AGREEMENT OF THE MEMBER STATE COMMITTEE

ON THE IDENTIFICATION OF

PHENOL, ALKYLATION PRODUCTS (MAINLY IN PARA POSITION) WITH C12-RICH BRANCHED ALKYL CHAINS FROM OLIGOMERISATION, COVERING ANY INDIVIDUAL ISOMERS AND/ OR COMBINATIONS THEREOF (PDDP)

AS SUBSTANCES OF VERY HIGH CONCERN

According to Articles 57 and 59 of

Regulation (EC) 1907/2006[1]

Adopted on 16 June 2021

This agreement concerns

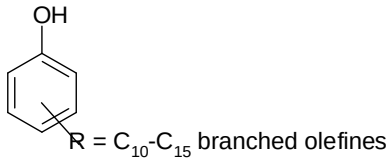
Substance names: Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP)

EC number: -

CAS number: -

Molecular formula: n.a. (UVCB[2])

Structural formula:



[1]Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC

[2] Substances of Unknown or Variable composition, Complex reaction products or Biological materials

Germany presented a proposal in accordance with Article 59(3) and Annex XV of the REACH Regulation (2 March 2021) on identification of *Phenol, alkylation products (mainly in para position) with C12-rich branched or linear alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP)* as substances of very high concern due to their toxic for reproduction properties and endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and the environment which give rise to an equivalent level of concern to those of other substances listed in paragraphs (a) to (e) of Article 57 of REACH Regulation.

The Annex XV dossier was circulated to Member States on 10 March 2021 and the Annex XV report was made available to interested parties on the ECHA website on the same day according to Articles 59(3) and 59(4).

Comments were received from both Member States and interested parties on the proposal.

Regarding the scope of the proposal, during the process the substance identity was changed, in response to a comment received in consultation, to exclude linear alkyl chains to *Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP).*

The dossier was referred to the Member State Committee on 24 May 2021 and discussed in the meeting on 14-17 June 2021 of the Member State Committee.

Agreement of the Member State Committee in accordance with Article 59(8):

Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP) are identified as substances meeting the criteria of Articles 57 (c) and 57 (f) of Regulation (EC) 1907/2006 (REACH) because they are substances with toxic for reproduction properties and endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and the environment which give rise to an equivalent level of concern to those for other substances listed in paragraphs (a) to (e) of Article 57 of REACH Regulation.

UNDERLYING ARGUMENTATION FOR IDENTIFICATION OF SUBSTANCES OF VERY HIGH CONCERN

Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP) are identified as substances of very high concern in accordance with Articles 57(c) and 57(f) of Regulation (EC) 1907/2006 (REACH) because of their toxic for reproduction properties and their endocrine disrupting properties for which there is scientific evidence of probable serious effects to the environment and human health which gives rise to an equivalent level of concern to those for other substances listed in points (a) to (e) of Article 57 REACH.

References to PDDP in this agreement include all the group members as described in Chapter 1 of the Support Document. The substances thus covered include, among others, the registered substance phenol, dodecyl-, branched (PDB, EC 310-154-3, CAS 121158-58-5). Further examples of substances in the scope of this agreement are given in section 1.2 of the Support Document. The conclusions drawn are mainly based on data from PDB but apply to all substances in scope of this agreement.

CMR assessment

PDB is covered by index number 604-092-00-9 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class reproductive toxicity category 1B (H360F[3]). In its respective opinion[4] on the dossier proposing harmonised classification and labelling of 5 December 2013 the Risk Assessment Committee (RAC) states that "the harmonised classification will apply to any substance which predominantly contains C12 (branched) alkyl-substituted phenols". Therefore, it can be concluded that PDDP meets the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH) owing to its classification in the hazard class reproductive toxicity category 1B[5].

Art 57(f) assessment

ED assessment

PDDP are proposed to be identified as substances of very high concern in accordance with Article 57(f) of Regulation (EC) 1907/2006 (REACH) because of their endocrine

[3] H360F: 'May damage fertility'

[4] https://echa.europa.eu/documents/10162/7e7b5949-9d0a-2896-fb10-1504496ab2eb

[5] Classification in accordance with section 3.7 of Annex I to Regulation (EC) No 1272/2008.

disrupting properties for which there is scientific evidence of probable serious effects to human health and the environment which gives rise to an equivalent level of concern to those of other substances listed in points (a) to (e) of Article 57 REACH.

Considering the results of all available studies, there is strong evidence that the adverse effects on fertility and sexual function (which led to classification of the substance as Repr. 1B), particularly in females, are due to the oestrogenic activity of PDDP. Mechanistic *in vitro* studies demonstrate oestrogen receptor (ER) binding and activation by PDDP (OECD level 2). The increase in uterus weight (as seen in two uterotrophic assays) and accelerated vaginal opening (as seen in four female pubertal assays and a two-generation study) are highly diagnostic parameters for oestrogenicity. Furthermore, reduced ovary weight, decreased corpora lutea and prolongation of the oestrus cycle were consistently observed in the majority of OECD Level 4 and 5 studies. Reproductive toxicity studies (OECD level 5) further demonstrated impacts on copulation index and apical fertility endpoints (decreased number of implantations and litter size). All of the above-mentioned parameters are considered as either EATS (oestrogeno-, androgeno-, thyroido-, and steroidogenesis)-mediated or sensitive to EATS modalities (OECD, 2018), and the overall observed effect pattern of PDDP is congruent with that of known model oestrogens.

In conclusion, there is strong evidence that the adverse effects on fertility and sexual function, particularly in females, are plausibly linked to the oestrogenic activity of the substance. Therefore, it is concluded based on the weight of evidence that PDDP is an endocrine disruptor with regard to human health according to the WHO/IPCS definition (as interpreted by the JRC Endocrine Disruptor Expert Advisory Group, 2013).

The evaluation of PDDP for the environment is based on mammalian data and supported by available fish *in vitro* tests and adverse outcome pathways. There are no aquatic *in vivo* long term data for fish and other aquatic vertebrates or investigations for endocrine disruption (ED) available. As effects on growth, development and reproduction in single species are generally regarded relevant for the maintenance of wild populations, the observed effects on reproduction and pubertal development in rats are relevant for mammalian populations in the environment. Therefore, it is concluded based on the weight of evidence that PDDP is an endocrine disruptor for the environment.

Equivalent level of concern assessment

Based on the above conclusion, evidence that PDDP is of an equivalent level of concern includes:

The effects of PDDP on mammals are considered to be of equivalent level of concern as those of CMR Cat 1, PBT or vPvB substances due to the severity and irreversibility of the effects on organisms and populations and the difficulties to quantify a safe level of exposure in the environment. Environmental effects observed after exposure to PDDP are considered to impair population stability and recruitment. The effects may influence a wide range of taxa in different ecosystems due to conservation of the reproductive endocrine system. For most species in the environment no data on endocrine effects that are caused by the substance are available. Furthermore, the organisms in the environment are exposed to a mixture of substances. Hence there can be additive or synergistic effects that might enhance the impact. For example, additive effects were seen for mixtures of long chain alkyl phenols and other estrogenic compounds like E2 (17β-Estradiol) and EE2 (17α-Ethinylestradiol). Increased sensitivity in an *in vitro* test was seen using 4-DPM (4-Dodecylphenol (mixture of isomers)) with co-exposure to E2 indicating enhanced mixture effects. Between exposure and effects might be a long time, which also hinders the derivation of a safe effect level.

PDDP severely affects reproduction and development-related processes in organisms. Different aspects of reproduction are affected such as decreased copulation index and impairment of fertility which are important for population stability. Furthermore, PDDP caused a developmental effect in term of precocious puberty in females in pubertal assays and in the two-generation study. This is also of environmental importance as a similar effect could appear regarding seasonal maturation of gonads. Many fish species exhibit seasonal maturation and reproduction cycles. Reproduction and rearing of offspring are energy demanding processes where enough food must be available. Mostly it is connected to a short time frame given by environment. If these energy demanding processes fall out of this time frame due to e.g. precocious puberty this could entail adverse effects on populations.

Thus, in summary, effects in mammals are relevant and serious for the environment. They are considered to be of equivalent concern due to the severity of the effects and the difficulties to quantify a safe level of exposure for oestrogen-like endocrine disruptors.

Therefore, it is concluded that the substances *Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof (PDDP)* meet the criteria of Articles 57(c) and 57(f) of REACH, due to their toxic for reproduction properties and their endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and the environment which give rise to an equivalent level of concern to those for other substances listed in paragraphs (a) to (e) of Article 57 of REACH Regulation.

Reference:

Support Document (Member State Committee, 17 June 2021)