



---

**Technical Consultation:  
Proposed Subgrouping of Bisphenol A (BPA)  
Structural Analogues and Functional Alternatives**

**Environment and Climate Change Canada  
Health Canada**

**December 2020**

Ottawa, ON, Canada

## PREFACE

The Chemicals Management Plan (CMP) is a Government of Canada initiative aimed at reducing the risks posed by chemicals to Canadians and the environment. The CMP builds on previous initiatives by assessing chemicals used in Canada and by taking action on chemicals found to be harmful to human health and/or the environment. Since 2006, assessment and management activities have been conducted under the CMP, which is a highly integrated program that addresses environmental and health risks under various laws, including the *Canadian Environmental Protection Act, 1999* (CEPA), the *Pest Control Products Act*, the *Canada Consumer Product Safety Act* (CCPSA), and the *Food and Drugs Act*. Under the CMP, Environment and Climate Change Canada (ECCC) and Health Canada (HC) have made significant progress in evaluating the substances identified as priorities following the categorization process and have implemented appropriate risk management measures where necessary.

Scientific information and regulatory actions on chemicals continue to evolve, as does the use of chemicals. ECCC and HC are highly engaged with other federal regulators and international programs and participate in a variety of fora related to the assessment and management of chemical risks. Both departments actively collect information on substances, monitor for emerging risks, and integrate newly acquired information into decisions about the assessment and management of chemicals and polymers, including the prioritization of substances for future risk assessments or reassessments.

Bisphenol A (commonly known as BPA) is an industrial chemical used to make polycarbonate plastics, epoxy resins, thermal paper, and other products available to consumers. Canada took action on BPA by banning the manufacture, importation, sale and advertising of polycarbonate baby bottles that contain BPA. This action is one of several taken under the CMP to protect the health of Canadians and the environment.

Regulatory action for BPA, as well as consumer and market shifts toward “BPA-free” products, has led to a rise in the use of BPA alternatives, such as bisphenol S (BPS) and Pergafast 201. Understanding the potential risk to the environment and human health from a substance used as a substitute for BPA is important to ensure the continued protection of Canadians and the environment.

The Identification of Risk Assessment Priorities (IRAP) process identified this concern, and in the 2017-2018 IRAP review 34 bisphenols (referred to as certain bisphenols) were identified for further scoping because they shared structural characteristics and identified uses with BPA and, therefore, had the potential to exert similar adverse effects. Based on the initial analysis conducted under the IRAP review, as well as similar work being conducted by other jurisdictions, the Government of Canada deemed it necessary to include other related substances that would merit further consideration. In so doing, a broad group of 343 BPA analogues and functional alternatives, in addition to BPA, was identified for further consideration in a problem formulation process.

Publication of a problem formulation document is proposed as a new initiative under the CMP, although it is commonly and explicitly used in other risk assessment programs internationally. The goal of the additional problem formulation step is to further scope potential emerging priorities and allow for flexibility in the proposed course of action to ensure that the Government of Canada is focusing efforts on the substances with greatest potential impact on human health and the environment. Early scoping and data mining supports program modernization through the opportunity to integrate new approach methods and tools for more efficient data collection, landscaping and gap analysis. This will be an important step in the identification of issues of concern, such as exposures related to vulnerable populations and multiple chemicals, potential for endocrine disruption, and considerations of chemical substitution to inform outcomes beyond risk assessment.

Problem formulation will also provide an opportunity for early consultation with stakeholders, thereby increasing communication and transparency for the identified priorities and associated regulatory considerations. This technical consultation document is the first step in the development of the problem formulation for structural analogues and functional alternatives for BPA. Comments received on this document will inform the subsequent problem formulation, as well as any potential future activities for these substances.

# Table of Contents

<b>1. Introduction</b> .....	<b>7</b>
<b>1.1 Scope and purpose</b> .....	<b>7</b>
<b>1.2 Consultation process</b> .....	<b>7</b>
<b>1.3 Prioritization of BPA analogues and functional alternatives under the Chemicals Management Plan</b> .....	<b>8</b>
<b>2. Regulatory status and international activity</b> .....	<b>9</b>
<b>2.1 Regulatory history of BPA in Canada</b> .....	<b>9</b>
<b>2.2 Current status of BPA</b> .....	<b>10</b>
<b>2.3 BPA analogues and functional alternatives</b> .....	<b>12</b>
<b>2.4 International regulatory activity on BPA, and BPA analogues and functional alternatives</b> .....	<b>13</b>
<b>3. Grouping of BPA analogues and functional alternatives</b> .....	<b>13</b>
<b>3.1 Results</b> .....	<b>14</b>
<b>3.2 Methods used to generate an initial broad pool of substances</b> .....	<b>15</b>
<b>3.3 Methods used to subgroup by structural similarity to BPA</b> .....	<b>17</b>
<b>3.4 Methods used to identify known or suspected functional alternatives to BPA</b> <b>20</b>	
<b>3.5 Methods used to form refined subgroups</b> .....	<b>22</b>
<b>3.6 Charge questions for the scoping and grouping approach</b> .....	<b>28</b>
<b>4. Next steps</b> .....	<b>28</b>
<b>4.1 Information gathering – mandatory survey</b> .....	<b>28</b>
<b>4.2 Problem Formulation</b> .....	<b>29</b>
<b>5. Summary</b> .....	<b>29</b>
<b>6. References</b> .....	<b>30</b>
<b>APPENDIX A</b> .....	<b>33</b>
<b>APPENDIX B. List of 204 BPA analogues and functional alternatives comprising Groups 3.1, 3.2, 3.3, 3.4, and Group 4</b> .....	<b>34</b>

## List of Figures

Figure 2-1. Conceptual model for current knowledge on exposure to and hazard from BPA. Heat-activated colour-developer in thermal paper, which has emerged as a prevalent source of exposure since the assessment of BPA under the CMP, is highlighted in orange.....	12
Figure 3-1. Schematic of the triage of the broad pool of substances. ....	14
Figure 3-2. Structural filter 1 (i.e., criteria for Group 1.1).....	17
Figure 3-3. Criteria for inclusion into Group 2.1 from structural filter 2. ....	18
Figure 3-4. Criteria for inclusion into Group 2.2 from structural filter 2. ....	18
Figure 3-5. Criteria for inclusion into Group 3.1 based on structural filter 3a.....	19
Figure 3-6. Criteria for inclusion into Group 3.2 based on structural filter 3a.....	19
Figure 3-7. Examples of structurally similar bisphenol analogues (solid box) sorted into Group 1.1 and structurally dissimilar chemicals based on criteria applied with evidence of use as functional alternatives for BPA (hashed box) sorted into Group 1.2. ....	21

## List of Tables

Table 3-1. Examples of chemical structures, molecular formula, and molecular weight for substances in each of the four structural groups. ....	15
Table 3-2. Group 4 substances identified as being known or suspected functional alternatives for BPA based on available information. ....	21
Table 3-3. Refined subgroups from Group 3.1 (A1 to A8) and Group 3.2 (B1 to B5). The final column identifies members of each subgroup that are more commonly recognized, and are therefore expected to have available data to support hazard evaluation. ....	23
Table 3-4. Refined subgroups from Group 3.3 (C1 to C3) and Group 3.4 (D1 to D5). The final column identifies members of each subgroup that are more commonly recognized, and are therefore expected to have available data to support hazard evaluation. ....	25
Table A-1. Thirty-four bisphenol substances identified through the 2017-2018 IRAP review .....	33
Table B-1. Complete list of BPA analogues and functional alternatives, and proposed groups and refined subgroups. ....	34

# 1. Introduction

## 1.1 Scope and purpose

This document outlines the scoping and subgrouping approach taken under Canada's Chemicals Management Plan (CMP) for certain bisphenols. The approach to identify analogues and functional alternatives of bisphenol A (BPA) is based on an analysis of substances having structural similarities or similar functional uses to that of BPA.

The intent of this consultation document is to obtain stakeholder input on the group of BPA analogues and functional alternatives identified on the basis of the approach described in this document. This document provides an overview of methods used to identify and triage a broad set of 343 substances for further consideration and outlines proposed next steps for problem formulation. The objectives of this consultation document are to solicit input specifically on:

1. the methods applied to identify the broader group of BPA analogues and functional alternatives;
2. the suitability of the chemicals as members of the broader group; and
3. the proposed subgrouping of substances.

Charge questions to specific aspects of this work are listed in Section 3.6 (BPA analogues and functional alternatives).

Importantly, it is not the purpose of this document to focus on information critical to determining whether the BPA analogues and functional alternatives included in the substances list meet the criteria as set out in section 64 of CEPA. Rather, the emphasis is on the approach used to identify the broader set of substances for further exploration in problem formulation. Depending on the outcome of the problem formulation, more specific and detailed examination of scientific information will be presented in draft screening assessment reports which, if developed, will incorporate a weight-of-evidence approach and precaution as relevant in developing conclusions.

This document was prepared by staff in the Existing Substances Risk Assessment Bureau at Health Canada and the Ecological Assessment Division at Environment and Climate Change Canada.

## 1.2 Consultation process

The Government of Canada is committed to providing interested parties with the opportunity to take part in consultations. Interested parties may provide comments on the proposed options in writing, by mail or email, to the contact information provided below.

Interested parties are invited to submit comments during the 60-day public comment period on the content of this consultation document or other information that would help to inform decision-making about future actions.

Comments and supporting information may be submitted prior to February 17, 2021 to Executive Director, Program Development and Engagement Division, Department of the Environment, Gatineau, Quebec K1A 0H3, or by email to [eccc.substances.eccc@canada.ca](mailto:eccc.substances.eccc@canada.ca)

Comments received on the consultation document will be taken into consideration in the development of the BPA analogues and functional alternatives problem formulation document.

### **1.3 Prioritization of BPA analogues and functional alternatives under the Chemicals Management Plan**

The Chemicals Management Plan (CMP) was announced by the Government of Canada in December 2006. The CMP is a comprehensive program aimed at reducing risks posed by chemicals to Canadians and their environment. Detailed information on the CMP is available at Canada.ca (ECCC, HC [modified 2016]). Under the CMP, the Identification of Risk Assessment Priorities (IRAP) process is one mechanism for priority setting. Detailed information on IRAP is available at Canada.ca (ECCC, HC [modified 2017]).

Problem formulation was identified as a new outcome of IRAP during the 2017-2018 cycle (ECCC, HC [modified 2019a]). It is recommended for substances or groups of substances that have indications of exposure and/or hazard but which are determined to require additional scoping to identify the most appropriate course of action. It also provides an opportunity for early stakeholder engagement. Thirty-four bisphenols (referred to as certain bisphenols) were identified in the 2017-2018 IRAP review (listed in Appendix A) and were recommended for problem formulation (ECCC, HC [modified 2019a]). These substances were identified because they shared structural characteristics with BPA and therefore had potential to exert similar adverse effects, along with evidence of potential use in applications in common with BPA. They were identified through a voluntary industry survey on “certain bisphenols” in 2017 and via screening of hazard and exposure data (in particular for BPS and BPF, which were also identified in the 2016 IRAP review for additional information gathering).

It was recognized that there are additional substances on the Canadian chemical inventory lists (i.e., the Domestic Substances List (DSL), the Non-Domestic Substances List (NDSL) and the Revised In-Commerce List (R-ICL)) beyond those identified during the IRAP review that may meet the criteria for this substance group. The methods and approach described in this document were therefore developed to capture a broader group of substances for consideration in the BPA analogues and functional alternatives group.



## 2. Regulatory status and international activity

### 2.1 Regulatory history of BPA in Canada

CEPA required the Minister of the Environment and the Minister of Health to identify—in an exercise called categorization—and assess substances that (1) are persistent or bioaccumulative (based on the *Persistence and Bioaccumulation Regulations*) and inherently toxic to humans or other organisms, or (2) present or may present, to individuals in Canada, the greatest potential for exposure. As BPA was found to meet these criteria, it was assessed under CEPA in 2008, and the Government of Canada determined that BPA met the criteria under sections 64(a) and (c) of CEPA, indicating the potential of this substance to cause harm to human health and the environment. BPA was therefore placed on the List of Toxic Substances (Schedule 1 of CEPA) (ECCC, HC [modified 2013]; ECCC, HC [modified 2019b]).

The 2008 assessment found that BPA is present in a wide range of environmental media, with detectable levels documented in several species of aquatic biota. BPA is not persistent under aerobic conditions, but was found to degrade slowly under conditions of low or no oxygen. It was also determined that BPA is bioavailable and can accumulate in tissues to some degree. BPA is acutely toxic to aquatic organisms and has been shown to adversely affect growth and development in both aquatic and terrestrial species. There is evidence that low-level exposure to BPA, particularly at sensitive life cycle stages, may lead to permanent alterations in hormonal, developmental or reproductive capacity. On the basis of expected continued or increasing exposure of biota, and information indicating the potential for long-term adverse effects to organisms within the range of concentrations currently measured in the environment, it was considered appropriate to apply precaution when characterizing risk. Accordingly, it was concluded that BPA is entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity.

The assessment also identified that human exposure to BPA in Canada can result from dietary intake (e.g., migration from food packaging, migration from repeat-use polycarbonate containers), from environmental media (i.e., ambient air, indoor air, drinking water, soil and dust), and from use of consumer products. Reproductive and developmental toxicity was the critical effect for characterization of risk to human health; however, the neurodevelopmental and behavioural datasets for rodents were considered to be suggestive of effects at lower doses. Given that toxicokinetics and metabolism data indicated potential sensitivity to the maternal-fetal unit and infant and that animal studies suggested a trend towards heightened susceptibility during stages of development in rodents, it was considered appropriate to apply a precautionary approach when characterizing risk. It was therefore concluded that BPA be considered as a substance that may be entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health (ECCC, HC [modified 2013]).

The CMP assessment recognized and accounted for the endocrine disruption potential of BPA. BPA is a xenoestrogen, which means that it is able to exert biological effects

using the same mode of action as estrogen. Estrogen is a hormone that works by binding to the estrogen receptor (ER), forming a complex that acts directly on the genome to alter gene expression. Because BPA is not the endogenous ligand for this receptor, it disrupts normal signalling pathways. BPA is therefore an endocrine disrupting chemical (EDC).

To address the ecological concerns identified, ECCC released a proposed risk management approach (ECCC, HC [modified 2010]). It included an environmental objective to prevent or minimize releases of BPA into the Canadian environment and a risk management objective to achieve the lowest level of release of BPA to water that is technically and economically feasible. To work towards these goals, the Government of Canada has taken risk management actions including a Pollution Prevention Planning Notice with respect to Bisphenol A in Industrial Effluents (Pollution Prevention Planning Notice for BPA) (Canada 2012) and an Environmental Performance Agreement Respecting Bisphenol A in Paper Recycling Mill Effluents (ECCC 2015).

In 2020, ECCC published the Evaluation of the Effectiveness of Risk Management Measures for Bisphenol A (BPA) – Ecological Component (ECCC 2020). The evaluation compared environmental concentration values to the Federal Environmental Quality Guidelines for BPA and found that the current concentration of BPA in surface water is below levels considered protective to aquatic life, and is generally decreasing in areas where risk management actions have taken place. The evaluation also found that 99% of sediment samples taken had concentrations of BPA below levels considered protective to aquatic life. Overall, the evaluation concluded that no further risk management action is required at this time but that sediment sampling should continue in order to monitor the concentration of BPA in sediment.

To address human health concerns, a risk management measure was applied under the CCPSA, which makes it illegal to manufacture, import, advertise or sell polycarbonate baby bottles containing BPA (ECCC, HC [modified 2010]). In 2012, Health Canada's Food Directorate published an updated assessment of BPA exposure from foods (HC2012). This report found that the updated dietary exposure estimates were lower than those estimated in the 2008 assessment. In 2018, Health Canada published a report measuring the effectiveness of the current risk management approach, which reported a 96% decrease in exposure to BPA in infants (HC 2018).

## **2.2 Current status of BPA**

Exposure to and effects of BPA remain areas of active investigation and evaluation. While early assessments focused on oral exposure to BPA, more recent international assessments have had an expanded scope that includes the dermal exposure scenario through the handling of thermal paper (ANSES 2014). While this exposure scenario is important for the general population, it is particularly relevant to some vulnerable populations, including women of reproductive age, especially those working as cashiers. Current knowledge on the status of BPA is well reviewed elsewhere (Geens et al. 2011; Ma et al. 2019; Pivnenko et al. 2015; Rathee et al. 2012) and is summarized in

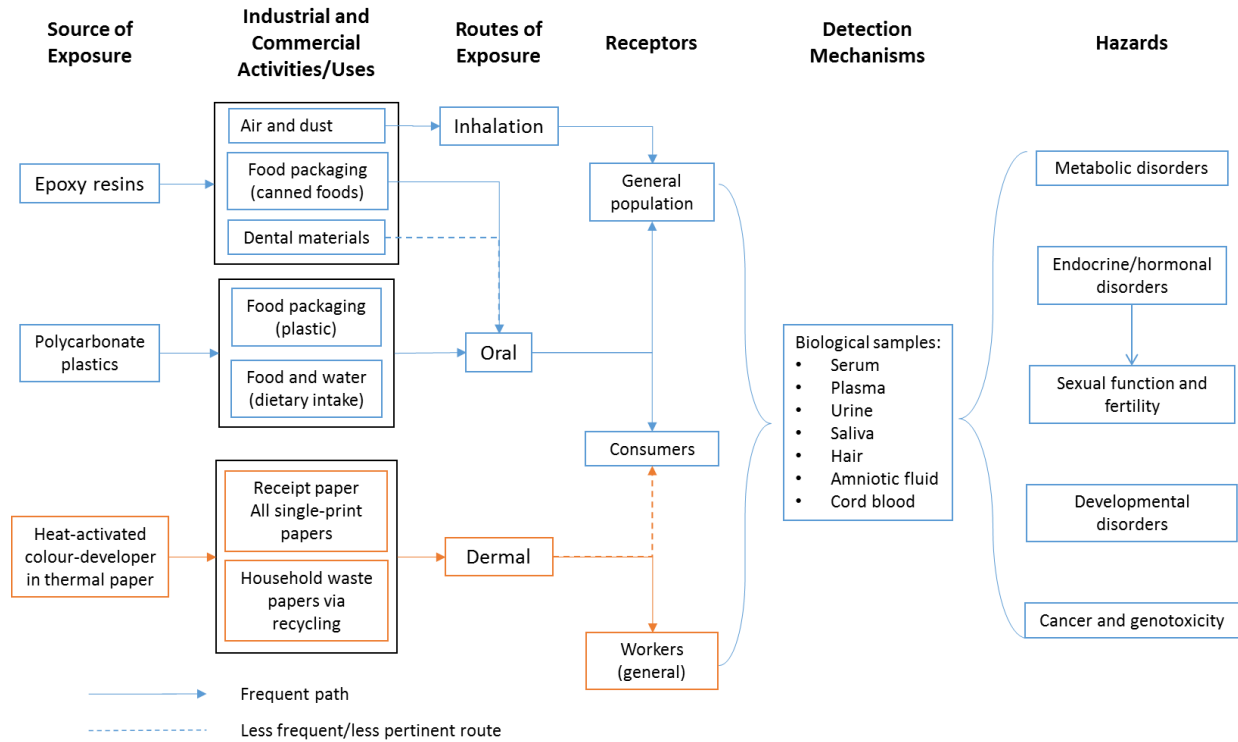
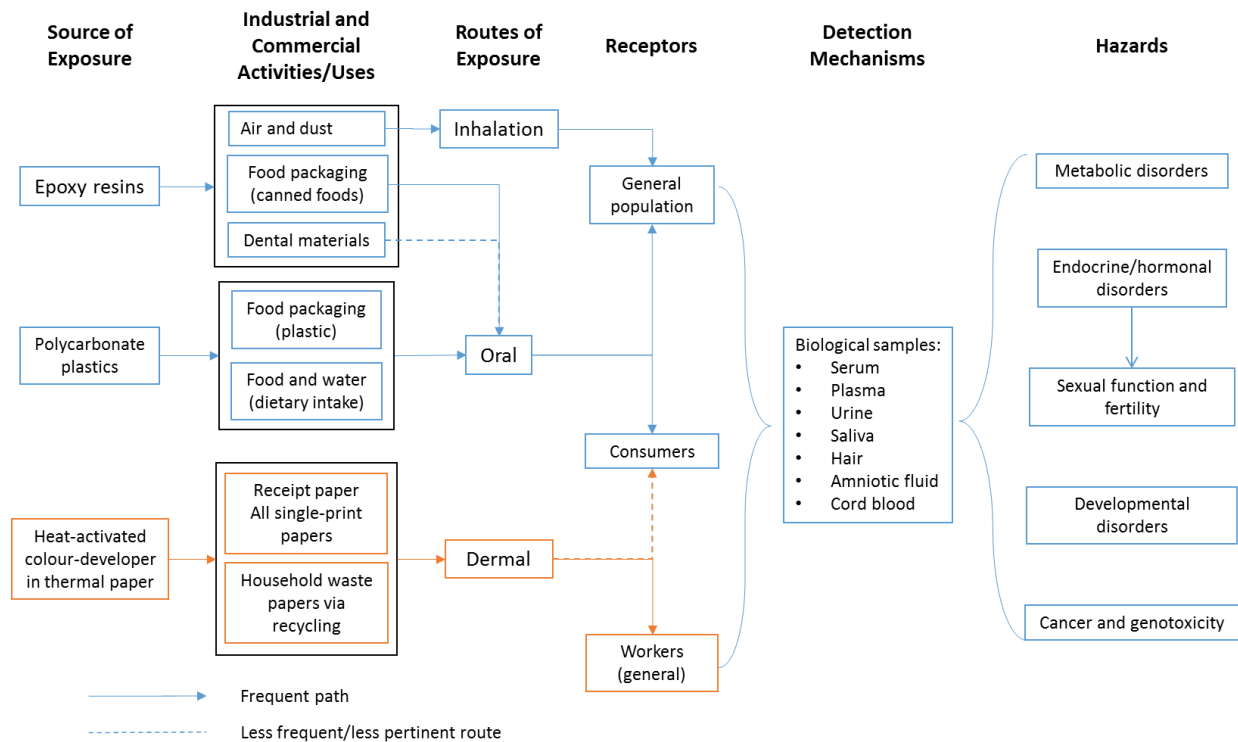


Figure 2-1.



**Figure 2-1.** Conceptual model for current knowledge on exposure to and hazard from BPA. Heat-activated colour-developer in thermal paper and its subsequent use, which has emerged as a prevalent source of exposure since the assessment of BPA under the CMP, is highlighted in orange.

[The above graphic depicts the conceptual model for current knowledge on exposure to bisphenol A (BPA) leading to potential human health hazards. The left most column describes the sources of exposure to BPA which include epoxy resins, polycarbonate plastics, and heat-activated colour-developer in thermal paper. The next column shows the industrial and commercial activities and uses. Epoxy resins may be released to air and dust and are used in food packaging (canned foods) and dental materials. Polycarbonate plastics are used to produce food packaging (plastic) and can be detected in food and water (dietary intake). The heat activated colour-developer in thermal paper is used in receipt paper, single-print papers and found in household waste papers via recycling.

The middle of the figure describes the routes of exposure and receptors related to each of the industrial and commercial activities and uses. BPA from air and dust are inhaled and the receptor is the general population. Food packaging, food and water are considered frequent pathways for oral exposure while dental materials are a less frequent route of oral exposure; receptors are the general population and consumers. Exposure to paper uses is through the dermal route; receptors include more frequently workers and less frequently consumers.

The receptors converge to column five describing the possible detection mechanisms which include biological samples from serum, plasma, urine, saliva, hair, amniotic fluid, and cord blood. The final column lists the possible hazards that have been documented in the literature from exposure to BPA and include metabolic disorders, endocrine/hormonal disorders, impact on sexual function and fertility, developmental disorders, and cancer and genotoxicity.]

## **2.3 BPA analogues and functional alternatives**

Regulatory action for BPA, as well as consumer and market shifts toward “BPA-free” products, has led to a rise in the use of BPA alternatives (e.g., bisphenol S (BPS) and Pergafast 201). As industry shifts away from the use of BPA, the increased use and abundance of possible alternatives have provided another level of complexity, namely, the lack of clarity as to whether statements like “BPA-free” actually equate with product safety. Therefore, the potential for regrettable substitution (i.e., substitution of one substance with another that poses an equivalent or greater risk to environmental or human health) is important in the context of the bisphenols and is reviewed elsewhere (Pelch et al. 2019).

While there has been success in managing the risks to Canadians and the Canadian environment associated with exposure to BPA, there is an ongoing need to consider the broader group of bisphenols. To reduce the potential for regrettable substitution, some

consideration of the possible substitutes for BPA is needed to understand their associated toxicity, exposure, and potential risk.

Based on the initial analysis of the BPA analogues conducted under the IRAP review (outlined in Section 1.3 and substances provided in Appendix A), as well as similar work being done by other jurisdictions, the Government of Canada deemed it necessary to conduct a more in-depth screening in order to capture other related substances that would merit further consideration. In so doing, a broad group of 343 BPA analogues and functional alternatives, including BPA was identified. This group and the associated methods for defining it are further described in Section 3.

## **2.4 International regulatory activity on BPA, BPA analogues and BPA functional alternatives**

BPA, BPA analogues (substances that share structural similarity to BPA) and BPA functional alternatives (substances that are known or suspected to be used as BPA replacements but are not structurally similar) are an active area of regulatory interest. For this work, BPA analogues are substances that are structurally similar to BPA, while BPA functional alternatives are substances that are known to have similar uses. Some recent regulatory publications include:

- a report by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) to restrict the use of BPA in thermal paper (ANSES 2014);
- two reports by the Danish Environmental Protection Agency on BPA on thermal paper (Danish EPA 2011, 2014);
- a report by the European Food Safety Authority (EFSA) on risks to public health related to the presence of bisphenol A (BPA) in foodstuff (EFSA 2015);
- a market survey by the European Chemicals Agency (ECHA) of use of BPA and its alternatives in thermal paper in the EU from 2014-2017 (ECHA 2017);
- a report by the U.S. National Toxicology Program (NTP) on a perinatal and chronic extended-dose-range study of BPA in rats (NTP 2018); and
- an NTP scoping review on BPA structural analogues and functional replacements (Pelch et al. 2019).

These reports were reviewed and considered to be key information sources informing the generation of the broad pool of BPA analogues and functional alternatives (described further in Section 3.2).

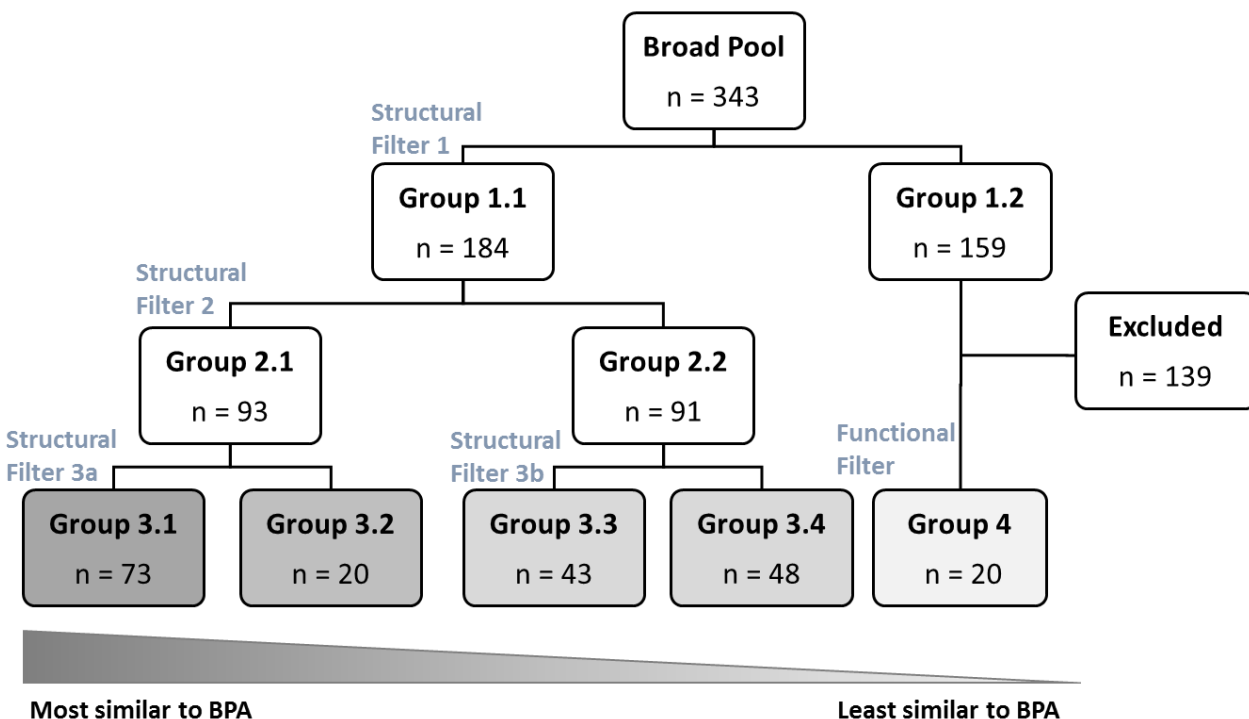
## **3. Grouping of BPA analogues and functional alternatives**

This section presents the approach to identifying and grouping BPA analogues and functional alternatives for further consideration in a future problem formulation. The results are presented first (Section 3.1), followed by a description of the methodology used (Sections 3.2-3.4).

### 3.1 Results

Using computational approaches and a comprehensive review of international inventories, a broad pool of 343 BPA analogues and functional alternatives were identified for consideration. These were then grouped either by structural similarity or based on their known or suspected use as functional alternatives; the structurally similar groups were further considered using more stringent filtering criteria to create refined subgroups.

The outcome of the triaging of the broad pool of substances is illustrated schematically in Figure 3-1. Examples of chemical structures for each group are described in Table 3-1. The methods used to identify the broad pool of substances can be found in Section 3.2, a description of the structural filters used can be found in Section 3.3, and the methods used to triage the functional alternatives group is described in Section 3.4. The approach to further refine structural groups into subgrouping consisting of the most structurally similar analogues is described in Section 3.5. The complete substance list can be found in Appendix B.



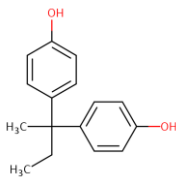
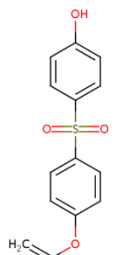
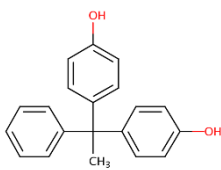
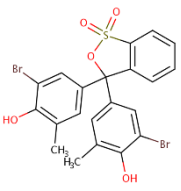
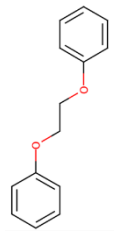
**Figure 3-1.** Schematic of the triage of the broad pool of substances.

[Figure 3-1 describes the results of the structure based triaging approach applied to the group of substances using hierarchical relationships progressing from top to bottom. An initial broad pool of 343 substances is shown in the top box which is then split by Structural Filter 1 into Group 1.1 (n=184) on the left and Group 1.2 (n=159) on the right. Structural Filter 2 is used to further split Group 1.1 into two refined groups, Group 2.1 (n=93) and Group 2.2 (n=91). Group 2.1 is split by further decision criteria under

Structural Filter 3a resulting in Group 3.1 (n=73) and Group 3.2 (n=20) on the left most part of the hierarchy. Group 2.2 is further split by Structural Filter 3b which creates Group 3.3 (n=43) and Group 3.4 (n=48). Finally, Group 1.2 on the far right side of the hierarchy is filtered using a Functional Filter which creates Group 4 (n=20) and excludes a total of 139 substances from the final groupings.

A scale bar is presented under the hierarchical relationships illustrating the decreasing level of structural similarity to BPA from left to right. Group 3.1 (far left) being the most similar and progressively decreasing between Group 3.2, Group 3.3 and Group 3.4 until Group 4 which is the least similar to BPA (far right).]

**Table 3-1.** Examples of chemical structures, molecular formula, and molecular weight for substances in each of the four structural groups.

	<b>Group 3.1</b>	<b>Group 3.2</b>	<b>Group 3.3</b>	<b>Group 3.4</b>	<b>Group 4</b>
<b>Number of substances</b>	N=73	N=20	N=43	N=48	N=20
<b>Summarizing description</b>	Most structurally similar to BPA	One or more hydroxyl groups on the phenyl rings	Ring functional group, light (< 450 g/mol)	Ring functional group, heavy (>or= 450 g/mol)	Lack of close structural similarity to BPA, but identified as a functional alternative
<b>Molecular weight range (g/mol)</b>	200.23-705.2	212.29-628.9	268.3-436.6	460.6-1103.6	110.11-1573
<b>Example substance</b>	 <p>Bisphenol B C<sub>16</sub>H<sub>18</sub>O<sub>2</sub></p>	 <p>BPS-MAE C<sub>15</sub>H<sub>14</sub>O<sub>4</sub>S</p>	 <p>Bisphenol AP C<sub>20</sub>H<sub>18</sub>O<sub>2</sub></p>	 <p>Bromocresol Purple C<sub>21</sub>H<sub>16</sub>Br<sub>2</sub>O<sub>5</sub>S</p>	 <p>Diphenyl Glycol C<sub>14</sub>H<sub>14</sub>O<sub>2</sub></p>

### 3.2 Methods used to generate an initial broad pool of substances

Two approaches were used to generate a broad pool of BPA structural analogues and known functional alternatives: (1) an automated workflow was used to identify structurally similar BPA analogues from Canadian chemical inventory lists; and (2) a

review was undertaken of published reports (national and international) on BPA analogues and replacements/alternatives and surveys conducted under the CMP with the aim of identifying known functional analogues for BPA. Together, this produced a pool of 343 unique substances. Details for each approach is described below.

#### *(1) Automated workflow*

Applying a computational approach, an automated workflow was developed using the Python programming language. This workflow was applied to screen the Domestic Substances List (DSL), the Non-Domestic Substances List (NDSL), and the Revised In-Commerce List (R-ICL). The inclusion of inventories beyond the DSL ensured a more comprehensive scoping of a broader chemical landscape for similar substances and further informed the potential for regrettable substitution.

The script searched for specified substructures to efficiently screen for chemical analogues. For a chemical from an inventory to be considered a BPA analogue, it needed to pass three filters designed to ensure that the substances ranked as most similar to BPA were discrete chemicals of two phenol groups attached by a single atom. The filters used were as follows:

1. exclusion of polymers;
2. inclusion of molecules containing two phenol rings connected by a single atom; and
3. inclusion of molecules with at least one aliphatic oxygen atom at any position on each phenyl ring.

The workflow identified 115 substances from the DSL, 189 from the NDSL, and 2 from the R-ICL that were considered BPA analogues. It should be noted that the two chemicals from the R-ICL were also found on the NDSL.

#### *(2) Review of lists of BPA analogues and functional alternatives*

Six lists of BPA analogues and functional alternatives were considered:

1. 34 bisphenols identified in the 2017-2018 IRAP cycle, plus 7 additional substances that were nominated after the publication of the IRAP report;
2. substances identified in response to the Bisphenol A voluntary survey (February 2018);
3. the U.S. EPA report 'Bisphenol A Alternatives in Thermal Paper' (US EPA 2012);
4. the NTP report 'Biological Activity of Bisphenol A (BPA) Structural Analogues and Functional Alternatives' (NTP 2017);
5. the ANSES report 'Substitution du bisphénol A' (ANSES 2013); and
6. the Danish EPA report 'Alternative Technologies and Substances to Bisphenol A (BPA) in Thermal Paper Receipts' (Danish EPA 2014).

The second approach identified an additional 39 substances that had not been identified by the first approach, increasing the final pool to 343 BPA analogues and functional alternatives. Twenty-one of the 39 substances were found on the DSL, NDSL, or R-ICL,



but had not met the structural criteria of the automated workflow approach, while the remaining 18 substances came from information sources external to the Canadian inventories identified above.

### 3.3 Methods used to subgroup by structural similarity to BPA

The broad pool of chemicals was sequentially passed through increasingly stringent structural similarity filters. Each chemical's molecular structure was screened with respect to the structural attributes of BPA; specifically, the chemical was considered more structurally similar to BPA if it more closely matched BPA's attributes. These structural filters are described below.

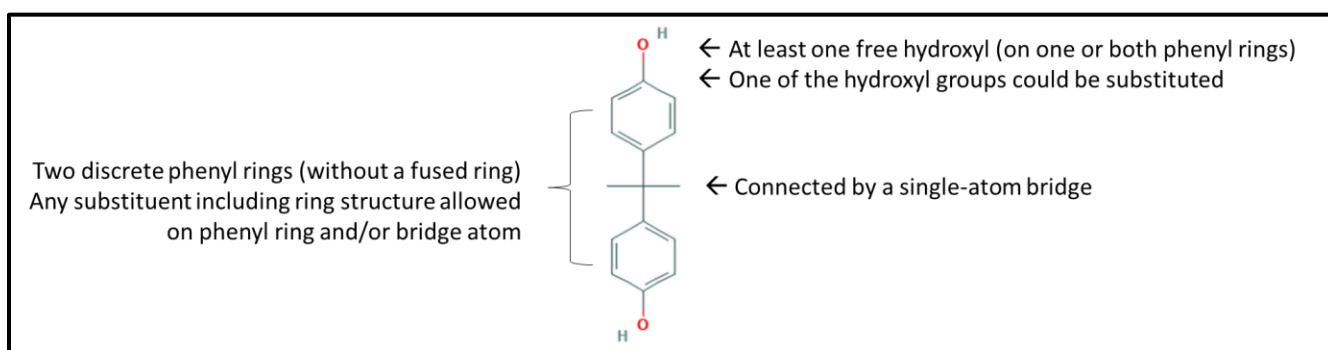
#### **Structural filter 1: Used to determine if a chemical meets the basic bisphenol definition**

The broad pool of substances was initially divided into two groups (1.1 and 1.2).

Group 1.1 (n = 184) met the following four criteria, which are further illustrated in Figure 3-2:

1. Presence of two phenyl rings connected by not more than one atom;
2. At least one of the phenyl rings to have minimum one free hydroxyl group in any position;
3. The two phenyl rings may not be multi-ring (e.g., naphthalene, anthraquinone, etc.) but may be substituted by other functional groups; and
4. Any ring(s) other than the two phenyl rings could exist in the structure.

Group 1.2 (n = 159) comprised those substances that did not meet these criteria.



**Figure 3-2.** Structural filter 1 (i.e., criteria for Group 1.1).

[Figure 3-2 depicts the chemical structure of BPA to schematically show the four criteria included in structural filter 1 and applied in the process of identifying substances that meet the basic structural skeleton of BPA for inclusion in Group 1.1.]

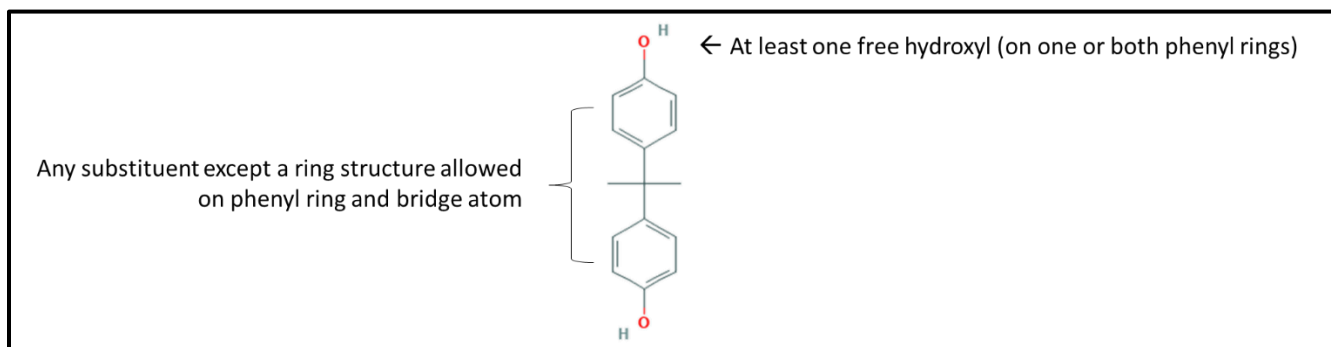
#### **Structural filter 2: Used to exclude bulky (poly rings) substances**

Substances from Group 1.1 were divided into two groups (2.1 and 2.2), which are further illustrated in Figure 3-3 and Figure 3-4. .

Group 2.1 (n = 93) met the following two criteria:

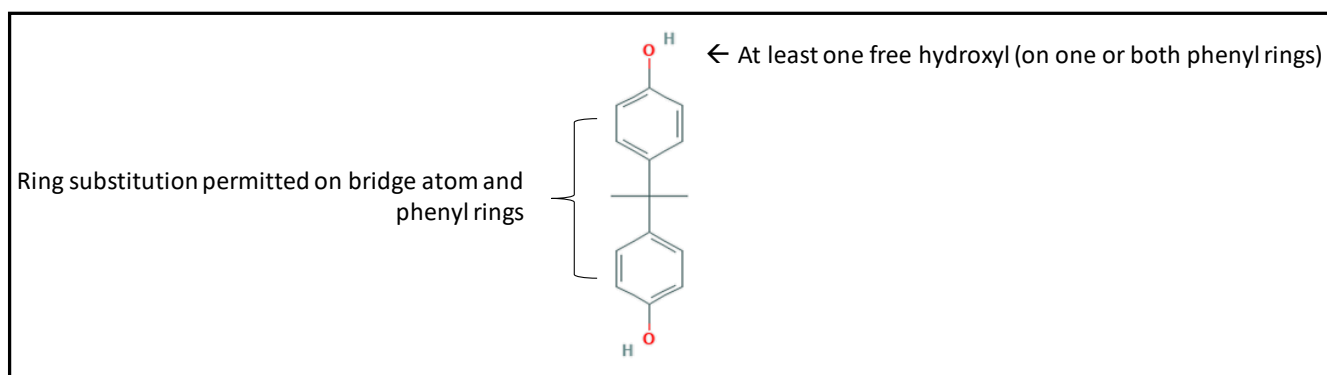
1. At least one free hydroxyl group on one or both phenyl rings; and
2. Substituents on phenyl ring can be anything other than a ring.

Substances in Group 2.2 (n = 91) met the following criterion: ring substitution allowed on either phenyl ring or at the bridge atom.



**Figure 3-3.** Criteria for inclusion into Group 2.1 from structural filter 2.

[Figure 3-3 depicts the chemical structure of BPA to schematically show the two criteria included in structural filter 2 and illustrates places on the two phenyl rings and the bridge atom where structures with rings are not allowed to be substituted for inclusion in Group 2.1.]



**Figure 3-4.** Criteria for inclusion into Group 2.2 from structural filter 2.

[Figure 3-4 depicts the chemical structure of BPA to schematically show the two criteria included in structural filter 2 and illustrates ring substitution is allowed on either phenyl ring or at the bridge atom for inclusion in Group 2.2.]

**Structural filter 3a: Used to refine the Group 2.1 that is most structurally similar to BPA**

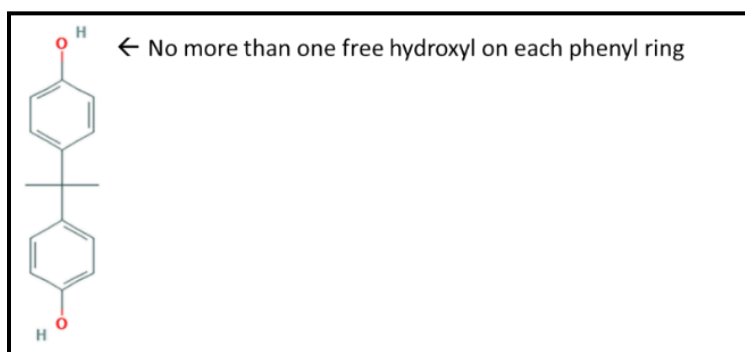
Substances in Group 2.1 were divided into two groups (3.1 and 3.2); Figure 3-5. and Figure 3-6 provide illustration of criteria as noted below.

Group 3.1 (n = 73) met the following criterion:

1. No more than one free hydroxyl group on each phenyl ring.

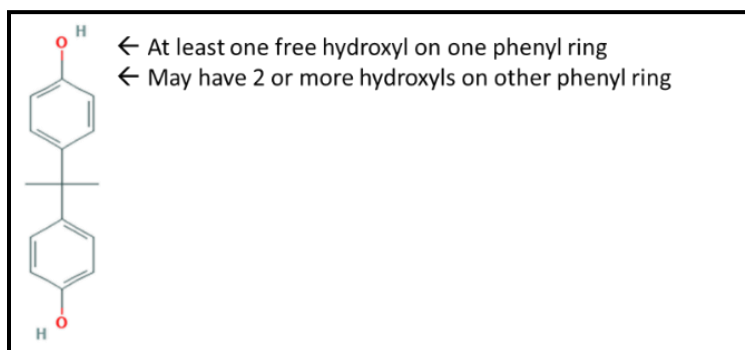
Group 3.2 (n = 20) met the following two criteria:

1. At least one free hydroxyl group on one phenyl ring; and,
2. May have 2 or more hydroxyl groups on the other phenyl ring.



**Figure 3-5.** Criteria for inclusion into Group 3.1 based on structural filter 3a.

[Figure 3-5 depicts the chemical structure of BPA to schematically show the criterion included in structural filter 3a and illustrates no more than one free hydroxyl group substituted on each of the phenyl rings for inclusion in Group 3.1.]



**Figure 3-6.** Criteria for inclusion into Group 3.2 based on structural filter 3a.

[Figure 3-6 depicts the chemical structure of BPA to schematically show the two criteria included in structural filter 3a and illustrates for requirement for at least one free hydroxyl group and 2 or more hydroxyl groups on the other phenyl ring for inclusion in Group 3.2.]

### **Structural filter 3b: Used to refine the group 2.2 that contains poly rings**

Substances in Group 2.2 were divided into two groups (3.3 and 3.4).

Group 3.3 (n = 43) met the following criterion:

1. Molecular weight of entire molecule is less than 450 g/mol.

Group 3.4 (n = 48) met the following criterion:

1. Molecular weight of entire molecule is greater or equal to 450 g/mol.

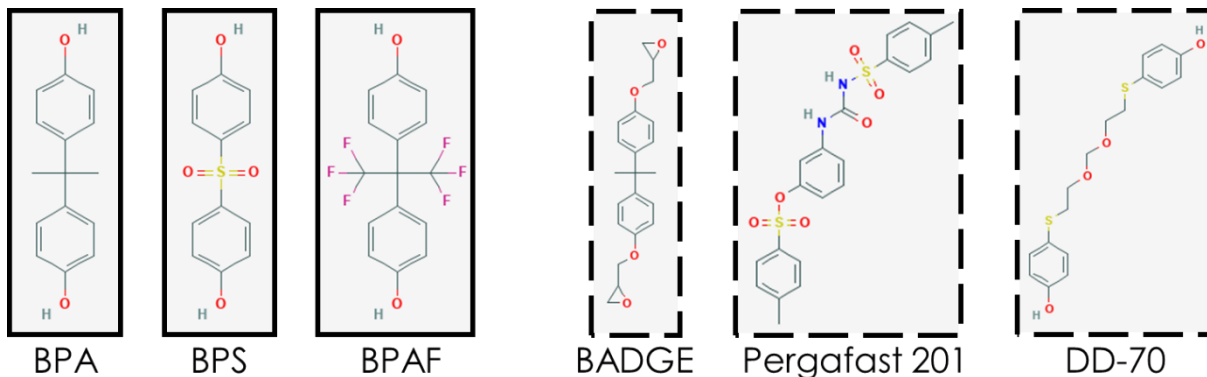
Molecular weight (MW) of 450 g/mol was used as cut-off based on predicted physical chemical properties, absorption, distribution, metabolism and excretion (ADME), and estrogen receptor flags. This was found to be the most suitable parameter because chemicals with MW greater than 450 g/mol had a higher probability of being inert/low activity compared to those less than 450 g/mol over a range of predicted activities/properties.

### **Functional Filter 4. Identification of known or suspected functional alternatives to BPA**

Expert judgement was used to identify 20 substances from the 159 substances in Group 1.2 that are either known to be (or suspected to be based on available information) functional alternatives for BPA. These 20 substances form Group 4 and their identification is further described in Section 3.4. The remaining 139 substances comprising Group 1.2 were not considered further in this grouping exercise as they are concluded to be structurally dissimilar or not currently being used as a BPA alternative based on the criteria described.

## **3.4 Methods used to identify known or suspected functional alternatives to BPA**

All substances that were deemed structurally dissimilar to BPA were sorted by structural filter 1 into Group 1.2. However, this removed some structures that are potential functional replacements (example structures shown in Figure 3-7).



**Figure 3-7.** Examples of structurally similar bisphenol analogues (solid box) sorted into Group 1.1 and structurally dissimilar chemicals based on criteria applied with evidence of use as functional alternatives for BPA (hashed box) sorted into Group 1.2.

[Figure 3-7 shows examples of structurally similar bisphenol analogues sorted into Group 1.1 and structurally dissimilar chemicals sorted into Group 1.2. On the left are chemical structures of three bisphenols, BPA, BPS and BPAF, which were denoted as being structurally similar and are outlined by a solid black line. Chemical structures of three other chemicals, BADGE, Pergafast 201, and DD-70, are shown on the right outlined by a dashed line, denoting them as being functionally similar although the structures lack structural similarity to BPA.]

Whereas determining structural similarity to a chemical could be done using automated workflows, functional alternatives needed to be identified using available information and expert judgement. For a chemical to be added to Group 4, it needed to meet one of the four criteria. In total, 20 unique substances, as presented in Table 3-2, met one or more of these criteria:

1. The substance was identified as a potential substitute through an IRAP review and/or further scoping activities;
2. The substance was identified by stakeholders in response to the 2018 Voluntary Survey;
3. The substance is a reactive epoxide. Epoxides were included as they are likely to serve functions similar to those of BPA in plastics and because their reactivity results in a higher likelihood that they will produce adverse health effects;
4. The substance appeared on 3 or more of the jurisdiction's lists; i.e., HC, US EPA, NTP, ANSES, and/or Danish EPA. Chemicals for which a consensus of functional replacement does not exist were not carried forward.

**Table 3-2.** Group 4 substances identified as being known or suspected functional alternatives for BPA based on available information

CAS RN	Common Name if Available	Name of Substance
80-07-9		Benzene, 1,1'-sulfonylbis[4-chloro-
94-18-8	PHBB	Benzoic acid, 4-hydroxy-, phenylmethyl ester
123-31-9	Hydroquinone	1,4-Benzenediol
1675-54-3	BADGE	Oxirane, 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bis-
2095-03-6	BFDGE	2,2'-methylenebis(p-phenyleneoxymethylene)bisoxirane
3188-83-8		Benzenemethanol, 5-[1-methyl-1-[4-(oxiranylmethoxy)phenyl]ethyl]-2-(oxiranylmethoxy)-
5945-33-5	Fyrolflex BDP	Phosphoric acid, P,P'-[(1-methylethylidene)di-4,1-phenylene] P,P',P',P'-tetraphenyl ester
7328-97-4		Oxirane, 2,2',2'',2'''-[1,2-ethanediylidene]tetrakis(4,1-phenyleneoxymethylene)]tetrakis-

25068-38-6	Polymerized BADGE w/ BPA resins	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane
39382-25-7	Bisphenol A propylene oxide fumarate polymer	2-Butenedioic acid (E)-, polymer with $\alpha,\alpha'$ -[(1-methylethylidene)di-4,1-phenylene]bis[ $\omega$ -hydroxypoly[oxy(methyl-1,2-ethanediyl)]]
39817-09-9		Oxirane, 2,2'-[methylenebis(phenyleneoxymethylene)]bis-
47758-37-2		Oxirane, 2,2'-[9H-fluoren-9-ylidenebis(4,1-phenyleneoxymethylene)]bis-
66072-38-6		Oxirane, 2,2',2''-[methylidynetris(phenyleneoxymethylene)]tris-
67786-03-2		Oxirane, 2,2'-[[[2-(oxiranylmethoxy)phenyl]methylene]bis(4,1-phenyleneoxymethylene)]bis-
93589-69-6	DD-70	Phenol, 4,4'-methylenebis(oxy-2,1-ethanediylthio)bis-
113693-69-9	Tetramethyl bisphenol F epoxy resin	Phenol, 4,4'-methylenebis[2,6-dimethyl-, polymer with 2-(chloromethyl)oxirane
151882-81-4	BTUM	Benzenesulfonamide, N,N'-[methylenebis(4,1-phenyleneiminocarbonyl)]bis[4-methyl-
191680-83-8	D-90	Phenol, 4,4'-sulfonylbis-, polymer with 1,1'-oxybis(2-chloroethane)
232938-43-1	Pergafast 201	Benzenesulfonamide, 4-methyl-N-[[[3-[(4-methylphenyl)sulfonyl]oxy]phenyl]amino]carbonyl]
321860-75-7	UU (urea-urethane compound)	Phenol, reaction products with 4,4'-sulfonylbis[benzenamine] and 2,4-TDI

### 3.5 Methods used to form refined subgroups

Substances in Groups 3.1 and 3.2 (i.e., the two groups that are most similar to BPA; see Figure 3-1), and Groups 3.3 and 3.4 (i.e., the two groups with poly rings in their molecular structure) were further divided into refined subgroups as described below as an approach to identify and address data gaps in properties of the substances. This step was taken in anticipation of the need to fill critical information gaps and data needs in the toxicological database for some of the newer or less commonly used or less studied BPA analogues to support recommendations and outcomes of the problem formulation using read-across. The structural subgroups were created using tools such as the OECD QSAR Toolbox (OECD 2014) and Leadscope software (Roberts et al. 2000). These chemistry-based tools aid in identifying the presence of specific functional groups and structural features in the molecular structure of the chemicals. The development of the refined subgroups was done by considering:

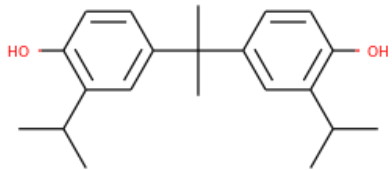
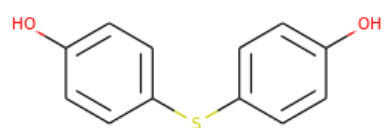
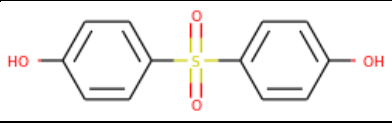

1. specific structural configuration (e.g., presence of steric hindrance);
2. similarity of functional groups at the bridge atom; and

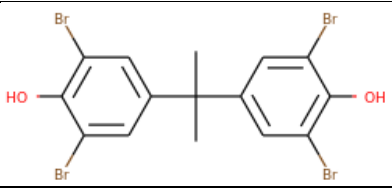
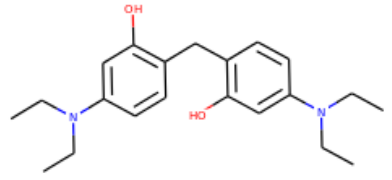
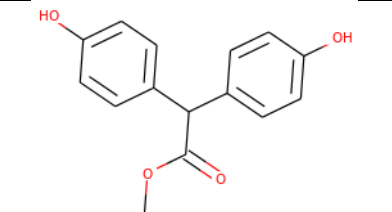
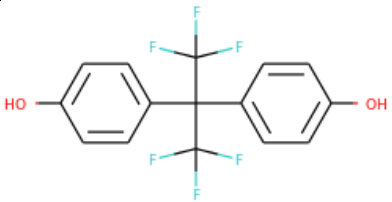
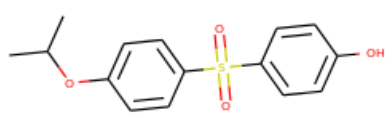
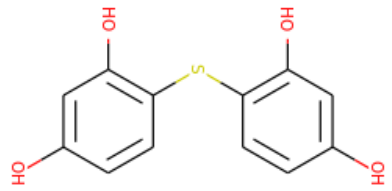
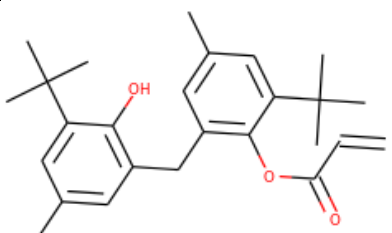
- specific functional group substitution (e.g., halogen, phosphate, amino, nitro groups) on phenyl ring(s).

The current approach for subgrouping only considered structural features in order to form provisional read-across groups. These read-across groups would be further substantiated with the absorption, distribution, metabolism and elimination (ADME), other physicochemical properties, and biological/toxicological activity data.

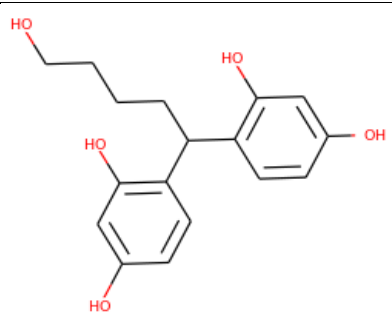
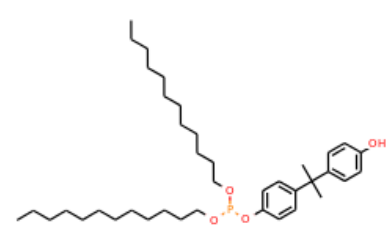
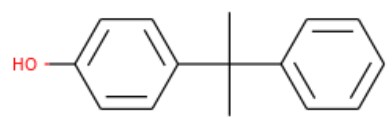
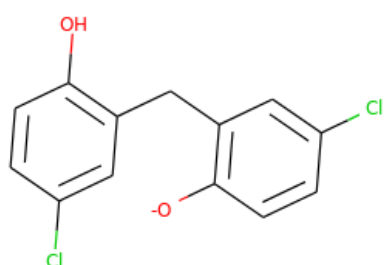
Preliminary literature scans suggest that many of the currently derived subgroups contain at least one well-studied chemical. Such chemicals have been studied for their toxicological effects (often in both *in vitro* and *in vivo* assays) and can therefore be used to build a weight of evidence in a category approach to read-across. From Group 3.1, eight subgroups (A1 to A8) were formed, while from Group 3.2 five subgroups (B1 to B5) were formed with two single substances remaining. From the Group 3.3, three subgroups were formed (C1 to C3), whereas from Group 3.4, four subgroups (D1 to D4) with two single substances were formed. Results for the refined subgroups are summarized in Table 3-3 and Table 3-4. The CAS RNs for each of the subgroups are listed in Appendix B.

**Table 3-3.** Refined subgroups from Group 3.1 (A1 to A8) and Group 3.2 (B1 to B5). The final column identifies members of each subgroup that are more commonly recognized, and are therefore expected to have available data to support hazard evaluation.

Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
A1 n = 18	(Partially) hindered bisphenols	 Bisphenol G C <sub>21</sub> H <sub>28</sub> O <sub>2</sub>	284 – 705	Bisphenol G
A2 n = 13	S/O/N bridge atom (no =O)	 4,4'-Thiodiphenol C <sub>12</sub> H <sub>10</sub> O <sub>2</sub> S	201 – 555	4,4'-thiobisphenol
A3 n = 12	=O at bridge atom	 Bisphenol S C <sub>12</sub> H <sub>10</sub> O <sub>4</sub> S	234 – 555	Bisphenol S 2,4-BPS
A4 n = 10	Structures most similar to BPA	 BPA C <sub>15</sub> H <sub>16</sub> O <sub>2</sub>	200 – 270	BPA BPB BPF

Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
A5 n = 7	Halogen on phenyl ring	 <p>TBBPA C<sub>15</sub>H<sub>12</sub>Br<sub>4</sub>O<sub>2</sub></p>	269 - 544	TetraBBPA Dichlorophen Dichloro-BPA
A6 n = 5	N-groups, COOH & Alkyl substituted (mixed group)	 <p>Phenol, 2,2'-methylenebis[5-(diethylamino)-] C<sub>21</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub></p>	286 - 425	
A7 n = 4	COO at bridge carbon	 <p>MBHA C<sub>15</sub>H<sub>14</sub>O<sub>4</sub></p>	244 - 300	MBHA
A8 n = 4	Halogenated alkyl groups on bridge carbon	 <p>Bisphenol AF C<sub>15</sub>H<sub>10</sub>F<sub>6</sub>O<sub>2</sub></p>	281 - 366	Bisphenol AF
B1 n = 7	=O at bridge atom	 <p>D-8 C<sub>15</sub>H<sub>16</sub>O<sub>4</sub>S</p>	230 - 294	D-8 BPS-MAE
B2 n = 5	S/O/N bridge atom (no =O)	 <p>4,4'-Thiodiresorcinol C<sub>12</sub>H<sub>10</sub>O<sub>4</sub>S</p>	215 - 362	
B3 n = 2	Ester	 <p>2-t-butyl-6-(3-t-butyl-5-methylbenzyl)-4-methylphenyl acrylate C<sub>26</sub>H<sub>34</sub>O<sub>3</sub></p>	395 - 409	

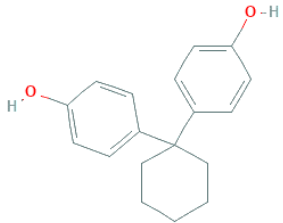
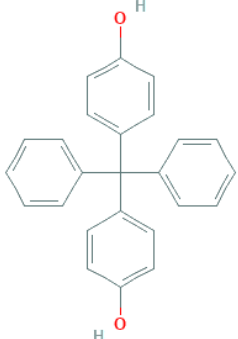
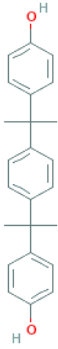
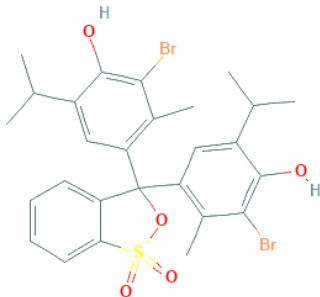


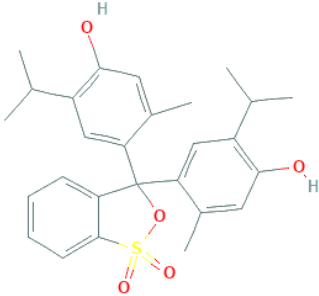
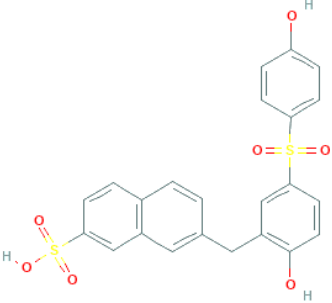
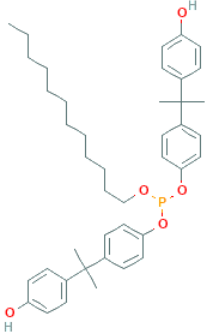
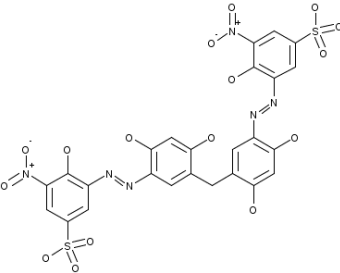
Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
B4 n = 2	Multi-OH on phenyl ring	 <p>4,4'-(5-Hydroxypentylidene) bis(1,3-benzenediol) C<sub>17</sub>H<sub>20</sub>O<sub>5</sub></p>	304 – 348	
B5 n = 2	Phosphate group	 <p>Phosphorous acid, didodecyl 4-[1-(4-hydroxyphenyl)-1-methylethyl]phenyl ester C<sub>39</sub>H<sub>65</sub>O<sub>4</sub>P</p>	388 – 629	
n = 1	Structure most similar to BPA	 <p>4-Cumylphenol C<sub>15</sub>H<sub>16</sub>O</p>	212	4-cumyl phenol
n = 1	Halogen on phenyl ring	<p>Na<sup>+</sup></p>  <p>Dichlorophen sodium salt C<sub>13</sub>H<sub>9</sub>Cl<sub>2</sub>NaO<sub>2</sub></p>	269	

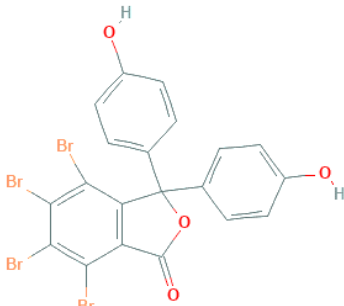
Abbreviations: A=Group 3.1; B=Group 3.2; n= number of chemicals in the subgroup

**Table 3-4.** Refined subgroups from Group 3.3 (C1 to C3) and Group 3.4 (D1 to D5). The final column identifies members of each subgroup that are more commonly

recognized, and are therefore expected to have available data to support hazard evaluation.

Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
C1 n = 20	Bridge atom inside ring	 <p>Bisphenol Z C<sub>18</sub>H<sub>20</sub>O<sub>2</sub></p>	268 – 430	Bisphenol TMC, Bisphenol FL (BHPF)
C2 n = 12	Substitution at ring atom	 <p>Bisphenol BP C<sub>25</sub>H<sub>20</sub>O<sub>2</sub></p>	290 – 435	Bisphenol AP
C3 n = 11	Ring substitution on phenyl ring	 <p>Bisphenol P C<sub>24</sub>H<sub>26</sub>O<sub>2</sub></p>	278 – 437	BPS-MPE, Bisphenol PH, Bisphenol M
D1 n = 23	Hindered	 <p>Bromothymol blue C<sub>27</sub>H<sub>28</sub>Br<sub>2</sub>O<sub>5</sub>S</p>	461 – 985	

Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
D2 n = 15	Partially hindered	 <p>Thymol blue C<sub>27</sub>H<sub>30</sub>O<sub>5</sub>S</p>	467 – 1104	
D3 n = 6	Sulfur atom bridge	 <p>2-Naphthalenesulfonic acid, 7-((2-hydroxy-5-((4-hydroxyphenyl)sulfonyl)phenyl)methyl)- C<sub>23</sub>H<sub>18</sub>O<sub>7</sub>S<sub>2</sub></p>	470 – 805	
D4 n = 2	Phosphate group	 <p>4,4'-Isopropylidenediphenol alkyl phosphite C<sub>42</sub>H<sub>55</sub>O<sub>5</sub>P</p>	514 – 671	
n = 1	Azo group	 <p>Iron, (mu-((3,3'-methylenebis((4,6-dihydroxy-3,1-phenylene)azo)bis(2(or 4)-hydroxy-5-nitrobenzenesulfonate))(6-)))di-, sodium hydrogen C<sub>25</sub>H<sub>18</sub>N<sub>6</sub>O<sub>16</sub>S<sub>2</sub></p>	(UVCB)	

Refined Subgroup	Basis	Example structure, with name and chemical formula	Molar mass range (g/mol)	Familiar member(s) in subgroup
n = 1	Bridge atom inside ring	 <p>4,5,6,7-Tetrabromophthaloin C<sub>20</sub>H<sub>10</sub>Br<sub>4</sub>O<sub>4</sub></p>	634	

### 3.6 Charge questions for the scoping and grouping approach

Charge questions for the BPA analogues and functional alternatives broad substances list and groupings:

1. Is the substance identification and grouping approach described for BPA analogues and functional alternatives adequate?
  - i. What are the strengths of the approach?
  - ii. Are there limitations to the approach, and if so, how do you recommend addressing them?
  
2. Have we captured the correct chemicals, consistent with the identified purpose?
  - i. Are there substances that were missed from the broad pool of structural analogues and known functional alternatives? If yes, please provide CAS RN and rationale for inclusion.
  - ii. Are there substances that should be omitted from the broad pool of structural analogues and known functional alternatives? If yes, please provide CAS RN and rationale for exclusion.
  - iii. Should any substance belong to a different refined subgroup than proposed? If so, please provide the rationale.

## 4. Next steps

### 4.1 Information gathering – mandatory survey

Further information gathering will be conducted through a section 71 notice under CEPA for substances identified as BPA analogues and functional alternatives. A mandatory survey (section 71 notice) is being considered for release in Summer 2021.

## 4.2 Problem formulation

Although problem formulation is commonly and explicitly used in other risk assessment programs internationally, it is proposed as a new formal initiative under the CMP. The goal of the proposed problem formulation step is to further scope potential emerging priorities and allow for flexibility in the proposed course of action to ensure that the Government of Canada is focusing efforts on the substances with greatest potential impact on human health and the environment. Problem formulation will also provide an opportunity for early consultation with stakeholders, thereby increasing communication and transparency for the identified priorities and associated regulatory considerations.

In the context of the CMP, problem formulation aims to further define the problem that was identified during the IRAP review and, if required, to develop a recommended course of action for resolving the stated problem. The main objectives of a problem formulation is to:

- 1) adequately scope substances that are applicable to the problem;
- 2) identify what is known about the use and potential exposure routes, as well as potential hazard for the substance/group;
- 3) identify any further considerations, which may include international activities; and
- 4) inform recommended outcomes and actions as relevant.

## 5. Summary

This document introduces and solicits feedback on the broad list and subgrouping of the BPA analogues and functional alternatives.

343 BPA analogues and functional alternatives were identified and triaged using structural filters into four groups based on structural similarity to BPA; a fifth group was derived based on filtering for evidence as a BPA functional alternative. The structures that were found to be most similar to BPA were further divided into 24 proposed subgroups (including four single substances) to support further information gathering and consideration.

Problem formulation is envisaged as having four main areas: (1) identifying the scope of substances; (2) reviewing the data landscape; (3) identifying considerations that are likely to impact the scope, direction, priority and timing of subsequent actions; and (4) recommending next steps.

## 6. References

- [ANSES] Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. 2013. Substitution du bisphénol A. (available in French only)
- Canada. 2012. Pollution Prevention Planning Notice for BPA. Canada Gazette. [accessed 2020 Feb 10].
- Danish Environmental Protection Agency. 2011. Migration of bisphenol A from cash register receipts and baby dummies.
- Danish Environmental Protection Agency. 2014. Alternative technologies and substances to bisphenol A (BPA) in thermal paper receipts [PDF] (Issue 1553).
- Dionisio KL, Frame AM, Goldsmith MR, Wambaugh JF, Liddell A, Cathey ., Smith D, Vail J, Ernstoff AS, Fantke P, Jolliet O, and Judson RS. 2015. Exploring consumer exposure pathways and patterns of use for chemicals in the environment. *Toxicology Reports*, 2, 228–237.
- Dionisio KL, Phillips K, Price PS, Grulke CM, Williams A, Biryol D, Hong T, and Isaacs KK. 2018. Data Descriptor: The Chemical and Products Database, a resource for exposure-relevant data on chemicals in consumer products. *Scientific Data*, 5(1), 1–9.
- [ECCC] Environment and Climate Change Canada. 2015. Bisphenol A in paper recycling mill effluents: environmental agreement. Ottawa (ON): Government of Canada. [accessed 2020 Feb 10].
- [ECCC] Environment and Climate Change Canada. 2020. Evaluation of the effectiveness of risk management measures for bisphenol A (BPA) – Ecological component. Gatineau (QC): Government of Canada.
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2010]. Proposed Risk Management Approach for Phenol, 4,4'-(1-methylethylidene) bis (Bisphenol A). Ottawa (ON): Government of Canada. [accessed 2020 Feb 11].
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2013]. Screening Assessment for The Challenge Phenol, 4,4'-(1-methylethylidene)bis-(Bisphenol A). Ottawa (ON): Government of Canada. [accessed 2020 Feb 11].
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2016]. Chemicals Management Plan. Ottawa (ON): Government of Canada. [accessed 2020 Feb. 10].
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2017]. The identification of risk assessment priorities. Ottawa (ON): Government of Canada. [accessed 2020 Feb 10].
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2019a]. Identification of Risk Assessment Priorities (IRAP). [accessed 2020 Feb 10].
- [ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified

- 2019b]. Toxic substances list. Ottawa (ON): Government of Canada. [accessed 2020 Feb. 10].
- European Chemicals Agency. 2017. Use of Bisphenol A and its alternatives in thermal paper in the EU 2014-16.
- European Food Safety Authority. 2015. Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. EFSA Journal, 13(1), 3978. [accessed 2020 Mar 19].
- Geens T, Goeyens L, and Covaci A. 2011. Are potential sources for human exposure to bisphenol-A overlooked? International Journal of Hygiene and Environmental Health, 214(5), 339–347. [accessed 2020 Feb 11].
- [HC] Health Canada. 2012. Health Canada’s Updated Assessment of Bisphenol A (BPA) Exposure from Food Sources. Ottawa (ON): Government of Canada. [accessed 2020 Feb 11].
- [HC] Health Canada. 2018. Bisphenol A (BPA) risk management approach: performance evaluation for BPA-HEALTH component. Ottawa (ON): Government of Canada. [accessed 2020 Feb 10].
- Isaacs KK, Goldsmith MR, Egeghy P, Phillips K, Brooks R, Hong T, and Wambaugh JF. 2016. Characterization and prediction of chemical functions and weight fractions in consumer products. Toxicology Reports 3, 723–732.
- Ma Y, Liu H, Wu J, Yuan L, Wang Y, Du X, Wang R, Marwa PW, Petlulu P, Chen X, and Zhang H. 2019. The adverse health effects of bisphenol A and related toxicity mechanisms. Environmental Research, 176(July).
- [NTP] National Toxicology Program (US). 2017. NTP Research Report on Biological Activity of Bisphenol A (BPA) Structural Analogues and Functional Alternatives.
- [NTP] National Toxicology Program (US). 2018. CLARITY-BPA Core Study: A Perinatal and Chronic Extended-Dose-Range Study of Bisphenol A in Rats. [accessed 2020 Mar 19]
- [OECD] Organisation for Economic Co-operation and Development. 2014. Guidance on grouping of chemicals. Series on Testing & Assessment 194.
- Pelch K, Wignall JA, Goldstone AE, Ross PK, Blain RB, Shapiro AJ, Holmgren SD, Hsieh JH, Svoboda D, Auerbach SS, Parham FM, Masten SA, Walker V, Rooney A, and Thayer KA. 2019. A scoping review of the health and toxicological activity of bisphenol A (BPA) structural analogues and functional alternatives. Toxicology, 424(June), 152235.
- Pivnenko K, Pedersen GA, Eriksson E, and Astrup TF. 2015. Bisphenol A and its structural analogues in household waste paper. Waste Management, 44, 39–47. [accessed 2020 Feb. 11].
- Rathee M, Singh J, and Malik P. 2012. Bisphenol A in dental sealants and its estrogen like effect. Indian Journal of Endocrinology and Metabolism, 16(3), 339. [accessed 2020 Feb 11].

Roberts G, Myatt GJ, Johnson WP, Cross KP, and Blower PE Jr. 2000. Leadscope: Software for exploring large sets of screening data. *J Chem Inf Comput Sci.* 40, 1302-1314.

United States Environmental Protection Agency. 2012. Bisphenol A Alternatives in Thermal Paper.

United States Environmental Protection Agency. 2017. [CompTox Chemicals Dashboard](#). [accessed 2020 Feb 11].



## APPENDIX A.

**Table A-1.** Thirty-four bisphenol substances identified through the 2017-2018 IRAP review

CAS RN	Common name (when available)	Name of Substance
77-40-7	BPB	4,4'-(1-methylpropylidene)bisphenol
79-97-0	BPC	Phenol, 4,4'-(1-methylethylidene)bis[2-methyl-
80-05-7	BPA	Phenol, 4,4'-(1-methylethylidene)bis-
80-07-9		Benzene, 1,1'-sulfonylbis[4-chloro-
80-09-1	BPS	Phenol, 4,4'-sulfonylbis-
127-54-8	BPG	Phenol, 4,4'-(1-methylethylidene)bis[2-(1-methylethyl)]-
599-64-4	4-Cumylphenol	Phenol, 4-(1-methyl-1-phenylethyl)-
620-92-8	4,4' BPF	Phenol, 4,4'-methylenebis-
843-55-0	BPZ	Phenol, 4,4'-cyclohexylidenebis-
1333-16-0; 87139-40-0	BPF (mixed isomers)	Phenol, 4,4'-methylenebis-
1478-61-1	BPAF	Phenol, 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]bis-
1571-75-1	BPAP	Phenol, 4,4'-(1-phenylethylidene)bis-
1675-54-3	BADGE	Oxirane, 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bis-
2081-08-5	BPE	Phenol, 4,4'-ethylidenebis-
2095-03-6	BFDGE	2,2'-methylenebis(p-phenyleneoxymethylene)bisoxirane
2167-51-3	BPP	Phenol, 4,4'-1,4-phenylenebis(1-methylethylidene)bis-
2467-02-9	BPF-ortho	Phenol, 2,2'-methylenebis-
2467-03-0	2,4'-BPF	Phenol, 2-[(4-hydroxyphenyl)methyl]-
2664-63-3	4,4'-Thiodiphenol	Phenol, 4,4'-thiobis-
3236-71-3	BHPF	Phenol, 4,4'-(9H-fluoren-9-ylidene)bis-
5129-00-0	MBHA	Benzeneacetic acid, 4-hydroxy- $\alpha$ -(4-hydroxyphenyl)-, methyl ester
5397-34-2	2,4'-BPS	Phenol, 2-[(4-hydroxyphenyl)sulfonyl]-
5613-46-7		Phenol, 4,4'-(1-methylethylidene)bis[2,6-dimethyl-
6807-17-6		Phenol, 4,4'-(1,3-dimethylbutylidene)bis-
13595-25-0	BPM	Phenol, 4,4'-[1,3-phenylenebis(1-methylethylidene)]bis-
24038-68-4	BPPH; BisOPP-A	1,1'-Biphenyl-2-ol, 5,5''-(1-methylethylidene)bis-
41481-66-7	TGSA	Phenol, 4,4'-sulfonylbis[2-(2-propenyl)-
63134-33-8	BPS-MPE	Phenol, 4-[[4-(phenylmethoxy)phenyl]sulfonyl]-
93589-69-6	DD-70	Phenol, 4,4'-methylenebis(oxy-2,1-ethanediythio)bis-
95235-30-6	D-8	Phenol, 4-[[4-(1-methylethoxy)phenyl]sulfonyl]-
97042-18-7	BPS-MAE	bis(4-Hydroxyphenyl) sulfone monoallyl ether
129188-99-4	Bisphenol TMC	Phenol, 4,4'-(3,3,5-trimethylcyclohexylidene)bis-
191680-83-8	D-90	Phenol, 4,4'-sulfonylbis-, polymer with 1,1'-oxybis(2-chloroethane)

## APPENDIX B. List of 204 BPA analogues and functional alternatives comprising Group 3.1, 3.2, 3.3, 3.4, and Group 4

**Table B-1.** Complete list of BPA analogues and functional alternatives, and proposed groups and refined subgroups

CAS RN	Name of Substance	Common Name (if available)	Group	Read-Across Group
79-96-9	Phenol, 4,4'-(1-methylethylidene)bis[2-(1,1-dimethylethyl)-		3.1	A1
85-60-9	Phenol, 4,4'-butylidenebis[2-(1,1-dimethylethyl)-5-methyl-		3.1	A1
88-24-4	Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-ethyl-		3.1	A1
118-82-1	Phenol, 4,4'-methylenebis[2,6-bis(1,1-dimethylethyl)-		3.1	A1
119-47-1	Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-		3.1	A1
127-54-8	Phenol, 4,4'-(1-methylethylidene)bis[2-(1-methylethyl)-	Bisphenol G	3.1	A1
1745-89-7	Phenol, 4,4'-(1-methylethylidene)bis[2-(2-propenyl)-		3.1	A1
5613-46-7	Phenol, 4,4'-(1-methylethylidene)bis[2,6-dimethyl-		3.1	A1
7292-14-0	Phenol, 2,2'-(3,5,5-trimethylhexylidene)bis[4,6-dimethyl-		3.1	A1
7786-17-6	Phenol, 2,2'-methylenebis[4-methyl-6-nonyl-		3.1	A1
13676-82-9	Phenol, 4,4'-(1-methylethylidene)bis[2,6-bis(1,1-dimethylethyl)-		3.1	A1
14362-12-0	Phenol, 2,2'-methylenebis[4,6-bis(1,1-dimethylethyl)-		3.1	A1
33145-10-7	Phenol, 2,2'-(2-methylpropylidene)bis[4,6-dimethyl-		3.1	A1
35958-30-6	Phenol, 2,2'-ethylidenebis[4,6-bis(1,1-dimethylethyl)-		3.1	A1
50378-93-3	Phenol, 2,2'-methylenebis[4,6-bis(1,1-dimethylpropyl)-		3.1	A1
67923-95-9	Phenol, methylenebis[dinonyl-		3.1	A1
72672-54-9	Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-(1-methylpropyl)-		3.1	A1
72672-55-0	Phenol, 2,2'-ethylidenebis[6-(1,1-dimethylethyl)-4-(1-methylpropyl)-		3.1	A1
90-66-4	Phenol, 2,2'-thiobis[6-(1,1-dimethylethyl)-4-methyl-		3.1	A2
96-66-2	Phenol, 4,4'-thiobis[2-(1,1-dimethylethyl)-6-methyl-		3.1	A2
96-69-5	Phenol, 4,4'-thiobis[2-(1,1-dimethylethyl)-5-methyl-		3.1	A2
97-18-7	Phenol, 2,2'-thiobis[4,6-dichloro-	Bithionol	3.1	A2
1752-24-5	Phenol, 4,4'-iminobis-		3.1	A2
1820-99-1	Benzoic acid, 3,3'-thiobis[6-hydroxy-		3.1	A2
1965-09-9	Phenol, 4,4'-oxybis-		3.1	A2
2664-63-3	Phenol, 4,4'-thiobis-	4,4'-Thiodiphenol	3.1	A2
3294-03-9	Phenol, 2,2'-thiobis[4-(1,1,3,3-tetramethylbutyl)-		3.1	A2

3818-54-0	Phenol, 4,4'-thiobis[3-(1,1-dimethylethyl)-5-methyl-		3.1	A2
13693-59-9	Phenol, 2,2'-thiobis-		3.1	A2
17755-37-2	Phenol, 2-[(4-hydroxyphenyl)thio]-		3.1	A2
68815-67-8	Phenol, thiobis[tetrapropylene-		3.1	A2
80-09-1	Phenol, 4,4'-sulfonylbis-	Bisphenol S	3.1	A3
131-53-3	Methanone, (2-hydroxy-4-methoxyphenyl)(2-hydroxyphenyl)-		3.1	A3
131-54-4	Methanone, bis(2-hydroxy-4-methoxyphenyl)-		3.1	A3
1774-34-1	Phenol, 4,4'-sulfinylbis-		3.1	A3
3121-60-6	Benzenesulfonic acid, 4-hydroxy-5-(2-hydroxy-4-methoxybenzoyl)-2-methoxy-, monosodium salt		3.1	A3
5397-34-2	Phenol, 2-[(4-hydroxyphenyl)sulfonyl]-	2,4'-BPS	3.1	A3
13288-70-5	Phenol, 4,4'-sulfonylbis[2,6-dimethyl-		3.1	A3
15038-67-2	Phenol, 2,2'-sulfonylbis-		3.1	A3
15452-89-8	Phenol, 2,2'-sulfonylbis[4-(1,1,3,3-tetramethylbutyl)-		3.1	A3
39635-79-5	Phenol, 4,4'-sulfonylbis[2,6-dibromo-		3.1	A3
41481-66-7	Phenol, 4,4'-sulfonylbis[2-(2-propenyl)-	TGSA	3.1	A3
63270-28-0	Benzenesulfonic acid, 3-hydroxy-2-(2-hydroxy-4-methoxysulfobenzoyl)-5-methoxy-, disodium salt		3.1	A3
77-40-7	4,4'-(1-methylpropylidene)bisphenol	Bisphenol B	3.1	A4
79-97-0	Phenol, 4,4'-(1-methylethylidene)bis[2-methyl-	Bisphenol C	3.1	A4
80-05-7	Phenol, 4,4'-(1-methylethylidene)bis-	Bisphenol A	3.1	A4
620-92-8	Phenol, 4,4'-methylenebis-	Bisphenol F	3.1	A4
837-08-1	Phenol, 2-[1-(4-hydroxyphenyl)-1-methylethyl]-		3.1	A4
2081-08-5	Phenol,4,4'-ethylidenebis-	Bisphenol E	3.1	A4
2467-02-9	Phenol, 2,2'-methylenebis-	Bisphenol F-ortho	3.1	A4
2467-03-0	Phenol, 2-[(4-hydroxyphenyl)methyl]-	2,4'-Bisphenol F	3.1	A4
3236-63-3	Phenol, 2,2'-methylenebis[4-methyl-		3.1	A4
6807-17-6	Phenol, 4,4'-(1,3-dimethylbutylidene)bis-		3.1	A4
70-30-4	Phenol, 2,2'-methylenebis[3,4,6-trichloro-		3.1	A5
79-94-7	Phenol, 4,4'-(1-methylethylidene)bis[2,6-dibromo-	TBBPA	3.1	A5
79-98-1	Phenol, 4,4'-(1-methylethylidene)bis[2-chloro-		3.1	A5
97-23-4	Phenol, 2,2'-methylenebis[4-chloro-		3.1	A5
1940-20-1	Phenol, 3,4,4',5',6,6'-hexachloro-2,2'-methylene-di-		3.1	A5
6386-73-8	Phenol, 2,6-dibromo-4-[1-(3-bromo-4-hydroxyphenyl)-1-methylethyl]-		3.1	A5
16669-42-4	Phenol, 4,4'-isopropylidenebis[2,3,5,6-tetrachloro-		3.1	A5
5329-21-5	Phenol, 4,4'-(1-methylethylidene)bis[2-nitro-		3.1	A6
6274-83-5	Phenol, 2,2'-methylenebis[5-(diethylamino)-		3.1	A6
27496-82-8	Benzoic acid, methylenebis[2-hydroxy-		3.1	A6

27725-17-3	Phenol, 2,2'-methylenebis[4-(1,1,3,3-tetramethylbutyl)-		3.1	A6
63468-95-1	Phenol, 2,2'-methylenebis[5-(dimethylamino)-		3.1	A6
126-00-1	Benzenebutanoic acid, 4-hydroxy- $\gamma$ -(4-hydroxyphenyl)- $\gamma$ -methyl-		3.1	A7
5129-00-0	Benzeneacetic acid, 4-hydroxy- $\alpha$ -(4-hydroxyphenyl)-, methyl ester	MBHA	3.1	A7
40232-93-7	Benzeneacetic acid, 4-hydroxy- $\alpha$ -(4-hydroxyphenyl)-		3.1	A7
71077-33-3	Benzeneacetic acid, 4-hydroxy- $\alpha$ -(4-hydroxyphenyl)-, butyl ester		3.1	A7
1478-61-1	Phenol, 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]bis-	Bisphenol AF	3.1	A8
2971-36-0	Phenol, 4,4'-(2,2,2-trichloroethylidene)bis-		3.1	A8
14868-03-2	Phenol, 4,4'-(dichloroethenylidene)bis-	Bisphenol C	3.1	A8
83558-87-6	Phenol, 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]bis[2-amino-		3.1	A8
131-55-5	Methanone, bis(2,4-dihydroxyphenyl)-		3.2	B1
519-34-6	Methanone, (3,4-dihydroxyphenyl)(2,4,6-trihydroxyphenyl)-		3.2	B1
1470-79-7	Methanone, (2,4-dihydroxyphenyl)(4-hydroxyphenyl)-		3.2	B1
7392-62-3	Methanone, (2,4-dihydroxyphenyl)(2-hydroxy-4-methoxyphenyl)-		3.2	B1
28341-67-5	1,3-Benzenediol, 4,4'-sulfinylbis[2-methyl-		3.2	B1
95235-30-6	Phenol, 4-[[4-(1-methylethoxy)phenyl]sulfonyl]-	D-8	3.2	B1
97042-18-7	bis(4-Hydroxyphenyl) sulfone monoallyl ether	BPS-MAE	3.2	B1
97-29-0	1,3-Benzenediol, 4,4'-thiobis-		3.2	B2
27151-54-8	Phenol, 4-[(4-methoxyphenyl)amino]-		3.2	B2
28341-66-4	1,3-Benzenediol, 4,4'-thiobis[2-methyl-		3.2	B2
28341-68-6	Resorcinol, 4,4'-thiobis[6-chloro-		3.2	B2
72361-37-6	1,2-Benzenediol, thiobis[4-(1,1-dimethylethyl)-		3.2	B2
61167-58-6	2-Propenoic acid, 2-(1,1-dimethylethyl)-6-[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]methyl]-4-methylphenyl ester		3.2	B3
61167-60-0	2-Propenoic acid, 2-methyl-, 2-(1,1-dimethylethyl)-6-[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]methyl]-4-methylphenyl ester		3.2	B3
3957-22-0	1,3-Benzenedimethanol, 5,5'-(1-methylethylidene)bis[2-hydroxy-		3.2	B4
67828-51-7	1,3-Benzenediol, 4,4'-(5-hydroxypentylidene)bis-		3.2	B4
59189-82-1	Phosphorous acid, didodecyl 4-[1-(4-hydroxyphenyl)-1-methylethyl]phenyl ester		3.2	B5
181028-79-5	Phosphoric trichloride, reaction products with bisphenol A and phenol		3.2	B5
599-64-4	Phenol, 4-(1-methyl-1-phenylethyl)-	4-Cumylphenol	3.2	B6
10187-52-7	Phenol, 2,2'-methylenebis[4-chloro-, monosodium salt		3.2	B7

77-09-8	1(3H)-Isobenzofuranone, 3,3-bis(4-hydroxyphenyl)-		3.3	C1
115-41-3	1,2-Benzenediol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis-, S,S-dioxide		3.3	C1
125-20-2	1(3H)-Isobenzofuranone, 3,3-bis[4-hydroxy-2-methyl-5-(1-methylethyl)phenyl]-		3.3	C1
125-31-5	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2,5-dimethyl-, S,S-dioxide		3.3	C1
143-74-8	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis-, S,S-dioxide		3.3	C1
596-27-0	1(3H)-Isobenzofuranone, 3,3-bis(4-hydroxy-3-methylphenyl)-		3.3	C1
596-28-1	1(3H)-Isobenzofuranone, 3,3-bis(3,4-dihydroxyphenyl)-		3.3	C1
843-55-0	Phenol, 4,4'-cyclohexylidenebis-	Bisphenol Z	3.3	C1
1733-12-6	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2-methyl-, S,S-dioxide		3.3	C1
1943-96-0	Phenol, 4,4'-bicyclo[2.2.1]hept-2-ylidenebis-		3.3	C1
1943-97-1	Phenol, 4,4'-(octahydro-4,7-methano-5H-inden-5-ylidene)bis-		3.3	C1
2303-01-7	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[3-methyl-, S,S-dioxide		3.3	C1
3236-71-3	Phenol, 4,4'-(9H-fluoren-9-ylidene)bis-	BHPF	3.3	C1
4430-20-0	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2-chloro-, S,S-dioxide		3.3	C1
34487-61-1	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis-, S,S-dioxide, monosodium salt		3.3	C1
47465-97-4	2H-Indol-2-one, 1,3-dihydro-3,3-bis(4-hydroxy-3-methylphenyl)-		3.3	C1
62625-29-0	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2-methyl-, S,S-dioxide, monosodium salt		3.3	C1
62625-31-4	Phenol, 4,4'-(3H-1,2-benzoxathiol-3-ylidene)bis[3-methyl-, S,S-dioxide, monosodium salt		3.3	C1
63665-75-8	Phenol, 4,4'-(1,2-benzisothiazol-3(2H)-ylidene)bis[2-methyl-, S,S-dioxide		3.3	C1
129188-99-4	Phenol, 4,4'-(3,3,5-trimethylcyclohexylidene)bis-	Bisphenol TMC	3.3	C1
81-90-3	Benzoic acid, 2-[bis(4-hydroxyphenyl)methyl]-		3.3	C2
569-58-4	Benzoic acid, 5-[(3-carboxy-4-hydroxyphenyl)(3-carboxy-4-oxo-2,5-cyclohexadien-1-ylidene)methyl]-2-hydroxy-, triammonium salt		3.3	C2
603-45-2	2,5-Cyclohexadien-1-one, 4-[bis(4-hydroxyphenyl)methylene]-		3.3	C2
1571-75-1	Phenol, 4,4'-(1-phenylethylidene)bis-	Bisphenol AP	3.3	C2
1844-01-5	Phenol, 4,4'-(diphenylmethylene)bis-	Bisphenol BP	3.3	C2
4431-00-9	Benzoic acid, 5-[(3-carboxy-4-hydroxyphenyl)(3-carboxy-4-oxo-2,5-cyclohexadien-1-ylidene)methyl]-2-hydroxy-		3.3	C2
7727-33-5	Phenol, 4,4',4'',4'''-(1,2-ethanediylidene)tetrakis-		3.3	C2

10143-03-0	Benzoic acid, 3,3'-[[4-(dimethylamino)phenyl]methylene]bis[6-hydroxy-5-methyl-		3.3	C2
25639-41-2	Phenol, methylidynetris-		3.3	C2
27955-94-8	Phenol, 4,4',4''-ethylidynetris-		3.3	C2
29036-21-3	Phenol, (1-propanyl-3-ylidene)tris-		3.3	C2
63450-78-2	Benzoic acid, 2-[bis(4-hydroxyphenyl)methyl]-, ethyl ester		3.3	C2
77-62-3	Phenol, 2,2'-methylenebis[4-methyl-6-(1-methylcyclohexyl)-		3.3	C3
1620-68-4	Phenol, 2,6-bis[(2-hydroxy-5-methylphenyl)methyl]-4-methyl-		3.3	C3
2167-51-3	Phenol, 4,4'-1,4-phenylenebis(1-methylethylidene)bis-	Bisphenol P	3.3	C3
2300-15-4	Phenol, 2,4-bis[1-(4-hydroxyphenyl)-1-methylethyl]-		3.3	C3
4066-02-8	Phenol, 2,2'-methylenebis[6-cyclohexyl-4-methyl-		3.3	C3
13595-25-0	Phenol, 4,4'-[1,3-phenylenebis(1-methylethylidene)]bis-	Bisphenol M	3.3	C3
14200-84-1	Phenol, 3-(3-phenoxyphenoxy)-		3.3	C3
24038-68-4	1,1'-Biphenyl-2-ol, 5,5''-(1-methylethylidene)bis-	Bisphenol PH	3.3	C3
31265-39-1	1,3-Benzenediol, 4,4'-[(5-chloro-2-hydroxy-1,3-phenylene)bis(methylene)]bis-		3.3	C3
63134-33-8	Phenol, 4-[[4-(phenylmethoxy)phenyl]sulfonyl]-	BPS-MPE	3.3	C3
71113-22-9	Phenol, 2,2'-methylenebis[4-(1-methyl-1-phenylethyl)-		3.3	C3
76-59-5	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2-bromo-3-methyl-6-(1-methylethyl)-, S,S-dioxide		3.4	D1
76-60-8	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromo-3-methyl-, S,S-dioxide		3.4	D1
76-62-0	1(3H)-Isobenzofuranone, 3,3-bis(3,5-dibromo-4-hydroxyphenyl)-		3.4	D1
90-68-6	Phenol, 2,6-bis[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]methyl]-4-methyl-		3.4	D1
115-39-9	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromo-, S,S-dioxide		3.4	D1
115-40-2	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2-bromo-6-methyl-, S,S-dioxide		3.4	D1
1611-35-4	Glycine, N,N'-[3H-2,1-benzoxathiol-3-ylidenebis[(6-hydroxy-5-methyl-3,1-phenylene)methylene]]bis[N-(carboxymethyl)-, S,S-dioxide		3.4	D1
2411-89-4	Glycine, N,N'-[(3-oxo-1(3H)-isobenzofuranylidene)bis[(6-hydroxy-5-methyl-3,1-phenylene)methylene]]bis[N-(carboxymethyl)-		3.4	D1
2588-24-1	Benzoic acid, 3,3'-(3H-2,1-benzoxathiol-3-ylidene)bis[6-hydroxy-5-methyl-, S,S-dioxide		3.4	D1
4430-25-5	Phenol, 4,4'-(4,5,6,7-tetrabromo-3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dibromo-, S,S-dioxide		3.4	D1
13027-28-6	1(3H)-Isobenzofuranone, 4,5,6,7-tetrabromo-3,3-bis(4-hydroxyphenyl)-		3.4	D1

31851-03-3	Phenol, 2,6-bis[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]octahydro-4,7-methano-1H-indenyl]-4-methyl-		3.4	D1
41699-00-7	Phenol, 2,2'-(octahydro-4,7-methano-1H-indenediyl)bis[6-(1,1-dimethylethyl)-4-methyl-		3.4	D1
57564-54-2	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[2,6-dinitro-, S,S-dioxide		3.4	D1
57569-40-1	1,4-Benzenedicarboxylic acid, bis[2-(1,1-dimethylethyl)-6-[[3-(1,1-dimethylethyl)-2-hydroxy-5-methylphenyl]methyl]-4-methylphenyl] ester		3.4	D1
57964-01-9	[1,1'-Biphenyl]-4-ol, 3,3''-thiobis[4',5-bis(1,1-dimethylethyl)-		3.4	D1
61931-71-3	Benzoic acid, 2-[bis(3,5-dibromo-4-hydroxyphenyl)methyl]-, ethyl ester		3.4	D1
64131-28-8	Phenol, 2,6-bis[(2-hydroxy-3,5-dinonylphenyl)methyl]-4-nonyl-		3.4	D1
67828-35-7	Phenol, 2,6-dibromo-4-[3-(3,5-dibromo-4-butoxyphenyl)-3H-2,1-benzoxathiol-3-yl]-, S,S-dioxide		3.4	D1
68510-93-0	1-Naphthalenesulfonic acid, 6-diazo-5,6-dihydro-5-oxo-, ester with phenyl(2,3,4-trihydroxyphenyl)methanone		3.4	D1
69119-80-8	Methanone, [methylenebis(2-hydroxy-4-methoxy-3,1-phenylene)]bis[phenyl-		3.4	D1
70367-99-6	1,2-Benzisothiazole-2(3H)-carboxylic acid, 3,3-bis(4-hydroxy-3,5-dimethoxyphenyl)-, 2-(methylsulfonyl)ethyl ester, 1,1-dioxide		3.4	D1
71113-23-0	Phenol, 2,2'-methylenebis[4,6-bis(1-methyl-1-phenylethyl)-		3.4	D1
103597-45-1	Phenol, 2,2'-methylenebis[6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)-		3.4	D1
76-61-9	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[5-methyl-2-(1-methylethyl)-, S,S-dioxide		3.4	D2
1843-03-4	Phenol, 4,4',4''-(1-methyl-1-propanyl-3-ylidene)tris[2-(1,1-dimethylethyl)-5-methyl-		3.4	D2
10496-54-5	1(3H)-Isobenzofuranone, 3-[4-hydroxy-2-methyl-5-(1-methylethyl)phenyl]-3-[2-methyl-5-(1-methylethyl)-4-(phosphonooxy)phenyl]-, magnesium salt (1:1)		3.4	D2
17016-43-2	1(3H)-Isobenzofuranone, 3-[4-hydroxy-2-methyl-5-(1-methylethyl)phenyl]-3-[2-methyl-5-(1-methylethyl)-4-(phosphonooxy)phenyl]-		3.4	D2
20227-53-6	Phosphorous acid, 2-(1,1-dimethylethyl)-4-[1-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]phenyl bis(4-nonylphenyl) ester		3.4	D2
28749-63-5	1(3H)-Isobenzofuranone, 3-[4-hydroxy-2-methyl-5-(1-methylethyl)phenyl]-3-[2-methyl-5-(1-methylethyl)-4-(phosphonooxy)phenyl]-, sodium salt		3.4	D2
32509-66-3	Benzenepropanoic acid, 3-(1,1-dimethylethyl)-β-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-4-hydroxy-β-methyl-, 1,2-ethanediyl ester		3.4	D2

36339-47-6	Phenol, 2-(1,1-dimethylethyl)-4-[[5-(1,1-dimethylethyl)-4-hydroxy-2-methylphenyl]thio]-5-methyl-, 1,1',1''-phosphite		3.4	D2
40703-84-2	Phenol, 2,2',2''-[1,3,5-triazine-2,4,6-triyltris[oxy[3-(1,1-dimethylethyl)-5-methyl-2,1-phenylene]methylene]]tris[6-(1,1-dimethylethyl)-4-methyl-		3.4	D2
62609-87-4	Benzenesulfonic acid, 3,3'-(3-oxo-1(3H)-isobenzofuranylidene)bis[6-hydroxy-, trisodium salt		3.4	D2
62625-21-2	Phenol, 4,4'-(3H-2,1-benzoxathiol-3-ylidene)bis[5-methyl-2-(1-methylethyl)-, S,S-dioxide, monosodium salt		3.4	D2
68134-20-3	2,7-Naphthalenedisulfonic acid, 4-amino-6-[(2-chloro-4-nitrophenyl)azo]-5-hydroxy-3-[[2-hydroxy-4-[[3-hydroxy-4-[[4-(4-nitro-2-sulfophenyl)amino]phenyl]azo]phenyl]amino]phenyl]azo]-		3.4	D2
68716-15-4	Methanone, [methylenebis(6-hydroxy-4-methoxy-3,1-phenylene)]bis[phenyl-		3.4	D2
72139-00-5	2-Naphthalenesulfonic acid, 3-[(2-chloro-4-nitrophenyl)azo]-4-hydroxy-7-[[2-hydroxy-4-[[3-hydroxy-4-[[4-(4-nitro-2-sulfophenyl)amino]phenyl]azo]phenyl]amino]phenyl]azo]-		3.4	D2
85186-33-0	Iron, [ $\mu$ -[[3,3'-methylenebis[(4,6-dihydroxy-3,1-phenylene)azo]bis[2(or 4)-hydroxy-5-nitrobenzenesulfonato]](6-)]di-, sodium hydrogen		3.4	D2
111850-25-0	Phenol, 4,4',4''-(1-methyl-1-propanyl-3-ylidene)tris[2-cyclohexyl-5-methyl-		3.4	D2
60247-61-2	Pentanamide, N-[2-chloro-5-[(hexadecylsulfonyl)amino]phenyl]-2-[4-[(4-hydroxyphenyl)sulfonyl]phenoxy]-4,4-dimethyl-3-oxo-		3.4	D3
66214-40-2	2-Naphthalenesulfonic acid, 7-[[2-hydroxy-5-[(4-hydroxyphenyl)sulfonyl]phenyl]methyl]-		3.4	D3
66327-55-7	2-Naphthalenesulfonic acid, 7-[[2-hydroxy-5-[(4-hydroxyphenyl)sulfonyl]phenyl]methyl](1-methylpropyl)-, monoammonium salt		3.4	D3
68310-82-7	2-Naphthalenesulfonic acid, 3-[[5-hydroxy-2-[(4-hydroxyphenyl)sulfonyl]phenyl]methyl]-		3.4	D3
68959-14-8	2-Naphthalenesulfonic acid, 3-[[5-hydroxy-2-[(4-hydroxyphenyl)sulfonyl]phenyl]methyl]-, monosodium salt		3.4	D3
71463-72-4	Phenol, 4-[(4-hydroxy-2-methylphenyl)thio]-3-methyl-, 1,1',1''-phosphate		3.4	D3
60381-07-9	Phosphorous acid, dodecyl bis[4-[1-(4-hydroxyphenyl)-1-methylethyl]phenyl] ester		3.4	D4
64022-67-9	Phenol, 4-[1-methyl-1-[4-[(9-phenoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undec-3-yl)oxy]phenyl]ethyl]-		3.4	D4
80-07-9	Benzene, 1,1'-sulfonylbis[4-chloro-		4	
94-18-8	Benzoic acid, 4-hydroxy-, phenylmethyl ester	PHBB	4	
123-31-9	1,4-Benzenediol	Hydroquinone	4	



1675-54-3	Oxirane, 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bis-	BADGE	4	
2095-03-6	2,2'-methylenebis(p-phenyleneoxymethylene)bisoxirane	BFDGE	4	
3188-83-8	Benzenemethanol, 5-[1-methyl-1-[4-(oxiranylmethoxy)phenyl]ethyl]-2-(oxiranylmethoxy)-		4	
5945-33-5	Phosphoric acid, P,P'-[(1-methylethylidene)di-4,1-phenylene] P,P,P',P'-tetraphenyl ester	Fyroflex BDP	4	
7328-97-4	Oxirane, 2,2',2'',2'''-[1,2-ethanediylidenetetrakis(4,1-phenyleneoxymethylene)]tetrakis-		4	
25068-38-6	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane	Polymerized BADGE with BPA resins	4	
39382-25-7	2-Butenedioic acid (E)-, polymer with $\alpha,\alpha'$ -[(1-methylethylidene)di-4,1-phenylene]bis[ $\omega$ -hydroxypoly[oxy(methyl-1,2-ethanediyl)]]	Bisphenol A propylene oxide fumarate polymer	4	
39817-09-9	Oxirane, 2,2'-[methylenebis(phenyleneoxymethylene)]bis-		4	
47758-37-2	Oxirane, 2,2'-[9H-fluoren-9-ylidenebis(4,1-phenyleneoxymethylene)]bis-		4	
66072-38-6	Oxirane, 2,2',2''-[methylidynetris(phenyleneoxymethylene)]tris-		4	
67786-03-2	Oxirane, 2,2'-[[[2-(oxiranylmethoxy)phenyl]methylene]bis(4,1-phenyleneoxymethylene)]bis-		4	
93589-69-6	Phenol, 4,4'-methylenebis(oxy-2,1-ethanediylthio)bis-	DD-70	4	
113693-69-9	Phenol, 4,4'-methylenebis[2,6-dimethyl-, polymer with 2-(chloromethyl)oxirane	Tetramethyl bisphenol F epoxy resin	4	
151882-81-4	Benzenesulfonamide, N,N'-[methylenebis(4,1-phenyleneiminocarbonyl)]bis[4-methyl-	BTUM	4	
191680-83-8	Phenol, 4,4'-sulfonylbis-, polymer with 1,1'-oxybis(2-chloroethane)	D-90	4	
232938-43-1	Benzenesulfonamide, 4-methyl-N-[[[3-[[4-methylphenyl]sulfonyl]oxy]phenyl]amino]carbonyl]	Pergafast 201	4	
321860-75-7	Phenol, reaction products with 4,4'-sulfonylbis[benzenamine] and 2,4-TDI	UU (urea-urethane compound)	4	