Section A6.2 Metabolism

Annex Point IIA6.2

			Official use only
		1 REFERENCE	
1.1	**Reference**	Sah, A. Mukherjee, S. Wickett, R.R (1998) An in vitro study of the effects of formulation variables and product structure on percutaneous absorption of lactic acid. J. Cosmet. Sci. 49, 257-273 Not GPL, Published	
1.2	**Data protection**	No	
1.2.1	Data owner	Purac Biochem BV	X
1.2.2	Companies with letter of access	No	X
1.2.3	Criteria for data protection	Data on existing or new [a.s. / b.p.] to [maintain or vary a.s. Annex I/IA entry / vary conditions of a b.p.'s authorisation]	X
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, Publication	
2.2	**GLP**	No, *Publication*	
2.3	**Deviations**	Not applicable, *Publication*	
		3 MATERIALS AND METHODS	
		L+[14C(u))] lactic acid, 150 mCi/mmol Synperonic PE/F127 Hpermer A60 Lactic acid Paraffin oil Propylene glycol Dermal penetration was studied on 3-4-week old female porcine dorsal skin, without adipose tissue and hair, thinned to 510 µm. 13 mm disks were mounted in flow-through cells. Viability was determined by transepidermal water loss measurements. Lactic acid was dissolved in oil-in-water, water-in-oil, and water-in-oil-in-wtaer emulsions, using appropriate surfactants and emulsification procedures. All test emulsions had a concentration of 8% lactic acid w/w. Emulsions were applied at two dose levels, viz. 2 µL / 0.64 cm^2 and 75 µL / 0.64 cm^2. Uptake of lactic acid into the skin layers and the receptor fluid (phosphate-buffered saline, pH 7.4, flow rate 5 mL/h) was studied for 6 hour penetration periods, for neat emulsions at pH 3.8 and 7, as well as emulsions at pH 3.8, with addition of 5% propylene glycol.	
		4 RESULTS AND DISCUSSION	
		Uptake from 2 µL o/w emulsion after 6 h pH 7: ca 7% in skin; 0.2% in receptor fluid.	

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		pH 3.8: ca. 25% in skin; 0.3% in receptor fluid. Uptake from 75 µL o/w emulsion after 6 h pH 7: ca 0.6%; 0.01% in receptor fluid. pH 3.8: ca. 0.95%; 0.01% in receptor fluid. Uptake from 2 µL o/w emulsion with 5% PG after 6 h pH 3.8: ca. 30% in skin; 0.7% in receptor fluid. Uptake from 75 µL o/w emulsion with 5% PG after 6 h pH 3.8: ca. 1.6%; 0.2% in receptor fluid. Penetration from water-in-oil and water-in-oil-in-water emulsions (2 µL, pH 3.8) is lower than from an oil-in-water emulsion.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Materials and methods appear appropriate for determining the dermal uptake of lactic acid from low concentration emulsions, as are encountered in cosmetics containing lactic acid as a relevant component.	
5.2	**Results and discussion**	It is clear that at low amounts of available lactic acid, the 6 hour potential dermal uptake from low concentration emulsions does not exceed 31%, at pH 3.8. Under these conditions propylene glycol enhances the uptake slightly. At higher doses, no significant effect of propylene glycol on dermal uptake percentage is observed. As such, it can be concluded that dermal uptake from large (‚infinite') amounts of lactic acid at high concentrations in aqueous solutions will not be higher than 31%.	
5.3	**Conclusion**	A worst case upper limit of the dermal uptake of lactic acid can be set at 31%	X
5.3.1	Reliability	1	X
5.3.2	Deficiencies	None	

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	The applicant's version is acceptable with the following amendments: 1.2.1 Not applicable, publication 1.2.2 Not applicable, publication 1.2.3 Not applicable, publication
Results and discussion	Applicant's version is acceptable.
Conclusion	5.3 A worst case upper limit of the dermal uptake of lactic acid can be set at 32 % in pig skin.
Reliability	2 (reliable with restrictions, see remarks)
Acceptability	Acceptable

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Remarks	No guideline, non-GLP data, in part results are only reported in diagrams (exact values missing).
	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	