

# ● Analysis Report

## Bruker IVDr BioBank QC B.I.BioBankQC™ in Plasma/Serum

Sample ID: test\_serum\_001

Measuring Date: 04-Oct-2017 12:01:12

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Quantification Method Version: BioBankQC PS 1.0.0

### Disclaimer

RESEARCH USE ONLY: This is no clinical diagnostic analysis report. Must not be used for clinical (medical or IVD) diagnosis or for patient management! Additional concentration range information (95% range) provided numerically or graphically in this report must not be used for clinical diagnostic interpretation.

### Summary

Test	Result	Flag
NMR Experiment Parameter Test	passed	●
NMR Experiment Quality Test	passed	●
NMR Preparation Quality Test	passed	●
Matrix Identity Test	Heparine plasma or Serum	●
Matrix Integrity Test	passed	●
Matrix Contamination Test	passed	●

## 1 NMR Experiment Parameters

Parameter	Target Value	Applied Value	Flag
EXP	PROF_PLASMA_NOESY	PROF_PLASMA_NOESY	●
PULPROG	noesygppr1d	noesygppr1d	●
AUNM	au_ivdr_noesy	au_ivdr_noesy	●
AUNMP	proc_ivdr_noesy	proc_ivdr_noesy	●
SOLVENT	Plasma	Plasma	●
TE	309.9 - 310.1	309.9996	●
P1	9 - 15	12.17	●
PRESAT	24 - 26	25	●
BF1	599 - 601	600.13	●
O1	2700 - 2900	2822.45	●
ERETIC	1000	4095.97	●
D1	4	4	●
SWH	18028.846	18028.8462	●
OVERFLOW	0	0	●
TD	98304	98304	●
NS	32	32	●
DS	4	4	●
LB	0.3	0.3	●
SI	131072	131072	●
PHC1	0	0	●

## 2 NMR and Preparation Performance Evaluation

### 2.1 NMR Spectral Quality Parameters

Parameter	Target Value	Measured Value	Flag
LineWidth in Hz	<1.5	1.3	●
Residual Water Signal in mmol/L	<30.0	14.7	●
BaseLine in mmol/L/Hz	<0.002	0.001	●

### 2.2 NMR Sample Preparation Quality Parameters

Parameter	Target Value	Measured Value	Flag
TSP region integral (-0.5ppm - 0.5ppm) in mmol/L	28.1 - 43.7	36.9	●
Intensity in (6ppm - 12ppm) in mmol/L	87.0 - 159.0	139.3	●
Alanine ppm shift delta from 1.48ppm in ppm	-0.0280 - -0.0140	-0.0228	●

### 3 Matrix Validation

#### 3.1 Matrix Identity Test

The spectral fingerprint of the sample is consistent with Heparine plasma or Serum.

	K-EDTA mmol/L	Ca-EDTA mmol/L	Citric acid-B mmol/L	Flag
Sample	<0.05	<0.01	0.18	
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	1.917	●
Citric acid-B	Conc. in mmol/L	0.03	<3.00	0.18	●
	Shift in ppm	-/-	2.672 - 2.680	2.678	●
Formic acid	Conc. in mmol/L	0.02	<0.20	<0.02	●
	Shift in ppm	-/-	8.458 - 8.460	8.459	●
D-Glucose-alpha	Conc. in mmol/L	0.20	<3.20	1.46	●
	Shift in ppm	-/-	5.237 - 5.239	5.238	●
Lactic acid	Conc. in mmol/L	0.03	<8.10	4.21	●
	Shift in ppm	-/-	1.327 - 1.329	1.329	●

#### 3.3 Matrix Contamination Parameters

Contamination	LOD	Measured Value	Flag
tert-Butanol in mmol/L	0.015	<0.015	●
Contamination-1.25ppm in mmol/L	0.015	<0.015	●
Isopropanol in mmol/L	0.020	<0.020	●

## 4 Explanations

### NMR Experiment Parameters

Related tests need to be passed successfully in order to document that NMR parameters applied to the sample are consistent with the parameters specified in the B.I.Methods™.

### NMR Spectral Quality Parameters

Shim performance is crucial, both, for water suppression quality and resolution. The linewidth measured at the Alanine doublet as well as the residual water signal absolute value intensity are used as respective indicators. Bad shim can have multiple reasons, from just non-optimum shim values, over concentration gradients in the sample, contrast agents from prior MRI investigations, sedimentation or particles in the sample, to tube imperfections. If NMR spectral quality parameter tests are not successfully passed, one may try one or more of the following steps in subsequent order:

- (1) Check standard shim file loaded prior to shimming.
- (2) Take out sample from magnet, shake it and re-run sample afterwards.
- (3) Do TopShim 3d. Re-run sample afterwards.
- (4) Fill sample in other NMR tube.
- (5) Re-prepare sample and then re-run sample.
- (6) Ask for a new sample from the same subject if study design allows for that.

### NMR Sample Preparation Quality Parameters

Plasma and serum sample preparation is straight forward. It is mixing of the sample with Bruker's IVDr plasma buffer at a ratio of 1:1. The TSP concentration as well as intensity of the protein background within the spectral range of 6ppm - 12ppm, both are important indicators for application of the correct buffer at correct concentration. If those parameter are outside specification, this would indicate either application of a wrong buffer or a wrong sample-to-buffer ratio. Either of the scenarios could result in deviations in peak intensities and peak positions (Alanine calibrated to chemical shift 1.48ppm is taken as reference) or in the worst case even changes of chemical equilibria in the mixture. As a consequence, subsequent application of NMR based plasma and serum quantification methods as well as lipoprotein parameter determination optimized for spectra acquired under B.I.Methods SOPs could provide wrong results.

### Matrix Identity Test

In this test, three categories of matrices are distinguished, i.e. (a) EDTA-plasma, (b) Citrate plasma, and (c) Heparine plasma and serum, i.e. Heparine plasma and serum spectroscopic fingerprints cannot safely be distinguished. Any plasma or serum sample should fall in one of the three categories. If a

given sample does not, this might indicate some mixing, e.g. mixing EDTA-plasma into serum which might hint to a serious QC issue in pre-analytical procedures, e.g. in sample collection or sample handling.

### **Matrix Integrity Parameters**

The integrity of a plasma or serum sample may be impaired due to inappropriate pre-analytics and inappropriate temperature exposure which may result in e.g. unwanted enzymatic activities or even bacterial growth. Both might affect concentrations and signal positions of characteristic, indicative metabolites tested for in the QC procedure.

### **Matrix Contamination Parameters**

Isopropanol may often be used in one or more steps of pre-analytics procedures and might show up as contamination in serum and plasma samples. Further contaminations sometimes showing up as singlets at 0.8ppm or 1.25ppm at the top of respective lipoprotein signals might indicate low quality cryovials used for sample storage.