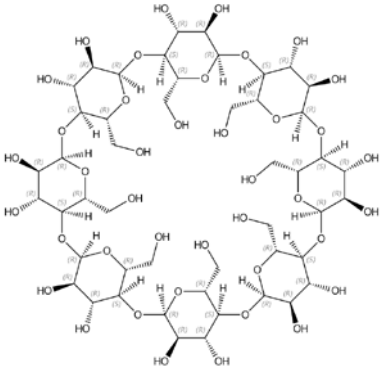
Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Group Name: Cyclic polysaccharides and their ether and ester derivatives

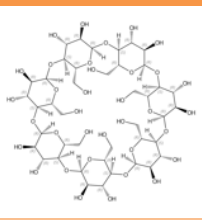
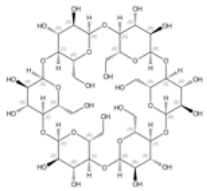
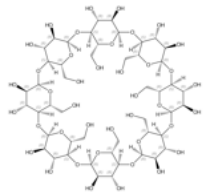
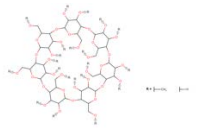
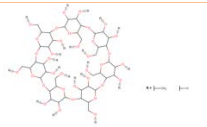
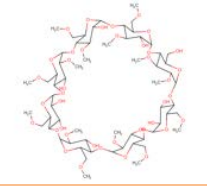
General structure: -



Revision history

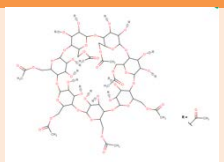
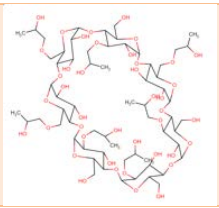
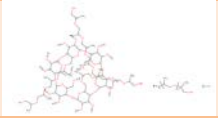
Version	*Date*	*Description*
1.0	28 June 2024	

Substances within this group:

EC / List no	CAS no	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
231-493-2	7585-39-9	Cycloheptapentylose, beta-cyclodextrin		Full, 100-1000
233-007-4	10016-20-3	Cyclohexapentylose, alpha-cyclodextrin		Full, not (publicly) available
241-482-4	17465-86-0	Cyclooctapentylose, gamma-cyclodextrin		Full, not (publicly) available
411-120-1[2]	-	β-cyclodextrine methyl ethers		NONS
603-270-3[2]	128446-36-6	Methyl-beta-cyclodextrin A.I.		C&L notification
418-710-8	-	γ-cyclodextrine methyl esters		Not registered

[1] The total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances

[2] When a dossier is submitted without EC/List number, REACH-IT automatically assigns a List number to the dossier. Sometimes, due to IT technical limitations, duplicate List numbers are created. In this group, the following are considered to be duplicate entries: EC/List no 603-270-3 and 411-120-1. In general, EC numbers take precedence over List numbers.

EC / List no	CAS no	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
418-780-1	-	ß-Cyclodextrin, acetyl		Full, not (publicly) available
418-850-1	-	α-cyclodextrine methyl ethers		Not registered
420-920-1	128446-35-5	2-Hydroxypropyl-β-cyclodextrine ethers		Full, 100-1000
430-870-0	-	GAMMA W8 HP		NONS
Substance A	-	No public or meaningful name is available		Not registered
443-280-3	-	ß-CDX-DERIVAT		Not registered
Substance B	-	No public or meaningful name is available		Full, not (publicly) available
Substance C	-	No public or meaningful name is available		NONS
619-816-9	128446-33-3	α-Cyclodextrin-2-hydroxypropylether		Full, not (publicly) available

This table contains also group members that are only notified under the CLP Regulation, however, the list is not necessarily exhaustive.

Contents

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The author does not accept any liability with regard to the use that may be made of the information contained in this document. Usage of the information remains under the sole responsibility of the user. Statements made or information contained in the document are without prejudice to any further regulatory work that ECHA, the Member States or other regulatory agencies may initiate at a later stage. Assessments of regulatory needs and their conclusions are compiled on the basis of available information and may change in light of newly available information or further assessment.

Foreword

The assessment of regulatory needs of a group of substances is an iterative, informal process to help authorities consider the most appropriate way to address an identified concern for a group of substances or a single substance and decide whether further regulatory risk management activities are necessary.

The grouping is mainly based on structural similarity and associations made by the registrants between substances through read-across and category approaches as well as category associations from external sources (e.g. OECD categories)[3]. These methods are different from grouping as defined in Section 1.5 of Annex XI to REACH because the scope and intended use of ECHA's grouping is different. Thus, in this context, grouping does not aim to validate read-across and category approaches according to the Annex XI requirements but rather to support a faster and more consistent approach for regulating chemicals and avoid regrettable substitution.

The focus of the assessment is largely based on information available in the registration dossiers and on properties requiring regulatory risk management action at EU level[4]. The information reported on uses is from the registration dossiers (IUCLID) and is used as a proxy for assessing how widespread uses are and whether potential for exposure to humans and releases to the environment can be expected. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

The outcome of these assessments are proposals for immediate (the first action) and subsequent regulatory action(s), including the foreseen ultimate regulatory action (last foreseen regulatory action) to address the identified concern(s) in case the potential hazards are confirmed. For example, further data generation through compliance check is suggested as a first action, to confirm the identified hazard.

Where hazards are confirmed, regulatory risk management actions could be considered for the whole group, for a subgroup or for individual substances within the group. The robustness of the group depends on the stage of assessment and the level of certainty this stage requires. For example, the needs for grouping under restriction may differ from the needs for grouping for the purpose of harmonised classification. Group membership is reconsidered accordingly throughout the iterative assessment of regulatory needs, for example, after further information is generated and the hazard has been clarified or when new insights on uses and risks are available.

The assessment of regulatory needs in itself does not represent a regulatory action, but rather a preparatory step to consider further possible regulatory actions at the level of individual substances or groups/subgroups of substances.

[3] Working with Groups - ECHA (europa.eu)

[4] Regarding hazard properties the focus is for instance on CMR (carcinogenic, mutagenic and/or toxic to reproduction), sensitiser, ED (endocrine disruptor), PBT/vPvB or equivalent (e.g. substances being persistent, mobile and toxic), aquatic toxicity hazard endpoints and therefore only those are reflected in the report. This does not mean that the substances do not have other known or potential hazards. In some specific cases, ECHA may consider additional hazards (e.g. neurotoxicity, STOT RE).

Publication of ARNs makes it easier for companies to follow the latest status of their substances of interest, anticipate potential regulatory actions and make strategic choices in their chemicals portfolio.

For more information on assessments of regulatory needs please consult ECHA's website[5].

[5] https://echa.europa.eu/understanding-assessment-regulatory-needs

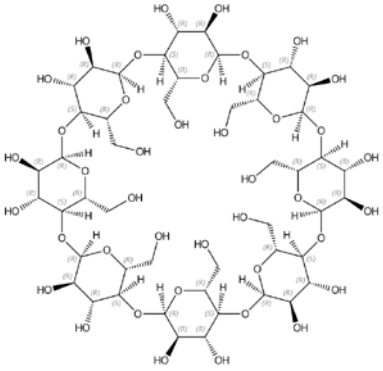
Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic / very persistent and very bioaccumulative
PMT/vPvM	Persistent, mobile, and toxic / very persistent and very mobile
RDT	Repeated dose toxicity
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SEv	Substance evaluation
STOT RE	Specific target organ toxicity, repeated exposure
SVHC	Substance of very high concern
TPE	Testing proposal evaluation
UVCB	Substances of unknown or variable composition, complex reaction products or biological materials

1 Overview of the group

Explanations on the scope of this assessment is available in the foreword to this document. Please read it carefully before going through the report.

ECHA has grouped together structurally similar substances based on the presence of a common cyclic polysaccharide core shown in the figure below.



The group consists of substances having different number of saccharide units which alcohol functionalities may be available as such or may have been derivatised as an ether or ester. The degree of derivatisation may be different from one substance to the other. The group includes mono-constituent substances and UVCB substances based on the variable position of the substituents on the saccharide units in the ring.

There are 15 substances in the group of which seven with full registrations. There are no harmonised classifications or classifications in registrations for the substances.

Based on information reported in the REACH registration dossiers, many of the substances are used by industrial and professional workers and consumers in washing and cleaning products, cosmetics and fragrances. Also use in food additives, pharmaceuticals, adhesives and sealants, coatings and paints and biocidal products is reported. There is potential for exposure for workers and consumers and release to the environment. Article service life in paper and board treatment products is explicitly reported for one substance, however, some of the substances may end up in coated articles including textiles where release cannot be excluded.

2 Conclusions and proposed actions

The conclusions and actions proposed in the table below are based mainly on the REACH and CLP information available at the time of the assessment by ECHA. The conclusions are preliminary suggestions from a screening-level assessment done by ECHA with the aim to propose the next steps for further work (e.g., strengthening of the hazard conclusions, clarification of the uses and/or potential for exposure). The main source of information is the registration dossiers. Relevant public assessments may also be considered. When new information (e.g., on hazards through evaluation processes, or on uses) will become available, the document may be updated, and conclusions and actions revisited.

Table 1: Conclusions and proposed actions

EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
411-120-1 **418-780-1** **420-920-1** **430-870-0** **619-816-9** **Substance B**	No hazard or unlikely hazard	Known or potential hazard for vPvM	Industrial, professional and consumer use (and formulation) in washing and cleaning products, air care products, plant protection/ biocidal products, hydraulic fluids, pharmaceutical, coatings and paints. Potential for exposure for workers and consumers and releases into environment (water compartment)	**First step:** CCH for EC 420-920-1 **Potential next steps (if hazard confirmed after data generation):** CLH <u>Justification</u>: Since there is high release potential to surface waters, soil and ground water due to the use in washing & cleaning products, CLH is proposed to confirm the potential PMT/vPvM hazards. However, for the time being no conclusions are drawn regarding possible additional EU regulatory risk management until more clarity is available on how to regulate PMT/vPvM
418-710-8 **418-850-1** **443-280-3**			Not registered or C&L notification	

EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
603-270-3 **Substance A**				substances.
231-493-2 **233-007-4** **241-482-4** **Substance C**	No hazard or unlikely hazard	No hazard or unlikely hazard	Industrial, professional and consumer uses in many different applications: washing and cleaning products, perfumes and fragrances, biocidal products, cosmetics and personal care products, adhesives and sealants, coatings and paints, food and feed additive (ECs 233-007-4, 241-482-4) etc. Potential for exposure for workers and consumers and release to the environment.	**No action** **Currently no need for EU RRM** Justification: Overall, no or unlikely hazard that would lead to concern for the reported uses.

3 Justification for the (no) need for regulatory risk management action at EU level (if hazards confirmed)

Suggested regulatory risk management action for substances EC/List 411-120-1, 418-710-8, 418-780-1, 418-850-1, 420-920-1, 430-870-0, Substance A, 443-280-3, Substance B, 603-270-3 and 619-816-9 if vPvM hazard is confirmed

Cyclodextrins have low oral bioavailabity which limits their potential for systemic toxicity.

β-Cyclodextrin is approved as food additive[6]. According to the EFSA Opinion "β-Cyclodextrin is poorly absorbed following oral administration in animals and humans. It is hydrolysed to maltose and glucose by the gut microflora and endogenous amylases in the colon; consequently, β-cyclodextrin levels in tissues and serum are low (< 1%) ;[…] Short-term and subchronic toxicity studies were available in rats and dogs. In rats, the main reported effect was an adaptive enlargement of the caecum, resulting from consumption of poorly digestible carbohydrates. From a 6-month study in rats, a no observed adverse effect levels (NOAEL) of 600 mg/kg bw per day was identified and from a 52-week dogs study, the NOAEL was 466 and 476 mg/kg bw per day in males and females, respectively." The Panel considered that there was no indication for genotoxicity of β-cyclodextrin. From a chronic toxicity study in rats, a NOAEL of 654 and 864 mg/kg bw per day in males and females, respectively, was identified. Carcinogenicity studies in mice and rats were available and no evidence for carcinogenicity was found.

Available information from the registration dossiers is in line with the conclusion of EFSA as unlikely CMR/ED, skin sensitisation and STOT RE. In vivo skin sensitisation studies as well as in vitro and in vivo mutagenicity studies were negative. Repeated dose toxicity and reproductive toxicity studies (one two generation reproductive toxicity study and two PNDTs) did not show any effects up to the limit dose tested. No effects in endocrine related organs have been observed in the systemic toxicity studies available.

The findings are extrapolated to substances where no information is available based on common functional moiety (cyclodextrin) and taking into account low bioavailability potential.

Based on ECHA's screening of currently available information there is a potential for P/vP hazard for eleven substances in the group as they are not readily biodegradable, i.e. degrade <60/70% in an OECD 301 test or they are extrapolated to be not readily biodegradable based on structural similarity to not readily biodegradable substances in the group. These substances are potentially mobile (M/vM) as the log Koc is less than 3 or they are extrapolated to be potentially M/vM based on structural similarity to other potentially not M/vM substances in the group.

Since there is high release potential to surface waters, soil and ground water due to the use in washing and cleaning products for some of the substances, data generation is proposed to clarify the potential persistency and mobility of the substances.

The first step of the regulatory risk management should the hazard exist, is the

[6] https://www.efsa.europa.eu/en/efsajournal/pub/4628

confirmation of hazard via harmonised classification (CLH) as vPvM hazard for the substances. When preparing the proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for the group of substances, to submit them individually or jointly.

Currently, CCH is proposed to be opened for EC 420-920-1. Two other substances, i.e. EC/List 418-780-1 and 619-816-9 have also uses reported in washing and cleaning products. Substances EC/List 411-120-1, 418-710-8, 418-850-1, 430-870-0, Substance A, 443-280-3 and 603-816-9 have limited uses and if the vPvM hazard for the group is confirmed, they are suggested for regulatory risk management action to avoid substitution.

For the time being no conclusions are drawn regarding possible additional EU regulatory risk management until more clarity is available on how to regulate PMT/vPvM substances.

Currently no need to suggest (further) regulatory risk management actions for substances EC 231-493-2, 233-007-4, 241-482-4, Substance C

Based on currently available information, hazards are considered unlikely for all four substances and there is no need for (further) EU regulatory risk management for the substances. The substances are used by workers and consumers in many different applications e.g. washing and cleaning products, perfumes and fragrances, biocidal products, cosmetics and personal care products, adhesives and sealants, coatings and paints, food and feed additive.

The use of substances ECs 231-493-2 and 233-007-4 as additive or polymer production aid are authorised in food contact materials.

Based on ECHA's screening of currently available hazard information for skin sensitisation, STOT RE, genotoxicity, carcinogenicity, reproductive toxicity and ED hazards are considered unlikely for all substances in the group (as indicated above).

Similarly, based on screening of currently available hazard information all members in this group are unlikely to have PBT/vPvB/PMT properties because they are all expected to have low potency for bioaccumulation and are unlikely to meet the T criteria for HH and ENV based on currently available information as ~~. In addition,~~ there is no indication of high toxicity to the environment or health in the available data for any of the substances. ~~and as a result, it is unlikely that any of them meet the T criteria under CLP or REACH~~. Also, the currently known aquatic toxicity of the substances in the group is low and as a result, none of the substances has harmonised or self-classification for environmental hazards. No relevant information is available on their potential endocrine disruption (ED) potential for the environment and there is no indication of ED potency in the available health data. In conclusion, all substances in the group are considered unlikely ED for the environment.

Annex 1: Overview of classifications

Data extracted on 30 October 2023.

There are no harmonised classifications or classifications in registrations for the substances.

Annex 2: Overview of uses based on information available in registration dossiers

Data extracted on 30 October 2023.

EC number	231-493-2	233-007-4	241-482-4	418-780-1	420-920-1	Substance B	619-816-9
PC 20: ph-regulators, flocculants, precipitants, neutralisation agents	I	F	F				
PC 2: Adsorbents		F, I	F, I				
PC 12: Fertilisers	I						
PC 27: Plant protection products		F, I	F, I	**P**			
PC 35: Washing and cleaning products	F, I, **P**, **C**	F, I, **P**, **C**	F, I, **P**, **C**	F, I	F, **C**		F, I, **P**
PC 8: Biocidal products (e.g. disinfectants, pest control)	**P**	F, I, **P**	F, I, **P**	**P**			F, **P**, **C**
PC 28: Perfumes, fragrances	F, I, **C**	F, I, **C**	F, I, **C**				
PC 3: Air care products	I, **P**			I	F, **C**		
PC 39: Cosmetics, personal care products	F, I, **P**, **C**	F, **P**, **C**	F, **P**, **C**				
PC 29: Pharmaceuticals	F, I	F, I	F, I		I	I	
PC 31: Polishes and wax blends		F	F				

EC number	231-493-2	233-007-4	241-482-4	418-780-1	420-920-1	Substance B	619-816-9
PC 24: Lubricants, greases, release products	F, I						
PC 25: Metal working fluids	I						
PC 17: Hydraulic fluids				I			
PC 32: Polymer preparations and compounds						F, I	
PC 1: Adhesives, sealants	**P**, **C**	F, I, **P**, **C**	F, I, **P**, **C**				
PC 9a: Coatings and paints, thinners, paint removes	F, I, **P**, **C**	F, I, **P**, **C**	F, I, **P**, **C**	F			F, I, **P**, **C**
PC 18: Ink and toners		F, I	F, I				
PC 26: Paper and board treatment products	I, **C**, **A**	F, I	F, I				
PC 34: Textile dyes, and impregnating products	I	F	F				
PC 21: Laboratory chemicals	F, I, **P**	F, I, **P**	F, I, **P**	F, **P**		I	F
PC 19: Intermediate	I	I	I				
PC x1: Food and feed additives		F	F				

F: formulation, I: industrial use, P: professional use, C: consumer use, A: article service life; P, C and A are highlighted in red to indicate widespread use with potential for exposure/release

Annex 3: Overview of completed or ongoing regulatory risk management activities

Data extracted on 13 November 2023.

EC / List No	RMOA, ARN	Authorisation		Restriction*	CLH	Actions not under REACH / CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
231-493-2						Food contact material
233-007-4						Food contact material

*Some of the broad restriction entries in the Annex XVII of REACH are not represented in the overview, e.g. when the scope of the restriction is defined by its classification or the substance identification is broad (e.g. entries 3, 28-30, 40 and 75).

There are no relevant completed or ongoing regulatory risk management activities for the other substances.