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		1 REFERENCE
1.1	**Reference**	[redacted] 1983. Acute dermal toxicity study in rabbits using SY-83 at a dose level of 2 grams per kilogram of body weight. Toxigenics Inc. Report nr. 410-1354.
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/OPP Guidelines 1982
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
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
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	Rabbit
3.2.2	Strain	New Zealand White albino
3.2.3	Source	Langshaw Farms, Augusta, MI, USA
3.2.4	Sex	Male and female
3.2.5	Age/weight at study initiation	Young adult / mean weight of 2.97 kg (males) and 3.02 kg (females)
3.2.6	Number of animals per group	5 of each sex
3.2.7	Control animals	No
3.3	**Administration/ Exposure**	Dermal
3.3.1	Postexposure period	14 days
		Dermal

3.3.2	Area covered	10 % of body surface	
3.3.3	Occlusion	Occlusive (impervious binder, consisting of a plastic wrap and adhesive tape)	
3.3.4	Vehicle	Not applicable, test article was applied neat	
3.3.5	Concentration in vehicle	Not applicable	
3.3.6	Total volume applied	25 milligrams of test article (2 gram / kg bw)	
3.3.7	Duration of exposure	24 hours	
3.3.8	Removal of test substance	Water	
3.3.9	Controls	Not applicable	
3.4	**Examinations**	Mortality, clinical observations, skin condition, body weight and gross necropsy	
3.5	**Method of determination of LD_{50}**	Limit test, statistics not applicable	
3.6	**Further remarks**	-	
		RESULTS AND DISCUSSION	
3.7	**Clinical signs**	No effects observed	
3.8	**Pathology**	No effects observed	
3.9	**Other**	Effects on skin were seen:	X
3.10	**LD_{50}**	No mortality was observed: LD50 > 2 g/kg bw	
		4 APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	The acute dermal toxicity test is performed according to EPA/OPP, 1982 guidelines. The test article was applied neat to the skin (clipped free of hair and abraded). After 24 hours the bandage (occlusive) was removed and the skin was cleaned with water.	
4.2	**Results and discussion**	All animals survived the 14-day observation period and gained body weight. No abnormal clinical signs were observed, however, skin effects were observed: severe erythema and severe edema were observed at the test sites of all animals after removal on day 1. Both decreased in severity in some animals by the end of the study. Other dermal reactions observed at the test site include blanching, eschar formation and desquamation. At necropsy brown crusted discolorations of the treated skin were found in 3 males and 3 females. Also multiple depressions (3 males / 1 female) and a dark red focus (1 male) were observed. No effects on mortality were observed and the LD50 is set at the limit test dose of > 2 g/kg bw.	
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.
Results and discussion	Applicant's version is acceptable with the following amendment: 3.9 For details on local skin effects see CA-table 1.
Conclusion	LD_{50}: > 2,000 mg/kg bw
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 LD_{50} of > 2000 mg/kg bw with 80 % L-(+)-lactic acid without any mortality suggests an LD_{50} higher than the limit dose for classification for 93 % L-(+)-lactic acid, too.
	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*
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	

Table A6_1-1. Table for Acute Toxicity (modify if necessary)

Dose [unit]	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
2000 mg/kg	0 / 5 per sex	Not applicable	Skin irritation
LD_{50} value	No effects on mortality were observed and the dermal LD50 is set at the limit test dose of > 2 g/kg bw.		

CA-Table 1 Local Skin Effects

Effect	No. of animals	Duration
Erythema	10/10	day 1- day 14
Oedema	10/10	day 1- day 14
Blanching	10/10 6/10	day 1 day 1- day 4
Necrosis	10/10 7/10 4/10	day 1- day 2 day 1- day 6 day 1- day 11
Eschar formation	10/10 7/10	day 2- day 11 day 2- day 14
Atonia	8/10	day 3/4- day 11/14
Desquamation	10/10	day 10/11- day 14
Fissures	5/10	day 5- day 14
Denuded areas along abrasion lines	1/10	day 14