MINISTRY OF HUMAN CAPACITIES

Justification Document for the Selection of a CoRAP Substance

Group Name: Cyclic nitramine explosives

EC	CAS	Substance public name
204-500-1	121-82-4	Perhydro-1,3,5-trinitro-1,3,5-triazine
220-260-0	2691-41-0	Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

Authority: Hungarian REACH Competent Authority

Date: 19/03/2019

Cover Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

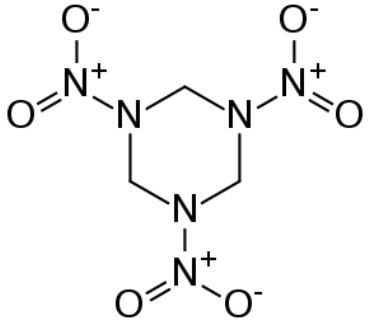
1 IDENTITY OF THE SUBSTANCES WITHIN THE GROUP

1.1 Other identifiers of the substances within the group

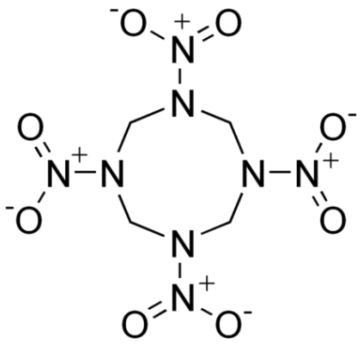
EC name (public)	IUPAC name (public)	Index number in Annex VI of the CLP Regulation:	Molecular formula:	Molecular weight or molecular weight range:	Synonyms:
Perhydro-1,3,5-trinitro-1,3,5-triazine	1,3,5-trinitro-1,3,5-triazinane	-	C3H6N6O6	222,12 g/mol	1,3,5 trinitroperhydro-1,3,5 triazine 1,3,5-Triazine, hexahydro-1,3,5-trinitro- 1,3,5-trinitro-1,3,5-triazacicloexano 1,3,5-Trinitroperhydro-1,3,5-triazine Perhydro-1,3,5-trinitro-1,3,5-triazine CYCLOTRIMETHYLENE TRINITRAMIDE RDX
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	1,3,5,7-tetranitro-1,3,5,7-tetrazocane	-	C4H8N8O8	296.155 g/mol	HMX Octagen 1,3,5,7-tetranitro-1,3,5,7-tetraazacyclooctane octahydro-1,3,5,7 tetranitro 1,3,5,7 tetrazocine

Type of substances ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formulas:



Perhydro-1,3,5-trinitro-1,3,5-triazine (RDX)



Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX)

RDX and HMX are structurally similar substances, both saturated heterocyclic compounds; the nitro groups, which give the compounds their explosive character are bound to the ring of nitrogen atoms. The RDX molecule is based on a six-membered ring and has three nitroamine groups while the HMX molecule is based on an eight-membered ring with four nitroamine groups. The physicochemical profiles of HMX and RDX are very similar, although HMX has a lower bioavailability than RDX.
RDX was found to be more toxic than HMX since it was absorbed more readily than HMX from the gastrointestinal tract. Absorbed HMX and RDX were both rapidly metabolised to polar metabolites which were excreted in urine.

1.2 Similar substances/grouping possibilities

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2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There is no ongoing or completed processes regarding the substances.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

The substance does not have harmonised classification according to the Annex VI of CLP regulation.

3.1.2 Self classification

- In the registration:

Perhydro-1,3,5-trinitro-1,3,5-triazine

- Acute Tox. 3 H301
- STOT SE 1 H370
- STOT RE 2 H373

Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

- Acute Tox. 3 H311
- Acute Tox. 4 H302
- Expl. Div. 1.1 H201

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

Perhydro-1,3,5-trinitro-1,3,5-triazine

- STOT RE 1 H372
- Skin Irrit. 2 H315
- Eye Irrit. 2 H319
- Acute Tox. 3 H311
- Acute Tox. 3 H331
- STOT SE 3 H335

Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

- Acute Tox. 4 H302, 312, 332
- Acute Tox. 3 H311, 201
- STOT SE 1 H370
- Aquatic Chronic 3 H412
- Repr. 1A H360

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

HU MSCA has no information about any proposal for harmonised classification regarding these substances.

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[1]

4.1 Tonnage and registration status

Table: Tonnage and registration status

Perhydro-1,3,5-trinitro-1,3,5-triazine

From ECHA dissemination site *		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☒ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

From ECHA dissemination site *		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☒ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

*****the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11):

https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0

[1] *The dissemination site was accessed 16/08/2018.*

4.2 Overview of uses

Table: Uses (in three parts)

Part 1:

Substance: **Perhydro-1,3,5-trinitro-1,3,5-triazine**						
☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system
Substance: **Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine**						
☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE OR GROUP

5.1. Legal basis for the proposal

☒ Article 44(2) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

5.2. Selection criteria met (why the substance or group qualifies for being in CoRAP)

☒ Fulfils criteria as CMR/ Suspected CMR

☐ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☐ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☒ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐ C ☐ M ☐ R	Suspected CMR[1] ☒ C ☐ M ☒ R	☐ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[2]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify):
Exposure/risk based concerns		
☒ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☒ Exposure of environment	☒ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

[2] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

RDX and HMX are used as explosive materials. The exposure concerns workers during manufacture, formulation and professional use of the subtances. No consumer use has been detected. According to SPIN database, occupational exposure is likely to occur (Use index: 5), and it indicated a potential exposure to air (Use index: 3).

Several repeated-dose animal assays reported neurological effects, including seizures, convulsions, tremors, hyperirritability, hyper-reactivity, and behavioural changes, associated with RDX exposure. In other studies there was no evidence of RDX-associated neurotoxicity.

Severe neurological disturbances include tonic-clonic seizures in factory workers, seizures, dizziness, headache, and nausea following nonwartime/nonoccupational exposures, and seizures in a child following ingestion of plasticised RDX from the mother's clothing were reported.

The available data suggest that RDX causes neurophysiological symptoms via interaction of GABA-receptors.

HMX, a structurally similar substance to RDX also shows neurotoxic potential. In one study a number of neurological effects including hyperkinesia, hypokinesia, clonic convulsions, and changes in aggressive behaviour were noted in rabbits administered a single dose of 168 mg/kg bw HMX or more. An increase in the severity of the convulsions, hindleg paralysis, and perivascular cuffing in the brain was observed in rabbits exposed to a single dose of 372 mg/kg HMX.

Although the substance has neurotoxic properties, harmonized classification of the substance is not recommended, because most of the notifiers already self-classified the substance as STOT SE/RE, therefore the risk is controlled adequately.

In an experiment the persistence of explosives in soil were investigated, and it was concluded that the estimated half-life of RDX in soil is 36 years, 39 years in the case of HMX. Other studies show that RDX only degrades under anaerobic conditions.

Additionally, in an earthworm reproduction test significant effects of RDX on reproduction were observed in artificial soil spiked with 189, 378 and 756 mg/kg of RDX. Productivity of juveniles was also reduced by exposure to 95 mg/kg of RDX, productivity of cocoons (total number) was reduced at 189 mg/kg of RDX.

However, the substance has low bioaccumulation potencial (BCF=5,9), thus it does not fulfil the PBT or vPvB criteria. Moreover, according to SPIN database, the uses do not indicate potential exposure to the soil.

The carcinogenicity of RDX has been examined in carcinogenicity bioassay in mice, and increased incidence of liver tumors was observed in female B6C3F1 mice. Although the re-evaluation of the data using revised diagnostic criteria resulted in a reclassification of several hepatocellular adenomas as foci of cytoplasmic alterations, there remained a statistically significant positive trend in the combined incidence of hepatocellular adenomas or carcinomas, consistent with the original findings. HMX carcinogenic potential has not been investigated.

Evidence of male reproductive toxicity is provided by the finding of testicular degeneration in male mice. An increased incidence of testicular degeneration (10−11%) was observed in male B6C3F1 mice exposed to ≥35 mg/kg/day RDX for 2 years in the diet compared to control. Reductions in absolute testicular weight were observed, but the magnitude of this effect was small (≤6% compared to controls) and not dose-related.

According to the SCR a rat developmental toxicity study reported spermatic granulomas in the prostates of rats exposed to 40 mg/kg/day RDX for 6 months, but this effect was not observed in rats exposed after 1 or 2 years of exposure. The study also reported an increase in the incidence of testicular degeneration in rats exposed to 40 mg/kg/day RDX for 6 months (3/10, not statistically significant) or 1 year (4/10), but not after 2 years (0/4).

An unpublished study indicates that RDX was found in the brain of rat pups whose mothers were administered RDX from gestation day 6 through to postnatal day 10. Significantly higher concentrations of RDX were found in the brain from pups sacrificed immediately after

birth than in the brain of pups sacrificed on postnatal day 10, therefore presumably transplacental exposure occurred. Since RDX was also found in the dam's milk, transfer of RDX to the offspring via the milk can also occur. However, according to the available data there is no sign for developmental toxicity of RDX, we cannot rule out the effects of RDX on the unborn child.

Regarding HMX, no reproductive toxicity study has been performed, in the registration dossier information requirements has been derived from read-across substance, RDX.

The available information on carcinogenicity and reproductive toxicity raise concern, thus the substances should be addressed in full evaluation.

5.4 Indication of information that may need to be requested to clarifyfy the concern

☒ Information on toxicological properties	☐ Information on physico-chemical properties
☐ Information on fate and behaviour	☐ Information on exposure
☐ Information on ecotoxicological properties	☐ Information on uses
☐ Information on ED potential	☐ Other (provide further details below)

In order to clarify the concerns identified further information on reproductive toxicity and carcinogenicity properties of the substances may be necessary.

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)

Depending on the outcome of the substance evaluation a harmonised classification is a possible risk management measure.