



**Committee for Risk Assessment
RAC**

Annex 2
Response to comments document (RCOM)
to the Opinion proposing harmonised classification and
labelling at EU level of

Benzoic Acid

**EC number: 200-618-2
CAS number: 65-85-0**

ECHA/RAC/CLH-O-0000001687-65-02/A2

**Adopted
25 November 2012**

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

[ECHA has compiled the comments received via internet that refer to several hazard classes and entered them under each of the relevant categories/headings as comprehensive as possible. Please note that some of the comments might occur under several headings when splitting the given information is not reasonable.]

Substance name: Benzoic acid
CAS number: 65-85-0
EC number: 200-618-2

General comments

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
2011/10/14	Germany/ AffiliatedWithOrganisation / Company-Downstream user / MENNO Chemie-Vertrieb GmbH, Norderstedt, Germany	MENNO Chemie-Vertrieb is the data submitter and authorisation holder for the use of benzoic acid as plant protection product and biocide, but not a manufacturer.	Noted.	Noted.
2011/10/14	United States/ BehalfOfAnOrganisation/ Company-Manufacturer/ Emerald Kalama BV (Formerly DSM/DSP)	DSP/DSM was the lead registrant for benzoic acid. Emerald Kalama BV is now the owner of this business. On a general point we note the RMS has references significant data not directly summarised within the REACH Registration dossier, and hence have proactively undertaken a re-review of existing data on benzoic acid and will be submitting this as a spontaneous update of the Registration in the coming months.	The data evaluation by the dossier submitter was initially prepared in the framework of directives 91/414/EEC and 98/8/EC.	Noted.
2011/10/14	France / Member State	FR agrees with the proposed classification for benzoic acid of Skin Irrit. 2/H315 and Eye Dam. 1/H318.	Thank you for the support.	Noted.
2011/09/12	Spain / Member State	We are in agreement with the environmental classification proposal submitted by DE.	Thank you for the support.	Thanks for the support.

Carcinogenicity

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		No comments provided		

Mutagenicity

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		No comments provided		

Toxicity to reproduction

/Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		No comments provided		

Respiratory sensitisation

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC response to comment
2011/10/14	United States/ BehalfOfAnOrganisation/ Company- Manufacturer/ Emerald Kalama BV (Formerly DSM/DSP)	Page 33 section 5.3.3 Respiratory irritation. We note the assessments drawn by the RMS based upon the data set available. In the REACH Registration dossier the lead registrant proposed classification as a respiratory irritant as follows: STOT Single Exp. 3 (Hazard statement: H335: May cause respiratory irritation). Affected organs: Lungs. Route of exposure: Inhalation. We note the comments on this being due to the physicochemical nature of the substance, however, our experience with manufacturing and handling this substance in a powder form leads us to consider this applicable and warranted.	The manufacturer proposes a classification with STOT-SE 3 (H335, R37) based on a repeated-dose inhalation study in rats and supported by occupational observations. The inhalation study is described in the dossier (section 5.6.2). The mentioned occupational information is not available to the dossier submitter and is not described in the registration dossier.	We consider this information relevant for the classification, as it reinforces the interpretation of the animal data. Based on the rat experiment (4 wk, 5 d/w, 6h/d) we propose a classification STOT RE Cat. 1, H372 (lungs, via dust inhalation)

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			It is within the remit of RAC to decide whether these data and information are sufficient for classification with STOT-SE 3 (H335, R37).	

Other hazards and endpoints

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
2011/10/14	Germany/ AffiliatedWithO rganisation / Company- Downstream user / MENNO Chemie- Vertrieb GmbH, Norderstedt, Germany	<p>5.3.1, page 27 - 31</p> <p>The proposed classification as skin irritant is not based on available studies on test animals according to EC or OECD guidelines. In these studies benzoic acid did not show skin irritating properties, and consequently up to now in no classification system worldwide benzoic acid is regarded to be a skin irritant.</p> <p>The proposal is based on experience on humans. It is known that a small part of the population shows pseudo-allergic reactions like irritated skin following a contact with benzoic acid. This contact may also be (and mostly is) oral ingestion. In our opinion R38/H315 should not be used for substances, which show irritating effects only in a very small part (far below 1%) of the population because of a special susceptibility.</p> <p>Because of the natural occurrence in food (e.g. tomatoes, some berries, cheese) and the widespread use of benzoic acid e.g. in food, cosmetics and cleaners, affected people usually are aware of their susceptibility. To warn these users, we are writing as a precaution the sentence "Contains benzoic acid. May produce pseudo-allergic reactions" on the label of benzoic acid containing plant protection products. The model for our course of action has been the warning sentence on food products like "Contains nuts".</p> <p>In more than 20 years use in commercial floriculture in greenhouses no reports at all from workers about any irritating or (pseudo-) allergic effects have been reported to the only authorisation holder of benzoic acid containing plant protection products. Therefore, we feel that a warning sentence naming benzoic acid and possible individual reactions is much more useful to protect sensitive people than a general and unspecific</p>	<p>Agree, that a more general discussion and more guidance would be helpful for the assessment of such effects.</p> <p>The proposed classification with H315/R38 was based on skin reactions in humans (as described in the dossier, section 5.3 and 5.10.2).</p> <p>Regarding observations in workers: We are not aware that there is a systematic study/evaluation of (irritative or pseudo-/allergic) skin reactions observed in workers upon or due to exposure to benzoic acid. It is noted that it is not compulsory to notify such effects.</p>	<p>We agree with the DS in the H315/R38 classification. We also agree that the guidance should be clarified to evaluate human results. Anyway, the fraction of human volunteers showing skin irritation upon contact to Benzoic acid is close to 100% in at least some tests in table 5.9; therefore, we cannot accept the argument that skin irritation only affects to a small part of the population.</p>

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		R38/H315 classification which is meaningless and unnecessary for more than 99% of the users. We appreciate a more general discussion on this issue at the Committee for Risk Assessment.	It is within the remit of RAC to decide whether the available and presented data and information are sufficient for classification with H315/R38.	Different reports (Basketter and Wilhelm, 1996; Lathi et al, 1995; Nair, 2001) indicate skin effects in a significant portion of the general (i.e., with no precondition) population
2011/10/14	United States/ BehalfOfAnOrganisation/ Company-Manufacturer/ Emerald Kalama BV (Formerly DSM/DSP)	Page 34 section 5.3.4: We note the proposed classification with R38 resp. H315 as a difference to the classification included by the lead registrant within the REACH Registration dossier.	Noted. The proposed classification with H315/R38 was based on skin reactions in humans (as described in the dossier, section 5.3 and 5.10.2).	We agree with the DS in the H315/R38 classification.
2011/10/14	France / Member State	<p>Repeated dose toxicity: inhalation: e.g. p.33, p.41 and p.43 about respiratory tract toxicity</p> <p>Regarding observations in animal studies, respiratory tract irritation was observed in a rat study. Compound-related microscopic lesions consisting of multifocal to generalised inflammation cell infiltrates and interstitial fibrosis of the lung were observed.</p> <p>Conclusions: According to these studies, it seems obvious that benzoic acid induces a lung irritation. Moreover, this compound also induces eye and skin irritation (H315 and H318). But, based on the available studies (for instance lack of details concerning the effects observed in the acute inhalation studies), it is difficult to determine the most appropriate classification. To FR point of view two options are possible:</p>	<p>No information on the effects in the acute inhalation studies is available. As indicated in the CLH-report, the information was mainly cited from reviews and these did not provide further details.</p> <p>Effects in repeated dose inhalation study: Reddish discharge around nares was observed in all animals treated with 0.25 mg/L</p>	We consider that the lung effects are clearer in the repeated dose inhalation study, which reports interstitial inflammation and lung fibrosis. These effects are considered severe, irreversible, and relevant to humans. Guidance values

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		<p>- STOT SE, cat. 3: H335 may cause respiratory irritation. The observed effects in the studies for acute toxicity by inhalation in rat (5.2.2) are not presented in the report. It may be possible that lung irritation effects of appear at the first exposure since the benzoic acid is a skin and eye irritant.</p> <p>- STOT RE, cat. 1: H372 Causes damage to organ (lung) through prolonged or repeated exposure. In the 4 weeks study in rats, the exposure dose at which adverse effects on lung appear (0.025 mg/L air) is a criterion that can lead to a STOT RE 1 classification, since the cut-off adjusted for exposure duration is 0.06 mg/L air for this category. In addition, it has been indicated in the report that benzoic acid can cause respiratory reactions such as rhinitis and asthma in humans following an oral, dermal or inhalation exposure.</p>	<p>or 1.2 mg/L (starting on day 4, with an dose-related increase in severity) and once (on day 13) in the group treated with 0.025 mg/L. No compound-related macroscopic lesions were reported in any of the animals from the test groups. Microscopic findings in lungs consisted (in all dose groups, i.e., \geq 0.025 mg/L air) of an increase in the intensity and extent of interstitial inflammatory cell infiltrate and an increase in the incidence and intensity of interstitial fibrosis.</p> <p>The manufacturer proposed STOT-SE 3 (see comment by Emerald Kalama BV).</p> <p>Considering, (1) that the effects in lungs in the repeated-dose inhalation study were most probably related more to local action than to systemic action, and (2) that benzoic acid induced severe damage to eyes (proposal for R41/H318)</p>	<p>for STOT RE Cat. 1 for dusts are $C < 0.06$ mg/litre/6h/day for, 28 day-experiments, above the reported LOAEL of < 0.025 mg/litre/6h/day (28 days, 5 days per week) for pulmonary effects (Interstitial inflammation, lung fibrosis) in rats. We therefore propose a classification STOT RE Cat. 1, H372 (lungs, via dust inhalation). The information present in the dossier is not sufficient to evaluate single exposure effects of benzoic acid inhalation.</p>

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			(which would be an acute effect, and (mechanistically thinking) no different effects would be expected after single or repeated exposure, whereas the severity might increase), we would tend more to a classification with STOT-SE than STOT-RE.	
2011/10/13	United Kingdom / UK CLP CA / HSE / Member State	<p>STOTE-SE The dossier does not make any reference to classification for STOT-SE and the section on acute toxicity does not contain details of the effects observed following single exposure. It would be useful if consideration was given to this hazard class in the response to comments table.</p> <p>Irritation – skin and eye We agree with the proposed classification for both skin and eye irritation.</p> <p>Respiratory Tract Irritation Adverse effects are reported in humans and experimental animals suggesting some respiratory tract changes (section 5.3.3), but not considered in the summary of irritation. It would be useful to come to a conclusion regarding classification for respiratory tract irritation in this section.</p>	<p>Regarding STOT-SE: As indicated in the CLH-report, the information about acute studies was mainly cited from reviews and these did not provide enough details for an assessment regarding STOT-SE 1/2.</p> <p>Regarding skin & eye irritation: Thank you for the support.</p> <p>Regarding respiratory tract irritation: see our response to the comments by France and by Emerald Kalama BV.</p>	<p>We agree that the information present on the dossier is not sufficient to evaluate single exposure effects.</p> <p>We agree with the DS on skin & eye irritation</p> <p>We propose a classification STOT RE Cat. 1, H372 (lungs, via dust inhalation)</p>
2011/10/10	Sweden / Member State	<p>Skin irritation and serious eye damage SE supports classification of benzoic acid (Cas No 65-85-0) as specified in the proposal. SE agrees with the rationale for classification into the proposed hazard classes and differentiations.</p>	Thank you for the support.	Noted

Attachments received: No received attachments