Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

3-Iodo-2propynyl butylcarbamate

EC Number: 259-627-5

CAS Number: 55406-53-6

CLH-O-0000001550-84-03/F

Adopted

28 November 2013

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 3-IODO-2-PROPYNYLBUTYLCARBAMATE

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: 3-Iodo-2-propynylbutylcarbamate
EC number: 259-627-5
CAS number: 55406-53-6

General comments

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
12/09/ 2011	France / Member State	General comment on environmental assessment: Some tables need to be edited: - table 21 (p.65), part of the frame misses - table 21: "Transfor-mation" needs to be corrected to "Transformation" - table 22: part of the frame misses (p.70 and 72)	Thank you for your comments, the tables will be corrected accordingly	Noted.
12/09/ 2011	Spain / Member State	We are in agreement with the classification proposal submitted by DK.	Ok thank you.	Noted.
09/09/ 2011	Germany / Member State	Overall, the CLH report is well written and covers adequately the specific end points for assessment. p.7 In contrast to the text of the heading there are no labelling proposals. Furthermore the difference between chapter 1.2 and 1.3 is not quite clear. p.8 The formal difference between classification and labelling should become more clear here. Concerning the proposed S-Phrases we suggest to omit S22 because having R37 and R23 should be a sufficient clear warning which implies automatically avoiding the inhalation of this substance. Secondly according to the criteria S46 should be omitted as S45 has been assigned already (higher priority).	Thank you for your comments. Each comment will be dealt with separately: p.7: We followed the format from ECHA. p.8: We agreed to omit S22 and S46. S1 and S38	p.11. The H-statement for environmental classification and labelling based on CLP H410 has been included in the resubmitted CLH report_3-Iodo-2-propynylbutylcarbamate_26 July 2011 p.65 A modified Zahn-Wellens test shows, that IPBC is rapidly

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		p.11 The conclusion on proposed labelling for technical material IPBC: The proposed H-statements for environmental classification and labelling based on CLP criteria (1272/2008/EC and 286/1022) are H400 and H410. Please add on this page the proposed labelling with H410. p. 19 & IUCLID section 1.2 Only minimum purity or rather the purity range is stated. Neither in the report nor in the IUCLID Dossier impurities or additives are stated. Furthermore no confidential document is attached. As a consequence, no detailed composition of IPBC is stated in the documents for C&L. DE is of the opinion that the detailed composition of a substance should be given. If the impurities and additives are confidential, the confidential information can be included in the IUCLID file and be flagged as such or, alternatively, a confidential annex can be attached to the Annex VI report. p. 65 Test on inherent biodegradability: The test parameter measured was not DOC as given in the table. IPBC and PBC were analysed specifically. The lacking information on DOC is the reason why IPBC cannot be classified as inherently biodegradable. p.8, 12, 13, 14 and 75-77 The proposed environmental classification and labelling based on Directive 67/548/EEC has to be completed with the risk phrase R 53. The M-factor for the proposed H-statement H410 has to be changed into 10. IPBC cannot be classified as readily or inherent biodegradable (see also our comment to p. 65: test on inherent biodegradability). This classification and labelling (R50/53) based on Directive 67/548/EEC is furthermore consistent with the classification and labelling based on CLP criteria for IPBC (H400, H 410/M-factor 10).	can also be omitted. p. 11: This will be corrected accordingly. p.19: In the IUCLID file information of impurities of IPBC is included; however it is marked as "confidential business information". All this information is also available in the confidential part in the CA-report for PT8 (biocide Directive 98/8/EC). A special agreement has been made not to double the work since for biocides/pesticides a	transformed under the conditions of the test into the major metabolite PBC (within 2 hours) by the elimination of iodine, nevertheless inherently biodegradation cannot be proven because of the lacking information of DOC. This test can be only used as additional information. "DOC" should be changed to "specific analysis of IPBC and the degradation product PBC" in the revised CLH report. p.8, 12, 13, 14 and 75-77 RAC discussed the different tests submitted in the report regarding degradation. The reported ready biodegradability test shows that the substance is not readily degraded, however, the concentration of the

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
			comprehensive Competent Authorities report has already been prepared. It must be up to ECHA to make this information available for the RAC classification group. p. 65: "DOC" will be changed to "specific analysis of IPBC and the degradation product PBC" p. 8 osv.: See argumentation in the end of this commenting table (Annex II)	test substance (50 mg/l) is close to the inhibition concentration of microorganisms (EC20 = 57 mg/l). On the other hand, the aerobic soil degradation study shows a rapid degradation of IPBC, and the result of this test is in agreement with other studies such as the inherent biodegradation test which can be used only as additional information because it had some deficiencies. Taking into account all the reported information and the expert judgment RAC concluded that IPBC is rapidly degradable in the aquatic environment. Therefore, RAC agreed to classify IPBC as Aquatic Acute 1 with M factor 10 and Aquatic Chronic 1 with M factor 1.

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 3-IODO-2-PROPYNYLBUTYLCARBAMATE

<table>
<tr><th>Date</th><th>Country / Organisation / MSCA</th><th>Comment</th><th>Dossier submitter's response to comments</th><th>RAC's response to comment</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>09/09/ 2011</td><td>An Organisation / Company-Manufacturer (IPBC task force)</td><td>In the CLH report on IPBC, the substance has been proposed by DEPA Denmark to be classified as "toxic by inhalation" (T, R23 acc. to the DSD and Acute Tox. 3, H331 acc. to the CLP). The IPBC Task Force hold the opinion that based on the information available on the acute inhalation toxicity, IPBC is eligible for a split-entry classification with respect to acute inhalation toxicity. A detailed argumentation of the IPBC TF is provided in Annex I "Proposal for split-entry classification of IPBC concerning inhalation toxicity" of the CLH-Report, which is not attached to the published version (see reference to Annex I in the CLH-Report on page 29). This argumentation should be considered in the evaluation.

The document attached "Comments of the IPBC Task Force on the CLH report of 3-Iodo-2-propynyl butylcarbamate (IPBC)[CAS No. 55406-53-6], (TF Comment_CLH report_IPBC_Public Cons. Phase_Sept 2011.doc)", is copied below:

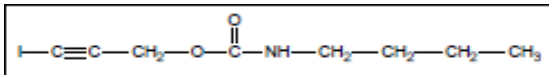
Comments of the IPBC Task Force on the

CLH report of 3-Iodo-2-propynyl butylcarbamate (IPBC)

[CAS No. 55406-53-6]

<table><tr><td>Substance name:</td><td>3-Iodo-2-propynyl butylcarbamate</td></tr><tr><td>CAS name:</td><td>Carbamic acid, N-butyl-, 3-iodo-2-propyn-1-yl ester</td></tr><tr><td>IUPAC name:</td><td>3-Iodoprop-2-yn-1-yl butylcarbamate</td></tr></table></td><td>Please refer to CA`s response to the split entry/Annex I proposal in the end of this document.</td><td>There is not enough information for justified split-entry classification concerning acute inhalation toxicity. It is not clear under which conditions different particle sizes and percentage distributions can occur.</td></tr>
</table>

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment

C number:	259-627-5
CAS number:	55406-53-6
Index number:	Not available
Molecular formula	C8H12INO2
Molecular weight	281.1 g/mol
Smiles notation	O=C(NCCCC)OCC#CI
Structural formula	
Annex VI Index number:	Not listed in Annex VI
Degree of purity:	≥ 98 % (w/w)
Submitted by:	DEPA Denmark

1.1 Harmonised classification and labelling proposal

Table 1: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation	**Directive 67/548/EEC (Dangerous Substances Directive; DSD)**
Current entry in Annex VI, CLP Regulation	**Not included in Annex VI, Table 3.1**	**Not included in Annex VI,**

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment

		Table 3.2 (CLP)
Task Force proposal for consideration by RAC for technical material containing more than 5% of particles < 10 µm	Acute tox 3 - H331 Acute Tox 4 - H302 Eye Dam.1 - H318 Skin sens.1 - H317 STOT SE3 - H335 Aquatic Acute 1 - H400, M=10 according to Commission Regulation (EU) No 286/2011(2nd ATP): Aquatic Chronic 1 - H410, M= 1	Xn: R22 Xi: R37 - 41 - 43 T: R23 N: R50
Task Force proposal for consideration by RAC for technical material containing less than 5% of particles < 10 µm	Acute Tox 4 - H302 Eye Dam.1 - H318 Skin sens.1 - H317 STOT SE3 - H335 Aquatic Acute 1 - H400, M=10 according to Commission Regulation (EU) No 286/2011(2nd ATP): Aquatic Chronic 1 - H410, M= 1	Xn: R22 Xi: R37 - 41 - 43 N: R50
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	-	-

1.2 Proposed harmonised classification and labelling based on CLP Regulation and/or DSD criteria

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		General: It is proposed that IPBC with less than 5% of particles < 10 µm should not be classified and labelled for inhalation toxicity, while IPBC with more than 5% of particles < 10 µm should be classified as T, R23 acc. to the DSD and Acute Tox. 3, H331 acc. to the CLP (see justification provided in Annex 1). **1. Classification based on DSD criteria** **Proposed classification based on DSD criteria (Directive 67/548/EEC) for the technical material IPBC containing more than 5 % of particles < 10 µm** Class of Danger T: Toxic N: Dangerous for the environment R-Phrases R22: Harmful if swallowed R23: Toxic by inhalation R37: Irritating to the respiratory system R41: Risk of serious damage to the eye R43: May cause sensitization by skin contact R50: Very toxic to aquatic organisms **Proposed classification based on DSD criteria (Directive 67/548/EEC) for the technical material IPBC containing less than 5 % of particles < 10 µm** Class of Danger Xn: Harmful N: Dangerous for the environment R-Phrases R22: Harmful if swallowed		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		R37: Irritating to the respiratory system R41: Risk of serious damage to the eye R43: May cause sensitization by skin contact R50: Very toxic to aquatic organisms **2. <u>Classification based on CLP criteria</u>** **<u>Proposed classification based on CLP criteria (Regulation 1272/2008/EC) for the technical material IPBC containing more than 5 % of particles < 10 µm</u>** Signal Word: Danger Classification: Acute Tox 3 Eye Dam. 1 Acute Tox 4 Skin Sens. 1 STOT SE3 Aquatic Acute 1, M = 10 Aquatic Chronic 1, M = 1 H-Statements: H331: Toxic if inhaled H318: Causes serious eye damage H302: Harmful if swallowed H317: May cause an allergic skin reaction H335: May cause respiratory irritation H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects (according to Commission Regulation (EU) No 286/2011(2nd ATP)) **<u>Proposed classification based on CLP criteria (Regulation 1272/2008/EC) for the technical material IPBC containing less</u>**		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		<u>than 5 % of particles < 10 µm</u> Signal Word: Danger Classification: Eye Dam. 1 Acute Tox 4 Skin Sens. 1 STOT SE3 Aquatic Acute 1, M = 10 Aquatic Chronic 1, M = 1 H-Statements: H318: Causes serious eye damage H302: Harmful if swallowed H317: May cause an allergic skin reaction H335: May cause respiratory irritation H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects (according to Commission Regulation (EU) No 286/2011(2nd ATP)) **3. <u>Labelling based on DSD criteria</u>** **<u>Proposed labelling for the technical material IPBC containing more than 5 % of particles < 10 µm</u>** Class of Danger: T, N R-Phrases: R22-23-37-41-43-50 S-Phrases: S1-2-22-24-26-37/39-38-45-46-61 **<u>Proposed labelling for the technical material IPBC containing less than 5 % of particles < 10 µm</u>** Class of Danger: Xn, N R-Phrases: R22-37-41-43-50 S-Phrases: S1-2-24-26-37/39-45-46-61		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		4. <u>Labelling based on CLP criteria</u> **<u>Proposed labelling for the technical material IPBC containing more than 5 % of particles < 10 µm</u>** Signal Word: Danger Pictograms: GHS05, GHS06, GHS09 (CLP, Article 26, 1b) H-Statements: H331 Toxic if inhaled H318: Causes serious eye damage H302: Harmful if swallowed H317: May cause an allergic skin reaction H335: May cause respiratory irritation H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects (according to Commission Regulation (EU) No 286/2011(2nd ATP)) **<u>Proposed labelling for the technical material IPBC containing less than 5 % of particles < 10 µm</u>** Signal Word: Danger Pictograms: GHS05, GHS07, GHS09 (CLP, Article 26, 1b) H-Statements: H318: Causes serious eye damage H302: Harmful if swallowed H317: May cause an allergic skin reaction H335: May cause respiratory irritation H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects (according to Commission Regulation (EU)		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		No 286/2011(2nd ATP)) **ANNEX I TO THE CLH REPORT** **PROPOSAL FOR SPLIT-ENTRY CLASSIFICATION OF IPBC CONCERNING ACUTE INHALATION TOXICITY** During the evaluation of the active substance dossier on IPBC, the RMS Denmark (DEPA) proposed a classification of IPBC as toxic by inhalation (T, R23). In the following, a justification is provided for a split-entry classification of IPBC with respect to acute inhalation toxicity. The principles defined by Pauluhn (2008) are the basis for the argumentation. According to Pauluhn (2008), the following conditions must be met so that the split-entry approach can be applied concerning inhalation toxicity: 1. The substance is either a powder or dust or a liquid with low volatility. 2. The substance acts *via* direct local effects and not *via* systemic toxicity. 3. The observed effects in inhalation toxicity studies are dependent on the particle size of the substance (proof of principle). IPBC meets these conditions: 1. IPBC is a powder, thus fulfilling the first criterion. Furthermore, the vapour pressure of IPBC is low: 2.36-4.5x10^{-3} Pa. 2. In the acute inhalation studies [redacted], 1985; [redacted] 1990; [redacted] 1994) and in the sub-chronic inhalation study [redacted] 1994), only local effects on the respiratory system were seen: In all studies, there were signs of irritation in the respiratory system. In the sub-chronic inhalation study, additionally,		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		epithelial hyperplasia were found in the larynx. They are considered as a protective or repair mechanism, secondary to the local irritation caused by IPBC. Since only local but no systemic effects were found in all inhalation studies, also the second criterion for the applicability of the split-entry approach is fulfilled. 3. From the studies reported in the "Overview on the results of acute-inhalation studies on IPBC" (see table below) it can be concluded that the size of the IPBC particles to which the test animals (rats) were exposed in inhalation toxicity studies influenced the toxicity of IPBC: In the study by [redacted] (1985), an LC_{50} of > 6.89 mg/L (not triggering classification for inhalation toxicity) was determined, whereas in the study by [redacted] (1990), considerably lower values were determined, i.e. an LC_{50} of 0.68 mg/L in case of exposure to IPBC as dust aerosol and an LC_{50} of 0.78 mg/L in case of exposure to IPBC as liquid aerosol. These results trigger T, R 23 (toxic by inhalation). These differences in toxicity can be explained by differences in the size of the particles used in the two tests: In the study by [redacted] (1985), non-micronized IPBC was used. Though the particle size was not determined in the study itself, a later performed study on particle-size distribution ([redacted], 2001: Particle size distribution of Troysan Polyphase P-100; Doc. No. 111-001; study is not listed in the table below since it is not a toxicity study), showed that in Troysan Polyphase P-100 less than 5% of particles have an aerodynamic diameter of less than 10 µm. For this reason, the study author concluded that "*there is little potential for inhalation of the dust of the material"*. It is confirmed by the Sponsor of the study (Troy Corporation Inc.) that the production process for Troysan Polyphase P-100 did not change between 1985 and 2001. Therefore, it is concluded that the material tested by [redacted] (1985) had a particle-size distribution similar to the one described by [redacted], so that the result obtained in the [redacted] study (LC_{50} > 6.89 mg/L) is applicable to any IPBC with less than 5% of particles < 10 µm, as		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		described in the [redacted] study. In the study by [redacted] (1990), when IPBC was applied as dust aerosol, 82% of the particles had a size < 10 µm. This means that the inhalable fraction was considerably higher than in the material tested by [redacted] (1985), resulting in the low LC_{50} of 0.68°mg/L, triggering T, R23 for the tested material. (The results concerning the liquid aerosol are not considered here since they are not relevant for the split-entry considerations). In the study by [redacted] (1994), only the test groups 2, 3 and 8 (corresponding to measured concentrations of 0.29, 0.58 and 0.16 mg IPBC/L) were exposed to micronized IPBC, while the test groups 4, 5 and 6 (corresponding to measured concentrations of 2.44, 1.19 and 0.49 mg IPBC/L) were exposed to non-micronized IPBC. For the micronized IPBC, no LC_{50} could be calculated because there was no dose-related trend in mortality at the three respective dose levels. From the groups exposed to non-micronized IPBC, an LC_{50} of 0.88 mg/L was calculated, while from all groups (groups exposed to micronized dust and groups exposed to non-micronized dust), an LC_{50} of 0.67 mg/L was derived. 19.2-26.7% of the particles of the non-micronized IPBC were below 6 µm in size, while 74.4-80.5% of the particles of the micronized IPBC were below 6 µm. Though in the study report, the percentages of particles ≤ 10 µm are not provided, it is evident that in the [redacted] study, the percentage of particles < 10 µm must be similar to the respective percentage (82 %) provided in the study by [redacted] (1990) (considering the groups with micronized material), and, (considering the non-micronized IPBC), still more than 4-5 times higher than in study by [redacted] (1985). This explains the low LC_{50} values in the [redacted] study. Consequently, the results of the [redacted] study are not in conflict with the conclusion drawn from the comparison of [redacted] (1985) and [redacted] (1990), i.e. they do not contradict the application of the split-entry approach to IPBC. **Overview on the results of acute-inhalation studies on IPBC**		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment

Author species	Particle size distribution	LC_{50} (mg/L)	Resulting classification
[redacted] 1985 / rats	Less than 5% of particles < 10 µm (from read-across to particle-size distribution as determined by [redacted] (2001)	> 6.89	none
[redacted] 1990 / rats	Dust aerosol: 82% of particles ≤ 10 µm Liquid aerosol: 94% of particles ≤ 10 µm	0.68 (dust aerosol) 0.78 (liquid aerosol)	T, R23 Acute Tox 3, H331
[redacted] 1994 / rats	Dust micronized: 3.5 µm MMAD*; % respirable (6 µm): 74.4-80.5% of particles Dust non-micronized: 9.6-14.2 µm MMAD* % respirable (6 µm): 19.2-26.7% of particles	LC_{50} could not be calculated From groups exposed to non-micronized dust: 0.88 mg/L From all mortality data: 0.67 mg/L	T, R23 Acute Tox 3, H331

*MMAD: Mass Median Aerodynamic Diameter

Thus, all three criteria as defined by Pauluhn (2008) are considered to be

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		fulfilled so that a split-entry classification of IPBC with respect to acute inhalation toxicity can be applied. It is proposed that IPBC with less than 5% of particles < 10 µm should not be classified for inhalation toxicity, while IPBC with more than 5% of particles < 10 µm should be classified as T, R23 (EU)/ Acute Tox. 3, H331 (GHS). **References** • [redacted] (1985): Acute Inhalation Limit Test in Rats 3-Iodo-2-propynyl butyl carbamate Revised Final Report; [redacted] (unpublished); this study is also included in the reference list of the CLH report • [redacted] (1990): (Troysan Polyphase P-100) – Acute Inhalation Toxicity Study in the Rat; [redacted] (unpublished); this study is also included in the reference list of the CLH report • [redacted] (1994): Acute Inhalation Toxicity Study in Rats – 4-Hour Exposure to Omacide® IPBC; [redacted] (unpublished); this study is also included in the reference list of the CLH report • [redacted] (2001): !!CONFIDENTIAL!! - Particle Size Distribution of TROYSAN Polyphase P-100; [redacted] (unpublished); this study is also included in the reference list of the CLH report; this study is confidential business information of Troy		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
		• [redacted] (1994): 13-week inhalation toxicity study in rats; [redacted] (unpublished); this study is also included in the reference list of the CLH report • Official Journal of the European Commission: Directive 1999/45/EC (1999): OJ L 200, Part B, chapter 1.1, Table 1, page 26 • Pauluhn, J. (2008): Inhalation toxicology: Methodological and regulatory challenges; Experimental and Toxicological Pathology, 60, p.111-124 *End of attachment*		
07/09/2011	United Kingdom / Member State	When possible it would be useful if more details of the available data were presented, including quantification of observed effects (e.g. state whether an effect is significant, the magnitude of the observed effect, the relevant dose(s) and the number of animals affected). This is particularly important for repeat dose toxicity, carcinogenicity, reproductive toxicity and where the effects are potentially relevant for classification. S-phrases – It is recommended that a maximum of 6 S-phrases be applied to a substance. We do not consider that that the S-phrases S22 and S38 and S46 are required.	Understandable and we fully agree. Which are why we with the submission of the CLH-report to ECHA referred to the IIIA documents of the CA-report for IPBC (product type 8; biocides Directive 98/8/EC) which are available from	OK

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
			circa portal. Doc IIIA contains all study summaries. Since ECHA has not included this information for the classification group we have now send doc IIIA to ECHA to be distributed to RAC members. Please keep in mind that the study summaries (Doc IIIA) should only be used by ECHA as supporting information and that these study summaries will not be published. Concerning S-phrases we	

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
			will delete. It is agreed that a maximum of 6 S-phrases should be used only. S1, S22, S38 and S46 are not necessarily required	
31/08/ 2011	Netherlands / RIVM / Bureau REACH / Behalf Of An Organisation / National Authority	Page 7, table 2: 'Resulting harmonised classification' should be filled in. Page 11, labelling according to CLP; please mention the applicable symbol. According to the 2nd ATP of CLP, H410 should be included in the labelling. And when H410 is mentioned H400 may be omitted (Annex III of CLP, as adapted by the 2nd ATP). Page 14: Why are some of the R phrases in bold? ☐Classification should only be discussed in the paragraphs 'Comparison with criteria' and 'Conclusions on classification and labelling', not in the paragraphs '(Non-)human information'. ☐In 'Comparison with criteria', also the criteria of DSD should be discussed.	Thank you for your comments Each comment will be dealt with separately: p.7: Resulting harmonized classification will be filled in (copy of "current proposal for consideration by RAC). p.11: This will be corrected accordingly p. 14:Bold R-phrases are a formatting error. Other: In most cases	p.11 The H-statement for environmental classification and labelling based on CLP H410 has been included in the resubmitted CLH report_3-Iodo-2-propynylbutylcarbamate_26 July 2011. RAC agrees with the comment to omit H400 in the label when H410 is mentioned (Annex III of CLP, as adapted by the 2nd ATP).

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comments	RAC's response to comment
			the CLP C&L criteria cover also the DSD C&L criteria. No repetition needed. Information on proposed C&L in the paragraphs (non)-human information should be maintained as it fits into the context. We find a degree of flexibility should be allow for the biocides/pesticides to minimise the workload for MS performing the CLH-report on basis of a fully comprehensive CA-report. Decision could be taken on current basis.	

Carcinogenicity

Date	Country /Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
12/09/2011	France / Member State	Agree with conclusion of RMS	Thank you	OK
09/09/2011	Germany / Member State	No classification for carcinogenicity is proposed because recorded hepatocellular adenomas in the mice feeding study were regarded as non-specific, high-dose toxicity effects in sensitive species. However, detailed incidence data for each dose group is missing, therefore the dose-response for hepatocellular adenomas cannot be assessed with respect to other signs of non-specific toxicity at doses significantly exceeding MTD. Ideally, the degree of correlation between the dose-dependent body weight reduction and adenoma incidence would help with interpretation of the significance of hepatocellular adenomas at the high dose. Some further discussion may be directed to the argument that CD-1 mice are specifically susceptible for liver tumours at doses exceeding MTD: background incidences in other mouse strains (i.e., B6C3F1) are significantly higher. Overall, considering the lack of mutagenicity in vivo and liver neoplasms in the rat study, and given there is no clear dose-response for the adenoma incidence, IPBC would not fulfil the criteria for classification as outlined in Table 3.5.1 of the CLP.	Detailed information on incidences of hepatocellular adenomas, MTD (based on body weight effects) and lack of dose-response can be found in the respective study summary of Document IIIA6. In males at 150 mg/kg bw/day a higher incidence in hepatocellular adenoma (11/50) was observed when compared to controls (4/10). However, in the dose groups treated with 20 mg/kg bw/day and 50 mg/kg bw/day, no significant increase in incidence (i.e. 3/50 and 5/50 at 20 and 50 mg/kg bw/day in males; 1/50 and 1/50 at 20 and 50 mg/kg bw/day in females) of hepatocytic adenoma was observed when compared to the control group animals (i.e. 4/50 in males and 0/50 in females). Thus, there is no clear dose-response relationship in the incidences for hepatocellular adenoma. Furthermore, at 150 mg/kg bw/d, the body weight gain was reduced by 23% and 20% in males and females, respectively, which demonstrates that the MTD was exceeded at the high dose level.	Agree with MSCA

07/09/2011	United Kingdom / Member State	It would be useful if further information could be provided in this section regarding the incidence of observed tumours. For example, in your description of the mouse study, it would be useful if you could specify the incidence of the hepatocytic adenoma observed in the 20 and 50 mg/kg bw/day dose groups, to allow the reader to establish whether a dose response pattern is followed. For the rat study, please state the incidence rates for the observed mammary fibroadenomas and pituitary adenomas.	Agree see comment above. Doc IIIA6 containing detailed study summaries from the CA-report for IPBC for biocides will/has now been submitted to ECHA for distribution to RAC-members. In rat females, the incidence of mammary fibroadenomas was increased (i.e. 20/50) in the low dose group of 20 mg/kg bw/day only. At 40 mg/kg bw/day and 80 mg/kg bw/day the incidence of mammary fibroadenomas (i.e. 12/50 and 13/50, respectively) was comparable to the control (i.e. 12/50). Thus, no dose-response relationship was evident and the increased incidence of mammary fibroadenomas in the low dose group is not of toxicological significance. The incidence of pituitary adenoma was increased (i.e. 39/50) at 40 mg/kg bw/day in female rats. At 20 mg/kg bw/day and 80 mg/kg bw/day the incidence of pituitary adenoma was not increased (i.e. 33/50 and 29/50, respectively) when compared to the control group (i.e. 32/50). In the absence of a dose-response relationship, these findings were considered to be incidental and not to be of toxicological relevance.	Agree with MSCA

31/08/2011	Netherlands / RIVM / Bureau REACH / Behalf Of An Organisation / National Authority	Table 18 + text 4.10.1.1: Rat study: An increase in fibro adenomas in the salivary gland was observed. Without more detailed information about incidence in all dose groups and historical controls, it is not possible to conclude that IPBC has no carcinogenic potential. Table 18 + text 4.10.1.1: Mouse study: An increase in hepatocellular adenomas was observed. Without more detailed information about incidence in all dose groups and historical controls, it is not possible to conclude whether the finding is of biological relevance to human and it is therefore not possible to conclude that IPBC has no carcinogenic potential. According to 4.10.4 the increase is statistically significant compared to controls (although only at the 95% level, but also outside the historical control range (such information should be included in 4.10.1.1 as well!). Neither the DSD criteria nor the CLP criteria indicate that, in analysing common neoplasms, the p value for significance (historical control incidence >1%) should be be $p<0.01$ rather than $p<0.05$. What are the incidences of hepatocellular carcinomas? Is there information on the time of onset? What is the incidence of other hepatocellular changes?	Rat study: Understandable. Please also see above for fibroadenomas. More details on the incidences and dose-response considerations for fibroadenomas in the salivary gland can be found in the respective study summary of Document IIIA6. A significant increased incidence (6/49) of fibroplasia in the salivary glands was noted in males at 80 mg/kg bw/day only when compared to the control group (0/49). However, this higher incidence was observed only at the highest dose level (80 mg/kg bw/day) where the Maximum Tolerated Dose (MTD) was exceeded (i.e. absolute bw/bw gain was markedly reduced (> 20%). Mouse study: Detailed information on incidences of hepatocellular adenomas, MTD (based on body weight effects) and lack of dose-response can be found in the respective study summary of Document IIIA6. In males at 150 mg/kg bw/day a higher incidence in hepatocellular adenoma (11/50) was observed when compared to controls (4/50). This was, however, not considered to be of biologically significance for the following reasons: (1) The incidence in hepatocellular adenoma observed in this study (11/50) is only slightly outside the observed historical control range (i.e. 1 to 8/50) for this type of neoplasm. (2) There was no statistically significantly increase in the incidence of hepatocellular carcinomas or in foci of cellular alteration. (3) Additionally, there was no evidence of progression to malignant hepatocellular tumours and no effect on tumour multiplicity observable. (4) Hepatocytotoxicity or genotoxicity was not observed. (5) In females, the incidence of hepatocellular adenoma (i.e 1/50 in all dosed groups; elicits no dose response) and no carcinoma (i.e. 0/50) was observed. The	Agree with MSCA

Mutagenicity

Date	Country/ Organisation/ MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
12/09/2011	France / Member State	Agree with conclusion of RMS	Thank you.	OK
31/08/2011	Netherlands / RIVM / Bureau REACH / Behalf Of An Organisation / National Authority	☐ Please include the source of metabolic activation, whether appropriate controls (positive and negative) were used and specify the doses used (not only min-max). Without this information it is difficult to conclude whether the studies are indeed performed according to guidelines.	Agree. Detailed information on materials and methods used in the genotoxicity studies can be found in the respective study summaries of Document IIIA6 in the biocide CA-report for IPBC. Doc III6A has now been submitted to ECHA for distribution to RAC-members	OK

Toxicity to reproduction

/Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
12/09/2011	France / Member State	Agree with conclusion of RMS	Thank you	OK

09/09/2011	Germany/ Member State	No classification for reproductive toxicity is proposed based on the lack of any selective impairment of reproduction and development in the tested species at systemically non-toxic dose levels. However, the CLH-report does not provide specific incidence data for both signs of parental toxicity (e.g., reduced body weight gain, acanthosis and hyperkeratosis at doses ≥ 30 mg/kg bw/d, and changes in fertility parameters - e.g. fertility/mating index in F0 at doses <100 mg/kg bw/d, in [redacted], 1996 study), which would allow assessing the dose-response concordance between severity of parental toxicity and effects on fertility. Similarly, incidence data for each dose group is missing for developmental toxicity end points such as reduced live birth index, viability, and cumulative survival index. Such dose-response data is much appreciated during review since it gives an indication for the weight (strength) of evidence when dismissing reproductive effects because of parental toxicities. In its present form, the CLH report does not provide sufficiently detailed information that can serve as a base for conclusive assessment of reproductive toxicity.	Agree. For details, please refer to the corresponding study summaries in Document IIIA6 of the BPD dossier. **<u>Parental toxicity:</u>** **Body weight/ body weight gain:** At 100 mg/kg bw/day, male body weight gains were generally lower (i.e. 312 g) than the control (i.e. 349 g) being statistically significant on several occasions. Females body weight gain at 100 mg/kg bw/day during pre-mating and pregnancy was comparable to controls. During the first week of lactation, however, there was a statistically significant reduction in group mean maternal body weight gain (i.e. 21 g) for the 100 mg/kg bw/day females compared to the control group (i.e. 30 g). **Hyperkeratosis and acanthosis:** At histopathology, diffuse acanthosis with hyperkeratosis in stomach were noted at 30 mg/kg bw/day in F1 males (minimal 3/10, slight 4/10 and moderate 3/10, respectively) and F1 females (minimal, slight and moderate: incidence of 5/10, 2/10, 0/10, respectively) compared to the respective control groups (males and females: 0/10). Stomach of the F0 animals was not examined by histopathology. The lesions (hyperkeratosis and acanthosis) observed in the stomach may be a result of the local irritant properties of IPBC and bolus administration by gavage, however the findings in the stomach are considered to be of toxicological relevance to humans. There were no other effects observed at histopathology. For further details on reproductive toxicity observed please refer to document IIIA6.	OK

31/08/2011	Netherlands / RIVM / Bureau REACH / Behalf Of An Organisation / National Authority	Quantification of effects is needed to conclude whether effects are biologically relevant and whether developmental effects are due to maternal toxicity. Table 19, study [redacted] 1994a: When are the females sacrificed? The amount of decreased food intake should be included to be able to conclude whether this is a biologically relevant effect (especially since there are no significant effects on body weight). How is it possible that there are no significant effects on body weight in the 40 mg group while 4 animals are sacrificed due to body weight loss? Also the NOAEL dev cannot be the same as the LOAEL dev. 4.11.4 and 5: Whether or not developmental effects are observed without biologically relevant maternal toxicity cannot be concluded without more information.	For details, please refer to Doc IIIA6 containing the detailed study summaries from the CA-report for IPBC for biocides. In group 3 (20 mg/kg bw/day) one female animal and in group 4 (40 mg/kg bw/day) four females were prematurely sacrificed between days 15 and 22 of pregnancy, after prolonged periods of bodyweight loss and negligible food consumption. These observations were considered to be related to treatment. In addition, one control female aborted on day 27 of pregnancy and was sacrificed. The remaining females were sacrificed on day 28 of pregnancy. Food consumption showed high group variability at 20 and 40 mg/kg bw/day. When premature decedents and not pregnant animals were excluded from group means, mean food consumption was comparable to controls at 10 mg/kg bw/day. On single occasions, mean food consumption was statistically significantly reduced at 20 mg/kg bw/day (i.e. 128 g/rabbit/day compared to 169 g/rabbit/day in the control group) on day 11 – 15 and also at 40 mg/kg bw/day (i.e. 123 g/rabbit/day compared to 182 g/rabbit/day in the control group) on day 7-11 and on day 11-15 (124 g/rabbit/day compared to 169 g/rabbit/day in the control group). Afterwards, food consumption recovered, but tended to be slightly lower in these dose groups when compared to controls. When treatment with the test substance had stopped (day 19 to 28) mean food consumption was comparable to controls (20 mg/kg bw/day) or even higher (40 mg/kg bw/day). Thus, reduction in food consumption was reversible when treatment had stopped. The females in group 3 and 4 (20 and 40 mg/kg bw/day) which were sacrificed prematurely, exhibited persistent body weight loss from the onset of dosing until they were sacrificed	

Respiratory sensitisation

Date	Country / Organisation /MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
12/09/2011	France / Member State	Agree with conclusion of RMS	Thank you.	

Other hazards and endpoints

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
12/09/2011	France / Member State	P28 : In the acute inhalation toxicity part, could you please add more information on observed effects as the applicant's proposed a split entry classification for this endpoint quoting « the substance acts via direct local effect and not via systemic toxicity » and « the observed effects are dependent on the particle size of the substance ». However, we are agree with RMS. In effect, we think that a split entry classification is not appropriate because there is no effect in the study of [redacted] in which less than 5% of particle has an aerodynamic diameter of less than 10µm whereas there are effects in the study of [redacted] in which particles have also a mean diameter between 9.6 et 14.2 µm. P30 : Could you please consider the neurotoxic property in the STOT-RE part and not in the STOT-SE part ?	Thank you for your comments Each comment will be dealt with separately: P28.Detailed information on the effects observed in the acute inhalation toxicity studies can be found in the respective study summaries of Document IIIA6. P30.On page 47/48 of the CLH report, this information on neurotoxicity is already included. P34. To be discussed and other MS´s view are appreciated. IPBC is a solid material and according to our knowledge R66/EUH066 has historically predominantly been assigned to solvents which have degreasing effects. Considering the exposure method with semi-occlusion of the skin for 91 days the effects such as skin dryness and cracking are not surprising. P42-43 and P47. To be corrected and amended as fare as possible. The CLH	Noted.

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		P32 : We agree with your suggestion for a classification R37 « irritating to respiratory system » or H335 « may cause respiratory irritation » because this classification is based on qualitative data and not quantitative data. But we agree that effects could appear at dose superior in humans. P34: Do you think that a classification R66 (repeated exposure may cause skin dryness or cracking) or EUH066 (repeated exposure may cause skin dryness and cracking) could be added considering that some effects (hyperkeratosis, acanthosis and ulcer) are observed in the 13-week dermal toxicity study? P42-43 : Could you please add in the summary table of relevant repeated dose toxicity studies : • for the study of [redacted] that the increase of relative kidney weight was observed at 30 mg/kg/d and above, the increase of incidence in alpha-2-microglobulin droplets and erosion and ulceration in the forestomach were observed at 30 and above and not only above 30 mg/kg/d. • for the study of [redacted] that reduce of body weight and body	report contains only a summary of the toxicological properties of IPBS since the report is based upon the comprehensive CA-reports containing doc IIIA6 summaries. The doc IIIA6 is supposed to acts as an annex to the CLH-report. In our opinion the CLH-report is not supposed to be a stand alone document *when* a full CA-report exists and an agreement (at the CARACOL-CA group for REACH) concerning cooperation between the different legislations (DG SANCO, DG ENVIRON and REACH) has been made to minimise the workload between governmental bodies. P68. This will be included P69. This will be corrected	

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		weight gain in males were observed at 250 mg/kg/d and above and not only above 250 mg/kg/d and that the reduce of body weight gain in females were observed at 500 mg/kg/d and above and not only above 500 mg/kg/d. P47 : In the repeated dose toxicity by oral route, could you please add that reduced food consumption was observed at 80 mg/kg/d in the gavage study. Could you please add in the summary table of relevant repeated dose toxicity the study of [redacted] (oral feeding 104 weeks study in rats) as the conclusion on food consumption and body weights in rats by diet were based on it ? Moreover, you quoted this study at the end of this part « in the two-year feeding study … ». Could you please add in the summary of this study the effects observed on the salivary gland? Could you please also add in the summary table the study on mice of [redacted] as you quoted it? Could you please add in the summary of this study the pneumonitis? Could you please consider the conclusion on carcinogenicity in the appropriate part?		

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		Environmental hazards: - Degradation P68: it could be added in this part that iodine won't change the classification of IPBC - Distribution modelling P69: this part seems to not be very relevant considering the section 5.2.2 above. Moreover, the Henry's law constant value could be correctly "copied and pasted" from the section above		
12/09/2011	Sweden / Member State	SE comments on the environmental classification: In general we do not agree with the proposed classification for the substance. While we agree with the assessment of the toxicity and bioaccumulation (although description of the studies is very scarce and according to our opinion this should be improved to allow an independent judgment of the results) we do not agree with the conclusion that based on the available information the substance is readily biodegradable. The available information on degradation of the substance includes results from: (i) two hydrolysis studies, (ii) one ready test, (iii) one inherent biodegradability test, (iv) one	Thank you for your comment. IPBC cannot be considered to be "**readily** " biodegradable but IPBC can be considered to be "**rapidly**" degradable. The "ready" biodegradability is only one criteria to demonstrate that a substance is "rapidly" degradable. The CLP classification categories for hazardous to the aquatic environment are based on aquatic ecotoxicity data and whether a substance can be considered to be "**rapidly**" degradable. The decision scheme (mentioned by SE above) in Annex II, II4 of the "Guidance on Application of the CLP Criteria" ("Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures) (04/2011)" is a general guidance to facilitate decisions in relation	RAC discussed the different tests submitted in the report regarding degradation. The reported ready biodegradability test shows that the substance is not readily degraded, however, the concentration of the test substance (50 mg/l) is close to the inhibition concentration of microorganisms (EC20 = 57 mg/l). On the other hand, the aerobic soil degradation study shows a rapid degradation of IPBC, and the result of this test is in agreement with other studies such as the inherent biodegradation test which can be used only as additional information because it had some deficiencies. Taking into account all the reported information and

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		anaerobic degradation test in water/sediment, and (v) one aerobic degradation test in soil. The decision logic presented in part II.4 of the Guidance document guides on how the available information should be used in assessment of whether the substance is or is not ready biodegradable. In general, the decision logic is composed of two parts: the first part defines the preferred information on which a decision on ready biodegradability should preferably be based. The second part defines other types of information that can be used in the absence of the information specified in the first part. The preferred information for the assessment of biodegradation according to the first part is the following: results from a ready-test, or results from a surface water simulation test, or evidence showing primary degradation (biotic or abiotic) in the aquatic environment to non classifiable degradation products. If this information is not available the following information may be used for deciding on whether a substance is or is not ready biodegradable: results from an aquatic sediment or soil simulation	to rapid degradability. The preferred data are o Ready test o Surface water simulation test o Tests (e.g. hydrolysis) which show that the substance is primarily degraded in the aquatic environment to degradation products which do not fulfill the criteria for classification as hazardous to the aquatic environment. For IPBC data for the first point (ready test) are available, which shows that IPBC is not readily biodegradable. However, according to Commission Regulation (EU) No. 286/2011 (point 4.1.2.9.2 and 4.1.2.9.5) "a fail in the ready test does not necessarily mean that the substance will not degrade rapidly in the environment . A substance can be considered as rapidly degradable in the environment if (c) other convincing scientific evidence is available to demonstrate that the substance can be degraded (biotically and/or abiotically) in the aquatic environment to a level of > 70% within a 28-day period (see argumentation concerning page 8,12,13,14 above and page 75-77 in the CLH-report). An aerobic water simulation test (preferred data according to the Decision	the expert judgment RAC concluded that IPBC is rapidly degradable in the aquatic environment. Therefore, RAC agreed to classify IPBC as Aquatic Acute 1 with M factor 10 and Aquatic Chronic 1 with M factor 1.

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		test, or BOD5 and COD data, or weight of evidence approach based on read-across. In selection of the relevant information it is also important to consider section II.2.3.7 of the Guidance document. According to this section "data regarding the anaerobic degradation cannot be used in relation to deciding whether a substance should be regarded as rapidly degradable, because the aquatic environment is generally regarded as the aerobic compartment where the aquatic organisms, such as those employed for aquatic hazard classification, live." Taking into account the above the following data from the available data set on the substance can be considered as the preferred: results from the ready test and results from the hydrolysis tests. The simulation test in the surface water is not taken into account since it was performed under anaerobic conditions. The aerobic simulation test in soil is neither taken into account since, according to the decision logic, other preferable data are available. The selected data show that the substance is not ready	Scheme) is not available, therefore point (d) of the Decision Scheme applies to IPBC which says that "…*rapid degradation may be demonstrated if …..*" *The substance is demonstrated to be ultimately degraded in an aquatic sediment* ***or soil simulation*** *test with a half-life of < 16 days (corresponding to a degradation of > 70 % within 28 days);* ..". Furthermore, the anaerobic water-sediment study shows rapid degradation with a DT50 of a few hours, which confirms the observations made in other studies that IPBC very rapidly degrades in natural environments. Therefore, IPBC is considered to be "**rapidly**" degradable (a detailed argumentation is provided in the CLH-Report on page 76-77). Hydrolysis is not relevant for IPBC; IPBC is hydrolytically stable. Degradation of IPBC occurs under natural conditions i.e. IPBC is biotically degradable. The main criteria for bioaccumulation are the Log K_{OW} and BCF in fish. Degradation data are only supporting information.	

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		biodegradable (results from ready test) and is stable in water (hydrolysis tests) showing no primary degradation. Therefore our conclusion is that the substance is not ready biodegradable. This conclusion (i.e. the substance is not readily biodegradable) will imply changes in section 5.3.1. on aquatic bioaccumulation and also in section 5.5. Comparison with the classification criteria, that would lead to different classifications according to both DSD and CLP (incl. ATP2).		
09/09/2011	Germany / Member State	Proposed classifications for acute oral, acute dermal and acute inhalative toxicities can be supported (we cannot comment on the split-entry proposal). For eye and skin irritation, only mean scores for all animals and over all observation times are reported. Specifically for eye irritation, scores for cornea and iris damage are below the criteria specified in CLP and DSD for classification as Cat. 1/R41. If classification is proposed solely on irreversibility of the effects	For study details please refer to Doc IIIA6 (study summaries). **Skin irritation:** In the skin irritation study of [redacted] (2000), 3 rabbits were used and a dose of 500 mg of test substance was administered per patch and animal. Post-exposure period was 5 days. In the study summary, only the average scores for all animals at 24-72 h are presented. The following average scores (24, 48, 72 h) for erythema and oedema for the individual animals have been calculated from the study report: Animal 1: Erythema: 0.67 / Oedema: 0	**Concerning proposal for STOT RE 1, H371 (resp. R48/23):** Information on **skin irritation** study of [redacted] (2000) has been added to the RAC box. Information on eye irritation study ([redacted] (1998) has been added to the RAC box. With respect to **skin sensitization** more information on control groups used in Vohr,

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		(observed for 7 days only, CLP recommends 21), additional information on severity of iris and cornea damage on day 7 suggesting permanent irreversibility would be helpful and support the proposal. With respect to skin sensitization, the high incidences in the positive GPMT study ([redacted], 2001) would lead to classification as Cat. 1A, however data on incidences in the control group is missing; such information can help to better understand the argumentation that challenge with 5% IPBC was too close to the lowest irritating concentration of 6%. For the human data, information on previous exposures specifically to IPBC among the measured collective (and thus potential for IPBC-sensitized individuals) would strengthen the evidence for classifying as Cat 1B based on rather low incidences of <1% in human population. No classification is proposed for repeated dose toxicity; instead, classification for STOT SE Cat. 3 (May cause respiratory irritation) and R37 (Irritating to respiratory system) is suggested based on effects on the larynx (hyperplasia,	Animal 2: Erythema: 0.33 / Oedema: 0 Animal 3: Erythema: 1.0 / Oedema: 0 Average score (all animals, 24-72 h): Erythema: 0.67 / Oedema: 0. Reversibility of skin effects after 4 days in animals 1 + 2, and on day 5 in animal 3 In the **eye irritation study** of [redacted] (1998), 6 rabbits (3 per sex) were used and a dose of 80 - 90 mg of test substance was instilled into the right eye of each animals. Post-exposure period was 7 days. In the study summary, only the average scores for all animals at 24-72 h are presented. The following average scores (24, 48, 72 h) for erythema and oedema for the individual animals have been calculated from the study report: Animal 4204: Corneal opacity: 2.0; Iris: 1.0; Conjunctival redness: 2.0; Chemosis: 4.0 Animal 4205: Corneal opacity: 1.0; Iris: 1.0; Conjunctival redness: 2.0; Chemosis: 4.0 Animal 4206: Corneal opacity: 2.0; Iris: 1.0; Conjunctival redness: 2.0; Chemosis: 4.0 Animal 4207: Corneal opacity: 2.0; Iris: 1.0; Conjunctival redness: 2.0; Chemosis: 4.0 Animal 4208: Corneal opacity: 1.0; Iris: 1.0; Conjunctival redness: 2.0; Chemosis: 4.0	2001 study has been added to the RAC box. Classification for STOT SE 3/STOT RE 1 was discussed by RAC. RAC agreed on classification for STOT RE 1; H372 (larynx) based on the high incidence of the effects in larynx in the 90-day inhalation study ([redacted], 1994). The effective dose for larynx toxicity (0.0067 mg/l) is below the cut-off level for classification for STOT RE 1 (0.02 mg/l).

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		squamous metaplasia and necrosis) observed in a 90-day inhalation study with rats. While criteria listed in 3.8.2.2.1 of CLP regulation permit the use of data from chronic studies for classifying as STOT SE (i.e., respiratory irritant), these refer mostly to reversible clinical signs of toxicity. Therefore, if such observations are available from the initial stages of the 90-day inhalation study (or any other studies), they should be used for classifying as respiratory irritant. In our view, it is worth considering classification for STOT RE Cat 1, H371 (resp. R48/23) based on the high incidence (all animals in the high dose group), severity and potential irreversibility of the necrotic damage to the larynx. We understand the argument that these effects are most likely local due to the irritating properties of the test substance, however, the CLP regulation does not specify that STOT RE classifications should be only based on systemic effects. In addition, several oral studies (i.e., [redacted], 2001; [redacted], 1984) provide indication for damage of the fore-stomach (erosions, ulceration, hyperkeratosis and acanthosis) of rats exposed to ≥30 mg/kg (resp. ≥50 mg/kg) IPBC. It should be	Animal 4209: Corneal opacity: 2.0; Iris: 2.0; Conjunctival redness: 3.0; Chemosis: 4.0 Mean scores (24-72 hours) from six animals: Corneal opacity: 1.67; Iris: 1.17; Conjunctival redness: 2.17; Chemosis: 4.0 All ocular effects (i.e. opacity, iritis, conjunctival redness and swelling) have not reversed by the end of the observation time (day 7) in all animals. C&L with R41 or H318 is required. **Skin sensitization:** In the key study by [redacted], 2001, IPBC showed strong effects up to encrustation at the injection sites of the test item animals after intradermal induction. The challenge with the 5 % test item formulation led to skin effects (grade 1) in 80 % of the test item group after 48 hrs and 90 % after 72 hrs, respectively. No skin effects were seen in the control group. Decision regarding which category is appropriate for skin sensitization to be decided. For further information on the human data please refer to DocIIIA6 study summaries. **Concerning proposal for STOT RE Cat 1, H371 (resp. R48/23):** IPBC has been demonstrated to be a respiratory irritant and to induce irritation of mucous membranes.	

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		discussed if these effects do not warrant classification for repeated toxicity as well.	According to chapter 3.8.2.5 ("Decision on classification of substances") of the Guidance on the Application of the CLP Criteria, Category 3 effects should be confined to changes, whether functional or morphological, occurring in the upper respiratory tract (nasal passages, pharynx and larynx). Localized irritation with associated adaptive responses (e.g., inflammation, epithelial metaplasia, goblet cell hyperplasia, proliferative effects) may occur and are consistent with Category 3 responses. The effects in the 90-day inhalation study with IPBC were epithelial hyperplasia in the central region of the larynx, hyperplasia or squamous metaplasia in the ventrolateral region of the larynx, and necrosis of the underlying cartilage of the larynx at concentrations in the air equal to 6,7 mg/m3 (LOAEC 6,7 mg/m^3 with a NOAEC 1 mg/m^3). These findings are in accordance with the definition for a classification with STOT SE 3 and a classification with STOT RE is, thus, not warranted. The irritational effects observed in the laryngeal region were not associated with functional changes or any organ dysfunction. Furthermore, the NOAEC as well as the effective dose (ED) in the 90-day inhalation study are even clearly above the guidance values (GV) for a classification with STOT RE 2 which further substantiates that a classification with STOT RE is not warranted. The local effects in the oral studies are	

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
			clearly related to sustained irritation at the site of first contact which deserves no classification with STOT RE. The lack of a need to classify is further confirmed by studies where for instance tumorigenic effects are caused by sustained irritation at the port of entry. In these cases, no classification with respect to carcinogenicity is required. The same principle applies to IPBC for the forestomach effects. Consequently, no classification with STOT RE is required	
09/09/2011	Germany / Behalf Of An Organisation / Company-Manufacturer	The data submitted show that IPBC and mixtures containing IPBC have to be classified only with respect to acute inhalation toxicity, if the technical material contains more than 5% of particles with a size of less then 10 microns. If the technical material contains less than 5% of particles with a size of less then 10 microns, no classification of the IPBC and mixtures containing IPBC is warranted. For this reason, the classification of IPBC is to be split and a proposal for this split-entry classification is included in the attached document. In addition the Annex I of the CLH-Report "Proposal for split-entry classification of IPBC concerning inhalation toxicity" is attached since it is not provided in the	Annex I was submitted together with the initial CLH-report to ECHA.	See comment above with respect to split-entry classification for inhalation toxicity

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		published version. *The document attached "Comments of the IPBC Task Force on the CLH report of 3-Iodo-2-propynyl butylcarbamate (IPBC)[CAS No. 55406-53-6], (TF Comment_CLH report_IPBC_Public Cons. Phase_Sept 2011.doc)", is copied under the section "General Comments" pages 2-11 of this document.*		
07/09/2011	United Kingdom / Member State	Acute Toxicity- In addition to the LD50/LC50 data, please present any relevant toxicological findings along with an indication of their severity, the number of animals affected and the relevant dose(s). This information is required to allow the reader to make a judgment on whether the classification criteria for STOT-SE are fulfilled. Acute Inhalation Toxicity- Although we agree that classification should be based upon the form the substance is placed on the market, we do not consider that sufficient information has been provided to justify a split entry in Annex VI to CLP. Also, we note that the applicant's justification for a spilt entry in Annex VI (Appendix I) has not been made publically available	We fully understand the comments.. Please refer to Doc IIIA6 containing the detailed study summaries from the CA-report for IPBC for biocides. Annex I was submitted together with the initial CLH-report to ECHA.	**STOT-SE3** Additional details on acute inhalation toxicity studies were added in the RAC box. RAC concluded that since dyspnoea, salivation, lacrimation and rhinorrhea were observed in the acute inhalation toxicity studies at toxic concentrations (LC50 values between 0.5 and 1 mg/l) and the criteria for classification for acute inhalation toxicity are met, the classification STOT SE 3 is not warranted. In addition, RAC considered that hyperplasia and metaplasia of the larynx epithelium, and necrosis of the underlying cartilage of the larynx are not clinical signs of respiratory tract irritation. Consequently, RAC did not support the STOT SE 3 classification.

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		in the CLH Report. Skin Irritation- please state the number of animals and the dose used in the [redacted] (2000) study. If more than 3 animals are used in this study then the data should be presented as the average score (across the time points (24-72 hours)) for each individual animal, to allow for the provisions for tests conducted with more than 3 animals outlined in the 'guidance of the application of the CLP criteria'. Eye Irritation- please state the number of animals and the dose used in the [redacted] (1998) study. If more than 3 animals are used in this study then the data should be presented as the average score (across the time points (24-72 hours)) for each individual animal, to allow for the provisions for tests conducted with more than 3 animals outlined in the 'guidance of the application of the CLP criteria'. Skin Sensitisation – Please provide a statement indicating whether the positive and negative controls behaved appropriately in each study. In addition, two further Guinea Pig Maximisation Tests	R37: The order in this table should remain. The C&L as a respiratory irritant will be deleted from this section.	Acute inhalation toxicity: See the comment above with respect to split-entry classification for inhalation toxicity. Skin irritation, eye irritation, skin sensitisation: the available details have been added in the RAC boxes.

Date	Country / Organisation / MSCA	Comment	Dossier submitter's response to comment	RAC's response to comment
		(Shimizu et al, 2000 and Zissu, 2002) and one further Buehler test ([redacted], 1993) have been mentioned in the CLH Report; it would be useful if you could present the data from these studies in the report. In the repeat dose toxicity section (table 16), it would be beneficial to the reader if the studies for each route of exposure were grouped together (i.e. present the oral studies, then the inhalation then the dermal). In addition, in section 4.7.1.10 "conclusions on classification and labelling for repeat dose toxicity", the proposed classification with R37 has been included. As this section relates to repeat dose toxicity we would suggest deleting this from here and including only a conclusion on the repeat dose toxicity.		

31/08/2011	Netherlands / RIVM / Bureau REACH / Behalf Of An Organisation / National Authority	Page 19: In table 9, under 'state of the substance': both data for the pure substance and technical have been given. Are the other data provided in this table (and in the rest of the dossier) relevant for the pure or the technical substance? In addition, units are missing for vapour pressure. page 20: Table 9, oxidising properties: the comment refers to explosive properties, not oxidising properties. We agree with no classification of IPBC with respect to physical-chemical properties Acute toxicity Page 26/27: In table 11, please also include the resulting classification according to CLP. Page 27/28: In 4.2.1.1-4.2.1.4 and 4.2.3 only the results of the studies should be described. Where possible, please include more detailed information on the number of mortalities and clinical symptoms per dose administered. Page 29: In 4.2.4, please compare the relevant LD50/LC50 values with the cut off values of the criteria. Acute inhalation toxicity: According to CLP guidance 3.1.2.3.2 Evaluation of non-human data, results from studies in which substances with particle size with a MMAD > 4 µm have been tested can generally not be used for	**In general for many of the comments:** Please refer to our response regarding flexibility when performing the CLH-report on basis of a CA-report. *Study details are available in Doc IIIA study summaries from the CA-report.* p.19. See comment regarding CA-report Unit for v.p. will be included p.20 The oxygen balance (OB) is an indicator for both explosive and oxidizing properties as both physical-chemical endpoints are interrelated to each other. Therefore, the same statement applies for explosive and oxidizing properties. From the structural point of view, IPBC does not contain any atoms or functional groups which would give rise to explosive and oxidizing properties. All the oxygen or iodine atoms are only bound to carbon atoms and do, thus, not impose any oxidizing or explosive properties on the overall molecule. In addition, IPBC contains only oxygen in the carbamate form which does not support oxidation. Page. 26/27: Classifications according to CLP can be added as well. STOT-SE Cat 3. We are grateful for the further substantiation of the	Noted The liver effects (weight and histopathological changes) after oral exposure as well as other effects of the available oral, dermal and inhalation repeated dose toxicity studies were assessed by RAC. As indicated above, RAC agreed on classification for STOT RE 1; H372 (larynx) based on the high incidence of the effects in larynx in the 90-day inhalation study ([redacted], 1994). The effective dose for larynx toxicity (0.0067 mg/l) is below the cut-off level for classification for STOT RE 1 (0.02 mg/l).

		classification. In the study by Hoffman, the MMAD of the dust used is 4.3 µm (close to the maximum particle size that can be used for classification) and the MMAD of the liquid aerosol is 2.4 µm. The results of this study can thus be used for classification. In the study by [redacted], there is no information on particle size (study cannot be used). In the study by [redacted], the MMAD of the non micronised dust (respirable fraction 19.2-26.7%) was 9.6-14.2 µm. Also this study is therefore not ideal for classification purposes. Based on the study by [redacted] (LC50 0.63-0.99 mg/L), we propose to classifiy the substance as Acute Tox. 3; H331 (CLP) or T; R23 (DSD). Page 29, 4.2.3 No comment or conclusion is provided by the dossier submitter regarding the split entry as proposed by industry. In principle we agree with the use of a split entry if the requirements of Pauluhn as stated in the CLP guidance 3.1.2.3.2. are fulfilled. To enable this evaluation for the reader of the CLH report please provide a comparison of the available data with these requirements. STOT-SE: ☐ Page 30: It is stated that 'Clinical signs noted during the acute inhalation studies … are suggestive for an irritant effect on the	classification and the arguments will be added. Page 29: Please see CA`s response to Split entry/Annex I proposal in the end of this document. STOT-SE: We are grateful for the further substantiation of the classification and rephrasing and arguments will be added. Agreed that respiratory tract irritation is one of the criteria for STOT-SE. The second part of the sentence "rather than indicative for specific target organ toxicity" will be deleted. The 90-day inhalation study is important in this context as effects in the 90-day inhalation study with IPBC are in accordance with the definition for a classification with STOT SE 3 according to chapter 3.8.2.5 of the Guidance on the Application of the CLP Criteria. Results of repeated dose toxicity studies can be used for STOT SE 3 classification.(see Annex 1: 3.8.2.2.1 Criteria for respiratory tract irritation, point d): there are currently no validated animal tests that deal specifically with RTI, however, useful information may be obtained from the single **and repeated inhalation toxicity tests.** For example, animal studies may provide useful information in terms of clinical signs of toxicity (dyspnoea, rhinitis etc) and histopathology (e.g. hyperemia,	

		respiratory tract rather than indicative for specific target organ toxicity'. However, respiratory tract irritation is one of the criteria for STOT-SE. In addition, results observed in repeated dose toxicity studies are not relevant for STOT-SE, unless effects observed in the first day are regarded. The 90 day study described under 4.3 is therefore not directly relevant for STOT-SE. However, it could be considered as supportive evidence because in a repeated dose inhalation study, irritation occurs normally as an acute effect followed by hyperplasia and metaplasia. Further, it is supported by the stomach and eye irritating properties of the substance. ☐ Page 31/32: 4.3.1-4.3.3: Based on the dyspnoea and rhinorrhea observed in the acute inhalation study, but NOT only on the results of the repeated dose study, STOT-SE Cat 3; H335 should be proposed. Classification as Xi; R37 is not relevant in this paragraph, but should be discussed under 4.4.3. Skin irritation: ☐ Page 33/34: The key study should be described more detailed (number of animals, scores per time point, dose, vehicle used etc.). ☐ Page 34: Skin occlusion is not a reason for not classifying for skin	edema, minimal inflammation, thickened mucous layer) which are reversible and may be reflective of the characteristic clinical symptoms described above. Such animal studies can be used as part of weight of evidence evaluation. Page 31/32: The classification with Xi, R37 or STOT SE 3, H335, is relevant in this paragraph as chapter 4.3 deals with "Specific target organ toxicity – single exposure" and respiratory irritation is relevant for STOT SE (Note: R37 translates to STOT SE 3). In addition, the 90-day inhalation study is important in this context as well because effects in the 90-day inhalation study with IPBC are in accordance with the definition for a classification with STOT SE 3 according to chapter 3.8.2.5 of the Guidance on the Application of the CLP Criteria. Results of repeated dose toxicity studies can be used for STOT SE 3 classification.(see Annex 1: 3.8.2.2.1 Criteria for respiratory tract irritation, point d): there are currently no validated animal tests that deal specifically with RTI, however, useful information may be obtained from the single **and repeated inhalation toxicity tests.** Skin irritation: In the skin irritation study of	

		irritation. ☐ Page 33/34:_Dose levels of non-standard studies should be compared on a mg/cm2 basis. ☐ Page 34, 4.4.1.4 and 4.4.1.5: R38 can be applied according to the criteria based on a non-acute study if the effects are comparable to those for an irritation study. It should be clarified (also in 4.4.1.1) whether the effects occur early in the repeated dermal study indicating irritation or later probably indicating skin sensitisation. Eye irritation: ☐ Page 35: The key study should be described more detailed (number of animals, scores per animal and time point, dose, vehicle used etc.). ☐ Page 35, 4.4.2.5: According to the mean scores of the eye irritation test (mean 24+48+72), Eye irritation Cat 2; H319 (CLP) or Xn; R36 (DSD) should be appropriate. However, because the effects are not reversible (not because of the scores) IPBC should be classified as Eye Damage Cat 1; H318 (CLP) or Xi; R41. We agree with the proposed classification for eye irritation. Respiratory tract irritation: ☐ Please also include the effects in the acute inhalation study (dyspnoea and rhinorrhea) and the	[redacted] (2000), 3 rabbits were used and a dose of 500 mg of test substance was administered per patch and animal. The dose level of 500 mg/animal was applied to an area of 6 cm^2 (= 83mg/cm^2). Post-exposure period was 5 days. In the study summary, only the average scores for all animals at 24-72 h are presented. The following average scores (24, 48, 72 h) for erythema and oedema for the individual animals have been calculated from the study report: Animal 1: Erythema: 0.67 / Oedema: 0 Animal 2: Erythema: 0.33 / Oedema: 0 Animal 3: Erythema: 1.0 / Oedema: 0 Average score (all animals, 24-72 h): Erythema: 0.67 / Oedema: 0. Reversibility of skin effects after 4 days in animals 1 + 2, and on day 5 in animal 3. A classification with R38 is not triggered considering the results of the skin irritation study of [redacted]. In the 91 day dermal study the effects were observed within the first few days of exposure. Respiratory tract irritation: Please refer to the respective study summaries in DocumentIIIA6 of the	

		irritating effect on the eyes and stomach in the decision to classify for respirator tract irritation. To be added in the argumentation ☐ Classification as STOT-SE (H335) is not relevant in this paragraph, but should be discussed under 4.3. Corrosion: We agree with no classification of IPBC with respect to corrosive properties Sensitisation: ☐ Please include more detailed information of the key study (i.e. results of negative controls). In addition, information is needed whether a dose of 5% is irritating or not. Without more detailed information, it is not possible to conclude from this summary of the study whether IPBC is sensitizing. ☐ Because human information on skin sensitization is available, this should be leading over the animal data. Therefore, we should propose to classify IPBC as Skin Sens. 1B; H317 or Xi, R43. Repeated dose toxicity: ☐ Quantitative changes (body weight, liver weight, cholinesterase activity etc) are needed to decide whether effects are biologically relevant and thus relevant for classification. In addition, histological changes should be specified in the text.	BPD dossier for more details on the results of the acute inhalation toxicity studies. As respiratory irritation is relevant for a classification with STOT SE 3, the classification is maintained in this chapter. Sensitisation: Please refer to the respective study summaries in DocumentIIIA6 of the BPD dossier for more details on the results of the skin sensitisation studies. Human data take preference over animal data. Based on the results of human data, a C&L with Skin Sens. 1B is justified as justified below: In the 6 available human studies submitted with the BPD dossier, the incidence of positive reactions of patch-tested individuals was < 1%: Five of 6 investigations were patch tests (Bryld, L.E. et al, 1997; Pazzaglia, M. and Tosti, A., 1999; Majoie, I.M.L and van Ginkel, C.J.W., 2000; Bryld, L.E. et al; 2001; Schnuch, A. et al, 2002), one investigation is a case report (Jensen, C. D. et al, 2003). In four of the six studies, Finn chambers were used for patch testing but no details on the dermal load were given. The majority of the available animal tests result in an overall classification of IPBC in Skin Sens.	

		☐ Page 47: In 4.7.1.1 it is stated that IPBC is an irritating substance. This needs either a reference or data indicating that in this study the substance was irritating (more than salivation alone). ☐ Page 47: In 4.7.1.1 it is stated that results indicated that IPBC was not neurotoxic when administered via the oral route. On which data (from the oral studies) is this conclusion based? ☐ In the text, a 78 week study in mice and a 2 year study in rats are mentioned. Please include these studies and the relevant data in table 16. ☐ 4.7.1.1 and 4.7.1.7: Carcinogenesis should be discussed in 4.10. It is not relevant for repeated dose toxicity. ☐ The severity of liver effects (weight and histopathological changes after oral administration should be further discussed to conclude whether the effects are severe enough for classification as STOT RE2; H373 (CLP) or Xn; R48/22 (DSD). ☐ Also the irritating effects on the stomach should be discussed as these effects are mentioned in the DSD 3.2.4 to lead to classification even if reversible. For CLP, irreversibility is not stated as a requirement in the criteria. Neurotoxicity Please include data on which the	1A. The human data show that IPBC is a skin sensitizer in humans. In most cases, the frequency of occurrence of hypersensitivity is < 1 % of the persons tested. However, the 2nd ATP to the CLP gives no guidance on what is regarded a low, moderate or high frequency in humans. Overall, a classification in Skin Sens. Cat. 1B would be more appropriate based on positive patch testing results in humans and the low frequency of occurrence of hypersensitivity (< 1%). Page 47: The irritating effects of IPBC can be derived from the results of the eye irritation study and partly from the repeated dose dermal study. For neurotoxicity a study is described in docIIIA ([redacted] (2001): Acute Oral Neurotoxicity Study with IPBC. In general the classification proposals made by the CA/RMS are stated in the report. If other MS have suggestions for further/other classifications it could be given with arguments taken into account the provided study summaries in doc IIIA.	

		conclusion is based that no neurotoxicity was observed. Which parameters were analyzed? Environment No comments		

ATTACHMENTS RECEIVED:

GENERAL COMMENTS and OTHER HAZARDZ AND ENDPOINTS

Comments of the IPBC Task Force on the CLH report of 3-Iodo-2-propynyl butylcarbamate (IPBC)[CAS No. 55406-53-6], September 2011 (**TF Comment_CLH report_IPBC_Public Cons. Phase_Sept 2011.doc**). Submitted by Germany / Behalf Of An Organisation

Please find CA´s response to Annex I/split entry proposal below:

We were not aware that principles of Pauluhn 2008 (mentioned only as a reference in the ECHA document on Guidance on Application of CLP Criteria) could overrule the OECD guidelines in general. If we are going to apply the principles of using the most realistic situation with respect to particles sizes, which of course makes sense, it would mean that probably the majority of the previously classified biocides and pesticides would be subject to reclassification. In general the particle size of active substances used in formulated products is bigger than the one prescribed to be tested by OECD (MMAD of 1-4 µm). That would mean that the data requirements should be re-evaluated for acute inhalation toxicity and the currently performed inhalation studies seems therefore useless.

In general we are not against a split entry if the data justifies it. However in this particular situation we basically find that the data are insufficient to establish a split entry for IPBC.
As stated in the CLH report three inhalation studies ([redacted], 1985, [redacted], 1990, [redacted], 1994) were evaluated of which only one, [redacted] 1985, did not lead to classification as toxic.
In the [redacted] study the actual used particle size of IPBC was not measured and the proportion of particle less than 10 µm is therefore uncertain.
The applicant states that in a study on particle-size distribution ([redacted] 2001) measuring the particle size of technical IPBC used in the representative products and products on the market ≤ 5% of the particles were smaller than 10 µm but it was not further subdivided into smaller particle sizes and percentage distributions. So the split entry classification should be based upon a study ([redacted], 1985) where the particles size is actually unknown but extrapolated from another study ([redacted] 2001) postulated to be representative for technical IPBC used in the products on the market today since according to the applicant the production process for IPBC did not change between 1985 and 2001. We have difficulties to base a split-entry under these conditions on a study where we formally have no documentation for the tested

particle-size and percentage distribution. The LC50 of the non-micronised dust in the study from [redacted] corresponds to the LC50 in the study from [redacted], which according to our opinion supports the proposal for classification as T, as we do not know exactly why the LC50 in the [redacted] study was much higher than in the other two studies.

As response to ANNEX I and the so-called Pauluhn principles CA have the following comments.

1. We agree with IPBC being a powder with a low vapour pressure.

2. In the Guidance on Application of CLP Criteria is it stated:

> "A scientific concept has been developed as a basis for relating the conditions of acute inhalation tests to those occurring in real-life, in order to derive an adequate hazard classification. This concept is applicable only to substances or mixtures which are proven cause acute toxicity through local effects and do not cause systemic toxicity (Pauluhn, 2008)."

To our knowledge the deaths observed cannot be attributed only to acute local effects of IPBC but are as well caused by systemic effects so the crucial premise for applying the Pauluhn principles is not fulfilled. In the acute inhalation studies substantial decreases in body weights were observed and in addition to this reduced motor activity, laboured breathing and gasping and failure of grooming were seen (all potential indicators of impending death or moribund conditions).

3. We agree that the particle size can have an impact on the acute toxicity observed in inhalation studies (LC_{50} values) in general. However this had not been documented for IPBC, since we do not accept a study ([redacted] 1985) in which the particle size has not been measured (please refer to arguments above as well).

Annex II

- Argumentation: IPBC cannot be classified as readily biodegradable.
  In the Commission Regulation (EU) No. 286/2011 (2nd ATP) it is stated under
  - Point 4.1.2.9.2: that a fail in the screening ready test does not necessarily mean that the substance will not degrade **rapidly** in the environment
  - Point 4.1.2.9.5 that substances are considered rapidly degradable in the environment if (c) other convincing scientific evidence is available to demonstrate that the substance can be degraded (biotically and/or abiotically) in the aquatic environment to a level of > 70% within a 28-day period.

These apply to IPBC (a detailed argumentation is provided in the CLH-Report on page 76-77)

- Argumentation: Based on the results of the inherent test, IPBC cannot be classified as inherently biodegradable.

  In the inherent test a specific analysis of IPBC and PBC was performed. Based on these results, it **cannot** be concluded, that IPBC is not inherently degradable. The results of the study show that IPBC degrades completely to PBC within 2 hours and on day 21 the PBC concentration was below the LOQ.

  In the "Guidance on Application of the CLP Criteria" ("Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures) (04/2011) it is stated under

  - Point 4.1.3.2.3.2 (page 406) "Selection of test systems" that "Inherent- (OECD 302) and sewage treatment simulation (OECD 303) tests are not normally used in this context, due to the high levels of adapted biomass.
  - Annex II, Point II.2.3.4 (page 458) Substances that are degraded more than 70% in tests for inherent biodegradability (OECD 302) have the potential for ultimate biodegradation. However, because of the optimised conditions in these tests, the rapid biodegradability of inherently biodegradable substances in the environment cannot be assumed.

An inherent study could therefore only be used as supporting information. The inherent test performed with IPBC is based on specific analysis and therefore no conclusion can be drawn from this study concerning the inherent biodegradability of IPBC. However, the results show that IPBC and also the degradation product PBC degrade rapidly.