B.I.BioBankTool™
Bruker IVDr BioBankTool
(for research use only)

Quality Control under Standardization

While the number of Biobanks worldwide is growing rapidly, quality control of the whole process Is a requirement to ensure the value of the biobanks. Standardization is needed to allow researchers to integrate results obtained of specimen tests from 1 or more biobanks.

Standardization also includes the QC Process, which needs to cover all aspects of pre-analytics and sample storage. In addition validation of specimen/donor metaparameters is of additional value. NMR is especially suited to perform QC-analysis of liquid biopsies and can deliver a large number of criteria based on one QC measurement per sample.

In addition to QC Information NMR can deliver a large number of metabolic information using the same spectra generated during the QC process. With this information in urine 150 metabolites in 2 age ranges are quantified. In plasma/serum 115 lipoprotein related parameters (including subclasses) and 41 metabolites/parameters are analyzed and quantified, the whole process is under push button automation and can be handled by a trained medical technical assistant.

NMR based Biobank QC delivers up to 46 criteria (depends on matrix type)

Table 1

Plasma QC Summary

Test	Result	Flag
NMR Experiment Parameter Test	not passed	
NMR Experiment Quality Test	passed	
NMR Preparation Quality Test	passed	
Matrix Identity Test	EDTA plasma	
Matrix Integrity Test	passed	
Matrix Contamination Test	not passed	

Urine QC Summary

Test	Result	Flag
NMR Experiment Parameter Test	not passed	
NMR Experiment Quality Test	not passed	
NMR Preparation Quality Test	passed	
Matrix Identity Test	Urine	
Matrix Integrity Test	not passed	
Matrix Contamination Test	not passed	
Medication Test	passed	
Protein Background Test	passed	
Further Indicative Parameter Test	not passed	

Table1 : Extract of the summary page of the B.I.BioBankQC-PS and B.I.BioBankQC-UR analysis report

Table 2

Plasma/Serum

3.1 Matrix Identity Test

The spectral fingerprint of the sample is consistent with EDTA plasma.

	K-EDTA mmol/L	Ca-EDTA mmol/L	Citric acid-B mmol/L	Flag
Sample	5.23	2.04	0.13	
EDTA plasma	2.50 - 13.00	1.30 - 3.60	<3.00	
Citrate plasma	<0.05	<0.01	3.10 - 20.00	
Heparine plasma	<0.05	<0.01	<3.00	
Serum	<0.05	<0.01	<3.00	

3.2 Matrix Integrity Parameters

Compound	Parameter	LOD	Target Value	Measured Value	Flag
Acetic acid	Conc. in mmol/L	<0.01	<0.10	0.01	
	Shift in ppm	-/-	1.916 - 1.918	1.918	
Citric acid-B	Conc. in mmol/L	<0.03	<3.00	0.13	
	Shift in ppm	-/-	2.657 - 2.659	2.658	
Formic acid	Conc. in mmol/L	<0.02	<0.20	0.04	
	Shift in ppm	-/-	8.458 - 8.460	8.459	
D-Glucose-alpha	Conc. in mmol/L	<0.20	<3.20	1.50	
	Shift in ppm	-/-	5.237 - 5.239	5.238	
Lactic acid	Conc. in mmol/L	<0.03	<8.10	4.45	
	Shift in ppm	-/-	1.327 - 1.329	1.329	

3.3 Matrix Contamination Parameters

Contamination	LOD	Measured Value	Flag
tert-Butanol in mmol/L	<0.008	0.009	
Contamination-1.25ppm in mmol/L	<0.008	<0.008	
Isopropanol in mmol/L	<0.020	<0.020	

Urine

3.1 Matrix Identity Test

The spectral fingerprint of the sample is consistent with Urine.

	Creatinine mmol/L	Alanine mmol/L	Fumaric acid mmol/L	Flag
Sample	1.79	0.30	0.04	
Urine	0.60 - 29.00	<2.20	<0.07	

3.2 Matrix Integrity Parameters

Compound	LOD	Range	Measured Value	Flag
Acetic acid in mmol/L	<0.030	<2.90	<0.030	
Benzoic acid in mmol/L	<0.040	<0.45	<0.040	
Citric acid in mmol/L	<0.300	>0.30	1.290	
Formic acid in mmol/L	<0.020	<0.71	2.321	
Hippuric acid in mmol/L	<0.200	<15.10	<0.200	
Lactic acid in mmol/L	<0.100	<2.00	0.179	
Succinic acid in mmol/L	<0.020	<0.44	0.057	

3.3 Matrix Contamination Parameters

Contamination	LOD	Measured Value	Flag
Propylene glycol in mmol/L	<0.020	7.227	
Isopropanol in mmol/L	<0.020	<0.020	

Table2 : detailed examples extracted from the automatic B.I.BioBankQC-PS and B.I.BioBankQC-UR analysis reports

Table 3

QC criteria	Plasma/Serum	Urine
Check Sample Preparation	■ TSP ■ Protein background intensity ■ Alanine shift position	■ TSP
Check NMR analysis	■ Shim performance ■ Baseline	■ Shim performance ■ Baseline
Validate Matrix Identity	■ EDTA plasma ■ Citrate plasma ■ Serum	■ Urine
Validate Matrix Integrity	■ Degradation ■ Matrix composition out of model reference ranges	■ Degradation ■ Matrix composition out of model reference ranges
Check Matrix Contamination	■ Cleaning agents ■ Desinfection material	■ Propylene glycol ■ Isopropanol
Check most frequent medication		■ Drugs ■ Drugs metabolites
Check Protein background		■ Protein concentration beyond reference range
Check further parameter		■ Fasting/non-fasting state

Table3: Criteria used for the QC analysis depending on matrix type

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

Rich spectral information

Based on the outstanding performance of NMR in reproducibility and transferability, high quality analysis of data is available to deliver additional information for the biobank specimens. Together with the biobank, tool packages are offered for plasma/serum and urine quantification as outlined before. A multitude of disease relevant as well as endogenous metabolites and lipoprotein information is delivered extracted from the QC spectra analysis.

Clinical trials: spectra instead of aliquots

Based on the IVDr Platform concept and its strict standardization for NMR data generation, it is possible to select spectra from multiple biobanks for large epidemiological studies on a worldwide basis or to expand the testing range of clinical trials, providing for example spectra from healthy cohorts out of the biobanks Instead of generating always new aliquots. This builds a new value proposition for biobanks, allowing to save cost and contribute to big data in an efficient way. New NMR based diagnostic tests can such be validated on a worldwide basis and multiple phenotypes without exploding the cost of the trial. Data generated from a 11 IVDr platform ringtest clearly proof this unique feature of NMR.

IVDr Platform Concept

Table 4

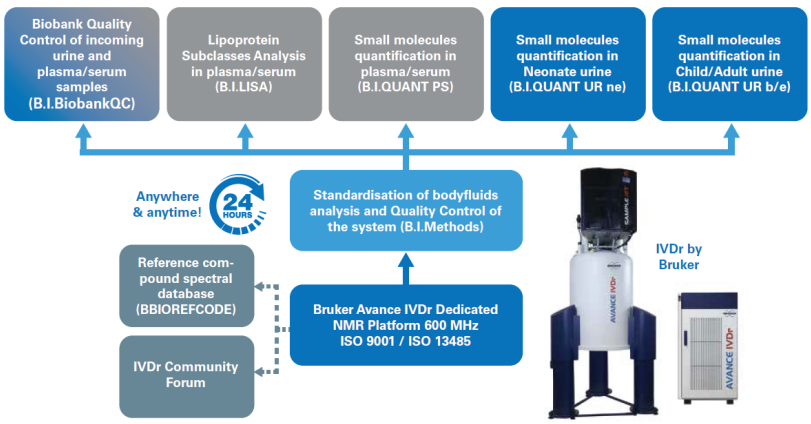

Table 4: Bruker IVDr Platform and embedded solutions

IVDr Platform quantification tools

Table 5

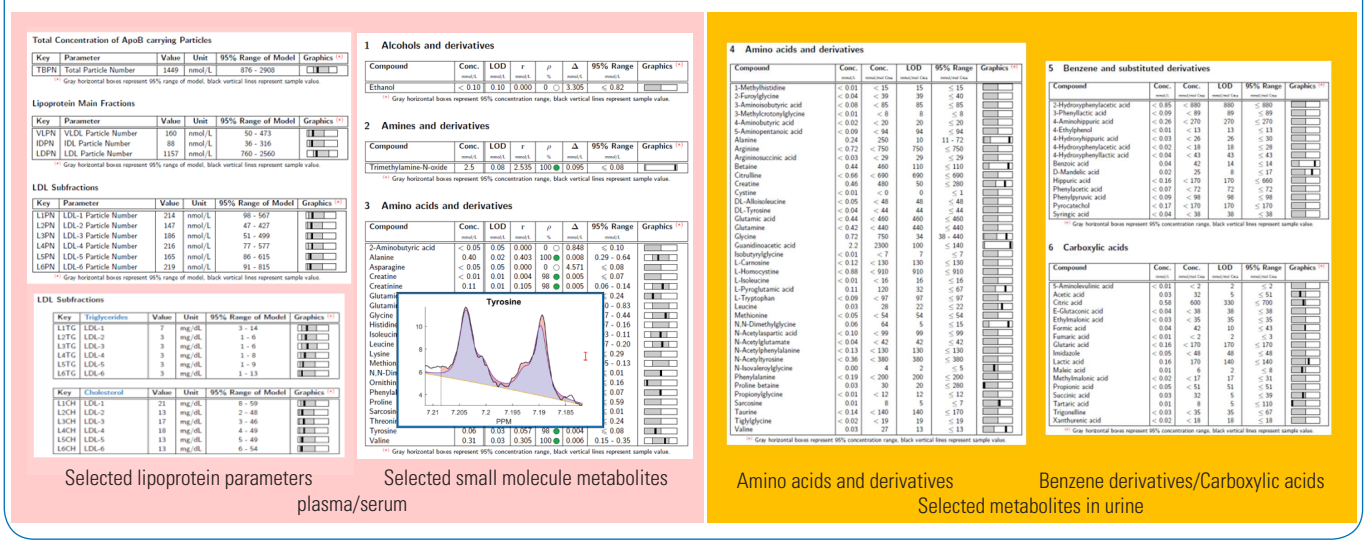

Table 5: Extract of the packages for plasma/serum and urine

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