

ERNDIM QUANTITATIVE ORGANIC ACIDS IN URINE: HIGHLIGHTS AND RECOMMENDATIONS

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Introduction

Can you use your organic acids profiling results for therapeutic monitoring?

Can they be used in multi-centre studies?

The ERNDIM Quantitative Organic Acids in Urine EQA scheme assesses accuracy, recovery, linearity and inter-laboratory variance (CV%) of quantitative measurements for 20 common and selected organic acids relevant to IEMs

Scheme Details

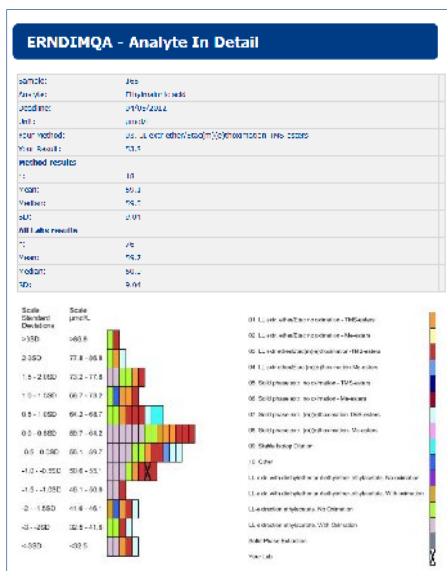
- 8 samples of lyophilised human urine spiked with physiologically relevant levels of 20 organic acids
- Results submitted via ERNDIM interactive website
- Scheme operated since 1993
- 107 participants from 33 Countries worldwide (2013)
- Cost (2013): 270 EURO

Participants' Annual Report

Analyte	Accuracy (CV%)		Precision (CV%)		Linearity (CV)		Recovery (%)		Data all labs
	Year Lab	All labs	Year Lab	All labs	Year Lab	All labs	Year Lab	All labs	
3-methylglutaric acid	149	140	11.8%	17.8%	0.003	0.050	81%	79%	71
4-hydroxybutyric acid	80.9	85.1	8.4%	9.4%	0.003	0.050	102%	103%	86
3-hydroxyisovaleric acid	115.9	115.1	9.0%	11.0%	0.004	0.040	100%	101%	74
2-hydroxyisovaleric acid	20.9	20.0	15.1%	12.6%	0.001	0.012	103%	103%	86
3-hydroxyvaleric acid	76.7	86.3	11.4%	10.4%	0.002	0.001	87%	86%	84
4-hydroxyvaleric acid	75.8	75.8	11.3%	11.8%	0.001	0.004	107%	107%	70
Glutaric acid	120.9	122.2	4.3%	3.2%	0.001	0.004	107%	107%	72
2-hydroxyglutaric acid	16.4	16.1	10.1%	10.1%	0.001	0.001	107%	107%	104
3-hydroxyglutaric acid	89.7	87.4	8.7%	11.3%	0.002	0.007	87%	100%	87
4-hydroxyglutaric acid	93.8	80.8	3.8%	12.1%	0.001	0.012	102%	104%	76
2-hydroxyglutamic acid	88.4	106	8.7%	4.0%	0.001	0.007	97%	87%	83
3-hydroxyglutamic acid	15.8	7.15	11.7%	7.1%	0.001	0.001	73%	80%	68
4-hydroxyglutamic acid	67.4	31.1	10.8%	18.6%	0.004	0.004	84%	104%	82
5-hydroxyglutamic acid	35.4	37.7	7.7%	7.1%	0.001	0.007	84%	84%	71
6-hydroxyglutamic acid	15.1	15.9	11.2%	10.7%	0.001	0.004	81%	69%	14
7-hydroxyglutamic acid	134.9	134.9	9.4%	12.1%	0.001	0.006	80%	100%	106
8-hydroxyglutamic acid	73.7	71.6	15.1%	8.1%	0.001	0.001	81%	80%	14
9-hydroxyglutamic acid	111	288.1	80.1%	26.8%	0.004	0.010	100%	79%	62
10-hydroxyglutamic acid	109.2	121.9	18.4%	19.4%	0.001	0.010	78%	78%	86
11-hydroxyglutamic acid	101	75.8	7.1%	11.1%	0.001	0.004	105%	94%	74
12-hydroxyglutamic acid	25.8	28.9	24.4%	12.1%	0.001	0.006	101%	91%	78
13-hydroxyglutamic acid	88.9	100.8	14.8%	19.1%	0.001	0.001	71%	89%	83
Overall	711	677	10.5%	6.4%	0.001	0.001	86%	86%	68

- Performance based on 4 parameters: Accuracy, Precision, Linearity, Recovery
- The parameters are scored for each analyte; those falling outside the 95th percentile for all laboratories are indicated with red shading
- Two or more parameters with red shading or insufficient submissions are equated to unsatisfactory performance for that particular analyte
- Green shading indicates satisfactory performance for that analyte

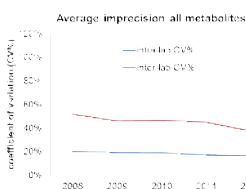
Example of Detailed Report



Ethylmalonic acid

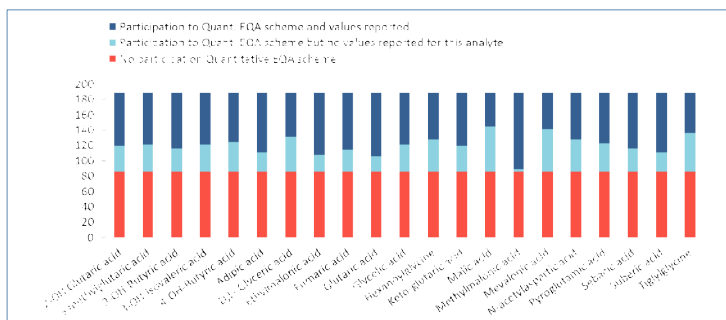
- Consensus concentration = median = 59 µmol/L (20 mmol/mol creatinine)
- Close to diagnostic threshold for EPEMA (ETH1 mutation ~ 35-45 mmol/mol creatinine)
- 5 labs (7%) reported values more than 3SD below consensus value: risk of missing ETH1
- 2 labs (3%) reported more than 3SD above consensus: risk of false positive ETH1 diagnosis

Variation within and between labs



- Large analyte-dependent differences in intra-lab CV% (precision): <10% to > 25%
- Inter-lab CV% discrepantly high as compared to intra-lab CV%: lack of method standardization
- A positive trend is seen for inter-lab CV% in the period 2008-2012

Scheme participation



Only 50% of the labs that participate in the Diagnostic Proficiency Scheme (ERNDIM Qualitative Organic Acids Schemes) participate in the Quantitative schemes. Does this mean that half of the labs does not care about accurate and precise quantification?

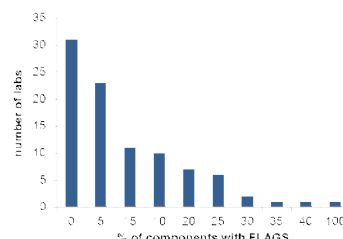
Feedback

General:

- 8 Monthly reports plus annual report
- Certificate issued once a year by ERNDIM Board

Personalized:

- Letters of support to poor-performers
- Offer training



Conclusions

- Accurate and precise quantification is important for therapeutic monitoring but also for diagnosis, e.g. subtle rises of ethylmalonic acid in SCAD or EPEMA, and 3-hydroxyisovaleric acid in biotinidase deficiency
- Surprisingly, only half of labs that use organic acids for clinical diagnosis feel the need to (quality-control if they can) report quantitative results
- From 2008-2012, the analytical performance in the Quantitative Organic Acids in Urine EQA scheme steadily improved, indicating the educational value of participation to such quantitative scheme.
- Inter-lab imprecisions remain, disproportionately high, calling for further standardization.

Ask your lab how they perform in ERNDIM EQA schemes!

For further information please contact: admin@erndim.org
www.erndim.org

