B.I.QUANT-UR 1.1™

Enhanced Reporting Features for Better Result Interpretation (for research use only)

The updated version of our automated urine quantification tool available on our IVDr platform is finally released! With B.I.QUANT-UR 1.1, routines and validation parameters have been improved and enables now more positive hits compared to the previous version B.I.QUANT-UR 1.0.

Indeed, the raw concentrations are accessible independent on our Limit of Detection and additional quantification result assessment information have been made available in order to be able to judge on quantification reliability.

New Features in B.I.QUANT-UR 1.1

- Summary on the first report page where the metabolites found with concentration outside the 95% range of the Bruker reference database are listed
- Raw concentration (r, mmol/L) is the calculated concentration and is always given independent of LOD
- Signal correlation (ρ,%) characterize the match between the lineshape metabolite signal and the calculated fit. Color coded flag have been added for better visualization
- Concentration error (Δ,mmol/L) is the concentration equivalent of the difference between metabolite signal and the calculated fit
- Comprehensive explanation page
- In additon to the pdf report and xml results file already accessible, results are also directly saved in csv format allowing direct input for follow-up calculations

The methods and solutions described here are for research use only and not for use in clinical diagnostic procedures.

In table 1 an extract of the report automatically generated by B.I.QUANT-UR 1.1 is shown. Metabolites are sorted into chemical classes. Absolute and relative to creatinine quantification values are given, LODs are listed as well as a 95% concentration range derived from the validation spectra set. The actual sample is shown as a black bar in the concentration range, if the corresponding metabolite is detected. The 3 new features, raw concentration (r), correlation (ρ) and error concentration (Δ) are listed too.

With the new version B.I.QUANT-UR 1.1, it is now possible to easily identify the key metabolites of phenylketonuria in this sample which would not have been the case with B.I.QUANT-UR 1.0. In fact, the concentration of 4-Hydroxyphenylacetic acid and phenylacetic acid are more than 2 times below LOD but the correlation is > 95%. The raw concentration in this case can be used as concentration estimate.

In table 2 another extract of a report generated by B.I.QUANT-UR 1.1 is shown.

Table 2

9 Hydroxy acids and derivatives

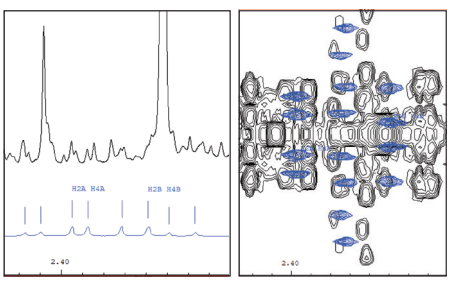
Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
3-Hydroxyglutaric acid	< 0.04	< 49	49	0.027	63 ○	0.613	≤ 49
3-Hydroxypropionic acid	< 0.03	< 35	35	0.000	0 ○	0.186	≤ 35
D-Galactonic acid	< 0.04	< 57	57	0.000	0 ○	0.279	≤ 57
D-Gluconic acid	< 0.07	< 99	99	0.000	0 ○	0.918	≤ 99
Glycolic acid	0.49	640	180	0.490	98 ●	0.109	≤ 180
Malic acid	< 0.07	< 97	97	0.000	0 ○	4.385	≤ 97

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

Extract of B.I.QUANT-UR 1.1 e (extended version) Pathological excretion of 3-Hydroxyglutaric acid characteristic of low excretor patients with glutaric aciduria type I (GA-1)

It can be seen that 3-Hydroxyglutaric acid has been quantified below LOD however the confidence value is only 63% which will require a visual inspection of the spectra for validation of the raw concentration (Figure 1). In this case, it could be confirmed, and it is typical for low excretor glutaric aciduria type I.

Figure 1



Visual inspection by using AMIX and BBIOREFCODE
Black spectra: low excretor patient with GA-1
Blue spectra : 3-Hydroxyglutaric acid reference at pH=7

Table 1

5 Benzene and substituted derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
2-Hydroxyphenylacetic acid	< 0.05	< 10	10	0.000	0 ○	0.726	≤ 10
3-Phenyllactic acid	0.88	180	89	0.879	85 ●	0.285	≤ 89
4-Aminohippuric acid	< 1.3	< 270	270	0.000	0 ○	0.499	≤ 270
4-Ethylphenol	< 0.06	< 13	13	0.000	0 ○	0.514	≤ 13
4-Hydroxyhippuric acid	< 0.13	< 26	26	0.000	0 ○	0.341	≤ 30
4-Hydroxyphenylacetic acid	< 0.09	< 18	18	0.035	99 ●	0.090	≤ 28
4-Hydroxyphenyllactic acid	< 0.21	< 43	43	0.000	0 ○	0.610	≤ 43
Benzoic acid	< 0.05	< 10	10	0.000	0 ○	0.026	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.000	0 ○	0.175	2 - 17
Hippuric acid	1.3	270	170	1.322	100 ●	0.081	≤ 660
Phenylacetic acid	< 0.35	< 72	72	0.152	98 ●	0.444	≤ 72
Phenylpyruvic acid	1.4	280	98	1.359	100 ●	0.069	≤ 98
Pyrocatechol	< 0.84	< 170	170	0.000	0 ○	0.550	≤ 170
Syringic acid	0.22	46	38	0.223	99 ●	0.107	≤ 38

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

Extract of B.I.QUANT-UR 1.1 e (extended version) Profile characteristic of phenylketonuria with pathological excretion of 3-phenyllactic acid, phenylpyruvic, 4-Hydroxyphenylacetic acid and phenylacetic acid.

The new version B.I.QUANT-UR 1.1 enables the quantification of more metabolites compared to the version 1.0. The combination of raw concentration with the quality assessment parameters available allow to obtain reliable quantification results even below LOD. For example, on a cohort with 500 urines, 45% of the Trigonelline and 1-Methylnicotinamide concentration values were below LOD but the correlation is >95% means that the raw concentration can be used. The same can be observed for other endogenous metabolites in table 3.

Metabolite	LOD (mmol/ mol Crea)	r < LOD (%)	ρ>95% (%)	ρ>85% (%)	ρ<85% (%)
Trigonelline	35	97	45	17	35
1-Methylnicotin-amide	32	77	45	19	13
Hippuric acid	170	58	34	9	15
Fumaric acid	2	61	26	19	16
Creatine	50	22	22	0	0
Inosine	19	82	20	27	35
Caffeine	45	46	16	19	11
Imidazole	48	99	15	11	73
Betaine	7	12	10	1	1
Trimethylamine	2	64	9	7	49
Proline betaine	25	50	9	9	33
Taurine	140	65	8	8	49
Dimethylamine	30	8	8	0	0
Pyruvic acid	9	30	7	9	14
Tartaric acid	5	33	7	13	13
D-Galactose	15	73	5	6	62
Guanidinoacetic acid	100	44	5	12	26
Formic acid	10	9	5	1	3

Table 3: Extract of results of a cohort quantification (500 spectra) with B.I.QUANT-UR 1.1 b (basic version)

Bruker BioSpin
info@bruker.com
www.bruker.com