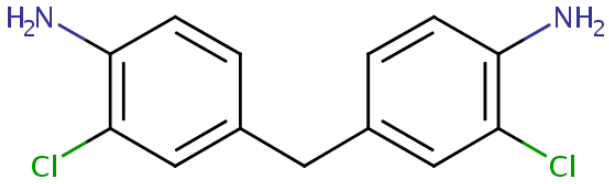
United States
Environmental Protection Agency

EPA Document# EPA-740-P-24-005
July 2024
Office of Chemical Safety and
Pollution Prevention

Proposed Designation of 4,4'-Methylene Bis(2-Chloroaniline) (MBOCA) as a High-Priority Substance for Risk Evaluation

CASRN 101-14-4



July 2024

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDIX TABLES

LIST OF APPENDIX FIGURES

ACKNOWLEDGEMENTS

This report was developed by the United States Environmental Protection Agency (U.S. EPA), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

Acknowledgements

The OPPT Assessment Team gratefully acknowledges participation or input from intra-agency reviewers that included multiple offices within EPA and assistance from EPA contractors ICF, Inc. (contract no. 68HERC23D0007) ERG (contract no. 68HERD20A0002); Abt Associates, Inc. (contract no. 68HERH22A0018); SpecPro Professional Services, Inc (contract no. 68HERC20D0021); General Dynamics Information Technology, Inc. (contract nos. HHSN316201200013W); SRC, Inc. (contract no. 68HEH19D0022).

Docket

Supporting information can be found in public dockets EPA-HQ-OPPT-2023-0601 and EPA-HQ-OPPT-2018-0464.

Disclaimer

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation, or favoring by the United States Government.

ABBREVIATIONS AND ACRONYMS

ADME	Absorption, distribution, metabolism, and excretion
AICIS	Australian Industrial Chemicals Introduction Scheme
ATSDR	Agency for Toxic Substances and Disease Registry
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
CAA	Clean Air Act
CalEPA	California Office of Environmental Health Hazard Assessment
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential business information
CDR	Chemical Data Reporting
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CSF	Cancer slope factor
CWA	Clean Water Act
ECHA	European Chemicals Agency
EC	European Commission
EC_x	Effective Concentration for x percent of exposed organisms
ECCC	Environment and Climate Change Canda
EPA	Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
EU	European Union
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FR	Federal Register
GHS	Globally Harmonized System
HAWC	Health Assessment Workplace Collaborative
HERO	Health and Environmental Research Online (database)
Hg	Mercury
HQ	Headquarters
HSDB	Hazardous Substances Data Bank
HSIS	Hazardous Substances Information System
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
K_{OC}	Organic carbon: water partition coefficient
K_{OW}	Octanol: water partition coefficient
LC_{10}	Lethal concentration of 10% test organisms
LC_{50}	Lethal concentration of 50% test organisms
LD_{50}	Lethal dose of an ingested substance that kills 50% of test organisms
LEC	Lowest effective concentration
LOEC	Lowest observed effect concentration
MBOCA	4,4'-Methylenebis (2- chloroaniline)
NICNAS	National Industrial Chemicals Notification and Assessment
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standard and Technology
NITE	National Institute of Technology and Evaluation
NLM	National Library of Medicine
NOEC	No observed effect concentration

NPDES	National Pollutant Discharge Elimination System
NTP	National Toxicology Program
OECD	Organization for Economic Co-operation and Development
OEHHA	California Office of Environmental Health Hazard Assessment
OEL	Occupational exposure limit
ONU	Occupational non-user
OPPT	Office of Pollution Prevention and Toxics
ORD	Office of Research and Development
OSHA	Occupational Safety and Health Administration
OQD	Overall Quality Determination
PECO	Population, exposure, comparator, and outcome
PESO	Pathways and processes or population, exposure, setting or scenario, and outcomes
PESS	Potentially exposed or susceptible subpopulation(s)
POTW	Publicly owned treatment works
PPE	Personal protective equipment
PPRTV	Provisional Peer Reviewed Toxicity Values
RCRA	Resource Conservation and Recovery Act
SDS	Safety data sheet
SDWA	Safe Drinking Water Act
TIAB	Title and abstract
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act

Proposed Designation and Rationale

EPA proposes to designate 4,4'-methylene bis(2-chloroaniline) (hereinafter referred to as MBOCA) as a High-Priority Substance under the Toxic Substances Control Act (TSCA) section 6(b)(2)(C) and implementing regulations (40 CFR 702.9). The basis for this proposed designation is the result of EPA's screening level review of MBOCA against the prioritization considerations identified in TSCA section 6(b)(1)(A) and implementing regulations cited above: the chemical substance's exposure and hazard potential, the chemical substance's persistence and bioaccumulation, potentially exposed or susceptible subpopulations (PESS), storage near significant sources of drinking water, the conditions of use or significant changes in the conditions of use of the chemical substance, the production volume or significant changes in production volume of the chemical substance manufactured or processed, and other risk-based criteria that EPA determines to be relevant.

Production Volume or Significant Changes in Production Volume

The annual national aggregate production volume of MBOCA is presented in Table 2-1, which includes the consideration of both confidential business information (CBI) and non-CBI reported production volume information to chemical data reporting (CDR). Since 1986, despite a decrease in production volume in 2002 and 2006, the annual national aggregate production volume of MBOCA has steadily increased and consistently has remained above 1 million pounds. The increase in production volume suggests a consistent potential source of exposure to MBOCA.

Conditions of Use or Significant Changes in Conditions of Use

EPA uses reasonably available information, such as data reported to CDR, to support the TSCA existing chemicals program for chemical prioritization, risk evaluation, and risk management. In addition to CDR, EPA reviewed MBOCA uses from other publicly available data sources, including public comments received following initiation, and identified sources. This information allows EPA to develop an understanding of the types, amount, end uses, and possible exposure to chemicals in commerce. The conditions of use of MBOCA demonstrate the continued manufacturing, distribution, processing, use (industrial, commercial and consumer) and disposal of MBOCA since 2016. While there have been some changes in use information reported to CDR in recent cycles, most reported conditions of use in CDR have remained unchanged between the 2016 and 2020 reporting periods. In the 2016 reporting period, MBOCA was identified as a finishing agent in all other basic organic chemical manufacturing, while in the 2020 cycle, it was labeled a catalyst in the same process. MBOCA was also reported in the 2016 period as a urethane curing agent in plastics product manufacturing and wholesale and retail trade. Moreover, the 2016 reporting cycle identified MBOCA as a process regulator in paint and coating manufacturing, while in the 2020 cycle, it was reported as a process regulator in plastics material and resin manufacturing. It is difficult to discern whether there are significant changes in conditions of uses for MBOCA based on reported information to CDR in 2016 and 2020 because information regarding the reporting guidance for categories and subcategories was updated between these periods, which may have led to use information being reported differently in 2020 compared to 2016. EPA is seeking additional information from the public on the uses presented in Section 2.3.

Potentially Exposed or Susceptible Subpopulations

EPA is required to account for sensitive subpopulations identified by EPA, referred to by TSCA as potentially exposed or susceptible subpopulation(s) (PESS), when implementing the TSCA existing chemicals program for chemical prioritization, risk evaluation, and risk management. EPA conducted a screening review of reasonably available information on factors that may make certain groups more vulnerable to adverse effects. These factors include lifestage, occupational exposures, certain consumer exposures, nutrition, lifestyle activities, and proximity to facilities that manufacture or process a chemical substance. For prioritization, EPA conducted a screening review of reasonably available

information to identify whether children may be exposed to MBOCA. EPA did not identify products intended for children regarding commercial and consumer uses for MBOCA in CDR reporting or from other sources. Based on public comments, however, EPA determined that there may be consumer products with the potential for exposure to children. Based on this information, EPA believes that women of reproductive age, overburdened communities, and children, may be PESS for MBOCA.

Persistence and Bioaccumulation

EPA determines the characteristics of a chemical to help understand how it behaves in the environment. A chemical's properties dictate its environmental fate- whether it is likely to be found in the air, the water, or the soil and how long it will stay there. These properties also help EPA predict how people and biota are likely to be exposed and whether or not the chemical will accumulate in the bodies of different species. EPA reviewed databases and previously conducted assessments to identify information for physical and chemical properties and fate endpoints to characterize the potential for MBOCA to persist in the environment or bioaccumulate (Section 2.5). Based on this information, there is evidence that MBOCA will preferentially partition to organic matter and sediment and therefore is likely to persist in those media, but not in the water column itself. MBOCA is expected to have low persistence in the atmosphere. MBOCA is expected to have some potential for bioconcentration in aquatic organisms.

Storage Near Significant Sources of Drinking Water

Drinking water is a possible source of chemical exposure and EPA is required to screen whether or not chemicals in the TSCA prioritization process are stored near significant sources of it. EPA identified facilities reporting MBOCA to the TRI in 2022 near potential sources of drinking water using public water systems data stored in EPA's Safe Drinking Water Information System Federal Data Warehouse (U.S. EPA, 2022). EPA determined whether TRI reporting facilities are located inside defined source water protection areas or within 4 miles of wellheads to identify potential storage of MBOCA near sources of surface water and groundwater, respectively. As shown in Table 2-4, from among 21 total TRI facilities that stored MBOCA on-site in 2022, EPA identified four facilities that were within source water protection areas and four that were within four miles of wellhead protection points.

Potential Hazard

In the TSCA existing chemicals program, through the prioritization process, EPA determines whether or not a chemical will undergo risk evaluation by making a priority designation. To support this proposed designation for MBOCA, EPA identified potential hazards to humans and ecological receptors, including plants, birds, other wildlife, and aquatic life. Should this chemical undergo risk evaluation, hazard information, along with exposure information, will be used to characterize risk. As described in Section 2.7.1, EPA identified potential environmental hazards for both aquatic and terrestrial organisms, such as mortality, growth, reproductive, and genetics effects resulting from MBOCA. Because environmental terrestrial data are limited, EPA is interested in continuing to screen new information as it becomes available. Additionally, as described in Section 2.7.2 EPA identified potential acute and chronic human health hazards (*e.g.*, carcinogenicity, genotoxicity, irritation, sensitization) resulting from exposure to MBOCA based on epidemiological and animal toxicity information.

Potential Exposure

EPA has identified potential occupational, consumer, and general population exposure to MBOCA (Section 2.8). Due to the annual releases of MBOCA to air, water, and land (Table 2-6 and Table 2-7), the presence of MBOCA in surface water, soil, groundwater, leachate, wastewater, and ambient air (Section 2.8.4.1), and the presence of TRI reporting facilities near significant sources of drinking water (Section 2.6), EPA has determined that various human populations (*e.g.*, general population, workers, consumers) and ecological receptors may be exposed to MBOCA via exposure pathways and routes

associated with the conditions of use. EPA did not identify other risk-based criteria relevant to the proposed designation of MBOCA.

Conclusion

Therefore, after screening the reasonably available information for MBOCA against the prioritization considerations above, EPA preliminarily finds that MBOCA may present an unreasonable risk of injury to health and/or the environment, including to potentially exposed or susceptible subpopulations (PESS), because of the potential hazards or exposure under the conditions of use. Should MBOCA be designated as a High-Priority Substance, additional information may be identified and considered for use in the risk evaluation during the scoping process. TSCA section 6(b)(4)(D) and implementing regulations require that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use, and PESS that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. In addition, a draft scope document is to be published pursuant to 40 CFR 702.41.

1 INTRODUCTION

Under TSCA section 6(b), after initiating prioritization for a chemical substance, the U.S. Environmental Protection Agency (EPA) must designate the chemical substance as a High-Priority Substance for risk evaluation or a Low-Priority Substance for which risk evaluation is not warranted at the time. In TSCA section 6(b)(1)(B) and EPA's implementing regulations (40 CFR 702.3), a High-Priority Substance for risk evaluation is defined as a chemical substance EPA determines, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations (PESS) identified as relevant by EPA. A Low-Priority Substance is defined as a chemical substance EPA concludes does not meet the standard for a High-Priority Substance (based on sufficient information and without consideration of costs or other non-risk factors).

On December 18, 2023, EPA issued a public notice (88 FR 87423) initiating the prioritization process for five chemical substances, including 4,4'-methylene bis(2-chloroaniline). 4,4'-Methylene bis(2-chloroaniline) (CASRN 101-14-4), hereinafter referred to as MBOCA, is a colorless or yellow-brown solid used as a urethane curing agent in the manufacturing and processing of plastics and resins. MBOCA is included in EPA's TSCA Work Plan for Chemical Assessments (U.S. EPA, 2014). Before proposing to designate a chemical substance's prioritization status, under EPA's regulations at 40 CFR 702.9 and pursuant to TSCA section 6(b)(1)(A), EPA will generally use reasonably available information, including relevant information received from the public, to screen the candidate chemical substance under its conditions of use against the following criteria and considerations:

- the chemical substance's production volume or significant changes in production volume (Section 2.2);
- conditions of use or significant changes in the conditions of use of the chemical substance (Section 2.3);
- PESS (Section 2.4);
- persistence and bioaccumulation (Section 2.5);
- storage near significant sources of drinking water (Section 2.6);
- the potential hazard (Section 2.7) and potential exposure (Section 2.8) of the chemical substance; and
- and other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority (Section 2.9).

The screening review of reasonably available information for MBOCA (CASRN 101-14-4) against these criteria and considerations will inform a finding of whether MBOCA may present unreasonable risk because of a potential hazard and a potential route of exposure under the conditions of use. That preliminary finding, proposed designation, and associated rationale can be found in the Proposed Designation Document Rationale section. Based on the information contained in this proposed designation document, EPA proposes that MBOCA be designated as a High-Priority Substance. EPA will take comment on this proposed designation for 90 days before finalizing its designation of MBOCA (EPA-HQ-OPPT-2018-0464). Relevant information received from the public and other information as appropriate will be considered for the final designation.

In developing this proposed designation and throughout the prioritization process, EPA has engaged and will continue to engage the public to obtain information on MBOCA relevant for use in the TSCA existing chemicals program. On December 18, 2023, EPA initiated a 90-day public comment period, during which EPA received information about conditions of use for MBOCA, including manufacturing,

processing, and consumer/commercial uses and products; release and exposure information; and potential hazards of MBOCA, as well as previously conducted hazard assessments. Specifically, in February 2024, EPA hosted a public webinar to discuss prioritization efforts and data gathering authorities utilized and considered for identifying potentially relevant information for the five chemical substances currently undergoing prioritization. Following this public webinar, there were follow-up discussions with stakeholders representing different sectors. During these meetings, comments and information submitted during the first public comment period were discussed to further EPA's understanding of the provided information and its relevance to this action. See docket ID number EPA-HQ-OPPT-2023-0601 for additional information on the information presented during the February 2024 public webinar (presentation materials and transcript). Final designation of the chemical substance as a High-Priority Substance would immediately initiate the risk evaluation process as described in EPA's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (40 CFR 702).

This proposed designation document contains additional information EPA believes will help inform the scope of the risk evaluation for MBOCA if it is designated as a High-Priority Substance. These additional data elements are considered preliminary draft products and are not intended to meet the requirements for scoping pursuant to 40 CFR 702.39(b). EPA expects to use information gained from public comments on these data elements to better inform and refine a draft scope of the risk evaluation if MBOCA is designated as a High-Priority Substance. For example, draft preliminary conceptual models for MBOCA are included in Section 2.8, Section 2.8.3, and Section 2.8.4. A draft preliminary regulatory history for MBOCA is included in Appendix A. Appendix B and Appendix C include a preliminary description of the reasonably available information used to perform the screening review for this proposed designation and that would also help inform the draft scope of the risk evaluation for MBOCA, if it is designated as a High-Priority Substance. These two appendices include a description of the searching methods (Appendix B) and the screening methods (Appendix C) EPA employed for MBOCA. Additional information regarding the process used to identify potentially relevant discipline-specific information for MBOCA is available in the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024). The proposed designation also includes a preliminary lifecycle diagram (Section 2.3.2), additional information about the physical and chemical properties (Appendix D), and environmental fate and transport property information (Appendix E) for MBOCA.

2 PROPOSED DESIGNATION OF MBOCA

2.1 Screening Review of the Reasonably Available Information for MBOCA

EPA's Office of Pollution Prevention and Toxics (OPPT) applies systematic review methods in the identification and review of reasonably available information in a manner that is objective, unbiased, and transparent for the purpose of screening the candidate chemical substance under its conditions of use against criteria and considerations listed in Section 1. EPA uses scientific information that is consistent with the best available science as required by the scientific standards in TSCA section 26(h) (15 U.S.C. 2625[h])). EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (U.S. EPA, 2021) (hereinafter referred to as "2021 Draft Systematic Review Protocol") to identify relevant information that informed the prioritization considerations set forth in 40 CFR 702.9. Based upon recommendations by the Scientific Advisory Committee on Chemicals regarding the 2021 Draft Systematic Review Protocol, EPA implemented improvements to its systematic review approaches and data gathering during the prioritization process. Specifically, EPA has incorporated additional data sources such as assessments published by other government agencies to identify potential hazards and exposures; clarified terminology to increase transparency in the systematic review process; and is presenting interactive literature inventory trees and evidence maps to better depict data sources containing potentially relevant information.

EPA conducted a comprehensive search for reasonably available information[1] to support the development of this proposed designation document for MBOCA. Chemical-specific literature searches and data source screening for relevance were conducted as described in Appendix B and Appendix C, respectively, for all disciplines (*i.e.*, physical and chemical properties, environmental fate and transport properties, occupational exposure and environmental release, general population, consumer and environmental exposure, environmental hazard, and human health hazard) from the following general categories of sources:

1. Databases containing publicly available, peer-reviewed literature;
2. Gray literature, which is defined as the broad category of data/information sources not found in standard, peer-reviewed literature databases;
3. Data and information submitted under TSCA sections 4, 5, and 8, as well as "for your information" (FYI) submissions; and
4. Data and information submitted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

While conducting a screening review of previous assessments identified to be potentially relevant for MBOCA, EPA identified additional primary data sources that were considered using the systematic review approach described in Appendix B. Public comments received during the public comment period following the initiation of prioritization were also considered for the proposed designation status of MBOCA. Note that information described in this document is as reported by the authors of the identified potentially relevant data sources, therefore some data sources may have different or conflicting conclusions for a given topic area. For the final designation status of MBOCA, EPA will consider

[1] *Reasonably available information* means information that EPA possesses or can reasonably generate, obtain, and synthesize for use, considering the deadlines specified in TSCA section 6(b) for prioritization and risk evaluation. Information that meets the terms of the preceding sentence is reasonably available information whether or not the information is confidential business information that is protected from public disclosure under TSCA section 14 (40 CFR 702.3).

additional relevant information that is made available through public comments on this proposed designation document as well as data call-in authorities (*e.g.*, TSCA section 8(d)), when applicable. Potentially relevant chemical-specific information received during the public comment period of data call-in authorities may also undergo systematic review approaches described in Appendix B and Appendix C.

2.2 Production Volume or Significant Changes in Production Volume

EPA considered current volume or significant changes in volume of MBOCA using information reported by manufacturers (including importers). EPA assembled reported information for years 1986 through 2019 on the production volume reported under the Chemical Data Reporting (CDR) rule, formerly known as the Inventory Update Rule (IUR) (40 CFR Part 711).

EPA considered both CBI and non-CBI reported production volume information reported to CDR and the annual national aggregate production volume, which is presented as a range to protect individual site production volumes that are CBI (Table 2-1). The screening review of production volume information indicates that since 1986, despite a decrease in production volume in 2002 and 2006, the annual national aggregate production volume of MBOCA has steadily increased and consistently has remained above 1 million pounds. The annual national aggregate production volume suggests a consistent potential source of exposure to MBOCA.

Table 2-1. 1986-2019 National Aggregate Production Volume Data for MBOCA

Year	Production Volume (lbs)
1986	>1M - 10M[a]
1990	>1M - 10M
1994	>1M - 10M
1998	>1M - 10M
2002	>500K - 1M
2006	500K - < 1M
2011	1M - 10M
2012	1M - 10M
2013	1M - 10M
2014	1M - 10M
2015	1M - 10M
2016	1M - 10M
2017	1M - 10M
2018	1M - 10M
2019	1M - 10M
[a] M = million	

2.3 Conditions of Use or Significant Changes in Conditions of Use

Under TSCA, the conditions of use of a chemical substance are "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of" (15 U.S.C. 2602(4); 40 CFR 702.3). The conditions of use or significant changes in conditions of use considered for the proposed designation of MBOCA were assembled from use information from CDR as well as other sources. Reporting requirements for the 2016 and 2020 CDR reporting cycles were different, as the function of the chemical in specific commercial and consumer uses was required beginning in 2020. Therefore, the

category and subcategory descriptions in Table 2-2 combine the use description and chemical function for commercial and consumer uses. EPA consulted a variety of other sources, including published literature, company websites, and government and commercial trade databases and publications to identify additional readily available information regarding the use of MBOCA. . Such additional information is organized in a separate table due to differences in how information was reported by the various data sources as compared to CDR (Table 2-3).

The categories and subcategories of conditions of use EPA identified from information reported to CDR for the proposed designation of MBOCA are presented in Table 2-2. It is difficult to discern whether there are significant changes in conditions of use for MBOCA based on reported information to CDR in 2016 and 2020 because guidance regarding the reporting of categories and subcategory information was updated between these periods. This update may have resulted in the use information being reported differently in 2020 compared to 2016, possibly leading to inaccurate implications that some uses may have commenced or ceased in recent years. Most reported conditions of use in CDR have remained unchanged between the 2016 and 2020 reporting periods, though some changes have been identified. In the 2016 reporting cycle, MBOCA was reported as a finishing agent in the category of all other basic organic chemical manufacturing. In 2020, MBOCA was reported as a catalyst in the same category. MBOCA was reported in the 2016 period as a urethane curing agent in plastics product manufacturing and wholesale and retail trade, while in the 2020 cycle, it was reported as a process regulator in plastics material and resin manufacturing. EPA is presenting information reported to CDR from both reporting cycles *as reported* to ensure all conditions of use information is captured and reduce any mischaracterization of the reported information.

In addition to the CDR information, EPA reviewed the uses of MBOCA from other publicly available data sources, such as the Toxics Release Inventory (TRI),[2] National Emissions Inventory (NEI), and Safety Data Sheets (SDS), and EPA Chemical and Product Categories (CPCat) (U.S. EPA, 2019). EPA also received public comments which can be found in docket ID number EPA-HQ-OPPT-2018-0464-0004 and EPA-HQ-OPPT-2018-0464-0008 containing potentially relevant information regarding the use of MBOCA. The relevant information is summarized in in Table 2-3.

Table 2-2 and Table 2-3 represent the initial information EPA has collected regarding the conditions of use based on CDR reporting and other sources for the purpose of prioritization. EPA plans to review and incorporate additional information on conditions of use, as relevant, received during the public comment period into the scope of the risk evaluation, should MBOCA be designated as a High-Priority Substance. As a result, EPA is seeking additional relevant information from the public during this second public comment period to clarify any inconsistencies regarding the conditions of use information identified by EPA thus far.

Table 2-2. Information Reported to CDR Regarding Conditions of Use of MBOCA

Life Cycle Stage[a]	Category[b]	Subcategory[c]	Reference(s)
Manufacture	Import	Import	2016 CDR
Processing	As a reactant	Finishing agent in all other basic organic chemical manufacturing	2016 CDR
		Intermediate in – plastic material and resin manufacturing – synthetic rubber manufacturing	2016 CDR; 2020 CDR
		Plasticizer in plastics material and resin manufacturing	2016 CDR; 2020 CDR

Life Cycle Stage[a]	Category[b]	Subcategory[c]	Reference(s)
		Plastics product manufacturing	2016 CDR
		Urethane curing agent in – plastics product manufacturing – wholesale and retail trade	2016 CDR
		Catalyst in all other basic organic chemical manufacturing	2020 CDR
	Incorporating into formulation, mixture or reaction product	Process regulator in paint and coating manufacturing	2016 CDR
		Process regulator in plastics material and resin manufacturing	2020 CDR
Distribution in commerce	Distribution in commerce	Distribution in commerce	
Commercial use	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere	2016 CDR
		Plasticizer in plastic and rubber products	2020 CDR
Disposal	Disposal	Disposal	

[a] Life cycle stage use definitions (40 CFR 711.3)
- "Industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed.
- "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services.
- "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use.
- Although EPA has identified both industrial and commercial uses here for purposes of distinguishing scenarios in this document, the Agency interprets the authority over "any manner or method of commercial use" under TSCA section 6(a)(5) to reach both.

[b] These categories of conditions of use appear in the preliminary life cycle diagram, reflect CDR codes, and broadly represent conditions of use of MBOCA in industrial and/or commercial settings.

[c] These subcategories reflect more specific conditions of use of MBOCA.

Table 2-3. Information Reported by Other Sources Regarding Conditions of Use of MBOCA

Use/Activity	Reference
Industrial surface coating and solvent use, and degreasing	U.S. EPA (2020)
Laboratory chemical	ECHA (2023)
Processing as a curing agent – polyurethane production used to manufacture semi-rigid foams, solid synthetic rubbers, and other urethane products. The curing process in polyurethane production can create materials as flexible as rubber tires or as rigid as solid wood	ATSDR (2017), OECD (2013b), ADC (2019), Tullo (2016)
Processing as a curing agent – epoxy resins	Danish EPA (2014)
Intermediate – polyurethane elastomers to produce polyurethane foams, synthetic urethane rubbers found in various commercial and consumer products	Tullo (2016), ATSDR (2017)

Use/Activity	Reference
Consumer products (public comment) – golf balls, robot wheels, roller skate wheels, sports boots, shoe soles, belts and rollers used in computer printers and photocopy machines, high-load wheels (caster wheels) for platform and tool-box carts, aftermarket rollers for boat trailers, snow-plow blades, glass polishing pads, glass wheels, glass rollers, paper, and corrugate cardboard	Docket ID numbers for public comments: EPA-HQ-OPPT-2018-0464-0004; EPA-HQ-OPPT-2018-0464-0008

The categories and subcategories of conditions of use from Table 2-2 are reflected in the preliminary life cycle diagram (Figure 2-1) and conceptual models in Section 2.8. In general, information reported to CDR are initially used to identify conditions of use due to EPA's ability to discern reporting entity-specific information and historical knowledge of connecting this information to conditions of use. However, information from public comments, stakeholder engagement and additional sources of publicly available relevant information are also routinely considered for determining conditions of use (Table 2-3). EPA plans to integrate the information in Table 2-3 with the categories and subcategories of conditions of use in Table 2-2 and plans to incorporate these activities, as relevant, into the life cycle diagram (Figure 2-1) and conceptual models (Section 2.8) during the scoping process should MBOCA be designated as a High-Priority Substance.

2.3.1 Activities That May Be Excluded

TSCA section 6(b)(4)(D) requires EPA, during scoping, to identify the conditions of use of a chemical substance that the Administrator expects to consider in a risk evaluation. In accordance with TSCA section 3(4)'s definition of conditions of use, EPA determines the circumstances appropriately considered to be conditions of use for a particular chemical substance.[2]

TSCA section 3(2) excludes from the definition of "chemical substance," among other things, "any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act [FFDCA] [21 U.S.C. 321]) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device" as well as "any pesticide (as defined in FIFRA [7 U.S.C. 136 et seq.]) when manufactured, processed, or distributed in commerce for use as a pesticide."

If MBOCA is designated as a High-Priority Substance, EPA plans to conduct a jurisdictional analysis during scoping on specific activities to determine whether they are excluded from the definition of a chemical substance under TSCA section 3(2).

[2] *Chemical substance* means any organic or inorganic substance of a particular molecular identity, including any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature, and any element or uncombined radical. Chemical substance does not include (1) any mixture; (2) any pesticide (as defined in FIFRA) when manufactured, processed, or distributed in commerce for use as a pesticide; (3) tobacco or any tobacco product; (4) any source material, special nuclear material, or byproduct material (as such terms are defined in the Atomic Energy Act of 1954 and regulations issued under such Act); (5) any article the sale of which is subject to the tax imposed by section 4181 of the Internal Revenue Code of 1954 (determined without regard to any exemptions from such tax provided by section 4182 or 4221 or any other provision of such Code); and (6) any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the FFDCA) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device (TSCA section 3(2)).

2.3.2 Overview of Conditions of Use and Preliminary Life Cycle Diagram

Figure 2-1 provides the preliminary life cycle diagram for MBOCA. The life cycle diagram is a graphical representation of the various life stages of the industrial, commercial, and consumer use categories of MBOCA. The preliminary life cycle diagram includes functional use codes for industrial uses and product categories for commercial and consumer uses.

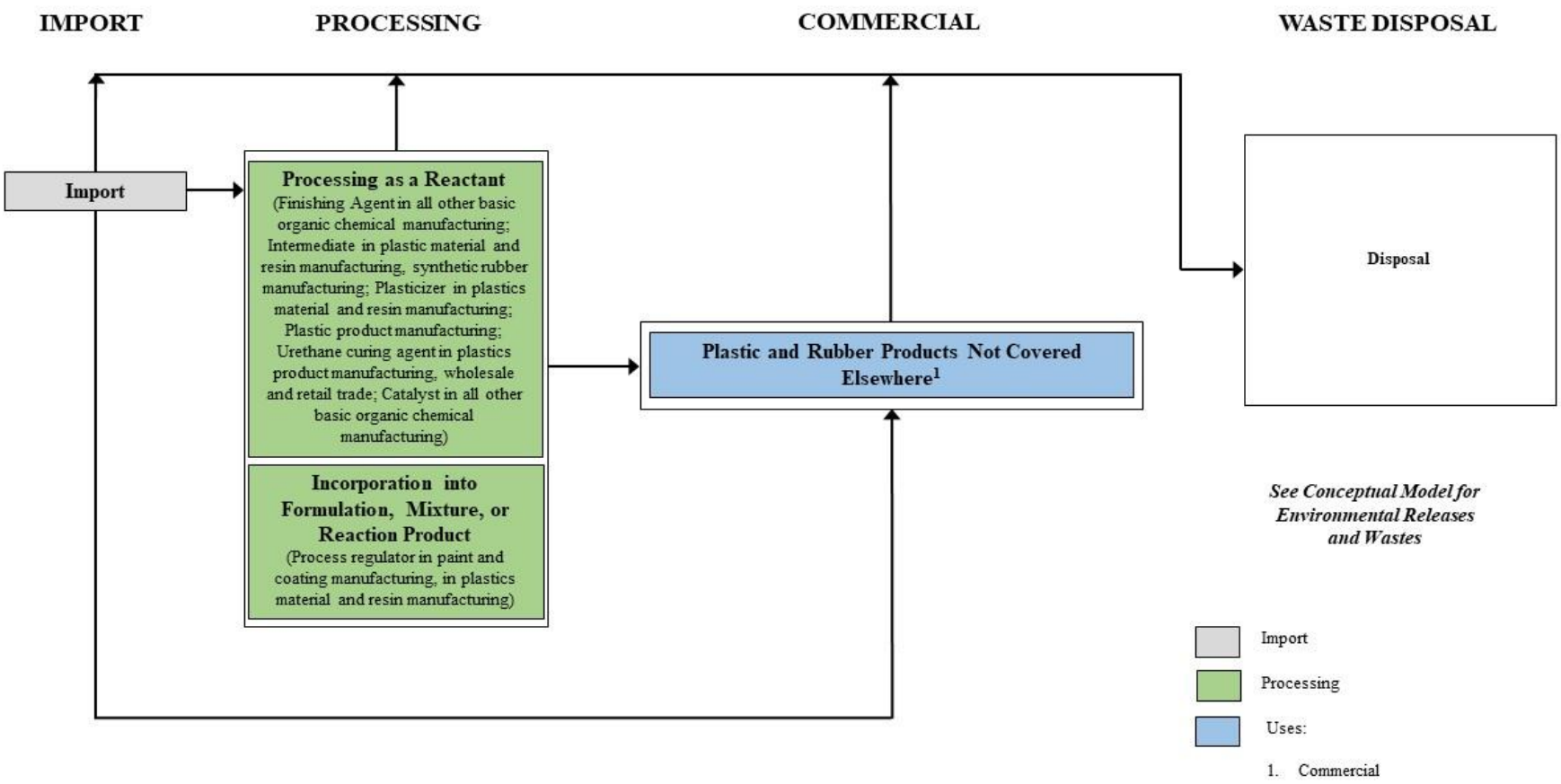


Figure 2-1. Preliminary Life Cycle Diagram for MBOCA

Distribution in commerce is not explicitly included in the life cycle diagram because its activities are associated with other conditions of use. Unloading and loading activities are associated with other conditions of use. The information in the preliminary life cycle diagram is grouped according to the 2016 and 2020 CDR processing codes and use categories from Table 2-2.

2.4 Potentially Exposed or Susceptible Subpopulations

Potentially exposed or susceptible subpopulation (PESS) means "a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly" (15 U.S.C. 2602(12)). General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

EPA conducted a screening review of reasonably available information on factors that may make population groups of concern more vulnerable to adverse effects (*e.g.*, unique pathways; behavioral, biological, or environmental factors that increase susceptibility), identifying unique considerations for subsistence populations when relevant and following best practices from the Agency's *Technical Guidance for Assessing Environmental Justice in Regulatory Analysis* (U.S. EPA, 2016). EPA has preliminarily identified a list of specific PESS factors that may contribute to a group having increased exposure or biological susceptibility. These factors include lifestage, occupational exposures, certain consumer exposures, nutrition, lifestyle activities, and proximity to facilities that manufacture or process a chemical substance.

For the proposed designation, EPA analyzed processing and use information included on the CDR Form U. These data provide an indication about whether children or other PESS may be exposed. EPA also used human health hazard information to screen against the PESS criterion for prioritization. During the screening review of data sources identified using the systematic review approaches described in Appendix C, information was identified that may be used to inform potential PESS considerations such as lifestage (*e.g.*, children and older adults), lifestyle activities (*e.g.*, subsistence fishing, Tribal lifeways), and site-related information (*i.e.*, information regarding either a specific site or the surrounding area near a site) associated with MBOCA. Based on this information, EPA believes that women of reproductive age and overburdened communities may be PESS for MBOCA. If MBOCA is designated as a High-Priority Substance, EPA will continue to use the information reasonably available information during the scoping process to identify those PESS the Agency plans to assess in the risk evaluation.

Children

EPA used data reported to the 2020 CDR to identify uses in products and articles intended for children for MBOCA. In addition, EPA considered information submitted during public comments about consumer uses (Table 2-3) and based on these comments determined that there might be potential for exposure in children given the consumer uses (*e.g.*, use in consumer products such as robot wheels, roller skate wheels, sports boots, shoe soles) identified for MBOCA. EPA did not identify MBOCA uses from other sources. Children's exposure to chemicals may differ from exposures among adults due to physiological and behavioral differences (U.S. EPA, 2008). For example, children have a higher ratio of body surface area to volume and higher inhalation rates per unit of body weight compared to adults. Additionally, children consume more of certain foods and water per unit of body weight. Children's behaviors that may increase exposure include oral exploration of their environment, touching the ground, surfaces, and objects, and ingesting human milk. In addition to consumer products, other media types of interest may include drinking water, indoor and outdoor air, soil, dust, human milk, and diet (*e.g.*, food) (U.S. EPA, 2011, 2008). Figure_Apx C-7 displays the media types identified for each data source. Through the implementation of systematic review approaches, as described in Section 8 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024), while EPA has identified no epidemiology data sources at this time that document reproductive and/or developmental effects in children, EPA has identified animal toxicity data used to

characterize human health reporting reproductive and/or development effects (see Figure_Apx C-10 in Appendix C.5.4). Furthermore, because screening through the systematic review approaches, as described in Appendix B, continues as new information becomes available, EPA may identify additional evidence of potential reproductive and/or developmental effects in children following exposure to MBOCA.

Women of Reproductive Age
EPA has not identified epidemiology data sources that document reproductive and/or developmental effects in women of reproductive age, but EPA has identified animal toxicity data used to characterize human health that reported reproductive and/or development effects (see Figure_Apx C-10 in Appendix C.5.4). Given that this is a screening review for data sources identified through the systematic review approaches, as described in Appendix B, as screening continues EPA may find additional evidence that women of reproductive age may be a PESS.

Consideration of women of reproductive age as a PESS was also based on exposure because women of reproductive age can also be workers in the manufacturing, processing, distribution in commerce, use, or disposal of MBOCA.

Overburdened Communities
EPA recognizes that some communities such as Tribal populations and fenceline communities (*i.e.*, communities in close proximity to facilities emitting air pollutants or living near effluent releases to water) may experience disproportionate environmental harms, risks, or multiple burdens from chemical exposure. Considerations that may be important for assessing chemical risks to such overburdened communities include aggregate exposure and sentinel exposures. EPA defines aggregate exposure as "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways (40 CFR 702.33)." Additionally, EPA defines sentinel exposure as "the exposure from a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures (40 CFR 702.33)." Environmental and socioeconomic stressors may also impact the health of these communities and their environment. In developing this proposed designation and throughout the prioritization process, EPA has engaged and will continue to engage the public to obtain information relevant to MBOCA.

Workers
Information about the uses and activities described in Section 2.8.2 was used to identify potential occupational exposure to MBOCA, indicating that workers are also likely to be PESS based on potentially greater exposure.

Consumers
Information about the uses and activities described in Section 2.8.3 was used to identify potential consumer exposure to MBOCA, indicating that consumers are also likely to be PESS based on potentially greater exposure.

2.5 Persistence and Bioaccumulation

EPA reviewed databases and previously conducted assessments to identify information for physical and chemical properties and fate endpoints to characterize the potential for MBOCA to persist in the environment or bioaccumulate. Table_Apx D-1 and Table_Apx E-1 summarize the information identified for physical and chemical properties and environmental fate and transport properties of MBOCA, respectively. Through the implementation of systematic review approaches, as described in

Sections 4 and 5 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024), EPA identified 41 data sources that contain potentially relevant physical and chemical property information and 50 data sources for the environmental fate characterization of MBOCA, as shown in Figure_Apx C-1 and Figure_Apx C-2, respectively.

With melting points reported between 101.19 and 110 °C (Reaxys, 2023; RSC, 2023; U.S. EPA, 2023), MBOCA exists as a colorless or yellow-brown solid with faint amine-like odor (NLM, 2023b; ATSDR, 2017). MBOCA has a water solubility of 13.9 mg/L at 24 °C (PhysProp, 2023), a vapor pressure of 1.0×10^{-5} mm Hg at 25 °C (NLM, 2023b; ATSDR, 2017), and an estimated Henry's Law Constant (HLC) ranging from 1.14×10^{-11} to 2.53×10^{-7} atm·m^3/mol (U.S. EPA, 2012), indicating negligible volatility from water.

Based on the octanol:water partition coefficient (log K_{OW}) of 3.66 at 25 °C (OECD, 2013b) in Table_Apx D-1 and organic carbon:water partition coefficient (log K_{OC}) of 3.56 at 35 °C (ECHA, 2023; OECD, 2013b) in Table_Apx E-1, although MBOCA will preferentially partition to organic phases over water, a small amount will also remain in water. When released to air, MBOCA is expected to have low persistence in the atmosphere. Once MBOCA is released to air (see Table 2-6), it will partition to particulate matter and to a lesser extent water vapor. Vapor-phase MBOCA absorbs wavelengths greater than 290 nm, and therefore, may be susceptible to direct photodegradation (NLM, 2023b; Reaxys, 2023). Additionally, MBOCA is expected to react with hydroxyl radicals (·OH) in the atmosphere, resulting in indirect photolysis half-life of 0.290-2.90 hours (ATSDR, 2017).

When released into water, aqueous-phase MBOCA is expected to have high persistence with negligible hydrolysis (half-life of 800 years at 25 °C (ECHA, 2023; NLM, 2023b; ATSDR, 2017)). Persistence in sediment and soil is also expected to be high with aerobic biodegradation results showing negligible biodegradability (ECHA, 2023; NITE, 2023; NLM, 2023b; ATSDR, 2017; OECD, 2013b). Two ready biodegradability MITI Test results were identified reporting degradation rates of 0 to 1 percent over 28 days and 0 percent over 8 weeks when testing 100 mg/L MBOCA (NITE, 2023; NLM, 2023b; OECD, 2013b). Though the MITI Tests employed a test concentration above MBOCA's water solubility, these results were supported by three additional biodegradation studies which reported biodegradability of 0 percent over 7 days, 0 percent over 6 weeks, and 10 percent over 7 days at MBOCA concentrations of 2.02, 2, and 2 mg/L, respectively (ECHA, 2023; NLM, 2023b; ATSDR, 2017). Additionally, MBOCA is expected to adsorb to suspended solids and sediment. Results from the STPWIN model of EPI Suite™ v 4.11 (assuming half-life of 10,000 hours) predicted low removal of MBOCA during wastewater treatment with a total of 26.13 percent removal, of which 14.9 percent was removed via sorption to primary sludge and 10.94 percent was removed via sorption to waste sludge (U.S. EPA, 2012).

MBOCA is expected to have some potential for bioconcentration in aquatic organisms. One study on bioaccumulation in fish (OECD 305) reported bioconcentration factor (BCF) values ranging from 114 to 398 L/kg in *Cyprinus carpio* (NITE, 2023; NLM, 2023b; OECD, 2013b). This was supported by the BCFBAF model of EPI Suite™ v 4.11 which estimated BCFs of 233.1, 234.8, 220.2 L/kg for lower, middle, and upper trophic levels, respectively, using the Arnot-Gobas method (U.S. EPA, 2012).

2.6 Storage Near Significant Sources of Drinking Water

To support the proposed designation, EPA screened MBOCA under its conditions of use with respect to the seven criteria in TSCA section 6(b)(1)(A) and 40 CFR 702.9. The statute specifically requires the Agency to consider the chemical substance's storage near significant sources of drinking water, which EPA interprets as direction to focus on the chemical substance's potential human health hazard and exposure.

EPA reviewed reasonably available information, including certain existing regulations or protections in place for the proposed chemical substance (Appendix A). To that end, EPA reviewed MBOCA's existing National Primary Drinking Water Regulations under the Safe Drinking Water Act (SDWA) (40 CFR Part 141 and regulations under the Clean Water Act (CWA) (40 CFR 401.15). In addition, EPA considered the consolidated list of chemical substances subject to reporting requirements under the Emergency Planning and Community Right-to-Know Act (EPCRA) section 302 (Extremely Hazardous Substances) and EPCRA section 313 [Toxic Chemicals]), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA; Hazardous Substances), and the Clean Air Act (CAA) section 112(r) (Regulated Chemicals for Accidental Release Prevention). MBOCA is regulated under EPCRA section 302 and CERCLA but is not regulated under the SDWA and CWA. MBOCA is regulated under EPCRA section 313, CERCLA sections 102(a) and 103, and section 112(b), 112(d) of the CAA. Regulation by one or more of these authorities is an initial indication that could be used to support a "may present an unreasonable risk of injury to human health or the environment" finding for the chemical the substance, if released near a significant source of drinking water.

EPA identified facilities reporting MBOCA to the TRI in 2022 near potential sources of drinking water using public water systems data stored in EPA's Safe Drinking Water Information System Federal Data Warehouse (U.S. EPA, 2022). This data warehouse is updated quarterly and provided by EPA's Office of Ground Water and Drinking Water (OGWDW). Specifically, EPA determined whether TRI reporting facilities are located inside defined Source Water Protection Areas or within 4 miles of wellheads to identify potential storage of MBOCA near sources of surface water and groundwater, respectively. TRI reporting facilities were used as a reasonably available indicator for locations where storage of MBOCA is likely to occur. Similarly, while the source water protection areas and wellhead protection points analyzed are not inclusive of all sources of drinking water, for the purposes of this document, they were used as a representation of likely drinking water sources.

As shown in Table 2-4, EPA identified 21 TRI reporting facilities that stored MBOCA on-site in 2022. Multiple facilities were identified to be within source water protection areas and/or near wellhead protection points. Should MBOCA be designated as a High-Priority Substance, additional information about potential exposure via drinking water identified during this and future public comment periods may be considered to help identify the appropriate pathways included in the scope of the risk evaluation during the scoping process.

Table 2-4. Summary of MBOCA TRI Facility Proximity to Drinking Water Sources

Group	Facility Count
All	21
Within source water protection area (surface water)	4
Within 4 miles of wellhead protection (ground water)	4

2.7 Hazard Potential

EPA considered reasonably available information from previous assessments, databases, as well as information sources identified in the systematic review approach outlined in Section 2.1 to conduct a screening review of potentially relevant hazard information for MBOCA. Furthermore, Section 8 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024) and Appendix C.5 specifically describe how information sources were identified and screened to characterize potential environmental and human health hazards resulting from exposure to MBOCA, respectively. A summary of references for hazards identified for MBOCA during the

screening step of systematic review is included in the interactive literature inventory tree in Appendix C.5.2. Through implementation of systematic review approaches, EPA identified 432 data sources that contain information that may be relevant for the characterization of potential hazard resulting from MBOCA exposure (Figure_Apx C-8). The evidence maps depicting a summary of data identified during the full-text screening of data sources considered through systematic review are also available in Appendices C.5.3 and C.5.4 for environmental and human health hazard, respectively.

2.7.1 Potential Environmental Hazard

EPA used the Agency's ECOTOXicology Knowledgebase (ECOTOX), previous assessments, and search results from chemical specific data sources using systematic review approaches to identify reasonably available information that may be relevant for characterizing potential environmental hazard resulting from exposure to MBOCA. Table_Apx B-3 lists the previous assessments used to identify potential environmental hazard information for MBOCA.

A summary describing the potential environmental hazard resulting from exposure to MBOCA is shown below. EPA has preliminarily characterized organisms into aquatic and terrestrial categories to summarize potentially relevant hazards that reflect exposure in these ecosystems. EPA recognizes that some organisms have home ranges or lifestages that span multiple ecosystems and therefore exposure can occur in a variety of media and pathways. Figure_Apx C-9 presents an evidence map that depicts health outcomes (*e.g.*, morphology, genotoxicity, reproduction), categorized by ecosystem and taxonomic group, from data sources identified for ecological receptors cited and reviewed in assessments and ECOTOX, and identified through the systematic review approach. EPA has identified one aquatic and one terrestrial data source that may be used to inform the potential environmental hazard resulting from exposure to MBOCA. These data sources underwent full-text screening as described in Appendix C.5 and met the screening criteria described in Appendix C.5.1. All the data sources reflected in Figure_Apx C-9 underwent a screening level review.

The search of reasonably available and relevant information by using systematic review approaches outlined in Appendix C.5.1 identified additional data sources that have not yet been characterized or extracted to the extent accomplished by previous assessments or ECOTOX. To identify quantitatively characterized environmental hazard endpoints resulting from MBOCA exposure, EPA identified reasonably available environmental hazard information cited by assessments and extracted in ECOTOX. Specifically, Figure 2-2 through Figure 2-4 present visualizations of environmental hazard endpoint categories organized by health outcomes that were identified using data sources cited and reviewed by previous assessments and ECOTOX.

Separate visualizations depict endpoints observed in taxa that inhabit different ecosystems and various types of exposure media. Generally, EPA has plotted endpoints as reported by previous assessments and ECOTOX, however some data processing (*e.g.*, de-duplication of endpoints reported by the same primary data source, standardization of effect concentration units) was conducted to ensure uniformity in the presentation of this hazard information. ECOTOX standardized effect concentration units for aquatic data were used where available. Additionally, where possible, author-reported effect concentration units were converted to mg/L (*e.g.*, ug/L values were divided by 1000, mol/L values were multiplied by the molecular weight and 1000, ppm values were re-coded to mg/L as they are equivalent) and mg/kg (*e.g.*, mmol/kg values were multiplied by the molecular weight, ug/g values were re-coded to mg/kg as they are equivalent) to maximize the amount of data that could be included in the visualizations. The visuals depict a summary of hazard endpoints resulting from MBOCA exposure concentrations (*e.g.*, mg/L, mg/kg) in different environmental media (*e.g.*, surface water, sediment). The shape of points represents the category of endpoint (*i.e.*, measurement of a biological effect in response to MBOCA exposure)

characterizing a respective hazard value. The color of points represents the data source the hazard value came from (*i.e.*, ECOTOX or the specific previous assessment name and publication year). Individual plot panels are presented for three general taxonomic groups: vertebrates, invertebrates, and vegetation and fungi. In situations in which endpoints were identified in both previous assessments and ECOTOX, EPA attributed and labeled those endpoints as being associated with ECOTOX to reduce duplication in representing reasonably available environmental hazard information.

Environmental hazard endpoints displayed represent measures of a biological effect in response to exposure to MBOCA and focused on the traditionally statistically derived endpoints (*e.g.*, LC_{50}, LOEC, NOEC). Although considered for identifying potential environmental hazard resulting from MBOCA exposure, uncommon endpoints (*e.g.*, effective concentration that causes a response that is x% of the maximum (EC_x) endpoints where x= uncommon percentages in which a statistically significant response was observed in specific studies) or taxa (*e.g.*, bacteria) cited by the previous assessments or available in ECOTOX may not be represented in these visualizations. As seen in the figures below, common endpoints were grouped into categories based on the quantitative nature of the biological effect in the exposed population and included no observed effect (*e.g.*, NO(A)EC[L], LC0, EC0), lowest observed effect (*e.g.*, LO(A)EC[L]), and effect observed in 10% of the population (*e.g.*, EC10, LC10), 20% of the population (*e.g.*, EC20, LC20), and 50% of the population (*e.g.*, EC50, IC50, LD50). Definitions of the health outcome terms displayed in these visualizations are located in ECOTOX *Appendix S. Effect Groups and Measurements*. The "multiple" health outcome term refers to hazard values for which multiple different biological effects were reported for a single endpoint. Definitions of endpoint terms displayed in these visualizations are located in ECOTOX *Appendix T. Endpoint Terms and Definitions*.

The health outcomes and endpoints selected for these visuals do not represent the entire data landscape of environmental hazard information. The visualizations mainly serve the purpose of depicting the results from a screening review of environmental hazard information resulting from exposure to MBOCA via various environmental media types and exposure routes.

2.7.1.1 Aquatic Organisms

Information was identified that may be used to identify toxicological effects for aquatic organisms resulting from MBOCA exposure via surface water and sediment. Figure 2-2 through Figure 2-3 depict reasonably available environmental hazard information sourced from previous assessments. Furthermore, one data source that underwent full-text screening contains environmental hazard information (*i.e.*, morphological data for aquatic invertebrates) that may inform potential hazard to aquatic organisms exposed to MBOCA (Figure_Apx C-9). More detailed information can be found in Appendix C.5.3.

Surface Water

As presented in Figure 2-2, environmental hazard information was identified from previous assessments for aquatic organisms (vertebrates, invertebrates, vegetation and fungi) via surface water exposure, however no aquatic surface water environmental hazard information was available in ECOTOX. In addition, the environmental hazard data from previous assessments span numerous health outcomes (*e.g.*, mortality, reproduction, growth) among the three taxonomic groups in Figure 2-2 in response to MBOCA exposure (0.0095 – 1.8 mg/L).

Specifically, data from previous assessments shown in Figure 2-2 represent empirical hazard values for a variety of aquatic vertebrates (*e.g.*, Japanese medaka (*Oryzias latipes*)), invertebrates (*e.g.*, water flea (*Daphnia magna*)), and plant and fungal species (*e.g.*, microalgae (*Pseudokirchneriella subcapita*); species name formerly known as *Selenastrum capricornutum* and more recently updated to

Raphidocelis subcapitata) (U.S. EPA, 2015; OECD, 2013a, c). Hazard values include endpoints such as lethal concentrations (*e.g.*, LC_{50}) and effect concentrations (*e.g.*, EC_{50}) as well as both lowest and no observed effect concentrations (*e.g.*, LOEC, NOEC). Reported MBOCA data includes acute aquatic toxicity values less than 1 mg/L for fish and invertebrate species, as well as chronic aquatic toxicity values less than 1 mg/L for algae and less than 0.01 mg/L for water fleas (OECD, 2013c). For instance, a four-day, semi-static exposure of Japanese medaka to MBOCA resulted in a LC_{50} value of 0.61 mg/L. While a 21-day chronic exposure of water fleas resulted in a LC_{50} value of 0.046 mg/L, the LOEC for inhibition of reproductive output for water fleas occurred at 0.03 mg/L (U.S. EPA, 2015; OECD, 2013a, c). The LOEC reported for growth inhibition of the microalgae *P. subcapita* was 0.45 mg MBOCA/L following a three-day exposure (OECD, 2013a).

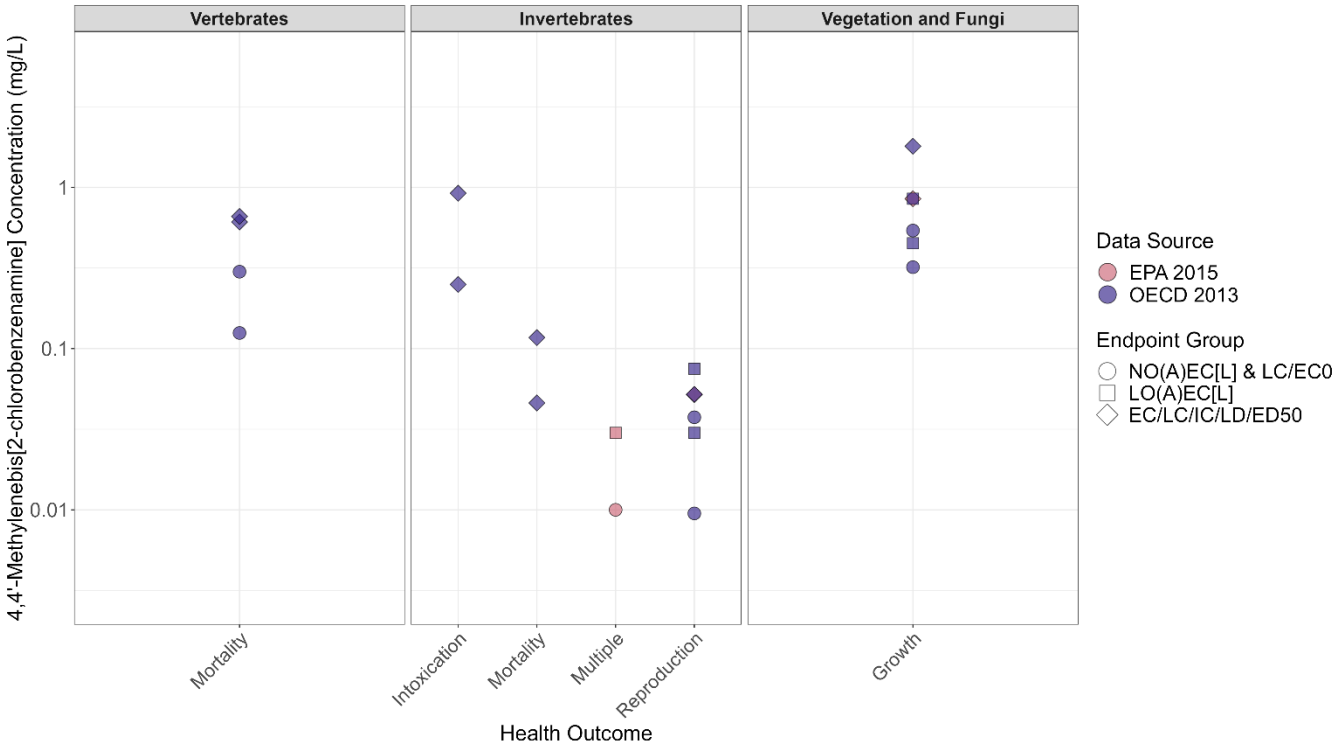


Figure 2-2. Summary of Select Environmental Hazard Information for Aquatic Organisms Resulting from Surface Water Exposure for MBOCA

Sediment

Figure 2-3 presents environmental hazard information identified from previous assessments for aquatic invertebrates via sediment exposure, however no aquatic environmental hazard information was available in ECOTOX. As shown in Figure 2-3, only growth health outcomes were identified in response to a relatively narrow range of MBOCA concentrations (84 - 182 mg/kg sediment dry weight).

Data identified in previous assessments suggest that MBOCA exposure in aquatic sediments can influence the emergence of sediment-dwelling midges (*Chironomus yoshimatsui*) (OECD, 2013a, c). Specifically, a 27-day, semi-static chronic exposure to MBOCA affected the emergence rate of midges resulting in an EC_{50} value of 150, LOEC value of 182, and NOEC value of 84 mg/kg dry sediment (OECD, 2013a, c).

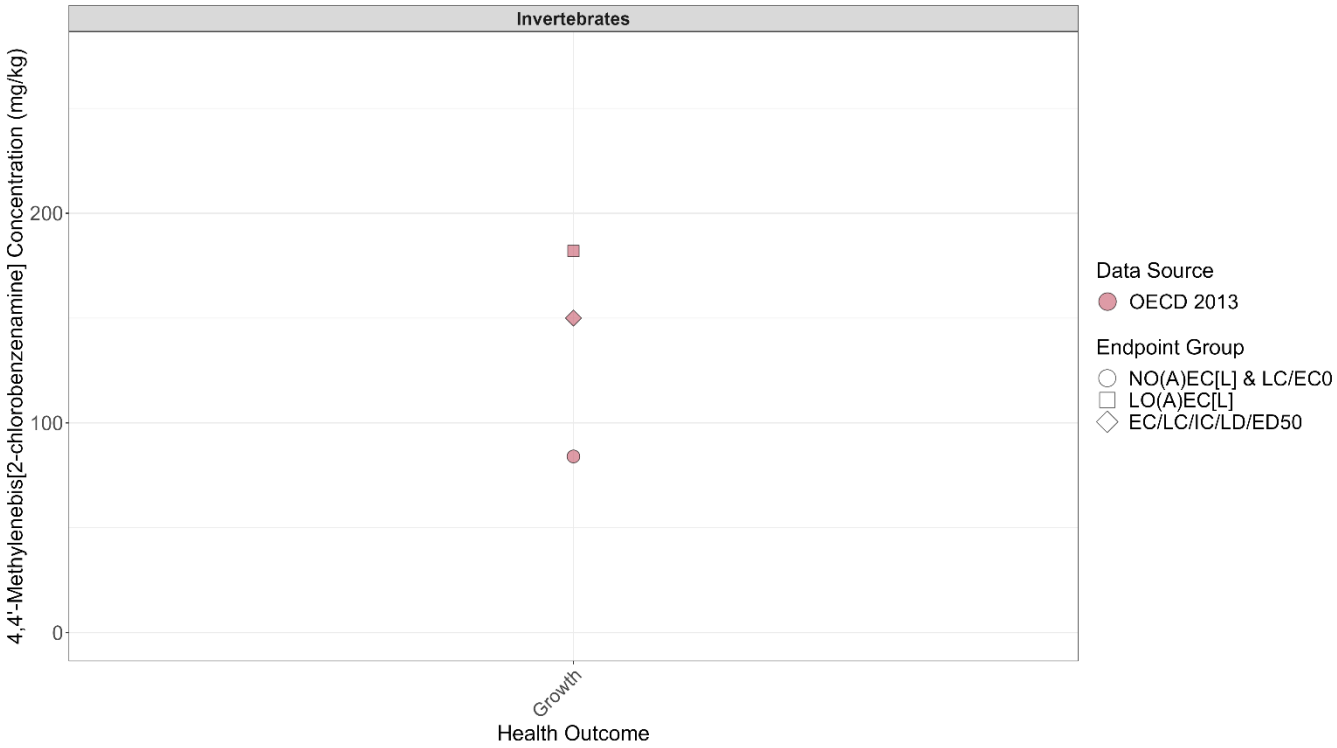


Figure 2-3. Summary of Select Environmental Hazard Information for Aquatic Organisms Resulting from Sediment Exposure for MBOCA

2.7.1.2 Terrestrial Organisms

Preliminary information was identified that may be used to identify toxicological effects for terrestrial organisms resulting from MBOCA exposure. Figure 2-4 depicts reasonably available environmental hazard information sourced from ECOTOX representing a single study. Furthermore, one data source that underwent full-text screening contains environmental hazard information (*i.e.*, genotoxicity and reproduction data for terrestrial invertebrates) that may inform potential hazard to terrestrial organisms resulting from MBOCA exposure (Figure_Apx C-9). Information on the health outcome identified for invertebrates can be found in Figure_Apx C-9. Additional health outcomes across taxonomic groups could potentially be identified as more information becomes available.

As shown in Figure 2-4, the terrestrial environmental hazard information identified for invertebrates was via dietary exposure. Only genetics health outcomes were identified in this ECOTOX study in response to one unique concentration of MBOCA (1,336 mg/L). Specifically, a 48-hour MBOCA exposure via food in larvae of the fruit fly *Drosophila melanogaster* resulted in a lowest observed effect level (LOEL) of 1,336 mg/L for mutagenic effects in wings (Kugler-Steigmeier et al., 1989). No other data were available in ECOTOX and no data were reported in any of the previous assessments for terrestrial organisms (U.S. EPA, 2015; OECD, 2013a, c). Thus, data are lacking for terrestrial vertebrate, invertebrate, and plant and fungal species.

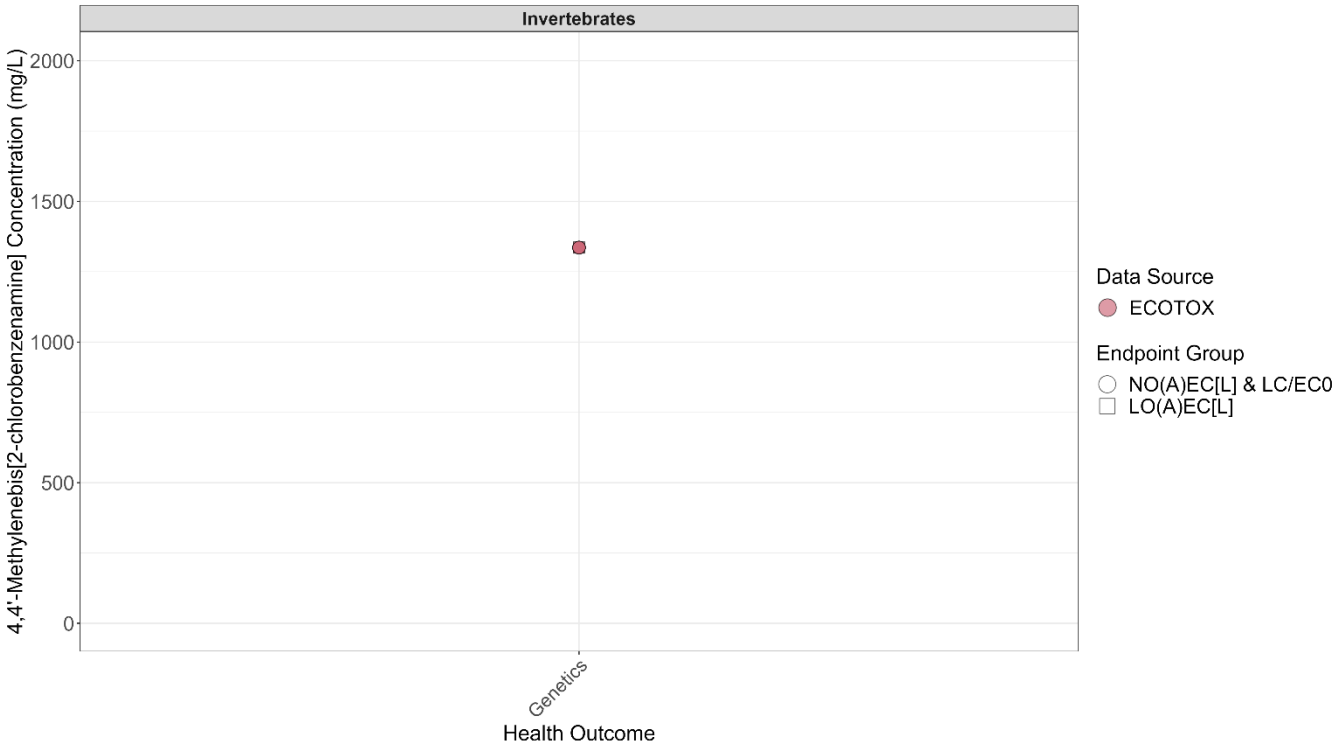


Figure 2-4. Summary of Select Environmental Hazard Information for Terrestrial Organisms Resulting from Exposure for MBOCA

2.7.2 Potential Human Health Hazard

EPA used previously published assessments and search results from EPA's identification of chemical-specific data sources using systematic review approaches to identify reasonably available information that is relevant for characterizing potential human health hazard resulting from exposure to MBOCA, based on both epidemiological and animal toxicity information.

Table_Apx B-4 lists the previous assessments used to identify potential human health hazards for MBOCA. Table 2-5 presents classifications assigned by various organizations associated with MBOCA exposure based on epidemiological and/or animal toxicity information (indicated by the "X" in the "Based on Epidemiology" and/or "Based on Animal Toxicity" columns. If the evidence (animal toxicity and/or epidemiological data) supporting the classification for a respective assessment is only based on either animal toxicity or epidemiological data, no table note was used to indicate the type of evidence in the "Exposure Route" column.

Table 2-5. Risk Assessment Classifications for MBOCA Based on Human Health Hazard Information

Risk Classification System	Health outcome	Classification	Assessment Label[a]	Exposure Route[b,c,d]	Based on Animal Toxicity Data	Based on Epidemiology Data
Approved Criteria, Hazardous Substances Information	Cancer	T; R45 (Category 2) – may cause cancer	NICNAS 2014	Diet; subcutaneous injection	X	

Risk Classification System	Health outcome	Classification	Assessment Label[a]	Exposure Route[b,c,d]	Based on Animal Toxicity Data	Based on Epidemiology Data
System (HSIS)						
Approved Criteria, Hazardous Substances Information System (HSIS)	Genotoxicity	Xn; R68 (Category 3) – possible risk of irreversible effects	NICNAS 2014	*In vitro*	X	
Approved Criteria, Hazardous Substances Information System (HSIS)	Acute toxicity	Xn; R22 – harmful if swallowed	NICNAS 2014	Oral	X	
Globally Harmonized System (GHS)	Cancer	H350 (Category 1) – may cause cancer	NICNAS 2014	NA	X	
Globally Harmonized System (GHS)	Cancer	Category 1B – may cause cancer	ECCC 2020	NA	X	
Globally Harmonized System (GHS)	Genotoxicity	H341 (Category 2) – suspected of causing genetic defects	NICNAS 2014	NA	X	
Globally Harmonized System (GHS)	Acute toxicity	H302 (Category 4) – harmful if swallowed	NICNAS 2014	Oral	X	
US Environmental Protection Agency (EPA)	Cancer	Reasonably anticipated to be a human carcinogen; Equivalent to "Likely to be Carcinogenic	ATSDR 2017	Oral	X	
			NTP 2021	Oral[d], subcutaneous injection[b], dermal[c], inhalation[c]	X	X

Risk Classification System	Health outcome	Classification	Assessment Label[a]	Exposure Route[b,c,d]	Based on Animal Toxicity Data	Based on Epidemiology Data
		to Humans" per EPA Guidelines for Carcinogen Risk Assessment, March 2005	ECCC 2020	Oral, subcutaneous injection	X	
US Environmental Protection Agency (EPA) – Health Affects Assessment Summary Tables (HEAST)	Cancer	Group B2 – probable human carcinogen	ORD 2006	Oral	X	
International Agency for Research on Cancer (IARC)	Cancer	Group 1 – carcinogenic to humans	ATSDR 2017	Based on IARC 2012	X	
			IARC 2012	Oral[d], dermal[d], subcutaneous injection[b], inhalation[c]	X	X
			ECCC 2020	Based on IARC 2012	X	
International Agency for Research on Cancer (IARC)	Cancer	Group 2A – probably carcinogenic to humans	ORD 2006	Oral, subcutaneous injection	X	
American Conference of Governmental Industrial Hygienists (ACGIH)	Cancer	A2 – suspected human carcinogen	ORD 2006	Based on ACGIH studies not available (no PDF)	X	
			ATSDR 2017	Based on ACGIH studies not available (no PDF)	X	

Risk Classification System	Health outcome	Classification	Assessment Label[a]	Exposure Route[b,c,d]	Based on Animal Toxicity Data	Based on Epidemiology Data

[a] "Assessment labels" refer to labels associated with previous assessments identified in various figures within Section 2.7.2. These are commonly secondary sources citing the risk classification system and outcome listed. Recent risk assessments may cite older outcomes that are still supported by current research.
[b] Exposure route is associated with an animal toxicity study.
[c] Exposure route is associated with an epidemiological study.
[d] Exposure route is associated with both an animal and epidemiological study.

Figure 2-5 presents quantitative endpoints identified by various organizations in the respective existing assessments of MBOCA (listed in Table_Apx B-4) based on epidemiological and animal toxicity studies, respectively. The Y-axis represents endpoint values (no units). The X-axis specifies exposure type and units (top) while also specifying health outcome type for each exposure type (bottom). As indicated by the key, circles specify an animal toxicity study outcome, triangles specify an epidemiology outcome, and squares denote an outcome that considered both animal data and epidemiology data in its determination. Each outcome specifies the assigning risk assessment by color (see key). Values listed as a range are depicted as two points – the minimum and maximum. Health outcome types have been generalized here so that the range of values for a particular category can be visualized (*i.e.*, "cancer index" includes cancer slope factor (CSF), unit risk factor, and other cancer-related endpoints). The range of endpoint values (EV) required that they be represented within ranges to allow for better clarify of individual points. The ranges can be seen in the grey boxes on the right of each row of dot plots. When the EV range is ≥ 1 the software (R, version 4.2.2, Tidyverse package) does not plot the "0" on the y-axis. Some assessments identified endpoint values that are not depicted in Table 2-5due to various reasons specific to how previous assessments reported hazard information from epidemiological and/or animal toxicity studies (*e.g.*, lack or use of units cited by previous assessments that do not represent the majority of information identified for a respective exposure route, observational endpoints without quantitative values) further described below. Table_Apx C-10 contains all endpoint values considered from previous assessments based on epidemiological and animal toxicity studies, including the subset depicted in Figure 2-7. All endpoint values shown below are greater than zero. To simplify the figure, endpoint values may occasionally exceed the upper bounds of the Y axis.

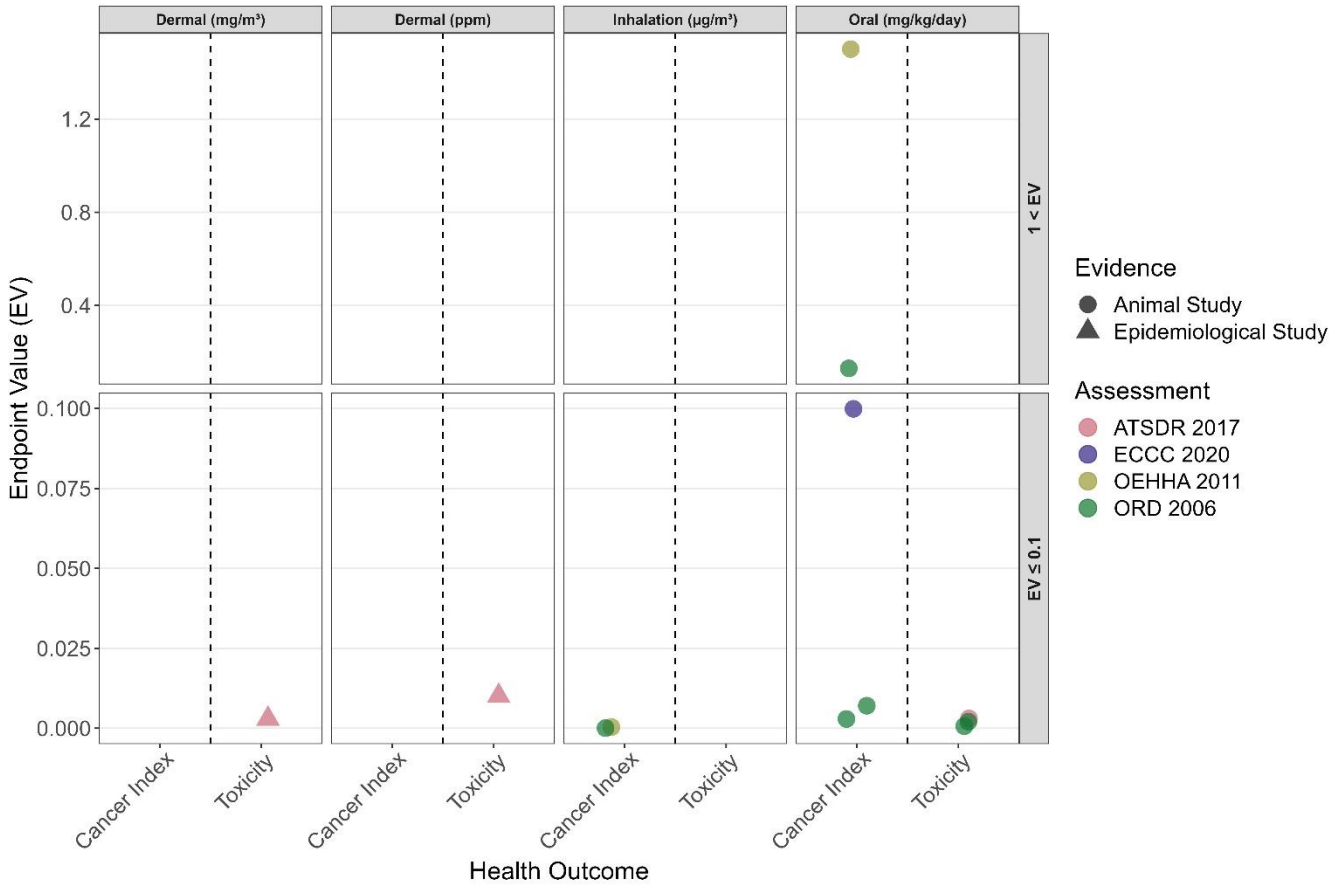


Figure 2-5. Summary of Quantitative Endpoints from Previous Assessments for Health Outcomes by Exposure Type for Animal Toxicity and Epidemiological Information

Figure 2-6 and Figure 2-7 present health outcomes associated with MBOCA exposure that are identified in previous risk assessments based on epidemiological or animal toxicity evidence, respectively. The Y-axis lists health outcomes associated with endpoints identified in previous assessments, which are listed in Table_Apx B-4. The X-axis serves to count the number of previous risk assessments that consider the corresponding health outcome. Blue segments denote counts of all the reported health outcomes considered and identified by various assessments. Red segments denote health outcomes utilized to characterize assessment-specific determinations: "primary outcomes" for epidemiological studies and "critical outcomes" for animal toxicology studies due to differences in discipline terminology. Designation as a primary or critical endpoint is otherwise equivalent.

Sections 2.7.2.1 and 2.7.2.2 summarize epidemiological and animal toxicity evidence that characterizes the potential human health hazard resulting from exposure to MBOCA, that supports the designation of MBOCA as a High-Priority Substance. Figure_Apx C-10 presents an evidence map depicting health outcomes categorized by exposure route from data sources identified using systematic review approaches.

2.7.2.1 Epidemiological Information

During prioritization, hazard information was identified for humans resulting from epidemiological studies, with exposure to MBOCA via ocular/eye contact, dermal/skin contact, and/or inhalation (see Figure_Apx C-10). Health outcomes considered include carcinogenicity, genotoxicity, and acute and chronic toxicity. This information is organized here according to endpoint descriptive type. Table 2-5 lists qualitative classifications reported by previous risk assessments. Meanwhile, Figure 2-5 contains

quantitative endpoints identified by various organizations. Figure 2-6 hallmarks the outcomes described in these risk assessments by organ system, noting critical epidemiological findings that were considered in the development of assessment-wide endpoints.

As identified in Table 2-5, carcinogenicity descriptions and designations for MBOCA by previous assessments range from "reasonably anticipated to be a human carcinogen" determined based on sufficient evidence of carcinogenicity from studies in experimental animals (NTP, 2021) and "carcinogenic to humans" (IARC, 2012). As presented in Figure 2-6, eight previous assessments described carcinogenic effects, but none were noted to be critical. No additional carcinogenicity qualitative endpoints were described by previous assessments.

No qualitative genotoxic effects for MBOCA were described in previous assessments.
As shown in Figure 2-6, within the "other" health outcome category, four of the previous assessments described genotoxic effect endpoints, however none were noted to be critical (ECCC, 2020; NICNAS, 2014; OECD, 2013a, c; IARC, 2012).

In addition, epidemiological data identified in previous assessments suggest that MBOCA exposure is associated with acute and chronic toxic effects (Figure 2-5). Critical chronic toxicity endpoints were identified resulting from dermal exposure (*e.g.*, potential increases in urinary bladder cancer following occupational exposure to MBOCA) (ATSDR, 2017). Although not included in Figure 2-5, acute toxic effects following exposure to MBOCA included skin and eye irritation, and conjunctivitis (ATSDR, 2017; OECD, 2013a, c). No additional acute or chronic toxicity endpoints from exposure to MBOCA were described by previous assessments. EPA would welcome additional information regarding toxicological effects resulting from exposure to MBOCA during this public comment period.

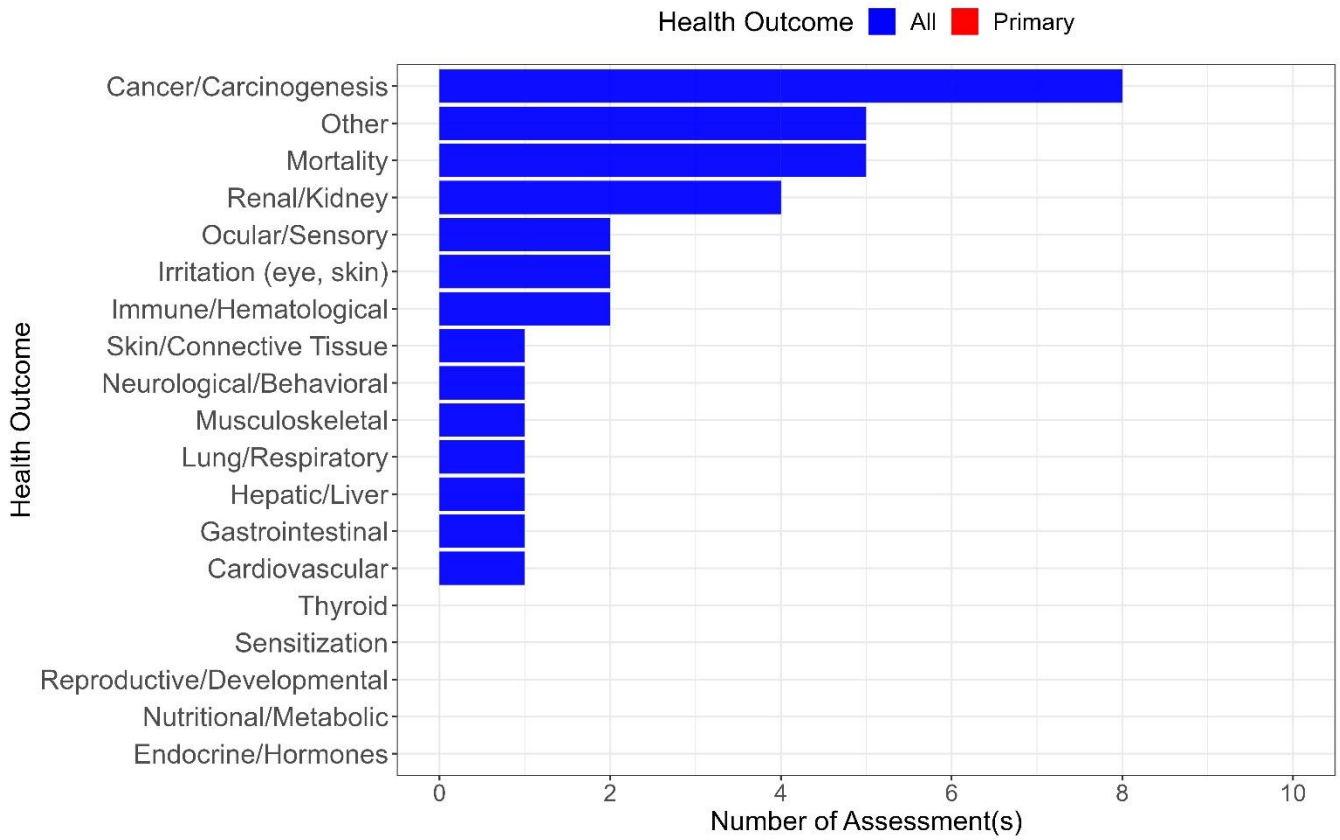


Figure 2-6. Summary of Epidemiological Data Cited by Previous Assessments

The "other" health outcome category in Figure 2-6 refers to outcomes (*e.g.*, absorption, distribution, metabolism, and excretion [ADME], genotoxicity and clinical signs) not explicitly listed as either a primary health outcome(s) or all health outcomes.

2.7.2.2 Animal Toxicity Information that Supports Human Health Hazard

EPA identified animal toxicity information resulting from MBOCA exposure via diet, oral gavage, dermal, eye, and/or inhalation (Table_Apx C-10). Health outcomes considered include carcinogenicity, genotoxicity, and acute and chronic toxicity. This information is organized here according to endpoint descriptive type. Table 2-5 lists qualitative classifications reported by previous risk assessments. Meanwhile, Figure 2-5 contains quantitative endpoints identified by these various organizations. Figure 2-7 summarizes the outcomes described in these risk assessments by organ system, noting critical animal findings that were considered in the development of assessment-wide endpoints.

As seen in Table 2-5, statements on MBOCA's carcinogenicity range from "May Cause Cancer" (ECCC, 2020; NICNAS, 2014), to "Carcinogenic to Humans" (ECCC, 2020; ATSDR, 2017; IARC, 2012). EPA found 37.5 percent of assessments described carcinogenic effects to be critical (Figure 2-7). These findings are based on a variety of observations in animals. Oral and injection studies in rats and mice resulted in liver hepatocellular adenoma or carcinoma (benign and malignant), lung adenoma and adenocarcinoma, Zymbal gland carcinoma, haemangiosarcoma, and mammary gland adenocarcinoma. Studies in dogs reported urinary bladder transitional-cell carcinoma, as well as urethra mixed transitional-cell carcinoma and adenocarcinoma (NTP, 2021; ECCC, 2020; ATSDR, 2017; NICNAS, 2014; OECD, 2013c; IARC, 2012; OEHHA, 2011; ORD, 2006). Based on these observed effects, human dose approximations were determined by previous risk assessments and are plotted in Figure 2-5.

Not visualized in this figure due to design limitations, ECCC (2020) reports a lifetime cancer risk (LCR) of $3x10^{-8}$, as well as a carcinogenic margin of exposure (MOE) of $2.78x10^{-8}$.

Genotoxicity effects for MBOCA outlined on Table 2-5 include "Possible Risk of Irreversible Effects" and "Suspected of Causing Genetic Defects" (NICNAS, 2014). Seven previous risk assessments described genotoxic effects, but none were noted to be critical (Figure 2-7). Genotoxic effects following exposure to MBOCA included chromosomal aberration and metabolic activation in hamster lung cells; unscheduled DNA synthesis in rat, mouse, and hamster hepatocytes; sister chromatid exchange in hamster ovary cells; and hypoxanthine-guanine phosphoribosyltransferase (HPRT) locus mutation in human lymphoblastoid (ECCC, 2020; NICNAS, 2014). These effects observed in animals were not described uniquely as genotoxicity-specific human endpoints in Figure 2-5. Rather, these data were considered with other chronic toxicity findings and were plotted as such.

Table 2-5 describes one qualitative acute toxicity effect of exposure to MBOCA: "Harmful if Swallowed" (NICNAS, 2014). No additional acute toxicity qualitative endpoints were described. In the previous risk assessments, acute toxic effects found in oral rat studies included weight loss, lethargy, cyanosis, deep breathing, and distended stomachs and bladders (NICNAS, 2014). Based on these observed effects, acute human dose approximations were determined by various previous risk assessments and are plotted in Figure 2-5.

Prior risk assessments did not describe chronic toxicity qualitative risk classifications related to MBOCA exposure. Rather, all reported data was quantitatively used by previous assessments. Chronic toxicity in oral rat studies resulted in anemia, methemoglobinemia, reproductive toxicity, hepatocytomegaly, bile duct proliferation, and enlarged spleen (OECD, 2013c; ORD, 2006). Finally, chronic studies in dogs resulted in hepatic hyperplasia and increased serum alanine aminotransferase (ATL) (ATSDR, 2017; ORD, 2006). Based on these observed effects, chronic human dose approximations were determined by various previous risk assessments and are plotted in Figure 2-5. As seen in Figure 2-7, 50 percent of the previous risk assessments indicate that described liver toxicity effects are critical for characterizing MBOCA toxicity, demonstrating liver cancer and noncancer effects following exposure. EPA would welcome additional information regarding toxicological effects resulting from MBOCA exposure during this public comment period.

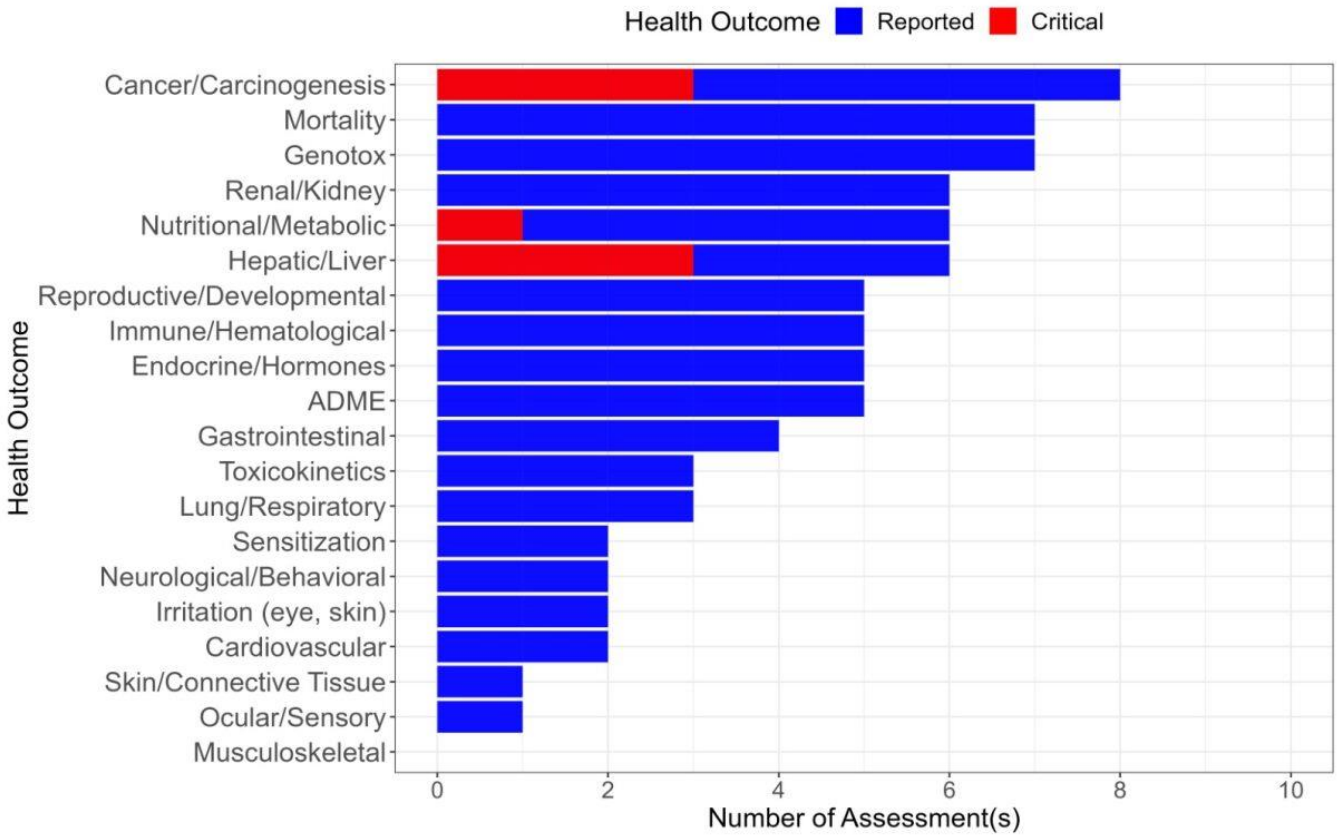


Figure 2-7. Summary of Human Health Animal Toxicity Data Cited by Previous Assessments

2.8 Exposure Potential

EPA considered reasonably available information from previous assessments, databases (*e.g.,* TRI, Water Quality Portal, National Emissions Inventory), as well as information sources identified in the systematic review approach outlined in Section 2.1 to conduct a screening review of relevant information for MBOCA. Section 7 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024) and Appendices C.3, and C.4 describe how information sources were identified and screened, respectively, to characterize potential exposure to MBOCA. Interactive literature inventory tree diagrams available in Appendices C.3.2 and C.4.2, summarize information identified during the screening step of systematic review that inform the exposure potential of MBOCA for different populations. Evidence maps depicting a summary of data identified through the full-text screening of data sources considered through systematic review are available in Appendices C.3.3 and C.4.3 for occupational exposure and environmental release and general population, consumer, and environmental exposure, respectively.

2.8.1 Release Information

Chemical releases to the environment from conditions of use are considered in identifying potential exposure and may be derived from reported data obtained through direct measurement, calculations based on empirical data or assumptions and models.

Toxics Release Inventory

EPA's TRI database contains information on chemical waste management activities reported to EPA by industrial and federal facilities, including quantities released into the environment (*i.e.*, to air, water, and disposed of to land), treated, burned for energy, recycled, or transferred off-site to other facilities for these purposes.

Under section 313 of EPCRA, MBOCA is a TRI-reportable substance effective January 1, 1987 (40 CFR 372.65). For TRI reporting, facilities in covered sectors in the United States are required to disclose release and other waste management activity quantities of MBOCA under the CASRN 101-14-04 if they manufacture, import, or process more than 25,000 pounds or otherwise use more than 10,000 pounds of the chemical in the previous calendar year by July 1 of the following year. For more detailed information about how facilities report information to EPA, see the Agency's web page on TRI reporting.

Table 2-6 provides total quantities of MBOCA released onsite to air, water, and land, and aggregated quantities of MBOCA transferred off-site to publicly owned treatment works (POTWs) and other wastewater treatment facilities (non-POTW). The table does not include any reported quantities pertaining to other waste management activities (*e.g.*, recycling, combustion for destruction) that occurred on- or off-site during reporting years 2013-2022. The "Number of Facilities" is the count of unique facilities that filed a TRI Form R report for MBOCA for reporting years 2013-2022. The TRI data presented in Table 2-6 reflect updates made to the publicly available TRI dataset in October 2023 regarding the addition of TRI information reported to EPA in 2022.

Table 2-6. Summary of TRI Data on MBOCA from Reporting Years 2013 through 2022 to Assess Exposure Potential

Year	Number of Facilities that Reported	Total Quantities Released On-Site to Air (lbs)	Total Quantities Released On-site to Water (lbs)	Total Quantities Released (Disposed of) On-Site to Land (lbs)	Total Quantities Transferred to POTW (lbs)	Total Quantities Transferred to Other (Non-POTW) Wastewater Treatment Facilities (lbs)	Total Release Quantity (lbs)
2013	28	4641	0	150	0	1671	6462
2014	27	3290	0	0	0	3563	6853
2015	26	3805	0	0	0	3628	7433
2016	25	1500	0	0	0	1281	2781
2017	30	439	0	0	0	1809	2248
2018	26	8	0	0	0	1633	1641
2019	26	8	0	0	0	1880	1888
2020	25	8	0	0	0	1628	1638
2021	22	17	0	0	0	500	517
2022	24	5	0	0	0	1436	1441

Of the more than 32,000 pounds of MBOCA disposed of or otherwise released to the environment during reporting years 2013-2022, about 58 percent was released or disposed of offsite, and about 42 percent was released or disposed of onsite. The majority of onsite releases were to air. The majority of offsite transfers were to other non-POTW wastewater treatment facilities. There has been a general downward trend in onsite air. Offsite transfers to other non-POTW wastewater treatment facilities show similar variability.

National Emissions Inventory (NEI)
The NEI was established to track emissions of Criteria Air Pollutants (CAPs) and CAP precursors and assist with National Ambient Air Quality Standard (NAAQS) compliance under the CAA. Air emissions data for the NEI are collected at the state, local, and Tribal (SLT) level. SLT air agencies then submit these data to EPA through the Emissions Inventory System (EIS). In addition to CAP data, many SLT air agencies voluntarily submit data for pollutants on EPA's list of hazardous air pollutants (HAPs). EPA uses the data collected from SLT air agencies in conjunction with supplemental HAP data to build the NEI. EPA releases an updated NEI every three years. The most recent version of the NEI was released in 2020 for reporting year 2017.

Table 2-7 presents the 2020 NEI data for MBOCA (U.S. EPA, 2020) Nearly 89 percent of the NEI reported air emissions are from industrial processes sources not elsewhere classified (NEC) indicating they could not be assigned to any specific industrial sector. For point/major sources, NEI reports emissions data at the emission unit-level. Emission units are the individual processes at a facility with the *potential* to emit a regulated air pollutant.

Table 2-7. Summary of 2020 NEI Air Emissions Data on MBOCA

Sector	Total Emissions (lbs.)
Industrial processes – NEC	6,245
Solvent – industrial surface coating & solvent use	739
Solvent – degreasing	74
Industrial processes – storage and transfer	7
Waste disposal	6

Discharge Monitoring Reports (DMR)
Under the CWA, EPA regulates the discharge of pollutants into receiving waters through the National Pollutant Discharge Elimination System (NPDES). A NPDES permit authorizes discharging facilities to discharge pollutants to specified limits. There are 2 types of effluent limits: technology-based and water quality-based. NPDES permits may also authorize facilities to process, incinerate, landfill, or beneficially use sewage sludge. Under the CWA, EPA may authorize state, Tribal, and territorial governments to write, administer, and enforce NPDES permits. NPDES permits apply pollutant discharge limits to each outfall at a facility. The permits require facilities to monitor their discharges and report the results to EPA and the state regulatory agency. Facilities report these results in DMRs. No NPDES data for MBOCA have been reported.

2.8.2 Industrial and Commercial Activities and Uses

Worker exposure to this chemical may be affected by many factors, including but not limited to volume produced, processed, distributed, used and disposed of; physical form and concentration; processes of manufacture, processing, and use; chemical properties such as vapor pressure; and exposure controls such as engineering controls, administrative controls, and use of a personal protective equipment (PPE) program.

MBOCA has a recommended exposure limit (REL) established by the National Institute for Occupational Safety and Health (NIOSH). The REL is 0.00027 ppm over up to a 10-hour workday, time-weighted average (TWA) in a 40-hours work week. American Conference of Governmental Industrial Hygienists (ACGIH) has also established a Threshold Limit Values (TLV) of MBOCA as 0.01 ppm (inhalable fraction and vapor) over an 8-hour workday, TWA. EPA has identified the NIOSH

REL and ACGIH TLV for MBOCA as indicators of potential workplace exposure to MBOCA via the inhalation route.

The pathways and routes of exposure EPA believes may be relevant to workers and occupational non-users (ONUs) are presented in Figure 2-8. This preliminary conceptual model is presented for public comment as part of this prioritization action, and EPA has not yet determined which pathways and routes would be included in the scope of the risk evaluation, should MBOCA be designated a High-Priority Substance.

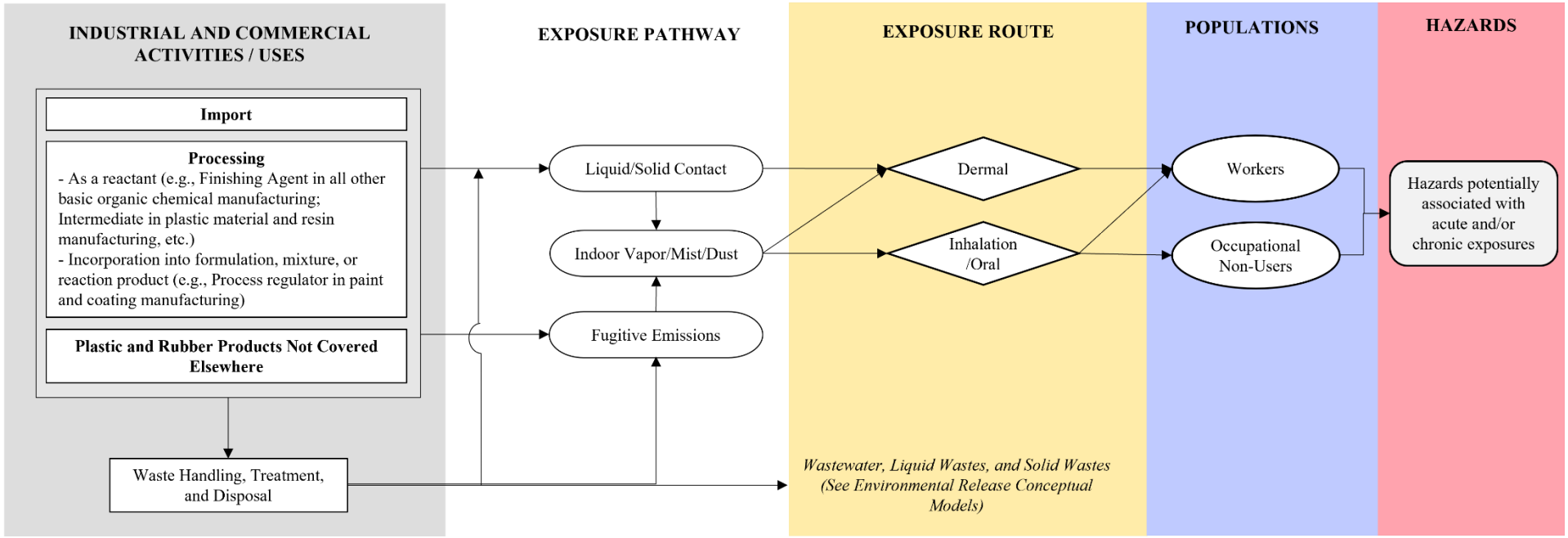


Figure 2-8. Preliminary Conceptual Model for Industrial and Commercial Activities and Uses: Potential Worker and ONU Exposures and Hazards for MBOCA

The preliminary conceptual model presents the potential exposure pathways, exposure routes, and hazards to human subpopulations from industrial and commercial activities and uses of MBOCA. Populations include PESS (see Section 2.4**).** The information in the preliminary conceptual model is group according to the 2016 and 2020 CDR processing codes and use categories from Table 2-2.

2.8.3 Consumer Activities and Uses

The 2016 and 2020 CDR cycles did not report consumer uses for MBOCA, therefore a preliminary consumer activity and uses conceptual model is not presented. Information regarding consumer use of MBOCA was also not identified in the ChemExpo database. Because reporting of MBOCA is not required, information regarding use in children's products was not identified in the HPCDS database. Based on EPA's screening review of reasonably available information, one study containing information relevant to consumer use was identified, see Figure_Apx C-7. EPA has and will continue to consider public comments received regarding the presence of MBOCA in consumer products and articles. Specifically, during the first comment period, Polyurethane Manufacturers Association submitted comments regarding use of MBOCA in consumer products. These comments are reflected in Table 2-3.

Based on the limited information on consumer uses, EPA seeks confirmation, comment or additional information on consumer uses. EPA will consider additional public comments received regarding the presence of MBOCA in consumer products and articles. EPA has not yet determined which pathways and routes would be included in the scope of the risk evaluation, should MBOCA be designated a High-Priority Substance.

2.8.4 Environmental and General Population Exposure

The manufacturing, processing, distribution, use, and disposal of MBOCA may result in releases to the environment and potential exposure to aquatic and terrestrial ecological receptors (biota), as well as the general human population. Environmental and general population potential exposure are informed by releases into the environment, overall persistence, degradation, and bioaccumulation within the environment and partitioning across different media. Concentrations of MBOCA in biota (*e.g.*, fish, shellfish, and breast milk) may also provide evidence that supports potential exposure.

As described in existing assessments (NTP, 2021; ECCC, 2020; ATSDR, 2017), MBOCA may be present in the outdoor environment as a result of releases from multiple industrial and commercial conditions of use identified in Section 2.3. Chemical manufacturing, manufacturing of products containing MBOCA, and use of MBOCA in other chemical manufacturing processes may contribute to releases to different media and to the outdoor environment.

Based on these environmental releases reported in Section 2.8, as well as physical and chemical and environmental fate and transport properties of MBOCA discussed in Sections 2.5, Appendix D, and Appendix E, MBOCA may be present in ambient air, surface water, wastewater, and soil. Data reported to TRI indicate releases of MBOCA to air, land, and wastewater. When released into water, aqueous-phase MBOCA is expected to have high persistence with negligible hydrolysis (ECHA, 2023; NLM, 2023b; ATSDR, 2017). MBOCA is expected to have a high persistence in sediment and soil because there is negligible biodegradation (ECHA, 2023; NITE, 2023; NLM, 2023b; ATSDR, 2017; OECD, 2013b). MBOCA is expected to have some potential for bioconcentration in aquatic organisms (NITE, 2023; NLM, 2023b; OECD, 2013b). EPA identified environmental concentration data to inform potential exposure to MBOCA (Table 2-8).

Table 2-8. Exposure Information for Potential Environment and General Population Exposure

Database	Environmental Concentration Data Present?	Human Biomonitoring Data Present?	Ecological Biomonitoring Data Present?	Reference
Air Monitoring Network	No	No	No	Washington State Department of Ecology (2008)
Biomonitoring California	No	No	No	CDPH, CalEPA (2006)
Biomonitoring in Washington State	No	No	No	Washington State Department of Health (2009)
Comparative Toxicogenomics Database	No	No	No	MDI, NC State University (2002)
Environmental Information Management (EIM) System	No	No	Yes	Washington State Department of Ecology (2019)
EPA AirToxScreen	Yes	No	No	U.S. EPA (2019)
EPA Ambient Monitoring Technology Information Center	Yes	No	No	U.S. EPA (1990)

Database	Environmental Concentration Data Present?	Human Biomonitoring Data Present?	Ecological Biomonitoring Data Present?	Reference
(AMTIC) – Air Toxics Data				
EPA Air Quality System (AQS)	No	No	No	U.S. EPA (1980)
EPA Fish Tissue Studies	No	No	No	U.S. EPA (2006)
EPA Six-year Review	No	No	No	U.S. EPA (2003)
EPA Unregulated Contaminant Monitoring Rule	No	No	No	U.S. EPA (1996)
Food and Drug Administration (FDA) Total Diet Study	No	No	No	FDA (1991)
Great Lakes Environmental Database	No	No	No	U.S. EPA (2018b)
International Council for the Exploration of the Sea	No	No	No	ICES (2018)
Targeted National Sewage Sludge Survey	No	No	No	U.S. EPA (2006)
The National Health and Nutrition Examination Survey	No	No	No	CDC (2013)
NWQMC, USGS, and EPA Water Quality Portal (WQP)	Yes	No	Yes	NWQMC, USGS, U.S. EPA (2021)

2.8.4.1 Environmental Exposure

Potentially relevant and reliable environmental monitoring data for MBOCA were considered from existing assessments, databases (*e.g.*, DMR and Water Quality Portal (WQP)) as well as peer-reviewed and gray literature data sources identified in the search of reasonably available information described in Section 7 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024). Table 2-8 identifies data sources that contain environmental concentration data that may be used to inform potential exposure to MBOCA for ecological receptors.

Disposal and waste treatment activities associated with MBOCA and products containing MBOCA are expected to result in releases to the outdoor environment. MBOCA may be present in ambient air, surface water, wastewater, and soil as a result of these releases. Environmental monitoring information as identified in databases and systematic review has indicated that MBOCA has been measured in ambient air, surface water, groundwater, and soil (U.S. EPA et al., 2023; ATSDR, 2017). Aquatic ecological receptors may be exposed to MBOCA due to the TRI-reported releases and MBOCA measured in surface water (0.01–399.4 mg/L) (U.S. EPA et al., 2023). Terrestrial ecological receptors may also be exposed to MBOCA due to TRI-reported releases and MBOCA measured in soil (4.6-1146 ppm) (ATSDR, 2017).

2.8.4.2 General Population Exposure

The 2016 and 2020 CDR cycles did not report consumer uses for MBOCA. EPA will consider public comments received regarding the presence of MBOCA in consumer products and articles. EPA has not yet determined which pathways and routes would be included in the scope of the risk evaluation, should MBOCA be designated a High-Priority Substance.

Environmental releases of MBOCA from certain conditions of use identified in Section 2.3, such as processing, commercial uses, and waste disposal may lead to general population exposure. Table 2-8 identifies data sources that contain environmental concentration data that may be used to inform general population exposure to MBOCA. Releases of MBOCA from certain conditions of use, such as processing, commercial activities, and waste disposal, may result in general population exposures. Elevated concentrations of MBOCA have been measured in the vicinity of chemical manufacturing plants, wastewater facilities, and industrial lagoons (NTP, 2021). The National Toxicology Program has indicated that dermal contact is the primary route of exposure to MBOCA for the general population (NTP, 2021).

The pathways and routes of environmental and general population exposure EPA believes may be associated with environmental releases and wastes are depicted in the preliminary conceptual model shown in Figure 2-9. This preliminary conceptual model is presented for public comment as part of this prioritization action. EPA has not yet determined which pathways and routes would be included in the scope of the risk evaluation, should MBOCA be designated a High-Priority Substance.

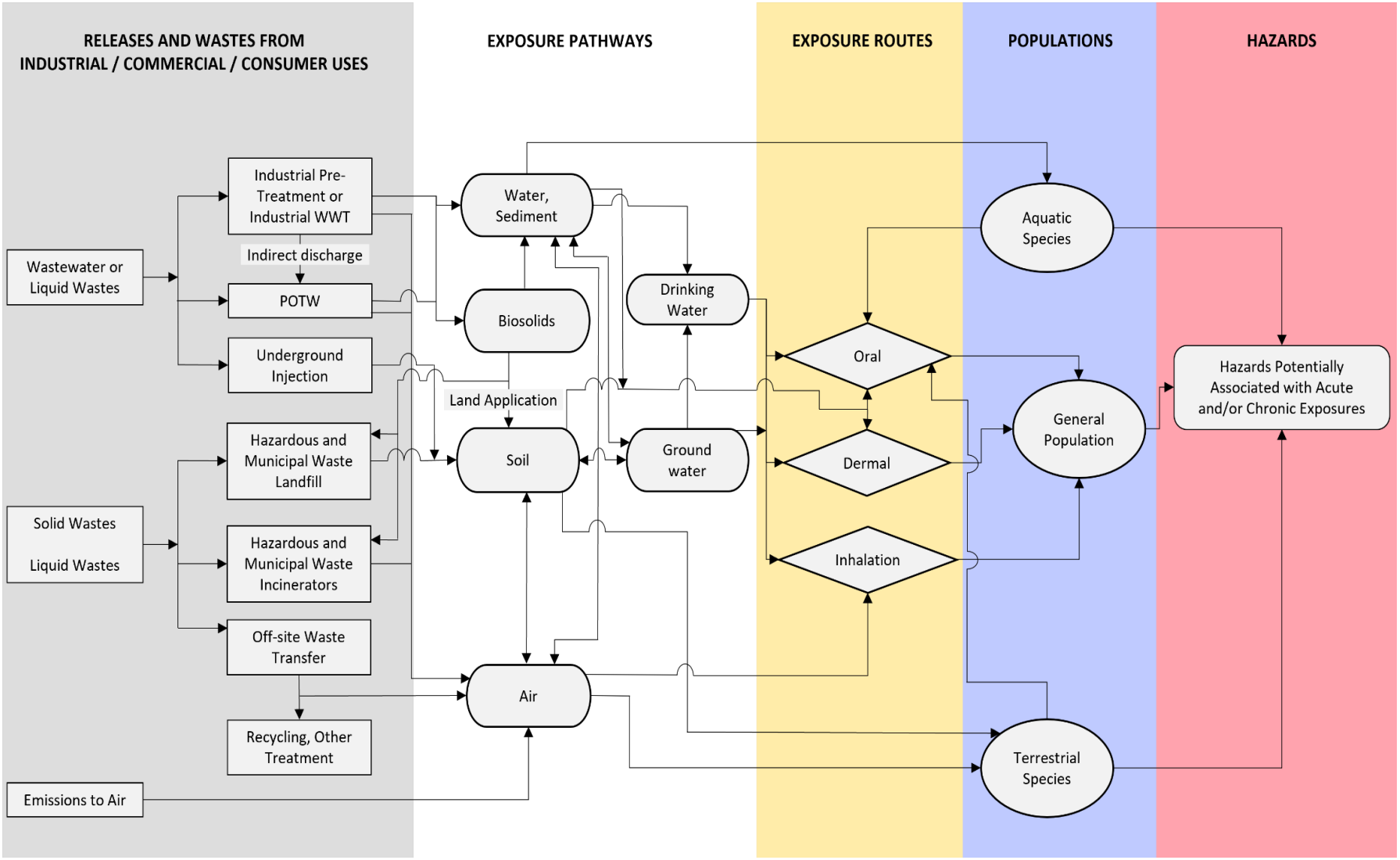


Figure 2-9. Preliminary Conceptual Model for Environmental Releases and Wastes: Potential Environmental and General Population Exposures and Hazards for MBOCA

Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTWs (indirect discharge). For consumer uses, such wastes may be released directly to POTWs. Drinking water will undergo further treatment in drinking water treatment plant. Groundwater may also be a source of drinking water. Inhalation from drinking water may occur via showering. Populations include PESS (see Section 2.4). The information in the preliminary conceptual model is grouped according to the 2016 and 2020 CDR processing codes and use categories from Table 2-2.

2.9 Other Risk-based Criteria Relevant to the Proposed Designation of MBOCA

EPA did not identify other risk-based criteria relevant to the proposed designation of MBOCA under TSCA.

REFERENCES

ADC. (2019). GHS Safety Data Sheet (SDS): Curene 442. Adrian, MI. http://www.martin-employees.com/MSDS/Urethane/Curene%20442%20SDS.pdf

ATSDR. (2017). Toxicological profile for 4,4'-Methylenebis(2-chloroaniline) (MBOCA). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=997&tid=209

Danish EPA. (2014). Hazardous substances in plastics. In Survey of Chemical Substances in Consumer Products. (132).

ECCC. (2020). Draft Screening Assessment: Aromatic Amines Group - Chemical Abstracts Service Registry Numbers: 86-30-6, 90-30-2, 95-55-6, 101-14-4, 101-96-2, 121-69-7, 122-39-4, 63449-68-3. Ottawa, Canada: Government of Canada. https://www.canada.ca/content/dam/eccc/documents/pdf/pded/aromatic-amines/Draft-screening-assessment-aromatic-amines-group.pdf

ECHA. (2023). ECHA Registration dossier: 4,4'-methylenebis[2-chloroaniline]. Available online at https://echa.europa.eu/registration-dossier/-/registered-dossier/14426

Howard, BE; Phillips, J; Miller, K; Tandon, A; Mav, D; Shah, MR; Holmgren, S; Pelch, KE; Walker, V; Rooney, AA; Macleod, M; Shah, RR; Thayer, K. (2016). SWIFT-Review: A text-mining workbench for systematic review. Syst Rev 5: 87. http://dx.doi.org/10.1186/s13643-016-0263-z

IARC. (2012). Chemical agents and related occupations: A review of human carcinogens [IARC Monograph]. Lyon, France. https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Chemical-Agents-And-Related-Occupations-2012

Kugler-Steigmeier, ME; Friederich, U; Graf, U; Lutz, WK; Maier, P; Schlatter, C. (1989). Genotoxicity of aniline derivatives in various short-term tests. Mutat Res 279: 279-289. http://dx.doi.org/10.1016/0027-5107(89)90011-0

NICNAS. (2014). Benzenamine, 4,4'-methylenebis[2-chloro-: Human health tier II assessment. Sydney, Australia: Australian Industrial Chemicals Introduction Scheme (AICIS). https://www.industrialchemicals.gov.au/sites/default/files/Benzenamine%2C%204%2C4%27-methylenebis%5B2-chloro-_Human%20health%20tier%20II%20assessment.pdf

NITE. (2023). Japan Chemicals Collaborative Knowledge (J-CHECK) database: CAS RN 101-14-4, Endpoints.

NLM. (2023a). Hazardous Substances DataBank (HSDB): 4,4'-Methylenebis(2-chloroaniline). Available online at https://pubchem.ncbi.nlm.nih.gov/source/hsdb/2629

NLM. (2023b). PubChem: 4,4'-Methylenebis(2-chloroaniline) - Chemical and Physical Properties. Available online

NTP. (2021). 4,4′-Methylenebis(2-chloroaniline): CAS No. 101-14-4. In Report on carcinogens, fifteenth edition (15th ed.). Research Triangle Park, NC: U.S. Department of Health and Human Services. https://ntp.niehs.nih.gov/ntp/roc/content/profiles/methylenebis_chloroaniline.pdf

OECD. (2013a). SIDS Dossier: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). Tokyo, Japan: National Institute of Health Sciences, Organisation for Economic Co-operation and Development. https://hpvchemicals.oecd.org/UI/handler.axd?id=93d3c71b-1608-4238-b29f-3c7a4af94e1f

OECD. (2013b). SIDS Initial Assessment Profile: 4,4'-Methylenebis(2-chloroaniline) (MBOCA) Paris, France: Organisation for Economic Co-operation and Development, CoCAM 5.

OECD. (2013c). SIDS Initial Assessment Report: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). Tokyo, Japan: National Institute of Health Sciences, Organisation for Economic Co-operation and Development. https://hpvchemicals.oecd.org/UI/handler.axd?id=93d3c71b-1608-4238-b29f-3c7a4af94e1f

OEHHA. (2011). Technical support document for cancer potency values, Appendix B: Chemical-specific summaries of the information used to derive unit risk and cancer potency values. Sacramento, CA: CalEPA. https://oehha.ca.gov/media/downloads/crnr/appendixb.pdf
OEHHA. (2014). Technical support document for noncancer RELs, Appendix D: Individual acute, 8-hour, and chronic Reference Exposure Level summaries. Sacramento, CA: CalEPA. https://oehha.ca.gov/media/downloads/crnr/appendixd1final.pdf
ORD. (2006). Provisional Peer Reviewed Toxicity Values (PPRTV) for 4,4'-Methylenebis (2-chloroaniline) (CASRN 101-14-4). Cincinnati, OH: EPA. https://cfpub.epa.gov/ncea/pprtv/chemicalLanding.cfm?pprtv_sub_id=1801
PhysProp. (2023). PhysProp experimental data: 4,4'-Methylenebis(2-chloroaniline): SRC, Inc.
Reaxys. (2023). Reaxys Query: 4,4'-Methylenebis(2-chloroaniline): Elsevier.
RSC. (2023). Merck Index: 4,4′-Methylenebis[2-chloroaniline] [Database]. Retrieved from https://merckindex.rsc.org/monographs/m7401
Rumble, JR. (2023). CRC Online: 4,4'-Methylenebis[2-chloroaniline].
Tullo, AH. (2016). Polyurethane makers prepare for a phase out. Retrieved from https://cen.acs.org/articles/94/i23/Polyurethane-makers-prepare-phase.html
U.S. EPA. (2008). Child-specific exposure factors handbook [EPA Report]. (EPA/600/R-06/096F). Washington, DC. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=199243
U.S. EPA. (2011). Exposure factors handbook: 2011 edition [EPA Report]. (EPA/600/R-090/052F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100F2OS.txt
U.S. EPA. (2012). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11 [Computer Program]. Washington, DC. Retrieved from https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface
U.S. EPA. (2014). TSCA work plan for chemical assessments: 2014 update. Washington, D.C.: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. https://www.epa.gov/sites/production/files/2015-01/documents/tsca_work_plan_chemicals_2014_update-final.pdf
U.S. EPA. (2015). Screening-level hazard characterization: 4,4'-Methylenebis(2-chlorobenzenamine) (MBOCA; CASRN 101-14-4). Washington, DC. https://chemview.epa.gov/chemview/proxy?filename=HC101144.pdf
U.S. EPA. (2016). Technical guidance for assessing environmental justice in regulatory analysis. Washington, DC. https://www.epa.gov/environmentaljustice/technical-guidance-assessing-environmental-justice-regulatory-analysis
U.S. EPA. (2019). Chemical and Products Database (CPDat). Available online at https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat
U.S. EPA. (2020). National Emissions Inventory (NEI): Acetaldehyde, Acrylonitrile, Benzenamine, MBOCA, and Vinyl Chloride [Database]. Washington, DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics Retrieved from https://www.epa.gov/air-emissions-inventories/national-emissions-inventory-nei
U.S. EPA. (2021). Draft systematic review protocol supporting TSCA risk evaluations for chemical substances, Version 1.0: A generic TSCA systematic review protocol with chemical-specific methodologies. (EPA Document #EPA-D-20-031). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0414-0005
U.S. EPA. (2022). Safe Drinking Water Information System (SDWIS) Fed Data Warehouse: Sensitive drinking water-related information, 2022Q2. Washington, DC. Retrieved from https://www.epa.gov/ground-water-and-drinking-water/safe-drinking-water-information-system-sdwis-federal-reporting

U.S. EPA. (2023). CompTox chemicals dashboard: 4,4'-methylenebis(2-chloroaniline). Washington, DC. Retrieved from https://comptox.epa.gov/dashboard/chemical/details/DTXSID5020865

U.S. EPA. (2024). Updated search strategies used to identify potentially relevant discipline-specific information: Systematic review support document for the proposed designation of acetaldehyde, acrylonitrile, benzenamine, vinyl chloride, and 4,4'-methylene bis(2-chloroaniline) as High-Priority Substances. Washington, DC: Office of Pollution Prevention and Toxics.

U.S. EPA; U.S.G.S.; NWQMC. (2023). 4,4-Methylene-bis(2-chloroaniline) (CAS RN: 101-14-4): WQP Output (NWIS, STEWARDS & STORET), Site data & sample results (physical/chemical metadata) [Database]: National Water Quality Monitoring Council. Retrieved from https://acwi.gov/monitoring/waterqualitydata.html

APPENDICES

Appendix A PRELIMINARY REGULATORY HISTORY

The chemical substance, MBOCA, is subject to federal and state laws and regulations in the United States (Table_Apx A-1 and Table_Apx A-2). Regulatory actions by other governments, Tribes, and international agreements applicable to MBOCA are listed in Table_Apx A-3.

Table_Apx A-1. Federal Laws and Regulations

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
EPA Regulations		
TSCA – section 6(b)	EPA is directed to identify High-Priority chemical substances for risk evaluation.	MBOCA is one of the High-Priority Substance candidates for which EPA initiated prioritization under TSCA (88 FR 87423, December 18, 2023).
TSCA – section 8(a)	The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States.	MBOCA manufacturing (including importing), processing and use information is reported under the CDR rule (40 CFR part 711).
TSCA – section 8(c)	TSCA section 8(c), as implemented at 40 CFR part 717, requires manufacturers (including importers) and processors to maintain records of significant adverse reactions to health or the environment alleged to have been caused by chemical substances or mixtures and to submit such records upon EPA's request.	EPA issued a Federal Register Notice requiring the submission of TSCA section 8(c) records associated with MBOCA (88 FR 88915, December 26, 2023). The Notice required records to be received by EPA on or before February 26, 2024.
TSCA – section 8(e)	Manufacturers (including importers), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.	One substantial risk report received for MBOCA (1993) (U.S. EPA, ChemView. Accessed August 23, 2023.).
EPCRA – section 313	EPCRA section 313 – also known as the Toxic Release Inventory (TRI) – requires annual reporting from facilities in specific industry sectors that employ 10 or more full-time equivalent employees and that manufacture, process or otherwise use a TRI-listed chemical in quantities	MBOCA is a listed substance (or part of a listed chemical category) subject to reporting requirements under 40 CFR 372.65 effective as of January 01, 1987.

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	above threshold levels. A facility that meets reporting requirements must submit a reporting form for each chemical for which it triggered reporting, providing data across a variety of categories, including activities and uses of the chemical, releases and other waste management (*e.g.*, quantities recycled, treated, combusted) and pollution prevention activities (under section 6607 of the Pollution Prevention Act). These data include on- and off-site data as well as multimedia data (*i.e.*, air, land and water).	
CAA – Section 112(b)	Contains the original list of 189 hazardous air pollutants (HAPs) that Congress added in 1990. Under 112(c) of the CAA, EPA must identify and list source categories that emit listed HAPs and then set emission standards for those listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAP by adding or deleting a substance. Since 1990, EPA has both removed HAPs from and added HAPs to the original list.	MBOCA is listed as a HAP (42 U.S. Code section 7412).
CAA – section 112(d)	Directs EPA to establish, by rule, NESHAPs for each category or subcategory of listed major sources and area sources of HAPs (listed pursuant to Section 112(c)). For major sources, the standards must require the maximum degree of emission reduction that EPA determines is achievable by each particular source category. This is generally referred to as maximum achievable control technology (MACT). For areas sources, the standards must require generally achievable control technology (GACT) though may require MACT. Section 112(d)(6) requires EPA to review, and revise, as necessary, (taking into account	EPA has established NESHAPs for a number of source categories that emit MBOCA to air. (See link)

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	developments in practices, processes and control technologies) the emission standards every 8 years.	
CAA – Section 112(f)	Section 112(f)(2) requires EPA to conduct risk assessments for each source category subject to section 112(d) NESHAP that require maximum achievable control technology (MACT) and to determine if additional standards are needed to reduce remaining risks; this is required within 8 years of promulgating the NESHAP.	EPA has promulgated a number of Risk and Technology Review (RTR) NESHAP and will do so, as required, for the remaining source categories with NESHAP.
Clean Water Act (CWA) – Section 301, 304, 306, 307, and 402	Clean Water Act Section 307(a) establishes a list of toxic pollutants or combination of pollutants under the CWA. The statute specifies a list of families of toxic pollutants also listed in the Code of Federal Regulations at 40 CFR Part 401.15. The list of "priority pollutants" lists the individual chemical names within the toxic pollutants and are found in 40 CFR Part 423 Appendix A. These are pollutants (along with non-conventional pollutants) for which best available technology effluent limitations must be established on either a national basis through rules (Sections 301(b), 304(b), 307(b), 306) or on a case-by-case best professional judgement basis in National Pollutant Discharge Elimination System (NPDES) permits, see Section 402(a)(1)(B). EPA identifies the best available technology that is economically achievable (BAT) for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology.	MBOCA is a non-conventional pollutant under section 301(b)(2)(F) of the CWA and as such is subject to effluent limitations and any associated monitoring requirements of NPDES permits. (Pollutants that are not found on the toxic pollutant list (40 CFR 401.15) or priority pollutant list (40 CFR 423 Appendix A), or conventional pollutant list (40 CFR 401.16) are non-conventional.)
CWA – section 301, 304, 306, 307, and 402	CWA section 307(a) establishes a list of toxic pollutants or combination of pollutants under the CWA. The statute specifies a list of families of toxic pollutants also listed in the Code of Federal Regulations at 40 CFR Part	MBOCA is a non-conventional pollutant under section 301(b)(2)(F) of the CWA and as such is subject to effluent limitations and any associated monitoring requirements of

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	401.15. The list of "priority pollutants" lists the individual chemical names within the toxic pollutants and are found in 40 CFR Part 423 Appendix A. These are pollutants (along with non-conventional pollutants) for which best available technology effluent limitations must be established on either a national basis through rules (Sections 301(b), 304(b), 307(b), 306) or on a case-by-case best professional judgement basis in National Pollutant Discharge Elimination System (NPDES) permits, see Section 402(a)(1)(B). EPA identifies the best available technology that is economically achievable (BAT) for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology.	NPDES permits. (Pollutants that are not found on the toxic pollutant list (40 CFR 401.15) or priority pollutant list (40 CFR 423 Appendix A), or conventional pollutant list (40 CFR 401.16) are non-conventional.)
Resource Conservation and Recovery Act (RCRA) – Section 3001	Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue and other related factors such as flammability, corrosiveness, and other hazardous characteristics.	MBOCA is included on the list of hazardous wastes pursuant to RCRA 3001. RCRA Hazardous Waste Code: U158 (40 CFR 261.33)
CERCLA – sections 102(a) and 103	Authorizes EPA to promulgate regulations designating as hazardous substances, in addition to those referred to in section 101(14) of CERCLA, those elements, compounds, mixtures, solutions, and substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103.	MBOCA is a hazardous substance under CERCLA. Releases of MBOCA in excess of 10 pounds must be reported (40 CFR 302.4).

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have knowledge of a release of a hazardous substance above the reportable quantity threshold. CERCLA Hazardous substances listed under 40 CFR Table 302.4 are subject to EPCRA Section 304 notification requirements.	
Superfund Amendments and Reauthorization Act (SARA) –	Amendments made several important changes to CERCLA, for example: requires the Agency to revise the hazardous ranking system and update the National Priorities List of hazardous waste sites, increases state and citizen involvement in the Superfund program and provides new enforcement authorities and settlement tools.	MBOCA is listed in SARA, an amendment to CERCLA and the CERCLA Priority List of Hazardous Substances. This list includes substances most commonly found at facilities on the CERCLA National Priorities List (NPL) that have been deemed to pose the greatest threat to public health.
Other Federal Regulations		
FFDCA – section 408	Provides the FDA with authority to oversee the safety of food, drugs and cosmetics, except residues of pesticides in food are regulated by EPA under FFDCA section 408 (discussed above where applicable).	FDA established a prohibition of MBOCA from Indirect Addition to Human Food Through Food-Contact Surfaces (21 CFR 189.280 and 34 FR 19073, December 2, 1969).
Occupational Safety and Health Act (OSH Act)	Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress or unsanitary conditions (29 U.S.C section 651 et seq.). Under the Act, OSHA can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure monitoring, engineering and administrative control measures, and respiratory protection.	OSHA has not issued a PEL for MBOCA.
Federal Hazardous Materials Transportation Act (HMTA)	Section 5103 of the Act directs the Secretary of Transportation to: • Designate material (including an explosive, radioactive material,	MBOCA is listed as a hazardous material with regard to transportation and is subject to regulations prescribing

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	infectious substance, flammable or combustible liquid, solid or gas, toxic, oxidizing or corrosive material, and compressed gas) as hazardous when the Secretary determines that transporting the material in commerce may pose an unreasonable risk to health and safety or property. • Issue regulations for the safe transportation, including security, of hazardous material in intrastate, interstate and foreign commerce.	requirements applicable to the shipment and transportation of listed hazardous materials (49 CFR 172).

Table_Apx A-2. State Laws and Regulations

State Actions	Description of Action
State Air Regulations	Allowable Ambient Levels: New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants): Toxicity Class I, 24-Hr AAL 0.39 (µg/m^3), Annual AAL[B] 0.26 (µg/m^3), 24-Hr De Minimis 0.0046 (lbs/day), Annual De Minimis 1.7 (lbs/yr) Rhode Island (Air Pollution Regulation No. 22): Annual AAL 0.002 (µg/m^3)
State Drinking Water Standards and Guidelines	Michigan (Mich. Admin. Code r.299.44 and r.299.49, 2017) State MCL: 1.1 (Residential) (µg/L), 4.5 (Nonresidential) (µg/L)
State PELs	California (PEL of 0.01 mg/m^3 and a STEL of N/A) (Cal Code Regs. Title 8, 5155) Hawaii PEL: 0.02 ppm (Hawaii Administrative Rules section 12-60-50).
State Right-to-Know Acts	Massachusetts (105 Code Mass. Regs. 670.000 Appendix A), New Jersey (N.J.A.C. 7:1G) and Pennsylvania (P.L. 734, No. 159 and 34 Pa. Code 323).
Chemicals of High Concern to Children	At least two states have adopted reporting laws for chemicals in children's products containing MBOCA, including Maine (38 MRSA Chapter 16-D, Chemical of High Concern)), and Minnesota (Toxic Free Kids Act Minn. Stat. 116.9401 to 116.9407).
Other	California listed MBOCA on Proposition 65 in 1987 due to cancer. (Cal Code Regs. Title 27, 27001). MBOCA is listed as a Candidate Chemical under California's Safer Consumer Products Program established under Health and Safety Code 25252 and 25253 (California, Candidate Chemicals List. Accessed September 8, 2023). MBOCA is on the MA Toxic Use Reduction Act (TURA) list of 2023 (301 CMR 41.00).

Table_Apx A-3. International Laws and Regulations

Country/Organization	Requirements and Restrictions
Canada	MBOCA is on the Domestic Substances List (Government of Canada. Managing substances in the environment. Substances search. Database accessed October 18, 2023). Other regulations include: Canada's National Pollutant Release Inventory (NPRI).
European Union	MBOCA is registered for use in the EU. (European Chemicals Agency (ECHA) database. Accessed October 18, 2023). In August 2014, MBOCA was added to Annex XIV of REACH (Authorisation List) with a sunset date of 1 March 2023. There have been 3 approved requests for authorization of the industrial use of MBOCA: in the manufacture of hot cast polyurethane products, the manufacture of high-performance polyurethanes specifically for custom-made rollers with high reliability requirements for steel and

Country/Organization	Requirements and Restrictions
	aluminium sectors, and in the manufacture of high-performance polyurethanes specifically for heavy-duty rollers, tensioner pads and spring blocks with high reliability requirements for offshore energy and renewables sectors. (European Chemicals Agency (ECHA) database. Accessed December 1, 2023).
Australia	MBOCA was assessed under Human Health Tier II of the Inventory Multi-Tiered Assessment and Prioritisation (IMAP). (National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Chemical inventory. Database accessed November 29, 2023). These assessments were carried out by NICNAS, but are now accessed through the Australian Industrial Chemicals Introduction Scheme (AICIS). No specific Australian use, import, or manufacturing information has been identified. The use of the chemical is restricted in Australia (NICNAS, 2014, *Human Health Tier II assessment for Benzenamine, 4,4'-methylenebis[2-chloro-*. Accessed November 29, 2023).
Japan	MBOCA is regulated in Japan under the following legislation: • Chemical Substances Control Law (CSCL) • Pollutant Release and Transfer Registers & Safety Data Sheet Law (PRTR-SDS Law) • Industrial Safety and Health Act (ISHA) • Air Pollution Control Law (National Institute of Technology and Evaluation [NITE] Chemical Risk Information Platform [CHIRP]. Accessed December 1, 2023).
Australia, Austria, Belgium, Canada, Denmark, European Union, Finland, France, Germany, Hungary, Ireland, Italy, Japan, Latvia New Zealand, Norway, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, The Netherlands, United Kingdom	Occupational exposure limits for MBOCA (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed December 1, 2023).

Appendix B IDENTIFICATION OF PUBLICLY AVAILABLE PEER-REVIEWED AND GRAY LITERATURE FOR MBOCA

As stated above, EPA conducted a comprehensive search for reasonably available information to support the proposed designation of MBOCA as a High-Priority Substance. This search included the following general categories of sources identified in Section 2 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024), which include publicly available peer-reviewed literature, gray literature, and other relevant information submitted to EPA (*e.g.*, public comments). There was no limit set on the search for reasonably available information on MBOCA regarding when or where the data in a respective data source were published, therefore there may be some data that are potentially more relevant than others.

Appendices B.1 and B.2 describe how EPA identifies potentially relevant peer-reviewed and gray literature for each chemical, respectively. As compared to the 2021 Draft Systematic Review Protocol, some updates have been made regarding how EPA identified discipline-specific information from the peer-reviewed literature search, and the gray literature sources considered for each chemical. These updates are described in the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024).

B.1 Identification of Potentially Relevant Peer-Reviewed Information for MBOCA

Section 4.2.1 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) provides an overview of how peer-reviewed literature was identified by an information specialist. The chemical-specific literature searches are broad and focus only on the chemical name (including synonyms and trade names) with no additional search limits. Using this approach and searching multiple databases, the search is designed to be comprehensive, using validated chemical descriptors to generate a wide capture of information and yield diverse information for all disciplines. Appendix B.1.2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) provides additional information regarding search term genesis for chemical-specific peer-reviewed literature searches implemented under TSCA section 6, whereas this section provides chemical verification for the identification of peer-reviewed MBOCA data sources.

After the broad search is completed, additional filtering steps are applied in SWIFT-Review (Sciome product) to narrow the literature pool to references that are potentially discipline-relevant. As described by Howard (2016), SWIFT-Review uses the Apache Lucene open-source software to provide a search engine and query language that can be used to interactively explore and filter references using both custom and built-in searches. The software identifies relevant references by automatically scanning for search terms characteristic of each of these disciplines in the title and abstract fields of each reference.

Broad searches are over-inclusive by nature and may lead to a literature pool of overwhelming size, as is the case with MBOCA. Additionally, discipline-specific keywords pertaining to desired information categories often overlap with information categories known to be off-topic for all disciplines. This additional filtering process identifies literature that is not expected to meet population, exposure, comparator, and outcome (PECO) or pathways and processes or population, exposure, setting or scenario, and outcomes (PESO) criteria (*e.g.*, chemical derivatives, nanotechnology, etc.), with the resulting subset of literature being deprioritized for later consideration.

The initial extraction step identified instances of the chemical name and synonyms of the chemical name that appeared as part of a separate, unrelated chemical or substance name (*e.g.*, 3,4-dichloroaniline), as well as generalized keywords relating to concepts falling outside of PECO and PESO criteria. The results of this

extraction were then examined for instances where the chemical name or a synonym appeared in conjunction with a chemical of non-interest, and also met at least one criteria point for a discipline. This subset of the extraction pool was then reintegrated into the peer literature pool for discipline-specific binning.

Table_Apx B-1. Filtering Strategies for Identifying Peer Literature Not Meeting PECO or PESO Criteria

Filtering Step	Filtering Queries
Initial extraction	tiab_punct:("aniline" OR "benzenamine" OR "phenylamine") tiab:("Polyaniline*" OR "Poly(aniline*" OR "Dimethylaniline" OR "nitrobenzene" OR "metal complex*" OR "ligand*" OR ("framework*" AND ("DNA" OR "metal")) OR "polymer*" OR "derivative*" OR "catalyst*" OR "photo*" OR "spectr*" OR "DFT" OR "density functional theory" OR "nano*" OR "synthesis" OR "dye-sensitized" OR "functionalized")
Reintegration	tiab:("DNA" OR "photodeg*" OR "spectro*") ((tiab_punct:("aniline" OR "benzenamine" OR "phenylamine") AND (tiab:("occupational health" OR "worker exposure" OR "occupational groups" OR "employee" OR "worker*" OR "worker exposed" OR "work* in a factory" OR "work* in a plant" OR "work* in a manufacturing plant" OR "hygienist" OR "OSHA" OR "NIOSH") OR tiab:("carcinogen*" OR "cancer" OR "etiology" OR "tumor" OR "mortality" OR "mortality rate" OR "mortality ratio" OR "rats" OR "mortality incidence" OR "cancer incidence" OR "hematuria" OR "intravenous" OR "intra-assay" OR "drosophila" OR "daphnia" OR "cytology" OR "atypia" OR (("dog" OR "dogs" OR "cats") NOT "human") OR "oral administration" OR "administration" OR "administered" OR "carcinoma" OR "Sprague-Dawley" OR "mice" OR "gene" OR "genetic" OR "mutagenicity" OR "genotoxicity" OR "cytotoxicity" OR "LD50" OR "LC50" OR "LT50" OR "TD50" OR "P450" OR "cytochrome" OR "bioassay" OR "immunoassay" OR "cholinesterase" OR "inhibitor" OR "*in vivo*" OR "*in vitro*" OR "enzyme" OR "transferase" OR "oxidase" OR "hydrogenase" OR "dehydrogenase" OR "bacteria*" OR "virus" OR "viral" OR "agar" OR "mutation*" OR "nucleotide" OR "malignant" OR "neoplasm" OR "tumor*" OR "tumour*" OR "benign" OR "neoplasia" OR "preneoplastic" OR "neoplastic" OR "metastases" OR "proliferative lesion" OR "hypertension" OR "neurological" OR "behavioral" OR "cardiovascular" OR "endocrine" OR "reproductive" OR "developmental" OR "gastrointestinal" OR "immune" OR "hematological" OR "hepatic" OR "musculoskeletal" OR "ocular" OR "sensory" OR "renal" OR "irritation" OR "sensitization" OR "gene therapy" OR "gavage" OR "radioactivity" OR "hypertrophy" OR "atrophy" OR "inbred strain" OR "congenic" OR "inbred A" OR "inbred AKR" OR "inbred BALB C" OR "inbred C3H" OR "inbred C57BL" OR "inbred mdx" OR "inbred CBA" OR "inbred CFTR" OR "inbred DBA" OR "inbred ICR" OR "inbred MRL Ipr" OR "inbred NOD" OR "inbred NZB" OR "inbred SENCAR" OR "inbred ACI" OR "inbred BB" OR "inbred BN" OR "inbred BUF" OR "inbred Dahl" OR "inbred F344" OR "inbred LEC" OR "inbred Lew" OR "inbred OLETF" OR "inbred SHR" OR "inbred WF" OR "inbred WKY" OR "transgenic" OR "founder animal" OR "GMO animal" OR "genetically engineered animal" OR "genetically modified animal" OR "knockout mice" OR "ApoE" OR "rabbit*" OR "goldfish") OR tiab:("biodegradability" OR "biodegradation" OR "bioisomerization" OR "biomagnification" OR "biotransformation" OR "dechlorination" OR "degradation" OR "dehalogenation" OR "fate" OR "food web" OR "hydrolysis" OR "photodegradation" OR "photolysis" OR "phototransformation" OR "trophic magnification" OR "evaporation rates" OR "reaction" OR "bioremediation" OR "bioaugmentation" OR "reverse osmosis" OR "sterilization" OR "kinetic*" OR "ultraviolet irradiation") OR tiab:(("physical form" OR "physical state" OR "physical chemistry" OR "physical properties" AND ("crystal structure" OR "crystalline structure" OR "morphology" OR "color")) OR "melting

Filtering Step	Filtering Queries
	point" OR "boiling point" OR "density" OR "vapor pressure" OR "vapour pressure" OR "vapor density" OR "vapour density" OR "water solubility" OR "aqueous solubility" OR "aqueous saturation point" OR "water saturation point" OR "octanol:water partition coefficient" OR "octanol-water partition coefficient" OR "octanol/water partition coefficient" OR "octanol water partition coefficient" OR "Kow" OR "Henry's Law constant" OR "heat of Henry" OR "Kaw" OR "air water partition" OR "pKa" OR "acid dissociation constant" OR "dissociation constant" OR "flash point" OR "autoflammability" OR "viscosity" OR "enthalpy of phase change" OR "enthalpy of vaporization" OR "heat of vaporization" OR "photoabsorption" OR "absorption spectra" OR "absorption spectrum" OR "transition state" OR "zeta potential" OR "individual fiber diameter" OR "average fiber outer diameter" OR "particle dimension" OR "decomposition temperature" OR "KOA" OR "K(OA)" OR "log KOA" OR "octanol-air partition coefficient" OR "1-octanol-air partition coefficient" OR "octanol/air partition coefficient" OR "n-octanol/air partition coefficient" OR "Kd" OR "association constant" OR "λmax" OR "absorption wavelength" OR "extinction coefficient" OR "molar absorptivity" OR "absorption maxima" OR "ε" OR "kOH" OR "kOC" OR "Langmuir isotherm" OR "isotherm" OR "thermodynamics") OR tiab:("direct product concentration" OR "direct article concentration" OR "direct weight fraction" OR "product emission*" OR "product test*" OR "article emission*" OR "chamber test*" OR "product migration" OR "article migration" OR "controlled human study" OR "simulated" OR "simulation" OR "test house" OR "test field" OR "building material" OR "consumer product" OR "emission rate" OR "emission factor" OR "migration rate" OR "emission*" OR "emission rate" OR "emission flux" OR "flux" OR "consumer product" OR ("concentration*" AND ("air*" OR "indoor" OR "outdoor" OR "product" OR "article")) OR "chamber" OR "chamber system" OR "exhaust system" OR "ventilation system" OR "air exchange rate" OR "release*" OR "release rate") OR tiab:("modeled indoor concentration*" OR "modeled outdoor concentration*" OR "modeled concentration*" OR "modeled dose*" OR "modeled intake*" OR "dust ingestion" OR "dermal absorption" OR "sensitivity analysis" OR ("exposure" AND "modeling")) OR tiab:(("contaminant*" OR "contaminat*" OR "media" OR "medias" OR "medium" OR "pollutant*" OR "pollution" OR "quality" OR "source*" OR "environment*" OR "monitor" OR "monitoring" OR "occurrence" OR "measured" OR "measurable" OR "measurements" OR "sample*" OR "compound" OR "compounds" OR "detected" OR "accumulate*" OR "analys*" OR "analyz*" OR "collected" OR "estimate" OR "estimated" OR "manufacture" OR "matrices" OR "matrix" OR "micropollutant" OR "microenvironment" OR "quantification" OR "quantified" OR "quantify" OR "quantitation" OR "residue" OR "ubiquitous" OR "trace" OR "monitoring well" OR "wells") AND ("bioconcentrat*" OR "concentrat*" OR "level" OR "levels" OR "mg/L" OR "ug/L")))) NOT tiab:("metal complex*" OR "ligand*" OR ("framework*" AND "metal") OR "polymer*" OR "*polymer*" OR "copolymer*" OR "derivative*" OR "catalyst*" OR "DFT" OR "density functional theory" OR "nano*" OR "synthesis" OR "dye-sensitized" OR "functionalized"))

B.1.1 Query Strings for Peer-Reviewed Literature Database Searches on MBOCA

Public database searches were conducted for all available years at the time of the search. The literature searches encompassed literature from the earliest date for which literature was available to be searched within each database through January 2023. Search strings were constructed using syntax provided in their respective online search manuals.

These are the search terms compiled from agency and industry databases for MBOCA used in the initial search strategies for each of the databases below.

- ProQuest: Includes Agricultural & Environmental collection, Agricola, Dissertations & Abstracts, and Toxline
- PubMed
- Scopus
- Web of Science: Includes WoS Core Collection and Current Contents Connect

Table_Apx B-2. Peer- Reviewed Literature Search Strategy for MBOCA

Source	Source-Specific Search Strategy	Results
ProQuest	TIAB("101-14-4" OR "4,4'-Methylene bis(2-chloroaniline)" OR "2,2'-Dichloro-4,4'-methylenedianiline" OR "4,4'-Methylenebis(2-chloroaniline)" OR "4,4'-Methylene-bis(2-chloroaniline)" OR "4,4'-Methylene-bis-2-chloroaniline" OR "Bisamine" OR "methylenebis(chloroaniline)" OR "MBOCA" OR "Kuralon" OR "Pandex" OR ("MOCA" AND "methylene"))	116
PubMed	("101-14-4"[rn] OR "4,4'-Methylene bis(2-chloroaniline)"[tw] OR "2,2'-Dichloro-4,4'-methylenedianiline"[tw] OR "4,4'-Methylenebis(2-chloroaniline)"[tw] OR "4,4'-Methylene-bis(2-chloroaniline)"[tw] OR "4,4'-Methylene-bis-2-chloroaniline"[tw] OR "Bisamine"[tw] OR "methylenebis(chloroaniline)"[tw] OR "MBOCA"[tw] OR "Kuralon"[tw] OR "Pandex"[tw] OR ("MOCA"[tw] AND "methylene"[tw]))	205
Scopus	TITLE-ABS({101-14-4} OR {4,4'-Methylene bis(2-chloroaniline)} OR {2,2'-Dichloro-4,4'-methylenedianiline} OR {4,4'-Methylenebis(2-chloroaniline)} OR {4,4'-Methylene-bis(2-chloroaniline)} OR {4,4'-Methylene-bis-2-chloroaniline} OR {Bisamine} OR {methylenebis(chloroaniline)} OR {MBOCA} OR {Kuralon} OR {Pandex} OR ({MOCA} AND {methylene}))	238
Web of Science	TS=("101-14-4" OR "4,4'-Methylene bis(2-chloroaniline)" OR "2,2'-Dichloro-4,4'-methylenedianiline" OR "4,4'-Methylenebis(2-chloroaniline)" OR "4,4'-Methylene-bis(2-chloroaniline)" OR "4,4'-Methylene-bis-2-chloroaniline" OR "Bisamine" OR "methylenebis(chloroaniline)" OR "MBOCA" OR "Kuralon" OR "Pandex" OR ("MOCA" AND "methylene"))	246
Total Literature	Total literature considered for systematic review	367

Following the identification of potentially relevant peer-reviewed literature on MBOCA, SWIFT-Review was used to further refine the peer-reviewed literature pool into discipline-relevant categories via positive and negative seed prioritization and/or discipline-specific keyword filtering depending on that discipline's information needs. Discipline-specific filters predict relevance to a respective discipline or topic based on the presence or absence of applicable keywords and phrases in titles and abstracts. Positive and negative seed prioritization priority ranks individual publications against a predetermined set of references containing desired information (positive seeds) and undesired information (negative seeds). For additional information on the strategies implemented to identify discipline-specific peer-reviewed information, see Section 4.1 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024).

B.2 Identification of Potentially Relevant Gray Literature for MBOCA

Gray literature generally contains data sources that do not contain abstracts, such as TSCA and FIFRA submissions, databases containing secondary information, and previous assessments, therefore making it difficult to ascertain chemical- or discipline-specific relevance. The publicly available data sources used to

identify discipline-specific gray literature are identified in Section 3.2 of the *Updated Search Strategies Used to Identify Potentially Relevant Discipline-Specific Information* (U.S. EPA, 2024).

B.2.1 Gray Literature Sources Considered for identifying Potential Hazard for MBOCA

Table_Apx B-3 outlines the bibliographical information for the assessments considered in Section 2.7.1. Information from both aquatic and terrestrial toxicity studies were considered from all listed assessments. The quantitative endpoints described in these previous assessments are depicted in the figures within Section 2.7.1.

Table_Apx B-3. Assessments Identified for Environmental Hazard

Assessment HERO ID	Reference	Assessment Label[a]
OECD (2013c)	SIDS Initial Assessment Report: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). Tokyo, Japan: National Institute of Health Sciences, Organisation for Economic Co-operation and Development.	OECD 2013
OECD (2013a)	SIDS Dossier: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). Tokyo, Japan: National Institute of Health Sciences, Organisation for Economic Co-operation and Development.	OECD 2013
U.S. EPA (2015)	Screening-Level Hazard Characterization: 4,4'-Methylenebis(2-chloro) (MBOCA; CASRN 101-14-4). Washington, DC.	EPA 2015

[a] "Assessment labels" refer to labels associated with previous identified in various figures within Sections 2.7.1.1 and 2.7.1.2.

Table_Apx B-4 outlines the bibliographical information for the previous assessments considered in Section 2.7.2. Both animal toxicity studies and epidemiological information were considered from all listed previous assessments. The quantitative and qualitative endpoints described in these previous assessments are visualized in the following table and figures: Table 2-5, Figure 2-5, Figure 2-6, and Figure 2-7. Table_Apx C-10 lists the quantitative endpoint values reported in these previous assessments.

Table_Apx B-4. Assessment Identified for Human Health Hazard (Animal Toxicity and Epidemiology)

HERO ID	Reference	Assessment Label[a]
ATSDR (2017)	Agency for Toxic Substances and Disease Registry (ATSDR). 2017. Toxicological profile for 4,4'-Methylenebis (2 chloroaniline) (MBOCA). U.S. Department of Health and Human Services, Public Health Service	ATSDR 2017
ECCC (2020)	Environment and Climate Change Canada (ECCC). 2020. Draft Screening Assessment: Aromatic Amines Group - Chemical Abstracts Service Registry Numbers: 86-30-6, 90-30-2, 95-55-6, 101-14-4, 101-96-2, 121-69-7, 122-39-4, 63449-68-3. Government of Canada	ECCC 2020
IARC (2012)	International Agency for Research on Cancer (IARC). 2012. Chemical agents and related occupations: A review of human carcinogens. International Agency for Research on Cancer. Series IARC Monographs on the Evaluation of Carcinogenic	IARC 2012

	Risks to Humans, vol. 100F. ISBN 9789283201380. IARC Monograph	
NICNAS (2014)	National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2014. Benzenamine, 4,4'-methylenebis [2-chloro-: Human health tier II assessment. Australian Industrial Chemicals Introduction Scheme (AICIS)	NICNAS 2014
NTP (2021)	National Toxicology Program (NTP). 2021. 4,4′-Methylenebis(2-chloroaniline): CAS No. 101-14-4 U.S. Department of Health and Human Services. Book Title Report on carcinogens, fifteenth edition.	NTP 2021
OECD (2013a)	Organization for Economic Co-operation and Development (OECD). 2013 SIDS Dossier: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). National Institute of Health Sciences, Organization for Economic Co-operation and Development	OECD 2013
OECD (2013c)	Organization for Economic Co-operation and Development (OECD). 2014. SIDS Dossier: 4,4'-Methylenebis(2-chloroaniline) (MBOCA). National Institute of Health Sciences, Organization for Economic Co-operation and Development	OECD 2014
OEHHA (2011)	California Office of Environmental Health Hazard Assessment (OEHHA). 2011. Technical support document for cancer potency values, Appendix B: Chemical-specific summaries of the information used to derive unit risk and cancer potency values. California Office of Environmental Health Hazard Assessment (OEHHA)	OEHHA 2011
OEHHA (2014)	California Office of Environmental Health Hazard Assessment (OEHHA). 2014. Technical support document for noncancer RELs, Appendix D: Individual acute, 8-hour, and chronic Reference Exposure Level summaries. California Office of Environmental Health Hazard Assessment (OEHHA)	OEHHA 2014
ORD (2006)	Office of Research and Development (ORD). 2006. Provisional Peer Reviewed Toxicity Values (PPRTV) for 4,4'-Methylenebis (2-chloroaniline) (CASRN 101-14-4) U.S. Environmental Protection Agency (U.S. EPA)	ORD 2006
U.S. EPA (2015)	U.S. Environmental Protection Agency (U.S. EPA). 2015. Screening-level hazard characterization: 4,4’-Methylenebis(2-chloroaniline) (MBOCA; CASRN 101-14-4) U.S. Environmental Protection Agency	US EPA 2015

[a] “Assessment labels” refer labels associated with previous assessments in various figures and tables within Sections 2.7.2.1 and 2.7.2.2.

Appendix C SYSTEMATIC REVIEW APPROACH – SCREENING OF REASONABLY AVAILABLE INFORMATION

Sections 4.2.5 and 4.3.2 of the 2021 Draft Systematic Review Protocol describe how TIAB and full-text screening respectively, are conducted to identify references that may contain relevant information for use in risk evaluations under TSCA using discipline-specific screening criteria (U.S. EPA, 2021). The manual screening process is similar for both TIAB and full-text screening phases, which starts with a calibration exercise for a set of references that are screened by all screeners. Differences in screening decisions during the calibration exercise are discussed, and clarification and refinements are provided for chemical-specific attributes as well as clarification on individual PECO or PESO screening criteria including which supplemental tags might be needed. Once the calibration exercise has concluded, screening proceeds for the remaining references identified during screening.

TIAB screening efforts are conducted manually as well as using the specialized web-based software programs DistillerSR[3] and SWIFT-Active-Screener[4] [5]; for the screening review of reasonably available information identified for MBOCA, TIAB screening efforts were conducted using SWIFT-Active-Screener, where machine learning helped to prioritize reference screening. Additional details on how SWIFT Active-Screener utilizes a machine-learning algorithm to automatically compute which unscreened documents are most likely to be relevant[6] are available in Section 4.2.5 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). During TIAB screening, if it was unclear whether a reference met the screening criteria without having the full reference to review, or if a reference was determined to meet the screening criteria, that reference advanced to full-text screening if the full reference could be retrieved and generated into a Portable Document Format (PDF).

Full-text screening is manually conducted in DistillerSR using the same discipline-specific screening criteria as those used in TIAB screening and consisted of independent screening being conducted by two individuals trained to identify potentially relevant discipline-specific information within the various types of data sources. As mentioned in Appendix B, gray literature identified in public sources as well as TSCA and FIFRA submissions undergo a pre-screening step to determine whether there is potentially relevant information for a respective discipline; those that are deemed potentially relevant undergo full-text screening using the same screening criteria used for the TIAB and full-text screening of peer-reviewed literature. The discipline-specific subsections below describe the methodology used to screen data sources identified for a respective discipline, as well as screening results. Specifically, the literature inventory trees convey TIAB and/or full-text screening results for the data sources identified and considered using the systematic review approach. For data sources that meet screening criteria during full-text screening, the evidence maps indicate data elements or characteristics relevant for a respective discipline and chemical. Available in Health Assessment Workplace Collaborative (HAWC), are chemical- and discipline-specific

[3] As noted on the DistillerSR web page, this systematic review software "automates the management of literature collection, triage, and assessment using AI and intelligent workflows...to produce transparent, audit ready, and compliant literature reviews." EPA uses DistillerSR to manage the workflow related to screening and evaluating references; the literature search is conducted external to DistillerSR.

[4] SWIFT-Active Screener is another systematic review software that EPA is adopting in the TSCA systematic review process. From Sciome's SWIFT-Active Screener web page: "As screening proceeds, reviewers include or exclude articles while an underlying statistical model in SWIFT-Active Screener automatically computes which of the remaining unscreened documents are most likely to be relevant. This 'Active Learning' model is continuously updated during screening, improving its performance with each reference reviewed. Meanwhile, a separate statistical model estimates the number of relevant articles remaining in the unscreened document list."

[5] SWIFT is an acronym for "Sciome Workbench for Interactive Computer-Facilitated Text-mining." SWIFT-Active Screener uses machine learning approaches to save screeners' time and effort.

[6] Description comes from the SWIFT-Active Screener web page.

projects containing interactive versions of both the literature inventory trees and evidence maps that enable users to identify specific data sources pertaining to elements in either figures via the Health and Environmental Research Online (HERO) database. The links to those HAWC project pages are available for each respective static image of the literature inventory trees and evidence maps. As indicated below, as additional relevant information is identified, the interactive versions of these figures may change.

As described in the discipline-specific sub-sections, EPA is interested in information that may help with the final designation of MBOCA as a High- or Low-Priority Substance. EPA is seeking information from the public on the various data elements described in this appendix. As additional information becomes available, EPA will continue to use the discipline-specific screening criteria during TIAB and/or full-text screening. Should this chemical be designated as a High-Priority Substance, screening decisions and data elements characterized in literature inventory trees and evidence maps presented in Appendices C.1, C.2, C.3, C.4, and C.5 for discipline-specific interactive visualizations may be updated for future actions.

C.1 Physical and Chemical Properties

During data screening, EPA followed the process described in Appendix H-1 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct TIAB and full-text screening for MBOCA guided by the data or information needs on various physical and chemical properties or endpoints as listed in the table in Appendix C.1.1. The same screening criteria was used during TIAB and full-text screening for references considered for the evaluation of physical and chemical properties of MBOCA. TIAB screening was performed used SWIFT Active Screener. Upon meeting the screening criteria during full-text screening, data or information sources will then undergo data quality evaluation and data extraction. Figure_Apx C-1 represents the number of references that report general physical and chemical property information that fulfilled the data needs for MBOCA and passed these criteria for TIAB and full-text screening.

C.1.1 Screening Criteria for Data Sources Reporting Physical and Chemical Properties

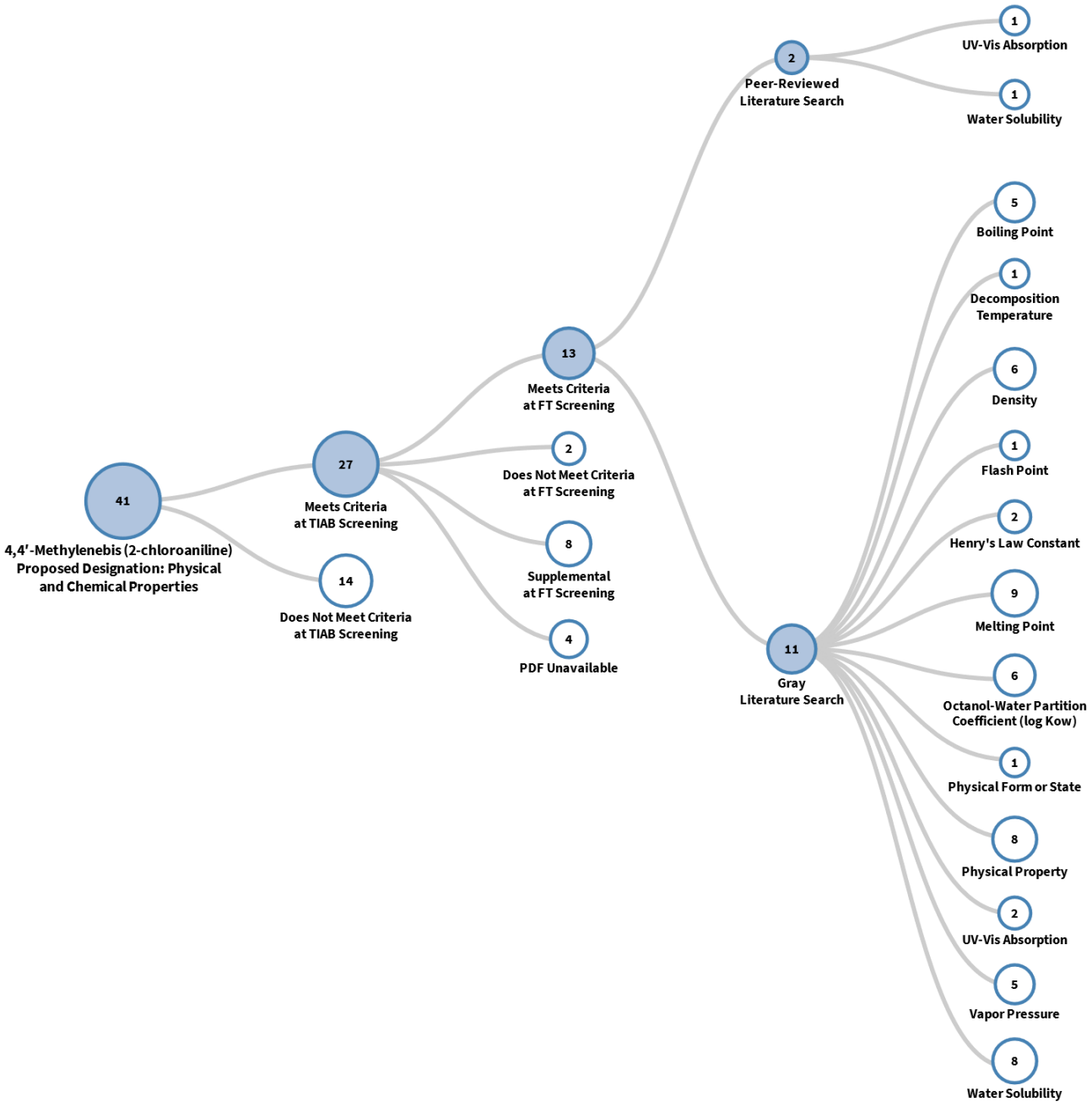
In order to be considered, a reference should present measured or modeled values on various physical and chemical properties or endpoints as listed in Table_Apx C-1.

Table_Apx C-1. Screening Criteria for Data Sources Reporting Physical and Chemical Properties for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

Property or Endpoint
Physical form or state (*e.g.*, solid, liquid, gas)
Physical properties (*e.g.*, color, scent)
Melting point
Boiling point
Density
Vapor pressure
Vapor density
Water solubility
Octanol-water partition coefficient (also reported as log K_{OW})
Octanol-air partition coefficient (also reported as log K_{OA})
Henry’s law constant
Dissociation constant

Property or Endpoint
Flash point
Auto-flammability (or flammability)
Viscosity
Decomposition temperature
UV-Vis absorption

C.1.2 Literature Inventory Tree – Physical and Chemical Property Search Results for 4,4'-Methylene bis(2-chloroaniline) or MBOCA



Figure_Apx C-1. Literature Inventory Tree for Physical and Chemical Properties for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent the references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of April 29, 2024. Additional data may be added to the interactive version as they become available. View the interactive version of the literature inventory tree in HAWC.

C.2 Environmental Fate and Transport Properties

During screening of reasonably available information, EPA followed the process described in Appendix H-2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) to conduct TIAB and full-text screening for MBOCA guided by the data or information needs on various environmental fate and transport properties or endpoints. Specifically, EPA used the PESO screening criteria in Table_Apx C-2 along with the information in Table_Apx C-3. During screening, EPA ensured that data and information provided a complete coverage of the processes, pathways and data or information relevant to the environmental fate and transport of MBOCA. Quantitative data for the endpoints in Table_Apx C-2 were included in the literature screening when data come from a primary source and are reported in the environmental media of interest.

C.2.1 Screening Criteria for Data Sources Reporting Environmental Fate and Transport Properties

Table_Apx C-2. Screening Criteria for Data Sources Reporting Environmental Fate and Transport Properties for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

PESO Element Relevance	Evidence

Pathways and **P**rocesses	• Fate will use transport, partitioning and degradation behavior across media to inform exposure pathways in conceptual models
	• Exposure pathways included in the conceptual models:
	  ○ Surface water
	  ○ Groundwater
	  ○ Wastewater
	  ○ Drinking water
	  ○ Soil
	  ○ Sediment
	  ○ Biosolids
	  ○ Air
	• Processes associated with the target exposure pathways
	• Bioconcentration and bioaccumulation
	• Destruction and removal by incineration

Exposure	• Exposures of aquatic and terrestrial organisms to the chemical substance, mixtures including the chemical substance, and/or degradation products and metabolites of the chemical substance • Environmental exposure pathways of humans to the chemical substance, mixtures including the chemical substance, and/or degradation products and metabolites of the chemical substance
Setting or **S**cenario	• All aquatic and terrestrial ecological, general population, and susceptible subpopulation exposure scenarios for releases of the chemical substance to the natural or built environment

Outcomes	• Fate properties which allow assessments of exposure pathways:
	  ○ Abiotic and biotic degradation rates, mechanisms, pathways, and products
	  ○ Bioaccumulation magnitude and metabolism rates
	  ○ Partitioning within and between environmental media (see Pathways)

Items listed in the PESO screening criteria guide the selection of possible and required data types used to complete the data needs table (Table_Apx C-2.2). Primary source literature containing quantitative data were included if that data described the following environmental fate endpoints in the corresponding media in the table.

Table_Apx C-3. Data Categories Included in Developing Fate and Transport Assessments

Fate Data Endpoint	Associated Processes	Associated Media/Exposure Pathways			
		Surface water	Soil	Ground water	Air
Abiotic reduction rates or half-lives	Abiotic reduction, abiotic dehalogenation	X			
Aerobic biodegradation rates or half-lives	Aerobic biodegradation	X	X		
Anaerobic biodegradation rates or half-lives	Anaerobic biodegradation	X	X	X	
Aqueous photolysis (direct and indirect) rates or half-lives	Aqueous photolysis (direct and indirect)	X			
Atmospheric photolysis (direct and indirect) rates or half-lives	Atmospheric photolysis (direct and indirect)				X
BCF BAF	Bioconcentration, bioaccumulation	X	X		X
Biomagnification and related information	Trophic magnification	X			
Desorption information	Sorption, mobility	X	X	X	
Destruction and removal by incineration	Incineration				X
Hydrolysis rates or half-lives	Hydrolysis	X	X	X	
K_{AW} and other volatilization information (but NOT Henry's Law constant)	Volatilization, vapor intrusion	X	X	X	X
K_{OC} and other sorption information	Sorption, mobility	X	X	X	
Wastewater treatment removal information	Wastewater treatment	X	X		

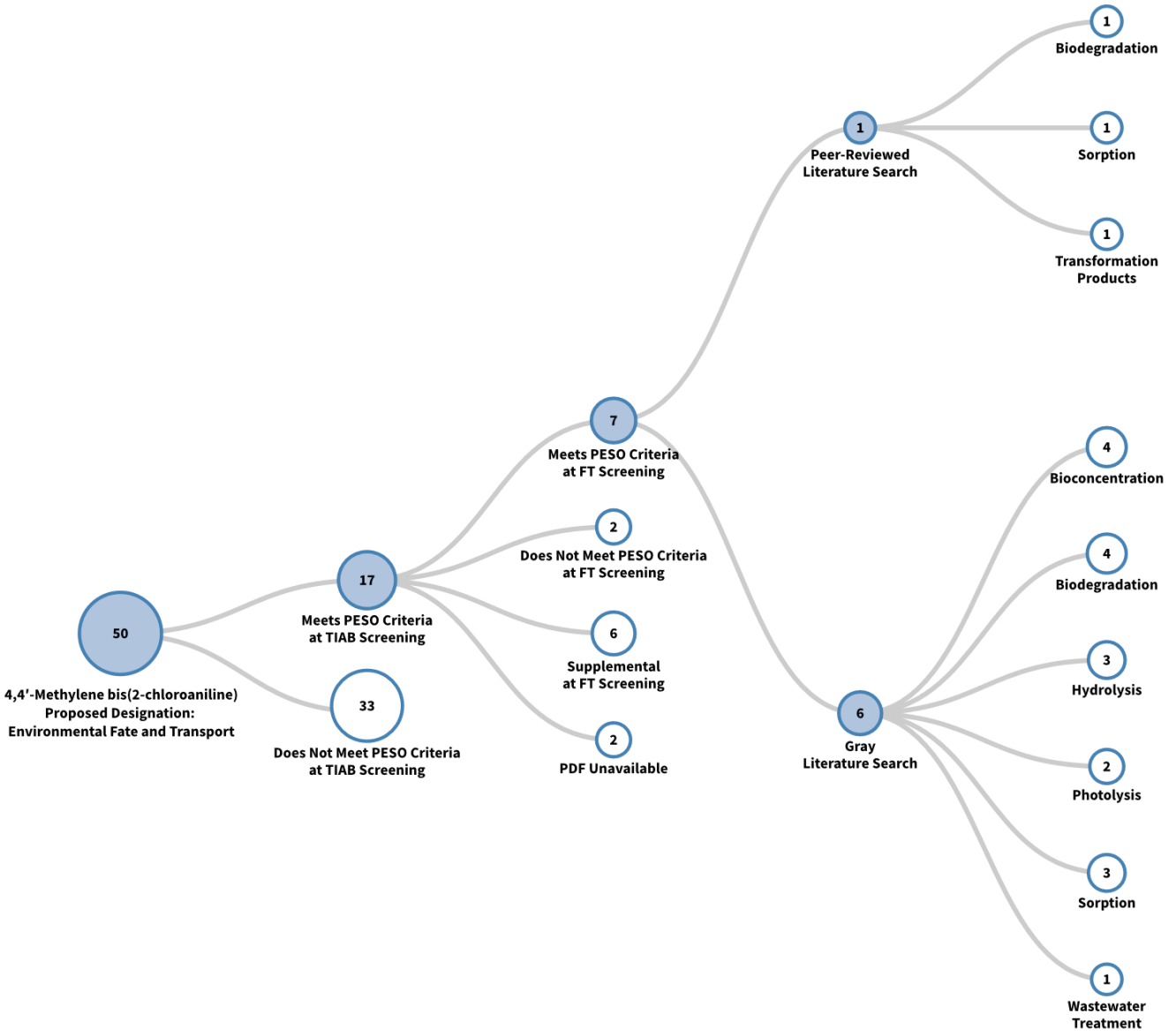
Supplemental information table

Other types of information that may be useful for completing fate assessments are listed in Table_Apx C-4. This is not an exhaustive list of potential supplemental information.

Table_Apx C-4. Examples of Supplemental Data Used in Developing Fate and Transport Assessments

Fate Data Endpoint	Associated Process(es)	Associated Media/Exposure Pathways			
		Surface water, Wastewater, Sediment	**Soil, Biosolids**	**Groundwater**	**Air**
Abiotic transformation products	Hydrolysis, photolysis, Incineration	X			X
Aerobic biotransformation products	Aerobic biodegradation	X	X		
Anaerobic biotransformation products	Anaerobic biodegradation	X	X	X	
Atmospheric deposition information	Atmospheric deposition				X
Coagulation information	Coagulation, mobility	X		X	
Suspension/resuspension information	Suspension/resuspension, mobility	X			

C.2.2 Literature Inventory Tree – Environmental Fate and Transport Property Search Results for 4,4'-Methylene bis(2-chloroaniline) or MBOCA



Figure_Apx C-2. Literature Inventory Tree of Environmental Fate and Transport Properties for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available, the interactive figure can be accessed in HAWC.

C.2.3 Evidence Map of Environmental Fate and Transport Property Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Endpoints	Media				
	Air	Soil	Wastewater/ biosolids	Water	Grand Total
Bioconcentration, Biomagnification, etc.	1	1		4	**4**
Biodegradation	2	3	1	5	**5**
Degradation products/ transformation pathways		1		1	**1**
Hydrolysis	2	2	1	3	**3**
Photolysis	2	1	1	2	**2**
Sorption to soil, sediment, or land-applied biosolids (Koc)	1	3	1	4	**4**
Wastewater treatment	1	1	1	1	**1**
Grand Total	**2**	**3**	**1**	**7**	**7**

Figure_Apx C-3. Evidence Map of Environmental Fate and Transport Properties for 4,4'-Methylene bis(2-chloroaniline) or MBOCA. View the interactive evidence map in HAWC.
Data in this figure represent the references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 15, 2024. The column totals, row totals, and grand totals indicate total numbers of distinct references. The various shades of color visually represent the distinct number of relevant references identified by medium or endpoint. The darker the color, the higher the number of references for any given medium or endpoint. Additional data may be added to the interactive version as they become available. View the interactive evidence map in HAWC.

C.3 Occupational Exposure and Environmental Releases

During data screening, EPA followed the process described in Appendix H-3 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct TIAB and full-text screening for MBOCA literature search results, as guided by the screening criteria in the PESO screening criteria (Table_Apx C-5). TIAB was performed using SWIFT Active-Screener. Full text screening occurred in DistillerSR for references that met the PESO screening criteria during TIAB.

EPA used the PESO screening criteria along with the information in Table_Apx C-5 when screening the occupational exposure and environmental release data.

C.3.1 Screening Criteria for Data Sources Reporting Occupational Exposure and Environmental Release Information

Table_Apx C-5. Screening Criteria for the Data Sources Reporting Occupational Exposure and Environmental Release Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

PESO Element Relevance	Evidence
Population	• **Humans:** Workers, including ONUs • **Environment:** All ecological receptors (relevant release estimates input to Exposure) Please refer to the conceptual models for more information about the ecological receptor and human subpopulations included in the TSCA risk evaluation.
Exposure	• Worker exposure to and relevant environmental releases of the chemical substance from occupational scenarios: o Dermal and inhalation exposure routes (as indicated in the conceptual model) o Oral route (as indicated in the conceptual model) Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation.
Setting or Scenario	• Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table 2-2..
Outcomes	• Quantitative estimates[a] of worker exposures and of relevant environmental releases from occupational settings • General information and data related and relevant to the occupational estimates*

[a] Metrics (*e.g.*, mg/kg/day or mg/m^3 for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; Table_Apx C-6 provides a list of related and relevant general information.

Table_Apx C-6. Engineering, Environmental Release, and Occupational Exposure Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments

Objective	Type of Data[a]
General Engineering Assessment (may apply to Occupational Exposures and / or Environmental Releases)	1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (*e.g.*, each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. 2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. 3. Description of processes, equipment, and unit operations during each industrial/ commercial life cycle step. 4. Material flows, use rates, and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). 5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. 6. Concentration of the chemical of interest
Occupational Exposures	7. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. 8. Potential routes of exposure (*e.g.*, inhalation, dermal). 9. Physical form of the chemical(s) of interest for each exposure route (*e.g.*, liquid, vapor, mist) and activity. 10. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). 11. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). 12. Sampling and analytical methodology 13. For solids, bulk and dust particle size characterization data. 14. Dermal exposure data. 15. Exposure duration (hr/day). 16. Exposure frequency (days/yr). 17. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. 18. PPE types employed by the industries within scope. 19. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions.
Environmental Releases (to relevant environmental media)	20. Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. 21. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) 22. Release or emission factors. 23. Number of release days per year. 24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions.

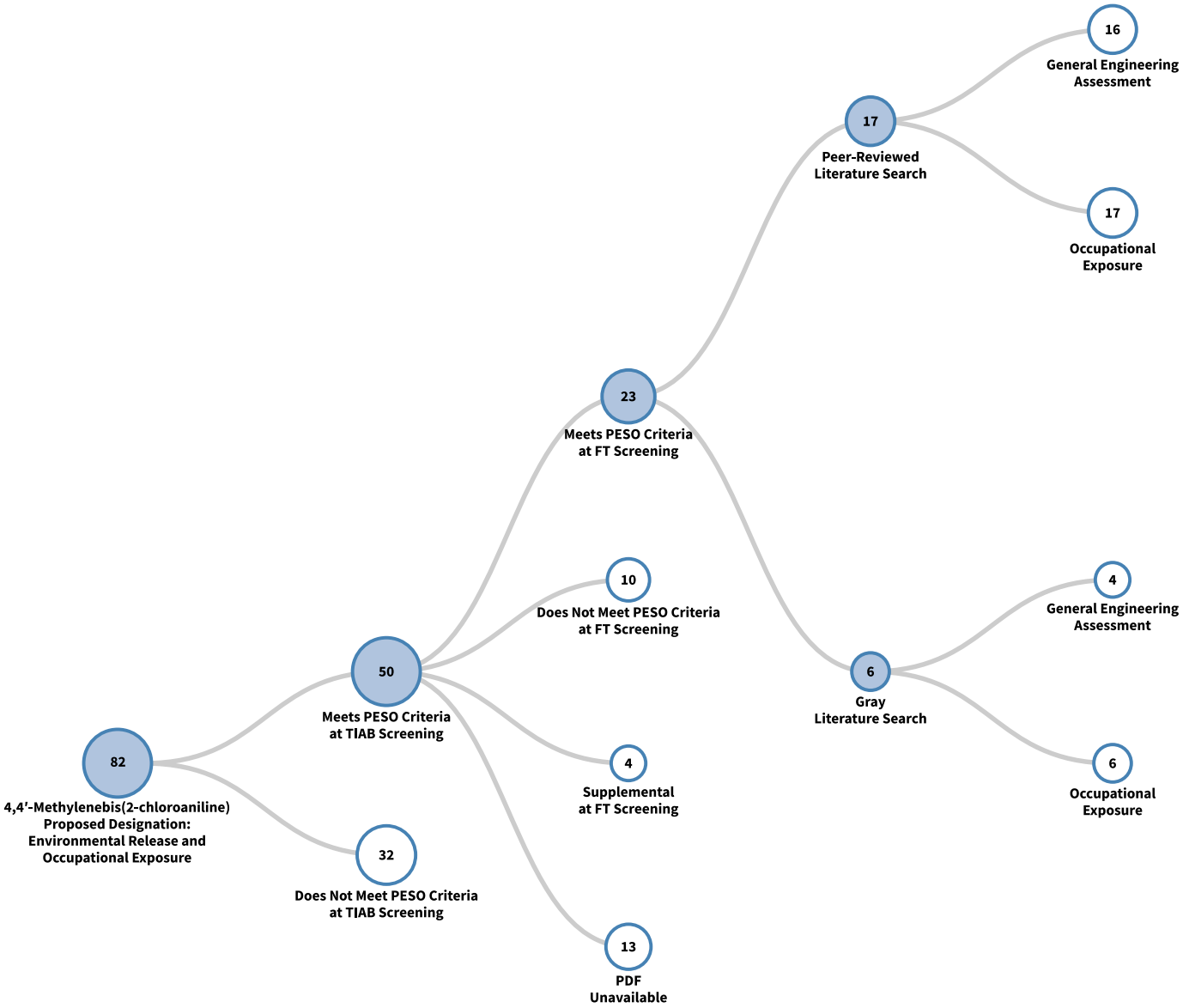
Objective	Type of Data[a]
	25. Accidental releases/spills

[a] These are the tags included in the full text screening form. The screener selects from these specific tags, which describe more specific types of data or information.

In addition to the data types listed above, EPA may identify additional data needs for mathematical modeling. These data needs will be determined on a case-by-case basis.

C.3.2 Literature Inventory Tree – Occupational Exposure and Environmental Release Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Figure_Apx C-4 presents the number of references that report general engineering data, environmental release, and occupational exposure data that passed PESO screening criteria at TIAB, and full-text screening for MBOCA Data or information sources that comply with the PESO screening criteria then undergo data quality evaluation and extraction.



Figure_Apx C-4. Literature Inventory Tree of Occupational Exposure and Environmental Release Search Results for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

Data in this figure represent the references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 14, 2024. Additional data may be added to the interactive version as they become available. View the interactive literature inventory tree in HAWC.

C.3.3 Evidence Map of Occupational Exposure and Environmental Release Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

Distinct count of Hero ID
1 17

Data Type	Evidence Tag	References
COU	Industrial/Commercial Use	1
	Manufacture - Domestic manufacture	12
	Manufacture-Import	4
	Processing - Processing as a reactant	12
	Processing - Processing incorporation into formulation, mixture, or reaction product	13
	Processing - Processing- incorporation into articles	9
	Total	22
General Engineering	Chemical Concentration	4
	Life cycle Description	2
	Number of sites	9
	Process description	14
	Production, Import, or Use Volume	9
	Throughput	2
	Total	20
Occupational Exposure	Area sampling data	13
	Dermal exposure data	8
	Engineering control	8
	Exposure duration	6
	Exposure frequency	3
	Exposure route	16
	Number of workers	17
	Personal protective equipment	16
	Personal sampling data	8
	Physical form	10
	Sampling and analytical methodology	4
	Worker Activity description	15
	Total	23
Grand Total		**23**

Figure_Apx C-5. Evidence Map of Occupational Exposure and Environmental Release Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent the references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 14, 2024. The column totals, row totals, and grand totals indicate total numbers of distinct references. The various shades of color visually represent the distinct number of relevant references identified by data type or engineering evidence tag. The darker the color, the more references are available for a given data type or engineering evidence tag. Additional data may be added to the interactive version as they become available. View the interactive evidence map in HAWC.

C.4 General Population, Consumer, and Environmental Exposure

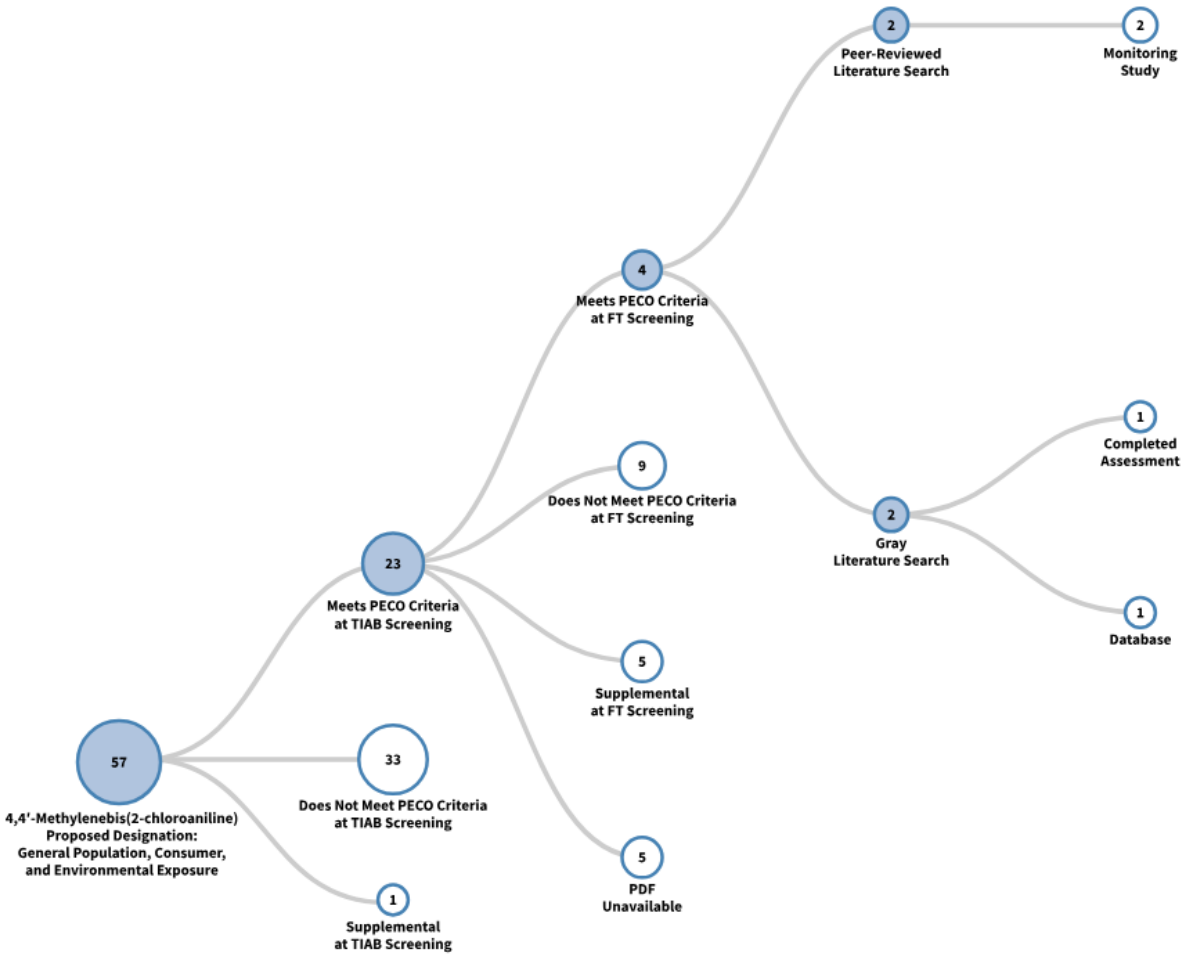
During data screening, EPA followed the process described in Appendix H-4 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) to conduct TIAB and full-text screening for MBOCA literature search results, as guided by the PECO screening criteria (Table_Apx C-7). The same PECO screening criteria was used during TIAB and full-text screening for references considered for the evaluation of general population, consumer, and environmental exposure information for MBOCA. TIAB screening was performed using SWIFT Active-Screener. Figure_Apx C-6 presents the number of references that report general population, consumer, and environmental exposure data that passed PECO screening criteria at TIAB and full-text screening.

C.4.1 Screening Criteria for Data Sources Reporting General Population, Consumer, and Environmental Exposure Information

Table_Apx C-7. Screening Criteria for the Data Sources Reporting Exposure Data on General Population, Consumers, and Environmental Receptors for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

PECO Element	Evidence
Population	**Human**: General population; consumers; bystanders in the home; near-facility populations (includes industrial and commercial facilities manufacturing, processing, or using the chemical substance); children; susceptible populations (lifestages, preexisting conditions, genetic factors), pregnant women; lactating women, women of childbearing age. Many human population groups may be exposed.
	Environmental: Aquatic species, terrestrial species, terrestrial plants, aquatic plants (field studies only).
Exposure	**Expected Primary Exposure Sources, Pathways, Routes**: **Pathways**: Indoor air/vapor/mist; indoor dust; particles; surface water; groundwater; outdoor/ambient air; drinking water; land disposal; biosolids/sludge; soil; sediment; aquatic species; terrestrial species; human biomonitoring; dietary; consumer product uses in the home (including consumer product containing chemical). **Routes of Exposure**: Inhalation, Oral, Dermal.
Comparator (Scenario)	**Human**: Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which human subpopulations are and are not reasonably exposed across the projected exposure scenarios.
	Environmental: Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
Outcomes for Exposure Concentration or Dose	**Human**: Acute, subchronic, and/or indoor air and water concentration estimates (mg/m^3 or mg/L). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. Characteristics of consumer products or articles (weight fraction, emission rates, etc.) containing chemical.
	Environmental: A wide range of ecological receptors will be considered (range depending on available ecotoxicity data) using surface water concentrations, sediment concentrations.

C.4.2 Literature Inventory Tree - General Population, Consumer, and Environmental Exposure Search Results



Figure_Apx C-6. Literature Inventory Tree of Consumer, General Population, and Environmental Exposure Search Results for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available. View the interactive literature inventory tree in HAWC.

C.4.3 Evidence Map of General Population, Consumer, and Environmental Exposure Information

Distinct count of Hero ID

1

Media	Study type						
	Completed Assessment	Database	Experimental	Modeling	Monitoring	Survey	**Grand Total**
Ambient (Outdoor) Air					1		1
Aquatic Species							0
Biosolids/Sludge							0
Building Material							0
Consumer Product or Article	1						1
Dietary/Food							0
Drinking Water							0
Dust (Indoor)							0
Groundwater							0
Human Biomonitoring - Blood							0
Human Biomonitoring - Dermal							0
Human Biomonitoring - Milk							0
Human Biomonitoring - Tissues, Other							0
Human Biomonitoring - Urine					1		1
Indoor Air							0
Leachate							0
Other Media		1					1
Personal Inhalation							0
Precipitation							0
Sediment							0
Soil							0
Surface Water		1					1
Terrestrial Species							0
Wastewater							0
Grand Total	1	1	0	0	2	0	4

The column totals, row totals, and grand totals indicate total numbers of distinct references. The various shades of color visually represent the distinct number of relevant references identified by study type or media tag. The darker the color, the more references are available for a given study type or media tag.

Figure_Apx C-7. Evidence Map of Consumer, General Population, and Environmental Exposure Information for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent the references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available. View the interactive evidence map in HAWC.

C.5 Environmental and Human Health Hazard

During data screening, EPA followed the process described in Sections 4.2.5 and 4.3.2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) to conduct TIAB and full-text screening. Specifically for MBOCA literature search results, screening was guided by the PECO screening criteria in Table_Apx C-8. The same PECO screening criteria was used during TIAB and full-text screening for references considered for the evaluation of environmental and human health hazard resulting from exposure to MBOCA. For TIAB screening, EPA utilized machine learning to help prioritize reference screening in SWIFT-Active-Screener. Full-text screening occurred manually in DistillerSR for references that either met the PECO screening criteria during TIAB screening or if it was unclear to EPA whether the reference would meet the PECO screening criteria based on the information available in the title and abstract. While the same PECO

screening criteria was used during TIAB and full-text screening, an update to the screening decision was made between TIAB and full-text screening to references that reported meta-analyses with epidemiological data in which originally these references met PECO screening criteria at TIAB screening but were later classified as supplemental information for full-text screening. The rationale for this update being that references with meta-analyses use information of individual studies from sources other than generated by the authors in order to perform their meta-analyses. Figure_Apx C-8 presents the number of references that report environmental and human health hazard data that passed PECO screening criteria at TIAB and full-text screening.

C.5.1 Screening Criteria for Data Sources Reporting Environmental and Human Health Hazard Information

Table_Apx C-8. Screening Criteria for Populations, Exposures, Comparators, and Outcomes (PECO) Criteria for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4)

PECO Element Relevance	Evidence
P	**Human (Epidemiology):** Any population and lifestage (*e.g.*, occupational, or general population, including children and other sensitive populations). **Animal:** Aquatic and terrestrial species (live, whole organism) of any life stage (*e.g.*, preconception, *in utero*, lactation, peripubertal, and adult stages). Animal models will be inventoried according to the categorization below: - Human health animal models: rat, mouse, rabbit, dog, hamster, guinea pig, cat, non-human primate, and pig. - Ecotoxicological animal models: All animal studies (invertebrates and vertebrates) excluding the models listed above as a human health model. All hen studies (including neurotoxicity studies) will ***meet screening criteria*** as ecotoxicological animal models. **Plants and Fungi:** All aquatic and terrestrial species (live) (vascular and non-vascular plants), including but not limited to algal species, diatoms, cyanobacteria, moss, lichen and macro fungi (*e.g.*, mushrooms (Phylum: Basidiomycota)) species. **Note on Yeast and Bacteria:** Any genotoxicity, mutagenicity, or hormone assay data utilizing yeast or bacteria are sorted under ***Yeast/Bacteria*** receptor, and tagged ***Supplemental, Mechanistic***. **Screener notes:** • Human Health Animal Hazard and Environmental Hazard: To identify human health and ecological hazards, other organisms not listed above each of these two respective categories can also be used. Non-mammalian model systems are increasingly used to identify potential human health hazards *(e.g.*, *Xenopus*, zebrafish), and traditional human health models (*e.g.*, rodents) can be used to identify potential ecological hazard. For SR screening and data evaluation and extraction purposes, the human health models listed above will be tagged or identified as human health models and all other animal studies will be tagged as ecotoxicological animal models, unless stated otherwise based on existing chemical-specific information. Neurotoxicity studies performed in hens (*e.g.*, OECD 418 and 419) are considered relevant to both human health and environmental hazard, but all hen studies will be tagged only as ecotoxicological animal models for SR screening and data evaluation and extraction purposes. • Environmental Hazard: Ecotoxicological studies that assess exposure effects on organisms such as protozoan, microbial fungi (*e.g.*, microsporidians), and molds will be

PECO Element Relevance	Evidence

	tagged as ***Supplemental, Deprioritized environmental organisms*** because an environmental hazard assessment will unlikely be driven by unicellular organisms or microbial organisms which are low in the natural ecosystem hierarchy.
	
	• Environmental Hazard: The Population (PECO) consideration should be directed toward direct effects on the **target species only** regardless of the type of effect or health outcome. Studies reporting only indirect effects expressed in taxa that are **not** the target species of the chemical exposure do not meet the PECO criteria and thus are ***Supplemental, Indirect exposure***. Examples of target species with direct effects *versus* not the target species with indirect effects include but are not limited to:
	  • *Plant studies*: Several studies conducted with plants investigate the chemical's ability to control pests. Substance is lethal to a **targeted** pest species leading to positive effects on plant growth due to diminished presence of the **targeted** pest species (*e.g.*, nematodes). In these scenarios: The **direct effects** are those on the **targeted** pest species (*e.g.*, increased mortality in nematodes); **indirect effects** are those on the plants that experience an effect (*e.g.*, increased yield) but only as a result of the effects of exposure on the **targeted** pest species. Thus, studies that use the substance to control pest species but only report the plant growth are tagged as ***Supplemental, Indirect exposure***.
	  • *Fish studies*: Substance is used to treat fungal/parasitic/bacterial infections, so increased survival or growth is an indirect effect of the improved health of fish due to diminished presence of pathogenic microbes. Thus, studies that use the substance to control pest species but only report fish health outcomes are tagged as ***Supplemental, Indirect exposure***.
	  • *Avian studies*: Substance is used to treat poultry eggs to prevent growth of bacteria on the eggshell which indirectly can increase the survival and health of chicks. Thus, studies that use the substance to control growth of bacteria on the eggshell and report chick health outcomes are tagged as ***Supplemental, Indirect exposure***.
	  • *Livestock studies*: Substance is used to treat fungal/parasitic/bacterial infections which indirectly results in positive effects of survival, growth of livestock. Thus, studies that use the substance to only control pathogenic microbes but only report livestock health outcomes are tagged as ***Supplemental, Indirect exposure***.
	
	• Human Health Animal Hazard and Environmental Hazard: Studies on gametes, embryos, or plant or fungal sections capable of forming whole, new organisms will be tagged as potentially ***Supplemental, Mechanistic***. **EXCEPTION**: Embryos for environmental hazard studies (*e.g.*, zebrafish, fathead minnow, copepod, bivalve embryos) ***meet the PECO screening criteria*** if they also meet all other PECO criteria.
	
	• Yeast and Bacteria: Bacteria and yeast studies specific for assessing genotoxicity, mutagenicity (*e.g.*, Ames assay), or hormone assay will be tagged as potentially ***Supplemental, Mechanistic.*** Otherwise, bacteria and yeast studies that are **not** used for assessing genotoxicity, mutagenicity, or hormone assays ***do not meet the PECO criteria***.
	
	• Human Health Animal Hazard and Environmental Hazard: Studies on viruses and any pathogenic microbes (unless bacteria or yeast used for assessing genotoxicity,

PECO Element Relevance	Evidence
	mutagenicity, or hormone assay; see bullet above) ***do not meet the PECO screening criteria***.
E	**Relevant forms and isomers:** • MBOCA aka MBOCA or MOCA (CASRN 101-14-4) • MBOCA hydrochloride Common synonyms of MBOCA include MBOCA, 2,2`-Dichloro-4,4`-methylenedianiline, 4,4`-Methylene-bis(2-chlroroaniline), 4,4`-Methylene-bis-2-chloroaniline, Bisamine, and Methylenebis(chloroaniline). For a full list of synonyms, see list of validated synonyms on the EPA CompTox Chemicals Dashboard. ○ Isomer(s) (these chemicals are included): ▪ No isomers identified Other ***Supplemental*** relevant structures (these should be tagged as ***Supplemental, Other Relevant Structures*** only if they meet the PECO and if exposure to MBOCA or MBOCA in hydrochloride are not explicitly mentioned). • Degradant(s)/Metabolite(s)/Biomarker(s): ▪ Degradants: N-monoacetyl MBOCA, N,N'diacetyl MBOCA (or MOCA) (also being considered as a metabolite), 4,4'-Diamino-3,3'-dichloro-benzophenone, N-hydroxyl-N-acetyl MBOCA, N-hydroxyl-N,N'-diacetyl MBOCA, and N-hydroxy MBOCA (or MOCA) (also being considered as a metabolite) ▪ Metabolites: N,N'diacetyl MBOCA (or MOCA) (also being considered as a degradant), N-acetyl MBOCA, β-N-glucuronide of MBOCA, N-hydroxy MBOCA (or MOCA) (also being considered as a degradant), Mononitroso-MBOCA, O-hydroxy-MBOCA (or MOCA), MBOCA Benzhydrol, N-nitroso-MBOCA, and 5-hydroxy-MBOCA ▪ DNA adducts used as biomarker of exposure: N-(deoxyadenosin-8-yl)-4-amino-3-chlorobenzyl ▪ Hemoglobin adducts used as a biomarker of exposure: MBOCA-globin adducts • MBOCA "Salts" other than MBOCA hydrochloride with a health outcome. **Human (Epidemiology):** Any exposure to MBOCA (CASRN 101-14-4) singularly or in mixture (including co-occurrence and mixtures as defined under TSCA), including exposure as measured by internal concentrations of these chemicals or metabolites of these chemicals in a biological matrix (*i.e.*, urine, blood, semen, etc.) if MBOCA or synonyms are mentioned. **Animal:** Any exposure to MBOCA (CASRN 101-14-4) via water (including environmental aquatic exposures), soil or sediment, diet, gavage, dermal (*i.e.*, exposure to skin), eye, and inhalation will ***meet screening criteria***. **Plants and Fungi:** Any exposure to MBOCA (CASRN 101-14-4) including via water, soil, sediment.

PECO Element Relevance	Evidence
	Screener notes: • Human Health Animal Hazard, and Environmental Hazard: Exposure routes not listed above are to be identified as ***Supplemental, Non-prioritized Exposure Routes***. Skin sensitization studies (*e.g.*, the guinea pig maximization protocol) that include an intradermal induction phase (with application onto the skin during the challenge phase) will ***meet screening criteria***. • Epidemiology, Human Health Animal Hazard, and Environmental Hazard: Exposure to the target chemical even if specific exposure concentrations are not reported is sufficient to ***meet the PECO screening criteria***. • Environmental Hazard: Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals, plants, and/or fungi are to be identified as ***Supplemental, Field Studies*** only if any biological effects are reported. • Human Health Animal Hazard and Environmental Hazard: Animal, plant and/or fungi studies involving exposures to mixtures will ***meet screening criteria*** only if they also include exposure to MBOCA (CASRN 101-14-4) or MBOCA hydrochloride **alone or in the presence of no other non-inert chemicals**. Otherwise, mixture studies (including chemical co-occurrence/co-exposure as well as mixtures as defined under TSCA) will be tagged as ***Unclear*** during **Title/Abstract Screening** and as ***Supplemental, Mixtures*** during **Full Text screening.** • Human Health Animal Hazard and Environmental Hazard: Chemical plus non-chemical stressor co-exposures (*i.e.*, chemical + temperature and/or pH, DO, nutrition, feeding rate, culture density, physical injury, light/dark cycles, etc.) will be tagged as ***Unclear*** during **Title/Abstract Screening** and as ***Supplemental, Chemical plus non-chemical stressor*** during **Full Text screening.** • Environmental Hazard: Controlled outdoor experimental studies (*e.g.*, controlled crop/greenhouse studies, mesocosm studies, artificial stream studies) are considered to be similar to laboratory studies (**not field studies**) because there is a known and prescribed exposure dose(s) and an evaluation of hazardous effect(s). On the contrary, field studies (*e.g.*, biomonitoring) where there is no prescribed exposure dose(s) will be tagged as ***Supplemental, Field studies*** only if there is an evaluated hazardous effect. • Epidemiology, Human Health Animal Hazard, and Environmental Hazard: Metabolite and MBOCA salts other than MBOCA hydrochloride should be tagged as ***Supplemental, Other relevant chemical structures*** if the study meets all PECO screening criteria. • Epidemiology, Human Health Animal Hazard, and Environmental Hazard: If biomarkers of **exposure** are used to assess exposure to the chemical of interest, they will ***meet the PECO screening criteria***. • Biomarkers of **exposure** include measurements of exposure, internal dose, and biologically effective dose (including adducts).
C	**Human (Epidemiology):**

PECO Element Relevance	Evidence
	Any study with a comparison group, control group, or referent group, including: • A comparison group that does not have the disease or outcome of interest (such as a case-control study); or Any study comparing exposed individuals to unexposed or lower-exposed individuals including: • A comparison group with no exposure to the chemical of interest or exposure below detection limits, or • A comparison group exposed to lower levels of the chemical of interest; or • A comparison group exposed to the chemical of interest for shorter periods of time; or Any study assessing the association between a continuous measure of exposure and a health outcome; or For studies in which humans are intentionally exposed to the chemical of interest, an individual can serve as their own control. **Animal, Plants, and Fungi:** A concurrent control group exposed to vehicle-only treatment and/or untreated control (control could be a baseline measurement). **<u>Screener notes:</u>** • <u>Epidemiology:</u> All epidemiology studies with a comparison group, control group, or referent group ***meet screening criteria:*** o Studies that mention that they used any of the following common study designs or methods listed (but not limited to): cohort (prospective cohort, retrospective cohort, etc.), case-control, case-crossover, case-referent, case-cohort, cross-sectional, nested case-control, regression, relative risk, risk ratio, odds ratio, hazard ratio, and standardized mortality ratio (SMR) will ***meet screening criteria***. These are not the only included designs but all epidemiology studies that use these designs will ***meet screening criteria*** – other designs may also ***meet screening criteria***. Intentional dosing epidemiology studies (controlled exposure studies or studies in which people are intentionally exposed to the chemical) with an individual serving as their own control will ***meet screening criteria***. (Ethics review will occur later). Otherwise, studies without a comparison group are ***Supplemental***: o All study designs such as case reports, case series, and case studies without a comparison group in any setting (*e.g.*, occupational, general population), will be tracked as ***Supplemental, Hazard value without negative control or appropriate vehicle control***. • <u>Human Health Hazard (Animal Hazard and Epidemiology)</u>: For studies in which humans or human health animal models are intentionally exposed to a chemical, the control could be a baseline measurement of the same individual (*i.e.*, the individual is assessed pre- and post-exposure), and these studies will ***meet screening criteria***. Also, for studies in which humans or human health animal models are intentionally exposed to a chemical, references that contain experimental designs that do not require a negative or vehicle control group (*i.e.*, skin sensitization (such as LLNA), LC50 and LD50 completed within an acute timeframe, or dermal irritation studies in which the experimental individual serves as their own control) will ***meet screening criteria***. • <u>Human Health Animal Hazard and Environmental Hazard</u>: If no control group is explicitly stated, the study will be marked as ***Unclear*** during **Title/Abstract Screening.** But if the study reports the following specific hazard values of interest (EC10, NOEC,

PECO Element Relevance	Evidence
	LOEC, or Environmental Hazard LC50) even if it does not explicitly report the use of a control, it will be tagged as ***Supplemental, Hazard value without negative control or appropriate vehicle control*** during **Full Text screening** because the data can be of value for data-poor chemicals. Otherwise, if no control group is explicitly stated AND the specific hazard values of interest listed in this paragraph are not reported, then the study ***does not meet the PECO screening criteria*.**
O	**Human (Epidemiology), Animal, Plants, and Fungi:** For *in vivo* studies, any health outcome measured at any level of biological organization (*e.g.*, DNA damage, apoptosis, organ damage, mortality) will ***meet screening criteria***. For *ex vivo* studies, only health outcomes measured at the organ level or higher, where exposure occurred in a live animal, will ***meet screening criteria***. *Ex vivo* studies where the live organism was not directly exposed to the chemical of interest are to be tagged as ***Supplemental, Mechanistic.*** For all non-*in vivo* studies, sub-organ level health outcomes are to be tagged as ***Supplemental, Mechanistic***. **Screener notes:** • Environmental Hazard: *In vivo* ADME studies designed to capture information regarding transformation (*i.e.*, ADME) will ***meet screening criteria***. • Human Health Animal Hazard and Epidemiology: *In vivo* and *in vitro* ADME studies designed to capture information regarding transformation (*i.e.*, absorption, distribution, metabolism, and excretion) without assessing a health outcome are to be tagged as ***Supplemental, Mechanistic, subtag: ADME*.** • Epidemiology and Human Health Animal Hazard: Studies that identify potentially susceptible subgroups but do not report a health outcome need to be tagged as ***Supplemental, Susceptible Population (no health outcome).*** • Epidemiology and Human Health Animal Hazard: Biomarkers of **effect** are to be considered outcomes. However, if the *only* outcomes assessed are biomarkers of exposure, with no health outcomes assessed, then it is ***Supplemental, Mechanistic***. o Biomarkers of **effect** include measurements of early biological effect (including altered enzymatic activities), altered structure/function, and disease. o Biomarkers of **exposure** include measurements of exposure, internal dose, and biologically effective dose (including adducts). o Biomarkers of **susceptibility** are relevant for potentially exposed or susceptible subpopulations (PESS) considerations. If a reference doesn't meet the O of the PECO but includes biomarkers of susceptibility, then the reference should be tagged as ***Supplemental, Susceptible Populations (no health outcome)***.
P, E, C, O	Meta-analyses are ***Supplemental.*** **Screener notes:** • Epidemiology: Meta-analyses (quantitative, formal, epidemiological study design used to systematically assess the results of previous research addressing a similar research question) may be advantageous when deriving a dose-response relationship and potentially offer improvement in the precision of effect estimates because the individual studies alone included in the meta-analysis may not offer study details (*e.g.*, more appropriate analytical methods, different model fit and more appropriate data inclusion/exclusion rules). Therefore, meta-analyses should be tagged as ***Supplemental, Other potentially relevant data sources, subtag: Meta-analyses***.

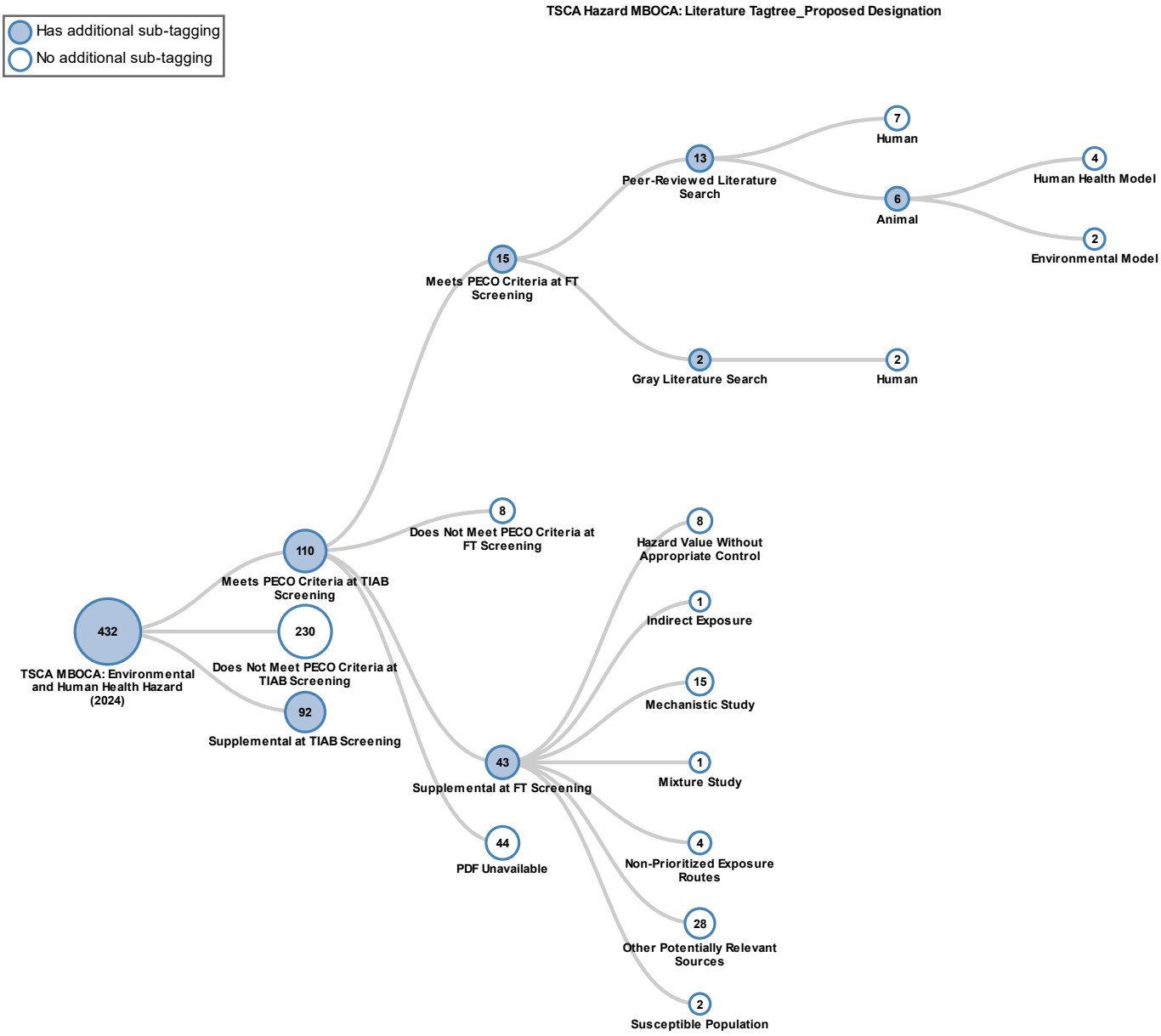
Table_Apx C-9. Major Categories of Potentially Relevant Supplemental Material for 4,4'-Methylene bis(2-chloroaniline) or MBOCA (CASRN: 101-14-4) – Title and Abstract and Full Text Screening

PECO Element Relevance	Category	Evidence
P	Deprioritized environmental organisms	Environmental Hazard: Studies that assess exposure effects on protozoans, microbial fungi (*e.g.*, microsporidians), and molds fall under this category because an environmental hazard assessment will unlikely be driven by unicellular organisms or microbial organisms which are low in the natural ecosystem hierarchy.
P	Indirect exposure	Environmental Hazard: Studies reporting only indirect effects expressed in taxa that are **not** the target species of the chemical exposure. Examples include but are not limited to: • Plant studies: Substance is used as a means to control pests (*e.g.*, nematodes), but the study does **not** report data on nematodes (*e.g.*, mortality) and **only** reports data on plant health outcomes (*e.g.*, plant growth) which are an indirect effect because it is a result of the decrease presence of nematodes. • Fish studies: Substance is used as a means to control pathogenic microbes and pests (*i.e.*, treatment of fungal/parasitic/bacterial infections), and the study only reports health outcomes in fish, which are an indirect effect of the improved health of fish due to diminished presence of pathogenic microbes. • Avian studies: Studies reporting increased survival and health of chicks following chemical substance treatment on eggs to prevent growth of bacteria on the eggshell fall in this supplemental category. Reminder: Studies on viruses and any pathogenic microbes (unless bacteria or yeast used for assessing genotoxicity, mutagenicity, or hormone assay; see screener notes under P) ***do not meet PECO screening criteria***.
E	Non-prioritized exposure routes	Human Health Animal Hazard, and Environmental Hazard: Examples include but not limited to injection (*e.g.*, intraperitoneal, intravenous, subcutaneous, intradermal), rectal exposures, intratracheal, intracranial, and bladder instilling (*i.e.*, exposure using a catheter).
E	Mixture studies	Human Health Animal Hazard and Environmental Hazard: Experimental mixture studies that are not considered to meet the PECO because they do not contain an exposure or treatment group assessing *only* the chemical of interest. The category does not apply to chemical mixtures of enantiomers and/or diastereomers, and the exposure in these cases would be marked as ***meeting the PECO screening criteria***. Mixture studies include chemical co-occurrence/co-exposure studies as well as mixtures as defined under TSCA.
E	Chemical plus non-chemical stressor	Human Health Animal Hazard and Environmental Hazard: Studies where organisms are exposed to the target chemical plus non-chemical stressor(s); *i.e.*, target chemical + temperature and/or pH, DO, nutrition, feeding rate, culture density, physical injury, light/dark cycles, etc. In these scenarios, the non-chemical stressor is a singular or a range of animal maintenance conditions that are **not** normal/standard. However, if a study includes a group exposure to the target chemical in normal/standard conditions, the study will ***meet screening criteria***.
E	Other relevant chemical structures	Epidemiology, Human Health Animal Hazard, and Environmental Hazard: PECO-relevant studies with other chemical structures such as metabolites

PECO Element Relevance	Category	Evidence
		may be useful later. Metabolites of MBOCA or MBOCA hydrochloride should be tagged as ***Supplemental, Other relevant chemical structures*** if the study meets all PECO screening criteria. If exposure to MBOCA or MBOCA hydrochloride are not explicitly mentioned, these metabolites and other structures of interest should be put into this supplemental category. Structures of interest currently include: - Degradants: N-monoacetyl MBOCA, N,N'diacetyl MBOCA (or MOCA) (also being considered as a metabolite), 4,4'-Diamino-3,3'-dichloro-benzophenone, N-hydroxyl-N-acetyl MBOCA, N-hydroxyl-N,N'-diacetyl MBOCA, and N-hydroxy MBOCA (or MOCA) (also being considered as a metabolite) - Metabolites: N,N'diacetyl MBOCA (or MOCA) (also being considered as a degradant), N-acetyl MBOCA, β-N-glucuronide of MBOCA, N-hydroxy MBOCA (or MOCA) (also being considered as a degradant), Mononitroso-MBOCA, O-hydroxy-MBOCA (or MOCA), MBOCA Benzhydrol, N-nitroso-MBOCA, and 5-hydroxy-MBOCA - DNA adducts used as biomarker of exposure: N-(deoxyadenosin-8-yl)-4-amino-3-chlorobenzyl alcohol - Hemoglobin adducts used as a biomarker of exposure: MBOCA-globin adducts - MBOCA salts other than MBOCA in hydrochloride with a health outcome.
E	Field studies	Environmental Hazard: Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants ***only if any*** biological effects (*i.e.*, apical and mechanistic) are reported.
C	Hazard value without negative control or appropriate vehicle control	Human Health Animal Hazard and Environmental Hazard: Studies that do not explicitly report the use of a control but report the following hazard values (EC10, NOEC, LOEC, or Environmental Hazard LC50) can be of value for data-poor chemicals. Human Health Animal Hazard LC50 and LD50 studies completed within an acute timeframe will ***meet PECO screening criteria***. Epidemiology: Study designs such as case reports, case series, and case studies without a comparison group will be tracked as ***Supplemental***. (This Supplemental category does NOT include cohort (prospective cohort, retrospective cohort, etc.), case-control, case-crossover, case-referent, case-cohort, cross-sectional, nested case-control, regression, relative risk, risk ratio, odds ratio, hazard ratio, or standardized mortality ratio (SMR) study designs, which all ***meet PECO screening criteria***).

PECO Element Relevance	Category	Evidence
O, P	Mechanistic studies	Human Health Animal Hazard and Environmental Hazard: Bacteria and yeast studies specific for assessing genotoxicity, mutagenicity (*e.g.*, Ames assay), or hormone assay will be tagged as potentially ***Supplemental, Mechanistic***. Studies on gametes, embryos, or plant or fungal sections capable of forming whole, new organisms will be tagged as potentially ***Supplemental, Mechanistic***. EXCEPTION: Fish and invertebrate embryo (*e.g.*, zebrafish, fathead minnow, copepod, bivalve embryos) studies ***meet screening criteria*** they also meet all other PECO criteria. Epidemiology, Human Health Animal Hazard, and Environmental Hazard: *Ex vivo* studies where the live organism was not directly exposed to the chemical of interest are to be tagged as ***Supplemental, Mechanistic***. For all non-*in vivo* studies, sub-organ level health outcomes are to be tagged as ***Supplemental, Mechanistic***. **ADME studies:** *In vitro* Environmental Hazard studies investigating ADME are to be tagged as ***Supplemental, Mechanistic, subtag: ADME***. *In vitro* and *in vivo* Human Health Animal Hazard and Epidemiology ADME studies designed to capture information regarding transformation (*i.e.*, ADME) without assessing a health outcome are to be tagged as ***Supplemental, Mechanistic, subtag: ADME***.
O	Susceptible populations (no health outcome)	Epidemiology and Human Health Animal Hazard: Studies that identify potentially susceptible subgroups but do not report a health outcome. **Screener note:** If biological susceptibility issues are clearly present or *strongly* implied in the title/abstract, this supplemental tag may be applied at the Title/Abstract Screening. If uncertain at title/abstract, do not apply this tag to the reference during the Title/Abstract Screening.
P, E, C, O	Non-English language records	Epidemiology, Human Health Animal Hazard, and Environmental Hazard: Non-English records will be tracked as potentially relevant supplemental information.
P, E, C, O	Other potentially relevant data sources	Epidemiology, Human Health Animal Hazard, and Environmental Hazard: Records that may not contain original data, such as other agency assessments, informative scientific literature reviews, editorials or commentaries and conference proceedings or abstracts. Epidemiology: Meta-analyses will be tagged as ***Supplemental, Other potentially relevant data sources, subtag: Meta-analyses***.

C.5.2 Literature Inventory Tree – Environmental and Human Health Hazard Search Results



Figure_Apx C-8. Literature Inventory Tree of Environmental and Human Health Hazard Search Results for 4,4'-Methylene bis(2-chloroaniline) or MBOCA

Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available. View the interactive literature inventory tree in HAWC.

C.5.3 Evidence Map of Environmental Hazard Information

Distinct count of Hero ID

1

Health outcome	Ecosystem / Taxonomic group						Grand Total
	Aquatic			Terrestrial			
	Invertebrate	Vertebrate	Vegetation and Fungi	Invertebrate	Vertebrate	Vegetation and Fungi	
Accumulation/ADME							0
Behavior							0
Biochemical/Biochemistry, Enzyme(s), Hormone(s)							0
Biomarkers							0
Cancer/Carcinogenesis							0
Cell signaling/function							0
Computation toxicology and data integration							0
Cytotoxicity							0
Development							0
Ecosystem processes							0
Enhanced adipogenesis							0
Epigenetics							0
Genotoxicity				1			1
Growth							0
Histology							0
Immobilization							0
Morphology	1						1
Mortality							0
Oxidative stress							0
Photosynthesis/Respiration							0
Physiology/organ function							0
Population							0
Receptor binding/regulation of receptor activity							0
Reproduction				1			1
Grand Total	1	0	0	1	0	0	2

Figure_Apx C-9. Evidence Map of Environmental Hazard Information for MBOCA

Data in this figure represent all references obtained from the publicly available databases and gray literature reference searches that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available. The left side of the evidence map depicts references obtained for aquatic ecosystems, while the right side depicts references obtained for terrestrial ecosystems. The column and row grand totals indicate total number of distinct references. The various shades of color represent the number of relevant references identified for each health outcome-taxonomic group pair. Darker colors indicate a higher number of references available for a given health outcome-taxonomic group pair. In cases where a given reference reported the same health outcome for multiple taxonomic groups and/or multiple health outcomes for a single taxonomic group, the number of references within the table may appear higher than the grand totals. View the interactive evidence map for environmental hazard in HAWC.

C.5.4 Evidence Map of Human Health Hazard Information

Health outcome	Exposure type					Grand Total
	Animal toxicity		Epidemiology			
	Dermal	Oral	Dermal	Inhalation	Ocular/Eye	
Cancer/Carcinogenesis		3	4	4	2	8
Cardiovascular		1	1			2
Gastrointestinal	1	1				1
Hepatic/Liver	1	3				3
Immune/Hematological		1	1	1	1	2
Lung/Respiratory	1	3	1			4
Mortality	1	4	1	1	1	5
Nutritional/Metabolic		2				2
Ocular/Sensory		1				1
Other		1	4	3	3	5
Renal/Kidney	1	3	1			4
Reproductive/Developmental		1				1
Skin/Connective Tissue	1	2				2
Thyroid		1				1
Grand Total	1	4	7	7	5	12

Figure_Apx C-10. Evidence Map of Human Health Hazard Information
Data in this figure represent all references obtained from the publicly available databases that were included in systematic review as of May 15, 2024. Additional data may be added to the interactive version as they become available. These references are reflected in the Hazard Literature Inventory Tree (Figure_Apx C-8), The X-axis lists exposure types: oral/food/drinking water (not yet available for epidemiology references), dermal, inhalation (not yet available for animal toxicity references), and ocular (not yet available for animal toxicity references). The Y-axis lists health outcomes described for each appropriate exposure type. The column totals, row totals, and grand totals indicate total numbers of distinct references. The various shades of color visually represent the distinct number of relevant references identified for each health outcome-taxonomic group pair. Darker colors indicate a higher number of references available for a given health outcome-exposure pair. View the interactive human health outcome heatmap in HAWC.

Table_Apx C-10 lists the quantitative endpoint data as reported in previous assessments considered for Section 2.7.2, potential human health hazard. Each endpoint was determined based on animal toxicity study data, epidemiology data, or both, per the two right-most columns. The data values in this table are visualized in Figure 2-5 .

Table_Apx C-10. Human Health Quantitative Endpoints from Previous Assessments

Assessment Label[a]	Endpoint Type	Health Outcome	Value	Exposure Type	Based on Animal Toxicity Data	Based on Epidemiology Data
OEHHA 2011	Unit Risk Factor (URF)	Cancer	4.3×10^{-4} $\mu g/m^3$	Inhalation	X	

Assessment Label[a]	Endpoint Type	Health Outcome	Value	Exposure Type	Based on Animal Toxicity Data	Based on Epidemiology Data
OEHHA 2011	Slope Factor	Cancer	1.5 mg/kg/day	Oral	X	
ATSDR 2017	Minimal Risk Level (MRL)	Chronic toxicity	3×10^{-3} mg/kg/day	Oral	X	
ATSDR 2017	Threshold Limit Value – Time-Weighted Average (TLV-TWA)	Chronic toxicity	0.01 ppm	Dermal		X
ATSDR 2017	Recommended Exposure Limit (REL) - (Up to 10-hour TWA)	Chronic toxicity	0.003 mg/m^3	Dermal		X
ECCC 2020	Slope factor	Cancer	0.1 mg/kg/day	Oral	X	
ECCC 2020	Lifetime cancer risk	Cancer	3×10^{-8} (no units)	Oral	X	
ECCC 2020	Margin of Exposure (MOE)	Cancer	2.78×10^{8} (no units)	Oral	X	
ORD 2006	Reference Dose (RfD), chronic and subchronic	Chronic toxicity	2×10^{-3} mg/kg/day	Oral	X	
ORD 2006	Slope Factor	Cancer	7×10^{-3} mg/kg/day	Oral	X	
ORD 2006	Slope Factor	Cancer	0.13 mg/kg/day	Oral	X	
ORD 2006	Inhalation Unit Risk (IUR)	Cancer	3.7×10^{-5} µg/m^3	Inhalation	X	
ORD 2006	Reference Dose (RfD), Chronic and Subchronic	Chronic toxicity	7×10^{-4} mg/kg/day	Oral	X	
ORD 2006	Minimal Risk Level (MRL)	Cancer	3×10^{-3} mg/kg/day	Oral	X	

[a] "Assessment labels" refers to the labels associated with previous assessments identified in various figures and tables within Section 2.7.2and Table_Apx B-4.

Appendix D PHYSICAL AND CHEMICAL PROPERTIES

Table_Apx D-1. Physical and Chemical Properties of MBOCA

Property	Value(s)[a]	Reference(s)
Molecular formula	$C_{13}H_{12}Cl_2N_2$	NLM (2023b)
Molecular weight	267.153 g/mole	Rumble (2023)
Physical form	Colorless crystals or yellow-brown pellets or flakes; faint amine-like odor	NLM (2023b), ATSDR (2017)
Melting point	110 °C	RSC (2023), U.S. EPA (2023)
	101.19 – 110 °C	Reaxys (2023)
Boiling point	Decomposes above 202 °C	PhysProp (2023), NLM (2023b), OECD (2013b)
Density	1.44 g/cm^3 at 20 °C	NLM (2023b), NLM (2023a), ATSDR (2017)
Vapor pressure	1.0 x 10^{-5} mm Hg at 25 °C	NLM (2023b), ATSDR (2017)
Vapor density	Not applicable	
Water solubility	13.9 mg/L at 24 °C	PhysProp (2023)
Octanol:water partition coefficient (log K_{OW})	3.91	PhysProp (2023)
	3.66 at 25 °C (OECD 107)	OECD (2013b)
	2.5 at 25 °C (OECD 117 & EU Method A.8)	ECHA (2023)
Octanol:air partition coefficient (log K_{OA})	12.781[b]	EPI Suite™ (KOAWIN)
Henry's law constant	1.14 x 10^{-11} (bond) to 2.53 x 10^{-7} (VP/WS)[b]	EPI Suite™ (HENRYWIN)
Flash point	113 °C (closed cup)	NLM (2023b)
Autoflammability	Not applicable	
Viscosity	Not applicable	
UV-Vis absorption	absorbs wavelengths >290 nm	Reaxys (2023)

[a] Measured unless otherwise noted
[b] Information was estimated using EPI Suite™ (U.S. EPA, 2012).

Appendix E ENVIRONMENTAL FATE AND TRANSPORT PROPERTIES

Table_Apx E-1. Environmental Fate and Transport Properties of MBOCA

Property or Endpoint	Value[a]	Reference(s)
Direct photodegradation (air)	Absorbs wavelengths > 290nm, therefore may be susceptible to direct photodegradation	NLM (2023b), Reaxys (2023)
Direct photodegradation (water)	No data identified	
Indirect photodegradation (air)	$t_{1/2}$ = 0.290 – 2.90 hours (based on reaction with •OH; rate constant and radical concentration not specified)	ATSDR (2017)
Indirect photodegradation (water)	$t_{1/2}$ = 39 – 72 days assuming alkoxy radical concentration of 1E-10M	NLM (2023b)
Hydrolysis half-life (water)	$t_{1/2}$ = 800 years at 25°C	ATSDR (2017), NLM (2023b), ECHA (2023)
Aerobic biodegradation (water)	0% over 7 days (Static Incubation Test) at 2.02 mg/L test substance concentration, inoculum source and adaptation not specified	ATSDR (2017)
	0-1% over 28 days (OECD 301C) at 100 mg/L test substance concentration, inoculum adaptation not specified	OECD (2013b), NITE (2023)
	0% over 6 weeks at 2 mg/L test substance concentration, inoculum source and adaptation not specified	NLM (2023b)
	0% over 8 weeks (MITI Test) at 100 mg/L test substance concentration, inoculum source and adaptation not specified	NLM (2023b)
	10% over 7 days at 2 mg/L test substance concentration, inoculum source and adaptation not specified	ECHA (2023)
Aerobic biodegradation (soil)	<1% over 24 weeks (CO_2 Evolution) at 4 mg/kg and 40 mg/kg test substance concentrations, in both uncontaminated and contaminated soils	ATSDR (2017), ECHA (2023)
Aerobic biodegradation (sediment)	No data identified	
Anaerobic biodegradation	No data identified	
Bioconcentration factor (BCF) (L/kg wet weight, unless noted)	BCF = 114 – 398 in *Cyprinus carpio* (OECD 305)	OECD (2013b), NITE (2023), NLM (2023b)
	Upper Trophic Level: 233.1 Middle Trophic Level: 234.8 Lower Trophic Level: 220.2	EPI Suite™ (BCFBAF, Arnot-Gobas method)[b]
Bioaccumulation factor (BAF)	Upper Trophic Level: 220.2 Middle Trophic Level: 235.7 Lower Trophic Level: 237.8	EPI Suite™ (BCFBAF, Arnot-Gobas method)[b]

Property or Endpoint	Value[a]	Reference(s)
(L/kg wet weight, unless noted)		
Organic carbon:water partition coefficient (log K_{OC}) (soil)	3.56 at 35 °C (OECD 121)	OECD (2013b), ECHA (2023)
	3.68	ATSDR (2017)
Removal in wastewater treatment	Total removal: 26.13 % Removal to primary sludge: 14.9 % Removal to waste sludge: 10.9 %	EPI Suite™ (STPWIN, with BIOWIN $t_{1/2}$s)

[a] Measured unless otherwise noted
[b] Information was estimated using EPI Suite™ (U.S. EPA, 2012).