Assessment of regulatory needs

Authority: ECHA

Date: 27 September 2021

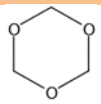
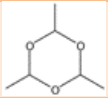
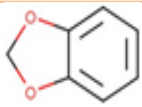
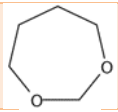
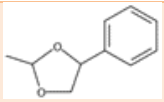
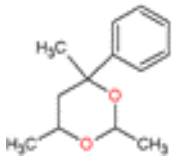
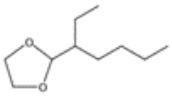
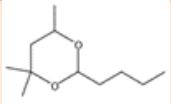
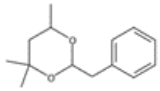
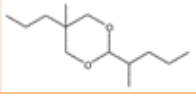
Group Name: Cyclic acetals from aldehydes

General structure: -

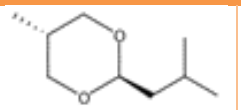
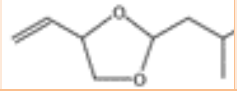
Revision history

Version	*Date*	*Description*
1.0	27 September 2021	

Substances within this group:

EC number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y)[1]
Subgroup 1: Cyclic acetals from formaldehyde and acetaldehyde				
203-812-5	**110-88-3**	1,3,5-trioxane		Full, >1000
204-639-8	**123-63-7**	2,4,6-trimethyl-1,3,5-trioxane		OSII or TII
205-992-0	**274-09-9**	1,3-benzodioxolane		OSII or TII
208-015-6	**505-65-7**	1,3-dioxepane		Full, not (publicly) available
211-463-5	**646-06-0**	1,3-dioxolane		Full, >1000
251-752-3	**33941-99-0**	2-methyl-4-phenyl-1,3-dioxolane		Full, not (publicly) available
945-924-3		Reaction mass of 2,4,6-trimethyl-4-phenyl-1,3-dioxane isomer 1 and 2,4,6-trimethyl-4-phenyl-1,3-dioxane isomer 2		Full, not (publicly) available
Subgroup 2: Cyclic acetals from other aldehydes				
224-436-8	**4359-47-1**	2-(1-ethylpentyl)-1,3-dioxolane		Full, not (publicly) available
259-210-8	**54546-26-8**	2-butyl-4,4,6-trimethyl-1,3-dioxane		Full, not (publicly) available
266-795-3	**67633-94-7**	2-benzyl-4,4,6-trimethyl-1,3-dioxane		Full, not (publicly) available
279-482-1	**80480-24-6**	5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane		Full, not (publicly) available

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

EC number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y)[1]
426-130-1	**166301-21-9**	A mixture of: cis-2-isobutyl-5-methyl 1,3-dioxane; trans-2-isobutyl-5-methyl 1,3-dioxane		Full, not (publicly) available
815-031-2	**1411949-02-4**	2-isobutyl-4-vinyl-1,3-dioxolane		Full, not (publicly) available

This table contains also group members that are only notified under the CLP Regulation. However, the list is currently non-exhaustive. Should further regulatory risk management action on one or more substances in the group be considered, ECHA will make an additional search for related C&L notified substances to be included in the group and develop an assessment of regulatory needs for them.

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. Assessment 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 purpose of the assessment of regulatory needs of a group of substances is to help authorities conclude on the most appropriate way to address the identified concerns for a group of substances or a single substance, i.e. the combination of the regulatory risk management instruments to be used and any intermediate steps, such as data generation, needed to initiate and introduce these regulatory measures.

An assessment of regulatory needs can conclude that regulatory risk management at EU level is required for a (group of) substance(s) (e.g. harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. While the assessment is done for a group of substances, the (no) need for regulatory action can be identified for the whole group, a subgroup or for single substance(s).

The assessment of regulatory needs is an important step under ECHA's Integrated Regulatory Strategy. However, it is not part of the formal processes defined in the legislation but aims to support them.

The assessment of regulatory needs can be applied to any group of substances or single substance, i.e., any type of hazards or uses and regardless of the previous regulatory history or lack of such. It can be done based on different level of information. A Member State or ECHA can carry out this case-by-case analysis. The starting point is available information in the REACH registrations and any other REACH and CLP information. However, more extensive set of information can be available, e.g. assessment done under REACH/CLP or other EU legislation, or can be generated in some cases (e.g. further hazard information under dossier evaluation). Uncertainties associated to the level of information used should be reflected in the documentation. It will be revisited when necessary. For example, after further information is generated and the hazard has been clarified or when new insights on uses are available. It can be revisited by the same or another authority.

The responsibility for the content of this assessment rests with the authority that developed it. It is possible that other authorities do not have the same view and may develop further assessment of regulatory needs. The assessment of regulatory needs does not yet initiate any regulatory process but any authority can consequently do so and should indicate this by appropriate means, such as the Registry of Intentions.

For more information on Assessment of regulatory needs please consult ECHA's website.[2]

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

Glossary

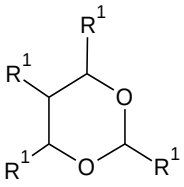
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
CSS	Chemicals Strategy for Sustainability
DEv	Dossier evaluation
ED	Endocrine disruptor
EOGRTS	Extended one-generation reproductive toxicity study
NONS	Notified new substances
OEL	Occupational exposure limit
OSH	Occupational safety and health
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic/very persistent and very bioaccumulative
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SCC	Strictly controlled conditions
SEv	Substance evaluation
SID	Substance identity
STOT RE	Specific target organ toxicity - repeat exposure
SVHC	Substance of very high concern

1 Overview of the group

ECHA has grouped together structurally similar substances based on the presence of the cyclic acetal moiety shown in the figure below.

The group contains 13 registered substances (10 full registrations, 1 NONS, 2 OSII or TII) and consists of mono- and multi-constituent substances. The main chemical feature of the group is more than one cyclic ether functionality with other varied structures e.g. alkyl chain or aromatic ring. The main type of chemical structure of these substances is the ether functionality.

Generic structure of the group members:



R^1: H, Me, Alkyl, Aryl,
The ring can be 5-, 6- or 7-membered and can contain 3 oxygen atoms as well.

Two subgroups were defined: (1) cyclic acetals from formaldehyde and acetaldehyde and (2) cyclic acetals from other aldehydes. In both subgroups there are quite a lot of differences in the chemical structures (e.g. number of atoms in ether ring, presence of aromatic ring, number, position and nature of substituents) however there are also substances that are structurally similar.

For one substance in the group (EC 211-463-5) there is an ongoing substance evaluation (studies clarifying skin irritation and serious eye damage have been requested), an intention from Germany for regulatory management option analysis (RMOA) and a harmonised classification proposal submitted by industry proposing to add Repr. 1B and Eye Irrit. 2 to the existing harmonised classification as Flam. Liq. 2.

Note on the scope of ECHA's assessment of regulatory needs

Regarding hazards, the focus of ECHA's assessment is 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 table in section 3. This does not mean that the substances do not have other known or potential hazards. In some specific cases, where ECHA identifies a need for regulatory risk management action at EU level for other hazards (e.g. neurotoxicity, STOT RE), such additional hazards may be addressed in the assessment. An overview of classification is presented in Annex 1.

On the exposure side, ECHA is mainly using the information on uses reported in the registration dossiers (IUCLID) as a proxy for assessing the potential for exposure to humans and releases to the environment. The potential for release / exposure is generally considered high for "widespread" uses, i.e. professional and consumer uses and uses in articles. For these uses, normally happening at many places, the expected level of control is *à priori* considered limited. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

Based on information reported in the REACH registration dossiers, most substances are used as a fragrance/odour agent in a variety of applications including washing and cleaning products, polishes and wax blends, cosmetics. The substances are used at industrial sites (including the formulation stage), by professional workers and consumers. High exposure potential for professional workers and consumers as well as high potential for releases to the environment cannot be excluded.

Two substances (EC 203-812-5 and 208-015-6) are used only as monomer/intermediate in polymer production by industrial workers. Even though there may be potential for releases to the environment and exposure for workers it is generically assumed that these are properly controlled in industrial settings.

Many substances in the group have been registered as intermediates where use under strictly controlled conditions (SCC) has been reported by the registrants.

2 Justification for the need for regulatory risk management action at EU level

Based on currently available information, there is a need for (further) EU regulatory risk management – restriction combined with authorisation for Repr. 1 B hazard due to the potential for release/ exposure of the substance 1,3-dioxolane (EC 211-463-5).

Substance EC 211-463-5 is self-classified for Repr. 1B by the lead registrant, fulfils the screening criteria for being P/vP and is expected to be mobile in the environment. The substance is used as monomer/intermediate in polymer production and as solvent in many applications (laboratories, washing and cleaning products, coatings, lubricants and metal working fluids/rolling oils) and therefore there is a high potential for exposure for both workers and consumers as well as high potential for releases to the environment.

The results from a pending extended one-generation reproductive toxicity study (EOGRTS) and an ongoing substance evaluation (SEv) will give clarification on the hazard. Furthermore, compliance check (CCH) will be initiated in order to clarify the persistency potential.

The first step of the regulatory risk management (RRM) action proposed, should the hazard exist, is the confirmation of hazard via harmonised classification (CLH[3]) as Repr. 1B.

CLH i) will trigger company level risk management measures (RMM) under the occupational safety and health (OSH) legislation for workers, ii) is needed or highly recommended for further regulatory processes under REACH and iii) is a prerequisite to restrict the presence of the substances in consumer mixtures, by means of the restriction entry 30 of REACH Annex XVII.

CLH will also support regulatory action under other regulations. For instance, in this specific case harmonised classification as CMR cat. 1 will trigger regulatory action under the Cosmetic products regulation (EC) No 1223/2009 for uses as fragrance, since CMR cat. 1 are restricted by this regulation.

[3] A CLH proposal has already been submitted by Industry, however, it has been suspended while the submitter awaits the results of the ongoing CCH (which will take several years). Consequently, in order not to delay regulatory action, CLH is still proposed and would be shared with MS in case there would be interest from their side to progress it further.

Reported use descriptors (e.g. rolling, brushing, spraying) suggest that there is high potential for exposure, particularly via dermal absorption and inhalation for both industrial and professional workers.

Professional use is typically widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with typically frequent exposures with a long duration. In addition, professional users may be self-employed and therefore not fully covered by the OSH legislation. Consumers may be co-exposed to the substances used by professionals. Therefore, a restriction of the substance as such or in mixtures (concentration limit in mixtures) used by professionals is suggested after CLH. If after generation of data, P/vP and mobility properties of the substance exist, those properties should be considered when developing the restriction as releases to the environment are expected.

Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses.

In addition, the use of the most harmful substances by professional workers has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability (CSS) which aims to extend to professional users under REACH the level of protection granted to consumers.

For the remaining industrial uses where potential for exposure cannot be excluded **it is suggested to use authorisation.** After being classified as repr. 1B SVHC identification could be initiated followed by inclusion in the Authorisation list. SVHC identification could also consider P/vP and mobility properties of the substance. Although, SVHC identification alone would likely send a message to Industry to seek alternatives, inclusion in Annex XIV would ensure that suitable substitutes are sought and that health risks in industrial settings are minimised.

Alternatively, to SVHC and authorisation, setting an EU-wide exposure limit for workers under OSH or REACH for industrial uses was also considered. Several national occupational exposure limits (OELs) are already in place[4]. However, the main use of the substance is as solvent and therefore it is assumed likely that viable (less toxic) alternatives are available and that it would actually be beneficial to rather push for substituting the substance to safer alternatives which authorisation would support. Therefore, for the time being, authorisation is suggested as the next regulatory risk management option to address potential exposure to workers on industrial sites. This proposal will be revisited, preferably based on further assessment when developing further the restriction on mixtures used by professionals which should also support clarifying what are those industrial uses in need for EU RRM action.

Germany has recently submitted an RMOA intention for this substance; the RMOA will focus mainly on its function/use as a solvent and its presence in consumer products, articles and mixtures. The current assessment of regulatory needs may need to be revisited to reflect the conclusions of the RMOA developed by Germany.

Based on currently available information, there is no need for (further) EU regulatory risk management for the remaining substances in the group.

One substance (EC 203-812-5) has a harmonised classification as Repr. 2(d), whereas another one (EC 208-015-6) is waiting for requested study results regarding possible reprotoxic effects. In addition to the (potential) reprotoxic properties, both substances as well as EC 204-639-8 are suspected to fulfil the P/vP

[4] https://www.dguv.de/ifa/gestis/gestis-internationale-grenzwerte-fuer-chemische-substanzen-limit-values-for-chemical-agents/index-2.jsp

screening criteria (substances being not readily biodegradable) and are expected to be mobile in the environment. The main use reported is as a monomer/intermediate in polymer production or as an intermediate under strictly controlled conditions (SCC) where release and exposure are expected to be low. Consequently, no further EU regulatory risk management is currently proposed, noting however that this may need to be revisited if the use profile changes.

Substance 205-992-0 is unlikely to have human health or environmental hazards and is only registered as intermediate under SCC.

The other substances have widespread uses as fragrance/odour agent in e.g. washing and cleaning products, polishes and wax blends, etc. where there is a high potential for release and exposure, however, no human health hazard is expected for most; for environmental hazard, proper self-classification by registrants should ensure adequate risk management are currently in place for these substances.

One substance (EC 224-436-8) has potential skin sensitisation properties and is self-classified as Skin sens. 1B by the registrant(s). Despite potential for exposure, the conclusion for this substance is that there is no need for further regulatory action at the moment. For industrial and professional uses, sufficient and consistent self-classification by registrants should trigger adequate RMM according to workplace legislation. Adequate product labelling should in principle provide consumers with sufficient information to manage risks arising from the use of mixtures containing the substance.

However, there is a concern related to skin sensitisers (potentially) present in consumer mixtures and the need to further investigate whether further regulatory actions are needed and what would be the best options to address this concern.

Such concern has already been identified in other groups of substances and was brought for further discussion to Member States. Work is ongoing on this generic issue by both Member States and ECHA which may affect the regulatory actions on substances in this group.

3 Conclusions and actions

The conclusions and actions proposed in the table below are based on the REACH and CLP information available at the time of the assessment by ECHA. 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 will be updated and conclusions and actions revisited.

EC number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
211-463-5	Known or potential hazard for reproductive toxicity	Known or potential hazard for persistence, mobility and toxicity	Several widespread uses reported including use in washing and cleaning products, lubricants, coatings**,** high potential for exposure for both workers and consumers	**Need for EU RRM: Restriction combined with authorisation** <u>Justification</u>: The harmonised classification as Repr. 1B would trigger the restriction entry 30 and by that ensure that the substances are not included in consumer mixtures above the limits specified in that entry. Professional use is typically widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with typically frequent exposures with a long duration.	**First step:** CCH **Next steps (if hazard confirmed):** • CLH • Restriction for professional uses • SVHC identification followed by authorisation for industrial uses

EC number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
				Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses. For industrial uses, authorisation is suggested as the most appropriate option but may need to be revisited once the hazard is clarified based on further assessment.	
203-812-5	Known or potential hazard for reproductive toxicity	Known or potential hazard for persistence, mobility and toxicity	Use as monomer/ intermediate in polymer production/ intermediate under SCC; low potential for exposure.	**Currently no need for EU RRM** <u>Justification:</u> Release and exposure/ hazards are expected to be low.	No action
208-015-6		Known or potential hazard for persistence and mobility			
204-639-8	No hazard or unlikely hazard				

EC number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
205-992-0	No hazard or unlikely hazard	No hazard or unlikely hazard			
224-436-8	Known or potential hazard for skin sensitisation	Known or potential hazard for aquatic toxicity	Widespread use as fragrance/ odour agent in washing and cleaning products, cosmetics, polishes and wax blends, biocidal products, air care products, high potential for exposure for both workers and consumers.	**Currently no need for EU RRM** Justification: For industrial and professional uses, sufficient and consistent self-classification by registrants should trigger adequate risk management measures according to workplace legislation. Sufficient risk management in place for environmental hazard.	No action
251-752-3, 945-924-3, 259-210-8, 266-795-3, 279-482-1, 426-130-1, 815-031-2.	No hazard or unlikely hazard				

Annex 1: Harmonised classifications and self-classifications reported by registrants

Data extracted on 29 September 2020.

EC/ List No	Substance name	Harmonised classification	Classification in registrations	Classification in C&L notifications
203-812-5	1,3,5-trioxane	Flam. Solid 1, H228 STOT SE 3, H335 (resp. Irrit.) Eye Irrit 2, H319*	Flam. Solid 1, H228 Repr. 2, H361d STOT SE 3, H335 (resp. Irrit.)	
208-015-6	1,3-dioxepane		Flam. Liquid 2, H225 Eye Irrit. 2, H319	Not classified
211-463-5	1,3-dioxolane	Flam. Liquid 2, H225 Repr. 1B, H360d *		
204-639-8	2,4,6-trimethyl-1,3,5-trioxane	Flam. Liquid 3, H226	Flam. Liquid 3, H226	Flam. Liq. 2, H225 Acute Tox. 4, H302 (oral)
205-992-0	1,3-benzodioxolane		Flam. Liquid 3, H226 Acute Tox. 4, H302 (oral) Eye Irrit. 2, H319 ** Skin Irrit. 2, H315 ** STOT SE 3, H335 (resp. Irrit.)**	Acute Tox. 4, H332 (inhal) Acute Tox. 4, H312 (dermal)
251-752-3	2-methyl-4-phenyl-1,3-dioxolane			Not classified Aquatic Chronic 3, H412
945-924-3	Reaction mass of 2,4,6-trimethyl-4-phenyl-1,3-dioxane isomer 1 and 2,4,6-trimethyl-4-		Aquatic Chronic 3, H412 Acute Tox. 4, H302 (oral)	

EC/ List No	Substance name	Harmonised classification	Classification in registrations	Classification in C&L notifications
	phenyl-1,3-dioxane isomer 2			
224-436-8	2-(1-ethylpentyl)-1,3-dioxolane		Aquatic Chronic 3, H412 Skin Sens. 1B, H317	Not classified
259-210-8	2-butyl-4,4,6-trimethyl-1,3-dioxane		Aquatic Chronic 3, H412	Not classified Eye Irrit. 2, H319
266-795-3	2-benzyl-4,4,6-trimethyl-1,3-dioxane		Aquatic Chronic 2, H411 Skin Irrit. 2, H315	Not classified
279-482-1	5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane		Aquatic Chronic 2, H411	Skin Irrit. 2, H315 Aquatic Chronic 3, H412
426-130-1	A mixture of: cis-2-isobutyl-5-methyl 1,3-dioxane; trans-2-isobutyl-5-methyl 1,3-dioxane	Aquatic Chronic 3, H412 Skin Irrit. 2, H315	Flam. Liquid 3, H226 Aquatic Chronic 3, H412 Skin Irrit. 2, H315	
815-031-2	2-isobutyl-4-vinyl-1,3-dioxolane		Aquatic Chronic 3, H412 Skin Irrit. 2, H315	

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

Data extracted on 29 September 2020.

Main types of applications structured by product or article types	Use in polymer preparations and compounds (plastic articles)	Use in laboratories	Use in coatings	Use in lubricants	Use in metal working fluids/ rolling oils	Use in de-icing agents	Use in metal surface treatment products	Use in washing and cleaning products	Use in cosmetics	Use in polishes and wax blends, biocidal products, air care products
203-812-5	I	I								
208-015-6	I									
211-463-5	I	I	F, I, **P, C**	F, I, **P, C**	F, I, **P**	F, **P**		F, I, **P, C**	F, **C**	
251-752-3								F, I, **P, C**	F, **P, C**	F, **P, C**
945-924-3								F, I, **P, C**	F, **P, C**	F, **P, C**
224-436-8								F, I, **P, C**	F, **P, C**	F, **P, C**
259-210-8								F, I, **P, C**	F, **C**	F, **P, C**
266-795-3								F, I, **P, C**	F, **P, C**	F, **P, C**
279-482-1								F, **P, C**	F, **C**	F, **P, C**
426-130-1							F, I	F, I, **P, C**	F, **P, C**	F, **P, C**
815-031-2								F, I, **P, C**	F, **P, C**	F, **P, C**

*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*includes only substances with a full registration; substances not included in this table have either (only) an intermediate registration or C&L notification*

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

Data extracted on 29 September 2020.

EC/List number	RMOA	Authorisation		Restriction *	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
203-812-5						Cosmetics (prohibited); FCM (authorised)
208-015-6						FCM (authorised)
211-463-5	YES				YES	FCM (authorised)
426-130-1						NONs

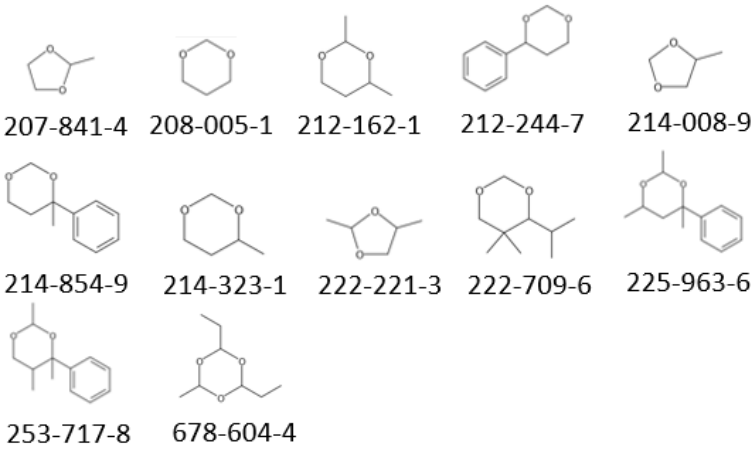
*Some of the broad restriction entries in the Annex XVII of REACH are not represented in the overview, e.g. when the scope of the restriction is defined by its classification or the substance identification is broad (e.g. entries 3, 28-30 and 40).

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

Annex 4: Non exhaustive list of substances in the C&L inventory that may fall into the group definition (optional)

Substances notified under C&L

Subgroup 1: Cyclic acetals from formaldehyde and acetaldehyde



Subgroup 2: Cyclic acetals from other aldehydes