HAZARD ASSESSMENT

OUTCOME DOCUMENT

for

Substance name

EC No 202-716-0

CAS No 98-95-3

Member State(s): Austria

Dated: 17 November 2015

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1. HAZARD SUBJECT TO ASSESSMENT

Nitrobenzene is on the short list 2015 established by ECHA under the common screening approach for REACH and CLP processes. Nitrobenzene has been listed because of its possible endocrine disrupting (ED) properties and selected by Austria for manual screening.

Thus, nitrobenzene was selected for hazard assessment in order to clarify suspected hazard properties: ED.

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.	x

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

3. BASIS FOR REASONING[1]

The adverse effects of nitrobenzene on testis (i.e. atrophy of the seminiferous epithelium, severe reduction of sperm numbers, testicular atrophy) and the resulting infertility of male animals (rat and mouse) is demonstrated by different animal studies. The harmonised classification of nitrobenzene as Repr. 1B substance reflects the adversity of the substance.

It has been shown that nitrobenzene has specific adverse effects on Sertoli cells, which are responsible to nourish the developing sperm cells and which secrete different hormones, including inhibin, which belongs to the hypothalamic-pituitary-gonadal axis (HPG-Axis). Further mechanistic investigations show that inhibin secretion of sertoli cells is increased due to nitrobenzene exposure: Inhibin levels were altered in sertoli cell systems exposed to nitrobenzene (ex vivo study) and also in seminiferous tubules cells of the testis when the rats were orally exposed to 300 mg/ kg bw nitrobenzene (in vivo study). These observations give some indication that nitrobenzene may have an endocrine disrupting potential.

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[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.

For the environment the available data are deemed to be insufficient for the identification of an endocrine disruptor for the environment.

AT presented the case in the Endocrine Disruptor Expert Group. In summary, no clear support has been provided for the identification of nitrobenzene as an endocrine disruptor. The majority of responses judged increased inhibin secretion as such as an endocrine mode of action, but stated that the available data are too limited to clearly identify nitrobenzene as endocrine disruptor. Some comments hypothesized that inhibin alteration might be secondary to a non-endocrine mode of action.

In principle, substance evaluation could be considered in order to require further testing for clarifying the endocrine disrupting effects. However, it does not seem justified to propose a substance evaluation process for this clarification, taking into consideration that this process would require considerable additional efforts, including testing and time, but would provide comparatively little additional benefits for risk management in this specific case. Nitrobenzene is already classified as Repr. 1B, and thus risk management measures could be taken on the basis of present knowledge without further delay.

Moreover, it needs to be acknowledged that the major volume of nitrobenzene is presently used as an intermediate.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

A RMOA analysis has been carried out by AT in parallel to the ED EG group consultation, since nitrobenzene is harmonised classified as Repr. 1 B (H360F). Based on the outcome of the performed analysis, taking into account also non-hazard criteria (use, volume, exposure), AT has submitted an Annex XV (SVHC) dossier (according to REACH Regulation, article 57 (c)), which is deemed a necessary further risk management option irrespectively of the not yet clarified ED hazard properties.

Follow-up action	Date for intention	Actor
RMOA	Already submitted	Austria
SVHC	Submission in August 2015	Austria