

## Industry Actions for Responsible Assessment and Classification of Cobalt Compounds – Reproductive Toxicity

The members of the Cobalt Institute (CI) and the Cobalt REACH Consortium (CoRC) have taken the decision to **self-classify** the following substances under the UN Globally Harmonized System for Classification and Labelling of Chemicals (UN GHS) as reproductive toxicants that may damage fertility (**Repr. 1B; H360F**) and are suspected of harming the unborn child (**Repr. 2; H361d**):

- Co dichloride (and its hydrates)<sup>1</sup> EC No. 231-589-4; CAS No. 7646-79-9  
CAS No. 7791-13-1
- Co sulphate (and its hydrates)<sup>1</sup> EC No. 233-334-2; CAS No. 10124-43-3  
CAS No. 10026-24-1; CAS 60459-08-7  
CAS 54887-51-3; CAS 13455-34-0
- Co diacetate (and its hydrates)<sup>1</sup> EC No. 200-755-8; CAS No. 71-48-7;  
CAS No. 6147-53-1
- Co carbonate<sup>1</sup> EC No. 208-169-4; CAS No. 513-79-1;  
EC No. 231-419-9; CAS No. 7542-09-8;  
CAS No. 51839-24-8
- Co dinitrate (and its hydrates)<sup>1</sup> EC No. 233-402-1; CAS No. 10141-05-6;  
EC No. 238-075-9; CAS No. 14216-74-1;  
CAS No. 10026-22-9
- Co(II) oxide EC No. 215-154-6; CAS No. 1307-96-6
- Co dihydroxide EC No. 244-166-4; CAS No. 21041-93-0
- Co lithium dioxide EC No. 235-362-0; CAS No. 12190-79-3
- Co(II) 4-oxopent-2-en-2-olate EC No. 234-855-6; CAS No. 14024-48-7
- Co oxalate EC No. 212-409-3; CAS No. 814-89-1
- Co propionate EC No. 216-333-1; CAS No. 1560-69-6
- Co borate propionate complexes EC No. 295-033-2; CAS No. 91782-61-5
- Co bis(2-ethylhexanoate) EC No. 205-250-6; CAS No. 136-52-7;  
EC No. 237-015-9; CAS No. 13586-82-8
- Co borate 2-ethylhexanoate complexes EC No. 295-032-7; CAS No. 91782-60-4

with the following comments,

- Using the UN GHS mixture rules, it is not foreseen to implement a specific concentration limit. Instead, the generic concentration limit should apply, resulting in all mixtures

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<sup>1</sup>Existing harmonised EU classification as Repr. 1B; H360F.

containing  $\geq 0.3\%$  of the above cobalt compounds carrying the same Repr. 1B; H360F classification (and mixtures containing  $\geq 3\%$  additionally carrying the developmental toxicity notation “d”).

- Companies are responsible for their own self-classification, labelling and communication within their supply chains (e.g. Safety Data Sheets), as appropriate for their products.

A list of classifications (including self-classifications) for each of these substances is available on the CoRC website (EU CLP<sup>2</sup> only) and CI website (according to UN GHS Model Regulations).

## BACKGROUND

There are 26 cobalt substances registered by the Cobalt REACH Consortium under the EU REACH<sup>3</sup> Regulation, with five of these substances<sup>4</sup> having harmonised classifications under the EU CLP Regulation as Repr. 1B; H360F (may damage fertility); and a sixth substance (Co metal) proposed for classification as Repr. 1B; H360F. Considering the existing reproductive toxicity classifications (indicating a potential hazard at high doses), the CI and CoRC have developed a read-across and grouping approach with the aim of predicting the potential for systemic bioavailability of the remaining cobalt compounds. The prediction is based on *in vitro* measurements of surrogate bioavailability (“bioaccessibility”) and short-term repeated-dose *in vivo* data. Substances are then grouped according to their toxicological properties, with classifications read across within a group, avoiding numerous long-term toxicity studies in animals.

The read-across group associated with the reproductive toxicity hazard consists of substances that show high bioavailability or high bioaccessibility in gastric fluid and contains the substances with harmonised/proposed harmonised classifications for reproductive toxicity – all of which are known or predicted to demonstrate a leading toxicological effect associated with the Co<sup>2+</sup> ion. The substances in this classification update show a high measured bioaccessibility (matched with high and moderate *in vivo* bioavailability in the case of Co dichloride and Co lithium dioxide, respectively; and upregulation of red blood cell parameters in a 28-day repeated-dose toxicity study with Co acetyl acetonate) and were therefore placed in the highly bioaccessible group. As a result, the members of the CI and CoRC have taken the decision to self-classify Co (II) oxide, Co dihydroxide, Co lithium dioxide, Co(II) 4-oxopent-

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<sup>2</sup> EU Regulation on Classification, Labelling and Packaging of substances and mixtures

<sup>3</sup> Registration, Evaluation, Authorisation and Restriction of Chemicals

<sup>4</sup> Five ‘soluble cobalt salts’: Co sulphate, Co dichloride, Co dinitrate, Co carbonate, Co diacetate (and respective hydrated forms)

2-en-2-olate, Co oxalate, Co propionate, Co borate propionate, Co bis(2-ethylhexanoate) and Co borate 2-ethylhexanoate under UN GHS as **Repr. 1B; H360F** by read-across from Co dichloride.

The CoRC has also conducted testing for the developmental toxicity endpoint under EU REACH. A first species (rat) pre-natal developmental toxicity (PNDT) study was conducted with Co dichloride as the source substance of the highly bioavailable/bioaccessible group. A lack of developmental toxicity was observed in this study, which triggered the need for testing in a second species according to the REACH Regulation. A second species (rabbit) PNDT study was then performed, using Co dichloride as the test substance. It was apparent that administration of the substance led to dose-dependent maternal gastrointestinal (GI) irritation, decrease in food consumption and decrease in body weight, leading to maternal mortality at high doses. An increase in foetal mortality was observed at doses toxic to the maternal animals. No increase in skeletal or soft tissue malformations were observed (no teratogenic potential). The available data were not adequate to exclude the possibility of developmental toxicity. Therefore, based on the results of the second species PNDT study, the members of the CI and CoRC have taken the decision to self-classify Co dichloride under UN GHS as **Repr. 2; H361d**. The members of the CI and CoRC have also taken the decision to self-classify Co sulphate, Co diacetate, Co carbonate, Co dinitrate, Co(II) oxide, Co dihydroxide, Co lithium dioxide, Co(II) 4-oxopent-2-en-2-olate, Co oxalate, Co propionate, Co borate propionate complexes, Co bis(2-ethylhexanoate) and Co borate 2-ethylhexanoate complexes under UN GHS as **Repr. 2; H361d** on the basis of read-across from Co dichloride.

The overall reproductive toxicity classification for the substances in this classifications statement is: **Repr. 1B; H360Fd**.

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