

Guideline Diagnostic Methods

The Swiss Rare Disease Registry (SRDR) distinguishes between 11 different **main categories** to classify the diagnostic method. Please only indicate the diagnostic method/test that was **decisive** for the diagnosis. Please do not indicate any auxiliary examinations or routine examinations that were indicative but not decisive for the diagnosis. Multiple entries are possible. The following list serves as a guideline for the classification of the diagnostic methods/tests into the 11 main categories. Please note that the list is **not exhaustive**.

The list is based on the following literature:

- Renz H. (2018). *Praktische Labordiagnostik*, 2. Auflage. DE Gruyter Verlag.
- Bruhn H. D., Junker R., Schäfer H., Schreiber S., & Bruhn, A. (2012). *LaborMedizin*, 3. Auflage. Schattauer Verlag.

1. Molecular Genetics

- Polymerase Chain Reaction (PCR): RT-PCR, Multiplex-PCR, real-time PCR
- Sanger Sequencing
- Next Generation Sequencing (NGS)
- Whole Exome Sequencing (WES)
- Multiplex Ligation-dependent Probe Amplification (MLPA) based techniques
- Microsatellite-DNA Analysis
- Array-based Comparative Genomic Hybridization
- Fluorescent in situ hybridization (FISH)
- Multiplex Fluorescent in situ hybridization (FISH)
- Liquid Biopsy
- Clonality Analysis
 - Ig Heavy-Chain Rearrangement
 - Ig Light Chain Rearrangement
 - TCR Rearrangement
- Mutation Analysis of single genes

2. Biochemistry

- Protein Diagnostic
 - Serum electrophoresis
 - Immunofixation electrophoresis

- SDS-polyacrylamide gel electrophoresis
- Isoelectric focusing
- High-performance liquid chromatography (HPLC)
- Ion-exchange chromatography
- Affinity chromatography
- Nephelometry
- Turbidimetry
- Analysis of special serum proteins e.g., complement components C3, C4
- Enzyme activity determinations
 - Lactate dehydrogenase (LDH)
 - g-glutamyl transferase
 - Creatine kinase
 - Urea (UV-test, colour test)
 - Uric acid (UV-test, colour test)
 - Glucose (e.g., Hexokinase methode, glucose dehydrogenase methode)
- Protein expression
 - Immunohistochemistry
 - Western blot
- Immunoassays
 - Areas of application: Serum-, urine, and cerebrospinal fluid proteins
 - Example of an analyte: Metabolites, amino acids, hormones, porphyrins
Proteins, tumour markers, vitamins
 - Special forms (detection of e.g., hormones):
 - Chemiluminescence immunoassay (CLIA)
 - Elektrochemiluminescence immunoassay (ECLIA)
 - Radioimmunoassay (RIA)
 - Luminescence immunoassay (LIA)
 - Enzyme-linked Immunosorbent Assay (ELISA)
 - Enzym immunoassay (EIA)
 - Immunfluorescence assay (IFA)
 - Immune nephelometry
 - Immunturbidimetry
 - Fecal immunochemical test (FIT)
- Blood gas analysis
- Colorimetric analysis
- Colour reactions or photometric methods
 - Special forms:
 - Reflectance photometry
 - Atomic absorption photometry
 - Flame photometry
- Ion-selective electrode (ISE)
 - Areas of application: Determination of Electrolytes, acid-base balance
 - Example of an analyte: pH; Na⁺, K⁺, Ca⁺; CL⁻)
- Flow cytometry
 - Areas of application: Immunohematology
 - Example of an analyte: Lymphocyte subpopulations

- Atomic absorption spectrometry and atomic emission spectrometry
 - Areas of application: Single element analysis of major and trace elements
Example of an analyte: Ag, Al, As, Cd, Cu, Fe, Hg, Li, Mg, Mn, Ni, Pb, Zn)
- Chromatography
 - Areas of application: universal
 - Example of an analyte: Metabolites, amino acids, hormones, porphyrins, vitamins
 - Special forms
 - Thin-layer chromatography
 - High performance liquid chromatography (HPLC)
- Coagulometry
 - Areas of application: Coagulation diagnostics
 - Example of analyte: APTT, Quick, coagulation factors
- Mass spectrometry
 - Areas of application: almost universal, prefers low molecular weight analytes
 - Example of an analyte: Amino acids, hormones, vitamins
- Spectroscopy
 - Areas of application: almost universal
 - Example of an analyte: Metabolites, amino acids, hormones, porphyrins, proteins, vitamins
 - Special forms
 - Absorption spectroscopy/Emission spectroscopy
 - UV/VIS-spectroscopy
 - Electrochemiluminescence spectroscopy
 - Fluorescence spectroscopy
 - Molecular spectroscopy
- Test strip analysis
 - Areas of application: almost universal
 - Example of an analyte: Metabolites, amino acids, hormones, porphyrins, proteins, vitamins
- Cell counting and cell differentiation
 - Areas of application: Hematology
 - Example of an analyte: Erythrocytes, leucocytes, platelets

3. Histology (microscopic examinations)

- Various biopsies

4. Clinical

The clinical picture refers to the totality of complaints or symptoms that occur in the context of a patient's illness.

5. Imaging

- X-Ray radiography
- Ultrasonography
- Doppler ultrasonography
- Magnetic resonance imaging (MRI)
- Endoscopy
 - Arthroscopy
 - Cytoscopy (baldder examination)
 - Bronchoscopy
 - Ophthalmoscopy
 - Colonoscopy
 - Gastroscopy
 - Rectoscopy
 - Laparoscopy
 - Thoracoscopy
- Elastography
- Positron emission tomography (PET)
- Single-photon emission computed tomography (SPECT)
- X-ray computed tomography (CT)
- Echocardiography
- Myelography
- Angiography

6. Electroencephalography EEG

- Auditory evoked potentials (AEP)
- Somatosensory evoked potentials (SEP)
- Visually evoked potentials (VEP)

7. Newborn Screening

The following 10 diseases are screened in the Newborn Screening:

- Phenylketonuria (PKU)
- Biotinidase Deficiency
- Hypothyroidism
- Cystic Fibrosis (CF)
- Medium-Chain Acyl-CoA Dehydrogenase (MCADD)
- Glutaric acidemia type 1 (GA1)
- Congenital Adrenal Hyperplasia (CAH)
- Maple syrup urine disease (MSUD)
- Galactosaemia
- Severe combined immunodeficiency (SCID) and severe T-cell lymphopenia

8. Prenatal Diagnostic

- Chorionic biopsy
- Aminocentese: Amniotic fluid examination
- Placental biopsy
- Triple-Test (alpha fetoprotein (AFP), oestriol, free beta-chorionic gonadotrophin (beta-hCG))

9. Cytology

- Blood smears for the determination of leukocytes and erythrocyte morphology
- Bone marrow smear
- Cytochemical reactions in leukocytes (e.g., detection of myeloperoxidase, detection of non-specific esterase)
- Cytology test on body fluids such as urine, sputum, cerebrospinal fluid (CSF), pleural fluid, pericardial fluid, bronchoalveolar lavage, peritoneal fluid
- Karyotyping
- Chromosome breakage analysis
- PAP test
- Banding analysis

10. Antibody Status (detection of specific antibodies)

- Radioimmunoassay (RIA)
- Enzyme immunoassay (EIA)
- Fluorescence immunoassay (FIA)
- Luminescence immunoassay (LIA)
- Enzyme-linked Immunosorbent Assay (ELISA)
- Immunofluorescence

11. Other (free text entry possible)

- Electrocardiography (ECG)
- Magnetoencephalography (MEG)
- EMG (electromyography)
- Parasitology
- Bacteriology
- Virology
- Mycology
- ¹⁴C-glycocholate breath test
- diverse H₂ breath tests
- Spirometry (Lufu – lung function test)
- Urinometer analysis
- Urine sediment analysis
- Oral glucose tolerance test

- Tactile imaging
- Sweat test
- Cardiac electrophysiology (EP)
- Perimetry