

How reliable are metabolite measurements in IEM: experience from ERNDIM Quality Assurance Schemes

Why do we need for Quality Assurance for Inborn Errors of
Metabolism

ERNDIM organisation

ERNDIM Schemes



Quality Assurance in IEM is essential

- agreed thresholds of metabolite levels for treatment
- validity of published data / inclusion of patients in multicentre studies
- agreed critical cutoff values in newborn screening (tandem MS)
- Mobility of patients

Email in metab-I

«...Our patient with Aciduria will be on vacation in XXX with his family; the parents ask if there is a metabolic center near XXX where a metabolic control for adapting the treatment could be done. »

Why is Quality Assurance in IEM essential

- agreed thresholds of metabolite levels for treatment
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- agreed critical cutoff values in newborn screening (tandem MS)
- Mobility of patients

Interpretation of data from different laboratories in a patient demands comparability of measurements of the two labs

ERNDIM Provides European-Wide Quality Assurance since 1994

Aims of ERNDIM

Consensus on procedures for diagnosis, treatment and monitoring of inherited metabolic diseases.

Quality control schemes operated according to accepted norms

Education

Meetings, Recommended Operating Procedures
Annual reports of schemes on the internet.

Value for money

Minimal administration costs and efficient subscription collection.

ERNDIM web-site: www.erndim.ch



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ERNDIM is now synonymous with quality control of laboratory measurements within the field of the study of inborn errors of metabolism. ERNDIM was founded in 1994 with its legal base in Maastricht, The Netherlands.

The full name of ERNDIM, the "European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism" reflects the original ideals and vision of its founders.

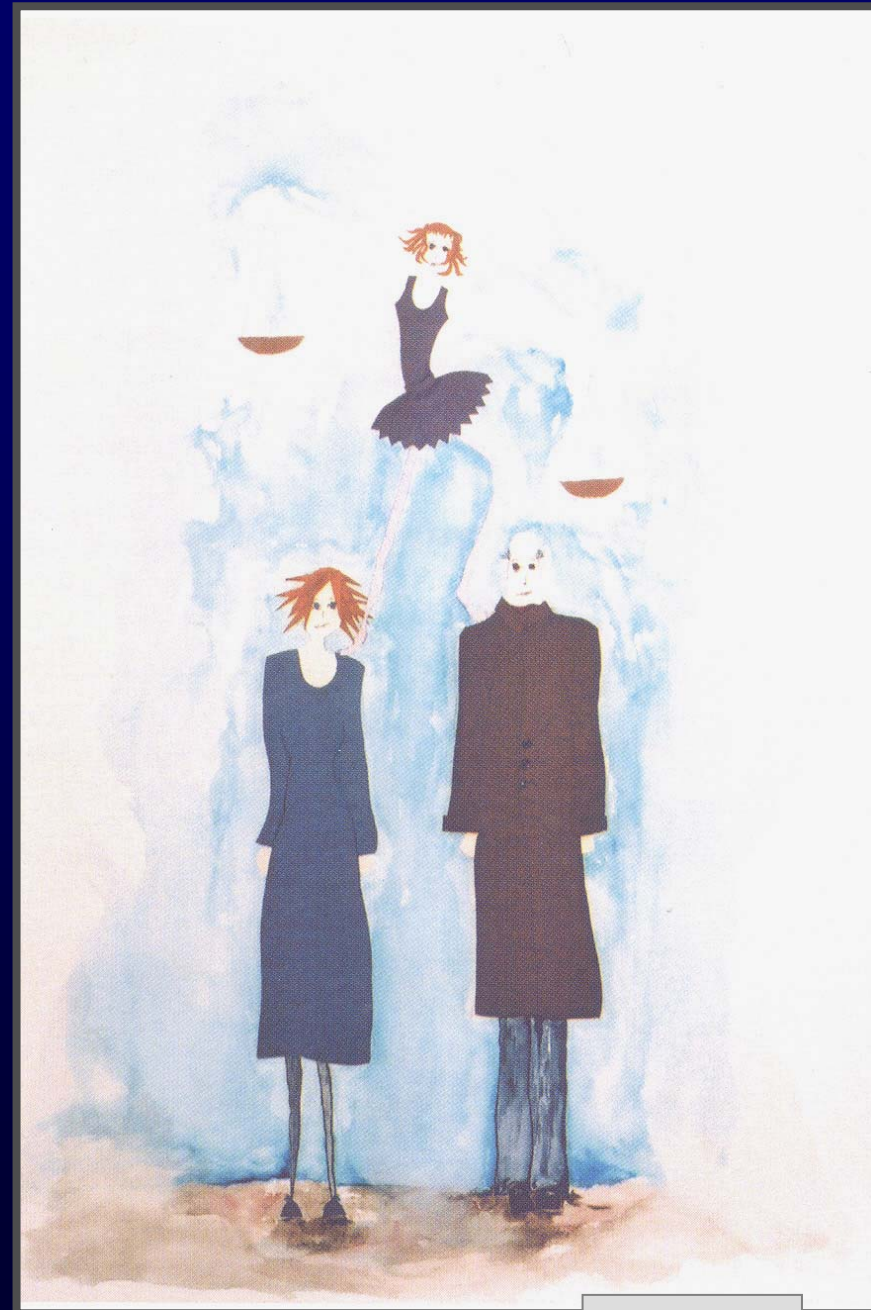


EuroGentest

Genetic Testing in Europe

Network for test development
harmonization, validation and
standardization of services

Co-ordinator: Jean-Jacques Cassiman
University of Leuven, Belgium



By Rebecca Kent

Current EQA Schemes

Plasma Amino
Acids (30)
177 participants

Serum Special
Assays
158 participants

Urine Special
assays
121 participants

O-1-6
J. Bonham et al

Organic Acids in
urine
Proficiency testing
137 participants

White Blood
P-18-21
M Henderson et al.

Diagnostic Proficiency
Testing in Urine
93 participants

Urine Purines
and pyrimidines
45 participants

Blood Spots
Acylcarnitines
67 participants

ERNDIM Special Assay Schemes: Analytes 2006

Urine

5-OH-Indolacetic acid
Carnitine free
Creatine
Creatinine
Guanidinoacetate
Homovanillic acid
Hydroxyproline
Lactic acid
Mucopolysaccharides
Orotic acid
Pipicolic acid
Sialic acid
Succinylacetone
Thiosulphate
Uric acid

Serum

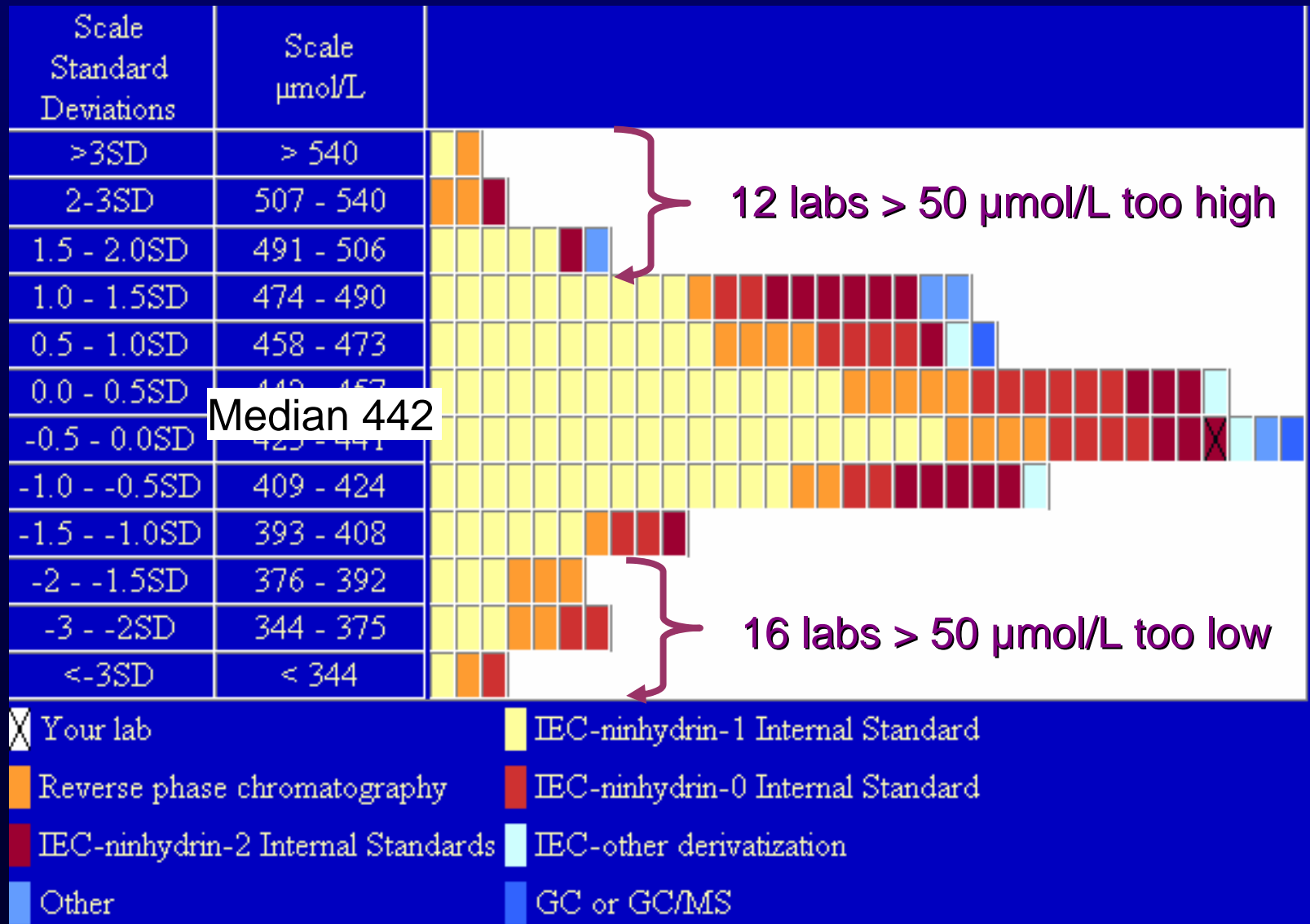
3-OH Butyric acid
7-Dehydrocholesterol
C22:0 Behenic acid
C24:0 Lignoceric acid
C26:0 Cerotic acid
Carnitine free
Cis-4-deconic acid
Creatine
Guanidinoacetate
Homocysteine
Phenylalanine
Lactic acid
Phytanic acid
Pipicolic acid
Pyruvic acid
Uric acid

ERNDIM Amino acid QC scheme:

Participants – 177 from 26 countries

Methods	Participants (%)
Ion-exchange chromatography + ninhydrin	82 %
Ion-exchange chromatography + other deriv.	2 %
Reverse phase HPLC	12 %
GC (MS)	1.5 %
Other	2 %

Amino acid QC scheme: Phenylalanine of 442 $\mu\text{mol/L}$



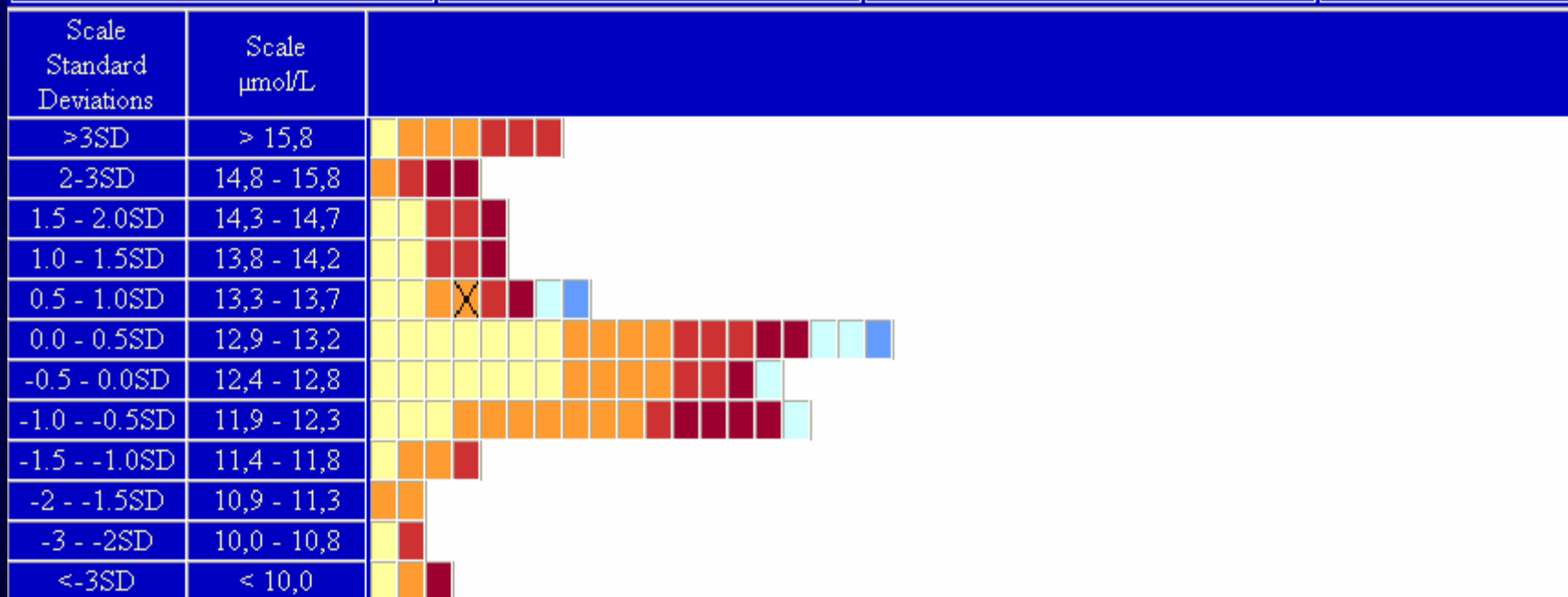
SA-Serum 59

Homocysteine

Method

Selections for Report

Hospital Name	Universitäts Kinderspital Beider Basel	Parameter	Your La
Department	Aminoacid lab	n	1
Contact Person	B. Fowler / M. Zaugg / M. Bill	Mean	13.5
Deadline	10-09-2004 23:59	Median	13.5
Unit	µmol/L	SD	



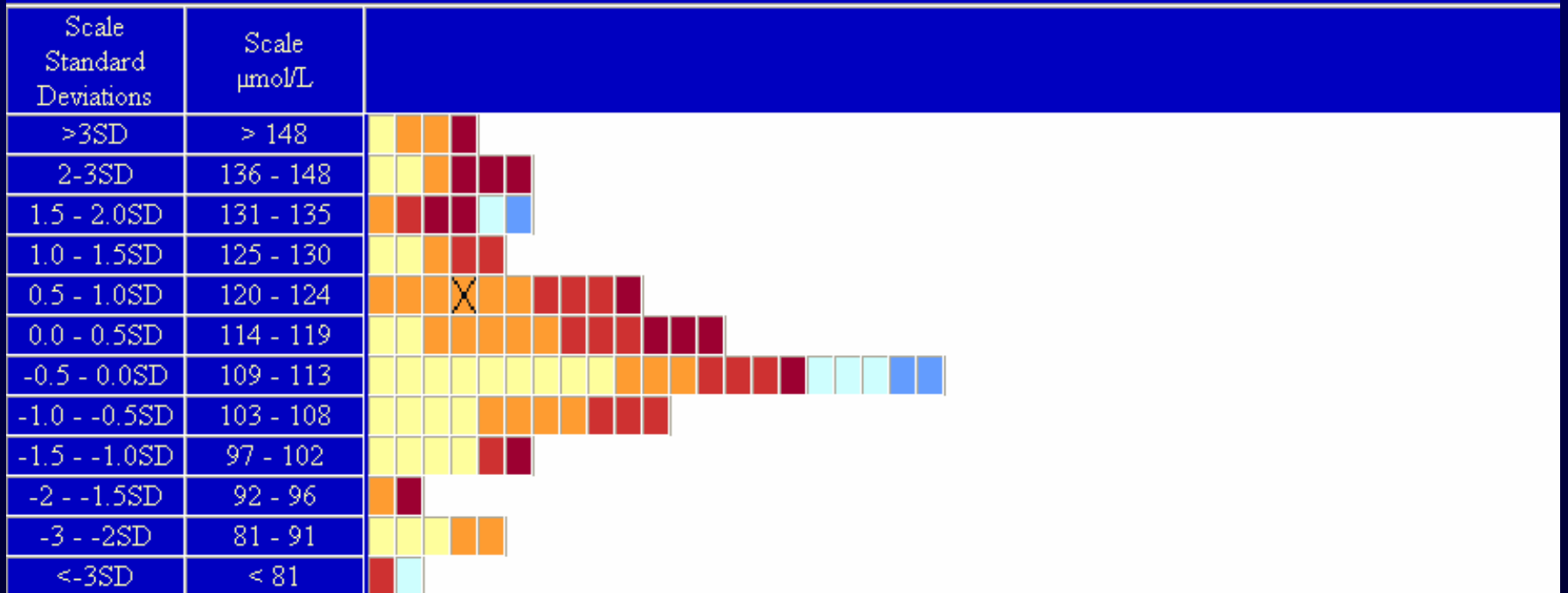
- Your lab
- Immunoassay
- HPLC-SBDF reagent
- Other
- Ion exchange/reduction DTT/ninhydrin
- ELISA
- HPLC-bromobimane reagent

Mean all labs 12.9
µmol/L

SA-Serum 62

Homocysteine

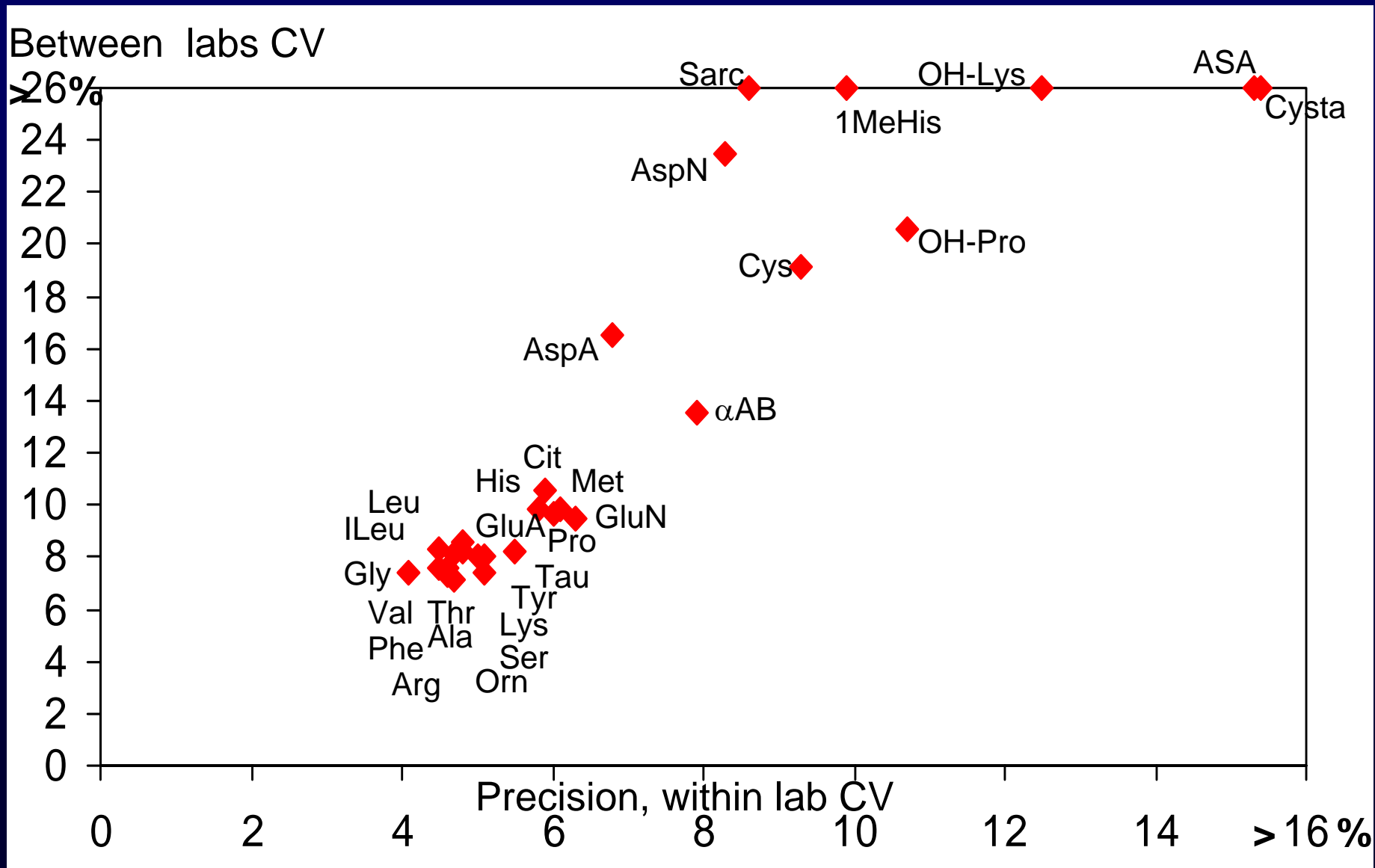
Method			
Selections for Report			
Hospital Name	Universitäts Kinderspital Beider Basel	Parameter	Your I
Department	Aminoacid lab	n	1
Contact Person	B. Fowler / M. Zaugg / M. Bill	Mean	121
Deadline	03-12-2004 23:59	Median	121
Unit	µmol/L	SD	



- Your lab
- Immunoassay
- HPLC-SBDF reagent
- Other
- Ion exchange/reduction DTT/ninhydrin
- ELISA
- HPLC-bromobimane reagent

Mean all labs 114
µmol/L

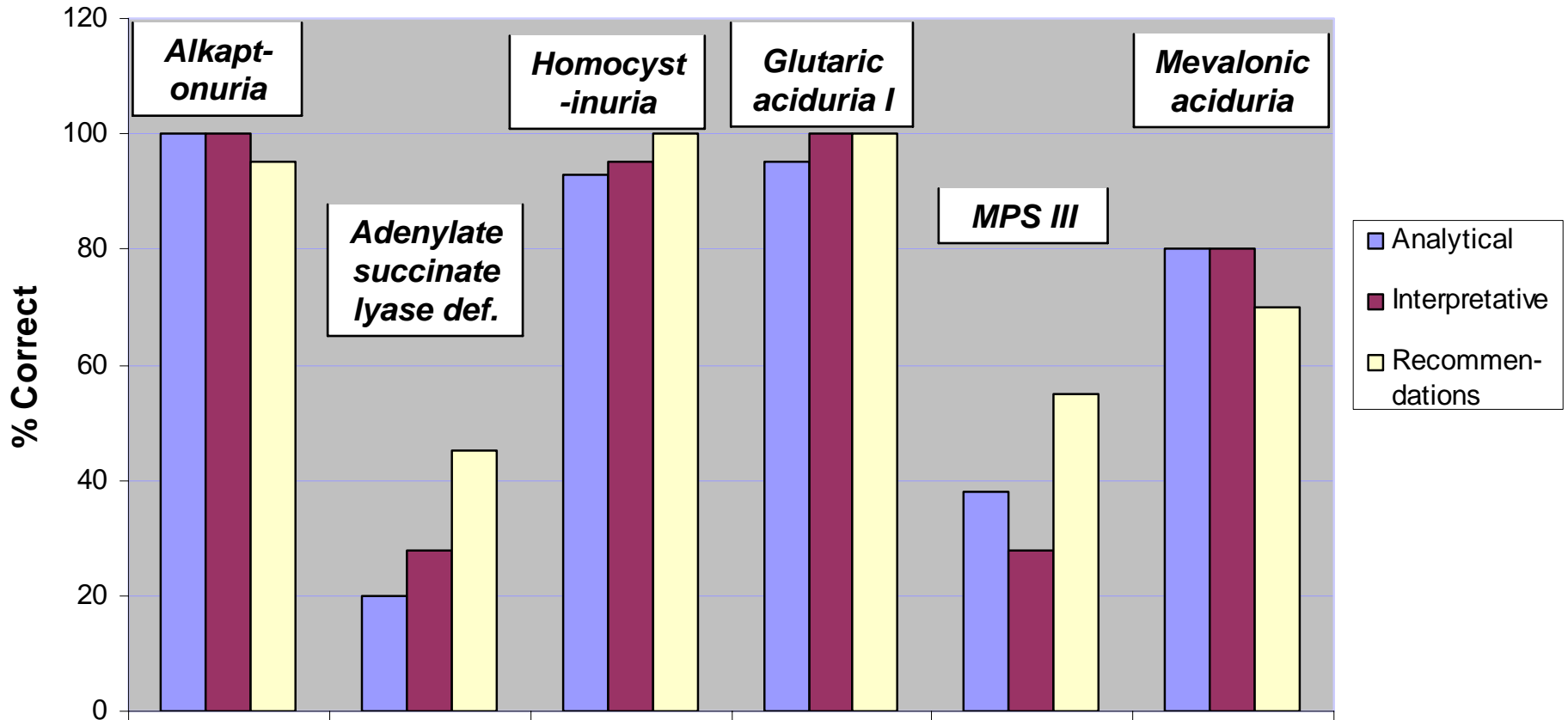
Amino acid QC scheme: Precision vs. Interlab variation



interlab CV for quantitative schemes 2005

Scheme	Best	Worst
Amino Acids	6.4 % (Valine)	253 % (hydroxyproline)
Special assays Urine	12.7 % (Carnitine)	198 % (sodium thiosulfate)
Special Assays Serum	3.5 % (Uric Acid)	190 % (cis-4-decanoic acid)
Organic Acids	42.5 % (ethylmalonate)	619 % (4-OH-Butyric acid)
Purines & Pyrimidines	6.1% (creatinine)	234 % (dihydro-uracil)
Cystine	12 % (protein)	104 % (cystine)

Diagnostic Proficiency Testing: Performance Prague Centre 2005



How can we improve quality

- Validation of methods and equipment
- Standard methods
- Internal QC
- External QC

EQA will play an increasing role in promoting the much needed improvements of quality of analyte measurement in IEM and will become essential for the accreditation of laboratories.

