United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention

Proposed Designation of 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-Hexamethylcyclopenta[γ]-2-Benzopyran (HHCB; CASRN 1222-05-5) as a High-Priority Substance for Risk Evaluation

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Acronyms and Abbreviations

Term	Description
ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
Biomon.	Biomonitoring
BOD	Biochemical oxygen demand
BP	Boiling point
CAA	Clean Air Act
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
Concen.	Concentration
CWA	Clean Water Act
ECOTOX	Ecotoxicology Database
EPA	U.S. Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
FDA	U.S. Food and Drug Administration
FR	Federal Register
GC	Gas chromatography
HPLC	High performance liquid chromatography
IRIS	Integrated Risk Information System
IUR	Inventory Update Rule
K	Thousand
K_{OC}	Organic carbon-water partition coefficient
K_{OW}	Octanol-water partition coefficient
M	Million

MITI	Ministry of International Trade and Industry
MP	Melting point
NAICS	North American Industry Classification System
NIH	National Institute of Health
NIOSH	National Institute for Occupational Safety and Health
NR	Not reported
OECD	Organisation for Economic Co-operation and Development
OH	Hydroxyl radical
OPPT	Office of Pollution Prevention and Toxics
OSHA	Occupational Safety and Health Administration
PEL	Permissible Exposure Limit
POTW	Publicly owned treatment works
PPE	Personal protective equipment
PPM	Parts per million
RCRA	Resource Conservation and Recovery Act
REL	Recommended Exposure Limit
RY	Reporting Year
SOP	Standard Operating Procedure
SMILES	Simplified Molecular-Input Line-Entry System
$T_{1/2}$	Half-life
TBD	To be determined
TG	Test guidance
TLV	Threshold Limit Value
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	Time weighted average
USGS	United States Geological Survey
VP	Vapor pressure
WS	Water solubility

1. Introduction

In section 6(b)(1)(B) of the Toxic Substances Control Act (TSCA), as amended, and in the U.S. Environmental Protection Agency's implementing regulations (40 CFR 702.3)[1], a high-priority substance is defined as a chemical substance that the U.S. Environmental Protection Agency (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 identified as relevant by EPA.

Before designating 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 to review the candidate chemical substance under its conditions of use against the following criteria and considerations:

- the hazard and exposure potential of the chemical substance;
- persistence and bioaccumulation;
- potentially exposed or susceptible subpopulations;
- storage near significant sources of drinking water;
- conditions of use or significant changes in the conditions of use of the chemical substance;
- the chemical substance's production volume or significant changes in production volume; and
- other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority.

This document presents the review of the candidate chemical substance against the criteria and considerations set forth in 40 CFR 702.9 for a may present risk finding. The information sources used are relevant to the criteria and considerations and consistent with the scientific standards of TSCA section 26(h), including, as appropriate, sources for hazard and exposure data listed in Appendices A and B of the *TSCA Work Plan Chemicals: Methods Document* (February 2012) (40 CFR 702.9(b)). Final designation of the chemical substance as a high-priority chemical substance would immediately initiate the risk evaluation process as described in the EPA's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (40 CFR 702).

1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2-benzopyran (HHCB) is one of the 40 chemical substances initiated for prioritization as referenced in the March 21, 2019 notice (84 FR 10491)[2]. EPA has determined that HHCB is a suitable candidate for the proposed designation as a high-priority chemical substance. The proposed designation is based on the results of the review against the aforementioned criteria and considerations as well as review of the reasonably available information on HHCB, including relevant information received from the public and other information as appropriate.

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[1] For all 40 CFR 702 citations, please refer to: https://www.govinfo.gov/content/pkg/CFR-2018-title40-vol33/xml/CFR-2018-title40-vol33-part702.xml and https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0654-0108

[2] https://www.federalregister.gov/documents/2019/03/21/2019-05404/initiation-of-prioritization-under-the-toxic-substances-control-act-tsca

EPA will take comment on this proposed designation for 90 days before finalizing its designation of HHCB. The docket number for providing comments on this chemical is EPA-HQ-OPPT-2018-0430 and is available at www.regulations.gov.

The information, analysis and basis used for the review of the chemical is organized as follows:

- *Section 1 (Introduction)*: This section explains the requirements of the amended TSCA and implementing regulations – including the criteria and considerations -- pertinent to the prioritization and designation of high-priority chemical substances.

- *Section 2 (Production volume or significant changes in production volume):* This section presents information and analysis on national aggregate production volume of the chemical substance.

- *Section 3 (Conditions of use or significant changes in conditions of use):* This section presents information and analysis regarding the chemical substance's conditions of use under TSCA.

- *Section 4 (Potentially exposed or susceptible subpopulations):* This section presents information and analysis regarding potentially exposed or susceptible subpopulations, including children, women of reproductive age, and workers, with respect to the chemical substance.

- *Section 5 (Persistence and bioaccumulation):* This section presents information and analysis regarding the physical and chemical properties of the chemical substance and the chemical's fate characteristics.

- *Section 6 (Storage near significant sources of drinking water):* This section presents information and analysis considered regarding the risk from the storage of the chemical substance near significant sources of drinking water.

- *Section 7 (Hazard potential):* This section presents the hazard information relevant to the chemical substance.

- *Section 8 (Exposure potential):* This section presents information and analysis regarding the exposures to the chemical substance.

- *Section 9 (Other risk-based criteria):* This section presents the extent to which EPA identified other risk-based criteria that are relevant to the designation of the chemical substance's priority.

- *Section 10 (Proposed designation)*: Based on the results of the review performed and the information and analysis presented, this section describes the basis used by EPA to support the proposed designation.

2. Production volume or significant changes in production volume

Approach

EPA considered current volume or significant changes in volume of the chemical substance using information reported by manufacturers (including importers). EPA assembled reported information for years 1986 through 2015 on the production volume for HHCB reported under the Inventory Update Reporting (IUR) rule and Chemical Data Reporting (CDR) rule[3].

Results and Discussion

The national aggregate production volume is presented in Table 1 as a range to protect individual site production volumes that are confidential business information (CBI).

Table 1. 1986–2015 National Aggregate Production Volume Data (Production Volume in Pounds)

Chemical ID	1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
HHCB (1222-05-5)	>500K to 1M	>1M to 10M	>1M to 10M	>1M to 10M	>1M to 10M	>1M to 10M	3,126,728	>1M to 10M	>1M to 10M	>1M to 10M	>1M to 10M

Note: K = thousand; M = million
Reference: U.S. EPA (2013) and U.S. EPA (2017)

The aggregate production volume of HHCB in 2015, as reported to EPA during the 2016 CDR reporting period, was between 1 and 10 million pounds. The exact aggregate production volume is available for one year, 2011, in which 3.1 million pounds of HHCB was produced or imported. Production volume of HHCB as reported to EPA has remained stable from 1986–2016 (Table 1). According to public comments received, HHCB is imported into the United States consistently at between 1 and 10 million pounds a year (EPA-HQ-OPPT-2018-0430-0004).

[3] Over time, the requirements for reporting frequency, production volume thresholds, and chemical substances under the Chemical Data Reporting (CDR) rule have changed. CDR was formerly known as the Inventory Update Rule (IUR). The first IUR collection occurred in 1986 and continued every four years through 2006. As part of two rulemakings in 2003 and 2005, EPA made a variety of changes to the IUR, including to change the reporting frequency to every five years to address burdens associated with new reporting requirements. Additional changes to reporting requirements were made in 2011, including to suspend and replace the 2011 submission period with a 2012 submission period, return to reporting every four years, and require the reporting of all years beginning with 2011 production volumes. The reporting of production volumes for all years was added because of the mounting evidence that many chemical substances, even larger production volume chemical substances, often experience wide fluctuations in production volume from year to year. In addition, also as part of the 2011 IUR Modifications final rule (76 FR 50816, Aug 16, 2011), EPA changed the name of the regulation from IUR to CDR to better reflect the distinction between this data collection (which includes exposure-related data) and the TSCA Inventory itself (which only involves chemical identification information).

3. Conditions of use or significant changes in conditions of use

Approach

EPA assembled information to determine conditions of use or significant changes in conditions of use of the chemical substance. TSCA section 3(4) defines, the term "conditions of use" to mean 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.

A key source of reasonably available information that EPA considered for determining the conditions of use for HHCB was submitted by manufacturers (including importers) under the 2012 and 2016 CDR reporting cycles. CDR requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the United States greater than 25,000 pounds per site, except if certain TSCA actions apply (in which case the reporting requirement is greater than 2,500 pounds per site). CDR includes information on the manufacturing, processing, and use of chemical substances. Based on the known manufacturing, processing and uses of this chemical substance, EPA assumes distribution in commerce. CDR may not provide information on other life-cycle phases such as distribution or chemical end-of-life after use in products (i.e., disposal). While EPA may be aware of additional uses, CDR submitters are not required to provide information on chemical uses that are not regulated under TSCA.

HHCB is not included on the TRI chemical list. For purposes of this proposed prioritization designation, EPA assumed end-of-life pathways that include releases to air, wastewater, and solid and liquid waste based on the conditions of use.

CDR and TRI Tables

Based on the publicly available[4] manufacturing information, industrial processing and use information, and consumer and commercial use information reported under CDR, EPA developed a list of conditions of use for the 2016 and 2012 reporting cycles (Tables 2 and 3, respectively).

Table 2. HHCB (1222-05-5) Categories and Subcategories of Conditions of Use (2016 CDR Reporting Cycle)

Life-Cycle Stage	Category	Subcategory	Reference
Manufacturing	Domestic manufacture/Import	CBI[5]	U.S. EPA (2019)
	Import	Import	U.S. EPA (2019)
Processing	Processing – incorporating into formulation, mixture, or reaction product	Odor agent in: - all other chemical product and preparation manufacturing;	U.S. EPA (2019)

[4] Some specific chemical uses reported by CDR submitters are confidential business information (CBI) under section 14 of TSCA. In these cases, EPA has indicated that the information is CBI.

[5] At this time, "CBI" indicates that a data element has been claimed CBI by the information submitter; it does not reflect the result of an EPA substantiation review.

Life-Cycle Stage	Category	Subcategory	Reference
		- miscellaneous manufacturing; - soap, cleaning compound, and toilet preparation manufacturing; - other: fragrance mixtures	
Processing	Processing – incorporating into articles	Odor agent in plastics material and resin manufacturing	U.S. EPA (2019)
Processing	Repackaging	Odor agent in all other chemical product and preparation manufacturing	U.S. EPA (2019)
Processing	Recycling	CBI[4]	U.S. EPA (2019)
Distribution in commerce[a,b]	Distribution in commerce	Distribution in commerce	
Industrial use	Surface active agents	Wholesale and retail trade	U.S. EPA (2019)
Commercial use	Air care products	Air care products	U.S. EPA (2019)
	Cleaning and furnishing care products	Cleaning and furnishing care products	U.S. EPA (2019)
	Laundry and dishwashing products	Laundry and dishwashing products	U.S. EPA (2019)
	Personal care products	Personal care products	U.S. EPA (2019)
	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere	U.S. EPA (2019)
	Other: aroma chemicals	Other: aroma chemicals	U.S. EPA (2019)
Consumer use	Air care products	Air care products	U.S. EPA (2019)
	Cleaning and furnishing care products	Cleaning and furnishing care products	U.S. EPA (2019)
	Laundry and dishwashing products	Laundry and dishwashing products	U.S. EPA (2019)
	Paper products	Paper products	U.S. EPA (2019)
	Personal care products	Personal care products	U.S. EPA (2019)
	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere	U.S. EPA (2019)
Consumer uses	Other: aroma chemicals	Other: aroma chemicals	U.S. EPA (2019)
	Non-TSCA use	Non-TSCA use	U.S. EPA (2019)
Disposal[a]	Disposal		

Life-Cycle Stage	Category	Subcategory	Reference
Note: CBI = confidential business information; TSCA = Toxic Substances Control Act [a] CDR includes information on the manufacturing, processing, and use of chemical substances. CDR may not provide information on other life-cycle phases such as distribution or chemical end-of-life after use in products (i.e., disposal). The table row is highlighted in gray to indicate that no information is provided for this life-cycle stage. **[b] EPA is particularly interested in information from the public on distribution in commerce.**			

Table 3. HHCB (1222-05-5) Categories and Subcategories of Conditions of Use (2012 CDR Reporting Cycle)

Life-Cycle Stage	Category	Subcategory	Reference
Manufacturing	Domestic Manufacture/Import	CBI[6]	U.S. EPA (2019)
	Import	Import	U.S. EPA (2019)
Processing	Processing – incorporating into formulation, mixture, or reaction product	Odor agent in: - all other chemical product and preparation manufacturing; - soap, cleaning compound, and toilet preparation manufacturing; - other: fragrance raw material	U.S. EPA (2019)
Processing	Processing – incorporating into articles	Odor agent in plastics material and resin manufacturing	U.S. EPA (2019)
Processing	Repackaging	Odor agent in all other chemical product and preparation manufacturing	U.S. EPA (2019)
Processing	Recycling	CBI[5]	U.S. EPA (2019)
Distribution in commerce[a,b]	Distribution in commerce		
Commercial use	Air care products	Air care products	U.S. EPA (2019)
	Cleaning and furnishing care products	Cleaning and furnishing care products	U.S. EPA (2019)
	Laundry and dishwashing products	Laundry and dishwashing products	U.S. EPA (2019)
	Personal care products	Personal care products	U.S. EPA (2019)
	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere	U.S. EPA (2019)

[6] At this time, "CBI" indicates that a data element has been claimed CBI by the information submitter; it does not reflect the result of an EPA substantiation review.

Life-Cycle Stage	Category	Subcategory	Reference
Consumer use	Air care products	Air care products	U.S. EPA (2019)
	Cleaning and furnishing care products	Cleaning and furnishing care products	U.S. EPA (2019)
	Laundry and dishwashing products	Laundry and dishwashing products	U.S. EPA (2019)
	Personal care products	Personal care products	U.S. EPA (2019)
	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere	U.S. EPA (2019)
	Non-TSCA use	Non-TSCA use	U.S. EPA (2019)
Disposal	Disposal		

Note: CBI = confidential business information; TSCA = Toxic Substances Control Act
[a] CDR includes information on the manufacturing, processing, and use of chemical substances. CDR may not provide information on other life-cycle phases such as distribution or chemical end-of-life after use in products (i.e., disposal). The table row is highlighted in gray to indicate that no information is provided for this life-cycle stage.
[b] EPA is particularly interested in information from the public on distribution in commerce.

CDR Summary and Additional Information on Conditions of Use

According to the 2016 CDR reports, HHCB was imported into the United States. However, due to CBI[7], EPA cannot disclose whether HHCB was manufactured in the United States. HHCB is processed in several ways: incorporated into formulation, mixture, or reaction products; incorporated into articles; and repackaged. Due to CBI[6], EPA cannot disclose whether HHCB is recycled. The functional use reported for HHCB is as odor agent that is used in several industrial sectors (e.g., miscellaneous manufacturing; soap, cleaning compound, and toilet preparation manufacturing; plastics material and resin manufacturing; and all other chemical product and preparation manufacturing).

The only industrial use reported in the 2016 CDR is as surface active agent for wholesale and retail trade. The 2016 CDR includes several reports of commercial and consumer uses of HHCB in air care products, cleaning and furnishing care products, laundry and dishwashing products, personal care products, plastic and rubber products, and as aroma chemicals. The consumer uses reported also include uses in paper products and non-TSCA uses. Consumer uses were also identified in additional databases, which are included in the Exposure Potential section (Section 8). Based on CDR reporting, the reported processing of HHCB in 2016 was similar to the reported processing in 2012.

According to public comments received, HHCB is manufactured outside the United States and nine sites import CDR-reportable quantities of HHCB. The only TSCA use is as fragrance ingredient in commercial and consumer products, and this use has not change significantly in

[7] At this time, "CBI" indicates that a data element has been claimed CBI by the information submitter; it does not reflect the result of an EPA substantiation review.

recent years (EPA-HQ-OPPT-2018-0430-0004). Another public comment provided information regarding the use of HHCB in consumer products, such as air fresheners, shampoos, and soaps, however, a complete list was not provided given the difficulty to search for ingredients in databases provided by the manufacturers (EPA-HQ-OPPT-2018-0430-0005). Similarly, another commenter indicated that HHCB is a fragrance commonly used in detergents and other consumer and personal care products (EPA-HQ-OPPT-2019-0131-0009). One other comment indicates that HHCB is found as an impurity in amounts less than 0.1 percent in paints, coatings, sealants, and adhesives (EPA-HQ-OPPT-2018-0430-0003).

Should the Agency decide to make a final decision to designate this chemical substance as a high-priority substance, further characterization of relevant TSCA conditions of use will be undertaken as part of the process of developing the scope of the risk evaluation.

4. Potentially exposed or susceptible subpopulations

Approach

In this review, EPA considered reasonably available information to identify potentially exposed or susceptible subpopulations, such as children, women of reproductive age, workers, consumers or the elderly. EPA analyzed processing and use information included on the CDR Form U that indicates whether the chemical substance is used in products and articles subject to TSCA and are intended for children. These data provide an indication about whether children or other susceptible subpopulation may be potentially exposed (e.g., workers, women of reproductive age). EPA also used human health hazard information to identify potentially exposed or susceptible subpopulations.

Results and Discussion

At this stage, EPA identified children, women of reproductive age, consumers and workers as subpopulations who may be potentially exposed or susceptible subpopulations for HHCB.

Children

EPA used data reported to the 2012 and 2016 CDR to identify uses in products and articles intended for children over time for HHCB. According to the 2016 CDR, one site reported use of HHCB in personal care products intended for children (Table 4). In the 2012 CDR, no uses in children's products were reported.

Existing assessments reviewed lacked discussion on the susceptibility of children to HHCB within children's products (U.S. EPA, 2014, U.S. EPA, 2008, EU, 2008). EPA also identified potential developmental hazards that would impact any stage of children's development. A public comment provided information regarding studies indicating the placental transfer of HHCB *in utero*. According to the comment, these studies indicate that infants and fetuses are vulnerable populations to consider with respect to HHCB exposure (EPA-HQ-OPPT-2018-0430-0005).

Table 4. Uses in Children's Products Information

Chemical	Year	Product Category (Product Concentration, Number of Workers)	Consumer or Commercial	Used in Products Intended for Children
HHCB (1222-05-5)	2012	Air care products (1% to <30% conc. by wt.; 50–499 workers)	Consumer and Commercial	No or NKRA
		Cleaning and furnishing care products (<1% to <30% conc. by wt.; 50–499 workers)	Consumer and Commercial	No or NKRA
		Laundry and dishwashing products (<1% to <30% conc. by wt.; 50–499 workers)	Consumer and Commercial	No or NKRA
		Personal care products (<1% to <30% conc. by wt.; 50–499 workers)	Consumer and Commercial	NKRA
		Plastic and rubber products not covered elsewhere (< 1% conc. by wt.; workers NKRA)	Consumer and Commercial	NKRA
		Non-TSCA use (1% to <30% conc. by wt.; workers NKRA)	Consumer	NKRA
	2016	Air care products (<1% to <60% conc. by wt.; <10–999 workers)	Consumer and Commercial	No or NKRA
		Cleaning and furnishing care products (<1% to <30% conc. by wt.; <10–999 workers)	Consumer and Commercial	No or NKRA
		Laundry and dishwashing products (<1% to <30% conc. by wt.; <10–499 workers)	Consumer and Commercial	No or NKRA
		Paper products (NKRA conc. by wt.; 100–499 workers)	Consumer	NKRA
		Personal care products (<1% to <30% conc. by wt.; 50–499 workers)	Consumer and Commercial	Yes or NKRA
		Plastic and rubber products not covered elsewhere (< 1% conc. by wt.; workers NKRA)	Consumer and Commercial	No
		Other: aroma chemicals (NKRA conc. by wt.; workers NKRA)	Consumer and Commercial	NKRA
		Non-TSCA use (1% to <30% conc. by wt.; workers NKRA)	Consumer	NKRA

TSCA = Toxic Substances Control Act; NKRA = not known or reasonably ascertainable
Reference: U.S. EPA (2019)

Women of reproductive age (e.g., pregnant women per TSCA statute)
EPA identified studies that observed developmental effects following exposure to HHCB (Section 7, Table 7). No reproductive hazards were identified. EPA considers women of reproductive age as a potentially exposed susceptible subpopulation. During the scoping and risk evaluation process, reproductive hazards will be considered again following a systematic search of the relevant scientific literature.

Consideration of women of reproductive age as a potentially exposed or susceptible subpopulation was also based on exposure because women of reproductive age are potential workers in the manufacturing, processing, distribution in commerce, use, or disposal of the chemical substance.

Workers
Please refer to the Exposure Potential section (Section 8) for a summary of potential occupational exposures, which EPA indicates that workers are potentially exposed or susceptible subpopulations based on greater exposure.

Consumers
Please refer to the Exposure Potential section (Section 8) for a summary of potential consumer exposures which EPA indicates that consumers are potentially exposed or susceptible subpopulations based on greater exposure.

5. Persistence and bioaccumulation

Approach
EPA reviewed reasonably available data, such as physical and chemical properties and environmental fate characteristics, to understand HHCB's persistence and bioaccumulation.

Physical and Chemical Properties and Environmental Fate Tables
Table 5 and Table Table 6 summarize the physical and chemical properties of HHCB, and environmental fate characteristics of HHCB, respectively.

Table 5. Physical and Chemical Properties of HHCB

Property or Endpoint	Value[a]	Reference
Molecular Formula	$C_{18}H_{26}O$	PhysProp Database (U.S. EPA, 2012b); HSDB (2007)
Molecular Weight	258.41	PhysProp Database (U.S. EPA, 2012b); HSDB (2007)
Physical State[b]	Liquid	OECD (2009); EU (2008)
Physical Form	Colorless crystals	HSDB (2007) citing O'Neil (2013)
Purity	Purity: ≥ 95% w/w (sum of isomers)	EU (2008)

Property or Endpoint	Value[a]	Reference
	Diluents typically added to HHCB include diethyl phthalate, benzyl benzoate, or isopropyl myristate	
Melting Point[b]	−5 ºC	PhysProp Database (U.S. EPA, 2012b)
	<−20 ºC at 101,325 Pa	EU (2008)
	(4S,7R) and (4R,7S) isomers 77–78 ºC (4R, 7R) and (4S, 7S) isomers 52–58 ºC	HSDB (2007) citing O'Neil (2013)
	57–58 ºC	HSDB (2007) citing O'Neil (2013)
Boiling Point	325°C	PhysProp Database (U.S. EPA, 2012b)
	318 ºC at 101,325 Pa	EU (2008)
	128 ºC at 0.8 mm Hg	HSDB (2007) citing O'Neil (2013)
Density/Specific gravity	1.0054 at 20 ºC/4 ºC	HSDB (2007) citing O'Neil (2013)
Vapor Pressure	5.45×10^{-4} mm Hg at ºC	HSDB (2007) citing Balk and Ford (1999)
	7.27×10^{-2} Pa at 25 ºC	OECD (2009); EU (2008)
Vapor Density	TBD	TBD
Water Solubility	1.75 mg/L at 25 ºC	HSDB (2007) citing Balk and Ford (1999)
	1.65–1.99 mg/L	EU (2008)
Log K_{OW}	5.9	EU (2008) citing Rudio (1993)
	5.3	OECD (2009); EU (2008) citing Artola-Garicanoa (2002)
Henry's Law Constant	1.32×10^{-4} atm-m^3/mol	Betterton and Hoffman (1988)
	3.60×10^{-4} atm-m^3/mol	EU (2008)
Flash Point	>100 ºC (closed cup)	IFF (2001)
Auto Flammability	Not a flammable liquid; it is a combustible liquid that can burn; no pyrophoric properties	IFF (2001)
Viscosity	12,914 mPa second	HSDB (2007) citing ECHA (2018)
Refractive Index	1.53 at 20 ºC	HSDB (2007) citing O'Neil (2013)
Dielectric Constant	TBD	TBD
Surface Tension	39.3 dyn/cm	EU (2008) citing IFF (2001)

[a]Measured unless otherwise noted

[b]HHCB is a mixture of various isomers that typically is a viscous liquid at room temperatures; the solid with higher melting points represent isolated isomers
TBD = to be determined, if reasonably available. **EPA is particularly interested in information from the public on these properties or endpoints.**

Table 6. Environmental Fate Characteristics of HHCB

Property or Endpoint	Value[a]	Reference
Direct Photodegradation	Direct photolysis is not expected to be an important fate process because HHCB does not contain chromophores that absorb at wavelengths >290 nm	HSDB (2007)
	Direct photolysis by sunlight and gas-phase reaction with ·OH radicals are considered to be the major degradation routes for HHCB in the atmosphere	OECD (2009)
Indirect Photodegradation	$t_{1/2}$ = 5 days (based on ·OH reaction rate constant of 2.6×10^{-11} cm^3/molecules·second 25 ºC and an ·OH concentration of 1.5×10^6 ·OH/cm^{-3})	OECD (2009)
Hydrolysis	Stable; HHCB is not expected to undergo hydrolysis in the environment due to its chemical structure, which lacks functional groups known to undergo hydrolysis under environmental conditions	HSDB (2007); OECD (2009)
Biodegradation	0%/28 days CO_2 evolution test (OECD test guideline 301 B) (aerobic water)	HSDB (2007); EU (2008)
	18%/200 days activated sludge; by-products identified were Galaxolide-lactone and Galaxolide hydroxy acid	HSDB (2007) citing Balk and Ford (1999)
Wastewater Treatment	92% total removal (0.76% by biodegradation, 91% by sludge and 0.14 by volatilization to air; estimated)[b]	U.S. EPA (2012b)
	91.5% removal activated sludge plant	EU (2008) citing Simonich et al. (2000)
Bioconcentration Factor	1,584 (whole fish, wet weight) bluegill sunfish (*Lepomis macrochirus*) OECD Test guideline 305E	HSDB (2007) citing Balk and Ford (1999)
	624 (fresh weight) 33,200 (lipid) zebrafish (*Brachydanio rerio*), OECD Test guideline 305E	EU (2008) citing Butte and Ewald (1999)
Bioaccumulation Factor	52,370 (crucian carp), 66,030 (common carp), 39,400 (silver carp)	Hu (2011)
Soil Organic Carbon:Water	4.87	EU (2008) citing MacGillivray (1996)
	3.6–3.9	EU (2008) citing Muller (2002)

Property or Endpoint	Value[a]	Reference
Partition Coefficient (Log K_{OC})	3.8	EU (2008) citing Artola-Garicanoa (2002)

[a]Measured unless otherwise noted
[b]EPI Suite™ physical property inputs: Log Kow = 5.90, BP = 325.00 ºC, MP = -5.00 ºC, VP = 0.000545 mm Hg, ·OH = hydroxyl radical, WS = 1.75 mg/L, BIOP = 10,000, BioA = 10,000 and BioS = 10,000, SMILES: O(CC(c(c1cc(c2C(C3C)(C)C)C3(C)C)c2)C)C1

Results and Discussion

HHCB, in a mixture of stereo-isomers, is a liquid at room temperature (with melting points from <−20 to −5 °C); however, purified isomers of HHCB are solids at room temperature with melting points of 52–78 °C. HHCB has moderate water solubility (1.75 mg/L). Given its measured Henry's Law constant (1.32×10^{-4} atm-m^3/mol) and vapor pressure (5.45×10^{-4} mm Hg), HHCB is expected to be moderately persistent in surface water and soil. In the air, HHCB may react with photochemically produced hydroxyl radicals at a rate corresponding to a half-life of 5 days. HHCB is not susceptible to direct photolysis because it does not absorb light at wavelengths >290 nm. Similarly, HHCB is not expected to hydrolyze due to a lack of hydrolyzable functional groups.

In aerobic aquatic environments, HHCB was not observed to be readily biodegradable, having only achieved 0 percent degradation over 28 days in an OECD 301B CO_2 evolution test. HHCB degraded 18 percent in activated sludge over 200 days, with HHCB-lactone and HHCB-hydroxy acid being the major by-products. HHCB is expected to persist in subsurface environments, groundwater, or enclosed pipes based on these data. HHCB has a bioconcentration factors of 1,584 in *Lepomis macrochirus* and 624 *Brachydanio rerio.* Additionally, bioaccumulation factors of 52,370, 66,030, and 39,400 were measured crucian carp, common carp, and silver carp, respectively. The measured bioaccumulation factor and bioconcentration factor values suggest that the potential for HHCB to bioaccumulate is high.

6. Storage near significant sources of drinking water

Approach

To support the proposed designation, EPA screened each chemical substance 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, specifically looking to identify certain types of existing regulations or protections for the proposed chemical substances. EPA considered the chemical substance's potential human health hazards, including to potentially exposed or susceptible subpopulations, by identifying 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 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). Regulation by one of these authorities is an indication that the substance is a potential health or environmental hazard which, if released near a significant source of drinking water, could present an unreasonable risk of injury to human health or the environment.

Results and Discussion

EPA has not established a Maximum Contaminant Level (MCL) or Maximum Contaminant Level Goal (MCLG) for HHCB under SDWA. HHCB is not considered a priority pollutant under the CWA. HHCB is also not subject to regulations under EPCRA, CERCLA, or CAA.

According to public comments received, HHCB is an extremely high-value industrial ingredient that is stored indoors, at manufacturing facilities, in structurally sound, non-leaking tanks and containers (EPA-HQ-OPPT-2018-0430-0004).

7. Hazard potential

Approach

EPA considered reasonably available information from peer-reviewed assessments and databases to identify potential human health and environmental hazards for HHCB (Tables 7 and Table 8, respectively).

Because there are few publicly available assessments for HHCB with cited environmental hazard data, EPA uses the infrastructure of ECOTOXicology knowledgebase (ECOTOX) to identify single chemical toxicity data for aquatic and terrestrial life (U.S. EPA, 2018a). It uses a comprehensive chemical-specific literature search of the open literature that is conducted according to the Standard Operating Procedures (SOPs)[8]. The environmental hazard information was populated in ECOTOX and is available to the public. In comparison to the approach used to survey human health hazard data, EPA also used a read-across approach to identify additional environmental hazard data for isomers of HHCB, if available, to fill in potential data gaps when there were no reported observed effects for specific taxa exposed to the HHCB (Table 8).

Potential Human Health and Environmental Hazard Tables and Additional Information on Hazards

EPA identified potential human health and environmental hazards based on a review of the reasonably available information for HHCB (Tables 7 and 8, respectively). In addition, EPA received comments with references to studies identifying potential human health and environmental concerns (EPA-HQ-OPPT-2018-0430-0005 and EPA-HQ-OPPT-2018-0430-0006).

[8] The ECOTOX SOPs can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4

Table 7. Potential Human Health Hazards Identified for HHCB

Human Health Hazards	Tested for Specific Effect	Effect Observed	Data Source
Acute Toxicity	X		U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Repeated Dose Toxicity	X		U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Genetic Toxicity	X		U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Reproductive Toxicity	X		U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Developmental Toxicity	X	X	U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Toxicokinetic	X		U.S. EPA (2014), EU (2008)
Irritation/Corrosion	X		U.S. EPA (2014), EU (2008)
Dermal Sensitization	X		U.S. EPA (2014), EU (2008)
Respiratory Sensitization			U.S. EPA (2014), EU (2008)
Carcinogenicity			U.S. EPA (2014), U.S. EPA (2008), EU (2008)
Immunotoxicity			
Neurotoxicity	X		U.S. EPA (2014), EU (2008)
Epidemiological Studies or Biomonitoring Studies	X		U.S. EPA (2014), EU (2008)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

Table 8. Potential Environmental Hazards Identified for HHCB

Media	Study Duration	Taxa Groups	High-Priority Chemical Candidate 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2 benzopyran (CASRN 1222-05-5)		Isomers of 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2 benzopyran (CASRN 1222-05-5) NONE		Data Sources
			Number of Studies	Observed Effects	Number of Studies	Observed Effects	
Aquatic	Acute exposure	Vegetation	1	X	-		Balk and Ford (1999)
		Invertebrate	6	X	-		Artola-Garicano et al. (2003); Chen et al. (2015); Gooding et al. (2006); Parolini et al. (2015); Wollenberger et al. (2003)
		Fish	12	X	-		Carlsson and Norrgren (2004); Fernandes et al. (2013); Fernandez et al. (2013); Ribalta and Sole (2014); Schnell et al. (2009); Yamauchi et al. (2008); Zhang et al. (2012)
		Non-Fish Vertebrates (i.e., amphibians, reptiles, mammals)	-		-		
	Chronic exposure	Vegetation	-		-		
		Invertebrate	6	X	-		Artola-Garicano et al. (2003), Balk and Ford (1999), Breitholtz et al. (2003), Parolini et al. (2015), Wollenberger et al. (2003)
		Fish	6	X	-		Balk and Ford (1999); Chen et al. (2012); Lefebvre et al. (2017); Van Dijk (1996); Zhang et al. (2012)
		Non-Fish Vertebrates (i.e., amphibians, reptiles, mammals)	2	X	-		Pablos et al. (2015)

Media	Study Duration	Taxa Groups	High-Priority Chemical Candidate 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2 benzopyran (CASRN 1222-05-5)		Isomers of 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2 benzopyran (CASRN 1222-05-5) NONE		Data Sources
			Number of Studies	Observed Effects	Number of Studies	Observed Effects	
Terrestrial	Acute exposure	Vegetation	-		-		
		Invertebrate	4	X	-		Chen et al. (2011); Liu et al. (2011); Liu et al. (2012); Mori et al. (2006)
		Vertebrates	-		-		
	Chronic exposure	Vegetation	3	X	-		Chen and Cai (2015); Chen et al. (2014); Wang et al. (2013)
		Invertebrate	4	X	-		Balk and Ford (1999); Chen et al. (2011); Liu et al. (2011)
		Vertebrates	-		-		

The dash indicates that no studies relevant for environmental hazard were identified during this initial review and thus the "Observed Effects" column is left blank.. The "X" in the "Observed Effects" column indicates when a hazard effect was reported by one or more of the referenced studies. The "N/A" in the "Observed Effects" column indicates when a hazard effect was not reported by one of the referenced studies' abstract (full reference review has not been conducted).

8. Exposure potential

Approach

EPA considered reasonably available information to identify potential environmental, worker/occupational, consumer, and general population exposures for HHCB.

Release potential for environmental and human health exposure

HHCB (CAS RN 1222-05-5) is not included on the TRI chemical list. EPA considered information from existing assessments (U.S. EPA 2014; EU, 2008), conditions of use reported in CDR and the physical and chemical properties to inform the release potential of HHCB.

Worker/Occupational and consumer exposure

EPA approach for assessing exposure potential was to review the physical and chemical properties, conditions of use reported in CDR, and information from existing assessments (U.S. EPA 2014; EU, 2008) for 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-Hexamethylcyclopenta[γ]-2-Benzopyran to inform occupational and consumer exposure potential. The results of this review is detailed in the following tables.

General population exposure

EPA identified environmental concentration and human biomonitoring data to inform HHCB's exposure potential to the general population (Table 10).

Results and Discussion

Release potential for environmental and human health exposure

In 2014, EPA noted that HHCB is produced solely outside of the United States (U.S. EPA, 2014). EPA anticipates releases of HHCB into the environment due to activities at import sites where HHCB is diluted and compounded onsite after import, disposal, or waste treatment activities, activities related to the blending of fragrance oils, as well as from the use of commercial and consumer products (EU, 2008). HHCB release into the environment from industrial sources would be dependent upon frequency of specific processes. Cleaning of HHCB mixing vessels in compounding operations that do not collect and incinerate remaining wash solution may result in discharge to waste water; this waste water may or may not be further treated, depending on the size of the processing plant and its capabilities, with the smaller facilities having less strictly controlled treatment of emissions (EU, 2008). The EU assessment noted HHCB releases to the environment through consumer product use would be primarily through detergents, rather than cosmetics, and release from disposal of residue in empty containers is expected to be minor (EU, 2008).

HHCB was reported in water, soil/sediment environmental concentrations, as well as in human blood. In 2014, EPA reported HHCB measurements in filtered and non-filtered drinking water, wastewater influent and effluent, wastewater sludge, municipal sewage treatment effluent streams, surface and groundwater located near wastewater discharge areas, bottom material from top bed deposits within bodies of water, downstream surface water sediment of streams and lakes, wastewater treatment biosolids subsequently disposed of through landfill/incineration or known to be used for agricultural land application, agricultural, and suburban soil (U.S. EPA, 2014). Measured concentrations within biota were also reported and included sampling of

aquatic organisms, aquatic mammals, birds, and higher trophic level aquatic organisms (U.S. EPA, 2014).

Research suggests moderate-range (regional) atmospheric transport of HHCB may occur; however, long-range transport is unlikely (U.S. EPA, 2014). HHCB is considered to be of low to moderate concern for bioaccumulation, with aquatic food-chain modeling indicating it is not subject to biomagnification (U.S. EPA, 2014, EU, 2008).

When chemical substances are used as reactants and as intermediates, the industrial releases may be a relatively low percentage of the production volume. Lower percentage releases occur when a high percentage of the chemical reacts without excess loss during its use as an intermediate. The actual percentages, quantities, and media of releases of the reported chemical associated with this processing or use are unknown.

When chemical substances are repackaged, the industrial releases may be a relatively low percentage of the production volume. Lower percentage releases occur when a high percentage of the chemical is repackaged without significant process losses during its repackaging. The actual percentages, quantities, and media of releases of the reported chemical associated with this processing or use are unknown.

When chemical substances have commercial or consumer use as cleaning products, the releases during end use may be a relatively high percentage of the production volume. Higher percentage releases occur when the product containing the chemical is used in a way that is often disposed to aqueous media. The actual percentage and quantity of release of the reported chemical associated with this category are unknown but could be high.

Worker/occupational exposure

Worker exposures 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, solubility, and water partition coefficient; local temperature and humidity; and exposure controls such as engineering controls, administrative controls, and the existence of a personal protective equipment (PPE) program.

HHCB does not have an Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) [9], a National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL)[10], or the Threshold Limit Value (TLV) set by American Conference of Governmental Industrial Hygienists (ACGIH).

HHCB has a vapor pressure of 5.45×10^{-4} mm Hg at 25 ºC/77 °F. EPA assumes that inhalation exposure is negligible when vapors are generated from liquids or solids with vapor pressures below 0.001 mm Hg at ambient room temperature conditions. Some handling activities of HHCB

[9] OSHA, 2009. Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs). https://www.osha.gov/dsg/annotated-pels/tablez-1.html

[10] NIOSH, 2005. NIOSH Pocket Guide to Chemical Hazards. https://www.cdc.gov/niosh/npg/npgdcas.html

may generate dust, particularly, when handled as a dry powder. Workers may be exposed to aerosolized particles.

Consumer exposure
According to EPA (2014), HHCB is present in a multitude of consumer products (Table 9). TSCA uses for HHCB include as an ingredient in detergents, fabric softeners, dishwashing detergents, and commercial and consumer general purpose cleaners. Non-TSCA uses include cosmetics and personal care products, which are regulated under the Federal Food, Drug, and Cosmetic Act (U.S. EPA 2014). The main route of exposure to consumers was assumed as dermal, with some inhalation exposures and no oral exposures (U.S. EPA 2014).

Table 9. Exposure Information for Consumers

Chemical Identity	Consumer Uses (List)
HHCB (1222-05-5)	Absorbent, adsorbent, air fresheners, air treatment, automotive care, automotive cleaner, candle, cleaner, detergent, detergent fragrance, dishwashing detergent, dry cleaning, floor cleaner, fluid property modulator, fragrance, furniture cleaner, paint, plastic, polish, propellant, soap, soap fragrance, textile cleaner, toilet cleaner

Reference: U.S. EPA 2014

The estimated exposure to HHCB on the skin from the use of a combination of all classes of consumer products on a daily basis was calculated by a European Union (EU) assessment to result in a "worst case situation" of 0.85 mg/kg body weight per day (EU, 2008). The inhalation exposure of consumers to HHCB in household cleaning products and air fresheners was estimated as lower, in total 0.0085 mg/kg body weight per day (EU, 2008). The 2008 EU assessment concluded there was no need for further information and/or testing and no need for risk reduction measures beyond those already being applied for consumers (EU, 2008).

General population exposure
HHCB was reported in water, and soil/sediment environmental concentrations, as well as in human blood.

Releases of HHCB from specific conditions of use, such as consumer and industrial use product processing through fragrance compounding and end-product formulation, disposal, or waste treatment activities may result in general population exposures due to ingestion of contaminated drinking water near industrial processing sites (U.S. EPA 2014, EU 2008). HHCB was reported in water, soil/sediment environmental concentrations, and in human blood. In the 2014 assessment EPA reported HHCB measured in filtered and non-filtered drinking water, wastewater influent and effluent, wastewater sludge, municipal sewage treatment effluent streams, surface and groundwater located near wastewater discharge areas, bottom material from top bed deposits within bodies of water, downstream surface water sediment of streams and lakes, wastewater treatment biosolids subsequently disposed of through landfill/incineration or known to be used for agricultural land application, agricultural and suburban soil (U.S. EPA 2014). Measured concentrations within biota were also reported in the 2014 assessment

describing sampling of aquatic organisms, aquatic mammals, birds, and higher trophic level aquatic organisms (U.S. EPA 2014). Research suggests moderate-range (regional) atmospheric transport of HHCB may occur, however long-range transport is unlikely (U.S. EPA 2014).

Table 10. Exposure Information for the Environment and General Population

Database Name	Environmental Concen. Data Present?[a]	Human Biomon. Data Present?[b]	Ecological Biomon. Data Present? [b]	Reference
California Air Resources Board	no	no	no	CARB (2005)
Comparative Toxicogenomics Database	no	no	no	MDI (2002)
EPA Ambient Monitoring Technology Information Center – Air Toxics Data	no	no	no	U.S. EPA (1990)
EPA Discharge Monitoring Report Data	no	no	no	U.S. EPA (2007)
EPA Unregulated Contaminant Monitoring Rule	no	no	no	U.S. EPA (1996)
FDA Total Diet Study	no	no	no	FDA (1991)
Great Lakes Environmental Database	no	no	no	U.S. EPA (2018b)
Information Platform for Chemical Monitoring Data	no	no	no	EC (2018)
International Council for the Exploration of the Sea	no	no	no	ICES (2018)
OECD Monitoring Database	no	yes	no	OECD (2018)
Targeted National Sewage Sludge Survey	no	no	no	U.S. EPA (2006b)
The National Health and Nutrition Examination Survey	no	no	no	CDC (2013)
USGS Monitoring Data –National Water Quality Monitoring Council	yes	no	no	USGS (1991a)
USGS Monitoring Data –National Water Quality Monitoring Council, Air	no	no	no	USGS (1991b)
USGS Monitoring Data –National Water Quality Monitoring Council, Ground Water	yes	no	no	USGS (1991c)
USGS Monitoring Data –National Water Quality Monitoring Council, Sediment	yes	no	no	USGS (1991d)
USGS Monitoring Data –National Water Quality Monitoring Council, Soil	yes	no	no	USGS (1991e)
USGS Monitoring Data –National Water Quality Monitoring Council, Surface Water	yes	no	no	USGS (1991f)
USGS Monitoring Data –National Water Quality Monitoring Council, Tissue	no	no	no	USGS (1991g)

[a] Concen.= concentration
[b] Biomon.= biomonitoring

Human exposure through ingestion of water and food including fish, root crops, and mother's milk was noted in the 2014 assessments as the main route of exposure to humans, as exposure by the inhalation route to the general population was considered to be negligible (U.S. EPA 2014). A EU assessment concluded there was no need for further information and/or testing and no need for risk reduction measures beyond those already applied for the general population exposed via the environment (EU, 2008).

9. Other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority

EPA did not identify other risk-based criteria relevant to the designation of the chemical substance's priority.

10. Proposed designation and Rationale

Proposed designation: High-priority substance

Rationale: EPA identified and analyzed reasonably available information for exposure and hazard and is proposing to find that HHCB may present an unreasonable risk of injury to health and/or the environment, including potentially exposed or susceptible subpopulations, (e.g., workers, consumers, women of reproductive age, children). This is based on the potential hazard and potential exposure of HCCB under the conditions of use described in this document to support the prioritization designation. Specifically, EPA expects that the manufacturing, processing, distribution, use and disposal of HHCB may result in presence of the chemical in surface water and groundwater, ingestion of the chemical in drinking water, exposure to workers, exposure to consumers and exposure to the general population, including exposure to children. In addition, EPA identified potential environmental (e.g., aquatic toxicity, terrestrial toxicity) and human health hazards (e.g., developmental toxicity).

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Note: All hyperlinked in-text citations are also listed below

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