Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	3,5-dimethylpyrazole
Chemical Group:	
EC Number:	200-657-5
CAS Number:	67-51-6
Submitted by:	Ministry of Health, Social Services and Equality, Spain
Date:	17/03/2015

Note

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

Contents

1 IDENTITY OF THE SUBSTANCE

1.1 Other identifiers of the substance

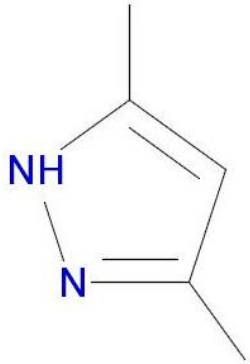
Table 1: Substance identity

EC name:	3,5-dimethylpyrazole
IUPAC name:	3,5-dimethyl-1H-pyrazole
Index number in Annex VI of the CLP Regulation	
Molecular formula:	C5H8N2
Molecular weight or molecular weight range:	96.1304
Synonyms/Trade names:	

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

Structural formula:

3,5-dimethylpyrazole



1.2 Similar substances/grouping possibilities

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2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

No harmonised classification available.

2.2 Self classification

The registration data includes the following self-classification:

Acute Tox. 4 (H302: Harmful if swallowed)

Repr. 2 (H361fd: Suspected of damaging fertility or the unborn child)

STOT RE 2 (H373: May cause damage to organs through prolonged or repeated exposure)

In addition, there are 193 entries for this substance in the C&L Inventory, grouped in 14 aggregated notifications. The following hazard classes are in addition notified among the aggregated self-classification in the C&L Inventory:

Acute Tox. 4 (H312: Harmful in contact with skin)

Acute Tox. 4 (H332: Harmful if inhaled)

Skin Irrit. 2 (H315: Causes skin irritation)

Eye Irrit. 2 (H319: Causes serious eye irritation)

STOT SE 3 (H335: May cause respiratory irritation)

In addition, there are 35 entries of no classification.

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

Currently, there is no proposal for harmonised classification for the substance 3,5-dimethylpyrazole.

3 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA 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

☒ Industrial use	☒ Professional use	☐ Consumer use	☐ Closed System

Industrial uses of the substance include formulation of polymer preparations and compounds, modification of polymers, use of substance as an intermediate, use for production of pre-blocked polymers, use of monomers in the production of polymers, plastics and polymerization processes, use of processing aids in processes and products. Professional workers can use products containing low percentage of the substance.

4 OTHER COMPLETED/ONGOING REGULATORY PROCESSES THAT MAY AFFECT SUITABILITY FOR SUBSTANCE EVALUATION

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	

5 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

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 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[1]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)
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)

The substance has no harmonised classification according to Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) but the registrant classified the substance as Repr. 2 (H361fd: Suspected of damaging fertility or the unborn child).

The only information available for the reproductive toxicity endpoint is a reliable GLP combined repeated dose toxicity study with the reproduction/development toxicity screening test in Wistar rats (OECD 422) dosed at 20, 60 and 200 mg/kg bw/day via oral gavage.

In this study, effects were observed on weight and histopathology of reproductive organs at the highest dose level (200 mg/kg bw/d) such as a decrease in absolute and relative testes and seminal vesicles weight, a decrease in absolute prostate and epididymides weight, oligospermia, increased incidence and/or severity of seminiferous cell debris, degeneration/depletion of spermatocytes and an increase in incidence and/or severity of spermatidic giant cells. The registrant states that these effects underlie the poor reproductive results, manifested in the lower fertility and conception index.

With regard to the developmental effects observed in this study, it was reported that thirteen pups were found dead or went missing during the first days of lactation in the highest dose group, compared with three, three and one pups in the control, low and medium dose group. Seven of the thirteen dead pups were attributable to one female of the high dose group who had a total litter loss by Day 3. Missing pups were most likely cannibalized. A case of a external malformation consisted in small lower jaw was observed in a single pup at the mid dose level (60 mg/kg bw/d). However, due to its single occurrence, it was considered an incidental effect not attributable to the treatment.

The screening test available gives indications of relevant reproductive effects that may have to be confirmed in a definitive reproductive toxicity study. As it is stated in the ECHA Guidance, chapter R.7a, the screening tests are not meant to provide complete information on all aspects of reproduction and development. In particular, postnatal effects associated with prenatal, postnatal or lactational exposure are not covered. In this case, more specific data on reproductive and developmental effects may be needed to confirm the present classification as Repr. 2 or even to change it to a more restrictive hazard category.

In addition, it has to be noted that some RCR for industrial workers are close to 1 (combined routes, systemic long-term).

[1] 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

5.4 Preliminary indication of information that may need to be requested to clarify 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 ED potential	☐ Other (provide further details below)
Hazard data to investigate further reproductive toxicity.	

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
If concern is confirmed, the substance should be harmonised classified as toxic to reproduction.			