard Endpoints Detailed Summary

Carcinogenicity (C)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. Based on professional judgment, it is expected to have few to no residual monomers. Additionally, crosslinking, swellability, dispersability, reactive functional groups, inhalation potential and hindered amine groups are not expected. Therefore, there is low potential for carcinogenicity.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Mutagenicity (M)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for genotoxicity.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Reproductive Toxicity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for reproductive effects.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Development Toxicity (D)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for developmental effects.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Endocrine Activity (E)			
Authoritative	**Screening**	**USEPA**	**Comment**

List	List		
		This polymer is large, with a MW >1,000. Based on professional judgment, polyphosphonate is not expected to have endocrine activity due to its poor bioavailability and inability to be readily metabolized in the body.	**LOW:** Based on the expert judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Acute Mammalian Toxicity (AT)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on experimental LD50 values > 2,000 mg/kg.	**LOW:** Based on USEPA report experimental study with LD50>2,000 mg/kg and the confidence in the data is high.
Systemic Toxicity/Organ Effects-Single Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Polyphosphonate was assigned a score of DATA GAP for single dose systemic toxicity/organ effects based on no data reported and located in literature.
Systemic Toxicity/Organ Effects-Repeat Exposure (ST)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; however, because the MW is >10,000, there is the possibility of lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.	**LOW:** Based on the expert judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Neurotoxicity-Single Exposure (N)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			DG: Polyphosphonate was assigned a score of DATA GAP for single dose neurotoxicity effects based on no data reported and located in the literature.
Neurotoxicity-Repeat Exposure (N)			

Authoritative List	Screening List	USEPA	Comment
		LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for neurotoxicity.	**LOW:** Based on the expert judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Skin Sensitization (SnS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on professional judgment, polyphosphonate is estimated not to have potential for skin sensitization.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Respiratory Sensitization (SnR)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		DG: Polyphosphonate was assigned a score of DATA GAP for Respiratory Sensitization based on no data reported.	DG: Polyphosphonate was assigned a score of DATA GAP for Respiratory Sensitization based on no data reported.
Skin Irritation/Corrosivity (IrS)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on professional judgment, polyphosphonate is estimated to not have potential for dermal irritation.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Eye Irritation/Corrosivity (IrE)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Based on expert judgment, polyphosphonate is estimated to not have potential for eye irritation.	**LOW:** Based on the expert judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Acute Aquatic Toxicity (AA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**

		LOW: Non-ionic polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to have no effects at saturation (NES). These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Bioavailability is limited because this chemical cannot be absorbed through membranes due to its large size.	**LOW:** Based on the professional judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Chronic Aquatic Toxicity (CA)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		LOW: Non-ionic polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to display NES. These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Bioavailability is limited because this chemical cannot be absorbed through membranes due to its large size.	**LOW:** Based on the expert judgment in the USEPA report a low score is designated and the confidence in the score is low due to absence of measured data.
Persistence (P)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
		VERY HIGH: This polymer is large, with a MW>1,000. It is expected to have negligible water solubility and poor bioavailability to microorganisms indicating that neither biodegradation nor hydrolysis are expected to be important removal processes in the environment. The polymer does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths. Evaluation of these degradation values suggest a half-life of >180 days.	**VERY HIGH:** Based on the expert judgment in the USEPA report a very high score is designated and the confidence in the score is low due to absence of measured data.
Bioaccumulation (B)			
Authoritative	**Screening**	**USEPA**	**Comment**

List	List		
		LOW: This polymer is large, with a MW >1,000. It is expected to have poor bioavailability indicating that this polymer should be of low potential for bioaccumulation.	**VERY LOW:** Based on the expert judgment in the USEPA report a low score is designated which is equivalent to very low score in GreenScreen assessment and the confidence in the score is low due to absence of measured data.
Reactivity (R)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Polyphosphonate was assigned a score of LOW for Reactivity based on professional judgment and structural similarity to other chemicals. Because of the lack of concrete data for this endpoint, the confidence in the score is low (Rosenblum Environmental 2016b).
Flammability (F)			
Authoritative List	**Screening List**	**USEPA**	**Comment**
			LOW: Based on the USEPA report which categorizes it as non-flammable.

References:

Rosenblum Environmental. (2016). *GreenScreen ® Assessment for [Polyphosphonate (CAS#68664-06-2)]*. (October 2014). Retrieved from https://store.greenscreenchemicals.org/gs-assessments/chemical/68664-06-2

USEPA. (2014b). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Pharos. (2021). 'CAS#68664-06-2 Polyphosphonate homopolymer / oligomers' Retrieved from https://pharosproject.net/chemicals/2037098#hazards-panel.

Appendix C1: Physicochemical Properties of Target and Alternative Chemicals.

Table C1: Physicochemical properties Literature Derived Values (LDV) and Final Adjusted Values (FAV) used in EQC

Chemical Name	Molar Mass (g/mol)	Melting Point C	Vapor Pressure (Ps) Pa			Solubility in Water (Ss)(g/m3)			Henry's Law Constant (H=P/S)(Pa-m3/mol) (FAV)	logKow (Used)		Half-live in air (h)	Half-live in water (h)	Half-live in soil (h)	Half-live in sediment (h)	Koc
			LDV	Adjustement (%)	FAV	LDV	Adjustement (%)	FAV		LDV	FAV					
Bis-(2-Ethylhexyl) phthalate (DEHP)	390.557	-55	2.00E-05	3.40E+01	2.68E-05	2.70E-01	-2.55E+01	2.01E-01	5.21E-02	7.6	7.30	17.0	550	5500	5500	8,196,333
Dibutyl phthalate (DBP)	278.3	-35	2.68E-03	4.70E+01	3.94E-03	1.12E+01	-3.20E+01	7.62E+00	1.44E-01	4.5	4.45	55	170	1700	5500	11,664
Benzyl butyl phthalate (BBP)	312.37	-35	1.10E-03	-1.69E+01	9.14E-04	2.69E+00	2.03E+01	3.24E+00	8.82E-02	4.7	4.55	17	55	1700	1700	14,400
ASE	368.58	-150	3.00E-04	2.20E+01	3.66E-04	2.2	-1.80E+01	1.80E+00	7.48E-02	8.2	7.71	6.23	360	720	3240	20,896,424
ATBC	402.49	-80	6.07E-04	-7.60E+01	1.44E-04	5	3.30E+01	6.65E+00	8.74E-03	4.9	5.06	17.8	208.8	416	1870	47,074
DEHT	390.57	-55	1.89E-05	2.69E+01	2.40E-05	2.70E-01	-2.12E+01	2.13E-01	4.40E-02	7.6	7.37	11.7	360	720	3240	9,659,282
DINA	398.63	-68	2.00E-07	6.95E+01	3.39E-07	0.0032	-4.10E+01	1.89E-03	7.16E-02	9.6	9.14	9.58	360	720	3240	562,610,723
DINCH	424.67	-54	2.20E-05	6.77E+01	3.69E-05	0.022	-4.98E+01	1.10E-02	1.42E+00	10.0	9.60	8.36	900	1800	8100	1,640,698,494
Hexabromocyclododecane (HBCD)	641.7	190	5.61E-07	5.74E+00	5.94E-07	3.00E-03	1.65E+01	3.50E-03	1.09E-01	5.6	5.82	31.2	2040	2040	8.40E+02	268,297
TBBPA-bis brominated ether derivative	971.68	110	4.40E-04	1.16E+02	9.49E-04	2.00E-02	-5.36E+01	9.27E-03	9.94E+01	12.4	11.61	16.6	4320	8640	3.89E+04	165,330,824,159
TBBPA bis(2,3-dibromopropyl) ether	943.62	117	2.93E-02	7.62E+01	5.17E-02	1.40E-04	-4.32E+01	7.95E-05	6.14E+05	11.52	10.76	24.4	4320	8640	3.89E+04	23,865,043,772
Decabromodiphenyl Ether (DecaBDE)	959.2	300	6.22E-10	-3.64E+01	3.95E-10	1.00E-04	1.13E+02	2.13E-04	1.78E-03	9.97	10.09	7620	3600	3600	1.44E+04	5,004,514,393

The References for the LDVs are shown in the Table C2,C3 and C4 below. (Only Henry's constant and Koc values are FAV incdicated below in the tables).

Table C2: Physicochemical properties for phthalates and alternatives.

Property	Values	Reference	Comment
Benzyl butyl phthalate (BBP) (CASRN 85-68-7)(EC-201-622-7)			
Molecular Weight: 312.37 g/mol			
Smiles: CCCCOC(=O)C1=CC=CC=C1C(=O)OCC2=CC=CC=C2			
Melting Point	1) -35C (BP 370)	1)ECHA (Measured)	1) The information is taken from a reliable peer reviewed source. The value is recommended. (NICNAS, 2020) also has the same value. The variance will be chosen as 1.
Vapor Pressure	1)1.1E-03 (Pa,25C)	1)ECHA (Measured) (Howard, 1985)	1) The information is taken from a reliable peer reviewed source. The peer-reviewed European Union Risk Assessment Report for BBP used this as one of its key studies (NICNAS, 2020). **The variance will be chosen as 1 due to reliable peer reviewed source.**
Water Solubility	1) 2.69 (mg/L, 25C)	1) ECHA (Measured) (Howard, 1985) (EPI Suite Experimental Database)	1) The value has been supported by peer reviewed studies. 4 studies have supported the value which shows BBP as slightly soluble. **The variance will be chosen as 1 due to reliable peer reviewed source.**
Partitioning Coefficient (logKow)	1) 4.85 (25C) **2) 4.73** Log Koa=8.78 Log Kaw= -4.78 (Cousins,2003)	1) ECHA (Measured) (Leyder and Boulanger, 1983, and Gledhill et al, 1985). **2) EPI Suite (Experimental Database)**	1) The information is taken from reliable key study. The peer-reviewed European Union Risk Assessment Report for BBP used this as one of its key studies. **2)** EPI Suite (Experimental Database) **This value will be chosen. It is also reported in (Cousins, 2003)** **The variance will be chosen as 1 due to EPI Suite experimental database.**
Henry's Law Constant (Pa-m3/mol)	8.82E-02	Calculated	The value is calculated from solubility and vapor pressure and this value was used in EQC.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	Koc=14,400	Calculated from 0.41x10^logKow	Calculated from FAV logKow
pKa	No ionisable atoms found.	Chemicalize	
Half-Lives (hours)	Air: 17 Water:55 Soil: 1700 Sediment: 1700	1)(Cousins, 2003)	1) (Cousins, 2003)
Dibutyl phthalate (DBP) (CASRN 84-74-2)			

Molecular Weight: 278.3			
Smiles: C(=O)(c1c(C(=O)OCCCC)cccc1)OCCCC			
Melting Point	**1) -35C (BP 340C)**	**1) USEPA ACToR (NICNAS, 2020)**	1**) The value has been reported by a lot of sources in the databases. -35C is used.**
Vapor Pressure	1) 2.68E-03 (Pa)	1) USEPA ACToR (NICNAS 2020)	1) The value has been reported by a lot of sources in the ACToR database. **The variance is chosen as 1.**
Water Solubility	1) 14.6 (mg/L, 25C) **2) 11.2 (mg/L, 25C)**	1) USEPA ACToR (NICNAS,2008) **2) EPI Suite Experimental Database**	1) The value has been reported by a lot of sources in the ACToR database. **2) 11.2 mg/L value will be used.** **The variance is chosen as 1.**
Partitioning Coefficient (logKow)	**1) log Kow 4.5** log Kaw -4.13 log Koa 8.631	1) USEPA ACToR (NICNAS,2008)	1) The value has been reported by a lot of sources in the ACToR database. **EPI Suite experimental database also has the same values. The variance will be chosen as 1.**
Henry's Law Constant	1.44E-01	Calculated	Calculated from solubility and vapor pressure.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	11,664	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.		
Half-Lives (Hours)	Air: 55 Water: 170 Soil: 1700 Sediment: 5500	(Cousins,2003)	These values will be used
DEHP (CASRN 117-81-7)			
Molecular Weight: 391 g/mol			
Smiles: C(=O)(c1c(C(=O)OCC(CCCC)CC)cccc1)OCC(CCCC)CC			
Melting Point	1) -55C (BP 374.15C)	1) USEPA ACToR (Measured) (NICNAS,2020)	1) The value has been reported by a lot of sources in the ACToR database.
Vapor Pressure	**1) 2.0E-05 (Pa,25C)**	1) USEPA ACToR (Measured) (Cousins and Mackay, 2000)(NICNAS,2020)	1) The value has been reported by a lot of sources in the ACToR database. **2x10^-5 Pa will be used. (EPI Suite Experimental database) The Variance will be 1 due to reliable data and source.**
Water Solubility	1) 0.017 (mg/L,25C) **2) 0.27 (mg/L, 25C)**	1) USEPA ACToR (Measured) (NICNAS,2019) **2) EPI Suite experimental database**	1) The value has been reported by a lot of sources in the ACToR database. (mg/L=g/m3) **2) 0.27 mg/L will be used.** **The Variance will be 1 due to reliable data and source.**

		(Defoe et al, 1990)	
Partitioning Coefficient (logKow)	log Kow 7.6 log Kaw-4.96 log Koa 12.6	1) EPI Suite (Experimental Database)	1) The values will be used because they are from EPI Suite experimental database. **The Variance will be 1 due to reliable data and source.**
Henry's Law Constant (Pa-m3/mol)	5.21E-02	Calculated	Calculated from solubility and vapor pressure.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	8,196,333	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa			
Half-Lives (Hours)	Air: 17 Water: 550 Soil:5500 Sediment:5500	(Cousins, 2003)	1) These values will be used.
Sulfonic acids, C10-21-alkane, Ph esters (ASE) CASRN: 91082-17-6			
Molecular Weight: 368.58 g/mol (EPI Suite)			
Smiles: O=S(=O)(Oc1ccccc1)C(CCCCCCC)CCCCCCC			
Melting Point	<-150C	1)ECHA (Measured)	The value has been gotten from (Currenta, 2010) study.
Vapor Pressure	1) 3E-04 (Pa, 20C)	1) ECHA (Measured) (Nielsen & Larson, 2014)	1) Based on OECD Guideline Study (104). Klimisch Score 1. **The variance is 1 due to Klimisch Score 1 reliable study.**
Water Solubility	1) 2.2 (mg/L, 20C)	1) ECHA (Measured) (Nielsen & Larson, 2014)	1) Based on OECD Guideline Study (105). Klimisch Score 1. **The variance is 1 due to Klimisch Score 1 reliable study.**
Partitioning Coefficient (logKow)	1) 5.7-11.3 (40C) **2) Log Kow 8.15** **Log Koa 12.80** **Log Kaw -4.69**	1) ECHA (Measured) **2) EPI Suite (Estimation)(KOWWIN)**	1) Based on OECD Guideline Study (117). Klimisch Score 1. **2) Based on EPI Suite estimation. 8.15 will be used.** **The Variance will be 5 due to EPI Suite Estimation.**
Henry's Law Constant (Pa-m3/mol)	7.48E-02	Calculated	Calculated from solubility and vapor pressure.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	20,896,424	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 6.23 Water: 360	1)EPI Suite	1) Based on estimation in EPI Suite.

	Soil: 720 Sediment: 3240		
Tributyl O-acetylcitrate (ATBC) (CASRN 77-90-7) (EC-201-067-0)			
Molecular Weight: 402.49 g/mol			
Smiles: O=C(OC(C(=O)OCCCC)(CC(=O)OCCCC)CC(=O)OCCCC)C			
Melting Point	1) -80C (BP 172C)	1) ECHA(Measured)	1) Peer Reviewed Reliable data. **(EPI Suite Experimental database as well has same value).**
Vapor Pressure	1) 6.07E-04 (Pa, 25C)	1) EPI Suite (MPBPVP v1.43) (Modified Grain Method)	1) Based on estimation data from EPI Suite. **The variance will be 5 due to estimation by EPI Suite.**
Water Solubility	1) 4.49 (mg/L,20C) **2) 5 (mg/L, 25C)**	1) ECHA (Measured) (EU Method A.6 (Water Solubility) **2) EPI Suite (Experimental database match)**	1) Based on experimental data with a Klimisch score 1. 2) **EPI Suite experimental database match and the value will be used.** **The variance will be 1 due to EPI Suite Experimental database match.**
Partitioning Coefficient (logKow)	**1) Log Kow 4.86** **Log Koa= 12.10** **Log Kaw=-4.71** **(Calculated)** 2) Log Kow= 4.29	**1) ECHA (Measured) (Nielsen & Larson, 2014)** (EPA OPPTS 830.7570) 2) EPI Suite (Estimation)(KOWWIN v1.68)	**1) Based on experimental data with a Klimisch score 1.** 2) Based on EPI Suite Estimation. **The variance will be 1 due to Klimisch score 1 data.** **For Koa and Kaw the Klimisch score will be 5 due to estimation of VP.**
Henry's Law Constant (Pa-m3/mol)	8.74E-03	Calculated	Calculated from solubility and vapor pressure.

Sediment/Soil Adsorption/Desorption Coefficient – Koc	47,074	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 17.8 Water: 208.8 Soil: 416 Sediment: 1870	1)EPI Suite (Estimation)	1) Based on EPI Suite Estimation.
COMGHA CASRN 736150-63-3			
Molecular Weight: 943 g/mol (which is gotten from adding two chemicals A and B addition) (Danish EPA Toys)			
Smiles: O=C(OC(COC(=O)CCCCCCCCCCCCCCCCC)COC(=O)C)C (It is for only element 2 in the mixture)			
Melting Point	-21.5C	1)Danish EPA (Measured)	1) Based on experimental data.
Vapor Pressure	1) 5x10^-8 (Pa,20C) 2) 1.1x10^-7 (Pa,25C)	1) ECHA (Measured) 2) Danish EPA (Measured)	1) Based on OECD Guideline (104) study with a Klimisch Score 1. 2) Based on the data submitted by the manufacturer to the Danish EPA. **8.25x10^-10 mmHg**

Solubility	1) <0.33 (mg/L, 20C)	1) ECHA (Measured)	1) Based on OECD Guideline (104) study with a Klimisch Score 1.
Partitioning Coefficient (logKow)	1) 6.4 (25C)	1) ECHA (Measured)	1) Based on OECD Guideline (117) study with a Klimisch Score 2.
Henry's Law Constant	1)4.86x10^-4 (atm-m3/mol)	1) EPI Suite (Estimation)	1) This is only calculated from element 2 in the COMGHA mixture so can this be used or not that's confusing.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	1) 5.4 (25C)	1) ECHA (Measured)	1) Based on OECD Guideline (121) study with a Klimisch Score 1.
pKa	Not found in Chamecalize.		

Half-Lives (Days)	Air: 0.36 Water: 15 Soil: 30 Sediment: 135	1)EPI Suite	1) This is only calculated from element 2 in the COMGHA mixture so can this be used or not that's confusing.
DEHT bis(2-ethylhexyl) terephthalate (CASRN 6422-86-2)(EC 229-176-9)			
Molecular Weight: 390.57 g/mol			
Smiles: C(=O)(c1c(C(=O)OCC(CCCC)CC)cccc1)OCC(CCCC)CC			
Melting Point	-55C (BP 384C)	1)EPI Suite (Experimental Database)	1) Based on experimental database of EPI Suite.
Vapor Pressure	1) 1.0x10^-3 (Pa, 25C) **2) 1.89E-05 (Pa, 25C)**	1)ECHA (Measured) ((EU Method A.4 (Vapor Pressure)) **2) EPI Suite (Experimental Database match)**	1) Based on experimental data with a Klimisch score of 2. **7.5x10^-6 mmHg.** **2) This value will be used.** **The variance will be 1 due to EPI Suite Experimental database match.**
Water Solubility	1) 0.4x10^-3 (mg/L, 22.5C) **2) 0.27 (mg/L, 25C)**	1) ECHA (Measured) **2) EPI Suite (Experimental database)**	1) Based on experimental data with a Klimisch score of 2. **2) EPI Suite (Experimental database match) so 0.27 mg/L is used.** **The variance will be 1 due to EPI Suite Experimental database match.**
Partitioning Coefficient (logKow)	1) 7.81 (25C) **2) LogKow= 7.60 (Experimental Database)** Log Kaw=-4.957 (Experimental Database) Log Koa=12.557 **(Estimated)**	1) ECHA (Estimation) **2) EPI Suite (Experimental Database)**	1) Based on QSAR (SPARC) with a Klimisch Score 2. **2) The value used is 7.60 due to presence in experimental database.** **The variance will be 1 due to EPI Suite Experimental database match.** **As Log Koa is estimated but value is dependent on Kow and Kaw which is from experimental database the variance chosen will be 2.**

Henry's Law Constant (Pa-m3/mol)	4.40E-02	Calculated	Calculated from solubility and vapor pressure.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	9,659,282	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 11.7 Water: 360 Soil: 720 Sediment: 3240	1)EPI Suite (Estimation)	1) Based on EPI Suite Estimation.
Diisononyl adipate (DINA) (CASRN 33703-08-1) (EC 251-646-7)			
Molecular Weight: 398.63 g/mol			
SMILES: O=C(OCCCCCCCCC)CCCCC(=O)OCCCCCCCCC			

Melting Point	-68C (BP 224C)	1) (Nielsen & Larson, 2014) (Measured)	1) Based on measured data submitted by the manufacturer.
Vapor Pressure	**1) 2E-07(Pa, 20C).** 2) 3.31x10^-6 (mmHg,25C)	**1) ECHA (Measured) (Dynamic method)** (Nielsen & Larson, 2014) 2)EPI Suite (Estimation) (Modified Grain Method)	**1) Based on experimental data with a Klimisch score of 2.** 2) Based on estimation data. **The Variance will be 3 because not guideline study and no detail provided.**
Water Solubility	**1) 0.0032 (mg/L, 22.5C)** 2) 3.98x10^-5 (mg/L, 25C)	**1) ECHA (Measured) (Read Across)** (Nielsen & Larson, 2014). 2) EPI Suite (Estimation) (WSKOWIN)	**1) Based on experimental read across data with a Klimisch score 2.** 1) Based on estimation from EPI Suite. **The Variance will be 3 due to read across data.**
Partitioning Coefficient (logKow)	1) 9.56-10.4 (25C) 9.56 used. **Log Kaw=-5** **Log Koa=14.6 (Calculated)**	1) ECHA (Measured)	1) Based on experimental OECD Guideline Study (117) with a Klimisch score 2. **The Variance will be 3 due to not exact value.** **The variance for Kaw and Koa will be 5 due to calculated value from VP and solubility.**
Henry's Law Constant (Pa-m3/mol)	7.16E-02	Calculated	Calculated from solubility and vapor pressure.

Sediment/Soil Adsorption/Desorption Coefficient – Koc	562,610,723	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 9.58 Water: 360 Soil: 720 Sediment: 3240	1)ECHA (Estimation)	1) Based on EPI Suite Estimation.
DINCH (CASRN 166412-78-8)			
Molecular Weight: 424.67 g/mol			
Smiles: CC(C)CCCCCCOC(=O)C1CCCCC1C(=O)OCCCCCCC(C)C			
Melting Point	**-54C**	1) Danish EPA (measured) (Nielsen & Larson, 2014)	1) Based on measured data submitted by the manufacturer.
Vapor Pressure	**1) 2.2E-05 (Pa, 20C)** 2) 9.62x10^-7 (mmHg, 25C)	**1) Danish EPA (Measured) (Nielsen & Larson, 2014)** 2) EPI Suite (Estimation) (Modified Grain Method)	1) Based on experimental data but Klimisch score is not provided. It is also provided in (NICNAS, 2012). **The variance will be 3 as it is provided in a reliable NICNAS report but Klimisch score is not provided.**

Water Solubility	**1) <0.02 (mg/L, 25C)** 2) 8.83x10^-6 (mg/L, 25C)	**1) Danish EPA (Measured) (Nielsen & Larson, 2014)** 2) EPI Suite (Estimation)	1) Based on experimental data but Klimisch score is not provided. **The variance will be 4 as it has no exact value and upper limit is used but it is experimental value.**
Partitioning Coefficient (logKow)	10 (25C) Log Kaw= -3.77 Log Koa= 13.8 (Calculated)	1) Danish EPA (Measured) (Nielsen & Larson, 2014)	1) Based on experimental data but Klimisch score is not provided. **The variance will be 3 as no Klimisch score is provided and no detail is given.** **The Variance for Koa and Kaw will be 5.**
Henry's Law Constant (Pa-m3/mol)	1.42	Calculated	Calculated from solubility and vapor pressure.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	1,640,698,494	Calculated from 0.41x10^logKow	**Calculated from FAV logKow**
pKa	No ionisable atoms found.	Chamecalize	

Half-Lives (Hours)	Air: 8.36 Water: 900 Soil: 1800 Sediment: 8100	1)EPI Suite (Estimation)	1) Based on Estimation.

References:

Cousins, I. T., Mackay, D., & Parkerton, T. F. (2003). Physical-chemical properties and evaluative fate modelling of phthalate esters. *Handbook of Environmental Chemistry*, *3*(July), 57–84. https://doi.org/10.1007/b11463

NICNAS. (2020). *Phthalate esters : Environment tier II assessment*. (March 2019), 1–38. Retrieved from https://www.industrialchemicals.gov.au/sites/default/files/Phthalate esters_ Environment tier II assessment.pdf

Nielsen, B. S., & Larsen, P. B. (2014). *Alternatives to classified phthalates in medical devices*. Retrieved from https://www2.mst.dk/Udgiv/publications/2014/03/978-87-93178-27-4.pdf

Table C3: Physicochemical properties for HBCD and alternatives.

Property	**Values**	**Reference**	**Comment**
Hexabromocyclododecane (HBCD) CASRN: 25637-99-4 (EC 247-148-4); **3194-55-6 (EC 221-695-9)(This one was used in Arnot) (Both are present in Turkish Inventory 1-1000 tons/year)**			
Molecular Weight: 641.70 g/mol			
(Smiles BrC1CC(CC(CC(CC(CC(C1)Br)Br)Br)Br)Br)Br (for CASRN 25637-99-4); BrC(C(Br)CCC(Br)C(Br)CCC(Br)C(Br)C1)C1 (for CASRN 3194-55-6)			
Melting Point	**1)190C** 2)185-195C	**1) (Arnot,2009)** 2) USEPA (Measured) (NAS, 2000).	**1) Based on experimental data. OECD Guideline 102 and EU method A.1 under GLP conditions.** 2) Based on experimental data and guideline study reported in

			secondary sources.
Vapor Pressure	1) 6.27E-05 (Pa, 21C). 2) 4.7E-07 (mmHg, 21C). 3) 7.9E-11 (mmHg,25C) **4)P_L= 2.41E-05 (Pa, 25C)(Subcooled VP)** **P_s=5.61E-07 (Pa,25C)**	1) ECHA (Measured) (Stenzel and Nixon, 1997) 2) USEPA (Measured) (EINECS, 2008). 3) USEPA (Measured) (Kuramochi, 2010) **4)(Arnot,2009)(Measured)**	1) Based on experimental data. OECD Guideline 104 study. 4.7x10^-7 mmHg. 2) The method is not recommended for substances with Vapor Pressure <10^-4 Pa. This value indicates low vapor pressure. 3) The method is not recommended for substances with Vapor Pressure 7.5X10^-10 to 0.008 mmHg. This value indicates low vapor pressure. **4) This is measured reliable value which will be used.** **The variance chosen by (Arnot, 2009) is 3.**
Water Solubility	1) 0.0034 (mg/L,25C) 2) 6.6X10^-2 (mg/L,20C) **3) S_s = 4.67E-06 (mol/m3)** **S_L=2.01E-04 (mol/m3)** **S_S =3E-03 (mg/L)**	1) ECHA (Measured) (Generator Column Method) 2) USEPA (Measured)(GLP Elution Column Method) **3) (Arnot,2009)(Measured)**	1) Based on experimental data. Recommended in ECHA Registration Dossier. 2) Based on experimental data. **3) Based on reliable experimental data. It will be chosen.** **The variance selected by (Arnot, 2009) is 2.**
Partitioning Coefficient (logKow)	1)5.625 (25C) 2)5.62 **3)Log Kow=5.63** **Log Kaw=-4.15** **Low Koa=10.71**	1) ECHA (Measured) ((Stenzel and Nixon, 1997). 2) USEPA (Measured) 3) (Arnot,2009) (Measured)	1) Based on experimental data. Recommended in ECHA Registration Dossier. 2) Based on experimental data. **3) Reliable data which will be used.** **The variance selected by (Arnot, 2009) is 3 for Kow and 4 for Kaw**

Henry's Law Constant (Pa-m3/mol)	1.09E-01	Calculated	Calculated from Solubility and Vapor Pressure values.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	268,297	Calculated from 0.41*10^logKow	FAV LogKow value is used.
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 31.2 Water: 2040 Soil: 2040 Sediment: 840	1) (Arnot, 2009) (Professional Judgment based on data)	1) Reliable Data.
TBBPA-bis brominated ether derivative CASRN 97416-84-7			
Molecular Weight: 971.68 g/mol			
Smiles: BrCC(Br)(C)COc1c(Br)cc(C(C)(C)c2cc(Br)c(OCC(Br)(C)CBr)c(Br)c2)cc1Br			
Melting Point	100-110C **110C** 115C	1)ECHA (Measured) **2)(USEPA, 2014a) (Measured)(DKS,2012)** 3)USEPA (Eurosarm MSDS, 2010)	1) Based on experimental data and considering the estimation by calculation ECHA has chosen the range. 2&3) Reported for PYROGUARD SR-130, containing approximately 100% CASRN 97416-84-7. No study details provided.
Vapor Pressure	1) 2.99E-13 (Pa, 25 °C) **2) <4.4E-04 Pa,25C)**	1)ECHA (MPBWIN v1.43 by the modified Grain method) **2) (USEPA, 2014a) (Measured) (ICL-IP, 2011)**	1) After considering all the data submitted ECHA suggested using this value. 2) The experimental details were not provided but it is consistent with the expected value based on the chemical structure. **3.3x10^-6 mmHg (4.4E-4 Pa) is used. The variance will be 4 because it is the upper limit.**

Water Solubility	**1)20E-3 (mg/L,20C)** 2) 4.2x10^-04 (mg/L,25C) 3) 20x10^-3 (mg/L)	**1)ECHA (Measured)(OECD Guideline 105)** 2)USEPA (Measured)((ICL-IP, 2011) 3)USEPA (Measured) (DKS,2012)	**1) After considering whole data set ECHA recommended the value. This value was used. USEPA, (2014a) also recommended the value.** 2) No experimental details were provided but this value is consistent with the expected value based on chemical structure. 3) Reported for PYROGUARD SR-130, containing approximately. No study details were provided. **The Variance is 4 because no detail provided and its upper value.**
Partitioning Coefficient (logKow)	**1)12.42** 2)12 Log Kaw= -2.06 Log Koa= 14.5	1) ECHA (Estimation) (KOWWIN v1.68) 2) USEPA (Estimation)	1) After considering the data set the value has been recommended. **12.42 is used. The variance is 5 due to estimated value.** 2) Estimated value is greater than the cut off value >10 according to methodology based on HPV assessment guidance.
Henry's Law Constant (Pa-m3/mol)	9.94E+01	Calculated	Calculated from Solubility and Vapor Pressure values.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	165,330,824,159	Calculated from 0.41*10^logKow	FAV LogKow value is used.

pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 16.6 Water: 4320 Soil: 8640 Sediment:3.89E+04	1)EPI Suite (Estimation)	
TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
Molecular Weight: 943.62			
Smiles: O(c1c(cc(cc1Br)C(c1cc(c(OCC(Br)CBr)c(c1)Br)Br)(C)C)Br)CC(Br)CBr			
Melting Point	1)113.39C **2)117C**	1) ECHA (Measured) (Differential Scanning Calorimeter). **2) (USEPA, 2014a) (Measured)**	1) Non Guideline not good laboratory study but reported in a secondary source. **2)Chemspider,2011 (selected value for assessment)**
Vapor Pressure	**1)2.2E-04 (mmHg) 0.029 (Pa, 20C)** 2)<10^-8 (mmHg)	**1) ECHA (Measured) (Static Method) (USEPA, 2014a)** 2) USEPA (Estimation)	**1) This is reported in ECHA and (USEPA, 2014a) as a guideline study.** 2) Cutoff value for nonvolatile compounds according to HPV assessment guidance. **The variance is chosen as 3 because details of the experiment are not provided.**

Solubility	**1) 0.144E-03 (mg/L, 20C).** 2)<10^-3 (mg/L)	**1) ECHA (Measured) (Column Elution Method).** 2) USEPA (Estimation)	**1) This is reported in USEPA. Cutoff value from a guideline study.** 2) Cutoff value for non-soluble compounds according to HPV assessment guidance. **The variance is chosen as 3 because cutoff value but from a Guideline Study.**
Partitioning Coefficient (logKow)	1)7.2 written as Pow 2)12 **3)11.52** Log Kaw= 1.90 Log Koa= 9.62	1)ECHA 2)USEPA (Estimation) **3)EPI Suite (Estimation) (KOWWIN v1.68)**	1) Written by ECHA but no comment or recommendation is made about the quality of data. 2) Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance. **3) Based on estimation from EPI Suite.** **The variance is chosen as 5 due to estimated value.**
Henry's Law Constant (Pa-m3/mol)	6.14E+05	Calculated	Calculated from Solubility and Vapor Pressure values.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	23,865,043,772	Calculated from 0.41*10^logKow	FAV LogKow value is used.

pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 24.4 Water: 4320 Soil: 8640 Sediment: 38900	1)EPI Suite (Estimation)	

Arnot, J., McCarty, L., Armitage, J., Toose-Reid, L., Consultant Frank Wania, E., & Cousins, I. (2009). *An evaluation of hexabromocyclododecane (HBCD) for Persistent Organic Pollutant (POP) properties and the potential for adverse effects in the environment*.

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Table B5:

Table C4: Physicochemical properties for DecaBDE.

Property	Values	Reference	Comment
Decabromodiphenyl ether (DecaBDE) CASRN: 1163-19-5			
Molecular Weight: 959.2			
Smiles: O(c1c(c(c(c(c1Br)Br)Br)Br)Br)c1c(c(c(c(c1Br)Br)Br)Br)Br			
Melting Point	1) **300C** 2) 307C	**1) (Palm, 2001)** 2) USEPA (Measured) (Differential Scanning Calorimeter) (Fu and Suuberg, 2011)	**1) Reliable data so this value will be used.** 2) Based on experimental data. Recommended by USEPA.

Vapor Pressure	**1)6.22E-10 (Pa)** 2) 9.02x10^-13 (mmHg,25C)	1) USEPA (ACToR database)(Chemical and Physical properties from Risk Assessment Information System (RAIS)) (Spinning Rotor Method) (European Chemicals Bureau, 2002) 2) USEPA (Extrapolated) (Knudsen Effusion Method)	**1) Reliable experimental study. This value will be used.** 2) Extrapolated using an indirect measurement technique but adequate value for low volatility. **The variance used will be 3 because it is experimental derived data nut no Guideline study details were provided.**
Water Solubility	**1) <1.0x10^-4 (mg/L,25C)** 2) 2.8x10^-11(mg/L, 25C)	**1) (USEPA 2014b) (GLP Column Elution Method) (European Chemicals Bureau, 2002).** 2)(Palm, 2001) Estimation (EU,1998)	**1) Experimental data based on guideline OECD 105 study. Klimisch score 1.** 2) It is from estimation. This value will be used because the experimental data gives the upper limit and we can't be sure about the value which we should use. **The variance will be 4 due to upper limit used.**
Partitioning Coefficient (logKow)	**1) 9.97** **Log Kaw= -1.75** **Log Koa= 11.72**	1) (Measured)(Palm, 2001)	2) Experimental data based on Guideline Study. **The variance used will be 1.** **The variance for Kaw and Koa will be 5 because of calculation.**
Henry's Law Constant	1) 1.78E-03	Calculated from FAV value of Solubility and Vapor Pressure.	Value was obtained from the measured (FAV) vapor pressure and water solubility.
Sediment/Soil Adsorption/Desorption Coefficient – Koc	Koc= 5,004,514,393	Calculated from Koc=0.41X10^logKow	FAV (log Kow) value was used.
pKa	No ionisable atoms found.	Chamecalize	
Half-Lives (Hours)	Air: 7620 Water: 3600	1) (Palm,2001)	Estimation.

	Soil: 3600 Sediment: 14400		

References:

Palm, A. (2001). The Environmental Fate of Polybrominated Diphenyl Ethers in the Centre of Stockholm- Assessment Using a Multimedia Fugacity Model. *Report to IVL Swedish Environmental Research Institute*, (January). Retrieved from https://www.ivl.se/download/18.343dc99d14e8bb0f58b73be/1445515453827/B1400.pdf

USEPA. (2014b). *An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE)*. (January), 1–901. Retrieved from https://www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde-publications

Appendix C2: Thermodynamic Consistency Check Report

In this report, the procedure by Schenker et al. (2005) has been explained stepwise for the thermodynamic consistency check to get internal consistency amongst the measured values of the physicochemical properties like (vapor pressure, aqueous solubility, octanol solubility, Henry's law constant, and octanol-air and octanol-water partition coefficients). A spreadsheet tool developed by Dr. Scheringer was obtained on request and was used for applying the least squares adjustment procedure for a new data.

All the steps are followed in a systematic way to understand the procedure and to clarify the details so that if anything is wrong or seems out of ordinary it can be detected.

Step 1: Fugacity Ratio:

The influence of the intermolecular interactions in the solid phase is not relevant to the partitioning of a chemical after dissolving in liquid phase or solution. Therefore the fugacity ratio F (unitless) is used to correct solid state property data to subcooled liquid state. The fugacity ratio is calculated by the following equation

$$F = \exp(6.79(1 - T_M/T))$$

Where T_M is the melting point of the material chosen and T is the system melting point which is taken as (298K). The entropy of fusion is taken as 56.5 J/K/mol as a constant (Arnot et al., 2009), for each chemical due to unavailability of data.

For HBCD (T_M= 463 K) if we calculate the fugacity ratio F

F= exp (6.79(1-(463/298)) =0.023

For all the chemicals the fugacity ratios were calculated.

Step 2: Subcooled Liquid State Data:

The following equations are used to convert the solid state property data to subcooled liquid data.

$$P_L = P_S/F$$

$$S_L = S_S/F$$

The subscript S is for solids and L is for subcooled liquid state.

Where P_S in units of Pascal and S_S is in units of mol/m^3.

(Solubility S_S which is usually given in g/m^3 was converted into mol/m^3 by dividing it with molecular weight of the chemical).

Step 3: (Log Kaw) and (Log Koa):

Some of the Kow and Koa values were found from literature. When not found in the literature mostly Koa and Kaw values were calculated by equations below but if done for all the misclosure columns were getting all negative or positive which a sign of biasness in the data that is why just to keep the miscalculation errors in check EPI Suite Kaw and Koa values for few chemicals were used as well.

Henrys Constant (H) = P_S/S_S or P_L/S_L

Log K_{AW} = Log (H/RT)

Where R= 8.314 J/K/mol

K_{OA} = K_{OW}/K_{AW}

The empirical relationships to convert the K_{OW} into K_{OW}* which is the dry octanol adopted as a reference solvent for adjusting partitioning coefficients for internal consistency (Beyer et al., 2002).

$$\log K_{ow} - 0.117 - \log K_{oa} - \log K_{aw} = 0 \quad \text{for } \log K_{ow} \leq 4$$

$$1.35\log K_{ow} - 1.58 - \log K_{oa} - \log K_{aw} = 0 \quad \text{for } \log K_{ow} > 4$$

Step 4: Variance Assumptions:

These assumptions are based upon logic not by some reference. The HBCD (Arnot et al., 2009) **study was helpful in the regard as well where the variance were derived as per very extensive knowledge of the experimental methods used but no Klimisch score was provided that is why Klimisch score is an excellent indicator of the validity and quality of data so why not use it as a variance indicator as well.**

Variance 1: Guideline study with Klimisch score 1 or the data which has been gotten from EPI Suite experimental database.

Variance 2: Guideline study with Klimisch score 2.

Variance 3: Guideline study but no Klimisch score is given or guideline study but from read-across or analogue data (solubility of DINA)

Variance 4: Guideline study but a range is given or upper limit is given e.g. (DINCH Solubility <0.02 mg/L)

Variance 5: Estimated data from EPI Suite.

The LDV and FAV values shown in Tables B3 and B4 below are subcooled VP and solubility. In EQC model we convert FAV to solid state and not use subcooled phase properties.

Table C5: Input Physicochemical Properties - Literature Derived Values (LDVs) used in the thermodynamic consisteny check

Chemical Name	Subcooled Vapor Pressure P (Pa)	Solubility (SubCooled Liquid)(mol/m3)	logKow (Used)	log Kaw	log Koa
Bis-(2-Ethylhexyl) phthalate (DEHP)	3.23E-06	1.12E-04	7.6	-5.0	12.6
Dibutyl phthalate (DBP)	6.83E-04	1.03E-02	4.5	-4.1	8.6
Benzyl butyl phthalate (BBP)	2.80E-04	2.19E-03	4.7	-4.8	8.8
ASE	5.56E-06	1.11E-04	8.2	-4.7	12.8
ATBC	5.55E-05	1.14E-03	4.9	-4.7	12.1
DEHT	3.05E-06	1.12E-04	7.6	-5.0	12.6
DINA	2.40E-08	9.64E-07	9.6	-5.0	14.6
DINCH	3.64E-06	8.56E-06	10.0	-3.8	13.8
Hexabromocyclododecane (HBCD)	2.41E-05	2.01E-04	5.6	-4.2	10.7
TBBPA-bis brominated ether derivative	3.05E-03	1.43E-04	12.4	-2.1	14.5
TBBPA bis(2,3-dibromopropyl) ether	2.39E-01	1.21E-06	11.5	1.9	9.6
Decabromodiphenyl Ether (DecaBDE)	3.27E-07	5.49E-05	10.0	-6.3	18.4

The adjustment percentages of the FAV and the misclosure errors after thermodynamic consistency check are shown in the Figure C1and C2 below

Chemical Name	% Adjustment of Partitioning Data					
	Vapor Pressure	Solubility in water	Solubility in Octanol	K_{AW}	K_{OW}	K_{OA}
Bis-(2-Ethylhexyl) phthalate (DEHP)	34%	-25%		90%	-50%	155%
Dibutyl phthalate (DBP)	47%	-32%		-21%	-10%	15%
Benzyl butyl phthalate (BBP)	-17%	20%		114%	-35%	78%
Sulfonic acids, C10-21-alkane, Ph esters (ASE)	22%	-18%		48%	-64%	300%
Tributyl O-acetylcitrate (ATBC)	-76%	33%		-82%	59%	-96%
bis(2-ethylhexyl) terephthalate (DEHT)	27%	-21%		61%	-41%	317%
Diisononyl adipate (DINA)	70%	-41%		189%	-62%	484%
DINCH	68%	-50%		237%	-60%	697%
Hexabromocyclododecane (HBCD)	6%	16%	-32%	-38%	53%	-9%
TBBPA-bis brominated ether derivative	116%	-54%		360%	-84%	1103%
TBBPA bis(2,3-dibromopropyl) ether	76%	-43%		212%	-82%	964%
Decabromodiphenyl Ether (DecaBDE) CASRN: 1163-19-5	-36%	113%		48%	31%	-31%

Figure C1: Adjustment Percentages after thermodynamic consistency check

	Partitioning Data						
	w1	w2	w3	w4	w5	w6	w7
Bis-(2-Ethylhexyl) phthalate (DEHP)	0.02			-1.09	-1.07		
Dibutyl phthalate (DBP)	-0.44			-0.02	-0.46		
Benzyl butyl phthalate (BBP)	0.49			-0.83	-0.34		
Sulfonic acids, C10-21-alkane, Ph esters (ASE)	-0.00			-1.37	-1.38		
Tributyl O-acetylcitrate (ATBC)	0.00			2.38	2.39		
bis(2-ethylhexyl) terephthalate (DEHT)	-0.00			-1.14	-1.14		
Diisononyl adipate (DINA)	0.00			-1.80	-1.80		
DINCH	0.00			-1.97	-1.97		
Hexabromocyclododecane (HBCD)	-0.16	-0.15	-0.48	0.50	0.34	0.02	-0.65
TBBPA-bis brominated ether derivative	-0.00			-2.82	-2.83		
TBBPA bis(2,3-dibromopropyl) ether	0.00			-2.55	-2.55		
Decabromodiphenyl Ether (DecaBDE) CASRN: 1163-19-5	0.69			0.15	0.84		
Number of entries (n)	14	1	1	14	14	1	1
Average value	0.05		-0.48	-0.74	-0.69		-0.65
Percent positive values	57%		0%	36%	36%		0%
Percent negative values	43%		100%	64%	64%		100%

Figure C2: The Misclosure Errors

The average misclosure errors are relatively closer to 0 and the misclosure error columns are not all minus or plus which shows that there is no inherent bias in the data or some error which is accumulating. Table C6 shows the FAVs which were obtained after thermodynamic consistency check.

Table C6: Physicochemical properties (Final Adjusted Values FAVs) after thermodynamic consistency check

Chemical Name	Subcooled Vapor Pressure P (Pa)	Solubility (SubCooled Liquid)(mol/m3)	logKow (Used)	log Kaw	log Koa
Bis-(2-Ethylhexyl) phthalate (DEHP)	4.33E-06	8.33E-05	7.3	-4.7	13.0
Dibutyl phthalate (DBP)	1.00E-03	6.97E-03	4.5	-4.2	8.7
Benzyl butyl phthalate (BBP)	2.33E-04	2.64E-03	4.5	-4.4	9.0
ASE	6.79E-06	9.07E-05	7.7	-4.5	13.4
ATBC	1.32E-05	1.51E-03	5.1	-5.5	10.7
DEHT	3.87E-06	8.80E-05	7.4	-4.8	13.2
DINA	4.07E-08	5.69E-07	9.1	-4.5	15.4
DINCH	6.10E-06	4.30E-06	9.6	-3.2	14.7
Hexabromocyclododecane (HBCD)	2.55E-05	2.34E-04	5.8	-4.4	10.7
TBBPA-bis brominated ether derivative	6.58E-03	6.62E-05	11.6	-1.4	15.6
TBBPA bis(2,3-dibromopropyl) ether	4.20E-01	6.85E-07	10.8	2.4	10.6
Decabromodiphenyl Ether (DecaBDE)	2.08E-07	1.17E-04	10.1	-6.1	18.3

References

Arnot, J., McCarty, L., Armitage, J., Toose-Reid, L., Consultant Frank Wania, E., & Cousins, I. (2009). *An evaluation of hexabromocyclododecane (HBCD) for Persistent Organic Pollutant (POP) properties and the potential for adverse effects in the environment*.

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