Minority opinion regarding the classification of lithium hydroxide as Repr cat 1 for fertility and development

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This minority opinion concerns the classification of lithium hydroxide to reproductive cat 1B for fertility and to 1A for development based on the data from soluble lithium salts (mainly lithium carbonate). There are uncertainties related to the read across from lithium carbonate to lithium hydroxide due to lithium hydroxide's corrosive properties and consequently the potential to reach high enough doses of the lithium cation to induce reproductive toxicity. As also noted in RAC opinion, even very diluted solutions of lithium hydroxide have a high pH around 13.0, which may result in corrosivity. Since there is no in vivo repeated dose toxicity data on lithium hydroxide it is not possible to verify the dose levels that can be repeatedly given to animals without resulting in local (e.g. gastrointestinal) toxicity. Although classification is based on intrinsic hazardous properties and not risk based considerations, reproductive effects occurring only at the dose levels causing clear general toxicity are not considered relevant for classification. Reproductive toxicity occurring at doses showing signs of general toxicity can also justify the lowering of hazard category from cat 1B to 2.

According to classification criteria, classification to cat 1 should be based either clear evidence on human epidemiological data or on clear evidence of adverse reproductive effects in animals in the absence of other toxic effects. If there are some evidence from humans or experimental animals, but the evidence is not sufficiently convincing to place the substance in Category 1 or there are deficiencies in the available dataset making the quality of evidence less convincing, Category 2 could be the more appropriate classification. In the case of lithium hydroxide, there are uncertainties related to its potential to reach high enough systemic doses of lithium to result in reproductive toxicity. According to my view, these uncertainties make the evidence less convincing and should – according to the CLP criteria – result rather to cat 2 classification than to cat 1 classification. It should be also noted that animal fertility data on lithium carbonate/chloride is not fully consistent either; guideline based GLP study was not showing any fertility effects at dose levels in which effects were seen in non-guideline studies with limitations in the conduct and reporting of the study. Thus, even the classification of carbonate and chloride for fertility can be considered as a borderline between cat 2 and cat 1B. The same applies also to developmental toxicity since the developmental toxicity data in animals remained negative, and human epidemiological evidence on the developmental effects is not very strong, either. These combined with uncertainties in the applicability of read across approach to lithium hydroxide makes classification of lithium hydroxide to repr cat 1B for fertility and repr cat 1A for development unjustified. Instead of cat 1 classification, cat 2 for both fertility and development should be considered.