Section A6.1.3 Acute Toxicity

Annex Point IIA6.1

Inhalation - rat

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] 1987. Acute inhalation toxicity study of SY-83 in the rat [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Purac Biochem BV	
1.2.2	Companies with letter of access	No	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing [a.s. / b.p.] for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes: EPA, 1985 and OECD, 1981	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	SY-83	
3.1.1	Lot/Batch number	Not presented	X
3.1.2	Specification	Formulated from Purac HS pharmaceutical grade (USP XX) L(+) lactic acid (88%) by dilution to a concentration of 80% in water.	
3.1.2.1	**Description**	Liquid	X
3.1.2.2	**Purity**	SY-83 is formulated from Purac HS pharmaceutical grade by dilution to a concentration of 80% with water: 83.5-76.5% lactic acid in water	
3.1.2.3	**Stability**	As given in section 2	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Fischer 344	
3.2.3	Source	Charles River Breeding Laboratories, Raleigh, North Carolina, USA.	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	197.5 gram (male) and 139.9 gram (female)	
3.2.6	Number of animals per group	5 of each sex	
3.2.7	Control animals	Yes: sham-exposed control group to observe the biological effects of restraint. The animals were exposed for 4 hours to air alone.	

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3.3	**Administration/ Exposure**	Inhalation		
3.3.1	Post exposure period	14 days		
		Inhalation		
3.3.2	Concentrations	Nominal concentration	7.94 mg/L	X
		Analytical concentration	5 mg/L	X
3.3.3	Particle size	*Only for studies with aerosols*		
		MMAD (mass median aerodynamic diameter) 2.03 – 2.14 µm		
		The respirable concentrations (<15 microns) of SY-83 was 7.9 mg/L		
3.3.4	Type or preparation of particles	*For studies with particles:*		
		Not applicable		
3.3.5	Type of exposure	Nose only		
3.3.6	Vehicle	Not applicable		
3.3.7	Concentration in vehicle	Not applicable		
3.3.8	Duration of exposure	4 hours		
3.3.9	Controls	sham exposure		
3.4	**Examinations**	Mortality, clinical observations, body weight and gross necropsy		
3.5	**Method of determination of LD_{50}**	Limit test, statistics not applicable		
3.6	**Further remarks**	Not applicable		
		RESULTS AND DISCUSSION		
3.7	**Clinical signs**	Rapid breathing and eye tearing were seen during and shortly after exposure. After 24 hours most animals appeared normal and no unusual behaviour or appearance was observed for the remainder of the test period. However, several treated female rats showed ruffled, ungroomed fur the first days after treatment and the treated female rats lost weight during the first week. At the end all surviving animals gained weight and no significant differences were observed in body weight between treated and control groups.		
3.8	**Pathology**	No gross lesions were observed at necropsy.		
3.9	**Other**	One female rat died on day 8 post-treatment, following labored breathing and gasping on day 7.		
3.10	**LD_{50}**	Based on the results of this study, the LC50 of SY-83 is greater than 7.94 mg/L.		

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4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines The acute inhalation toxicity test is performed according to EPA/OPP, 1985 guidelines (Vol 50, no 188) and OECD guidelines (1981). The test article was applied by nose-only for four hours.
4.2	**Results and discussion**	Rapid breathing and eye tearing were seen during and shortly after exposure. After 24 hours most animals appeared normal and no unusual behaviour or appearance was observed for the remainder of the test period. Although one treated animal died, the LC50 of SY-83 is set as greater than 7.94 mg/L.
4.3	**Conclusion**	
4.3.1	Reliability	1
4.3.2	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/06/27
Materials and Methods	Applicant's version is acceptable with the following amendments: 3.1.1 Lot number: AP6853 3.1.2.1 Description: colourless liquid 3.3.2 Nominal concentration: 5 mg/L (incorrect value given in the study report) Analytical concentration: 7.94 mg/L
Results and discussion	Applicant's version is acceptable.
Conclusion	LC_{50}: > 7.94 mg/L air x 4 h
Reliability	1
Acceptability	Acceptable without restrictions
Remarks	The study was conducted with 80 % L-(+)-lactic acid instead of 93 % (concentration of the active substance, the highest obtainable concentration). However, the LC_{50} of > 7.94 mg/L air x 4 h with 80 % L-(+)-lactic acid with only one mortality suggests an LC_{50} higher than the limit concentration for classification for 93 % L-(+)-lactic acid.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*

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Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	