Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Thixatrol® MAX

(Reaction mass of N,N'-ethane-1,2-diylbis(hexanamide) and 12-hydroxy-N-[2-[(1-oxyhexyl)amino]ethyl]octadecanamide and N,N'-ethane-1,2-diylbis(12-hydroxyoctadecanamide))

EC Number: 432-430-3

CAS Number: Not assigned

ECHA/RAC/CLH-O-0000002529-68-01/F

Adopted

3 May 2012

3 May 2012
CLH-O-0000002529-68-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT COMMUNITY LEVEL

In accordance with Article 37 (4) of the Regulation (EC) No 1272/2008 (CLP Regulation), the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling of

Trade Name: **Thixatrol® MAX**

Substance Name: **Reaction mass of N,N'-ethane-1,2-diylbis(hexanamide) and 12-hydroxy-N-[2-[(1-oxyhexyl)amino]ethyl]octadecanamide and N,N'-ethane-1,2-diylbis(12-hydroxyoctadecanamide)**

EC Number: **432-430-3**

CAS Number: **Not assigned**

The proposal was submitted by **United Kingdom** and received by RAC on **30 August 2011**.

The proposed harmonised classification

	CLP Regulation (EC) No 1272/2008	**Directive 67/548/EEC**
Current entry in Annex VI of CLP Regulation (EC) No 1272/2008	Skin Sens. 1 - H317 Aquatic Chronic 4 - H413	Xi; R43 R53
Proposal by dossier submitter for consideration by RAC	Removal of Skin Sens. 1 - H317	Removal of Xi; R43
Resulting harmonised classification (future entry in Annex VI of CLP Regulation) as proposed by dossier submitter	Aquatic Chronic 4 - H413	R53

PROCESS FOR ADOPTION OF THE OPINION

United Kingdom has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/web/guest/harmonised-classification-and-labelling-previous-consultations*** **on 30 August 2011**. Parties concerned and MSCAs were invited to submit comments and contributions by **14 October 2011**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Marianne van der Hagen**
Co-rapporteur, appointed by RAC: **Marian Rucki**

The opinion takes into account the comments of MSCAs and parties concerned provided in accordance with Article 37 (4) of the CLP Regulation.

The RAC opinion on the proposed harmonised classification and labelling has been reached on **3 May 2012,** in accordance with Article 37 (4) of the CLP Regulation, giving parties concerned the opportunity to comment. Comments received are compiled in Annex 2.

The RAC Opinion was adopted by **consensus**.

OPINION OF RAC

The RAC adopted the opinion that **Thixatrol® MAX** should be classified and labelled as follows:

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
616-200-00-1	Reaction mass of N,N'-ethane-1,2-diylbis(hexanamide) and 12-hydroxy-N-[2-[(1-oxyhexyl)amino]ethyl]octadecanamide and N,N'-ethane-1,2-diylbis(12-hydroxyoctadecanamide)	432-430-3	not assigned	Aquatic Chronic 4	H413	-	H413	-	-	

Classification and labelling in accordance with the criteria of Directive 67/548/EEC

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits	Notes
616-200-00-1	Reaction mass of N,N'-ethane-1,2-diylbis(hexanamide) and 12-hydroxy-N-[2-[(1-oxyhexyl)amino]ethyl]octadecanamide and N,N'-ethane-1,2-diylbis(12-hydroxyoctadecanamide)	432-430-3	not assigned	R53	R: 53 S: 61	-	-

SCIENTIFIC GROUNDS FOR THE OPINION

HUMAN HEALTH HAZARD ASSESSMENT

Skin sensitisation

Summary of dossier submitter's proposal:

The proposal was produced by Elementis UK Limited and submitted by United Kingdom according to CLP article 37(6).

Thixatrol® MAX (Reaction mass of N,N'-ethane-1,2-diylbis(hexanamide) and 12-hydroxy-N-[2-[(1-oxyhexyl)amino]ethyl]octadecanamide and N,N'-ethane-1,2-diylbis(12-hydroxyoctadecanamide)) was notified in the UK under the Notification of New Substances (NONS) Regulation (00-06-1340) in 2000. The existing classification is based upon read-across to a structural analogue (Thixatrol® Plus, EC# 430-050-2, reaction product of decanoic acid, 12-hydroxystearic acid and 1,2-ethandiamine (mol1:1:1)). Based on the results of a GPMT study on Thixatrol® Plus, Thixatrol® MAX was classified as a skin sensitizer. This GPMT study and a previous GPMT study on Thixatrol Plus were reported by the dossier submitter and considered unreliable.

However, sensitisation is an intrinsic property of the substance itself and, hence, it was considered justified to test the substance in mice for evaluation of safe use of the substance. Based on a key study Local Lymph Node Assay (LLNA) upon the substance itself and the weight of evidence of two supporting LLNA studies, also on the substance itself, the dossier submitter proposes to delete the existing classification in CLP (Regulation (EC) No. 1272/2008) and DSD (Directive 67/548/EEC) of Thixatrol® MAX as a sensitizer (Skin Sens. 1: H317; Xi: R43: May cause sensitisation). The studies show that the substance does not meet the criteria for classification as a skin sensitizer.

Comments received during public consultation:

The proposal to delete the classification as a sensitizer was supported by two MSCAs. One MSCA asked the dossier submitter to include information on substance identity and physico/chemical properties. This MSCA also asked for clarification on the methodology used in the key study. This concerned the highest test concentration, timing of the positive control study, and identity of the vehicle Pluronic L92. Due to deficiencies and unreliability the MSCA disagreed with the characterization of the two additional LLNA studies as supportive evidence. Another MSCA recommended deleting the test data from the structural analogue (Thixatrol® Plus) from the summary table of relevant studies, to avoid confusion. One MSCA noted that Thixatrol® Max contains an impurity classified as a sensitizer, and that this would trigger classification of Thixatrol® Max if the concentration is ≥ 1 %.

Outcome of RAC assessment - comparison with criteria and justification:

The LLNA key study (Reference 10)[1] is considered to be reliable. RAC appreciates the response from the dossier submitter in the RCOM with clarification concerning the maximum test concentration at 25% due to the physical nature of the test item. RAC also appreciates the response from the dossier submitter describing Pluronic® L92 as a polyoxypropylene-poloxyethylene block copolymer non-ionic surfactant, used at the concentration of 1% in water to improve the wettability of the mouse ears by the

[1] References are cited in Annex 1, the Background Document.

formulated test item in LLNAs. The positive control study reported in the key study was carried out two months previous to the key study itself, and this RAC regards as a weakness. However the test facility had also conducted nine other LLNA positive studies within the six months prior to the study on Thixatrol® Max with a satisfactory response.

RAC disagrees with the dossier submitter that the two other negative LLNA studies on Thixatrol® Max can be described as supporting studies in the weight of evidence analysis for sensitisation. In the first LLNA study (Reference 1), the max test dose was only 10 % in propylene glycol and there was no positive control. In the second LLNA study (Reference 5), at testing of up to 25% in corn oil, the positive control study was negative and judged non-valid. Based on these deficiencies RAC disregards the two LLNA studies on Thixatrol® Max preceding the key study.

Thixatrol® Max was previously classified by applying read-across to Thixatrol® Plus and available Guinea Pig Maximisation Test (GPMT) studies were reported by the dossier submitter (Reference 11 and 12). RAC has not assessed the GPMT studies, as these were carried out on another substance (Thixatrol® Plus) and RAC agrees with the dossier submitter that valid studies on the test substance itself should take precedence over these unreliable studies. RAC has no information on the substance identity of Thixatrol® Plus beyond the information that it is a reaction product of decanoic acid, 12-hydroxystearic acid and 1,2-ethandiamine (mol1:1:1).

The LLNA key study (Reference 10) is considered to be reliable due to the concentration of samples tested, the choice vehicle and the methodology employed.

A stimulation index of less than 3 was recorded for the test material at concentrations of 25%, 10% and 5% w/w in 1% Pluronic L92 in distilled water. Therefore Thixatrol® Max should not be classified.

In conclusion RAC recommends that Thixatrol® Max should not be classified as a skin sensitizer according to CLP (Regulation (EC) No. 1272/2008) and DSD (Directive 67/548/EEC).

ANNEXES:

Annex 1 Background Document (BD)[2]

Annex 2 Comments received on the CLH report, response to comments provided by the dossier submitter and RAC (excl. confidential information).

[2] The Background Document (BD) is based on the CLH report prepared by a dossier submitter; the evaluation performed by RAC is contained in RAC boxes.