

## Targeted consultation

### **Additional information relevant for the acute inhalation toxicity classification of 3-iodo-2-propynyl butylcarbamate, 3-iodoprop-2-yn-1-yl butylcarbamate (IPBC); EC number 259-627-5; CAS number 55406-53-6**

#### **Comments of the European IPBC Task Force**

On 21-April-2023 a targeted consultation was launched related to the CLH process to harmonized the acute inhalation toxicity of the active substance IPBC<sup>1</sup>.

On behalf of the European IPBC Task Force taking care of the active substance IPBC in terms of approval and/or renewal of several biocidal product types under the BPR, the following concerns regarding the two acute inhalation studies and their use during the CLH process are herewith communicated.

The two studies do not belong to the IPBC data set used for the approval of IPBC as biocidal product and those studies were also not available for the renewal of IPBC as PT8 under the BPR.

Interestingly, those two studies were already finalized / reported in 2014 but were not included by Denmark in the CLH report for which a public consultation was started in December 2022<sup>2</sup>.

After thorough review of the two robust study summaries in the targeted consultation, the European IPBC Task Force has major reservations to use those studies for harmonized classification and labelling for the following reasons since the results of the study are not considered reliable:

#### **OECD 403 (2009) Test Guideline was not followed**

Paragraph 5 of OECD 403 indicates that *“Before considering testing in accordance with this Test Guideline all available information on the test article, including existing studies (e.g. TG 436)(4) whose data would support not doing additional testing should be considered by the testing laboratory in order to minimize animal usage.”*

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<sup>1</sup> [https://echa.europa.eu/de/harmonised-classification-and-labelling-targeted-consultations/-/substance-rev/73003/term?\\_viewsubstances\\_WAR\\_echarevsubstanceportlet\\_SEARCH\\_CRITERIA\\_NAME=3-iodo-2-propynyl+butylcarbamate&\\_viewsubstances\\_WAR\\_echarevsubstanceportlet\\_SEARCH\\_CRITERIA\\_EC\\_NUMBER=259-627-5](https://echa.europa.eu/de/harmonised-classification-and-labelling-targeted-consultations/-/substance-rev/73003/term?_viewsubstances_WAR_echarevsubstanceportlet_SEARCH_CRITERIA_NAME=3-iodo-2-propynyl+butylcarbamate&_viewsubstances_WAR_echarevsubstanceportlet_SEARCH_CRITERIA_EC_NUMBER=259-627-5), accessed 27-April-2023

<sup>2</sup> <https://echa.europa.eu/de/registry-of-clh-intentions-until-outcome/-/dislist/details/Ob0236e1875f99fa>, accessed 27-April-2023

IPBC was approved as active substance for PT8 already in 2008<sup>3</sup> and an assessment report was publicly available providing information on acute inhalation toxicity. In fact in 2012<sup>4</sup>, the Risk Assessment Committee (RAC) published their opinion with detailed information regarding acute inhalation toxicity. Thus, when following OECD 403 (2009), additional studies would not have been required.

Paragraph 16 and 17 indicate that proper justification related to the vehicle other than water should be given. When this is not available, a negative control group should be considered. However, based on the study summary neither an explanation for using the vehicle nor a negative control group is available.

### **IPBC Concentration in air is not accurately reported**

Modern acute inhalation toxicity studies like those two studies being finalized in 2014 have exact determination of the test item concentration in the air. Thus, a detailed description on the analytical procedures including sample collection is key for such types of studies. This is in detail described in paragraphs 21-24 of OECD 403 (2009).

Although the IPBC used during the two studies had high purity, it is entirely unclear whether or not the animals were inhaling IPBC since there is no information at all.

For example in study 1 the only information given is that the *"test item was aerosolized using a rotating brush powder dispenser located at the top of the exposure chamber. The dispenser was connected to a compressed air supply"*. However, there is no information how the "achieved concentrations" of 0.05, 0.05, and 0.494 mg IPBC/L were determined. If the concentrations to which the animals were exposed, were higher and the achieved concentrations were not correctly reported, the resulting LC50 is too low. The only information is that a Mercer style 7-stage impactor was available to determine the particle sizes.

For high reliability studies, more information is expected.

In line with OECD 403 (2009), the expectation would be that a device is used to collect the dust / aerosol and it would be common practice to have further information / descriptions like the next steps for determining the achieved concentration such as drying filters, weighing filters or even extraction of the test material from the filters followed by analytics such as HPLC for verification of the amount of the active substance. Together with the known amount of air sucked through the collecting device a precise determination would be possible. However,

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<sup>3</sup> <https://echa.europa.eu/documents/10162/9d72fc6a-6a37-045e-7609-975327cca21d>, accessed 27-April-2023

<sup>4</sup> <https://echa.europa.eu/de/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e180a0b8d7>, accessed 27-April-2023

based on the information available for study one, this was not done during the study and consequently the reliability of the result is low since we do not know to which concentration of IPBC in the air the animals were exposed.

The same uncertainty of applicable to study 2.

Furthermore, no information is available in the robust study summary whether a stable test atmosphere was achieved and regarding monitoring intervals.

### **High uncertainty regarding identity of the chemical(s) being applied to the animals**

For study 2, the situation is even worse since it is mentioned that IPBC could not be aerosolized without the help of a solvent. This is discrepant to acute inhalation studies submitted by the European IPBC Task Force for biocidal active substance approval and renewal as well as to study 1 presented in the targeted consultation.

However, the most problematic issue with study 2 is that the IPBC concentration, homogeneity, and stability in the vehicle ethanol was not performed. Thus, it is entirely unclear to what material the animals were exposed: IPBC may have degraded during the unknown storage time / period between test item preparation and exposure of the animals.

Since there is no information on stability of IPBC in ethanol, an analytical verification on the IPBC concentration in the air would have increased the quality of the study, however, the doubts about potential formation of degradation products would not have been dismissed even when such information would have been available.

Again in this study summary, there is only information on how the particle size was determined (by means of a Marple Personal Cascade Impactor). However, it is difficult to follow the details given in the study summary since it is mentioned that the *“test item was aerosolised using a glass jet nebuliser located at the top of the exposure chamber. The nebuliser was connected to glass syringe attached to an infusion pump, which provided a continuous supply of the test item, and to a metered compressed air supply.”* This is somewhat discrepant to other information in the study summary since the test item would have been solid IPBC and on the other hand it was solubilized in ethanol. Thus, a key element of animal exposure is not clearly described.

**To summarize,** based on the available information there are several major deviations to OECD 403 (2009) and to GLP requirements: The most important points are the uncertainty regarding the chemical atmosphere to which the animals were exposed, the identity of the material in the exposure chamber in study 2. There are also reservations against the use of the study since from an animal welfare perspective those two studies would not have been necessary.

Overall, the 2 studies do not qualify for a reliable assessment of acute inhalation toxicity of IPBC and should not be used for harmonized classification and labelling.