Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at Community level of

acequinocyl

ECHA/RAC/CLH-O-0000001401-89-01/F

Adopted

28 October 2010

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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

Substance Name: ***acequinocyl*** (3-dodecyl-1,4-dihydro-1,4-dioxo-2-naphthyl acetate)

EC Number: ***611-595-7***

CAS Number: ***57960-19-7***

The proposal was submitted by ***the Netherlands***
and received by RAC on ***08 January 2010***

The harmonised classification originally proposed by *the Netherlands*

	Directive 67/548/EEC	CLP Regulation (EC) No 1272/2008
Current entry in Annex VI CLP Regulation	no entry (table 3.2)	no entry (table 3.1)
Proposal for consideration by RAC from dossier submitter	Xi; R37 Xi; R43 N; R50/53	Skin Sens. 1 - H317 STOT SE 1 - H370 STOT RE 2 - H373 Aquatic Acute 1 - H400
Resulting harmonised classification as proposed by the dossier submitter	Xi; R37 Xi; R43 N; R50/53	Skin Sens. 1 - H317 STOT SE 1 - H370 STOT RE 2 - H373 Aquatic Acute 1 - H400

PROCESS FOR ADOPTION OF THE OPINION

The Netherlands have 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/consultations/harmonised_cl/harmon_cl_prev_cons_en.asp*** on 22

February 2010. Parties concerned and MSCAs were invited to submit comments and contributions by 08 April 2010.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Olivier Le Curieux-Belfond***
Co-rapporteur, appointed by RAC: ***Céu Nunes***

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 ***28 October 2010,*** 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 ***acequinocyl*** should be classified and labelled as follows:

Classification & Labelling in accordance with the CLP Regulation:

Classification:

Skin Sens. 1 - H317
STOT SE 1 - H370 Causes damage to organs (lung) (if inhaled).
STOT RE 2- H373 May cause damage to organs (blood system) through prolonged or repeated exposure.
Aquatic Acute 1 - H400
Aquatic Chronic 1 - H410

Specific concentration limits: None
M-factors: 1000

Notes: None

Labelling:

GHS08, GHS09, Dgr, H317, H370, H373, H410

Classification & labelling in accordance with Directive 67/548/EEC

Classification[1]:

T; R39/23
Xi; R43
N; R50/53

[1] This section should reflect all relevant entries for the C&L: classification, R-phrases, S-phrases, concentrations limits, nota.

Specific concentration limits:

N; R50/53, C ≥ 0.025%
N; R51/53, 0.0025% ≤ C < 0.025%
R52/53, 0.00025% ≤ C < 0.0025%

Notes:

None

Labelling: T, N; R39/23-43-50/53, S(2-)24-37-38-60-61

SCIENTIFIC GROUNDS FOR THE OPINION

Acequinocyl is an active substance in the meaning of Directive 91/414/EEC and therefore subject to harmonised classification and labelling (CLP Regulation Article 36(2)).

Acute toxicity

Acequinocyl does not need to be classified on the basis of its acute oral and dermal toxicity in rats. Although one of the high dose animals in the inhalation study died at a concentration of 0.84 mg/L, it was the highest attainable concentration. Therefore no classification for acute inhalatory toxicity (lethality) is required. However, the observed lung effects in all animals are aggregates of alveolar macrophages, thickening of alveolar walls, apparent alveolar collapse, bronchiolar epithelial erosion or necrosis, hyperplasia or squamous metaplasia of bronchiolar epithelium, peribronchiolar inflammatory cells, and bronchiolar obliteration/obstruction with recanalisation or giant cells with mineralisation. These (severe) effects started at a dose of 0.62 mg/L, which is below the guidance value of 1 mg/L for STOT SE category 1. Therefore, according to the CLP Regulation acequinocyl should be classified as STOT SE 1 - H370: Causes damage to organs (lung) after inhalatory exposure. Since irreversibility cannot be excluded for some of the microscopic lesions found in the lungs (e.g. alveolar collapse, bronchiolar epithelial erosion or necrosis), classification with T; R39/23 according to Directive 67/548/EEC is appropriate.

Skin, Eye and respiratory irritation

The results of the skin (OECD 404) and eye irritation studies (OECD 405) in rabbits were negative and would raise the conclusion that no classification is needed for skin and eye irritation. In an acute inhalation test (OECD 403) all treated rats showed pulmonary lesions (see section on acute toxicity). Some of these effects should be considered as severe and especially it cannot be asserted that these effects are reversible. They are indicative of severe lung damage rather than just respiratory tract irritation, and are already covered by the proposed classification STOT SE 1 – H370 according to the CLP Regulation and T; R39/23 according to Directive 67/548/EEC.

Skin sensitisation

Six out of 20 guinea pigs showed a positive response in a Maximisation test (OECD 406). Therefore, acequinocyl should be classified as sensitising to the skin with Skin Sens. 1 - H317 according to the CLP Regulation and with Xi; R43 according to Directive 67/548/EEC. As this sensitisation can be achieved by intradermal induction higher than 1.0%, it can be qualified as “moderate” sensitiser according to CLP Regulation. This is covered by the generic concentration limit of 1%.

Repeated dose toxicity

Based on mortality, liver effects, haemorrhages and haematological effects (including effects on clotting) observed in several studies and several species at dose levels at or below the guidance levels, according to the CLP Regulation acequinocyl should be classified for specific target organ toxicity / repeated exposure as STOT RE 2 - H373 May cause damage to organs (blood) through prolonged or repeated exposure.

Based on effects in the longest studies in rats (104 weeks) and mice (80 weeks), classification for repeated dose oral toxicity at the effective dose level in comparison to the guidance levels according to Directive 67/548/EEC seems however not necessary. In addition, neither of the shorter repeated dose toxicity studies provides reasons for classification according to Directive 67/548/EEC.

Based on the dermal toxicity study in rats, classification for the dermal route according to Directive 67/548/EEC seems not necessary.

Mutagenicity

Results of *in vitro* tests such as Ames test, chromosome aberration test and TK gene mutation test, and *in vivo* micronucleus tests results were found negative. On the basis of these above results, acequinocyl is not considered genotoxic and thus does not need to be classified for mutagenicity.

Carcinogenicity

Neither in rats (OECD 453 oral study) nor mice (OECD 451 oral study), did acequinocyl show a carcinogenic potential. Thus, acequinocyl does not need to be classified for carcinogenicity.

Reproductive Toxicity

No fertility effects were observed in the available studies including a 2-generation study. Therefore, no classification for effects on fertility is proposed.

In a 2-generation reproduction study in rats, post-weaning adverse clinical and macroscopic effects (haemorrhages, discoloured and swollen body parts, pallor), and mortality were observed almost exclusively at the highest dose of 1500 mg/kg food. These effects were a direct consequence of pups consuming acequinocyl in the diet.

In a teratogenicity study in rats, 3 out of 246 pups had major abnormalities – all of a different nature - at high dose that also induced marked maternal toxicity including mortality. These were considered to be incidental findings.
In rabbits, a statistically significant increased incidence of 13th rib was observed in a teratogenicity study, at a dose that also induced marked maternal toxicity including mortality. These minor variations do not require classification.

Environmental hazard

The reported 48 hr EC50 for immobility of the water flea *Daphnia magna* (according to OECD 202) was 3.9 µg/L and the reported 96 hr EC50 on the marine mysid shrimp *Mysidopsis bahia* (according to OPPTS 850.1035) was 0.93 µg/L. In fish acute toxicity tests with four different species and in the algae growth test, no effects were observed up to the water solubility level.

Regarding the environmental classification according to the CLP Regulation, acequinocyl has reported EC50 values in crustaceans at concentrations lower than 1 mg/L and thus fulfils the criteria for classification as hazardous to the aquatic environment Acute category 1 - H400. Based on an EC50 value of 0.93 µg/L obtained for the marine crustacean *Mysidopsis bahia* in a 96-h flow-through study, it is concluded that an M-factor of 1000 should be applied.

Acequinocyl is considered not readily biodegradable according to the result of the OECD 301B (CO2 Evolution (Modified Sturm test)) test. Therefore, the additional information on degradation has been assessed and compared with the additional criteria for rapid degradation. In the water sediment study total mineralisation of acequinocyl was measured 30.2-32.6% after 100 days, one of the major metabolites formed, R1 (2-dodecyl-3-hydroxy-1,4-naphathalenedione) showed acute aquatic toxicity recorded with a 48hr-EC50 for the crustacean *Daphnia magna* equal to 13 µg/L (according to the DAR 2007) and thus meeting the criteria for classification. Therefore, based on the above, it can be concluded that acequinocyl is not rapidly biodegradable.

Acequinocyl has its log Kow > 6 and its solubility in water equals to 6.69 µg/L which may indicate some bioaccumulation potential. The measured BCF values for whole fish (according to OCDE 305E) were 366 at concentration in water of 0.17 µg/L and 288 µg/L at concentration in water of 1.7 µg/L (geometric mean: 327 L.kg-1). If these values were standardised to lipid content as recommended in the above mentioned guideline, the BCFs become 779 and 670 L.kg-1 (geometric mean: 724.5 L.kg-1), respectively. However, these values were based on total radioactivity and the chromatograms showed that acequinocyl and

its metabolite R1 were not present in fish tissue extracts indicating that both compounds were probably metabolised.

Based on the results of the substances' aquatic toxicity and the lack of rapid degradability it is concluded that acequinocyl also fulfils the criteria for classification as hazardous to the aquatic environment Chronic category 1 - H410.

Regarding the environmental classification according to Directive 67/548/EEC, acequinocyl has reported EC50 values in crustaceans at a concentration below 1 mg/L. The substance is not readily biodegradable, with a log Kow value above 3 and its BCF possibly above the threshold value of 100. Acequinocyl therefore fulfils the criteria for classification as dangerous for the aquatic environment and should be classified with N; R50/53.

As the lowest EC50 value for this substance is between 0.0001 and 0.001 mg/l (for *crustacea*) the following specific concentration limits based on Directive 67/548/EEC should be applied:

N; R50/53, $C \geq 0.025\%$

N; R51/53, $0.0025\% \leq C < 0.025\%$

R52/53, $0.00025\% \leq C < 0.0025\%$

Additional information

The Background Document, attached as Annex 1, gives the detailed scientific grounds for the Opinion.

ANNEXES:

Annex 1	Background Document (BD)[2]
Annex 2	Comments received on the CLH report, response to comments provided by the dossier submitter and rapporteurs' comments (excl. confidential information)

[2] The Background Document (BD) supporting the opinion contains scientific justifications for the CLH proposal. The BD is based on the CLH report prepared by a dossier submitter. The original CLH report may need to be changed as a result of the comments and contributions received during the public consultation(s) and the comments by and discussions in the Committees.