Dear users of the laboratory services

On the following pages, we would like to give you important information on preparing the patient, collecting samples, shipping samples to the laboratory and measuring uncertainty of our measurement results. If you have further questions, especially regarding medical aspects, do not hesitate and use the contact options below. All information and declarations of consent for investigations to be carried out are available on our website.

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Acceptance times

Mo-Fr 8:30-18:00

Preparation and educating the patient

For this purpose, concrete indications are given under the following points, such as: maintaining a fasting or certain diets prior to sample collection, discontinuation of certain medicines in certain examinations, etc.

Sample collection

Blood collection

Preparation

- skin disinfectant spray
- non-sterile swabs
- plaster, possibly a first wound dressing
- tourniquet
- several drawing needles of different sizes: green (21G, nNr.2, 0,8mm) or yellow (20G, nr.1, 0,9 mm) and butterflies with adapters
- sample collection tubes according to the requested test. These have to be labelled unambiguously with surname, first name, and birth date of the patient or with barcode sticker, collection date and time
- non-penetrable disposable container for cannulas
- protective gloves
- possibly a forearm pad

The order of the blood sample collection should be as follows:

1. blood cultures
2. native blood (serum)
3. citrate blood (coagulation)
4. EDTA- / heparin blood
5. fluoride blood

Blood collection tubes with additives of anticoagulants have to be mixed immediately by panning the sample (5 to 10 times over the head) – do not shake!

Blood collection systems – colour coding:

Sample material	Vacutainer®	Sarstedt Monovette®
Serum	red (brown)	white
Serum with separation aid / gel monovette	golden yellow	brown
EDTA blood	purple	red
Blood typing tubes	purple/large	red/large
Citrate blood [1+9, coagulation]	light blue	green
Citrate blood [1+4, BSG]	black	purple
Heparin blood Na-/NH4	green	blue
Lithium heparin blood	orange	orange
Fluorid [NaF]	grey	yellow
Urine monovette	-	yellow

Identification, patient education

- Introduction to unknown persons
- Ensuring the identity of the person. Ask unknown patients for their names!
- Check all collection tubes for correct labelling
- Explain the indication of the measure
- Ensure the consent of the patient or guardian

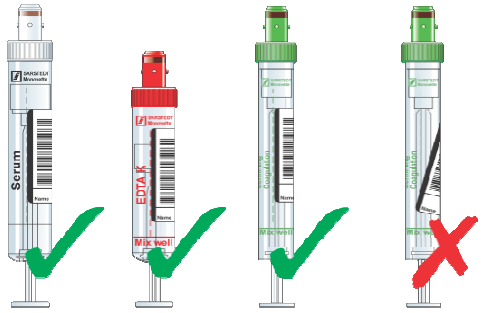
Sample labelling

A clear unambiguous labelling of the samples is the prerequisite for carrying out the examination!

The assignment of the request form to the sample can be made via the name or via barcode adhesive, which can be obtained from the laboratory. In addition to the acceptance date, the acceptance period should also be noted on the request form, which is especially important for parameters that show strong circadian fluctuations.

Collection tubes are labelled correctly, if:

- a clear view of the content is guaranteed
- controlling the filling level is possible
- the plug can be removed unhindered
- the tube and the label do not jam or stick together in the centrifuge
- the barcode sticker are upright and glued as straight as possible and are not dirty (see figure below)



Never place the identification of the sample on the lid, outer packaging or transport container!

Mark infectious material clearly on the tube and the request form!

Request for laboratory tests

The tests are requested on referral forms or on the request forms provided by the laboratory. All necessary information about the patient, such as age, sex and diagnosis should be noted on the appropriate form.

All information must be readable!

Packaging the samples

The first packaging is the tube. The vessels must be tight and must not contain more than 500 ml.

Absorbent material must be used between the first container and the second package. If multiple containers are placed in a single second package, they must either be individually wrapped or separated so as to prevent mutual contact. The absorbent material, such as e.g. cotton wool must be sufficient to hold all the samples contained in the first tubes. The second packaging must be tight.

Transport of the samples

The samples are sent to the laboratory by courier services or sent by post according to the relevant transport regulations (identification as diagnostic sample **UN 3373**). Special requirements for transport (e.g. cooling, keeping hot, immediate delivery) are to be taken from the specifications, if necessary.

Subsequent requests for additional tests from previously submitted sample material can only be accepted if there is still sufficient stability of the analyte in the sample material. We ask therefore for telephone demand.

Storage

The time between blood collection and sample collection should be as short as possible. If this is not possible for technical reasons, it is recommended that, with a few exceptions (for example, examination of vital cells such as immunophenotyping of leucocytes, HLA cross-match tests, cryoglobulins, cold agglutinins and microbiological materials), the material is stored in the refrigerator.

Samples for the determination of light-sensitive analytes such as bilirubin, vitamins, porphyrins must be stored dark, e.g. tubes packed in aluminium foil.

Criteria for the rejection of laboratory tests

- Sample material that is not sufficiently labeled (identity must be secured; for samples for blood group serology, the material must be labeled with the patient's surname, first name, and date of birth). In the case of sample material which cannot be recovered in the same quality or obtained in the patient's critical condition it is decided, in consultation with the client whether the requested laboratory tests are nevertheless carried out. The result of the consultation must be documented.
- Sample material in which the type and amount of added substances (e.g., anticoagulants) are unknown
- Citrate tubes (e.g. for coagulation tests) that are not filled sufficiently
- Citrate tubes for coagulation tests and EDTA tube for blood analysis in which (micro)clots are detectable
- Frozen whole blood samples
- Samples that have been stored and / or transported at over 42 ° C

General interfering factors in laboratory tests

Nutritional differences can be eliminated by a 12 to 14-hour food abstinence, and alcoholic differences by alcohol-free time of 24 hours before blood collection.

Many measures are subject to considerable daily rhythmic fluctuations. These extreme differences are the reason that the blood sample is usually taken in the morning between 7.00 and 9.00 in the fasting patient.

Depending on the body position, there is a considerable inflow and outflow of fluid from the intravascular space into the interstitium. Concentration fluctuations of proteins, protein-bound hormones, blood lipids and cellular components are the result.

Blood should therefore always be taken in the same body position of the test person (sitting or lying down).

Prolonged venous stasis causes an increase in the concentration of proteins, protein-bound and corpuscular constituents of the blood. A reason for this is a hemoconcentration just like when changing the body position or physical stress.

Recommendation: In case of venous sampling should be punctured within one minute (better 30 seconds) after beginning of blood stagnation. As soon as blood flows, the jam can be released. For repetitions, the opposite arm is preferable.

Strong physical stress before blood collection leads to changes in the following parameters::

- Hemoconcentration (blood thickening due to reduction of plasma water) and hypoxia.
- Increased hormone release during stress and anxiety (e.g. renin, catecholamine, cortisol, HGH).
- Alteration of parameters after muscle work (e.g. CK-MM increase in athletes)
- Avoid opening and closing the fist. "Pumping" of the fist leads to increases in potash and magnesium.
- Drugs can alter the results due to a variety of interferences.
- Samples that are hemolytic, lipemic or icteric are only of limited use for laboratory analysis. Hemolysis - removal error / lipemia - usually not sober patient / bilirubinemia - due to illness..

If it is unavoidable to analyze such samples, the results must be interpreted with special caution!

Corrupt measurements on hemolytic samples:

- LDH (160-fold concentration in erythrocytes)
- potassium (25-fold concentration in erythrocytes)
- GOT (40-fold concentration in erythrocytes)

A too long interval (> 1 hour) between blood collection and separating the cellular elements leads to hemolysis (potassium +).

As a general rule, sampling should always be carried out under standard conditions as far as possible:

- Blood collection between 7:00 and 9:00
- No extreme physical activity in the last three days
- No alcohol excesses several days before taking blood
- sober, i.e. food abstinence for 12 to 14 hours and 24 hour alcohol abstinence
- Always take blood samples in the same position (sitting or lying down)
- Rest for at least ten minutes before taking blood
- Avoid opening and closing the fist: "pumping" of the fist results in significant potassium increase (up to 2 mmol / L)
- Block for a maximum of one minute (better 30 seconds), release stasis, remove blood

Blood collection for drug determinations (Therapeutic Drug Monitoring).

Blood collection before next dose

The control of a medication (dose adjustment, compliance control) usually takes place via the so-called steady-state concentration (syn. basic concentration, equilibrium concentration). This requires a blood sample immediately before the next dose. If the so-called C1 or C2 drug concentrations are to be determined, the blood is taken one or two hours after the last administration.

Optimal gel-free blood collection tubes

Since adsorption (attachment) of drugs and their metabolites (degradation products) to the gel barrier of gel-containing blood tubes is not tested for each drug and therefore cannot be ruled out, the use of drug monitoring (the Therapeutic Drug Monitoring) -free blood collection systems is recommended.

Drug-free venous access

Detection of drugs (therapeutic drug monitoring) from venous access carries the risk of incorrect determinations (high drug concentrations) due to the washing-in of drug residues from the venous access. Therefore, the blood should generally not be taken from the venous access. If this is unavoidable, the volume of blood corresponding to 2 times the dead volume of the venous access must be discarded before the blood volume required for Therapeutic Drug Monitoring is collected.

Never collect blood proximally from an intravenous venous catheter because then the blood sample is diluted and possibly contamination by foreign substances can occur.

Sample materials

A prerequisite for the meaningfulness of laboratory medical test is that the state of the measured variables present in vivo in the body fluid investigated is transferred unchanged into the analytical process. This is ensured by the use of suitable collection and shipping materials.

Our **list of services** contains precise information about which material should be sent in which quantity and which delivery tubes should be used.

For special tests, we will also send you specially designed vessels on request and give you detailed descriptions of how to proceed with the collection.

If, according to the **list of services**, samples are frozen for certain tests, please observe the information on the corresponding pages in the specifications.

Anticoagulants:

Anticoagulants inhibit blood coagulation either by binding calcium ions (EDTA and citrate) or by antithrombin activity (heparin and hirudin):

EDTA: ethylendiamintetraacetic acid

Hematology (BB), blood typing, immunohematology, molecular genetic testing, HLA typing

Citrate: Tri-sodium citrate dihydrate

Pay attention to the exact mixing ratio. The tubes should be filled to the mark during blood collection.

Coagulopathy

Heparin: Either sodium, lithium or ammonium heparin. Enhances the effects of AT III, cytogenetics, clinical chemistry

Hirudin: binds thrombin

ThromboExact: For platelet determination in pseudothrombocytopenia

Additives:

NaF-citrate: For the determination of a correct glucose value, the measurement of glucose in NaF-citrate plasma (GlucoEXACT tube with light gray cap) is recommended; Sodium fluoride in combination with citrate inhibits glycolysis and thus the degradation of glucose. The GlucoEXACT Monovette contains NaF as well as citrate. By this addition, the initial drop in glucose level is inhibited until the full onset of NaF effect (after about 30 min). Glucose levels in the GlucoEXACT Monovette are up to 10% higher than in the pure NaF Monovette.

Whole blood

Whole blood should only be shipped for tests where it is explicitly noted. For serum or plasma samples, the shipment of whole blood is not suitable because the inevitable hemolysis of the results of many studies can be significantly distorted.

Serum

For serum samples take the double amount of blood: For example, use 4-5 ml of blood for 2 ml of serum. Remove whole blood with special serum tubes (e.g. serum vacutainer or serum monovette) and swirl tubes several times. Leave blood at room temperature for about 30 minutes (maximum 1 hour). Then centrifuge for about 10 to 15 minutes at about 3000 rpm. If no tube with separating gel is used, transfer the supernatant (serum) to shipping tubes and ship as specified.

Plasma

Procedure

- collect blood with specially coated tubes (e.g. EDTA Vacutainer or EDTA monovette);
- exactly observe the filling quantities (mixing ratio);
- mix thoroughly (tilt, do not shake).

If plasma is required for the test, the EDTA or Heparin whole blood is centrifuged for about 15 minutes at 3000 rpm and the supernatant is transferred to a corresponding test tube and shipped as indicated.

Urine

Impeccable test results are obtained in the 24h collection only if the patient is instructed exactly. For the laboratory tests, the 24h amount is collected, of which only a part, e.g. 30 ml of urine, must be sent.

Never forget: specifying the 24h volume on the request form!

24hour collection:

Hand over the patient a clean container (urine collection container with collection instructions is available on request)

Please instruct the patient:

- Pay attention to normal hydration (1.5-2 l per day) and no alcohol.
- Empty the bladder in the morning after getting up. But do not catch this urine yet. Write down time.
- Collect all urine from there, even during bowel movements. Keep sample cool and do not place in bright light. Last collection the next morning at the time noted the day before (empty bladder, even without urgent need).
- Collect urine completely at each micturition, DO NOT discard the first serving, as with midstream urine.
- Mix 24h urine well. Read the urine volume at the scale on the collecting flax and note it. Put the amount of urine required for the required test into the appropriate urine tubes (if necessary, use boric acid tubes), mix well. Possibly. add the indicated acid, e.g. 25% hydrochloric acid, then mix well. Label the urine tubes with personal data (surname, first name, gender, date of birth) or the barcode and the amount of urine collected (... ml / 24 hrs).

Urine collection for catecholamines and 5-hydroxy-indoleacetic acid:

- Please note: no acid must be presented in the collecting vessel!
- Immediately after collection of urine, mix 24h urine well, measure urine volume and state!
- Put 0.5 ml of 25% hydrochloric acid in the urine delivery tube. Fill tubes with urine and mix!
- Do not use acetic acid or boric acid!
- Vanillinmandelic acid, metanephrine, homovanillic acid can also be determined from these samples.

One urine tube (30 ml) is sufficient if all 5 parameters are requested.

Stool

In the examination of stool samples the proper collection is a crucial prerequisite for a meaningful test result.

For a safe and hygienic chair collection, you can request so-called "Stuhlfänger" with application description in our laboratory.

Stool tests

In addition, the following general instructions must be kept in mind:

- During collection, it must be ensured that the stool sample contains no urine.
- The stool sample must be taken from different parts of the stool.
- It is preferable to convert these sites in the stool tube if the stool contains any conspicuous ingredients that do not conform to normal stool consistency, (e.g. as mucus or blood or aqueous fractions).
- The stool tube should be about one quarter full and kept in a cool place until transport to the laboratory.

Bone marrow

For immunophenotyping (flow cytometry) and for molecular biological methods we need EDTA bone marrow.
For chromosome analysis and FISH technique, we need heparinized bone marrow.

Measurement uncertainty and significance

Each measurement result is subject to measurement uncertainty resulting from errors and uncertainties from the various stages of sampling to analysis and partial ignorance of the factors that influence the outcome. It is defined as an estimate that indicates the range of values within which the true value is expected.
Knowledge of measurement uncertainty can be very helpful in assessing the significance of medical laboratory findings. Two essential questions should be mentioned, which the medical findings should serve:

- What is the absolute position of the parameter relative to a reference range (deviation and degree of deviation from the norm, achievement of a therapy goal, etc.)?
- Is the value obtained significantly different from a pre-value (progress check)?

In the assessment of "measurement uncertainty" all sources must be included, in particular the sampling, which plays a crucial role in the medical laboratory.
The overall measurement uncertainty in the medical laboratory, which is decisive for the significance of the analysis, depends at least on:

- Influencing factors (= in vivo determinants):
    - biological physiological influences (e.g. gender differences, age, nutrition, state of stress, body position, daily rhythm)
    - Influences of diagnostic and therapeutic measures, e.g.
        - intramuscular injection
        - pharmacological changes in the metabolism
        - pathological influences (trauma, operations, shock)
    - Influences resulting from the sampling (see below)
- Confounding facts (= in vitro determinants):
    - as a consequence of diagnostic and therapeutic measures, in particular interference by drugs
    - confounding by sample components that occur in vivo prior to acceptance in vivo or due to incorrect storage of the sample
- especially the sampling as a source of error
    - Influencing variables (type of samples, body position, statis time, time of day, lipemia, haemolysis, etc.)
    - Confounding factors (coagulation, hemolysis, storage, light exposure, room air, etc.)
- the preanalytics (transport temperature, transport time, sample preparation etc.)
- the precision of the analytical laboratory process (measure of statistical error in repeated measurement = scattering). The measure of precision is the coefficient of variation. Its size can be highly dependent on the position of the measured value (for example, a method can have a larger relative dispersion with low measuring signals than with higher values).

- the correctness of the analytical laboratory process (measure of the measuring system-dependent deviation from the "true value")

A number of these points, which determine the "total measurement uncertainty", are highly dependent on the individual circumstances of the patient. An estimate of the contribution of this uncertainty can only be done with knowledge of the individual concerned and the medical conditions.

It is crucial to realize that these contributions are much larger for many analytes than the actual analytic variables of uncertainty (accuracy and precision).

For the assessment of the overall measurement uncertainty, we have tried to list important specifics of the individual analytes, such as half-life as well as influencing factors and confounding factors for sampling and transport in this laboratory information.

As part of quality control, the calculation of analytical precision and accuracy for all quantitative parameters is constantly updated.

The doctors of the laboratory are available to discuss the significance of findings at any time. They will introduce the current data on analytical uncertainty and considerations of preanalytics in the discussion of individual findings.