25 October 2023

SUMMARY REPORT OF THE 26th ED EXPERT GROUP MEETING

The 26th ED EG meeting took place on 3-4 October 2023. The EG provided scientific advice on ED assessments of three REACH substances and of one biocidal active substance.

The meeting was attended by 61 participants (both in person and online) representing 16 Member States and EEA countries (AT, BE, CZ, DK, DE, ES, FI, FR, IE, IT, LT, NL, NO, SE, SI, SK), Switzerland, European Commission and 7 accredited stakeholder organisations (CHEM Trust, Cefic, Concawe, CropLife Europe, ECETOC, EEB, PETA Science Consortium International e.V.).

Main outcomes of the substance discussions

Closed session

- [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (1,3-bis-TBP) (CoRAP 2015, follow-up evaluation): The presented ED assessment focused on thyroid modality, and the experts considered that in the OECD TG 443 with rats the observed effects on T4 (thyroxine) and TSH (thyroid stimulating hormone) were sufficient to conclude that there is T-mediated activity, which is relevant for both ED HH and ED ENV. The experts thought that the effects on auditory startle reflex are treatment related and cannot be dismissed. The observed effects on thyroid gland were considered as representing T-mediated adversity. Auditory startle and brain effects were considered supportive as they are considered "sensitive to" but not diagnostic of T-modality. In the experts' view there were no indications of non-human relevance, and the pattern of all T-modality related effects observed in experimental animals, e.g. causing behavioral changes, were considered as population relevant. The experts thought that the substance may be a suitable candidate for harmonised classification as ED cat. 1 for both HH and ENV.

- 3-(3,4-dichlorophenyl)-1,1-dimethylurea (diuron) (biocidal active substance): Regarding ED for ENV assessment, several studies with fish are available. While most experts considered the FSDT (Fish sexual development test, OECD TG 234) using zebrafish as not reliable enough to conclude on the ED properties of diuron, further data with clear indications of EAS concern (e.g. skewed sex ratio) were presented from studies on several other fish species. The experts advised that the data are sufficient to identify diuron as ED for non-target organisms although some uncertainties on the exact endocrine mode of action remain. Regarding ED for HH assessment, the effects seen in carcinogenicity studies were considered adverse, but it was not possible to conclude if they were caused by an endocrine mode of action. The possibility to read across with the structurally similar linuron was raised but was reported to be challenging. Some experts supported the proposal of conducting *in vitro* mechanistic studies to explore the potential endocrine mode of action but acknowledged that this might not sufficient (e. g., involvement and cross-talk of other receptors such as aryl hydrocarbon receptor). A number of experts also considered further *in vivo* testing might address the data gap, but concerns were raised about conducting additional animal testing of diuron since the substance already has a harmonised classification of Carc. 1B.

Open session

- Butanoic acid, 4-amino-4-oxosulfo-, N-coco alkyl derivs., monosodium salts, compds. with triethanolamine (CoRAP 2023): Many of the ED EG members were of the opinion that the substance is a potential anti-androgen, albeit other modalities may be involved and that further testing is needed to clarify the concern. Different studies were suggested, including *in vitro* tests, PNDT (prenatal developmental toxicity study, OECD TG 414), long term fish study and EOGRTS (Extended One-Generation Reproductive Toxicity Study, OECD TG 443) as well as repeating the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) at higher dose level.

- Dioctyltin oxide (DOTO) (planned CoRAP 2024): The presented preliminary ED assessment suggested several different endocrine modes of action (MoA). The data on the MoA via glucocorticoid receptor leading to thymus effects was considered as the most advanced while the experts suggested to look more also into RXR (retinoid X receptor) and PPAR (peroxisome proliferator activated receptor) data in invertebrates as well as using e.g. aromatase inhibition data in rodents for the assessment of non-target organisms.

General ED-related topics

ECHA presented a summary of the ongoing discussions on the ED EG's role in supporting RAC (Risk Assessment Committee) on the classification of ED substances and gave an update on the CLP guidance revision.

The next ED EG meeting will be held online on 14 November.

25 October 2023

Substances discussed at the 26th ED EG meeting:

MS	EC#	Substance name	Outcome of the discussion	Session	Notes
NL	246-678-3	[1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (1,3-bis-TBP)	ED HH ED ENV	Closed	CoRAP 2015
DK	206-354-4	3-(3,4-dichlorophenyl)-1,1-dimethylurea (diuron)	ED ENV	Closed	Biocidal active substance
FR	308-662-5	Butanoic acid, 4-amino-4-oxosulfo-, N-coco alkyl derivs., monosodium salts, compds. with triethanolamine	Testing needed	Open	CoRAP 2023
AT	212-791-1	Dioctyltin oxide (DOTO)	Refine assessment	Open	Planned CoRAP 2024