STUDY PROTOCOL TEMPLATE

INSTRUCTIONS:

- Explanations to the corresponding sections are provided in black.
- Proposed *text in green/italics* is provided for your consideration
- Depending on study design, not all sections may apply.
- Content has to be in compliance with local legal and regulatory requirements.
- A study synopsis may be inserted but is not mandatory.

General information	
Full study title and acronym	Please state: · **Full study title** · **Version number and date of the study protocol** · **Acronym** (if applicable)
Name and contact details of principal investigator	· Please provide name and contact details of the principal investigator and, if applicable, of the study coordinator · Signature of the principal investigator
Study duration	· Please state the estimated study start date (first subject/first visit/first sample analyzed) and study end date (completion of analysis) *Study start (first subject first visit) is anticipated to take place in MM/YYYY.* *Study completion is anticipated to take place in MM/YYYY."*
Study sites	· Please indicate where the study will take place; usually expressed as an approximate number of sites, location(s), and subjects per study site · Please provide the address/contact details of the sites, if applicable · Please indicate in which Laboratory the tests are performed

Instrument	· Please indicate which Roche instrument is used *(e.g. Cobas e411, 601, 602, BenchMark ULTRA, BenchMark XT, DP200)* · Please indicate whether instrument placement is required? *(Y/N)*
1. Introduction, study rationale and study objective(s)	
Introduction and rationale	· Please provide background information e.g. on the specific disease to be studied. This may include information on epidemiology, natural history of the condition, current clinical best practice, and unknown / controversial aspects · Based on the foregoing, please provide a study rationale why the study is to be conducted (without repeating the introduction section) · Please elaborate, if applicable, on the IVDs (=In Vitro Diagnostics) used in this study, the gold standard, and the characteristics of the investigated Roche product using the package insert as a reference
Medical Value/ Novelty of the Study	Please provide further detail on the significance and value of the study (locally and globally)
Study Hypothesis *(if applicable)*	Please state the hypothesis being tested, if applicable *"A research **hypothesis** is a specific, clear, **and** testable proposition or predictive statement about the possible outcome of a scientific research study"*
Study objective(s)	· Please state the primary objective and (if applicable) the secondary objective(s) Please make brief statements. The objectives should be specific and measurable and should relate to the endpoints of the study as well as to the statistical section and assessments, where applicable.

2. Investigational material	
Investigational material and comparator product(s)	· Please indicate the Roche assay(s) used in this study · Please indicate the comparator product(s) used in this study, if applicable · Please indicate the quantity of kits requested, if information is available
3. Study population	
Recruitment, enrollment period, and sample size	· Please indicate the number of subjects and/or sample size to be included in the study and for prospective studies, the estimated time needed to enroll this number using wordings such as *"approximately N subjects, [N per study group] will be recruited over a planned recruitment period of N months."*
Inclusion criteria	· Please list the inclusion criteria
Exclusion criteria	· Please list the exclusion criteria
4. Study design and study procedure	
Study design	· Please state the study design (e.g. prospective/retrospective/blinded)
Study Type	☐Interventional Study ☐Non-Interventional Study Please state the study type (e.g. pilot study, observational study, interventional study (e.g. medical decisions based on device / diagnostic / IVD test), diagnostic utility study*, clinical utility study**, open, randomized, number of study arms, control group, comparator IVD/gold standard, monocenter/multicenter, national/multinational, adjudication, etc) * A diagnostic utility study proves the likelihood that an in-vitro diagnostic test will lead to an improved clinical performance, either alone or in combination with other diagnostic procedures

	** A clinical utility study proves the likelihood that an in-vitro diagnostic test result will lead to an improved health outcome and/or improved patient management. The evaluation of outcomes is thereby associated with testing and clinical interventions

Study procedure	· *For prospective studies:* Please describe the study procedure, the visits and the time points (including time windows = allowed deviation from a fix date) of investigations (e.g. laboratory investigations and other investigations / follow-up) and the parameters that will be assessed · Please describe the specimen types, sample collection schedule, sample handling, transport, (long term) storage, and sample destruction (if applicable) You may provide a data collection overview table or a flow chart, if desired · For randomized and/or blinded studies: Please describe procedure for randomization (method/program, access and storage of the list for group allocation), the procedure for blinding and conditions for unblinding (e.g. in case of emergencies) · Please describe criteria for premature withdrawal considering wordings such as: *Subjects have the right to withdraw from the study at any time for any reason. If lost to follow-up, the assigned study staff will try to contact the subject by telephone followed by registered mail to establish and document as completely as possible the reason for the withdrawal.* *Subjects will be informed of circumstances under which their participation may be terminated by the responsible investigator without the subject's consent. The investigator may withdraw subjects from the study in the event of intercurrent illness, adverse events, lack of compliance with the study and/or study procedures (e.g., study visits), or any reason where it is felt that it is in the best interest of the subject to be terminated from the study. Any administrative or other reasons for withdrawal will be documented and explained to the subject. If the reason for removal of a subject from the study is an Adverse Event, the principal specific event will be recorded in the medical record.* If applicable: *"No subject prematurely discontinued from the study for any reason will be replaced."* *An excessive rate of withdrawals can render the study non-interpretable; therefore, unnecessary withdrawal of subjects will be avoided.* · For randomized and/or blinded studies: Please describe procedure for randomization (method/program, access and storage of the list for group allocation), the procedure for blinding and

	conditions for unblinding (e.g. in case of emergencies) *For retrospective studies:* please describe the time frame used to select samples, any clinical and demographic data collected for the samples, the preanalytics and storage of the samples, and if the samples were collected from a biobank under informed consent
5. Statistics	

Primary and secondary endpoint(s)	· Please define the primary and (if applicable) the secondary endpoint(s) matching the objective(s) defined in section 1
Statistical methods	· Please describe the planned statistical methods, statistical analysis plan, and state if an interim analysis is planned · *For prospective studies*: Please estimate the dropout rate, and define the study groups for evaluation (e.g. according to protocol population and full study population)
Sample size, level of significance, and power	· Please provide the sample size calculation, significance level, and statistical power for the primary endpoint (ideally including assumptions on effect size and variability of the primary endpoint). Consider dropouts and a minimal sample size limit. This may not apply to pilot studies with the objective to determine the sample size of subsequent studies
6. Safety assessment	
	In general this section should include information on: · Definitions of (serious) adverse events, time period in which you will report all serious adverse events and device deficiencies, where appropriate, to Ethics Committee, regulatory authorities, and to Roche · Study risk determination · List of anticipated adverse events and device deficiencies, if appropriate · Details of the process for recording and reporting adverse events (date of the adverse event, treatment, resolution, assessment of both the seriousness and the relationship to the investigational device/IVD) · Details of the process for reporting device deficiencies Please make sure that the safety section of your study protocol is in **compliance with your hospital's processes for SAE handling, and local legal and**

	regulatory requirements. **The text provided below in green is provided for general considerations only!** The correctness of the statements fully remains in your responsibility

Definitions	***Adverse Event (AE)*** *An AE is any untoward medical occurrence in a patient or clinical investigation subject which does not necessarily have a causal relationship with the medicinal product, or the device or diagnostic test under investigation. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporarily associated with the use of the medicinal product or the device. AEs might occur in any phase of the clinical investigation whether or not considered related to the medicinal product, or the device or the use of the diagnostic test. This also includes exacerbations of pre-existing conditions and events, intercurrent illnesses, or drug interactions. Anticipated day-to-day fluctuations of pre-existing conditions that do not represent a clinically significant exacerbation are not considered AEs in contrast to pre-existing conditions that worsen during a study except those associated with the disease being studied. Discrete episodes of chronic conditions occurring during a study period should be recorded as AE in order to assess changes in frequency or severity.* *Note 1: This includes events related to the investigational device or the comparator* *Note 2: This includes events related to the procedures involved* *Note 3: For users or other persons, this definition is restricted to events related to the investigational devices* ***Serious Adverse Event (SAE)*** *SAEs are a subset of AEs.* *An SAE is defined as any untoward medical occurrence or effect that:* *1) Leads to death, 2) Results in a life-threatening illness or injury, 3) Results in a permanent or significant disability/incapacity, impairment of a body structure or a body function, 4) Requires in-patient hospitalization or prolongation of existing hospitalization (usually involving at least an overnight stay), 5) Results in an important medical event or requires intervention to prevent one or other of the outcomes listed above , 6) Leads to fetal distress, fetal death or a congenital abnormality or birth defect* ***Anticipated SAE*** *Effect which by its nature, incidence, severity or outcome has been identified in a risk assessment* ***Unanticipated SAE*** *Effect which by its nature, incidence, severity or outcome has not previously been identified in a risk assessment.*

Classification of AEs/SAEs (if appropriate) and AE/SAE recording and reporting	If appropriate from a local legal/regulatory point of view, please classify between anticipated and unanticipated AEs/ SAEs such as e.g: *AEs or SAEs will be classified as either anticipated or unanticipated. Recording and reporting procedures differ accordingly as described below. An attempt to establish a diagnosis based on the presenting signs, symptoms, and/or other clinical information will be made and AE/SAE will be documented as a diagnosis and not as individual signs/symptoms.* *Anticipated AEs/SAEs are AEs/SAEs that are associated with <the disease investigated>, unless judged as more severe than expected for the subject's condition. Anticipated AEs/SAEs will be recorded but not reported in line with local, legal and regulatory requirements. These anticipated AEs or SAEs include, but are not limited to:* *<Please list the AEs/SAEs>* *All AEs/SAEs which do not meet the criteria mentioned above of Anticipated AEs/SAEs, are considered as Unanticipated AEs/SAEs. All* *Unanticipated AEs/SAEs will be recorded in terms of nature of the event, date, outcome and action taken. All unanticipated SAEs will be reported in line with local, legal and regulatory requirements.* *Please note: SAEs which will be reported irrespective of being classified as anticipated or unanticipated include: Myocardial infarction, Stroke, Pulmonary embolism, Subarachnoid hemorrhage, Cerebral hemorrhage, Cerebral thrombosis* *All AEs will be recorded, even if the AE is assessed as unlikely to be causally related to the investigated <diagnostic test>. Patients will be instructed to contact the responsible study investigator immediately should they experience any signs or symptoms they perceive as serious during the period from start visit until study completion <define time point when the study is completed; e.g. delivery>.*

If applicable: Laboratory abnormalities and other abnormal assessments	*Laboratory test value abnormalities and other abnormal assessments will not be recorded as AEs unless they result in a clinically significant condition as judged by the assigned investigator and meet the definition of an AE, or SAE. However, clinically significant abnormal laboratory findings and other abnormal assessments that are associated with <state the investigated disease> are anticipated in the study population. These Anticipated AEs/SAEs will be captured/recorded in the study documentation <at each visit>. Such anticipated abnormalities will not be reported as SAEs.* *Anticipated laboratory abnormalities and other abnormal assessments related to <state the disease area> include but are not limited to:* *<Please provide here a list of anticipated laboratory abnormalities>* *The assigned investigator will exercise his or her medical and scientific judgment in deciding whether an abnormal laboratory finding or other abnormal assessment is clinically significant and whether or not it is associated with <state the disease area>.*
If applicable: Malfunction / incidents and indirect harm reporting	For open studies and when medical decisions are taken based on the medical device / IVD test results you may, if appropriate, consider wordings such as: *During the course of this clinical study incidents and indirect harms might occur. The documentation and reporting of the incidents and indirect harms will follow the guidance provided in MEDDEV 2.7/3, December 2010 <please update if appropriate> and local regulations and guidelines. These incidents and indirect harms will be determined by the responsible study investigator during the scheduled patient visits, and must be reported to the manufacturer immediately.* *An incident is any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequate in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a subject, or user or of other persons or to a serious deterioration in their state of health. An indirect harm may occur as a consequence of the medical decision, action taken/ not taken on the basis of information or result(s) provided by the device.* *Examples include: misdiagnosis, delayed diagnosis, delayed treatment, inappropriate treatment, transfusion of inappropriate materials.* *All incidents and indirect harms will be recorded in the medical record. A description of the event, including the start date, resolution date, action taken, and the outcome will be reported. As a general principle, a pre-disposition to report rather than not to report in case of doubt on the reportability of an incident will be applied.* *Any report will not be unduly delayed because of incomplete*

	information.
Follow up of ongoing AEs and SAEs	*If the event has resolved, the documentation in the medical record will be completed. If the frequency or severity of an already recorded AE changes significantly, a new AE will be recorded. If the AE becomes serious, the procedures for reporting of SAEs will be followed. Ongoing AEs will be followed until <define until when>.*
Treatment of any AE / SAE	*Treatment of any AE / SAE will be according to current available best clinical practice. The applied measures will be recorded in the medical record.*
Assessment of causality (relationship to IVD and indirect harm)	For blinded, observational studies a text as follows may be considered: *Due to the double-blind study design no diagnosis will be made, no treatment will be initiated and no medical decision will be taken based on the investigated <diagnostic tests>). In this study, the occurrence of AEs / SAEs will therefore be considered unrelated to the investigated <diagnostic tests>. Therefore no indirect harm related to the investigated immunoassays <define> is anticipated in the context of this study.*

7. Compliance Statements	
	General requirements: The study will be conducted in compliance to this study protocol, the current version of the Declaration of Helsinki, ICH GCP, and applicable local legal and regulatory requirements. *Submission of study documents: Before study start, the study protocol, and subject information / informed consent and any other study-related document as required by applicable laws and regulations will be submitted to the Ethics Committee and regulatory authorities for written approval. Any protocol amendments or new or amended information that requires ethical consideration will be submitted for written approval, too. In addition, a study report (interim and /or full report) will be submitted to regulatory authorities in line with applicable timelines.* *Subject insurance: Sufficient insurance coverage according to legal requirements for subjects participating in the study is ensured. Subjects will be informed about this and will be asked to inform the assigned investigator about any harm they believe to be associated with their participation in this study.* *Subject information and informed consent: Subjects/legal representatives will be informed orally and in writing about the objectives of the study, study procedures, potential risks, and about the fact that to some extent data will be accessible for third parties (see below) for the purpose of controlling the study conduct - provided that data confidentiality is ensured at any time.* *Before any study-related activities are initiated, the subjects / legal representatives will have to sign the written informed consent. The participation in the study is entirely voluntary. The subjects have the right to withdraw their willingness to participate in the study at any time without affecting their future medical care in any way.* *Clinical study results and publication: The results of the clinical study will be documented in a clinical study report and if possible, will be published (e.g. in a journal or presented in a scientific meeting).*
8. Data confidentiality and protection	
Data confidentiality and data protection	*Auditors, Ethics Committee, and the regulatory authorities will be granted direct access to the subject's medical records to the extent permitted by the applicable law and regulation for verification of clinical study procedures, and/or data control, ensuring subject data confidentiality. The subject's file and the source data will be archived in line with national and international legal requirements.*
9. Quality controls and assurance	

Quality controls and quality assurance	· If applicable, please describe the procedures for data review, database cleaning, and issuing and resolving data queries · If applicable, please describe the procedures for verification, validation and securing of electronic clinical data systems
10. References	
Literature references	· Please provide a list of literature references unless mentioned within the protocol