

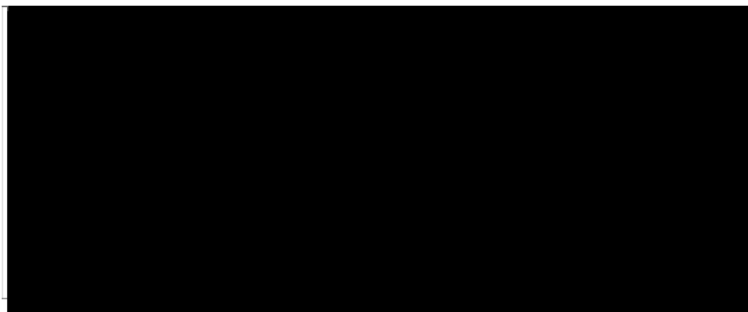
Section A4.1**Analytical Methods for Detection and Identification****Annex Point IIA4.1/4.2 & IIIA-IV.1**Official
use only

	1 REFERENCE	
1.1 Reference	Van Nieuwenhuizen, S. (1999) Determination of the chiral purity of lactic acid and derivatives Thesis, Hogeschool van Rotterdam Not GLP, Unpublished	
1.2 Data protection	Yes	
1.2.1 Data owner	Purac Biochem	
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/IA / authorisation]	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	This thesis forms the basis and validation for the chiral purity method described in A4_1_06.	
2.2 GLP	No	
2.3 Deviations	Not applicable	
	3 MATERIALS AND METHODS	
3.1 Preliminary treatment		
3.1.1 Enrichment	See A4_1_06.	
3.1.2 Cleanup	See A4_1_06.	
3.2 Detection		
3.2.1 Separation method	See A4_1_06.	
3.2.2 Detector	See A4_1_06.	
3.2.3 Standard(s)	See A4_1_06.	
3.2.4 Interfering substance(s)	None;	
3.3 Linearity		
3.3.1 Calibration range		
	all the points are lying between the 5% deviation lines ($R_c \cdot 1.05$ and $R_c \cdot 0.95$). So there can be concluded that all the points over the range of 0.1 until 5.5% chiral impurity have a linear relation.	

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3.3.2 Number of
measurements

9

3.3.3 Linearity

$r^2 = 0.9996$

**3.4 Specificity:
interfering
substances**

None:



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IIIA-IV.1

Table 4: peak table samples in S-form

component	retention time [min]
methyl-(R)-lactate	5.68
methyl-(S)-lactate	6.18

Table 5: peak table samples in R-form

component	retention time [min]
methyl-(R)-lactate	5.57
methyl-(S)-lactate	6.29

Table 6: list of possible impurities with their retention times

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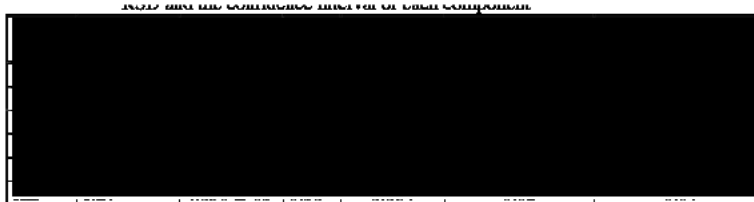
3.5 Recovery rates at different levels Not applicable

3.5.1 Relative standard deviation

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3.6 Limit of determination



Since the determination of an absolute amount or concentration is not the objective of this method, samples can always be analysed at the optimum method response point; LoD therefore is not applicable.

3.7 Precision

3.7.1 Repeatability

sample name:	measured area ratio [%]		theoretical area ratio [%]		recovery [%]
	R-HL	S-HL	R-HL	S-HL	
VALAC04	1.26	98.74	1.25	98.75	100.80
VALAC05	1.26	98.74	1.25	98.75	100.80
VALAC06	1.27	98.73	1.25	98.75	101.60
VALAC07	3.14	96.86	3.10	96.90	101.29
VALAC08	3.14	96.86	3.10	96.90	101.29
VALAC09	3.17	96.83	3.10	96.90	102.26
VALAC10	0.47	99.53	0.50	99.50	94.00
VALAC11	0.48	99.52	0.50	99.50	96.00
VALAC12	0.48	99.52	0.50	99.50	96.00

3.7.2 Independent laboratory validation

Not applicable

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

4.2 Conclusion



4.2.1 Reliability

1

4.2.2 Deficiencies

No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
Date	EVALUATION BY RAPPORTEUR MEMBER STATE 2014-10-30
Materials and methods	

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Conclusion	<i>The information given above is only in addition to the analytical methods for detection and identification presented in the other DOC III A 4.1.06 documents. It would be more useful and comprehensible to merge all information on the analytical methods for detection and identification and their validation in one DOC III A 4.1.06</i>
Reliability	
Acceptability	
Remarks	<i>Additional information.</i>
	COMMENTS FROM ...
Date	<i>Give date of comments submitted</i>
Results and discussion	<i>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</i>
Conclusion	<i>Discuss if deviating from view of rapporteur member state</i>
Reliability	<i>Discuss if deviating from view of rapporteur member state</i>
Acceptability	<i>Discuss if deviating from view of rapporteur member state</i>
Remarks	