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USE OF ANTICOAGULANTS IN DIAGNOSTIC LABORATORY INVESTIGATIONS

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Stability of blood, plasma and serum samples

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The WHO document "Use of Anticoagulants in Diagnostic Laboratory Investigations" (WHO/DIL/LAB/99.1 Rev. 1) received a surprising resonance and experts around the world provided many additional observations. This information has been included in the 2nd revision of the document. The document provides an extensive summary of observations on the effects of anticoagulants in blood, plasma and serum. Information on the effects of haemolysis, hyperbilirubinaemia and hyperlipoproteinaemia on measurement procedures has been added.

WHO is grateful for the efforts made by the group of experts in collecting all the information necessary for this revised version.

Geneva, 15 January 2002

Contents

1 Serum, Plasma or Whole Blood? Which Anticoagulants to Use?

It is imperative that the in-vivo state of a constituent remains unchanged after withdrawal from the body fluid of a patient to obtain a valid medical laboratory result. This may not always be possible when measuring extra-cellular and cellular components of blood. Platelets and coagulation factors are activated when blood vessels are punctured, and their activation continues in sample containers that do not contain anticoagulant.

Historically, serum was the preferred assay material for determining extracellular concentrations of constituents in blood. Today, plasma is preferred for many, but not all, laboratory investigations because the constituents in plasma are better reflecting the pathological situation of a patient than in serum. Some changes of constituents can be avoided by using anticoagulants. The types and concentrations of anticoagulants used in venous blood samples were defined in the international standard (86) in 1996. The standardized anticoagulants are now used to prepare standardized plasma samples for laboratory investigations throughout the world.

This document summarizes the findings published in the literature and those observed by the contributors on the use of anticoagulants. The overview was prepared in collaboration with experts from clinical diagnostic laboratories and the diagnostics industry (68, 71).

1.1 Definitions

1.1.1 Whole blood

A venous, arterial or capillary blood sample in which the concentrations and properties of cellular and extra-cellular constituents remain relatively unaltered when compared with their in-vivo state. Anticoagulation in-vitro stabilizes the constituents in a whole blood sample for a certain period of time.

1.1.2 Plasma

The virtually cell-free supernatant of blood containing anticoagulant obtained after centrifugation.

1.1.3 Serum

The undiluted, extracellular portion of blood after adequate coagulation is complete.

1.1.4 Anticoagulants

Additives that inhibit blood and/or plasma from clotting ensuring that the constituent to be measured is non-significantly changed prior to the analytical process. Anticoagulation occurs by binding calcium ions (EDTA, citrate) or by inhibiting thrombin activity (heparinates, hirudin). The following solid or liquid anticoagulants are mixed with blood immediately after sample collection:

1.1.4.1. EDTA

Salt of ethylene diamine tetraacetic acid. Dipotassium (K_2), tripotassium (K_3) (41) and disodium (Na_2) salts are used (86); concentrations: 1.2 to 2.0 mg/mL blood (4.1 to 6.8 mmol/L blood) based on anhydrous EDTA.

1.1.4.2. Citrate

Trisodium citrate with 0.100 to 0.136 mol/L citric acid. Buffered citrate with pH 5.5 to 5.6: 84 mmol/L trisodium citrate with 21 mmol/L citric acid. Differences were noticed between 3.2% and 3.8% (v/v) citrate when reporting results in INR (1, 145, 192, 210). WHO and NCCLS recommend 0.109 mol/L (3.2%) citric acid. The International Society for Thrombosis and Haemostasis (ISTH) recommends the use of Hepes buffered citrate for all investigations of haemostastic functions (114).

a. A mixture of one part citrate with nine parts blood is recommended for coagulation tests (86, 136).
b. One part citrate mixed with four parts blood is recommended to determine the erythrocyte sedimentation rate (86).

1.1.4.3. Heparinates

12 to 30 IU/mL of unfractionated sodium, lithium or ammonium salt of heparin with a molecular mass of 3 to 30 kD is recommended to obtain standardized heparinized plasma (86).

Calcium-titrated heparin at a concentration of 40 to 60 IU/mL blood (dry heparinisation) and 8 to 12 IU/mL blood (liquid heparinisation) is recommended for the determination of ionized calcium (22).

1.1.4.4. Hirudin

Hirudin is an antithrombin extracted from leeches or prepared by a genetic engineering process. Hirudin inhibits thrombin by forming a 1:1 hirudin-thrombin complex. Hirudin is used at a concentration of 10 mg/L (40).

The *colour codes* of anticoagulants described in ISO/DIS 6710 are:
EDTA = lavender/red;
citrate 9 + 1 = light blue/green;
citrate 4 + 1 = black/mauve;
heparinate = green/orange;
no additives (for serum) = red/white (86).

1.2 Plasma or serum?

1.2.1 Advantages of using plasma

The following aspects support the preferential use of plasma versus serum in laboratory medicine:

Time saving: Plasma samples can be centrifuged directly after sample collection, unlike serum, in which coagulation is completed after 30 minutes,

Higher yield: 15 to 20 % more in volume of plasma than of serum can be isolated from the same volume of blood.

Prevention of coagulation-induced interferences: Coagulation in primary and secondary tubes that were already centrifuged, may block suction needles of the analyzers when serum tubes are used; this is prevented by using anticoagulants.

Prevention of coagulation-induced interferences: The coagulation process changes the concentrations of numerous constituents of the extra-cellular fluid beyond their maximum allowable limit (70, 202). The changes are induced by the following mechanisms:

a. Increase in the concentrations of platelet components in serum as compared to plasma (e.g. potassium, phosphate, magnesium, aspartate aminotransferase, lactate dehydrogenase, serotonin, neurone-specific enolase, zinc). Release of amide-NH_3 from fibrinogen induced by action of clotting factor XIII.

b. Decrease in the concentration of constituents in serum as a result of cellular metabolism and the coagulation process (glucose, total protein, platelets).

c. Activation of the cell lysis of erythrocytes and leukocytes in non-coagulated blood (cell-free haemoglobin, cytokines, receptors).

Certain constituents should only be measured in plasma (e.g. neurone-specific enolase, serotonin, ammonia) to obtain clinically relevant results.

1.2.2 Disadvantages of plasma over serum

The addition of anticoagulants may interfere with certain analytical methods or change the concentration of the constituents to be measured:

a. Contamination with cations: NH_4^+, Li^+, Na^+, K^+.

b. Assay interference caused by metals complexing with EDTA and citrate (e.g. inhibition of alkaline phosphatase activity by zinc binding, inhibition of metallo-proteinases, inhibition of metal-dependent cell activation in function tests, binding of calcium (ionized) to heparin (22)).

c. Interference by fibrinogen in heterogeneous immunoassays (202).

d. Inhibition of metabolic or catalytic reactions by heparin: e.g., Taq polymerase in the polymerase chain reaction (PCR) (137).

e. Interference in the distribution of ions between the intracellular and extracellular space (e.g. Cl^-, NH_4^+) by EDTA, citrate (70).

f. Serum electrophoresis can be performed only after pre-treatment to induce coagulation in plasma.

1.2.3 Analytical samples in the serological diagnosis of infectious diseases

A variety of methods are used for serological diagnosis of infectious diseases. They include immuno-diffusion, immuno-precipitation, counter immuno-electrophoresis, agglutination of bacteria, haemagglutination and agglutination inhibition, particle-enhanced agglutination, complement fixation, indirect immuno-fluorescence (IFA), enzyme-linked immunoassay (ELISA), radio-immunoassay (RIA), neutralisation of toxins or virus-activity, immunoblot (Western blot) and others.

In general, serum is used for the serological diagnosis of infectious diseases; serum must be used for certain immunological techniques such as complement fixation or bacterial agglutination tests; for other tests, including some haemagglutination tests, ELISAs or immunoblots, either serum or plasma may be used.

1.3 Recommendations

Table 5.1 indicates materials that are recommended for a specific test. The table also contains information on the utility of other sample materials as long as the results measured by that method do not exceed the maximum allowable deviation of measurement (152) as defined by the biological variation (153). A maximum deviation of 10% is acceptable for a constituent if it is not included in the list.

1.3.1 Sample collection and transport time

The following sequence for filling tubes with blood from a patient is recommended to avoid contamination (70):

blood for blood culture,
serum [avoid serum as first tube when electrolytes shall be measured (116)],
citrate, heparinate, EDTA containing tubes,
tubes containing additional stabilizers (e.g. glycolytic inhibitors).

Only the recommended quantity of anticoagulant should be added, wherever required, to avoid errors in results.

Tilt the tube repeatedly (do not shake and avoid foaming) immediately after filling to mix the sample thoroughly with the anticoagulant. Leave the containers at room temperature for at least 30 minutes to separate serum from blood cells in blood that was taken from non-anticoagulated patients. This period is shorter when coagulation has been activated. Leave the sample at room temperature no longer than the period indicated in the table [see 5.1, (66)].

1.3.2 Centrifugation

Blood cells are rapidly separated from plasma/serum by centrifugation at increased relative centrifugal force (rcf). Rcf and rotations per minute (rpm) are calculated using the rotating radius r (the distance between the axis of rotation and the base of the container in mm) by the following equation:

$$rcf = 1{,}118 \times r\ (rpm/1000)^2$$

Centrifuge blood containers in 90°-swing-out rotors that the sediment surface forms a right angle with the container wall. This helps to prevent contact between the sampling needle and the surface of the cell layer or separating gel in the tube, when the centrifuged blood containers are directly transferred to an autoanalyzer for analysis.

1.3.2.1. Plasma

Centrifuge the anticoagulated blood (citrated, EDTA or heparinized blood) for at least 15 minutes at 2000 to 3000 *g* to obtain cell-free plasma.

1.3.2.2. Serum

When plasma coagulation is complete, centrifuge the sample for at least 10 minutes at a minimum speed of 1500 *g*.

When separating serum or plasma, the temperature should not drop below 15 °C or exceed 24 °C.

1.3.3 Storage

Non-centrifuged samples should be stored at room temperature for the time specified in the recommendations for stability [see table 5.1(66)]. After centrifugation, the serum or plasma should be analyzed within the time as recommended for whole blood, if the sample is stored without using a separating gel or a filter separator in primary tubes. When the sample shall be refrigerated or frozen for preservation, blood cells must first be separated from serum or plasma. Do not freeze whole blood samples before or after centrifugation, even when polymer separating gels are used.

1.3.4 Evaluation of new analytical procedures

Before using a new reagent or method, examine the suitability of the procedure by comparing the results of at least 20 blood samples with normal, and 20 with pathological concentrations of the constituent to be measured. The criteria for biological and clinical interpretation (reference intervals, clinical decision limits) may have to be changed, if the mean of the difference between the samples tested deviates by more than the maximum deviation allowed (152) (alternatively by more than 10 %).

2 The Optimal Sample Volume

The progress in the development of laboratory analyzers has led to a reduction of the sample volume for analysis. The development, however, is not necessarily accompanied by an adaptation of sample tubes and therefore often excessive sample volumes are collected. Studies revealed (30) that 208 mL blood for 42 tests is taken during an average stay of a patient in a department of internal medicine. In intensive care the total volume drawn for 125 tests was 550 mL of blood. Previous publications describe that in half of the patients who received blood transfusion, more than 180 mL of blood were taken for laboratory tests (174). "Iatrogenic anaemia" caused by excessive blood sampling is a well-known phenomenon in paediatrics (27), whereas iatrogenic anaemia is hardly recognized as an important phenomenon in the acute and intensive care of adult patients. The following recommendations were made for sampling reduced blood volumes for analysis (67):

2.1 Definition

The amount of sample needed for laboratory diagnostic purposes (Vol b) is defined by:

1. The analytical sample volume (Vol a),
2. The dead-space volume of the analyser (Da), measured as mL plasma/serum,
3. The dead-space volume of the primary sample tube (Dp), measured as mL blood,
4. The dead-space volume of secondary sample tubes (Ds), measured as mL plasma/serum,
5. The amount of sample needed for number (N) repetitive analysis and additional follow-up tests,
6. The plasma sample yield according to the respective haematocrit.

Assuming that plasma/serum yield is 50 % of blood volume the total blood needed can be calculated as follows:

$$Vol\ b = 2x\ [N\ x\ (Vol\ a + Da) + Ds] + Dp$$

2.2 Recommendations

Assuming a haematocrit of 0.50 and a need for a repetition and follow-up of laboratory tests, four times the analytical sample volume can be considered to be sufficient when plasma or serum shall be used. The following standard blood volumes are recommended for analysis using advanced analytical systems. These volumes may be sufficient in 95 % of cases to provide the laboratory results as requested:

— Clinical chemistry: 4 – 5 mL (when using heparin plasma: 3 – 4 mL)

— Haematology: 2 – 3 mL EDTA blood

— Coagulation tests: 2 – 3 mL citrated blood

— Immunoassays including proteins etc: 1 mL whole blood for 3 – 4 immunoassays

— Erythrocyte sedimentation rate: 2 – 3 mL citrated blood

— Blood gases, capillary sampling: 50 µl, arterial and venous sampling: 1 mL heparin blood

The request form for laboratory analyses should include clear information on the required sample volumes and tubes. Tubes of uniform size (for instance 4 – 5 mL tubes) with different filling volumes should be used. The length of the tubes should be at least four times the tube diameter. The criteria are met by standard tubes of 13 x 75 mm (diameter x length).

2.2.1 Measures which can help to reduce the required blood volume

— Introduction of primary tube reading in analyzers

— Deletion of sample distribution into secondary tubes

— Use of tubes with smaller diameter

— Use of analyzers requiring a smaller analytical sample volume

— Storage of samples in primary tubes, using separators for plasma or serum

— Use of plasma instead of serum

2.2.2 Documentation

1. Any method description should include the required analytical sample volume.
2. A quality manual should document the requested sample volumes and their handling procedure.
3. The manual should describe the procedures how to handle patient samples that have an insufficient sample volume.

3 Analyte Stability in Sample Matrix

The aim of a quantitative laboratory investigation is to determine the concentration or activity of a diagnostically relevant analyte in a body fluid in order to provide information on the clinical situation of a patient. This implies that the composition of the samples for analysis must not change during the pre-analytical phase (sampling, transportation, storage, sample preparation; 70).

3.1 Stability and Instability

Stability is the capability of a sample material to retain the initial property of a measured constituent for a period of time within specified limits when the sample is stored under defined conditions (87).

The measure of the instability is described as an absolute difference, as a quotient or as a percentage deviation of results obtained from measurement at time 0 and after a given period of time.

Example:
The transportation of whole blood for 3 to 4 hours at room temperature rises the concentration of potassium from 4.2 mmol/L to 4.6 mmol/L.

Absolute difference:	0.4 mmol/L
Quotient:	1.095
Percent deviation:	+ 9.5 %

The maximum permissible instability is the deviation of a result that corresponds to the maximum permissible relative imprecision of the measurement. This was defined as 1/12th of the biological reference interval (152). The deviation should be smaller than half of the total error derived from the sum of biological and technical variability (153). The stability of a blood sample during the pre-analytical phase is defined by the temperature, the mechanical load in addition to other factors. As time has also a major influence, the stability is stated as the maximum permissible storage time under defined conditions.

The maximum permissible storage time is the period of time at which the stability requirement of 95 % of the samples is met. This is a minimum requirement, since under pathological conditions the stability of an constituent in the sample can be considerably reduced (See examples in Table 5.1).

The storage time is stated in suitable units of time (days, hours, minutes). A clear distinction must be made between the storage of the primary sample (blood, urine, cerebrospinal fluid) and the storage of the analytical sample (e.g. plasma, serum, sediment, blood smear). The storage times are adopted for:

1. Storage of the primary sample at room temperature (20 to 25 °C)
2. Storage of the analytical sample at room temperature (20 to 25 °C), refrigerator temperature (4 to 8 °C) and deep-frozen (-20 °C).

3.2 Quality assurance of the time delay during the pre-analytical phase

3.2.1 Transport time
The transport time is the difference between the blood sampling time (in general with an accuracy of at least a quarter of an hour) and the registration time of the request and/or the arrival of the sample at the laboratory. The transportation time should be documented for each sample by the laboratory.

3.2.2 Pre-analytical time in the laboratory
The pre-analytical time in the laboratory is the difference between the time of analysis and the registration time of the sample. When the time at the end of the analytical phase (i.e. printing time of the result) is noted, the analysis time stated in the description of the method must be subtracted.

3.2.3 Documentation
It is recommended to state the sampling time and the arrival time of the sample in the laboratory in the report for the documentation of the transport time.

3.2.4 Actions to be taken when the maximum permissible pre-analytical times are exceeded
A medically relevant change of the results must be considered, when the maximum permissible transport and pre-analytical time of the sample was exceeded. The laboratory has the responsibility to mark the results of such samples with a note in the report, or to refuse to carry out the test. The latter

decision is advisable, when medical conclusions may be derived from the result that may be detrimental to the patient. The following example illustrates the problem:

> An EDTA blood sample shows a rise in monocyte number from 4 to 10 % after four hours of storage measured by an automatic cell counter system. When this results is reported without comment, it could lead to an erroneous medical diagnosis that the patient suffers from a viral infection. Therefore, the clinician should be informed with a comment or a refusal, such as:
>
> *Comment:* "The monocyte count may give incorrectly high values with the method used in our laboratory when EDTA blood is stored more than 2 hours. A control in the smear resulted in normal monocyte counts."
>
> *Refusal:* "The maximum permissible transportation time was exceeded. Therefore the monocyte results are not stated, because they cannot correctly be determined. For the determination of correct monocyte counts, a transportation time of maximally two hours is acceptable."

4 The Haemolytic, Icteric and Lipaemic Sample

Medical laboratory tests are affected by endogenous and exogenous factors in the sample matrix. Certain potentially interfering factors may be recognized by a coloured appearance of the sample, whereas other factors (e.g. drugs) are detected only by additional information and/or direct analysis. Reference books provide useful information on drug interferences in laboratory analysis (178, 194, 214). Publications of standard setting organizations describe the methodology and statistical methods for the recognition and quantitative estimation of interferences in clinical chemical investigations (52, 135).

It is difficult to predict the effects of haemolysis, turbidity (lipaemia) and bilirubin (icterus), especially when reagents and analytical systems undergo modification (58,59). This document provides information that the laboratory can consider appropriate actions to ensure that the results of measurement are clinically relevant.

4.1 Definition of a clinically relevant interference

The maximal allowable deviation (bias) is expressed in % deviation of the result without interference as determined by a reference method. A clinically relevant bias should be considered if the change of the result caused by the interfering substance is more than the maximal allowable deviation of the analytical procedure (152). The bias usually amounts to 1/12 (which is about 8%) of the reference interval.

Data on the biological variability were published to define the medical needs. The desirable bias (B) derived from intra-individual (CV_w) and inter-individual (CV_b) variation was established for 316 analytes (153).

> Example:
> A result for plasma creatinine of 125 µmol/L (1.41 mg/dL) was measured in an icteric sample by a routine method, whereas a creatinine concentration of 90 µmol/L (1.02 mg/dL) was measured in the same sample by a reference method. For creatinine the maximum allowable deviation amounts to 9 % (158), the specification for B to 3.4 % (153). The result deviates by 35 µmol/L, which is 39 % from the expected value. Both criteria confirm that hyperbilirubinaemia is a clinically relevant interference when creatinine is measured using the routine method established in the laboratory.

4.2 General recommendations

4.2.1 Documentation of interferences

Documentation of method: Each clinical laboratory should specify the constituents in the quality manual that are affected by any of the following properties of the sample. The limits, beyond which the analysis shall not be performed, should be stated for each method that is subject to an interference. The

European Directive for In Vitro-Diagnostics (IVD) states that providers of reagents must define the appropriate limiting conditions (42). The procedure for the detection of interfering properties as well as actions that should be taken with the sample, should be documented in the quality manual.

4.2.2 Detection of a potentially interfering property and handling of sample and request

Each sample must be visually examined immediately after arrival or (in case of blood samples) after centrifugation and the potential interfering property recorded in the laboratory journal and report. When no visible interference is observed, it should be registered in the list by the notation: “appearance unremarkable”.

The requests should be reviewed to identify analytes that could be affected by the observed interference in the sample. Analytes that are not affected by the interference in the sample, are measured like in samples that contain no interference using the routine method of analysis. A sample that may be expectedly affected by an identified interference, must be pre-treated to eliminate the interference before measurement is made; alternatively a measurement method may be used that is not subject to the interference. The analysis should not be made when a clinically relevant bias is expected, or if the interference cannot be eliminated or circumvented by an appropriate alternative method.

4.2.3 Reporting results

Each report should include a notation characterising the samples' “appearance”. The observation should be documented for each sample: e.g. “haemolytic”, “icteric”, “opalescent”, “turbid”, or “lipaemic”, if a relevant colour or turbidity was identified.

The report should indicate, that the analysis was made despite a remarkable appearance of an interference in the sample. The report should also indicate when the sample was pre-treated prior to the analysis. If the interference in a sample cannot be eliminated for a subsequent analysis, the text “impaired by...” should replace the report of the result.

4.3 The haemolytic sample and the effect of therapeutic haemoglobin derivatives

4.3.1 Haemolysis

Haemolysis is defined as the release of intracellular components of erythrocytes and other blood cells into the extracellular space of blood (65). Haemolysis can occur in-vivo (e.g. through a transfusion reaction or during malaria parasite infection affecting the invaded erythrocytes), and in-vitro during all steps of the pre-analytical phase (sampling, sample transport and storage).

Haemolysis is caused by biochemical, immunological, physical and chemical mechanisms (18, 65). During blood transfusion, complement-dependent haemolysis may be caused by antibodies reacting with the major blood group antigens. Physical haemolysis is caused by destruction of erythrocytes by hypotonicity (e.g. dilution of blood with hypotonic solution), as well as decreased (vacuum) or increased pressure. Mechanical haemolysis may occur during the flow of blood through medical devices (e.g. catheters, heart valves) in-vivo, during inadequate centrifugation as well as at elevated temperature in-vitro. Contaminating substances may also cause in-vitro haemolysis. Finally, detergents (residual cleaning agents and disinfectants) and other contaminating substances may cause haemolysis.

After the separation of blood cells, haemolysis may be visible by the red colour of serum or plasma. The sample may concomitantly be contaminated by constituents of other blood cells (leukocytes and platelets). For example, cell breakdown may result in changes in blood of patients with leukaemia; the disintegration of platelets during coagulation results in higher concentrations of intracellular platelet constituents in serum (70). On the other hand, the intracellular components of erythrocytes are also released into plasma without a concomitant increase in haemoglobin concentration during storage of whole blood in refrigerators.

4.3.2 Haemoglobin based oxygen carriers used as blood substitutes

Therapeutic haemoglobin derivatives (so-called HbOC = haemoglobin-based oxygen carriers) were recently developed as blood substitutes. The substitutes occur at concentrations of up to 50 g/L in

plasma of patients under blood substitute treatment. Plasma or serum containing blood substitutes has a strong red colour (24, 92, 211).

4.3.3 Detection and measurement of haemoglobin in serum or plasma

4.3.3.1. Visual detection

At extracellular haemoglobin concentrations above 300 mg/L (18.8 mmol/L), haemolysis is detectable by the red colour of serum or plasma. Samples with therapeutic haemoglobin derivatives (in therapeutically effective concentration) are always intensely red coloured.

4.3.3.2. Spectrophotometric detection

Some analytical systems measure the extent of haemolysis by comparing the absorption of samples at two wavelengths (61). The absorption spectrum of the haemoglobin derived oxygen carriers used as blood substitutes does not differ substantially from that of natural haemoglobin.

4.3.3.3. Analytical measurement

Haemoglobin in plasma or serum is measured at concentrations that are below the concentration visible to the human eye (13, 110, 188).

4.3.4 Distinction between in-vivo haemolysis and in-vitro haemolysis

In-vivo haemolysis may be distinguished from in-vitro haemolysis by comparing a haemolytic sample of a patient with other samples from the same patient, arriving at the same time.

4.3.4.1. In-vivo haemolysis

Free haemoglobin in-vivo rapidly binds to haptoglobin and the complex is eliminated from the circulating blood (as in haemolytic anaemia). Consequently, haptoglobin is reduced during intra-vasal haemolytic process. The measurement of low concentration of haptoglobin thus permits an imperative assessment of haemolysis (exceptions are inborn haptoglobin deficiency and newborn children (199)). Likewise, the measurement of haemopexin and/or methaemoglobin/albumin was used to characterize in-vivo haemolysis (199).

A rise in concentration of indirect bilirubin and reticulocyte counts is a typical sign of in-vivo haemolysis, which in turn leads to increased erythropoesis. Other consequences of in-vivo haemolysis, such as a change in the LDH iso-enzyme pattern, seem less suitable for the identification of haemolysis because of their low diagnostic sensitivity and specificity.

4.3.4.2. In-vitro haemolysis

After in-vitro haemolysis all constituents of erythrocytes, including potassium concentration, lactate dehydrogenase and aspartate aminotransferase activities, increase in addition to the concentration of free haemoglobin in plasma or serum(208). In contrast, haptoglobin concentration in plasma/serum of haemolytic samples remains unchanged. Certain immunological methods differ in their ability to distinguish haemoglobin/haptoglobin complexes from free haptoglobin (199).

4.3.4.3. Identification of haemoglobin derived oxygen carriers

Therapeutic haemoglobin derivatives yield a visible haemoglobin concentration within the range of 10 - 50 g/L. The absorption spectrum of haemoglobin derived oxygen carriers is not distinguishable from that of haemoglobin (24, 92, 211). However, haemoglobin concentrations of this magnitude rarely occur in vivo; therefore the use of therapeutic haemoglobin derivatives must be suspected at this plasma haemoglobin concentration. Haptoglobin cannot be used for discrimination, since the oxygen carriers form complexes with haptoglobin only slowly.

4.3.5 Mechanisms of interference by haemolysis

Haemolysis in-vivo or in-vitro can cause an apparent decrease or increase of results. A variety of mechanisms are contributing to these effects, some of which are summarized below:

4.3.5.1. Rise of intracellular constituents in the extra-cellular space

Cell constituents with an intracellular concentration 10 times higher than the extra-cellular concentration will increase in plasma/serum during haemolysis (e.g. potassium, lactate dehydrogenase,

aspartate aminotransferase). Differences of analyte concentrations between plasma and serum are also due to lysis of blood cells (essentially by platelets): Thus, neurone-specific enolase, potassium and acid phosphatase are higher in serum.

4.3.5.2. Interference with analytical procedure

Blood cell constituents can directly or indirectly interfere in the measurement of analytes. Adenylate kinase released from erythrocytes causes an increase of creatine kinase and CK-MB activity especially when inhibitors of adenylate kinase in the assay mixture are inadequate (182). In contrast, adenylate kinase does not affect the immunochemical quantification of CK-MB. Pseudo-peroxidase activity of free haemoglobin interferes in the bilirubin procedure of Jendrassik and Groof by inhibiting the diazonium colour formation (198). Proteases released from blood cells reduce the activity of coagulation factors while fibrin split product formation may increase.

4.3.5.3. Optical interference by haemoglobin

The effect of haemolysis on various analytes measured in clinical chemistry has been thoroughly investigated (18, 58, 176). Most often, the colour of haemoglobin increases the absorption at a respective wavelength or changes the blank value. An apparent increase or decrease of a result by haemoglobin is therefore method- and analyte concentration-dependent. Likewise, the changes caused by therapeutic haemoglobin derivatives are primarily due to optical interference (24, 92, 211).

4.3.6 Means to avoid haemolysis and its interferences

Haemolysis in-vitro can almost always be avoided, when the mechanism of haemolysis is known. Therefore each haemolytic sample should be documented and the cause of haemolysis identified.

The most frequent causes of haemolysis, such as errors during sampling, are avoided using standardized materials and methods for the pre-analytical processes and by training and individual counselling.

Sometimes reliable results can only be obtained from a truly non-haemolytic sample. In some cases, the interference can be reduced or excluded using a method that is not sensitive to haemolysis or by pre-treatment of the sample. Procedures, including de-proteinisation or molecular sieving (51) and others have not found to be useful, because of the work load involved. Today, a modification of the methodology, e.g. by using a blanking procedure by means of measurement at a second, appropriate wavelength, is preferred; although, this procedure may not be applicable for the analysis of blood from patients who received blood substitutes (59). Likewise the ultrafiltration procedure, as applied in the multi-layer film technology, reduces the effect of interference by haemolysis (178).

4.3.7 Reaction upon the receipt of haemolytic samples

Each laboratory should document the procedures that are affected by haemolysis and to what extent they are affected. The procedures how to handle haemolytic samples should be described in the quality manual. This includes the criteria for rejecting the execution of analysis.

The haemolysis of each sample must be documented and reported to the clinician who ordered the analysis.

When haemolysis occurs in all samples of a patient, haemolysis in-vivo may be suspected. This must be immediately reported to the clinician to verify the possible causes of haemolysis or the possible use of synthetic haemoglobin derivatives.

After estimation of the degree of haemolysis the sample is treated for analysis according to the degree of interference. The results of measurement may be reported as follows:

- Method not impaired: Report results as with non-haemolysed samples.
- Method impaired , but eliminated by pre-treatment: Report results after pre-treatment.
- Method impaired in a clinically relevant way: Instead of providing a result, report: "Impaired by haemolysis".

It is not recommended to correct a measured result for haemolysis arithmetically using the haemoglobin concentration as an indicator.

4.4 The Lipaemic Sample

4.4.1 Definition

Lipaemia is a turbidity of serum or plasma which is caused by elevated lipoprotein concentrations and which is visible by the eye. A sufficiently transparent sample container is a prerequisite to detect lipaemia. Visible detection of lipaemia is also dependent on the type of plasma lipoproteins at elevated concentrations in the sample. Post-centrifugal coagulation of serum samples of heparinized patients can also be the cause of turbidity.

4.4.2 Causes of lipaemia (turbidity)

Most often, lipaemia results from increased triglyceride concentration in plasma/serum. This can be due to food intake, altered lipid metabolism or infusion of lipids. After intestinal absorption, triglycerides are present in plasma as chylomicrons and their metabolites (remnants) for 6 to 12 h.

One to four hours after intake of a “Continental” or “American” breakfast, plasma triglyceride concentrations increase substantially. As they cause turbidity of the sample, the patient should be requested to fast, before investigations are made that are affected by lipaemia.

Metabolic disorders causing hypertriglyceridemia can hardly be distinguished from lipid infusions, cold agglutinins and monoclonal immunoglobulins.

4.4.3 Identification and quantification of lipaemia

4.4.3.1. Optical and photometric methods for serum and plasma samples

In whole blood triglyceride concentrations above 1000 mg/dL (11.3 mmol/L) cause turbidity that is detected by visual inspection. Lipaemia in plasma or serum is visually observed at triglyceride concentrations above 300 mg/dL (> 3.4 mmol/L). The extent of turbidity of serum/plasma samples is measured at wavelengths above 600 nm (e.g. 660/700 nm) (178).

4.4.3.2. Detection in EDTA-blood

Haematological tests are influenced by lipaemia. Thus, haemoglobin concentration is apparently increased by light scattering. The turbidity is detected by spectrophotometric analysis. The result of a centrifuged sample from the same patient taken at the same time can be used for comparison.

4.4.4 Mechanisms of the interference by lipaemia on analytical methods

4.4.4.1. Interferences in spectrophotometric analysis

Lipaemia interferes in photometric measurement by light scattering and light absorption. The apparent result can be either increased or reduced depending on the blanking procedure. At high turbidity, no measurement may be possible due to the limits of the linearity of the method (8).

4.4.4.2. Volume depletion effect

Lipoproteins decrease the apparent concentration of the analyte by reducing the available water of sample volume, since the volume occupied by lipoproteins in plasma or serum is included in the calculation of the analyte concentration. This explains why lower sodium and potassium concentrations are found in lipaemic sera, when plasma or serum is measured by flame photometry and by indirect measurement using ion-sensitive electrodes, in contrast to direct potentiometry (107). The same observation is made after centrifugation, when the lipoproteins are not homogeneously distributed in serum/plasma samples: the concentration of an analyte dissolved in the aqueous phase is less in the upper layer than in the lower phase of the sample. The converse is true for concentration of lipids and lipid soluble constituents, including certain drugs that are taken up by lipoproteins.

4.4.4.3. Interference by physico-chemical mechanisms

A constituent that is extracted by lipoproteins may not be accessible for the reagent, such as an antibody, for detection. Similarly, electrophoretic and chromatographic procedures may be affected by lipoproteins present in the matrix.

4.4.5 Means to avoid lipaemia and interferences caused by turbidity

To avoid interference of lipoproteins on measurement after oral intake of fat, the patient should fast at least 12 hours before blood samples are taken (186). In patients receiving parenteral infusion of lipids a period of 8 hours of interruption of the treatment is necessary to avoid interfering turbidity (70). If these measures do not provide a non-turbid sample, other causes of turbidity should be suspected.

Several methods were recommended to remove lipids from serum or plasma, such as centrifugation, to produce a clear infranatant sample. Other methods include the extraction of lipids with organic solvents or fluorine chlorinated hydrocarbons (e.g. Frigen®) and the precipitation of triglyceride-rich lipoproteins by polyanion and cyclodextrin (169).

4.4.5.1. Centrifugation

Centrifugation at 1000 *g* is effective, when chylomicrons cause turbidity. In contrast, at least 10 min, centrifugation at 12 000 *g* separates serum or plasma lipids by flotation.

The clear infranatant must be carefully separated for analysis. Ultra-centrifugation must be employed for the separation of low density lipoproteins and high density lipoproteins. A centrifugation time of at least 30 min at a speed above 40 000 *g* is recommended. The separation of lipaemic plasma from EDTA-blood in samples used in haematology can be performed by centrifugation and exchange of the cell-free supernatant with the same volume of isotonic NaCl solution.

4.4.5.2. Fluorine chlorinated hydrocarbon extraction

The extraction with fluorine chlorinated hydrocarbons, suggested many years ago, can no longer be recommended for reasons of environmental protection.

4.4.5.3. Polyethylene glycol

The plasma/serum sample is mixed 1 + 1 (v/v) with 8 % polyethylene glycol 6000, incubated for 30 min in a refrigerator at 4 °C and centrifuged afterwards for 10 min at 4 °C and approx. 1000 x *g*. The results determined in the clear supernatant are multiplied by the dilution factor 2 (148, 161).

4.4.5.4. a-Cyclodextrin

200 g α-cyclodextrin are dissolved in 1 L distilled water and kept in a refrigerator. Before use, α-cyclodextrin solution must be brought to ambient temperature. Thoroughly mix one part of α-cylodextrin solution with two parts of serum, and centrifuge for 1 min at 10 000 *g*. The clear supernatant can be used for analysis. The dilution must be considered when calculating the concentration of the constituent in the original serum sample.
Experiments revealed that the results on 20 serum constituents are not affected by the precipitation of lipoproteins using α-cyclodextrin (169).

4.4.5.5. Magnetic beads

With the exception of sodium, calcium, magnesium, chloride and creatinine, various clinical chemistry constituents can be determined using magnetic beads, with dextran sulfate (50 kD) coated in a concentration of 5 g/L and 250 mmol/L $MgCl_2$ for delipidation. Add 100 µL reagent to 500 µL serum, and mix briefly on the Vortex mixer. Leave the tube upright in a rack for a few minutes, containing a magnet at the bottom. It is absolutely necessary to centrifuge the sample briefly, because some magnetic beads may still remain in the supernatant and bind to the cuvette of the analytical system. Multiply the results using a dilution factor 1.2.

4.4.5.6. Other methods for delipidation

Four different procedures for the extraction of lipids from serum samples were examined (3), including Freon 113®, dextrane sulfate 500 S, Aerosil 300 and a butanol/di-isopropylether mixture. It was found that the delipidation methods may substantially alter the concentrations of certain analytes.

4.4.5.7. Optical clearing systems

Commercial test kits may contain detergents such as triton X-100, cholic and desoxycholic acid, lipase or cholesterol esterase to remove turbidity in plasma or serum samples. The assigned concentrations of these substances are method dependent and should not be changed by the user.

4.4.6 Recommendation

A visible turbidity of a sample must be documented and reported with the results. Transparent sample containers must be used to detect turbidity. The methods used for the measurement of certain analytes that are affected by lipaemia must be listed, the methods for delipidation and the criteria for their application must be documented in the quality manual.

The method of choice for removal of turbidity from serum and plasma is a 10 min centrifugation in a micro-centrifuge with 10 000 *g*.

When chemicals are added (e.g. polyethylene glycol, α-cyclodextrin), the laboratory must prove that assigned method for measurement is not disturbed by the agent.

Samples submitted for the determination of lipids and other analytes may be delipidated only after measurement of the lipids. This applies also to lipid soluble drugs.

4.4.7 Test of interference by lipaemia

Various problems should be considered to examine the influence of lipaemia on analytical methods. Unfortunately, there is no uniform human lipid standard available. Patient samples with high lipid concentrations should not be frozen.

A 10 or 20 % emulsion of vegetable fat emulsion as applied in parenteral nutrition (4, 21, 27, 59, 61, 112, 131, 155) is suitable to simulate lipaemia . Significant differences between the effects of "physiological" and the artificially produced lipaemia were observed, particularly in measurements of urea and potassium (27). Therefore, the effect of lipaemia may not be examined using exclusively a model that contains artificial fat emulsions, because the observations may not be transferable to the biological condition.

4.5 The icteric sample

4.5.1 Appearance of different bilirubin species

Bilirubin occurs in plasma as a free molecule and covalently bound to albumin. In addition, water-soluble bilirubin conjugates exist as mono- and di-glucuronides (11). Studies on bilirubin interference mainly based on experiments in which free bilirubin or water-soluble di-taurobilirubin was added to serum (135). Under certain conditions the bilirubin molecules differ qualitatively and quantitatively in their effects of interference(61).

Conjugated bilirubin appears in urine, when present at increased concentrations in blood. In patients with proteinuria, bilirubin bound to albumin can also appear in urine.

After intra-cerebral bleedings non-conjugated (free) bilirubin causes xanthochromia of the cerebrospinal fluid. At increased permeability of the blood-brain barrier bilirubin bound to albumin can appear in the CSF.

4.5.2 Mechanisms of bilirubin interference

4.5.2.1. Spectral interference

Bilirubin has a high absorbance between 340 nm and 500 nm wavelengths. Therefore, the range of the linearity of a spectrophotometric procedure, using these wavelengths for the measurement of an analyte, can be a limiting factor because of the high background absorbance caused by bilirubin (48, 49). In coagulation analyzers using turbidimetric principle, a bilirubin concentration exceeding 25 µmol/L causes clinically relevant changes of the measured values of antithrombin III. Interference of bilirubin at higher concentrations will also be significant in certain coagulation tests (156).

The reduction of absorption as a result of oxidation bilirubin in alkaline solution is the main cause for bilirubin interference in modifications of the Jaffé method without deproteinisation (48).

In a strongly acid solution the absorption of conjugated bilirubin shifts to the UV wavelengths. Therefore bilirubin interferes in the determination of phosphate using the phosphomolybdate method through its reducing effect (37, 61).

4.5.2.2. Chemical interference

Bilirubin interferes in oxidase/peroxidase based test systems. Proportionally to its concentration bilirubin reacts with H_2O_2 formed in the test system which causes systematically lower results in enzymatic procedures that are used for the measurement of glucose, cholesterol, triglycerides, urate and creatinine (61, 179). Bilirubin competitively interferes with dyes binding to albumin (115). However, di-taurobilirubin does not interfere in the procedure of dye binding to albumin (61).

4.5.3 Detection and documentation of increased bilirubin concentrations in clinical samples

The visual inspection of plasma or serum samples for the detection of hyperbilirubinaemia is often not sensitive enough. This is particularly true when samples are simultaneously stained by other pigments (e.g. haemoglobin and its derivatives). Moreover, adhesive labels on primary containers can impair visual inspection.

Hyperbilirubinaemia is directly detected in diluted samples that are measured at 450 and 575 nm (177). (The direct procedure of bilirubin measurement is only applied for the determination of hyperbilirubinaemia in newborns.) With the nutritional supply of carotines or carotinoids, bilirubin concentration by direct measurement is overestimated (53). The common clinical chemical methods are applied to quantitatively measure the interference caused by bilirubin. It is advisable to separate and measure the different bilirubin fractions to assess the mechanism of interference(11).

4.5.4 Prevention of bilirubin interference

4.5.4.1. Method selection

The high prevalence of hyperbilirubinaemia in patients from intensive care, gastroenterological, surgical or paediatric departments makes it pertinent to select analytical methods that are less susceptible towards bilirubin interference.

Blanking procedures are useful to eliminate spectral bilirubin interferences, (48, 61). Parallel sample blank values give better results than methods in which reagents are added successively into a cuvette (61). Blanking procedures are often part of the analytical procedure, e.g. in the kinetic method for creatinine determination according to the Jaffé principle, when autoanalyzers are used (165).

The chemical interference of bilirubin in an analytical reaction is not eliminated by blanking procedures. K_4 [$Fe(CN)_6$] effectively eliminates bilirubin interference in H_2O_2-forming enzymatic methods based on the Trinder reaction (4). Moreover, optimal concentrations of components of the Trinder reaction can reduce the interference by bilirubin. A mixture of non-ionic tensides may reduce bilirubin interference like in the spectrophotometric determination of inorganic phosphate using phosphomolybdate (58).

4.5.4.2. Actions recommended to use in procedures sensitive to bilirubin

When procedures susceptible to bilirubin interference are used, the laboratory must know the limit of bilirubin concentrations where interference-free measurements are possible (application limit). The limit depends on the maintenance status of the analytical system and other variables. Unfortunately, manufacturers' data are not always available. For the determination of the application limit, 2 mL of 20 mg free bilirubin, dissolved in 0.1 mol/L NaOH, are mixed with 20 mg di-taurobilirubin, dissolved in 2 mL distilled water, in the dark. Five mL of non-icteric pool serum are added to 0.1 mL of the master solution to prepare a final bilirubin concentration of approximately 340 µmol/L (20 mg/dL). Serial dilutions are prepared by mixing a non-icteric pool serum with the master solution at different proportions. The test solution must be used on the same day (135).

Suitable alternative procedures must be applied for samples that have bilirubin concentrations beyond the application limit. The procedures may require a pre-treatment of samples to remove bilirubin. For the determination of serum creatinine using a bilirubin susceptible enzymatic method the sample is pre-incubated with 4.4 kU/L bilirubin oxidase for 30 seconds (7). However, the low stability of bilirubin oxidase limits the practical application of this procedure. Ultrafiltration of serum was also used for the

elimination of bilirubin interference in creatinine assays (51). As bilirubin binds to proteins, serum is centrifuged in a centrifugable ultrafilter (cut off ≈ 20 kD) for 15 min at 2000 *g* to remove bilirubin and obtain a completely protein-free ultrafiltrate. The volume depletion effect of proteins results in an approximately 4 % higher value for creatinine in the ultrafiltrate (51). The distribution of ionised low-molecular weight analytes on the diaphragm may be pH dependent which has an effect on the measurement results (49).

If procedures for the elimination of bilirubin are not applicable, alternative analytical principles should be applied. Immunological procedures for the measurement of serum albumin can be used to replace dye binding methods that are susceptible to bilirubin interference.

5 Samples and Stability of Analytes

Key for tables

⊕ Recommended sample
\+ Can be used without changes of result
(+) Can be used with limitations (see comments, in case of citrated plasma this indicates the need to consider dilution by citrate (74)).
– Not recommended
Decreased (↘) or increased (↗) values may be measured in comparison to recommended samples.
Blank field means no data were found in literature.
Greek letters refer to the information provided by diagnostic companies, numbers in brackets to the references.

Information provided by Diagnostic Companies
α: ORTHO-Clinical Diagnostics; Vitros Systems
β: Abbott; Axsym, Architect
γ: Roche Diagnostics; Hitachi, Elecsys, Modular
γγ: Roche Diagnostics; Cobas®INTEGRA
δ: Beckman-Coulter; Synchron LX/CX, Immage/Array, Access
ε: Dade Behring; Dimension®, BN Systems, Stratus CS
κ: DPC Immulite
λ: Bio-Rad
μ: Bayer; ADVIA Centaur/ACS 180

Stability and half-life times
min = minute(s)
h = hour(s)
d = day(s)
w = weak(s)
m = month(s)
y = year(s)

5.1 Blood

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Acetaminophen see Paracetamol															
Acetylsalicylate	+	+β	+ β	(+)β				15 - 30 min							45
α_1-Acid glycoprotein (orosomucoid)	+	+ γ	+ γ, γγ	(+)					12 d	1 y	5 m	5 m			191
Adenovirus antibodies	+		(+)											Complement fixation test, ELISA IgG, IgM	
Alanineaminotrans-ferase (ALAT, ALT, GPT)	+	+	+	(+)				47 h	4 d ↘	7 d	7 d	3 d			76, 106
Albumin	+	+*	(+)↘	(+)				3 w	6 d 14 d (2 – 6 °C)	4 m	5 m	2,5 m		*Bichromatic assay recommended for colorimetric assay (72),	35, 191, 202
Aldosterone	+	+	⊕					min	1 d ↘	4 d	4 d	4 d	EDTA		216
Alkaline phosphatase, - total - bone isoenzyme	+↗ +	⊕ +	- -	(+) (+)↘					4 d ↘ 4 d	2 m 2 m	7 d 7 d	7 d 7 d		EDTA binds essential cofactor zinc	76, 202
Aluminium	-	-	-	-					days	1 y	2 w	1 w		Special tube needed	164
Amikacin	+	+	+ β	(+)β				30 min – 3 h				2 h			205
Amiodarone	+	+	+					4 h – 25 d						HPLC	
Amitriptyline	+	+	+					17 – 40 h				1 d		HPLC	205
Ammonia (NH_4^+)	-↗	(+) ↗	⊕	-	+			min	15 min in EDTA	3 w	2 h	15 min	Serin 5 mmol/L+ borat 2 mmol/L (13)	Do not use ammonium heparin. Contamination by sweat ammonia.	50
Amphetamines	+	+	+												

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Amylase - pancreatic - total	+ +	+ +	+γ, γγ +γ, -γγ, δ, ↘↘*	(+) (+)*				9 - 18 h 9 - 18 h	4 d ↘ 4 d ↘	1 y 1 y	7 d 7 d	7 d 7 d		* Possible decrease of the activity by Mg and Ca binding at > 25 °C	76, 121, 186, 202, 216
Amyloid A (SAA)	+	+								3 m at 25 °C	8 d ε	3 d ε			
Androstendione	+								1 d ↘	1 y	4 d	1 d			99
Angiotensin converting enzyme (ACE)	+		-	-						1 y	7 d	1d			
Anticonvulsive drugs see phenobarbital, valproic acid, phenytoine	+														
Antimitochondrial antibodies (AMA)	+									1 m	7 d	1d			
Antineutrophil cytoplasmic antibodies (ANCA)	+									1 m	7 d	1d			
Antinuclear antibodies (ANA)	+									1 m	7 d	1d			
Antiphospholipid antibodies	+									1 m	2 – 3 d	1 d			
Antistaphylolysine	+	+	+							6 m	2 d	2 d			
Antistreptodornase B	+									3 m	8 d				
Antistreptokinase	+														
Antistreptolysine	+	+ β, γ, δ, -γγ	+ β, γ, δ, - γγ							6 m	8 d	2 d			

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Antithrombin III - functional - immunochemical	-	-	- + δ, ε	⊕ (+) δ, ε			+*	30 h	8 h 2 d**	1 m 1 y	2 w 8 d	2 d		*Test by Pharmacia-Upjohn **After centrifugation	75, 148, 192
α_1-Antitrypsin	+	+γ	+γ, -γγ	(+) γ					11 d 7 w (2- 6 °C)	3 m	5 m	3 m		EDTA and citrate ↘	186, 187, 191, 216
APC resistance - functional screening test - genotyping factor V Leiden	-	-	-	⊕		⊕	⊕		30 min	6 m (-70 °C)	3 h	3h		Centrifuge within 30 min	
Apolipoproteins AI, B	+↗	+ γ, δ	⊕ γ, δ	(+)						3 m	8 d	1 d			29, 43
Apolipoprotein E	+		+						1 d	3 m	8 d				162
ApoE-genotyping						⊕			1 w (4 –8 °C)	3 m	1 w			Stability of $ApoE_2$ > $ApoE_4$ > $ApoE_3$	162, 170
Aspartate aminotransferase (ASAT, AST, GOT)	+↗	⊕	+, - α↘	(+)				17 h	7 d ↘	3 m	7 d	4 d			76, 106, 186, 216
Aspergillus - antigene detection - antibody	+ +														
Atrial natriuretic peptide (ANP) - prohormone (proANP)			+* +						Unstable 6 h	4 w	3 d	6 h	*Aprotinin	Centrifuge at 4 °C	134, 138, 195
Barbiturates (see also phenobarbital)	+	+						50 - 120 h	2 d	6 m	6 m	6 m			26, 45, 196
Bartonella spp. antibodies	+														
Batroxobin time	-	-	-	⊕						1 m	4 h	8 h		Avoid heparinate contamination ↗	75, 186, 192

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Benzodiazepine (see also diazepam, flunitrazepam)	+	+						25 - 50h	<1 d*		5m↘	5m↘			45, 102, 117, 196
Bicarbonate	+	+			⊕			min	Unstable ↘ (30 min – 2 h at +4°C)	2 w	7 d	1 d *	Keep tube closed	*1 h after opening the tube, see also blood gases	22, 106, 216
Bilirubin - conjugated - total (also in newborns)	 + +	 + +	 + +	 (+) (+)				 h 17 d	Unstable ↘	 6 m 6 m	 7 m 7 d	 2 d 1 d		Darkness required, when stored > 8 h	76, 202, 216
Blood cell surface markers (immunocytometry)					+	+			CD4 1d in heparinized blood					Special stabiliser recommended (Cyfix II) (157)	157
Blood gases (CO_2, O_2, pH)					⊕			min	< 15 min ↘ pO_2 < 30 min pH, pCO_2 < 60 min on ice		2 h *		*In heparinized blood and closed tubes	Use closed gas tight tubes or capillaries	15, 22
Bordetella pertussis antibodies	+														
Borrelia burgdorferi antibodies (Lyme disease)	+		(+)											ELISA, Western blot	
Brain natriuretic peptide (BNP) - pro BNP	+	+	⊕ ⊕						4 – 5 h 2 d	5 d	5 d	5 d	EDTA		44
Brucella antibodies (Brucellose)	+														
C_1-esterase inhibitor - functional assay - immunochemical	 + +		+	(+) ε + ε						 1 m 1 y	 2 d 8 d	 6 h		Stabilise plasma by freezing	186
CA 125	+	+ α, γ, μ	+ α, γ, μ	(+) γ				5 – 10 d	2 d ↘	3 m	5 d	3 d			17, 163

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
CA 15-3	+	+ α, γ, - μ	+ α, β, γ, - μ	(+) γ				5 - 7 d		3 m	7 d				163, 175
CA 19-9	+	+ γ, μ	+ γ, μ	(+) γ				4 - 8 d	7 d ↘	3 m	30 d	7 d			163
CA 72-4	+	+ γ	+ γ	(+) γ				3 - 7 d	3 d ↘	3 m	30 d	7 d			163
Cadmium	-		⊕	-				10 - 35 y	1 d in trace element tube				Special tube	Released from red stopper	164, 186, 216
Calcitonin	+	+	+					min	1h stabilized*				*Aprotinin 400 KIU/mL		186
Calcium - total - ionised (free)	+ -	+ (+)	-↘ -↘	-↘ -↘	+ ⊕*			h min	2 d↘ 15 min↗ 1 d*	8 m	3 w 2 h	7 d 3 d**	*Use calcium-titrated heparin (9)	pH-dependent **Stable in gel tubes for 25 h & 72 h after centrifugation in closed tube (^91)	78, 202, 216 19, 22, 91
Campylobacter jejuni/fetus antibodies	+														
Candida albicans - antibodies - antigen detection	+ +														
Carbamazepine	+	+ α↗, β, γ, δ	+ β,γ	(+)α ↗, β, γ				10 - 25 h	2 d	1 m	7 d	5 d		10 % higher results in plasma (α)	26, 45
Carbohydrate deficient transferrin (CDT)	+	-						14 - 18 d	3 d	y	7 d	7 d		Method-dependent	167
Carcino-embryonic antigen (CEA)	+	+ α, β, γ, μ	+ α↘, β, γ, μ	+ γ				3 - 11 d	7 d	6 m	7 d	1 d		EDTA reduces by 13 % ↘ α	63, 133, 163, 175, 200, 216
Cardiolipin antibody	+									1 m	2-3 d	1d			

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Catecholamines (epinephrine, norepinephrine)	-	⊕	(+)	-				3 - 5 min	1 h if not stabilized	1 m 6 m stabilised	2 d	1 d	Glutathione 1.2 g/L +EGTA (34)	EGTA plasma to be separated within 15 min and frozen at -20°C	
Chinidin	+	+β, γγ	+ β	(+) β				6 – 9 h		1 – 2 w	1 d				45, 205
Chlamydia antibodies (C. trachomatis, C. pneumoniae)	+		(+)											After thawing leave for 3 – 4 d at room temperature before sampling DNA	129
Chloramphenicol	+	+β	+	(+)				2 – 5 h							205
Chloride	+	+	-	-	+			1 h	1 d ↘	y	7 d	7 d			22, 76
Cholesterol	+	+, - α, γγ, δ	+, - α, γγ, δ	(+)					7 d ↗	3 m	7 d	7 d			10, 29, 43, 76
Cholesterol, HDL	+	+	+ δ, - α	-					2 d ↗	3 m	7 d	2 d			10, 29, 43
Cholesterol, LDL	+	-, + γ	+, - γ	-					1 d ↘	3 m	7 d	1 d			10, 29, 43
Cholinesterase, including dibucain number	+	+	+, - γ					10 d	7 d ↘	1 y	1 y	1 y			63, 76, 84
Circulating immuno-complexes (CIC)	+								4 h	1 y	8 h	4 h			
Clostridium tetani toxine antibodies	+														
Coagulation factors															75, 189
Factor II	-	-	-	⊕				41 - 72 h		1 m		6 h			189
Factor V	-	-	-	⊕				12 - 15 h		1 m	2 d	6 h		Centrifuge at 4°C	75, 136, 189
Factor VII	-	-	-	⊕				2 - 5 h			Unstable	6 h			189
Factor VIII	-	-	-	⊕				8 - 12 h		2 w	4 h	3 h			75, 136, 189
Factor VIII R: Ag	-	-	-	⊕				6 - 12 h		6 m	7 d*	7 d*	* Sodium azide	Five freezing-thawing cycles are possible	193

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Factor VIII R: Co				⊕				6 h		6 m	2 w*	2 d	* Sodium acide		193
Factor IX	-	-	-	⊕				18 - 30 h		1 m		6 h			193
Factor IX: Ag	-	-	-	⊕											
Factor X	-	-	-	⊕				20 - 42 h		1 m		6 h			189
Factor XI	-	-	-	⊕				3 – 4 d			Unstable	6 h			189
Factor XII	-	-	-	⊕				50 – 70 h			Unstable	6 h			189
Factor XIII	-	-	-	⊕				4 – 5 h		1 m		4 h			189
Cocaine Benzoylecgonin Ecgoninmethylester	+	+	-						< 10 min 5 d 10 d	4 d	30 d 5 d 10 d	<30 min 5 d 10 d	Fluoride, pH 5	Cocaine is converted in vitro into its metabolites.	79, 117, 172
Coeruloplasmin	+	+	+, -γγ					4 d		1 y	2 w	8 d			187, 191, 202
Cold agglutinins														Keep whole blood at 37°C (water bath)	
Complement C3	+	+, -γγ	+ γ, -γγ	(+)				min	1 d 2 d (C3c) (2 – 6°C)	8 d	8 d	4 d		Dependent on antibody, during storage C3c ↗ C3 ↘	191, 202, 216
Complement C4	+	+	+	(+)				12 h – 1 d	1 d 2 d (2 – 6 °C)	3m	8 d	2 d		During storage C4↘,C4c↗	202, 216
Copper	+	+	-	-					7 d	y	2 w	2 w		Special tube to avoid contamination	206, 216
Corticotropin (ACTH)		+	⊕					min	Unstable ↘	6 w	3 h	1 h	Aprotinin 400-2000 KIU/mL Mercaptoethanol 2µL/mL	Prevent binding to glass tubes by using plastic for storage	44, 132, 186
Corticotropin releasing hormone	+↘	+	⊕								1 d	11 – 18 h			44
Cortisol	+	+ α, µ	+ α, γ, µ					1 h	7 d	3 m	7 d	7 d		11 % less in EDTA (α)	34, 93, 216

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Corynebacterium diphtheriae toxine antibodies	+														
Coxiella burnetii-antibodies (Q-Fieber)	+														
Coxsackie virus antibodies	+														
C peptide	+	+	⊕					min	6 h	2 m	5 d	5 h	EDTA		44, 54, 132
C-reactive protein (CRP)	+	(+)** + α, γ, δ, ε	(+)* + α, γ, δ, ε	(+), + γ				2 - 4 h	3 w (2 - 6 °C)	3 y	2 m	11 d		*Method-dependent **Patient-dependent lower results	191, 216
Creatinine	+	+	+	(+)				min	2 - 3 d↗	3 m	7 d	7 d			76, 202, 216
Creatine kinase (CK)	+	+ α, β, γ, δ	+ β, γ, δ	(+)				18 h	7 d↘	1 m	1 m	4 h	Darkness	CK-BB not stable	76, 186, 202, 216
Creatine kinase MB															124
- enzyme activity	+	+, -α	+ γ, δ	(+) δ				12 h	7 d↘	1 y	7 d	2 d	SH reagent		
- molecular mass	+	+ β,γ, δ, - μ	+β,γ,δ , - μ	(+) γ				12 h	7 d↘	4 w	7 d	2d			
C-terminal telopeptide of type I collagen (ß-CrossLaps™)	+	+	+						8 h	3 m	7 d	1 h	pH 8.0	Stability pH-dependent	139
Cyclosporin A + G	-	-	-	-		⊕		10 - 27 h	13 d	3 m	13 d	21 d	EDTA	Store haemolysate	6, 46, 88, 205
CYFRA 21-1	+	+ γ	+ γ	(+) γ				min	7 d	6 m	1 m	7 d			163
Cystatin C	+	+	+					min	7 d	6 m	1 m	7 d		More stable in EDTA	47, 130
Cytokines			⊕						2 h (heparinized blood)		2 d				12, 32
- IFN-α, IFN-γ, -1α		+↗													
- IL-6	-↘	+							1 h (EDTA)						
- IL-1β, sIL-2R , sIL, 6R, TNFα	-↘										12 h ↘				

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Cytomegalovirus - antigen detection (pp65) - DNA amplification - (CMV) antibodies	+ +	+β	+β	(+)β		⊕ ⊕									
D-Dimer	(+)	+	-	⊕				6 – 8 h	8 - 24 h	6 m	4 d	8 h			16, 23, 189
Dehydroepiandosterone-sulfate (DHEA-S)	+								2 d ↘	y	2 w	1 d			34, 99
Dengue virus antibodies	+														
Diazepam	+	+	+					25 – 50 h			5 m	5 m			45, 117, 196
Differential leucocyte count - Band neutrophiles - Segmented neutrophiles - Eosinophiles - Basophiles - Monocytes - Lymphocytes	-	-	-	-		⊕	+	2 h-3 y 6 – 7 h 1.5 – 3 y	2 h-7 d* 2 – 12 h 3 – 12 h 12 h – 6 d 2 h – 2 d 2 – 12 h 3 h – 7 d				Dry blood smear stable	K_3-or K_2-EDTA: Stability temperature- and instrument-dependent *Prepare blood smear within 3 h after sampling. Do not store EDTA blood in refrigerator	73, 77, 159, 180
Digitoxin	+	+α,β, γ, μ	+γ, μ					6 – 8 d		6 m	3 m	2 w			45, 216
Digoxin	+	+α, β, γ, δ, μ	+ β, γ, δ, μ	(+)β				1 – 2 d		6 m	3 m	2 w			45, 216
Disopyramide	+	+	+	(+)				4 – 9 h		5m	2 w				45
DNA und RNA analysis by amplification (PCR)	(+)	-*			-*	⊕	+		DNA 1 w RNA 2 h				RNA: 5 mmol/L Guanidinium-isothiocyanate	*Heparin inhibits Taq polymerase and restriction enzymes LiCl 1.8 mol/L eliminates this error.	81, 82, 90, 201

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Dopamine			+					3 - 5 min		1 m	2 d	1 d			
Echinococcus spp. antibodies	+														
ECHO virus antibodies	+														
Elastase						+									
Electrophoresis, proteins; see also lipid electrophoresis	⊕	(+)								3 w	3 – 7 d	1 d		Fibrinogen to be considered when using heparinate plasma, may be eliminated by fibrin precipitation	186, 190
Entamoeba histolytica antibodies	+														
Enterovirus antibodies	+														
Epstein Barr virus - heterophilic antibodies (Paul Bunnel test) - anti-EBNA, -VCA, -EA);	+ +		(+)											IgG, IgM, IgA; ELISA, Western Blot	
Erythrocyte count					(+)	⊕	(+)		4 d 7 d (4 – 8 °C)		7 d*	7 d*		*EDTA-blood	62, 77
Erythrocyte sedimentation rate (ESR)							⊕		2 h	-	-	-		1 part citrate, 4 parts blood	186
Erythropoietin	+	+	+					4 - 11 h	6 - 24 h	5 m		2 w		Shipped frozen	96, 186
Estradiol (E_2)	+	(+) γ, μ, +α	(+) γ, μ, + α	(+)γ					1 d	1 y	3 d	1 d			34, 99, 216
Estriol (E_3)	(+)	+								1 y	2 d	1 d			63
Ethanol	+	⊕ α, β, γ, δ	+β, γ, δ	(+)β, δ		+*		2 – 6 h	2 w ↗ ↘**	6 m	6 m	2 w	EDTA/ Heparin	*10 g/L NaF recommended to stabilise **Evaporation, use closed tubes	57, 117, 128

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Ethosuximid	+	+	+					30 - 60 h		5 m	4 w				45
Fatty acids	+	(+)↗*	(+)↘					2 min	30 min↗*	2 d	12 h	30 min		*Activation of lipase by heparin. Freeze serum/ plasma immediately	202, 216
Ferritin	+	+ α, β, γ, δ, μ	(+)* γ, - γγ	(+) γ, γγ						1 y	7 d	7 d		*Method-dependent	186, 216
α_1-Fetoprotein (AFP)	+	+α, β, γ, μ	+ α,β,γ , μ	(+)β, γ				4 d	7 d	3 m	7 d	3 d			17, 95, 216
Fibrin(ogen) degradation products (FDP)	(+)*	-	-	(+)**					unstable↗↗	1 m	1 d	3 h	10 U thrombin and 150 KU kallikrein/mL blood	*Special tube **Aprotinin or soybean trypsin inhibitor	132, 187, 189
Fibrin monomers	-	-	-	⊕				<1h	1 d	3 m	1 d	2 h			150, 189
Fibrinogen - Clauss - immunochemical	 - -	 - -	 - -	 ⊕ ⊕				 4 -5 d 4 -5 d	8 h	 1 m 1 m	 1-7 d 7 d	 1-7 d 7 d		Stability method-dependent	2, 75, 189, 192
Fibrinopeptide A	-	-	-	⊕				3 min			2 h				189
Flunitrazepam	+								< 1 d*					*Store protected from light	102
Folate - in erythrocytes	+	+α, δ, μ	+β, - μ	(+)β	+ + μ	+β, δ +		min	30 min ↘, 5 d (2 – 8 °C)	8 w	1 d	30 min	Ascorbate 2g/L	Haemolysate, prepared by 0.5 mL blood +4.5 mL ascorbic acid (2 g/L). Na-heparin interferes with Axsym-Test (β).	63, 108, 186, 216
Follitropin (FSH)	+	+α, β, γ, μ	+α, β, γ, μ	(+) γ				min	7 d↘	1 y	2 w	2 w			94, 216
Francisella tularensis-antibodies (tularemia)	+														

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Fructosamine	+	+	+					12 d	12 h↗	2 m	2 w	3 d			183, 186
Galactose 1-p-uridyl-transferase (Beutler test)						+								Erythrocytes	
Gastrin	+	⊕*	+	(+)					2 h		1 w*	1 w*	*With aprotinin 2000 KIU/mL	Freeze serum as soon as possible	45, 186, 218
Gentamicin	+	+β, γ, δ	+β,γ, δ	(+)β				0.5 - 3 h (< 30 y of age) 1.5 – 15 h (> 30 y of age)	4 h	4 w	4 w	4 h			45
Glucagon	+	+	⊕						Unstable		1.5 d	30 h	Aprotinin 500-2000 KIU/mL	Stabilise	132
Glucose - capillary - venous	- -↘	- - ↘	- - ↘	- - ↘	(+)	⊕		min min	10 min↘ 10 min↘	1 d* 1 d*	7 d* 7 d*	2 d* 2 d*	Fluoride, mono-iodoacetate, mannose	*Stabilised haemolysate and plasma	39, 56, 63, 186, 202, 216
Glutamate dehydrogenase	+	+	+					18 h		4 w	7 d	7 d			186, 216
Glutamate oxaloacetic transaminase (GOT) see aspartate aminotransferase															
Glutamate pyruvate transaminase (GPT) see alanine aminotransferase															
γ-Glutamyl transferase (γ-GT)	+	+	(+)↘ , + α	(+)↘ , -γγ				3 - 4 d	1 d ↘	y	7 d	7 d			76, 106, 186, 216
Glycated albumin see fructosamine															183
Gold	+														
Haematocrit					+	⊕			1 d 4 d (4 – 8 °C)		4 d*		*EDTA-blood,	K_2-superior to K_3-EDTA	77
Haemoglobin A_{1c}						⊕		2 m	3 d (EDTA blood)	6 m*	7 d*	3 d*		*Haemolysate	63, 183

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Haemoglobin F (HbF)						+									
Haemoglobin (whole blood)						⊕		2 m	4 d		7 d*	4 d*		*EDTA blood	62, 77
Haemoglobin (plasma)	(+) ↗	⊕	(+) ↗	+										Haemolysis during clotting (49dt)	13, 69, 110
Hanta virus - antibodies - RNA amplification	+ 				 -	 ⊕	 -								
Haptoglobin	+	+	+, - γγ	(+) γ				3.5 - 4 d	8 d	3 m	8 m	3 m			187, 191, 202
HBeAg	+		+ β	(+) β											
HBsAg	+	+ α, δ	+ α, δ	(+)α, δ											
Helicobacter pylori antibodies	+														
Heparin (anti Xa)				⊕								4 h			
Heparin associated thrombopenia; HIPA test	+						+	1 d		4 w					
Hepatitis antibodies - anti-HAV - anti-HAV IgM	 + +	 + β, δ + α	 + β, δ + α	 (+) β, δ + α								 4 w			
- anti-HBsAg	+	+ α, β	+ β	+ α, β								4 w			
- anti-HBc	+	+ α, β, δ	+ α, δ	(+)α, β, δ								4 w			
- anti-HBe	+	+ β	+ β	(+) β								4 w			
- anti-HCV	+	+ α, β, δ	+ α, β, δ	+ α,- β, δ								4 w			
- anti-Hepatitis D	+	+β	+ β	(+)β											
- anti-Hepatitis E	+														

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Hepatitis B virus DNA	+		+												
Hepatitis C virus - RNA amplification	+		+												81
Hepatitis D virus - RNA amplification	+		+												
Hepatitis E - RNA amplification	+		+												
Herpes simplex 1 or 2 virus antibodies	+														
HHV 6 antibodies (human herpes virus 6)	+														
HHV 6-, 7-, 8-DNA amplification						⊕									
HI virus 1 - (provirus)DNA amplification - RNA amplification			⊕			⊕		5 – 14 d	7 d↘		5 d γ	7 d 1 – 2 d		Several freezing/thawing cycles possible	81, 83, 118
HI virus 1 and 2 antibodies	+	+ α, β	+β, δ	(+) α β, δ											
HIV, viral load					+	+	+	5 – 14 d	7 d						197
HLA-ABC typing					⊕									Ammonium heparinized blood	
HLA- B27						⊕						1 d	Citrate-phosphate-dextrose (CPD)	Ammonium heparinized blood	
HLA DR typing						⊕									
Homocysteine	+ ↗	+	+	(+)		⊕λ			1 h↗ 6 h (2 – 6 °C)	4 y	4 w	4 d	Sodium fluoride 4 g /L blood	Sample with EDTA/acidic citrate (0,5 mol/L). Store blood at 0 – 4 °C (207). haemolysed EDTA sample in detergent stable for 2 d (146). Serum>plasma	5, 144, 146, 149, 207, 214

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
HTLV I - antibodies (T-cell leukemia) - (provirus) DNA amplification - RNA amplification	+ 		 +			⊕									81
Human chorion gonadotropin (βhCG) - free - total	 + +	 + α, β, γ	 + β, γ	 (+)α ↗, γ				 12 - 36 h	 24 h (2 – 8 °C)	 4 w 1 y	 2 d 7 d	 1 d			94
3-Hydroxybutyrate					⊕									De-proteinisation of whole blood	
IgA	+	+ γ, δ	+ γ, δ					6 d	8 d 1 m (2 – 6 °C)	8 m	8 m	8 m		EDTA and citrate↘	191, 202, 216
IgD	⊕		- ↘					5 d		6 m	7 d	7 d			
IgE antigenspecific IgE	⊕ +	+ γ, δ, ε, μ	-↘, + γ, δ, ε, μ	(+) γ				2.5 d		6 m	7 d	7 d			
IgG IgG subclasses	+ +	+ γ, δ	↘, + γ	-				3 w	11 d 1 m (2 – 6 °C)	8 m	8 m	4 m			191, 202, 216
IgM	+	+ γ, δ	+ γ, δ, - ↘γγ					5 d	17 d 1 m (2 – 6 °C)	6 m	4 m	2 m			191, 202, 216
Immunoglobulin light chains (κ, λ)	+	+γ	+γ							6 m	1 m	7 d			
Influenza virus ABC antibodies	+														
Insulin	(+) ↘	+	+					min	15 min	6 m	6 d	1 d			44, 54, 186, 216

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Iron (Fe)	+	+	-↘	-↘				3 h	2 h↗	y	3 w	7 d			63, 202, 206, 216
JC polyoma virus - antibodies (progressive multifocal leukoence-phalopathy, PML) - DNA-amplification (PML)	+					⊕									
Lactate	-↗	-↗	-↗	-	(+)			min	<5 min, unstable↗↗	1 m* 2 w*	3d	8 h 6 d*	Mannose/ fluoride, monoiodo-acetate, deproteinisation	Use glycolysis inhibitor tube, if not immediately deproteinised *Deproteinised in whole blood	9, 63, 186, 202, 216
Lactate dehydrogenase (LDH)	(+)↗	⊕	+	(+)				10 - 54 h LDH 5 < LDH 1,2	1 h↗	6 w	4 d	7 d		LDH platelet-dependent (42, 82, 137)	76, 126, 202, 216
Lead (Pb)	-	-	+	-	(+)							7 d		Special tube	164
Legionella antibodies	+														
Leishmania spp. antibodies (visceral leishmaniosis)	+														
Leptin	+	+	+							2 y	2 m	3 – 6 d		Five freeze/thaw cycles possible	44, 203
Leptospira spp. antibodies (Leptospirosis)	+														
Leucocyte count					+	⊕	+	6 - 7 h	7 d		7 d			See also differential count	41, 62, 77, 143
Lidocaine	+	+β, γγ	+β					1 – 3 h			6 h			Separator gel	100
Lipase	+	+↘α	-↘	-				7-14 h		1 y	3 w	7 d		EDTA binds calcium (activator), 15 % less activated in heparin (α)	186, 187, 202

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Lipoprotein(a)	+	+ γ, ε	+γ	- γ						3 m	2 w	2 d			119, 142, 169, 216
Lipoprotein electrophoresis	⊕	-	-	-							2-5d			Store at –20 ° C with 15 % sucrose	
Listeria monocytogenes – antibodies - DNA amplification	+ 					⊕									
Lithium	+	+*, α	-, + α	-				8 – 24 h	1 h ↘	6 m	7 d	1 d		*Do not use Li-heparin	205
Lupus anticoagulant	-	-	-	⊕						6 m		4 h		Centrifuge platelet free	
Lutropin (LH)	+	+ α, β, - μ	+ α, β, μ						7 d	1 y	5 d	3 d			34, 44, 94, 216
Lymphocytic chorio-meningitis virus (LCM) - antibodies - RNA amplification	 +					⊕									
Lymphocyte subtypes						(+)								Special stabiliser recommended (Cyfix II) (157)	157
Magnesium (Mg)	+↗	+	-	- ↘	⊕				1 d↗*	1 y	7 d	7 d		*Separate blood cells before analysis (95)	39, 76, 166, 206, 216
Malaria -plasmodium antibodies - plasmodium spp. - trypanosoma gambiense	 +					 ⊕ (+)								 Microscopic examination of whole blood Blood film of capillary blood	
Measles virus - antibodies - RNA amplification	 +					 ⊕									
Mercury (Hg)					+									Special tube	

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Methadone	+	+													
Methotrexate	+							2 – 4 h		6 m	3 d			Light ↘	45, 187
Microfilarias					+	+								Concentrated sample	
β_2-Microglobulin	+	+γ	+γ	(+)					1 d	6 m	3 d	3d			187
Morbilli virus - antibodies - DNA amplification	+	+				⊕									
Morphine, total*	+	+							21 d 6 m (4 °C)	6 m	6 m	3 m		Light ↘ *After hydrolysis	173
Mumps virus antibodies	+														
Mycobacterium spp. DNA amplification						⊕									
Mycoplasma pneumoniae antibodies	+														
Myoglobin	+	+ γ, δ, ε, μ	+ γ, δ, ε, μ	(+) γ				15 min	1 h ↘	3 m	1 w	2 d			14, 33, 124, 186, 213
Neisseria gonorrhoeae antibodies	+														
Netilmycin	+							2 – 3 h							
Neuron specific enolase (NSE)	+ ↗	⊕						<24 h	2 h ↗	3 m	3 d	2 d	Heparin	Increased in thrombocytosis Serum>plasma	64, 186
Nitrazepam	+	+ β	+ β	(+) β					1 w	1 w	1 w			Light ↘	117, 196
Opiates (see also morphine)	+	+													
Osmolality	+	+								3 m	1 d	3 h			186, 216
Osteocalcin	+*	+*	⊕*					min	15 min	8 w (-30 °C)	2 d*	8 h	*Aprotinin 2500 KIU/mL + EDTA (5mmol/L)	Three freezing/thawing cycles are possible.	38, 111, 209

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Pancreatic elastase	+		+	+						6 m	2 w				
Pancreatic polypeptide	+	+	+								6 d	2 d			44
Paracetamol	+	+ α, β	+ α, β	(+) β				1 – 4 h		45 d	2 w				45, 205
Parathyrin (PTH)	+ κ↘	+ γ, κ	⊕	(+) γ				min	6 h (2 – 3 d in EDTA blood)	4 m	1 d	6 h	EDTA	15 % lower concentrations in serum compared to EDTA plasma	158
Partial thromboplastin time (aPTT)	-	-	-	⊕					8 – 12 h	1 m	2-8 h	2-8 h		Stability reduced in plasma of patients heparinized	75, 101, 136, 189
Parvovirus B 19 - antibodies (erythema infectiosum) - DNA amplification	+					⊕									
Phencyclidine	+														
Phenobarbital	+	+ β, γ, γγ, δ	+β, γ, δ	(+)β, γ, δ				2 – 6 d	2 d	6 m	6 m	6 m			26, 45
Phenytoin	+	+α,β,γ, δ	+β,γ, δ, -α	(+) β,γ, +α				1 – 8 d	2 d	5 m	1 m	2 d		Unstable in SST tubes (10) Biological half-life shorter in children	26, 45
Phosphate, inorganic	(+) ↗	⊕	-α, γγ, + μ	(+)μ, -α				min	1 h↗↗	1 y	4 d	1 d		Platelet-dependent in serum (123)	76, 202, 216
Polio virus 1, 2 , 3 antibodies	+													Neutralisation test	
Potassium (K)	(+) ↗	⊕	-	-	+			min	1 h↗↗	1 y	6 w	6 w		Platelet-dependent in serum > plasma (123, 202), haemolysis ↗	39, 70, 76, 202, 216
Pre-albumin	+	+ γ	+ γ							1 y	6 m	3 d			

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Primidone	+	+	+	(+)				6 - 8 h		5 m	4 w				45
Procainamide and N-acetyl-procainamide	+	+β, γ	+β, γ	(+)β				3 - 5 h 6 – 10 h		6 m	2 w				45, 187
Pro-calcitonin	+	+δ	+	(+)					1 - 2 d		1 d	4 h			127
Progesterone	+	+ β, - α, μ	+ β, μ, - α						7 d	1 y	7 d	1 d			34, 63, 216
Prolactin	+	+ β, δ, μ	+ β, μ	-					2 d	1 y	6 d	5 d			34, 44, 216
Propaphenone	+	+													
Propoxyphene	+	+													
Prostata specific antigen (PSA) - free - total	 + +	 + γ + γ, μ, - α	 + γ + γ, μ, -κ	 (+)γ				 2 h – 7 d 4 - 7 d	 2 h 1 d	 1 m↗ 3 m↘ - 2 y	 1 d 30 d	 7 d		Three freezing thawing cycles possible	25, 89, 114, 140, 141, 151, 163, 168, 212
Protein, total	+ ↘	⊕	+ γ, γγ, δ	(+)				Complex	1 d	1 y	4 w	6 d		Plasma results higher due to fibrinogen (Biuret method)	186, 216
Protein C	-	-	-	⊕				6 - 8 h	1 d	3 m	7 d	7 d		Avoid freezing/thawing cycles	75, 122
Protein S	-	-	-	⊕				24 - 58 h		4 h	4 h	4 h		Separate cell-free plasma directly after centrifugation	16, 75, 189
Protein S100	+														
Prothrombin time (thromboplastin time, Quick)	-	-	-	⊕					4 h – 1 d*	1 m	8 h - 1 d*	4 h – 1 d*		Reagent-dependent	2, 75, 147, 189, 192
Pyruvate	- ↘	- ↘	-	-	+*				< 1 min					*Only stable in deproteinised blood	

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Renin	-	-	+	-											
Reovirus antibodies	+														
Respiratory syncytial virus (RSV) antibodies	+														
Reticulocyte count					(+)	⊕		12 h	1 d		1 d*			*EDTA-blood	63
Rheumatoid factors subfractions IgA, IgG	+ +	(+) γ	(+) γ	(+)γ						3 m	8 d	1 d			216
Rickettsia antibodies	+														
Rotavirus antibodies	+														
Rubella virus - antibodies - RNA amplification	+	+ β	+ β	(+) β		⊕									
Salicylate	+	+	+	(+)				15 – 30 min		6 m	2 q	7 d			45, 205
Sandfly (pappataci-) fever antibodies	+														
Selenium (Se)	-	-	-	-		+*			2 d	1 y	2 w	1 w		*Special tubes, contamination	164
Sodium (Na)	+	+	-	-	+*			min	4 d↘	1 y	2 w	2 w		* Use 140mM Na-stabilized heparin 8-12 IU/mL blood (9)	39, 76, 216
Soluble transferrin receptor (sTfR)	+	+ε	-ε						2 h	2 w	7 d	3 d		Freeze only once	32, 186
Somatotropin (STH) (growth hormone)	+	-	+					min	1 d	3 m	8 d	3 d	EDTA		34, 44, 216
Squamous cell carcinoma antigen (SCC)	+								7 d	1 m	1 m	7 d	Closed tubes	Increase by contamination (skin)	133, 163
Staphylococcal antibodies - antistaphylolysin O	+	+ γ	+ γ												

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Streptoccoccal antibodies - anti-DNAse B - antihyaluronidase - antistreptokinase - antistreptolysin O	+ + + +	+, β, γ, δ + β, γ, δ	+, β, γ, δ + β, γ, δ												
Tacrolismus	-	-	-	-	-	⊕		6 – 12 h	7 d	1 y	2 w	7 d			6, 205
Testosteron	+	+ α, γ, δ, μ	+ α, γ, μ	(+) γ					7 d 1 d in women↗	1 y	3 d	1 d			34, 99, 202
Tetrahydrocannabinol carbonic acid (THC)	+	+						~45 h		6 m	6 m	2m	Na-azide	Unstable in plastic tubes	45, 117
Theophylline	+	+	+	(+)α, β				3 - 12 h		3 m	3 m	3 m			45, 205
Thrombin time	-	-	-	⊕					1 - 4 h↗ 1 h – 2 d (2 – 6 °C)	1 m	1 h – 2 d*	1 - 4 h		*Stability reagent- and heparin-dependent	75, 136, 189, 192
Thrombocyte antibodies			+	+											
Thrombocyte count					(+)↘	⊕	(+)	9 - 10 d	4 d		7 d*	4 d*	* in EDTA-blood	Aminoglycosides, avoid Pseudothrombocyto-penia in EDTA (160)	75, 77, 120, 160
Thrombocyte function using platelet function analyzer (PFA) (ε)	-	-	-	-			⊕	9 - 10 d	4 d			1 h		Special stabiliser (157)	157
Thyreoglobulin	+							3 w	2 d	1 m	3 d	1 d			63, 186, 216
Thyreotropine (TSH)	+	+ β, γ, μ, - α	+ α, β, γ, - μ	(+)γ				min	7 d	3 m	3 d	1 d		Spot blood in newborns	34, 202, 216
Thyreotropine receptor antibodies (TRAb)	+														

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Thyroid antibodies Thyreoidea peroxidase antibodies (anti-TPO) Thyreoglobulin antibodies (anti-TG)	+	+									2 d				
Thyroxine (T_4)	⊕	+ β, γ, γγ, - α, μ	+ α, β, γ, γγ, - α, μ	(+) γ				6 m	7 d	1 m	7 d	5 d			34, 202, 216
Thyroxine, free (fT_4)	+	+ β, γ, μ	+ γ, μ	(+) γ						3 m	8 d	2 d			216
Thyroxine binding globulin (TBG)	+	+							7 d	1 m	5 d	5 d			39, 187, 216
Tick borne encephalitis virus antibodies	+		(+)												
Tobramycin	+	+β, γ, δ	+ δ	(+)β				0.5 - 3 h		1 m	3 d	< 2 h		Lower results obtained in heparinized plasma	45, 154, 205
Toxoplasma gondii anti-bodies (IgA, IgG, IgM)	+	+ β	+ β	+β							8 d	8 d			
Transferrin	+	+ γ, γγ	+					8.5 d	11 d 3 w (2 – 6 °C)	6 m	8 m	4 m			191, 202, 216
Treponema pallidum - antibodies - DNA amplification	+					⊕								TPHA, IFT, FTA abs., VDRL, immunoblot	
Tricyclic antidepressants	+	+β	+β	(+)β											31
Triglycerides	+	+	+, -α	(+)				3 h - 3 d	7 d↗*	y	7 d	2 d		*Decrease of triglycerides, increase of free glycerol, but only minor increase of total glycerol	29, 76, 202, 216

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Triiodothyronine (T_3)	⊕	(+) ↗ β, γ, δ, μ	+ μ					19 h		3 m	8 d	2 d		Serum-plasma difference method-dependent	208, 216
- free (fT_3)	+	+ β, γ, μ	+ β, γ, μ	(+)γ						3 m	2 w	1 d			
Troponin I	+	+* δ, - α, μ↘	+ δ, - α, μ ↘			+		2 d		4 w	3 d	3 h		*Reduced concentration described in some patients (55, 181)	74, 124
Troponin T	+	+γ*	(+)γ						8 h	3 m	7 d	1 d		*Reduced concentration described in some patients (55, 181)	124, 186
Urea	+	+	+					min	1 d↗	1 y	7 d	7 d		Do not use NH_4-heparin	76, 216, 217
Uric acid	+	+	+ ↘	(+)				min	7d↗	6 m	7 d	3 d			202, 216
Valproate	+	+ β, γ, δ	+β,γ, δ	(+) β				8 - 15 h	2 d	3 m	7 d	2d			26, 45
Vancomycin	+	+ β	+	(+)β				4 - 10 h							45, 205
Varicella Zoster virus - antibodies - DNA amplification	+					⊕									
Vasoactive intestinale polypeptide (VIP)	↘	↘	⊕							> 6 d	6 d	1 d	EDTA + aprotinin		44, 132
Vasopressin (ADH)	↘	+	+								6 d	1 d	EDTA	Freeze plasma	44
Vitamin A (retinol)	+							11 h		2 y	1 m				63, 186
Vitamin B_1 (thiamine)		+	+							1 y					63, 85
Vitamin B_2 (riboflavin)		+	+							1 m					63
Vitamin B_6 (pyridoxal phosphate)			⊕							d	h	30min	EDTA, darkness		63, 85
Vitamin B_{12} (cobalamin)	+	+	⊕							8 w	1 d	15min	EDTA, darkness		63, 108

Samples									Stability						
Analytes	Serum	Heparinate Plasma	EDTA Plasma	Citrated Plasma	Whole blood Hep	Whole blood EDTA	Whole blood Citrate	Biological half-life	Stability in blood at room temperature	Stability in serum/plasma -20°C	Stability in serum/plasma 4-8°C	Stability in serum/plasma 20-25°C	Stabiliser	Remarks / Comments	Reference
Vitamin C (ascorbic acid)		+							3 h (4 °C)	3 w*	3 h		60g/L metaphosphate, deproteinised	*Only with stabiliser	63
Vitamin D - 1.25-dihydroxy-cholecalciferol - 25-hydroxy-cholecalciferol	 + +								 3 d 3 d			 3 d 3 d			63, 186, 216
Vitamin E (tocopherol)	+		⊕						8 h↘	1 y	1 m		EDTA		63, 186
Vitamin K (transphyllochinone)			+						unstable	3 m	unstable			UV light↘	63, 186
Yersinia enterocolitica antibodies	+														
Zinc (Zn)	-	+	-	-					30 min↗	1 y	2 w	1 w		Special tube, avoid contamination by stopper	164, 202, 216

5.2 Urine

Analyte	Stability in urine at			Stabilizer	Comments	Reference
	- 20 °C	4 – 8 °C	20 – 25 °C			
Albumin	6 m	1 m	7 d			80, 113, 184
Aluminium	1 y	7 d	3 d			63, 164
δ-Aminolevulinic acid	1 m	4 d	1 d	pH 6 - 7, stabilized with 0.3 % $NaHCO_3$	Drugs ↗ Light ↘	184, 216
Amphetamine	1 y					36
α-Amylase	> 3 w	> 10 d	2 d		Saliva contaminates ↗↗	121
Bence Jones protein (light chains κ, λ)	6 m	1 m	7 d			184
Calcium	> 3 w	4 d	2 d	Acidify, pH < 2	Crystallisation at cool temperature	28
Catecholamines Norepinephrine Epinephrine Dopamine	Unstabilised 20 d Unstabilised 1 y	4 d 1 y	4 d 3 w	Acidify, pH < 2 or EDTA (250 mg/L) and sodium metabisulfite (250 mg/L)		20
Citrate	4 w*		1 d*	*pH <1,7	Unstable in native urine	78
Cocaine metabolite Benzoylecgonine	4 m	3 w		pH 5, ascorbic acid		36, 79, 117
Codeine	1 y					36
Copper	1 y	7 d	3 d			164
Cortisol, free	1 w	1 w	2 d	10 g/L boric acid		28, 93, 206
C-peptide		6 d	19 h			44
Creatinine	6 m	6 d	2 d			28, 186

Analyte	Stability in urine at			Stabilizer	Comments	Reference
	- 20 °C	4 – 8 °C	20 – 25 °C			
Cystine	> 1 y*	3 m*	7 d*	*Stabilised in HCl		78
Ethanol		30d				57, 117
Glucose	2 d	2 h↘	2 h ↘	10 mmol/L azide	Bacteria decrease stability.	28, 186, 187
5-Hydroxyindole acetic acid	2 d	2 d	2 h	Acidify		186, 216
Hydroxyproline	5 d	5 d	5 d			186
Immunoglobulin G (IgG)	Unstable	1 m	7 d			80, 113, 184
Iron	>1 y	7 d	3 d			28
Lysergic acid diethylamide (LSD)	2 m	1 m	1 m			36, 117
α_2-Macroglobulin		7 d	7 d			
Magnesium	1 y	3 d	3 d	Acidify, pH < 2		28, 78
α_1-Microglobulin	6 m	1 m	7 d			80, 113, 184
Morphine	1 y					36, 45, 119
Myoglobin	>12d*	12d*	12d*	*pH >8.0	Unstable at acid pH	213
N-Acetyl-β,D-glucosaminidase (β-NAG)	1 m	7 d	1 d			125
N-telopeptides (NT_x)	4 w	5 d				
Osmolality	> 3 m	7 d	3 h			28
Oxalate	> 4 m (at pH 1.5)	unstable↘	< 1 h	pH <2, HCl 1 vol %, thymol 5 mL/L	Vitamin C ↗	78
pH	unstable↗				Increase by NH_4 formation	28
Phosphate, inorganic			2 d at pH <5.0	1 vol % thymol, 5 mL/L	precipitates at alkaline pH	28, 78

Analyte	Stability in urine at - 20 °C	4 – 8 °C	20 – 25 °C	Stabilizer	Comments	Reference
Porphobilinogen	1 m*	7 d*	4 d*	*pH 6 – 7 by $NaHCO_3$	Acid pH↘ Light↘	186, 216
Porphyrines Total porphyrine Uroporphyrine Heptacarboxyporphyrine Hexacarboxyporphyrine Pentacarboxyporphyrine Coproporphyrine Tricarboxyporphyrine Dicarboxyporphyrine	1 m	7 d Stabilized at pH 6 - 7	4 d	0.3 % $NaHCO_3$, pH 6-7	Light ↘	63, 186
Potassium	1 y	2 m	45 d			28
Protein	1 m	7 d	1 d			28
Pyridinium crosslinks (collagen crosslinks)	>1 y		6 w		UV light ↘↘	204, 209
Sediment		1 - 8 h	1 – 2h	Osmolality >300 mosmol/kg	*>300 mosmol./kg **pH <6,5 ***pH >7,5 Do not freeze	28, 103, 105
Acantocytes			2 d 1 d*			
Casts (hyaline and others)			2 d			
Bacteria		24 h	1 – 2 h↗***			
Epithelial cells			3 h			
Erythrocytes		1-4 h	1 h, 24 h*			
Leukocytes		1-4 h	24 h** <1 h ***			
Sodium	1 y	45 d	45 d			28

Analyte	Stability in urine at			Stabilizer	Comments	Reference
	- 20 °C	**4 – 8 °C**	**20 – 25 °C**			
Test-strip fields Erythrocytes Leukocytes Protein		1 - 3 h 1 d*	4 – 8 h 1 d ↗ >2 h**		* >300 mosmol./kg ** Unstable at pH >7.5	28, 103, 105
Transferrin	4 w	1 w	7 d			113
Urea	4 w	7 d	2 d	pH < 7		28
Uric acid	Unstable		4 d	pH >8	Precipitation at pH <7	28, 78
Vanillyl mandelic acid (VMA)	>1 y	>7d	7d at pH 3 - 5	pH <5		28, 186, 216

5.3 Cerebrospinal Fluid (CSF)

Analyte	Stability in urine at			Stabilizer	Comments	Reference
	- 20°C	4-8°C	20-25°C			
Albumin	>1 y	2 m	1 d	Up to 1h: Do not cool Up to 3 h: Transport on ice No additives No partial fixation Long term storage Immediately –70 °C in glass or polypropylene vessels tightly closed	Glucose lactate: Stability depends on cell content IgG: Freezing is not recommended Leukocytes, tumor cells: Store cells as dry smears	97, 98
Glucose	>1m	3 d	5 h ↘			
IgA, IgG, IgM	unstable	7 d	1 d			
Lactate	m	1 h	30 min↗			
Leukocytes		3-5 h	1-2 h			
Protein, total	> 1 y	6 d	1 d			
Tumor cells		1 – 12 h				

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