Risk Management Option Analysis Conclusion Document

Substance Name: Cholecalciferol/Vitamin D3
EC Number: 200-673-2
CAS Number: 67-97-0

Authority: Dutch National Institute for Public Health and the Environment
Date: October 2022

Version 2.1
October 2015

DISCLAIMER

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 or the Member States may initiate at a later stage. Risk Management Option Analyses 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 Risk Management Option analysis (RMOA) is to help authorities decide whether further regulatory risk management activities are required for a substance and to identify the most appropriate instrument to address a concern.

RMOA is a voluntary step, i.e., it is not part of the processes as defined in the legislation. For authorities, documenting the RMOA allows the sharing of information and promoting early discussion, which helps lead to a common understanding on the action pursued. A Member State or ECHA (at the request of the Commission) can carry out this case-by-case analysis in order to conclude whether a substance is a 'relevant substance of very high concern (SVHC)' in the sense of the SVHC Roadmap to 2020[1].

An RMOA can conclude that regulatory risk management at EU level is required for a substance (e.g. harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. Any subsequent regulatory processes under the REACH Regulation include consultation of interested parties and appropriate decision making involving Member State Competent Authorities and the European Commission as defined in REACH.

This Conclusion document provides the outcome of the RMOA carried out by the author authority. In this conclusion document, the authority considers how the available information collected on the substance can be used to conclude whether regulatory risk management activities are required for a substance and which is the most appropriate instrument to address a concern. With this Conclusion document the Commission, the competent authorities of the other Member States and stakeholders are informed of the considerations of the author authority. In case the author authority proposes in this conclusion document further regulatory risk management measures, this shall not be considered initiating those other measures or processes. Since this document only reflects the views of the author authority, it does not preclude Member States or the European Commission from considering or initiating regulatory risk management measures which they deem appropriate.

[1] For more information on the SVHC Roadmap: http://echa.europa.eu/addressing-chemicals-of-concern/substances-of-potential-concern/svhc-roadmap-to-2020-implementation

1. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Vitamin D3 is an endogenous substance which is actively regulated in organisms, among which the human body. The discussion in the PBT EG considering the PBT properties was confounded by the discussion if the PBT concept is applicable for endogenous substances. The NL-CA thinks that it is important to separate these discussions and firstly establish the PBT status before considering the handling perspective of this substance. However, by means of this RMOA the regulatory management options are included to address the handling perspective. Given the application of the substance as a rodenticide it is applied in the environment at higher concentration levels than normally present, possibly leading to long term environmental risks and in turn also for human indirectly exposed via the environment. The NL-CA would like to address this concern, accordingly. However, since the handling perspective is considered too limited, the RMOA is shared with the evaluating CA Sweden of cholecalciferol within the framework BPR to take the considerations into perspective at the time of re-evaluation (mid 2024).

General timeline on assessment within frameworks

2013 - The evaluating Competent Authority Sweden accepted the dossier on cholecalciferol on June 28th, and assessed it under Regulation (EC) no 528/2012 (BPR). In spite of the BPR requirements to submit data, which enable the assessment of the exclusion criteria, the dossier had data-gaps for carcinogenicity and reproduction toxicity. The applicant submitted extensive reasoning for waiving.

2014 - The strategy on how to proceed with respect to the missing data was discussed at an early-working group meeting (WG III/2014) as well as at the 57th CA-meeting. Both committees concluded that it would not be justified to require more testing for this substance. Similarly, the information to assess the PBT-properties was not considered sufficient. At an early-working group meeting (WG III 2014) it was concluded, that additional information on persistency in soil should be requested. At WG III 2014, it was also concluded that more testing on bioaccumulation should be considered, as soon as the results of the additional requested degradation studies became available. However, methodological difficulties were already expected in assessing the bioaccumulation potential.

2016 - A final version of the report of the requested degradation study was received in October 2016. The CAR was sent to the Biocidal Products Committee (BPC) in the first half of 2017. Proposal: cholecalciferol is potentially PBT.

2017 - At WG I 2017 the results of this study were discussed, after consultation with the ECHA PBT EG. The soil degradation study (using tritiated substance) helped to establish that cholecalciferol is not persistent. BPC concluded that Cholecalciferol is not PBT (see ECHA 2017)[2]. This decision was based on the draft opinion of evaluating Competent Authority (eCA) Sweden that the PBT-assessment is not the correct way to assess the risks of substances that are essential for organisms, actively regulated or even synthesized by organisms (see RCOM (PBT Written Procedure)).

[2] ECHA 2017. Opinion of the biocidal products committee on the approval of the active substance Cholecalciferol for product type 14. 16 pg.

2018 - The assessment report 2018 (KEMI 2018)[3] has been established as a result of the evaluation of the existing active substance cholecalciferol in product-type PT 14 (Rodenticides), submitted under Article 11 of the Biocidal Products Directive 98/8/EC, with the proposal for approval of this substance.

Cholecalciferol/Vitamin D3 is proposed as an alternative to anticoagulant rodenticides. The Cholecalciferol Biocide Opinion 2017 (ECHA 2017) acknowledges that it could not be assessed at that time whether cholecalciferol causes less suffering than the anticoagulant rodenticides or non-chemical alternatives. Despite this information gap the use of cholecalciferol as a chemical alternative was granted since there are concerns about development of resistance against anticoagulant rodenticides.

2. CONCLUSION OF RMOA

Additional hazard information is needed to draw a final conclusion on the P, B and ED-status of the substance. It is suggested to generate the data by performing the studies needed as can be required by the evaluating Competent Authority. The RMOA is therefore shared with KEMI as the eCA. The NL-CA is willing to support the actions needed and to support the assessment of the data when appreciated.

Conclusions	**Tick box**
Need for follow-up regulatory action at EU level:	
Harmonised classification and labelling	
Identification as SVHC (authorisation)	
Restriction under REACH	
Other EU-wide regulatory measures	
Need for action other than EU regulatory action	X
No action needed at this time	X

3. NEED FOR FOLLOW-UP REGULATORY ACTION AT EU LEVEL

Table: SVHC Roadmap 2020 criteria

	Yes	No
a) Article 57 criteria fulfilled?[1]	X	
b) Registrations in accordance with Article 10?		X
c) Registrations include uses within scope of authorisation?		X
d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution?		X

[1]Article 57 is/could be fulfilled due to STOT RE 1, endocrine disrupting properties and PBT-properties.

Approval of cholecalciferol as biocide

The assessment report 2018 (KEMI 2018) has been established as a result of the evaluation of the existing active substance cholecalciferol in product-type PT 14 (Rodenticides), submitted under Article 11 of the Biocidal Products Directive 98/8/EC, with

[3] KEMI: Assessment Report 2018. Cholecalciferol Biocide Assessment Report. 54 pg.

the proposal for approval of this substance. Cholecalciferol/Vitamin D3 is proposed as an alternative to anticoagulant rodenticides. The Cholecalciferol Biocide Opinion 2017 (ECHA 2017) acknowledges that it could not be assessed at that time whether cholecalciferol causes less suffering than the anticoagulant rodenticides or non-chemical alternatives. Despite this information gap the use of cholecalciferol as a chemical alternative is granted since there are concerns about development of resistance against anticoagulant rodenticides.

Since cholecalciferol is a pro-hormone and fulfils the criteria set in Article 5(1) of Regulation (EU) No 528/2012 (BPR) and further defined in Regulation (EU) No 2017/2100, the most appropriate conclusion seems that cholecalciferol should normally not be approved unless one of the conditions for derogation set in Article 5(2)[4] of the BPR is applicable (ECHA 2017). It appeared that one of the conditions for derogation set in Article 5(2) of the BPR is indeed applicable: rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It has been recognised during the evaluation of the anti-vitamin K rodenticides (AVKs) that such substances do cause suffering in rodents. However, it was considered that it was not in conflict with the requirements of Article 5.1 of Directive 98/8/EC (replaced by the BPR) 'to avoid unnecessary pain and suffering of vertebrates', as long as effective, but comparably less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are unavailable. It is therefore suggested by the eCA that similar arguments also apply to cholecalciferol when considering the requirements of Article 19.1 of the BPR.

Cholecalciferol is potential candidate for substitution

Cholecalciferol meets one of the criteria for substitution listed in Article 10(1) of the BPR. It concerns the criterion specified in Article 10(1)(e): "reasons for concern linked to the nature of the critical effects which, in combination with the use patterns, amount to use that could still cause concern, even with very restrictive risk management measures".

In the case of cholecalciferol the critical effect is primary and secondary poisoning. The biocide opinion (ECHA, 2017) concluded that there is unacceptable risk for mammals and birds in several environmental scenarios. For example, there is long-term primary and secondary poisoning of birds when the diet consist largely of poisoned rodents. For this reason Cholecalciferol was identified as a potential candidate for substitution by competent authority Sweden in one of the previous consultations in 2017 (https://echa.europa.eu/nl/potential-candidates-for-substitution-previous-consultations/-/substance-rev/17101/term).

3.1 Harmonised classification and labelling

Harmonized classification and labelling has been established for Cholecalciferol, which is listed in Annex VI:

[4] Without prejudice to Article 4(1), active substances referred to in paragraph 1 of this Article may be approved if it is shown that at least one of the following conditions is met: (a) the risk to humans, animals or the environment from exposure to the active substance in a biocidal product, under realistic worst case conditions of use, is negligible, in particular where the product is used in closed systems or under other conditions which aim at excluding contact with humans and release into the environment; (b) it is shown by evidence that the active substance is essential to prevent or control a serious danger to human health, animal health or the environment; or (c) not approving the active substance would have a disproportionate negative impact on society when compared with the risk to human health, animal health or the environment arising from the use of the substance.

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
603-180-00-4		200-673-2	67-97-0	Acute Tox. 2	H300	inhalation: ATE = 0,05 mg/L (dusts or mists) dermal: ATE = 50 mg/kg bw oral: ATE = 35 mg/kg bw STOT RE 1; H372: C ≥ 3 % STOT RE 2; H373: 0,3 % ≤ C < 3 %'	
				Acute Tox. 2	H310		
				Acute Tox. 2	H330		
				STOT RE 1	H372		

3.2 Identification as a substance of very high concern, SVHC (first step towards authorisation)

The use to be addressed is the application as a biocide, however this falls outside the scope of authorisation. Given the uncertainties in the PBT assessment, the identification of cholecalciferol as an SVHC based on PBT-properties seems not appropriate option. Since the BPC itself concluded that cholecalciferol is considered to be an endocrine disrupting substance, the identification of cholecalciferol as ED or STOT RE 1 SVHC does not further impact the use. Both SVHC identification as authorisation are therefore concluded to be out of scope.

In the final BPC opinion (ECHA, 2017) it is stated that cholecalciferol fulfils the criteria for having endocrine disrupting properties laid down in Article 5(1)(d) of Regulation (EU) No 528/2012 and further defined in Regulation (EU) No 2017/2100. This may imply that biocidal products containing cholecalciferol should not be used for the general public according to Article 19(4)(d) of Regulation (EU) No 528/2012. Reference is made to ongoing discussions on the draft note from the Commission on "The implementation of scientific criteria for the determination of endocrine-disrupting properties in the context of biocidal product authorisation" (CA-Nov17-Doc.7.2.c).

3.3 Restriction (under REACH)

Restriction under REACH applies if there is an unacceptable risk to human health or the environment arising from the manufacture, use or placing on the market of substances, with an urgency for community-wide measures. However, biocidal active substances are outside of the scope of restriction. As pointed out in the section with respect to the BPR, a ban on the use of this substance seems a more appropriate option which should be addressed by the corresponding framework. It is already concluded by the BPC (ECHA, 2017) that cholecalciferol is a candidate for substitution. The validity of approval for the use of cholecalciferol as an active ingredient for biocides ends at 30th of June 2024. It is recommended to address the uncertainties with respect to the SVHC properties PBT and ED before this date to take into account at the time of the evaluation for a new period of approval.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

An indicate a preliminary timetable for the risk management measures discussed above are indicated in the table below.

Follow-up action	Date for intention	Actor
Re-evaluation within BPR	June 2024	SE CA*

* The NL-CA is willing to support the actions needed and to support the assessment of the data when appreciated.