Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.4

Human skin

			Official use only
		1 REFERENCE	
1.1	**Reference**	York, M., Griffiths, H.A., Whittle, E., Basketter, D.A. (1996) Evaluation of a human patch test for the identification and classification of skin irritation potential Contact Dermatitis, 34, pp 204-212	
		No GLP, published	X
1.2	**Data protection**	No	
1.2.1	Data owner	Not applicable	
1.2.2	Companies with letter of access	Not applicable	
1.2.3	Criteria for data protection	Not applicable	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Not according to a guideline	
2.2	**GLP**	Yes	
2.3	**Deviations**	Not applicable	
		3 MATERIALS AND METHODS	
3.1	**Test material**	88% lactic acid	
3.1.1	Lot/Batch number	Not mentioned	
3.1.2	Specification	Obtained from Sherman	
3.1.2.1	**Description**	Not specified	
3.1.2.2	**Purity**	88%	
3.1.2.3	**Stability**	Not mentioned	
3.2	**Test Animals**	Not applicable, tests performed *in vitro* with human skin (full thickness breast or abdomen tissue obtained from cosmetic surgery) and *in vivo* using human patch test on human volunteers (18-65 years old)	
3.2.1	Species	Not applicable	
3.2.2	Strain	Not applicable	
3.2.3	Source	Not applicable	
3.2.4	Sex	Not applicable	
3.2.5	Age/weight at study initiation	Not applicable	
3.2.6	Number of animals per group	Not applicable	
3.2.7	Control animals	Not applicable	

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3.3	**Administration/ Exposure**	Dermal	
3.3.1	Application		
3.3.1.1	**Preparation of test substance**	Test substance was used undiluted	
3.3.1.2	**Test site and Preparation of Test Site**	*In vitro* corrosivity test: The skin, epidermal side uppermost, was sealed to polytetrafluoroethylene (PTFE) tubes, which was placed inside a separate plastic container containing electrolyte solution (154 mM MgSO4 in distilled water). The test substance was applied to the epidermis and removed using a jet of water after a 24-h application. The corrosive effect was determined by measuring the transcutaneous electrical resistance (TER). Human patch test: The sequential single patch test procedure was used. 0.2 mL (0.2 g for solid test materials) was applied onto a 25 mm Plain Hill Top Chamber containing a Webril pad (moistened for solid test materials). The test materials were applied progressively from 15 and 30 minutes through 1, 2,, 3, and 4 hours.The upper outer arm was used as the treatment site for all experiments. Treatment sites were assessed for the presence of irritation using a 4 point scale at 24, 48, and 72 h after patch removal.	
3.3.2	Occlusion	Not applicable	
3.3.3	Vehicle	Not applicable	
3.3.4	Concentration in vehicle	Not applicable	
3.3.5	Total volume applied	Not applicable	
3.3.6	Removal of test substance	Not applicable	
3.3.7	Duration of exposure	Not applicable	X
3.3.8	Post exposure period	Not applicable	
3.3.9	Controls	Not applicable	
3.4	**Examinations**		
3.4.1	Clinical signs	No	
3.4.2	Dermal examination	Yes	
3.4.2.1	**Scoring system**	Presence of irritation was scored on a 4 point scale: 0 – no reaction + – weakly positive reaction (usually characterized by mild erythema across most of the treatment site) ++ – moderately positive reaction (usually distinct erythema possibly spreading beyond the treatment site) +++ – strongly positive reaction (strong, often spreading erythema with oedema)	

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3.4.2.2	**Examination time points**	24, 48, 72 hours after treatment	
	Other examinations	Not applicable	
3.5	**Further remarks**		
		RESULTS AND DISCUSSION	
3.6	**Average score**	Lactic acid was corrosive in the *in vitro* corrosivity test. In the human patch test, no positive reactions were observed at assessment at 24, 48, and 72 hours after treatment when volunteers were treated for 15 minutes, 30 minutes, or 1 hour. However, at 2, 3, and 4 hours, a total of 21 of the 26 volunteers who completed treatment had an irritant reaction to lactic acid.	X
3.6.1	Erythema	Not applicable	
3.6.2	Edema	Not applicable	
3.7	**Reversibility**	Not applicable	
3.8	**Other examinations**	No	
3.9	**Overall result**	88% lactic acid has corrosive properties and is irritating to the human skin.	
		4 APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	The corrosive and irritating properties of lactic acid on human skin were investigated using the *in vitrocorrosivity test and the in vivo* human patch test	
4.2	**Results and discussion**	Lactic acid was corrosive in the *in vitro* corrosivity test. In the human patch test, no positive reactions were observed at assessment at 24, 48, and 72 hours after treatment when volunteers were treated for 15 minutes, 30 minutes, or 1 hour. However, at 2, 3, and 4 hours, a total of 21 of the 26 volunteers who completed treatment had an irritant reaction to lactic acid.	
4.3	**Conclusion**	88% lactic acid has corrosive properties and is irritating to the human skin.	X
4.3.1	Reliability	2, study conducted with generally accepted scientific principles.	
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	2008/12/18
Materials and Methods	1.1 Work was conducted according to GLP Otherwise, the applicant's version is acceptable.

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Results and discussion	The applicant's version is acceptable with the following amendment: 3.6 In the human patch test, no positive reactions were observed at assessment at 24, 48, and 72 hours after treatment when volunteers were treated for 15 minutes, 30 minutes, or 1 hour. After application times of 2, 3, and 4 hours, a total of 21 of the 26 volunteers who completed treatment had an irritant reaction to lactic acid at either 24, 48 or 72 h.
Conclusion	4.3 88% lactic acid has corrosive properties *in vitro* and is irritating to human skin *in vivo*.
Reliability	2
Acceptability	Acceptable
Remarks	None

	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	