27.01.2010
CLH-O-0000000793-71-03/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 ("the CLP Regulation"), the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling of

Substance Name: ***Indium Phosphide***

EC Number: **244-959-5**

CAS Number: **22398-80-7**

The proposal was submitted by ***France***
and received by ECHA on ***02 June 2009***

PROCESS FOR ADOPTION OF THE OPINION

France 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/doc/consultations/cl/clh_axrep_france_indium_phosphide.pdf on ***12 June 2009***. MSCAs and parties concerned were invited to submit comments and contributions by ***27 July 2009***.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Bert-Ove Lund***
Co-rapporteur, appointed by RAC: ***Andrew Smith***

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 ***27 January 2010,*** in accordance with Article 37 (4) of the CLP Regulation, giving parties concerned the opportunity to comment. Comments received are compiled in Annex II.

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

OPINION OF RAC

The RAC adopted the opinion that ***indium phosphide*** should be classified and labelled as follows[1]:

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

Classification: **Carc. Cat. 2; R45**

Repr. Cat. 3; R62

T; R48/23

Specific concentration limits:

Conc. ≥0.1%	**Carc Cat 2; R45 T; R48/23**
0.01% ≤ Conc. < 0.1%	**Carc Cat 2: R45 Xn; R48/20**

Notes: **Note E**

Labelling: **T; R45 – 48/23 – 62; S45- 53**

Classification & Labelling in accordance with the Classification, Labelling and Packaging Regulation:

Classification: **Carc. 1B – H350**

Repr. 2 - H361f[2]

STOT RE 1 – H372 ("Causes damage to lungs through prolonged or repeated inhalation exposure")

Specific concentration limits:

Conc. ≥0.1%:	**Carc 1B-H350 STOT RE 1 - H372 ("Causes damage to lungs through prolonged or repeated inhalation exposure")**
0.01% ≤ Conc. < 0.1%:	**Carc 1B-H350 STOT RE 2 - H373 ("Causes damage to lungs through prolonged or repeated inhalation exposure")**

M-factors: None
Notes: **None**

Labelling: **GHS08; Dgr; H350, H361f, H372**

[1] Note that all hazard classes have not been evaluated.
[2] It is the view of RAC that hazard statement H361f is the most appropriate, given the available toxicological profile of indium phosphide, but RAC recognised that H361 could be applied if the available criteria are applied strictly.

Opinion on justification for need for action at Community level

In accordance with the REACH and CLP Regulations, the proposals to harmonise classification of indium phosphide for carcinogenic and reproductive effects do not require a special justification for action at Community level.

Indium phosphide is a "transitional substance", because the dossier was initially prepared under the old legislation (prior to REACH and CLP) with a view to it being considered by the TC C&L expert group. However, that group did not get to discuss it before responsibility for C&L was passed to ECHA. As the data on the high potency lung toxicity was already compiled, a proposal for a harmonised classification of indium phosphide for adverse effects on the lungs after repeated inhalation exposure was included in the submission to ECHA. RAC concluded that this was justified by the need to ensure consistent and helpful labelling for this substance. Application of labelling for repeated dose toxicity will enable information about the key route of exposure of concern to be provided. Provision of this information, about the lungs being a target organ following inhalation exposure, will further help protect against the toxicity/carcinogenicity of indium phosphide.

In relation to repeated dose toxicity, the complexities in deriving a specific concentration limit (SCL) for this endpoint were noted by RAC deliberations, and setting a harmonised SCL therefore also seems of importance for this substance.

SCIENTIFIC GROUNDS FOR THE OPINION

The opinion relates only to those hazard classes that have been reviewed in the proposal for harmonised classification and labelling, as submitted by France.

Carcinogenicity

Carcinogenicity studies in two species (rats and mice) gave clear and consistent evidence of carcinogenic activity in the lung in both sexes after inhalation exposure to very low concentrations of indium phosphide, and the criteria for Category 2 (in accordance with Directive 67/548/EEC) and Category 1B (in accordance with the CLP Regulation) are therefore met.

Based on the weight of available evidence, including the relatively low concentrations of indium phosphide needed to induce lung tumours in rats and mice, RAC is of the opinion that indium phosphide can be defined as a high potency carcinogen and that a Specific Concentration Limit (SCL) of 0.01% should be set. This is judged by RAC to be in accordance with the available guidance on setting SCLs for carcinogens.

No information opposing the proposal has been received in the public consultation.

Reproductive Toxicity

As to potential effects on fertility, there are no multi-generation reproductive toxicity studies available. However, repeated dose toxicity studies are available in hamsters via intra-tracheal instillation, and in mice and rats via inhalation. In the hamster study, the most important observation was a decreased sperm count, accompanied by decreased weights of testes and epididymes, as well as histopathological lesions in the testes. Indium phosphide was also shown to accumulate in the rat testis following inhalation exposure. On this basis of effects on

male reproductive organs observed in hamsters and of toxicokinetic data showing the potential for accumulation of indium in testis, the criteria for classification in Category 3 (in accordance with Directive 67/548/EEC) for reproductive toxicity (fertility) are met. Similarly, according to the criteria of the CLP Regulation, indium phosphide should be classified in Category 2 for reproductive toxicity.

No information opposing the proposal has been received in the public consultation.

Repeated dose toxicity

In addition to the harmonised endpoints mentioned above, repeated dose toxicity has been evaluated. In inhalation studies in rats and mice, consistent observations of severe lung toxicity have been reported. In addition, the toxicity occurred at very low levels of inhalation exposure, with mortality observed in mice exposed to 100 mg/m^3 for 14 weeks. Interstitial fibrosis was evident in mice from 1 mg/m^3 and in rats from 3 mg/m^3 in the 14 weeks studies, which is well below the classification cut-off values of 25 and 20 mg/m^3 (according to the criteria in Directive 67/548/EEC and CLP, respectively), thus warranting classification with T; R48/23 and STOT RE.1 H372. The recommended wording of H372 according to CLP is "Causes damage to lungs through prolonged or repeated inhalation exposure".

Fibrosis was noted in the 2 year mice study already at the 3 months interim sacrifice, and at very low exposure levels (0.03 mg/m^3) warranting a SCL of 0.1% and 0.01% for repeated dose toxicity, T;R48/23, STOT RE 1 H372 and Xn; R48/20, STOT RE 2 H373 (recommended wording: "May cause damage to lungs through prolonged or repeated inhalation exposure"), respectively.

No information opposing the proposal has been received in the public consultation.

Additional information

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

ANNEXES:

Annex 1 Background Document (BD).[3]
Annex 2 Comments received on the CLH report and response to comments provided by the dossier submitter (excl. confidential information).

[3] 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.