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Chemicals of High Concern. Triennial Update Documentation. 2015

Maine Center for Disease Control and Prevention

Chemicals of High Concern

Triennial Update Documentation

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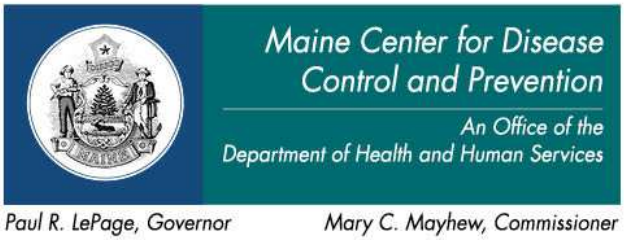

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Appendix I. Chemicals of High Concern 2015 Triennial Update Chemical-Specific Inclusion Criteria.

Appendix II. 2015 List of Chemicals of High Concern.

1. Summary

Maine Revised Statute Title 38, Chapter 16-D: *Toxic Chemicals in Children's Products* requires the Maine Department of Environmental Protection (MEDEP), in concurrence with the Maine Center for Disease Control and Prevention (MECDC), to develop and maintain a list of Chemicals of Concern (COC), a list of Chemicals of High Concern (CHC) and subsequently a list of priority chemicals which are subject to potential reporting requirements and/or regulation. The COC list was developed in 2010 and revised in 2011 according to statutory revisions and contains 1,384 chemicals[1]. The CHC list, which can contain no more than 70 chemicals, was derived from the COC list following statutory requirements and a prioritizing methodology developed by the MECDC and described in detail in the 2012 Deriving Chemicals of High Concern Process documentation[2]. The CHC list was published in 2012 and listed 49 chemicals of high concern. Since 2012, eight chemicals from the CHC list have been designated as priority chemicals.

The *Toxic Chemicals in Children's Products* statute requires the MEDEP Commissioner to update the CHC list once every 3 years[3]. Per statute, the update requires the removal of chemicals from the CHC list that are designated as priority chemicals, as well as removal of chemicals that no longer meet the CHC criteria. The statute also permits the MEDEP Commissioner to identify additional chemicals of high concern, so long as the chemicals meet the CHC listing criteria and the CHC list contains no more than 70 chemicals.

This document presents the first triennial update of the CHC list published in July 2012. The triennial update was focused on removing chemicals from the CHC list now designated as priority chemicals, and removing chemicals that do not meet the CHC criteria. The updated CHC list now contains 36 chemicals. For the 2015 update, 13 chemicals were removed from the 2012 CHC list. Eight chemicals were removed because they are now listed as priority chemicals. In response to petitions to delist specific chemicals, one chemical was removed from the CHC list, while another chemical CHC listing was modified. Based on review, four chemicals were removed because they do not meet the statutory CHC identification criteria.

The MEDEP and MECDC intend to review and update the CHC selection process to identify new chemicals of high concern and subsequent priority chemicals during the next three years. One approach under consideration would be to revise the interpretation of weight-of-evidence toxicity criteria initially used to generate the 2012 CHC list to meet the standard of "*strong* credible scientific evidence" (e.g., include probable human carcinogens rather than just known human carcinogens, consider both category 1A and 1B reproductive classifications by the Japanese GHS). This approach would expand the potential CHC list considerably, which would then be narrowed based on exposure information, such as biomonitoring data.

[1] http://www.maine.gov/dep/safechem/concern/index.html

[2] http://www.maine.gov/dep/safechem/highconcern/index.html

[3] MRS Title 38, Chapter 16-D:TOXIC CHEMICALS IN CHILDREN'S PRODUCTS. 38 §1693-A. Subsection 3. http://www.mainelegislature.org/legis/statutes/38/title38ch16-Dsec0.html

2. 2012 Derivation of Chemicals of High Concern

The 2012 chemicals of high concern (CHC) identification process began with the list of chemicals of concern (COC) published in 2011. The COC list contained 1,384 chemicals that in accordance with statute were listed by an authoritative governmental entity on the basis of credible scientific evidence[4] as being:

A. A carcinogen, a reproductive or developmental toxicant or an endocrine disruptor;

B. Persistent, bioaccumulative and toxic; or

C. Very persistent and very bioaccumulative.

According to statute the CHC list can contain no more than 70 chemicals. Identification of CHC requires that the chemical is on the COC list and meets additional toxicity and exposure criteria as defined by statute. The toxicity criteria are defined as *strong* credible scientific evidence that the chemical is a reproductive or developmental toxicant, endocrine disruptor or human carcinogen. The exposure criteria are defined as *strong* credible scientific evidence that:

A. The chemical has been found through biomonitoring to be present in human blood, including umbilical cord blood, breast milk, urine or other bodily tissues or fluids;

B. The chemical has been found through sampling and analysis to be present in household dust, indoor air or drinking water or elsewhere in the home environment; or

C. The chemical is present in a consumer product used or present in the home.

To narrow the list of 1,384 COC to no more than 70 CHC, the MECDC followed an approach developed by Washington State for their Children's Safe Products Act[5] and detailed in the 2012 Deriving Chemicals of High Concern Process documentation. Briefly, Washington State identified 476 chemicals that had both evidence of toxicity and exposure from two larger lists (a list of 2,044 high priority chemicals, which contained all of the 1,384 chemicals of concern identified by the State of Maine, and a list of 2,219 chemicals with evidence of potential child exposure). The list of 476 chemicals was reduced to 184 chemicals through removal of chemicals that were regulated under existing laws, chemicals that were combustion products, and chemicals with limited toxicity data or toxicity primarily concerned with ecological endpoints.

[4] Credible scientific evidence is defined by statute as the results of a study, the experimental design and conduct of which have undergone independent scientific peer review, that are published in a peer-reviewed journal or publication of an authoritative federal or international governmental agency, including but not limited to the United States Department of Health and Human Services, National Toxicology Program, Food and Drug Administration and Centers for Disease Control and Prevention; the United States Environmental Protection Agency; the World Health Organization; and the European Union, European Chemicals Agency.

[5] Washington State's Children's Safe Products Act. http://www.ecy.wa.gov/programs/swfa/cspa/

The MECDC then applied a three-step process to the Washington State list of 184 chemicals to derive a final CHC list of no more than 70 chemicals. Step 1 included removal of chemicals that were not on the State of Maine COC list, chemicals that were already regulated under existing Maine directive, or chemicals unlikely to be added to consumer products. Step 2 included exclusion of chemicals that did not meet the Maine statutory definition of credible scientific evidence (i.e., chemicals that were listed solely by State governments; not by federal or international authoritative governmental entities). Step 3 involved the use of toxicity and exposure prioritizing criteria developed by the MECDC and MEDEP to identify chemicals that met the statutory requirements for chemical of high concern listing (e.g., strong credible scientific evidence for toxicity) and to help identify the most potentially harmful chemicals.

After application of Steps 1 and 2, the potential CHC list was narrowed to 107 chemicals. For Step 3, multiple databases maintained by federal or international authoritative governmental programs were used to narrow the list of 107 potential CHC to no more than 70 CHC (Table 1). Database-specific toxicity prioritizing criteria for meeting the test of *strong* credible scientific evidence that the chemical is a reproductive or developmental toxicant, endocrine disruptor or human carcinogen were developed and applied (Table 1).

Table 1. CHC identification databases and applied prioritizing criteria.

Database	**Prioritizing criteria**
National Toxicology Program Center for Evaluation of Risks to Human Reproduction (NTP-CERHR)	"Serious Concern" or "Concern" for adverse effects in humans
National Toxicology Program Report on Carcinogens (NTP-ROC)	Known to be a human carcinogen
Globally Harmonized System of Classification and Labelling of Chemicals (GHS)	Category 1A reproductive hazard Category 1A carcinogen
European Commission Endocrine Disruptor Program (EU-EDP)	Category 1 endocrine disruptor
U.S. Environmental Protection Agency Integrated Risk Information System (USEPA IRIS)	1986 category A, 1996, 1999, or 2005 known human carcinogen
European Union List of Carcinogens (EU cancer)	Category 1A carcinogen
International Agency for Research of Cancer (IARC)	Group 1 carcinogenic to humans

In addition, MECDC considered chemicals that were categorized with credible scientific evidence as being persistent, bioaccumulative and toxic (PBT) as candidate CHC, since two of the three listing criteria for COC specified in statute were related to being a PBT. Two PBT lists were identified and used to identify potential CHC chemicals (Table 2).

Table 2. Databases and toxicity prioritizing criteria for identifying PBT related chemicals.

Database	**Prioritizing criteria**
Health Canada Persistent Bioaccumulative and inherently Toxic	Present on list
Washington State Persistent Bioaccumulative and Toxic	Present on list and confirmed with review of studies published in peer reviewed publications

Seven candidate CHC chemicals were identified solely based on a PBT listing. The MECDC previously performed extensive reviews of peer-reviewed published studies for four of the seven PBT-related chemicals (tetrabromobisphenol A, deca-brominated diphenyl ether, hexabromocyclododecane, and perfluorooctane sulfonic acid) and determined there was a sufficient body of peer-reviewed publications to conclude there was strong credible scientific evidence for either reproductive or developmental toxicity, endocrine disruption, or other toxic health effects.

To meet the CHC strong credible scientific evidence criteria for presence in human blood, urine or other bodily fluids or presence in household indoor air, dust or drinking water, MECDC conducted peer-review literature searches to identify chemical-specific human biomonitoring studies or indoor air/dust monitoring studies. For presence in a consumer product used or present in the home, the MEDEP examined 12 federal and international authoritative governmental databases to identify chemicals present in consumer products.

Forty-nine chemicals were identified from the list of 107 potential CHC that met both the toxicity and exposure prioritizing criteria. These 49 chemicals became the list of Chemicals of High Concern published on July 1, 2012.

3. 2015 Triennial Update

By statute, the MEDEP Commissioner is required to review the CHC list every three years and remove any chemical from the CHC list that has been designated a priority chemical or that no longer meets the listing criteria.[6] Additional chemicals may be added to the CHC list according to the listing requirements. The final list is to include no more than 70 chemicals and no fewer than 10. The 2015 CHC update consisted of an initial review to confirm the current status of chemical listings by authoritative national and international agencies, identify and remove chemicals that had been designated as priority chemicals, and identify and remove any chemicals not meeting the listing criteria. This update additionally identified and addressed a number of minor corrections to documentation that do not change any chemical's current CHC status.

[6] MRS Title 38, Chapter 16-D:TOXIC CHEMICALS IN CHILDREN'S PRODUCTS, 38 §1693-A Subsection 3. http://www.mainelegislature.org/legis/statutes/38/title38ch16-Dsec0.html

3.1. Chemicals of High Concern delisting

The delisting of chemicals from the CHC list is based on the removal of chemicals now listed as priority chemicals and chemicals not meeting the CHC listing requirements. Chemicals that do not meet the statutory CHC identification criteria were identified by chemical-specific petitions to delist chemicals from the CHC list or by the MECDC as not meeting the CHC identification criteria following review for the three year update.

3.1.1. Removal of chemicals listed as priority chemicals

Since the publication of the CHC list in 2012, eight CHC have been elevated from CHC status to priority chemical status (Table 3). These eight chemicals have gone through the priority chemical designation process and are now listed as priority chemicals. Due to their priority chemical listing status these chemicals were removed from the CHC list.

Table 3. Chemicals of high concern removed due to priority chemical listing status.

Chemical	CAS number	Year of priority status designation
Arsenic and arsenic compounds	7440-38-2	2014
Mercury and mercury compounds	7439-97-6	2014
Cadmium	7440-43-9	2014
Diethyl phthalate	84-66-2	2015
Dibutyl phthalate	84-74-2	2015
Benzyl Butyl phthalate	85-68-7	2015
Di-(2-ethylhexyl) phthalate	117-81-7	2015
Formaldehyde	50-00-0	2015

3.1.2. Removal of chemicals not meeting the CHC identification criteria

Table 4. Chemicals of high concern delisted because they do not meet the CHC criteria.

Chemical	CAS number	Reason for delisting
Beryllium and beryllium compounds	7440-41-07	Biomonitoring and presence in consumer products data did not meet the finding of strong credible scientific evidence
Metallic nickel [a]	7440-02-0	Does not meet the toxicity prioritizing criteria of a known human carcinogen.
Di-n-hexyl phthalate	84-75-3	Does not meet current toxicity prioritizing criteria used to identify CHC
Hexachlorobutadiene	87-68-3	Only listed as a PBT with no formal review
Tris(2-chloroethyl) phosphate	115-96-8	Only listed as a PBT with no formal review
2-Naphthalenol, 1-[(4-methyl-2-nitrophenyl)azo]-	2425-85-6	Only listed as a PBT with no formal review

[a] Nickel compounds (CAS N/A) remain on the CHC list as they meet CHC identification criteria.

Beryllium and beryllium compounds (CAS 7440-41-07)

In response to a recent petition[7] to remove beryllium and beryllium compounds from the CHC list, MECDC concurred with MEDEP that beryllium and beryllium compounds do not meet the CHC identification criteria due to insufficient biomonitoring data and the apparent lack of data related to exposure in the home or use in children's products[8]. As such, beryllium and beryllium compounds were removed from the CHC list during the 2015 update. While beryllium and beryllium compounds were removed from the CHC list, they remain on the COC list as they appropriately meet COC eligibility criteria.

Metallic nickel (CAS 7440-02-0)

The listing of nickel and nickel compounds (CAS 7440-02-0) as a CHC was challenged through petition[9] in 2014. Nickel and nickel compounds were identified on the 2012 CHC list under a single CAS number 7440-02-0, which specifically identifies only metallic nickel. However, metallic nickel itself does not meet the CHC criteria for strong credible scientific evidence of carcinogenicity[10]. Based on the CHC prioritizing toxicity criteria, metallic nickel should not be included on the final CHC list, as currently the CHC prioritizing toxicity criteria used for carcinogens is the chemical must be listed by an authoritative federal or international governmental agency as a known human carcinogen. Metallic nickel is listed as reasonably anticipated to be a human carcinogen. Accordingly, metallic nickel CAS 7440-02-0 was removed from the CHC list as it does not meet the CHC identification criteria. Removal of metallic nickel from the CHC list does not warrant removal from the COC list, as metallic nickel following current COC eligibility criteria is appropriately identified as chemical of concern.

Nickel compounds as a class are listed by authoritative federal and international governmental agencies as known human carcinogens and thus appropriately meet the toxicity inclusion criteria for CHC listing[8]. Consequently, nickel compounds will remain on the CHC list. As there is no single CAS number to identify nickel compounds as a group, the CHC listing for nickel compounds will not have an associated CAS number on the COC and CHC lists.

[7] "Petition to Remove Beryllium and Compounds from the Maine DEP List of Chemicals of Concern and from the List of Chemicals of High Concern under the Maine Toys and Children's Products Law" submitted by Materion June 6th, 2014.

[8] MECDC review of the "Petition requesting the removal of beryllium and beryllium compounds from the Toxic Chemicals in Children's Products list of Chemicals of Concern and Chemicals of High Concern", memorandum submitted to the MEDEP December 3rd, 2015.

[9] "Petition to Remove Nickel and Nickel Compounds from the Maine Kid's Safe Products Act" submitted by the Nickel Institute July 28th, 2014.

[10] MECDC review of the "Petition to Remove Nickel and Nickel Compounds from the Maine Kid's Safe Products Act", memorandum submitted to the MEDEP January 23rd, 2015.

Di-n-hexyl phthalate (CAS 84-75-3)

The National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) previously published a number of monographs assessing the potential human reproductive and developmental health effects of specific chemicals, including several phthalates[11]. The NTP-CERHR monographs were used as a database to identify CHC that met the statutory requirement of strong credible scientific evidence for human reproductive or developmental toxicants (Table 1), if NTP-CERHR determined there was "Serious Concern" or "Concern" for adverse effects in humans. The NTP-CERHR used a two phase process to classify the weight-of-evidence for potential human reproductive and/or developmental health effects[12]. Phase 1 consisted of a weight-of-evidence approach for hazard identification with a seven-tier classification scale as follows: Clear evidence of adverse effects; Some evidence of adverse effects; Limited evidence of adverse effects; Insufficient evidence for a conclusion; Limited evidence of no adverse effects; Some evidence of no adverse effects; Clear evidence of no adverse effects. For Phase 1 hazard identification, the weight-of-evidence for effects in laboratory animals and humans were classified separately. Phase 2 consisted of combining the hazard identification outcomes for experimental animal studies and human studies, if available, with current human exposure data or pharmacokinetic data needed to extrapolate results observed in experimental animals to potential effects in humans to generate a final "Level of Concern". The Phase 2 level of concern of adverse effects in humans were broken down into five categories: Serious concern for adverse effects; Concern for adverse effects; Some concern for adverse effects; Minimal concern for adverse effects; Negligible concern for adverse effects and a sixth category for insufficient data on hazard identification and/or exposure.

In the 2012 Deriving Chemicals of High Concern documentation the toxicity prioritizing criteria for CHC identification for chemicals with NTP-CERHR monographs is listed as "Clear" or "Some" evidence of adverse effects in humans. Although the NTP-CERHR prioritizing criteria as defined in the 2012 documentation is not clear regarding the use of Phase 1 or Phase 2 classifications, the intent was to identify chemicals with strong evidence of adverse reproductive or developmental health effects in humans.

For di-n-hexyl phthalate (DnHP) (CAS 84-75-3), the NTP-CERHR concluded for Phase 1 hazard identification that there was "Clear evidence of adverse effects" for reproductive toxicity and "Limited evidence of adverse effects" for development toxicity in laboratory animals, and a lack of data to assess the weight-of-evidence of adverse effects in humans[13]. The NTP-CERHR Phase 2 conclusion for the level of concern in humans was "Insufficient hazard and/or exposure data" [13]. Both Phase 1 and Phase 2 assessments concluded that there is insufficient data to assess the potential reproductive or developmental health effects of DnHP in humans. Consequently, DnHP

[11] Jahnke, G.D., Iannucci, A.R., Scialli, A.R., and Shelby, M.D. 2005. Center for the Evaluation of Risks to Human Reproduction-The First Five Years. Birth Defects Research (Part B) 74:1–8.

[12] Bucher, J.R., Wolfe, M.S., Thayer, K. 2011. National Toxicology Program: Evaluation of Reproductive and Developmental Hazards. http://www.oehha.ca.gov/prop65/public_meetings/pdf/071211NTPCalEPADART.pdf

[13] NTP-CERHR. 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n -Hexyl Phthalate (DnHP). NIH Publication No. 03-4489.
http://ntp.niehs.nih.gov/ntp/ohat/phthalates/dnhp/dnhp_monograph_final.pdf

does not meet the current MECDC toxicity prioritizing criteria designed to identify chemicals with strong evidence of adverse reproductive or developmental health effects in humans. The 2012 CHC selection process mistakenly recorded DnHP as meeting the prioritizing criteria for the Phase 2 NTP-CERHR evaluation, when in fact it only met "Clear" evidence of adverse effects for the Phase 1 evaluation for experimental animals. Consequently, the CHC listing of DnHP (CAS 84-75-3) as a reproductive or developmental toxicant under the NTP-CERHR database was removed in the 2015 update.

In the 2012 CHC selection process DnHP did not meet any of the toxicity prioritizing criteria in any of the additional toxicity databases used to identify chemicals of high concern. For the 2015 triennial update all of the toxicity databases were reviewed for potential updates since 2012 that would apply to listing DnHP as a chemical of high concern. The Japanese GHS database for reproductive health effects does not include any classification for DnHP. The European Union (EU) Endocrine Disruptor database continues to lists DnHP as a Category 2 endocrine disruptor. Only Category 1 endocrine disruptors from the EU endocrine disruptor list were considered for CHC designation. The NTP, IARC, IRIS 1986, IRIS 1996 or the EU carcinogen databases do not include classifications for DnHP. Following the 2012 CHC prioritizing criteria, DnHP does not meet the toxicity prioritizing criteria within any database used to identify chemicals of high concern and was removed from the CHC list. Removal from the CHC list does not affect the listing of DnHP as a chemical of concern. While DnHP was removed from the CHC list for the 2015 three-year update, this chemical may be listed as a CHC following review and use of additional toxicity databases as described in the Identifying New Chemical of High Concern section.

Hexachlorobutadiene (CAS 87-68-3), Tris(2-chloroethyl) phosphate (CAS 115-96-8), and 2-Naphthalenol, 1-[(4-methyl-2-nitrophenyl)azo]- (CAS 2425-85-6)

As part of the triennial review, MECDC identified three chemicals that were listed as CHC solely based on the criteria of persistent, bioaccumulative, and toxic (PBT). While PBT is a clear toxicity criterion for the COC list, it is not a criterion for listing as a CHC. Hexachlorobutadiene, tris(2-chloroethyl) phosphate, and 2-Naphthalenol, 1-[(4-methyl-2-nitrophenyl)azo]- are on the 2012 CHC list due to their exclusive presence on Washington State's PBT list and/or Health Canada's PBiT list. However, MECDC has not undertaken a substantial review of the peer-reviewed scientific literature regarding carcinogenic, reproductive and/or developmental, or endocrine disrupting health effects for these chemicals. The toxicity database listings for these three chemicals were reviewed for any potential updates or changes and in 2015 they do not meet any of the toxicity prioritizing criteria other than being listed as PBTs (i.e., none are known human carcinogens, none are listed by NTP-CERHR as reproductive or development toxicants with Serious Concern or Concern for adverse effects in humans and none are listed as Category 1 endocrine disruptors). Accordingly, hexachlorobutadiene, tris(2-chloroethyl) phosphate, and 2-Naphthalenol, 1-[(4-methyl-2-nitrophenyl)azo]- were removed from the CHC list as they do not meet the statutory CHC toxicity criteria, which do not include bioaccumulative or persistent criteria. These chemicals remain on the COC list as they appropriately meet statutory COC listing criteria.

Four additional chemicals are listed as CHC (Tetrabromobisphenol A (CAS 79-94-7), BDE-209 (CAS 1163-19-5), hexabromocyclododecane (CAS 25637-99-4), perfluoroocatane sulfonic acid and its salts (CAS 1763-23-1)) due to their listing as PBTs by Washington State or Health Canada. However, MECDC previously reviewed these chemicals and concluded that they met the toxicity listing criteria for CHC with strong credible scientific evidence. Tetrabromobisphenol A and hexabromocyclododecane have previously undergone review by the MECDC for listing as priority chemicals for brominated flame retardants in 2010[14] and BDE-209 was reviewed for legislation passed in 2007[15] banning specific brominated flame retardants.

For perfluorooctane sulfonic acid (PFOS) and its salts, the MECDC in the process of developing a drinking water guidance value for perfluorooctanoic acid (PFOA) and PFOS performed a review of the current scientific literature published in peer-reviewed journals. Through this process the MECDC identified multiple peer-reviewed scientific studies documenting endocrine disrupting effects and adverse reproductive and developmental effects in animals[16]. There were also a number of epidemiological studies identified that demonstrated adverse reproductive and developmental effects associated with PFOS in humans[16]. Based on this previous work and review the MECDC concluded that PFOS meets the toxicity criteria of an endocrine disruptor and reproductive or developmental toxicant with strong credible scientific evidence to be appropriately listed as a CHC. For the 2015 triennial update, the chemical-specific inclusion criteria (Appendix I) contains toxicity criteria references for PFOS in support of its CHC listing.

3.2. General updates

A number of general updates were made to the 2012 CHC list in this update. These represent minor changes or corrections and do not change any chemical's current CHC status.

3.2.1. Database classification updates

There are several chemicals in which the original 2012 CHC listing failed to include an appropriate toxicity prioritization from an individual database. For example, benzene is listed in NTP, IRIS, EU, IARC and GHS databases as a known human carcinogen; however, the 2012 CHC list and documentation failed to capture the GHS known human carcinogen categorization. Several of these types of database updates were made in the 2015 update (Table 5).

[14] Rationale for Concurrence by Maine Center for Disease Control and Prevention on the Designation of Brominated Flame Retardants as a Priority Chemical, November 22, 2010.

[15] Brominated Flame Retardants: Third annual report to the Maine Legislature, Prepared by the Maine Center for Disease Control & Prevention and the Maine Department of Environmental Protection, January 2007.

[16] See Appendix I 2015 Triennial Update Chemical Specific Inclusion Criteria for specific references.

Table 5. Toxicity database classification updates.

Chemical	CAS number	Toxicity database correction
Benzene	71-43-2	Added GHS known human cancer categorization
2-Naphthylamine	91-59-8	Added GHS known human cancer categorization
Benzidine and its salts	92-87-5	Added NTP known human cancer categorization; Added GHS Category 1A cancer categorization; Added European Union Category 1A cancer categorization
1, 2-Dibromoethane	106-93-4	Removed the IRIS 1996 cancer classification; it is classified as *likely to be carcinogenic to humans*, not *known to be a human carcinogen*
Nickel compounds	No CAS available	Added IARC Group 1 carcinogenic to humans categorization

3.2.2. COC and CHC nomenclature updates

Two general updates were made regarding how specific chemicals are identified by name on the final CHC list, as the naming convention of several CHC was not consistent between the COC and CHC lists.

Perfluorooctane sulfonic acid (CAS 1763-23-1)

Perfluorooctane sulfonic acid and its associated salts are identified on the COC lists as "Acid [Perfluorooctane sulfonates (PFOS)]"; while on the CHC list they are identified as "Perfluorooctanyl sulphonic acid and its salts". The COC and CHC nomenclature for PFOS was meant to capture the parent chemical, (i.e., perfluorooctane sulfonic acid) and structurally analogous salts that disassociate or breakdown into the parent chemical, such as perfluorooctane sulfonic acid potassium salt. The COC nomenclature, Acid [Perfluorooctane sulfonates (PFOS)], intended to capture the associated salt compounds through use of the term sulfonates, which denotes any salt of a sulfonic acid. The CHC nomenclature directly lists the parent chemical, perfluorooctanyl sulphonic acid and then includes the associated salts. For consistency between the COC and CHC lists, the identification by chemical name of perfluorooctane sulfonic acid and its associated salts was changed to "Perfluorooctane sulfonic acid (PFOS) and its salts" on both the COC and CHC lists. The perfluorooctane sulfonic acid nomenclature is the standard terminology used by the U.S. National Library of Medicine Hazardous Substances Database[17]. Identification by CAS number on both COC and CHC lists remains as 1763-23-1, which specifically identifies perfluorooctane sulfonic acid[17]. Compound-specific CAS numbers for perfluorooctane sulfonic acid salts are not included for CAS number identification for PFOS.

[17] U.S. National Library of Medicine Hazardous Substances Database, Perfluorooctane sulfonic acid CASRN: 1763-23-1. http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~9gR4Dw:1

Quartz (CAS 14808-60-7)

Quartz is identified by name on the COC list as “Silica, crystalline (inhaled in the form of quartz or cristobalite from occupational sources)” and by CAS number as 14808-60-7. On the CHC list quartz is identified by name as “Quartz” and by CAS number as 14808-60-7. The three toxicity prioritizing databases used to identify quartz/silica as a chemical of high concern use the following nomenclature and CAS numbers: NTP - “Silica, Crystalline (Respirable Size)” CAS No.: none assigned; IARC - “Crystalline silica in the form of quartz or cristobalite dust” no separate CAS numbers listed; GHS - “Quartz” CAS 14808-60-7. For consistency between the COC and CHC lists and the naming conventions used by federal and international authoritative governmental agencies, the chemical name for quartz was updated to “Silica, crystalline (in the form of quartz or cristobalite dust)” on both the COC and CHC lists. Identification by CAS number remains unchanged as 14808-60-7.

Chemicals listed with accompanying salts

Two chemicals on the CHC list are listed as a single chemical with associated salts compounds, Benzidine and its salts (CAS 92-87-5) and Perfluorooctane sulfonic acid (PFOS) and its salts (CAS 1763-23-1). For these two chemicals a clerical note was added to the COC and CHC lists describing that the listed CAS number is specific for the parent chemical, but the listing encompasses all parent chemical related salts. The salts have individual salt-specific CAS numbers separate from the parent chemical CAS number, but they are not individually listed.

3.2.3. 2012 Deriving chemicals of high concern process documentation corrections and updates

During the triennial review several minor documentation and reference errors in the 2012 MECDC Deriving Chemicals of High Concern Process document were identified. Several reference updates to documentation were also identified (e.g., the latest NHANES biomonitoring data). These errors and updates are described below as general documentation corrections, reference corrections, and reference updates.

General documentation corrections

In Figure 2 of the 2012 State of Maine Chemicals of High Concern Prioritization Process, the wording in the second bullet under the Step 3 exclusion criteria (“Chemicals with low toxicity values from U.S. EPA’s IRIS data base”) was revised to read “Chemicals with low toxicity values from ATSDR or RTECs databases”. The ATSDR and RTEC databases were used by Washington State to identify chemicals with low toxicity values rather than the IRIS database.

Di-*n*-hexyl phthalate (DnHP) (CAS 84-75-3) was identified in Table 6 of the 2012 CHC documentation as listed by the State of Washington only because of its presence on California’s PROP 65 list as reproductive or developmental toxicants. This is incorrect. DnHP is listed by an authoritative federal governmental agency, the NTP-CERHR, and should not be listed in Table 6 in the 2012 process documentation. The NTP-CERHR lists DnHP as having “Clear evidence of

adverse effects" for reproductive toxicity and "Limited evidence of adverse effects" for developmental toxicity in laboratory animals, and a lack of data to assess the weight-of-evidence of adverse effects in humans.[18] Due to this NTP-CERHR toxicity listing, DnHP was appropriately listed as a COC and remained in the potential CHC selection pool in 2012. However, as described in section 3.1.2 above, following review for the 2015 update, it was determined that DnHP did not meet the CHC listing criteria and was removed from the 2015 CHC list, while remaining on the COC list.

The abbreviation for Globally Harmonized System of Classification and Labelling of Chemicals (GHS) in the 2012 Appendix I - Deriving Chemicals of High Concern Process Documentation and 2012 Appendix II - Final List of Chemicals of High Concern was corrected from GSH to GHS in the 2015 appendices.

Reference corrections

The 2012 CHC listing for 2-naphthylamine included one reference for indoor air/dust exposure, Wilson, W. E., Lioy, P. J. (1994). "Sources of organic acids in indoor air: a field study." Journal of Exposure Analysis and Environmental Epidemiology 4(1): 25-47. However, there is no mention of 2-naphthylamine measurement in indoor air or dust or any type of monitoring for 2-naphthylamine in this publication or additional publications from these authors. The reference as listed in Appendix III is also missing an author, it should have been Zhang, J., Wilson, W. E., Lioy, P. J.. This reference was removed from the CHC listing as a reference for the presence of 2-naphthylamine in indoor air or dust. Removal of this reference does not warrant the removal of 2-naphthylamine from the CHC list, as it meets both toxicity criteria as a known human carcinogen and exposure criteria as present in consumer products.

Reference updates

The reference link for the European Commission Endocrine Disruptor Program was updated to: http://ec.europa.eu/environment/chemicals/endocrine/documents/index_en.htm#SubThemes5

For the chemical-specific inclusion criteria, the 2005 and 2009 CDC/NHANES biomonitoring data references were updated to 2015 data references. For each chemical that listed a CDC/NHANES biomonitoring reference, the latest 2015 NHANES biomonitoring report was reviewed to ensure that the specific chemical of high concern continues to be detected in human blood or urine. Appendix I - 2015 Chemical-Specific Inclusion Criteria, includes the most recent updates to biomonitoring and indoor dust/air monitoring references identified for individual CHC.

[18] NTP-CERHR. 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n -Hexyl Phthalate (DnHP). NIH Publication No. 03-4489. http://ntp.niehs.nih.gov/ntp/ohat/phthalates/dnhp/dnhp_monograph_final.pdf

4. Identifying New Chemicals of High Concern

4.1. Challenges to identifying new chemicals of high concern

In the 2012 CHC derivation process, the toxicity prioritizing criteria were focused on top-tier toxicity classifications used in individual toxicity databases, as a way to identify chemicals with strong credible scientific evidence. For carcinogens, for example, only known human carcinogens classified by the NTP or IARC were considered (Table 1). Similar top-tier classifications were used to identify reproductive or developmental toxicants and endocrine disruptors (Table 1). These top-tier toxicity classifications were also relied upon to narrow the list of potential CHC from 107 to fewer than 70 chemicals. While the application of the top-tier toxicity prioritizing criteria was efficacious in meeting these objectives, the chosen criteria may have been overly stringent in identifying chemicals of high concern. Additionally, the 2012 CHC derivation process identified only two authoritative databases for reproductive and/or developmental toxicants with weight-of-evidence determinations. One of these authoritative databases no longer works to exclusively evaluate and identify reproductive and developmental toxicants and does not appear to be currently involved in evaluations of any new chemicals.[19] Only one authoritative government list of endocrine disruptors was identified, and there appears to have been no new activity in recent years to add chemicals to this list or revise the categorization methodology.

4.2. Potential strategies to identify new chemicals of high concern

4.2.1. Toxicity classification strategies

Typically, chemicals that meet top-tier toxicity classifications, such as a known human carcinogen, have both human exposure and human health effects data to demonstrate a causal relationship. These data are commonly from occupational studies where chemical exposures are generally far greater in frequency and amount than most non-occupational exposures. Chemicals falling into a second-tier toxicity classification, such as reasonably anticipated to be a human carcinogen, typically have substantial data demonstrating adverse health effects in experimental animals with some exposure data in humans demonstrating a potential for human exposure, but limited or no human health data to validate a causal relationship. It is not necessarily the case that chemicals with lesser toxicity classifications are less harmful than chemicals with a higher toxicity classification. It may simply be that there is less information available regarding adverse health effects specifically observed in humans.

One way to identify additional CHC would be to adopt the second highest weight-of-evidence determination as representing strong credible scientific evidence. While credible scientific evidence is defined in the statute, strong credible scientific evidence is neither defined in the statute or in rule. The MECDC feels that the use of a second-tier toxicity classification coupled with sound evidence that the chemical is commonly detected in humans would satisfy the criteria of strong credible scientific evidence for CHC identification. Chemicals of concern that meet a

[19] http://ntp.niehs.nih.gov/pubhealth/hat/noms/index.html

second-tier carcinogen or reproductive or developmental toxicant classification could then be evaluated further to determine if there are relevant human exposure data, such as USCDC NHANES biomonitoring data. If the chemical meets a second-tier toxicity classification by a federal or international authoritative governmental agency and is found in humans through either large scale national biomonitoring studies or relevant peer-reviewed scientific studies, the chemical may be considered for CHC listing pending information about presence in products.

This approach would be a large undertaking, and there would be a need to develop either additional toxicity or exposure criteria to constrain the list to the required 70 chemicals. For example, for carcinogens alone, the NTP classifies nearly 200 chemicals as reasonably anticipated to be human carcinogens.

Table 6. Potential toxicity prioritizing criteria expansions to identify chemicals of high concern.

Database	**Second-tier cancer classifications**
Carcinogenesis	
NTP ROC	Reasonably anticipated to be a human carcinogen
USEPA IRIS	B1 probable human carcinogen (1986 guidelines) Likely to be carcinogenic to humans (1999 and 2005 guidelines)
Japanese GHS	Category 1B presumed to have carcinogenic potential for humans
EU Cancer	Category 1B presumed to have carcinogenic potential for humans
IARC	Group 2A probably carcinogenic to humans
Reproductive or developmental toxicity	
Japanese GHS	Category 1B presumed human reproductive toxicant

4.2.2. Strategies focusing on reproductive and developmental toxicity

The MECDC utilized two databases, the NTP-CERHR and the Japanese GHS, to identify chemicals of high concern that were reproductive or developmental toxicants. In 2011 the NTP-CERHR was reorganized into the Office of Health Assessment and Translation (OHAT). OHAT has the same general mission as the previous CERHR, but expanded to evaluate additional health effects. Since the 2011 transition OHAT has not published a formal chemical evaluation. To strengthen the CHC selection process for chemicals that exhibit reproductive or developmental toxicities, the MECDC would like to review the feasibility of using the USEPA IRIS and EU REACH databases for identifying chemicals of high concern based on reproductive and/or developmental health effects. The USEPA IRIS database, which is currently used to identify human carcinogens, also derives health-based reference doses for non-cancer toxicities such as reproductive and developmental endpoints. The EU REACH database maintains a Candidate List of Substances of Very High Concern which lists chemicals that have been reviewed and

identified as “Toxic for reproduction”. These two databases could be examined to determine if any COC are currently classified as reproductive or developmental toxicants and whether or not they would meet CHC identification criteria.

4.2.3. Endocrine disruptors

For endocrine disrupting status the MECDC relied on the only authoritative federal or international governmental database available that categorically classifies endocrine disrupting chemicals, the EU endocrine disruptor database. The EU list did not use a weight-of-evidence approach to classify potential endocrine-disrupting chemicals. Rather they defined endocrine-disrupting chemicals as Category 1: evidence of endocrine-disrupting activity in at least one species using intact animals; Category 2: at least some in vitro evidence of biological activity related to endocrine disruption; Category 3: no evidence of endocrine-disrupting activity or no data available[20]. While it was not a formal weight-of-evidence approach, chemicals that were classified as Category 1 endocrine disruptors were included as potential CHC largely because the EU endocrine disrupting list is the only authoritative federal or international governmental database available to identify potential endocrine-disrupting chemicals. Currently, the MECDC does not feel that it would be appropriate to expand the endocrine disruptor toxicity prioritizing criteria for the EU endocrine disruptor list because the classification method is not a robust weight-of-evidence approach and the Category 2 classification requires only some evidence of biological activity in vitro, not in intact animals or humans. It is also unclear whether or not this database is being updated as new chemical-specific information regarding endocrine disruption is made available. Short of an extensive chemical-by-chemical review for potential endocrine disrupting health effects, there remains a deficiency in the CHC selection process regarding identification of endocrine-disrupting chemicals.

[20] http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm

Table 7. 2015 Chemicals of High Concern.

CAS Number	Chemical Name
71-43-2	Benzene
75-01-4	Vinyl chloride
79-94-7	Tetrabromobisphenol A
84-61-7	Dicyclohexyl phthalate; DCHP
91-59-8	2-Naphthylamine
92-69-3	4-Hydroxybiphenyl; 4-Phenylphenol
92-87-5*	Benzidine and its salts
94-13-3	Propyl paraben
94-26-8	Butyl paraben
95-53-4	2-Aminotoluene
99-76-3	Methyl paraben
99-96-7	p-Hydroxybenzoic acid
100-42-5	Styrene
101-14-4	4,4´-Methylenebis(2-Chloroaniline)
106-89-8	Epichlorohydrin
106-93-4	1,2-Dibromoethane
106-99-0	1,3-Butadiene
108-88-3	Toluene
118-74-1	Hexachlorobenzene
120-47-8	Ethyl paraben
131-55-5	Benzophenone-2 (Bp-2), 2,2',4,4'-tetrahydroxybenzophenone
131-56-6	2,4-Dihydroxybenzophenon; Resbenzophenone
131-70-4	Mono-n-butylphthalate
140-66-9	4-tert-Octylphenol; 1,1,3,3-Tetramethyl-4-butylphenol
556-67-2	Octamethylcyclotetrasiloxane
608-93-5	Benzene, pentachloro-
1163-19-5	2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether; BDE-209
1634-04-4	Methyl tert-butyl ether; MTBE
1763-23-1*	Perfluorooctane sulfonic acid (PFOS) and its salts
1806-26-4	Phenol, 4-octyl-
5466-77-3	2-ethyl-hexyl-4-methoxycinnamate
14808-60-7	Silica, crystalline (in the form of quartz or cristobalite dust)
25013-16-5	Butylated hydroxyanisole
25637-99-4	Hexabromocyclododecane
27193-28-8	Phenol, (1,1,3,3-tetramethylbutyl)-; Octylphenol
No CAS	Nickel compounds

*CAS numbers are specific for the parent chemical, but the CHC listing includes both the parent chemical and parent chemical-related salt compounds.