baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

HAZARD ASSESSMENT

OUTCOME DOCUMENT

for

p-(1,1-dimethylpropyl)phenol

EC No 201-280-9

CAS No 80-46-6

Member State(s): Germany

Dated: 15 June 2016

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Version 1.3

1. HAZARD SUBJECT TO ASSESSMENT

p-(1,1-dimethylproply)phenol (ptPP) was originally selected for hazard assessment in order to clarify suspected hazard properties:

Endocrine Disruption with regard to the environment

2. OUTCOME OF HAZARD ASSESSMENT

The available information on the substance and the hazard assessment conducted has led the assessing Authority to the following considerations, as summarised in the table below.

Hazard Assessment Outcome	**Tick box**
According to the authority's assessment the substance is not an ED in accordance with the WHO (2002) definition based on the currently available information.	
According to the authority's assessment the substance is an ED in accordance with the WHO/IPCS (2002) definition.	✓
According to the authority's assessment further information would be needed to confirm the ED properties but follow-up work is not relevant or carried out at present.	

This outcome is based on the REACH and CLP data as well as other available relevant information.

3. BASIS FOR REASONING[1]

For ptPP several in vitro and in vivo studies are available which clearly show that ptPP acts as an estrogen agonist both in vitro and in vivo. In vivo data for several fish species show that this alteration of the function of the endocrine system results in adverse effects in intact organisms. They provide a clear link between the mode of action and the adverse effects observed. Data for other fish species substantiate the estrogen mode of action and adverse effects observed fit to this mode of action:

Available in vitro data show, that ptPP is able to bind to the estrogen receptor and activate it:

- All in vitro receptor binding studies showed that ptPP binds to the estrogen receptor in fish and rat and binds to sex steroid binding proteins in fish. The relative binding affinity in the studies with rainbow trout estrogen receptors ranged from 4E-5 to 7E-5

[1] Assessments of ED properties are based on the WHO/IPCS definition of an endocrine disruptor.

"An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations."

WHO/IPCS Report 2002: Global Assessment of the state-of-the-science of Endocrine disruptors, Executive Summary (Chapter 1) page 1 section 1.1

Under the REACH Regulation endocrine disruptors may be identified in accordance with Article 57(f) on a case-by-case basis as substances of very high concern (SVHCs), where there is scientific evidence of probable serious effects to human health or the environment, which give rise to an equivalent level of concern to CMR or PBT/vPvB substances.

and the RBA for the sex steroids was in a similar range.

- Studies analyzing vitellogenin induction demonstrated that exposure to ptPP resulted in a dose-dependent increase in vitellogenin expression levels with a range of 3.3E-5 to 1E-4. Liver slice gene expression showed vtgmRNA induction. All reporter gene assays available show, that ptPP acitivate human and fish estrogen receptor. The relative potency was higher for fish receptors than for human receptors.

Available in vivo data with 5 fish species show the estrogen mode of action results in severe adverse effects in fish:

- Changes of sex-ratios towards less males, increased number of females or undifferentiated fish or sex-reversal of genetic males was observed for *P.promelas*, *D.rerio* and *O.latipes* and – less comparable - in *C. carpio*. This endpoint is considerd to be indicative for an estrogen agonist mode of action and is an apical adverse effect. Other effects observed for these species substantiate the estrogen mode of action. Adverse effects observed fit to this mode of action.

- Indication of an estrogenic mode of action is available for one additional species (*C. variegatus*) for which no apical endpoints were assessed.

Compared to 4-nonylphenol and 4-tert-octylphenol, 4-tert-pentylphenol resulted in similar effects in *P.promelas, D.rerio*, and *O.latipes*. Some effects occurred at similar concentrations while for some endpoints concentrations causing effects were up to factor 100 higher.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

Indication of a tentative plan is not viewed as a commitment by the authority. Any commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Follow-up action	Date for intention	Actor
SVHC Dossier due to endocrine disruption for the environment	August 2016	Germany