



October 2011

CHEM Trust comments on 4-(1,1,3,3-tetramethylbutyl)phenol or (4-tert-octylphenol) - referred to as octylphenol (OP)

http://echa.europa.eu/consultations/authorisation/svhc/svhc_cons_en.asp

[A] General Comments on the Annex XV dossier:

CHEM Trust supports the inclusion of 4-(1,1,3,3-tetramethylbutyl)phenol also known as (4-tert-octylphenol) which is referred to as 'octylphenol' as a SVHC in the REACH candidate list based on the evidence presented that shows it to be a substance having endocrine disrupting properties. However, CHEM Trust considers that it should be determined as having ED (endocrine disrupting) properties of relevance for both the environment and human health.

[B] Specific comments on Part I 'Justification' Environment – Chapter 6.2.1

The justification for this chemical having endocrine relating properties that give rise to probable serious effects on the environment and an equivalent level of concern as other Article 57 chemicals, such as CMRs and PB(T)s is well presented. We consider that it is particularly the likelihood of delayed irreversible effects due to endocrine disrupting chemicals de-railing normal development during sensitive windows of exposure that gives rise to equivalent levels of concern as the PB(T) chemicals. This is because effects may not become evident until the animal reaches maturity, such that, like the vPvB chemicals, if adverse effects do come to light in future they will be ongoing for many years.

We understand the approach taken in the dossier with regard to leaving open some of the issues relating to the criteria, but it needs to be made very clear that potency should not play a part in the identification of a chemical with ED properties. It is only the intrinsic properties of ED that must be fulfilled. Consideration of the potency is only possible at a later stage when the risk management is considered.

We consider that this chemical is a potent ED in wildlife, however, this should not set a precedent that such a high degree of potency is required for subsequent chemicals, because as noted above, potency should not be considered at this stage. Furthermore, discussions on lead effect are also not appropriate. (For more detailed argumentation, please see the enclosed document from CHEM Trust which had significant input from WWF-European Policy Office “CHEM Trust’s Contribution to the Ongoing Debate on Criteria for EDCs – September 2011”).

Page 143:

CHEM Trust does not agree that “a substance should fulfill at least the definition of an ED provided by IPCS/WHO in order to be considered as of equivalent concern based on ED properties. The legal wording is “having endocrine disrupting properties.” The problem of the IPCS/WHO definition is that it requires considerable data to prove the exact mechanism behind an adverse effect. It can take years to establish this and while this is rather clear for octylphenol which has been well investigated, this should not be the level of proof required for all future EDs. Moreover, the IPCS definition requires ‘consequently causes adverse effects’ whereas the legal text of REACH requires ‘probable serious effects’. Here it can be seen that the word ‘probable’ allows some degree of uncertainty. It is imperative that the requirements of the legal text are used rather than some other definition. (Again, see aforementioned position paper – “CHEM Trust’s Contribution to the Ongoing Debate on Criteria for EDCs – September 2011”)

CHEM Trust considers that the data is well presented to show OP has ED properties in many species including fish, amphibians and invertebrates.

Human health – Chapter 6.2.2

CHEM Trust considers that it would be better to re-structure this chapter and not mix the discussion on potency and lead effect with the identification of the ED properties. There are normally no potency considerations in the identification of CMRs, where instead it is based on the level of evidence, so it is inappropriate to include potency considerations in the identification of ED properties. Furthermore, neither the IPCS/WHO definition, nor the OECD draft Guidance document requires any consideration of the potency of the chemical for it to be determined to have ED properties.

CHEM Trust considers that the data presented provide clear evidence that octylphenol does exhibit ED properties in vitro and in vivo. As the prepubertal oral uterotrophic study (Laws et al., 2000) showed an increase in uterine weight this is a clear indication of ED properties in an intact animal, which is of relevance for adverse effects in young girls.

The LOEL was lower using the s/c (subcutaneous) route of exposure which indicates that when there are exposure routes that bypass metabolism there should be added concern for estrogenic effects. We consider that information gained using the s/c route of exposure should inform the overall assessment.

CHEM Trust considers that given the conservation of the endocrine system in the evolution of vertebrate animals, the default should be to assume that a chemical with ED properties in one vertebrate species will also have such properties in others. If data contradict this, then the possible reasons should be examined. For example, in fish it can be seen that OP is clearly active as an ED. However, aqueous exposure of fish is via uptake through the gills and skin, which essentially bypasses metabolism in the small intestine and liver, and allows direct entry to the blood stream. Therefore, it is possible to visualize a scenario in which the endocrine activity of a substance can be markedly decreased by metabolism after oral exposure. This could lead to no or little endocrine related findings in the oral studies in mammalian animals, whereas endocrine activity may manifest itself in fish where the substance is not metabolized before reaching the site of action or the relevant organ. If this were the case with OP, then the oral exposure of mammals would not be representative of the inhalation or dermal routes of exposure, which also bypass metabolism. There are no data for either exposure routes for this chemical, and without such data – it should certainly not be concluded that this is not a potent ED chemical in humans. It is noted that this chemical is found in dust and in biomonitoring of housekeepers, suggesting that inhalation is a route of concern. Moreover, it is also found in textile workers suggesting that either or both dermal and inhalation exposure may be important. We note that OP is found in many imported textiles, such that dermal exposure should be a concern.

With regard to a related chemical, there was a discussion many years ago under the Existing Substances Regulation, where there was concern for a potential risk with regard to the use of nonyl phenol ethoxylate, because it was suggested that the dermal application of a de-greasing hand cleaner might result in significant exposure to nonyl phenol, a related compound. This highlights the need to consider the likely effects from dermal exposure and the precedent for this.

An alternative explanation for the low potency for ED effects seen in oral studies might be either that too high a dose had been used, or that the tests used were not sensitive enough. CHEM Trust suggests that when OECD study results are discussed, the year that the study was conducted should always be noted. This is because, for example, it might be that a chemical had been tested using the 2-Gen (TG416) which was in use prior to the last update in 2001, when it was made more sensitive to chemicals with ED properties. It should also be noted that even this 2001 updated version of the TG416 is still missing many important end points which would make it more sensitive for ED.

We consider that the most likely explanation for the results which indicate lower potency for ED in oral studies in rodents is that there is some metabolism in the gut. CHEM Trust therefore considers that the activity in mammalian animals using the subcutaneous route should indeed be taken into account, particularly as it is found in humans in some biomonitoring studies, and dermal and inhalation exposure via dust is likely. Nevertheless, we stress that potency considerations are not relevant for the identification of ED properties.

It should also be recognized that for potency considerations, test methods for ED effects need to be improved. For example, given the effects of estrogenic compounds on the mammary gland, we consider that tests need to be further improved with regard to including looking for effects of chemicals with ED properties on the mammary gland of both females and males. This is because in some chemicals tested to date, mammary gland development in males and females is altered at lower doses than the levels that cause changes in other tissues. The effects that have been observed after disrupted mammary gland development include impaired lactation and increased susceptibility to cancer, both of which are of potentially great public health significance. Key gaps in testing include lack of early life exposure in tests for carcinogenic effects; lack of assessment of lactation function other than nonspecific measures; and inadequate examination of mammary gland morphology and pathology.

Therefore overall, we consider that there are sufficient data for OP to be considered to have ED properties relevant for both the environment and human health.

Attachment (additional non-confidential information)

**CHEM Trust's Contribution to the Ongoing Debate on Criteria for EDCs –
September 2011**