Ministry of Environment of Denmark
Environmental Protection Agency

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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

Background

This document presents summaries (Study Summaries) complied by the Danish EPA (DEPA) for two Acute Inhalation Toxicity Studies of IPBC not included in the CLH Report for IPBC of 11.11.2022. Refer to Annex 1 for the Study Summaries.

Brief summary of the studies and their results

Study 1

Performed according to OECD TG 403 and under GLP. Reliability score of 1.

CRL:(WI) Wistar strain rats (5 individuals of both sexes, 3 exposure groups) were exposed (nose-only) to mean achieved atmosphere concentrations of IPBC dust of 0.050, 0.205 and 0.494 mg/L, with acceptable particle size distribution at all exposure concentrations: MMAD (mean & range for the 3 groups) of 2.69 (2.47 – 2.90) µm.

Mortality was observed on Day 1 and 2 post-exposure, with 7 of 10 animals in the highest exposure group, and 6 of 10 animals in the mid exposure group, dying during this period. Refer to the summary of mortality table below.

Study 1: Summary of Mortality

Group number	Dose [mg/L]	Type of exposure	Sex	Number of dead / number of investigated	Time of death [day]
2	0.050	Aerosol (dust) of IPBC	male female	0/5 0/5	– –
3	0.205	Aerosol (dust) of IPBC	male female	4/5 2/5	Day 1 or Day 2 Day 1
1	0.494	Aerosol (dust) of IPBC	male female	4/5 3/5	Day 1 or Day 2 Day 1 or Day 2

All animals that died on-study had collapsed lungs, with the lungs described as "dark discoloration, red, diffuse, all lobes".

Acute inhalation median lethal concentrations (4h LC_{50}) and 95% confidence limits for the IPBC test material were:

Females: 0.33 (not calculated) mg/L
Males: 0.17 (0.05 – 0.42) mg/L
Both sexes: 0.23 (0.13 – 0.45) mg/L

The values for males, females, and the combined sexes fall with the range > 0.05 to ≤ 0.5 mg/L that characterises Category 2 for acute inhalation of dust/mist in the Globally Harmonised Classification System, i.e. Acute Tox. 2, H330 – Fatal if inhaled.

Study 2

Performed according to OECD TG 403 and under GLP. Reliability score of 2.

RccHan™:WIST strain rats (5 individuals of both sexes, 5 exposure groups) were exposed (nose-only) to mean achieved atmosphere concentrations of IPBC as a liquid aerosol (absolute ethanol as solvent) of 0.05, 0.21, 0.52, 0.53 and 5.03 mg/L, with acceptable particle (droplet) size distribution at all exposure concentrations: MMAD (mean & range for the 5 groups) of 1.83 (1.23 – 2.30) µm.

Mortality occurred predominantly during the exposure period and first hour post exposure; all 10 animals in the highest exposure group, and 12 of the 13 animals from the 0.52 and 0.53 mg/L groups that died on-study died during this period. Refer to the summary of mortality table below.

Study 2: Summary of Mortality

Group number	Dose [mg/L]	Type of exposure	Sex	Number of dead / number of investigated	Time of death [day]
5	0.05	Liquid Aerosol (20% w/w IPBC)	male female	0/5 0/5	– –
3	0.21	Liquid Aerosol (20% w/w IPBC)	male female	2/5 2/5	During exposure or Day 1 During exposure or Day 1
4	0.52	Liquid Aerosol (20% w/w IPBC)	male female	3/5 4/5	During exposure During exposure
2	0.53	Liquid Aerosol (40% w/w IPBC)	male female	3/5 3/5	During exposure or 1 hour post-exposure During exposure or Day 1
1	5.03	Liquid Aerosol (40% w/w IPBC)	male female	5/5 5/5	During exposure or 1 hour post-exposure During exposure or 1 hour post-exposure

All animals that died on-study had lungs described as either "pale", "unusually dark", or with "dark patches"; the lungs of some of the animals that survived also showed dark patches. Gaseous distention of the intestine and/or stomach showed a tendency for dose-proportionality, being observed in 5 of the 10 animals (both male and female) the highest exposure group.

Acute inhalation median lethal concentrations (4h LC_{50}) and 95% confidence limits for the IPBC test material were:

Females: 0.303 (non-calculable) mg/L
Males: 0.365 (0.256 – 0.514) mg/L
Both sexes: 0.337 (0.267 – 0.418) mg/L

The values for males, females, and the combined sexes fall with the range > 0.05 to ≤ 0.5 mg/L that characterises Category 2 for acute inhalation of dust/mist in the Globally Harmonised Classification System, i.e. Acute Tox. 2, H330 – Fatal if inhaled.

Key data from the two studies are summarised in the table below.

Key data from the two studies

Study, test animal, form of test item, and mode of exposure	**MMAD** µm (mean & range for exposure groups)	**4h LC_{50} mg/L (median & 95% confidence limits)**		
		females	**males**	**Combined sexes**
Study 1 (2014) CRL:(WI) Wistar rats Dust Nose only	2.69 (2.47 – 2.90)	0.33 (-)	0.17 (0.05 – 0.42)	0.23 (0.13 – 0.45)
Study 2 (2014) RccHan™:WIST rats Liquid aerosol Nose only	1.83 (1.23 – 2.30)	0.303 (-)	0.365 (0.256 – 0.514)	0.337 (0.267 – 0.418)

Conclusion

The two studies are considered to support amendment of the Harmonised Classification of IPBC for the end-point acute inhalation toxicity from 'Acute Tox. 3, H331 – Toxic if inhaled' to 'Acute Tox. 2, H330 – Fatal if inhaled'.

The most appropriate ATE is the value of 0.17 mg/L obtained for male CRL:(WI) Wistar strain rats in Study 1.

Annex 1

Study 1 — Acute Toxicity

Inhalation, Rat, LC_{50}

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (2014): [redacted] – Acute Inhalation Toxicity Study (Nose Only) in the Rat; [redacted]; Laboratory Study/Report Number [redacted]; (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	[redacted]	
1.2.2	Companies with letter of access	Not relevant in relation to use of the data in relation to Regulation (EC) No. 1272/2008 (CLP).	
1.2.3	Criteria for data protection	Not relevant in relation to use of the data in relation to Regulation (EC) No. 1272/2008 (CLP).	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes: OECD TG 403 (September 2009) (current version) Method B2 (Inhalation) of Annex part B of Commission Regulation (EC) No. 440/2008 US EPA OPPTS 870.1300	
2.2	**GLP**	Yes.	
2.3	**Deviations**	Yes. A number of minor discrepancies are evident: 1) It is not stated if the animals were acclimatised to the restraining tubes (see paragraph 11 of OECD TG 403). 2) Humidity was not recorded during the exposure period due to failure of a temperature-humidity sensor (see paragraph 19 of OECD TG 403). 3) A higher frequency of clinical observations on the first few days post-exposure, and notation of the time of death, appears warranted based on the response of the animals to treatment (as recommended in paragraph 41 of OECD TG 403). 4) The following information was not reported: sufficient information on the method of randomisation of animals to treatment groups; CAS number of IPBC; dimensions of the inhalation chamber, and location of temperature and humidity sensors in the chamber; information regarding the equipment used to measure oxygen and carbon dioxide levels; number of volume changes per hour; clear rationale for selection of the test concentrations; likely cause of death. The implications of the relationship between nominal- and actual test item concentrations, and the respirability of particles in light of the overall findings, were not addressed in the interpretation and discussion of the results. These issues are among those specified in paragraph 41 of OECD TG 403.	
		3 MATERIALS AND METHODS	

Study 1		Acute Toxicity Inhalation, Rat, LC_{50}
3.1	**Test material**	A source of IPBC [redacted] subsequently agreed by ECHA as being technically equivalent* to the Reference source of IPBC under the BPD. (**Decision on Technical Equivalence under Article 54(4) Regulation (EU) No. 528/2012; Decision number:* [redacted].)
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	See 3.1
3.1.2.1	Description	White-yellowish powder
3.1.2.2	Purity	99.95%
3.1.2.3	Stability	The IPBC test material was stable for at least 6 months after the exposure tests (according to the Sponsor's Certificates of Analysis).
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	CRL:(WI) Wistar
3.2.3	Source	[redacted]
3.2.4	Sex	male, female
3.2.5	Age/weight at study initiation	Animals were ca. 8 to 9 weeks of age. On the day of exposure, male body weight ranged from 306 to 442 g, and female body weight ranged from 191 to 254 g. Females were nulliparous and non-pregnant.
3.2.6	Number of animals per group	5 animals/sex/group; 3 groups
3.2.7	Control animals	Not required
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post-exposure period	14 days
3.3.2	Concentrations	Nominal concentrations: 2.452, 4.707 and 5.261 mg IPBC/L air Achieved concentrations: 0.050, 0.205 and 0.494 mg IPBC/L air
3.3.3	Particle size	Particle size of the generated atmosphere inside the exposure chamber was determined 3 times during each exposure period using a Mercer style 7-stage impactor. Particle size distributions of the aerosols generated are given in *Table 1 (Study 1): Summary of Particle Size Distribution*. Particle size distribution analysis of the aerosols showed a group average MMAD of 2.69 µm and a group average GSD of 2.33. An average of 68.0% of the particles were < 4 µm in size.
3.3.4	Type or preparation of particles	The test item was aerosolised using a rotating brush powder dispenser located at the top of the exposure chamber. The dispenser was connected to a compressed air supply.
3.3.5	Type of exposure	Nose only

3.3.6	Vehicle	None
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	4 h
3.3.9	Controls	Not required for this type of study.
3.4	**Examinations**	Animals were observed for clinical signs at hourly intervals during exposure, as soon as practicable after the end of exposure, 1 hour after termination of exposure, and subsequently once daily for up to 14 days. Body weight was recorded prior to treatment on the day of exposure (Day 0), and on Days 1, 3, 7 and 14, or at death. All animals were subject to a gross necropsy that included detailed examination of the abdominal and thoracic cavities. Special attention was given to the respiratory tract for macroscopic signs of irritancy or local toxicity.
3.5	**Method of determination of LC_{50}**	LC_{50} values were calculates SPSS software and a log/probit method. 95% confidence limits were not stated for female rats; no explanation was provided.
3.6	**Further remarks**	None.

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	Mortality rates are given in *Table 2 (Study 1): Summary of Mortality and Acute Inhalation Toxicity*. Deaths occurred on Day 1 or 2 post-exposure, the majority on Day 1: 5 of 6 in Group 3 (mid exposure level), 5 of 7 in Group 1 (high exposure level). During the exposure period, slight to severe laboured and noisy respiration were noted for all animals in the 3 treatment groups, with gasping also noted for animals the mid- and high exposure levels groups. For several days after exposure, prostration and hunching were noted in the mid- and high exposure level groups, with sneezing and distended abdomen also noted in the high exposure level group. No clinical signs were noted from Day 3, 7 or 8 in the low-, mid- and high exposure level groups, respectively.
4.2	**Pathology**	Diffuse, dark red discolouration of the lungs was observed in animals of Groups 3 and 1 (mid- and high exposure levels) that died during the study. One male animal in Group 1 had red, liquid material on the fur of the perinasal and ventral cervical and thoracic area. No macroscopic changes were observed in the lungs of animals in sacrificed at the end of the recovery period.
4.3	**Other**	Normal body-weight gain was noted for all surviving animals during the post-exposure period with the exception of occasional, slight losses in the mid- and high exposure level groups at the beginning of the recovery period.
4.4	**LC_{50}**	Acute inhalation median lethal concentrations (4h LC_{50}) and 95% confidence limits for IPBC:

		Females: 0.33 mg/L Males: 0.17 (0.05 – 0.42) mg/L Combined sexes: 0.23 (0.13 – 0.45) mg/L
		5 SUMMARY AND CONCLUSION
5.1	**Materials and methods**	The study was performed to assess the acute toxicity of IPBC via the inhalation route (OECD TG 403). Three groups of 5 animals per sex were treated once with 0.050, 0.205 or 0.494 mg IPBC/L as an aerosol (IPBC dust). Animals were exposed nose-only for 4 hours. After exposure, animals were observed for 14 days.
5.2	**Results and discussion**	The LC_{50} for females, males, and the combined sexes were 0.33, 0.17 and 0.23 mg/L, respectively. Slight to severe laboured, gasping and noisy respiration were observed during the exposure period. Prostration and hunching (and sneezing and distended abdomen at the high exposure level) were observed for several days post-exposure. Body-weight gain was generally normal, though occasional, slight losses occurred at the beginning of the recovery period. Post-mortem findings were essentially limited to discoloured, red lungs in animals that died on-study.
5.3	**Conclusion**	LC_{50}: Females: 0.33 mg/L Males: 0.17 mg/L Combined sexes: 0.23 mg/L
5.3.1	Reliability	1
5.3.2	Deficiencies	Yes; refer to section 2.3.

Study 1 **Acute Toxicity**

Inhalation, Rat, LC_{50}

Table 1 (Study 1): Summary of Particle Size Distribution

Group number	Dose [mg/L]	Type of exposure	Mean Mass Median Aerodynamic Diameter (MMAD) (µm)	GSD	Fraction (%) < 4 µm (i.e. inhalable fraction)
1	0.494	Aerosol (dust) of IPBC	2.47	2.52	69.9
2	0.050	Aerosol (dust) of IPBC	2.70	2.28	68.3
3	0.205	Aerosol (dust) of IPBC	2.90	2.20	65.8

Table 2 (Study 1): Summary of Mortality and Acute Inhalation Toxicity

Group number	Dose [mg/L]	Type of exposure	Sex	Number of dead / number of investigated	Time of death [day]
2	0.050	Aerosol (dust) of IPBC	male female	0/5 0/5	– –
3	0.205	Aerosol (dust) of IPBC	male female	4/5 2/5	Day 1 or Day 2 Day 1
1	0.494	Aerosol (dust) of IPBC	male female	4/5 3/5	Day 1 or Day 2 Day 1 or Day 2
LC_{50} values	Females: 0.33 mg/L Males: 0.17 mg/L Combined sexes: 0.23 mg/L				

Study 2 **Acute Toxicity**

Inhalation, Rat, LC_{50}

		1 REFERENCE	**Official use only**
1.1	**Reference**	[redacted] (2014): IPBC (3-iodo-2-propynyl bytyl carbamate): Acute Inhalation Toxicity (Nose Only) Study In The Rat; [redacted]; (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	[redacted]	

1.2.2	Companies with letter of access	Not relevant in relation to use of the data in relation to Regulation (EC) No. 1272/2008 (CLP).
1.2.3	Criteria for data protection	Not relevant in relation to use of the data in relation to Regulation (EC) No. 1272/2008 (CLP).

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes: OECD TG 403 (September 2009) (current version) Method B2 (Inhalation) of Annex part B of Commission Regulation (EC) No. 440/2008 US EPA OPPTS 870.1300
2.2	**GLP**	Yes.
2.3	**Deviations**	Yes. A number of minor discrepancies are evident: 1) Peak relative humidity in the range 72 – 75% was measured during exposure to the 4 lowest test concentrations; 70% is the ideal maximum according to OECD TG 403, paragraph 11. 2) Historical inhalation toxicity data to support the lack of acute inhalation toxicity of the vehicle (ethanol absolute) were not presented (as required by paragraph 17 of OECD TG 403), however the harmonised classification for ethanol (CAS no. 64-17-5) does not include acute inhalation toxicity. 3) Two different batches of test item were used, one for the initial tests of the highest exposure concentration and a second for the subsequent tests of the 4 lower concentrations; purity of the batches was high and comparable (99.9% and 99.63%, respectively). OECD TG 403, paragraph 22, recommends that one lot (batch) of the test article should be used if possible. 4) 6 of 17 individual chamber concentration samples for the group exposed to 0.53 mg/L of the test item deviate from the mean concentration by more than ± 20% (the limit specified in paragraph 23 of OECD TG 430), though situation did not occur in the group exposed to 0.52 mg/L. 5) A higher frequency of clinical observations post-exposure on the day of exposure, and on the first few days after exposure, appears warranted based on the response of the animals to treatment (as recommended in paragraph 41 of OECD TG 403). 6) The following information was not reported: method of randomisation of animals to treatment groups; CAS number of IPBC; justification for choice of a vehicle other than water. The implications of the relationship between nominal- and actual test item concentrations, and the respirability of particles in light of the overall findings were not addressed in the interpretation and discussion of the results. These issues are among those specified in paragraph 41 of OECD TG 403. The homogeneity, concentration and stability of the IPBC test material in liquid test formulations prepared by dissolving IPBC in absolute ethanol were not determined, which is a GLP deviation.

3 MATERIALS AND METHODS

3.1	**Test material**	An Alternative source of IPBC [redacted] subsequently agreed by ECHA as being technically equivalent* to the Reference source of IPBC under the BPD. (**Decision on Technical Equivalence under Article*

		54(4) Regulation (EU) No. 528/2012; Decision number: [redacted].)
3.1.1	Lot/Batch number	[redacted] (used for exposure Group 1), and [redacted] (used for exposure Groups 2, 3, 4 and 5)
3.1.2	Specification	See 3.1
3.1.2.1	Description	White crystalline solid
3.1.2.2	Purity	99.9% (used for exposure Group 1), 99.63% (used for exposure Groups 2, 3, 4 and 5)
3.1.2.3	Stability	The IPBC test material was stable for at least 3 months after the exposure tests (according to the Sponsor's Certificates of Analysis). The stability of the IPBC test material in the liquid test formulations prepared by dissolving IPBC in absolute ethanol was not determined.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	RccHanTM:WIST
3.2.3	Source	[redacted]
3.2.4	Sex	male, female
3.2.5	Age/weight at study initiation	Animals were ca. 8 to 12 weeks of age. On the day of exposure, male body weight ranged from 247 to 326 g, and female body weight ranged from 206 to 242 g. Females were nulliparous and non-pregnant.
3.2.6	Number of animals per group	5 animals/sex/group; 5 groups
3.2.7	Control animals	Not required based the original study protocol to test IPBC as an aerosol (dust). On revision of the study protocol to test a liquid aerosol, historical inhalation toxicity data to support the lack of acute inhalation toxicity of the vehicle (ethanol absolute) should have been included in the study report.
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post-exposure period	14 days
3.3.2	Concentrations	Nominal concentrations: 0.31, 1.16, 2.33, 4.08 and 36.5 mg IPBC/L air Achieved concentrations: 0.05, 0.21, 0.52, 0.53 and 5.03 mg IPBC/L air
3.3.3	Particle size	Particle size of the generated atmosphere inside the exposure chamber was determined 3 times during each exposure period using a Marple Personal Cascade Impactor. Particle size distributions of the aerosols generated are displayed in *Table 1 (Study 2): Summary of Particle Size Distribution*. Particle size distribution analysis of the aerosols showed a group average MMAD of 1.83 µm and a group average GSD of 2.2. An average of 83.6% of the particles were < 4 µm in size.
3.3.4	Type or preparation	The test item was aerosolised using a glass jet nebuliser located at the top of the exposure chamber. The nebuliser was connected to glass

	of particles	syringe attached to an infusion pump, which provided a continuous supply of the test item, and to a metered compressed air supply. A suitable atmosphere could not generated from the test material as supplied (crystalline solid). To improve the aerosolisation properties of the test material, IPBC was dissolved in absolute ethanol at a concentration of 40% w/w (exposure Groups 1 and 2) or 20% w/w (exposure Groups 3, 4 and 5). The homogeneity, concentration and stability of IPBC in liquid test formulations were not determined. It was not stated how soon after their preparation the solutions of IPBC were used in the exposure studies.
3.3.5	Type of exposure	Nose only
3.3.6	Vehicle	Absolute ethanol
3.3.7	Concentration in vehicle	IPBC (in absolute ethanol): 40% w/w (exposure Groups 1 and 2) or 20% w/w (exposure Groups 3, 4 and 5).
3.3.8	Duration of exposure	4 h
3.3.9	Controls	Not required for this type of study.
3.4	**Examinations**	Animals were observed for clinical signs at hourly intervals during exposure, immediately on the end of exposure, 1 hour after termination of exposure, and subsequently once daily for up to 14 days. Body weight was recorded on arrival, prior to treatment on the day of exposure (Day 0), and on Days 1, 3, 7 and 14, or at death. Necropsy: All animals were subject to a full external and internal examination, and any macroscopic abnormalities recorded. The respiratory tract was subject to a detailed macroscopic examination for signs of irritancy or local toxicity.
3.5	**Method of determination of LC_{50}**	LC_{50} values were calculated using ToxCalc software. The LC_{50} values for males and for the combined sexes were calculated by the Maximum Likelihood Regression method (Finney, 1971). Due to nature of the data obtained for females, their LC_{50} was estimated by Linear Interpolation (US EPA, 1989)
3.6	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	Mortality rates are shown in *Table 2 (Study 2): Summary of Mortality and Acute Inhalation Toxicity*. Deaths occurred between the exposure period and Day 1. Mortality occurred predominantly during the exposure period and first hour post exposure; all 10 of the animals in the highest exposure group, and 12 of the 13 animals (6 male, 7 female) from the 0.52 and 0.53 mg/L groups that died during the study died during this period. During the exposure period, decreased respiration rate was observed in all or many of the animals in Groups 1, 3 and 4, with instances of increased respiration rate. In Groups 2 and 5, increased respiration rate with instances of decreased respiration rate, were observed. Laboured breathing was noted for all or most of the animals in each treatment

group.

All animals in Group 1 (highest exposure level) were dead at the end of the exposure period. On removal from the treatment chamber, surviving animals in all treatment groups exhibited laboured/noisy breathing, and instances of increased or decreased respiration rate. One day after exposure, instances of increased and/or decreased respiration rate, and laboured breathing, were observed in Groups 2 to 5. Isolated cases of noisy respiration, red/brown staining around the eyes or snout, hunched posture and pilo-erection were observed. Surviving animals recovered slowly in Groups 2 to 4, and first appeared normal around Day 6 to 9 post-exposure (earliest at the lower exposures).

4.2 Pathology

All animals that died during the course of the study had lungs described as either pale, abnormally dark or with dark patches. Gaseous distention of the small and large intestine and/or stomach showed a tendency for dose-proportionality, being observed in 5 of the 10 animals (both male and female) the highest exposure group. With the exception of dark patches on the lungs of 3 animals, no macroscopic abnormalities were observed amongst animals that survived to the end og the recovery period.

4.3 Other

No animals in Group 1 (highest exposure level) survived past the day of exposure, so post-exposure body-weight data could not be collected for this group. In the remaining groups (Groups 2 to 5), all animals (though males only in Group 4) exhibited body-weight loss or showed no body-weight gain on Day 1 post-exposure. With occasional exceptions (mainly during Day 1 to 3) all surviving animals showed reasonable weight gains during the recovery period.

4.4 LC_{50}

The laboratory noted that the first exposure tested (the limit exposure of 5.03 mg/L) was far higher than necessary (causing all animals to die very quickly) and proposed excluding this group when calculating the LC_{50} (as it would not have any significant bearing on the LC_{50} value generated). The laboratory also proposed excluding data for the group exposed to 0.53 mg/L IPBC due to variability in the achieved atmospheric concentration during the 4-h exposure period (see Section 2.3). Data for both groups were used in calculation of LC_{50} values.

Acute inhalation median lethal concentrations (4h LC_{50}) and 95% confidence limits for IPBC:

Females: 0.303 (non-calculable)[1] mg/L

Males: 0.365 (0.256 – 0.514) mg/L

Combined sexes: 0.337 (0.267 – 0.418) mg/L

5 SUMMARY AND CONCLUSION

5.1 Materials and methods

This study was performed to assess the acute toxicity of IPBC via the inhalation route (OECD TG 403). Five groups of 5 animals per sex were treated once with 0.05, 0.21, 0.52, 0.53 or 5.03 mg IPBC/L as a liquid aerosol (IPBC in absolute ethanol). Animals were exposed nose-only for 4 hours. After exposure, animals were observed for 14 days.

5.2 Results and

The LC_{50} for females, males, and the combined sexes were 0.303, 0.365,

[1] Not calculable using the data evaluation method employed for analysing the mortality data for females.

Study 2		Acute Toxicity Inhalation, Rat, LC_{50}	
	discussion	and 0.337 mg/L, respectively. Decreased or increased respiration rate and laboured breathing were observed during the exposure period, the immediate post-exposure period, and during the first week post-exposure. Body-weight loss or no body-weight gain on Day 1 post-exposure was observed in most animals, though with occasional exceptions (mainly during Day 1 to 3) all surviving animals showed reasonable weight gains during the recovery period. Post-mortem findings included discoloured lungs and gaseous distention of the small and large intestine and/or stomach.	
	Conclusion	LC_{50}: Females: 0.303 mg/L Males: 0.365 mg/L Combined sexes: 0.337 mg/L	
5.2.1	Reliability	2	
5.2.2	Deficiencies	Yes; refer to section 2.3.	

Table 1 (Study 2): Summary of Particle Size Distribution

Group number	Dose [mg/L]	Type of exposure	Mean Mass Median Aerodynamic Diameter (MMAD) (µm)	GSD	Fraction (%) < 4 µm (i.e. inhalable fraction)
1	5.03	Liquid Aerosol (40% w/w IPBC)	1.83	2.25	83.4
2	0.53	Liquid Aerosol (40% w/w IPBC)	1.23	1.92	96.5
3	0.21	Liquid Aerosol (20% w/w IPBC)	1.59	2.53	84.2
4	0.52	Liquid Aerosol (20% w/w IPBC)	2.20	2.32	76.3
5	0.05	Liquid Aerosol (20% w/w IPBC)	2.30	2.09	77.5

Table 2 (Study 2): Summary of Mortality and Acute Inhalation Toxicity

Group number	Dose [mg/L]	Type of exposure	Sex	Number of dead / number of investigated	Time of death [day]
5	0.05	Liquid Aerosol (20% w/w IPBC)	male female	0/5 0/5	– –
3	0.21	Liquid Aerosol (20% w/w IPBC)	male female	2/5 2/5	During exposure or Day 1 During exposure or Day 1
4	0.52	Liquid Aerosol (20% w/w IPBC)	male female	3/5 4/5	During exposure During exposure
2	0.53	Liquid Aerosol (40% w/w IPBC)	male female	3/5 3/5	During exposure or 1 hour post-exposure During exposure or Day 1
1	5.03	Liquid Aerosol (40% w/w IPBC)	male female	5/5 5/5	During exposure or 1 hour post-exposure During exposure or 1 hour post-exposure
LC_{50} values		Females: 0.303 mg/L Males: 0.365 mg/L Combined sexes: 0.337 mg/L			