

Assessment of regulatory needs

Authority: European Chemicals Agency

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Group Name: Alkyl nitrates

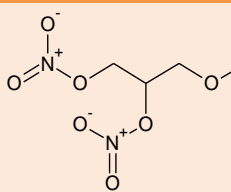
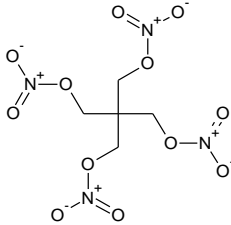
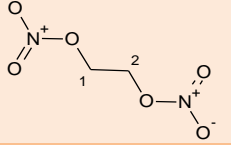
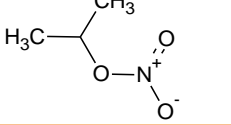
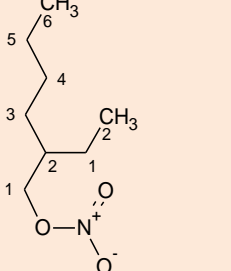
Chemical structure: -

Revision history

<i>Version</i>	<i>Date</i>	<i>Description</i>
1.0	07/12/2021	

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Substances within this group:

EC/List number	CAS number	Substance name (acronyms)	Chemical structures	Registration type (full/OSI/TII/NONS), highest tonnage band among all the registrations (t/y) ¹
200-240-8	55-63-0	glycerol trinitrate		Full, >1000
201-084-3	78-11-5	pentaerythrityl tetranitrate (PETN)		Full, >1000
211-063-0	628-96-6	ethylene dinitrate		Full, >1000
216-983-6	1712-64-7	isopropyl nitrate		Full, N/A
248-363-6	27247-96-7	2-ethylhexyl nitrate		Full, >1000

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>

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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 the ECHA website².

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
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TSII	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
SEv	Substance evaluation
SVHC	Substance of very high concern

1 Overview of the group

ECHA has grouped together structurally similar substances. The alkyl nitrates group consists of 5 well-defined substances with one or several nitrate moiety(ies) connected to (or connected by) a single alkyl chain.

Based on information reported in the REACH registration dossiers, the alkyl nitrate group substances are used mainly as explosives and fuel additives, resulting in potential exposure to workers, consumers, and professional users who handle the substances either on their own or in mixtures (see overview of uses in Annex 2). The main concern comes from the use as fuel additive where neither potential exposure to human nor to environment can be ruled out. One substance (EC 248-363-6, 2-ethylhexyl nitrate) has additional widespread uses (e.g. coatings, runner production and processing, lubricants, use in road and construction applications).

There is one substance ethylene dinitrate (EC 211-063-0) that has been under substance evaluation by Italy due to concern over reproduction/developmental toxicity (as well as endocrine disrupting-like effects), sensitisation, genotoxicity/carcinogenicity and PBT/vPvB properties. Italy concluded their evaluation with a no need for regulatory follow up action at EU level³. The hazard properties have not been clarified because the substance is characterized by extremely high explosive properties and therefore performing laboratory studies with this substance is extremely dangerous.

Because all these substances are explosives, requests for new studies may require non-standard preparation and handling of test material under controlled conditions. Furthermore, specific risk management measures are most probably in place in particular in industrial settings to ensure safety of workers related to the explosiveness of those substances. This has been considered when assessing the regulatory needs of the substances in the group (see section 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.

³ See also the SEV conclusion document available at: [7f62c8aa-9ee1-08ae-20f2-57ef117f3397 \(europa.eu\)](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:7f62c8aa-9ee1-08ae-20f2-57ef117f3397)

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 for potential reproductive toxicity of ECs 216-983-6 and 248-363-6 and potential PBT properties of EC 248-363-6 when used as fuel additives.

Potential reproductive toxicity (fertility/sexual function and/or developmental toxicity) and target organ toxicity has been identified for 3 substances in the group (EC 200-240-8 glycerol trinitrate, EC 211-063-0 ethylene dinitrate and EC 248-363-6 ethylhexyl nitrate). Due to common structural elements (presence of nitrate) in all substances in the group, the potential for reproductive and target organ toxicity applies to all 5 substances.

Three substances of the group (EC 200-240-8 glycerol trinitrate, EC 201-084-3 pentaerythrityl tetranitrate and EC 216-983-6 isopropyl nitrate) are deemed unlikely to have PBT/vPvB properties. For EC 248-363-6, 2-ethylhexyl nitrate the conclusion is less clear. This substance appears comparatively much more lipophilic than the other substances of the group. With a log Kow reported to be >4.5, the screening B criterion is met. The substance may be persistent. Toxicity cannot be ruled out either, in particular because there is potential for reproductive toxicity and target organ toxicity. Based on ECHA's assessment of currently available hazard information, EC 248-363-6 fulfils the screening PBT criteria and therefore is considered as potential PBT/vPvB substance. For EC 211-063-0 ethylene dinitrate, the potential PBT/vPvB properties have not been clarified due to the reasons described in section 1.

The first step of the regulatory risk management action proposed, should the hazard exist, is the confirmation of hazard via harmonised classification (CLH) as reproductive toxicity (ECs 216-983-6 and 248-363-6).

The CLH i) will trigger company level risk management measures (RMM) under OSH legislation for workers, ii) is needed or highly recommended for further regulatory processes under REACH (e.g. restriction) 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. Note that the supply of motor fuels to consumers is exempted from entry 30.

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 covered by Occupational Health and Safety (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. 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. The best legislative tool (e.g. fuel quality directive - Directive 2009/30/EC) to introduce the restriction when used as fuel additive will be further investigated while data is being generated.

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 which aims to extend to professional users under REACH the level of protection granted to consumers.

Furthermore, for EC 248-363-6, should the PBT hazard exist, confirmation of the PBT properties via candidate listing (SVHC) will need to be initiated. This hazard needs to be taken into account in the proposed restriction together with the potential for reproductive toxicity.

The other widespread uses of EC 248-363-6, 2-ethylhexyl nitrate are not yet covered under the actions proposed as the first step is to clarify whether or not they are relevant (e.g. whether the uses actually exist, if the substances are really used in those applications and not only as intermediates). Industry should update their registration dossiers and clarify whether or not the uses reported for this substance are supported. In the next iteration to this assessment of regulatory needs, if no update of the registration dossiers has been submitted, those uses will be considered to be of relevance and if the potential hazard properties confirmed, then further regulatory risk management will be considered.

Based on currently available information, there is no need for (further) EU regulatory risk management for ECs 200-240-8, 201-084-3 and 211-063-0, when used only as explosives.

For those substances used only as explosives it is proposed that there is currently no need for further regulatory risk management. The risk management measures in place due to the classification as unstable explosives should already ensure the protection of the workers (including the potential for toxicity to reproduction).

Environmental releases cannot be excluded from the use of those substances however it seems that improving the environmental classification and labelling (EC 200-240-8 already classified as aquatic toxic category 2) after generation of additional hazard data would not have a significant impact on the safety of those substances in practice for the following reasons:

- Under the SEVESO Directive (2012/18/EU), the classification as unstable explosives (P1a explosives) triggers much more stringent controls compared to those that would be triggered by classification Aquatic Chronic 1 (E1 environmental hazards).
- Under Directive 2014/28/EU⁴, the manufacture, storage, use, import, export, transfer or trade of explosives is strictly regulated and monitored by authorities.
- Under the Waste Framework Directive (2008/98/EC), wastes containing those substances would be regarded as hazardous waste. They would probably be considered 'ecotoxic waste' (HP14)⁵ irrespective of their

⁴ DIRECTIVE 2014/28/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 26 February 2014 on the harmonisation of the laws of the Member States relating to the making available on the market and supervision of explosives for civil uses (recast).

⁵ As a matter of fact, there is no precise definition of 'ecotoxic waste' in the legislation. Some guidance or guidelines have been proposed at the national level, which take into account both the concentration and the environmental classification of the hazardous substances present in the waste. A less stringent environmental classification could therefore make a difference in the handling of wastes if the concentrations of the substances in the disposed products/articles are low. However, such situation is not likely for uses as explosives, as the concentration of the explosive in the products/articles should be high enough to be effective.

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environmental classification as Aquatic Chronic 1 or Aquatic Chronic 2. Besides, they would be regarded anyway as explosive (HP1) and toxic for human health (at least HP5 and HP6).

- Under the Industrial Emission Directive (2010/75/EU), a substance is regarded as 'hazardous' as long as it is classified. Therefore, a more severe classification for environment would not change the obligations under this Directive.

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.

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
216-983-6, isopropyl nitrate	Known or potential hazard for reproductive toxicity and for STOT RE	Inconclusive hazard for aquatic toxicity	Used as fuel additive with potential exposure to industrial and professional workers and releases to the environment.	<p>Need for EU RRM: Restriction</p> <p><u>Justification:</u> The harmonised classification as repro 1 would trigger the restriction entry 30 and by that ensure that the substances are not included in consumer mixtures above 0.3% w/w.</p> <p>Restriction is proposed to ensure protection of workers. The best</p>	<p>First step: CCH</p> <p>Next steps (if hazard confirmed):</p> <ul style="list-style-type: none"> • CLH • restriction

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Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
				legislative tool (e.g. fuel quality directive - Directive 2009/30/EC) to introduce the restriction will be further investigated while data is being generated.	
248-363-6, 2-ethylhexyl nitrate	Known or potential hazard for reproductive toxicity and for STOR E	Known or potential hazard for PBT/vPvB and for aquatic toxicity	Used as fuel additive with potential exposure to consumers, industrial and professional workers and releases to the environment. In addition, other widespread uses reported which needs to be clarified (e.g. coatings, runner	Need for EU RRM: Restriction <u>Justification:</u> The harmonised classification as repro 1 would trigger the restriction entry 30 and by that ensure that the substances are not included in consumer mixtures above 0.3% w/w. Restriction is proposed to ensure protection of	First step: CCH Next steps (if hazard confirmed): <ul style="list-style-type: none"> • CLH for reprotoxicity • SVHC identification on PBT properties • restriction

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Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
			production and processing, lubricants, use in road and construction applications).	workers. The best legislative tool (e.g. fuel quality directive - Directive 2009/30/EC) to introduce the restriction will be further investigated while data is being generated. For other uses it is recommended first to clarify whether or not they are relevant (e.g. whether the uses actually exist, if the substances are really used in those applications and not only as intermediates).	
200-240-8, glycerol trinitrate	Known or potential hazard for reproductive toxicity and for STOT RE (ECs 200-240-8 and 201-084-3)	Known or potential hazard for aquatic toxicity (ECs 200-240-8 and 211-063-0)	Used only as explosives with no potential for exposure.	Currently no need for EU RRM <u>Justification:</u>	CCH for EC 200-240-8

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Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
<p>201-084-3, pentaerithrityl tetranitrate</p> <p>211-063-0, ethylene dinitrate</p>	<p>Known or potential hazard for reproductive toxicity and for STO RE (EC 211-063-0)</p> <p>Inconclusive hazard for carcinogenicity, skin sensitisation and ED (EC 211-063-0) – according to SEv</p>	<p>No hazard or unlikely hazard (EC 201-084-3)</p> <p>Inconclusive hazard for PBT/vPvB and ED (EC 211-063-0) – according to SEv</p>		<p>The risk management measures in place due to the classification as unstable explosives should already ensure the protection of the workers. Environmental releases cannot be excluded from the use of explosives. However, for these substances it seems that improving the environmental classification and labelling e.g. after generation of additional hazard data would not have a significant impact on the safety of those substances in</p>	

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Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
				practice as further detailed in the text above	

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

Data extracted on 16 April 2019.

EC/List No	CAS No	Substance name	Harmonised classification		Self-classification	
			Hazard class	Hazard code	Self-classification in registration dossier	Additional classification in C&L notifications
200-240-8	55-63-0	glycerol trinitrate	Unst. Expl. (or Expl. 1.1 if >40 % phlegmatiser]) Acute Tox. 1 Acute Tox. 2 Acute Tox. 2 STOT RE 2 Aquatic Chronic 2	H200 (or H201 if >40 % phlegmatiser]) H310 H330 H300 H373 H411		
201-084-3	78-11-5	pentaerithrityl tetranitrate	Unst. Expl. (or Expl. 1.1 if >20 % phlegmatiser])	H200 (or H201 if >20 % phlegmatiser])		
211-063-0	628-96-6	ethylene dinitrate	Unst. Expl. Acute Tox. 1 Acute Tox. 2 Acute Tox. 2 STOT RE 2	H200 H310 H330 H300 H373		
216-983-6	1712-64-7	isopropyl nitrate	None	None	Flam. Liq. 2, H225 Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 (Lungs)	None
248-363-6	27247-96-7	2-ethylhexyl nitrate	None	None	Acute Tox. 4, H302 Acute Tox. 4, H312 Acute Tox. 4, H332 Aquatic Chronic 2, H411	Asp. Tox. 1, H304 Acute Tox. 3, H311 Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 (Resp.) Aquatic Acute 1, H400 Aquatic Chronic 1, H410

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

Data extracted on 16 April 2019.

Main types of applications structured by product or article types	EC/ List 200-240-8	EC/ List 201-084-3	EC/ List 211-063-0	EC/ List 216-983-6	EC/ List 248-363-6
	I, F, P, C, A	I, F, P, A	I, F, P, A	I, F, P, C	I, F, P, C, A
Explosives, propellants, detonators, ammunition, boosters, blastings	x	x	x	x	x
Fuel additive				x	x
Use as laboratory reagent				x	
Metal working fluids/rolling oils					x
Coatings					x
Release agents or binders					x
Rubber production and processing					x
Use in oil and gas field drilling and production operations					x
Use as a fuel					x
Use of substance as intermediate					x
Lubricants					x
Use as functional fluids					x
Use in Road and Construction Applications					x

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 16 April 2019.

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
200-240-8				*	Yes	IOEL**
201-084-3				*	Yes	
211-063-0				*	Yes	
216-983-6				*	Yes	
248-363-6				*	Yes	

*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).

** Recommended indicative occupational exposure limit value for the European Union. A national occupational exposure limit value has to be set. 8 hours limit value: 0,095 mg/m³ (0,01 ppm).