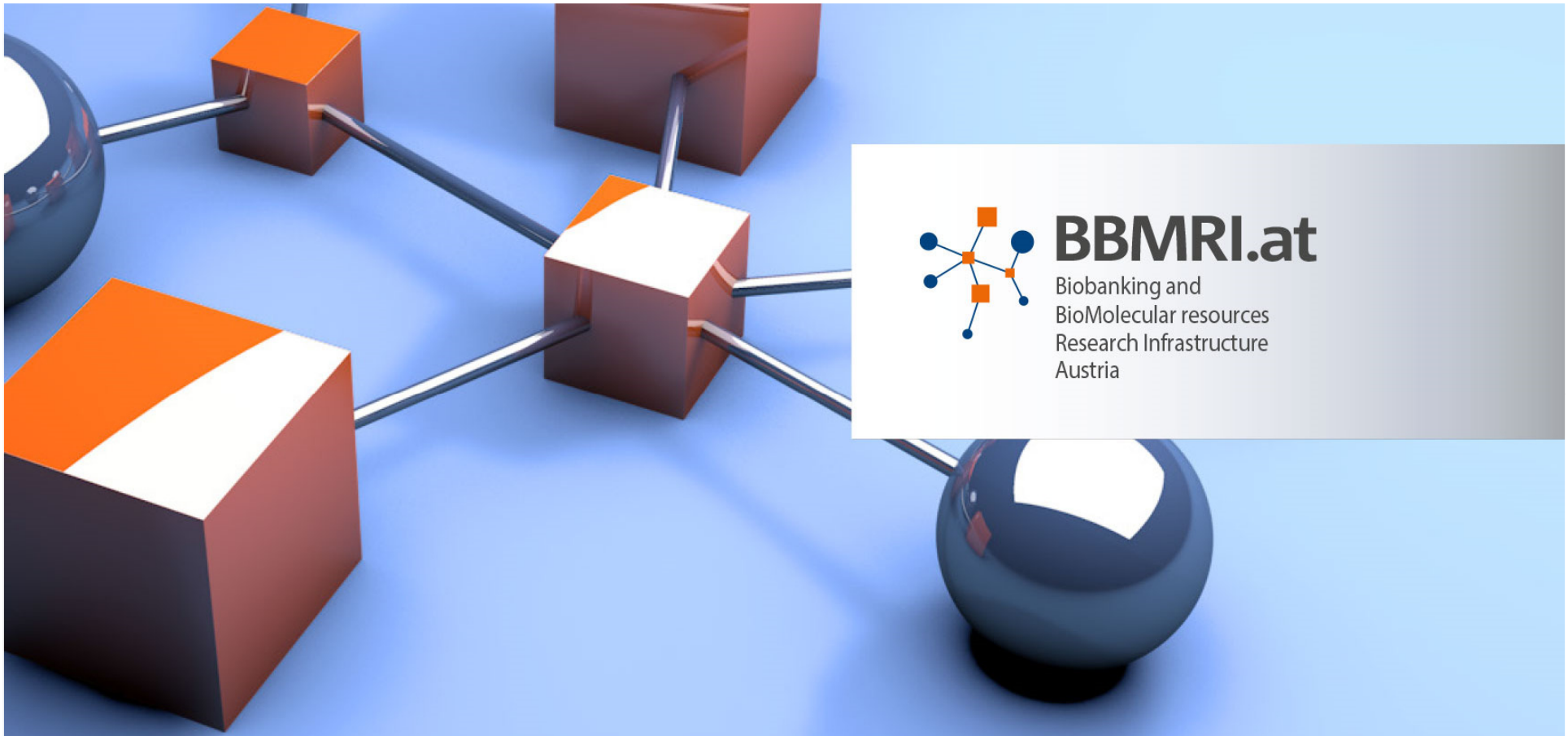

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Metabolomics in Urin, Serum und Plasma

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Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for metabolomics in urine, venous blood serum and plasma (CEN/TS 16945:2016)

Molekularanalytische in-vitro-diagnostische Verfahren — Spezifikationen für präanalytische Prozesse für Metabolomuntersuchungen in Urin, venösem Blutserum und -plasma (CEN/TS 16945:2016)

Tests de diagnostic moléculaire in vitro — Spécifications relatives aux processus préanalytiques pour l'analyse du métabolome dans l'urine et le sang veineux (sérum et plasma) (CEN/TS 16945:2016)

Overview

- **Outside the laboratory**
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- **Inside the laboratory**
  - Specimen Reception
  - Storage requirements between sample receipt and sample processing
  - Sample Processing
  - Optional: Transport of processed samples to another laboratory or biobank
  - Storage
  - Thawing

Outside the laboratory

Primary Sample Collection

Venous blood: Serum/Plasma
1.1.1 Information about the primary sample donor a) primary donor/ patient ID b) health status and relevant lifestyle factors c) treatment prior to sample collection d) instructions for the preparation of the patient for the blood draw procedure (e.g. fasting status) e) type and purpose of proposed analytical test
1.1.2 Selection of the blood collection tube a) Documentation of anticoagulant b) Documentation of stabilizers Notes: in dependence of the downstream application suitable collection tubes should be used Plasma: for metabolite analyses EDTA, sodium fluoride or citrate can be used as anticoagulants; Heparin-based anticoagulants shall be avoided for NMR analysis.
1.1.3 Primary sample collection from the sample donor and stabilization procedures a) Documentation: identity of the person collecting the sample & time of blood collection (EN ISO15189:2012) b) sample labelling: routine procedure (EN ISO15189:2012) or procedure with additional information c) For metabolite analyses blood should be collected after a minimum of 8 hours fasting. (Deviations must be documented) d) Application of standard venipuncture techniques; steps for preventing possible backflow e) Blood collection tubes shall be filled according the manufacturers' instructions f) Blood collection tube manufacturers' instructions for mixing or inverting after blood collection shall be followed
1.1.4 Pre-processing of blood specimens a) Documentation of time and date b) Processing of the blood specimen shall start within 30 min from collection (when specimens are kept at RT). For specific metabolites, longer times may be appropriate, if validated. c) All the steps in the specimen pre-processing shall be documented and validated.

Outside the laboratory

Primary Sample Collection

Urine
1.1.1 Information about the primary sample donor should include (not limited to) a) primary donor/ patient ID b) health status and relevant lifestyle factors c) treatment prior to sample collection
1.1.2 Selection and labelling of the urine collection containers a) The laboratory shall define the container intended for urine collection. b) A sufficient minimum volume of urine should be collected according to the requirements of the preanalytical preparation steps and the analytical test. c) For the labelling (specimen identification) of the urine collection tube a routine procedure (EN ISO 15189:2012, 5.4.4.3, e)) or a procedure with additional information (e.g. 2D-barcode) shall be used. Note: if additives are required, impact on analytical performance and outcome shall be analyzed
1.1.3 Urine collection and reception from the specimen donor a) Instructions for the urine collection shall be given to the donor (incl. safety measures) b) Any clinical procedure affecting the specimen collection shall be documented. The total volume to be collected shall be documented c) Documentation: identity of the person receiving the sample & time of urine collection (EN ISO15189:2012) Note: The first midstream urine of the morning should be collected after a minimum of 8 h fasting. Drinking can influence urine metabolite concentrations. This requires a normalization. Specify, if collected at different times, or for 24-h collection. Any variations to standard instructions shall be validated.
1.1.4 Information on the primary urine sample storage requirements at the urine collection site a) Documentation of time and date of urine collection b) sample should be kept refrigerated (2°C-8°C) for max. 2h and shall be not frozen prior to centrifugation and/or filtration Note: The allowed urine specimen total storage duration includes the time for storage at the point of urine collection, transportation to the testing laboratory and further storage at the testing laboratory or other institutions.

Outside the laboratory

Transport requirements

Venous blood: Serum/Plasma
1.2.1. Temperature and conditions a) If primary blood is not processed at the collection site, the blood specimen shall be transported and validated in accordance to 1.1.4. b) Appropriate measures shall be taken to secure temperature specifications and to reduce time for the delivery. c) The use of a pneumatic tube transport system should be validated, as it can impact specimen quality due to high acceleration/deceleration forces.
1.2.2. Documentation a) time for storage at the point of collection b) transportation to laboratory c) further storage at the laboratory or other institutions Note: For metabolite analyses the sample should be kept cool during transport. Processing of the primary blood sample shall start with 30 min from collection when samples are kept at RT. The use of a pneumatic tube transport system should be validated, as it can impact specimen quality due to high acceleration/deceleration forces.

Outside the laboratory

Transport requirements

Urine
1.2.1. Temperature and conditions a) specimen should be kept cool (temperature range 2 °C to 8 °C). b) Appropriate measures shall be taken to secure temperature specifications and to reduce time for the delivery, which should be completed within 2 h from collection. c) The use of a pneumatic tube transport system should be validated, as it can impact specimen quality due to high acceleration/deceleration forces.

Inside the laboratory

	Venous blood: Serum/Plasma
2.1. Specimen Reception	**2.1.1. Documentation of blood sample arrival time and conditions (volume, nonconformities of labelling, storage, transport, … should be recorded)** Note: in case of nonconformities: a new sample should be obtained
2.2. Storage Requirements between sample receipt and sample processing	**2.2.1 Documentation of storage temperature** Note: For metabolite analyses sample processing should start within 30 min at RT from blood collection. **2.2.2. Documentation of time interval** a) storage time at the point of collection b) time for transportation to laboratory c) storage time inside the laboratory or any other institution
2.3. Sample Processing	**2.3.1. Processing information** a) for metabolite analyses processing should start within 30 min from collection when samples are kept at RT (for specific metabolites longer times may be appropriate, if validated) **2.3.2. Centrifugation** a) Serum requires about 30 min clotting time at RT before centrifugation. If clotting problems occur, these should be annotated. b) Serum and plasma shall be prepared according to documented standard procedures. c) if processed sample is intended to be stored frozen, it should be aliquoted into cryo-vials in the suitable volume needed for the downstream applications.
2.4. Optional: Transport of processed samples to another laboratory or biobank	**2.4.1. Conditions** a) If samples are transported to a laboratory for immediate analysis, the transport conditions should be validated. b) specimens should be transported to and from a biobank as frozen c) Documentation of processed sample arrival time and conditions (volume, nonconformities of labelling, storage, transport, … should be recorded) Note: in case of nonconformities: a new sample should be obtained

Inside the laboratory

	Urine
2.1. Specimen Reception	**2.1.1. Documentation of urine sample reception time and conditions (volume, nonconformities of labelling, storage, transport, … shall be recorded)** Note: in case of nonconformities: a new sample should be obtained
2.2. Storage Requirements between sample receipt and sample processing	**2.2.1 Documentation of storage temperature** Note: For metabolite analyses sample should be kept refrigerated (2°C-8°C). Some downstream analyses need special storage/ archiving conditions; therefore manufacturers' instructions should be followed.
	2.2.2. Documentation of time interval a) storage time at the point of collection b) time for transportation to laboratory c) storage time inside the laboratory or any other institution
2.3. Sample Processing	**2.3.1. Centrifugation and/ or filtration (removal of particulate matter and cells)** a) 1000xg to 3000xg, 5 min, 2°C to 8°C b) filtration: e.g.: 0.2µm cut-off filter c) if processed sample is intended to be stored frozen, it should be aliquoted into cryo-vials in the suitable volume needed for the downstream applications. d) alternative processing shall be validated Note: Alternatively, only filtration can be used. Filter material and devices should be proven neither to absorb nor to release metabolites or interfere with their analyses by increasing the blank.

Inside the laboratory

	Venous blood: Serum/Plasma
2.5 Storage	**2.5.1 Documentation of storage temperature** a) The temperature and durations between sample receipt, sample processing and freezing of the processed sample shall be documented. b) For Nuclear magnetic resonance metabolite analyses: storage at -70°C is recommended (for at least 5 years) c) For Mass spectrometry based metabolite analyses: storage below -130°C is recommendet
	2.5.2. Documentation of time interval between sample receipt, sample processing and freezing of the processed sample
2.6. Thawing	**2.6.1. Documentation of thawing** a) time elapsing after the thawing until the analysis Note: For metabolite analyses the thawing procedure and duration until commencing the subsequent analysis shall be validated.

Inside the laboratory

	Urine
2.5 Storage	**2.5.1 Documentation of storage temperature** a) The temperature and durations between sample receipt, sample processing and freezing of the processed sample shall be documented. b) For Nuclear magnetic resonance metabolite analyses: storage at -70°C is recommended (for at least 5 years) c) For Mass spectrometry based metabolite analyses: storage below -130°C is recommended
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