Template for an In vitro diagnostic (IVD) medical device Clinical Performance Study Plan (CPSP)

General information and instructions

This document is the Clinical Performance Study Plan (CPSP) for In vitro diagnostic (IVD) device performance studies.

The purpose of the CPSP is to ensure the clinical performance study is performed to yield high quality, accurate and reliable data for the IVD device under investigation. The CPSP shall be developed by Investigators or Sponsors appropriately qualified by education, training, or experience.

This template provides a general format applicable to performance studies with IVD devices:

- initiated by (academic) Investigators,
- performed in Switzerland, respectively where the Sponsor is located in Switzerland,
- where the study is undertaken to establish or confirm the analytical or clinical performance of a IVD device,
- where the Federal Act on Medicinal Products and Medical Devices (TPA) applies,
- where the Swiss law on human research (Federal Act on Research involving Human Beings (HRA)) and the ordinance ClinO-MD (KlinV-Mep, OClin-Dim, OSRUm-Dmed) apply.

The template is based on:

- HRA and the ordinance ClinO-MD (KlinV-Mep, OClin-Dim, OSRUm-Dmed).
- Standard ISO 20916
- In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR)

Performance studies of category A1 and A2 do not need Swissmedic approval, the CPSP must be adapted accordingly.

The CPSP must be adapted in case of international performance studies.

You can also use this template to write a Post-Market Performance Follow-up (PMPF) Plan. In such case this template can be simplified. Annex XIII Part B Art. 5 IVDR legislates on the minimum set of information the PMPF Plan must include.

Projects that are performed for reasons other than pre- and post-market regulatory purposes, such as for re-imbursement purposes, are out of the scope of this document. This template can nonetheless be used, but must be adapted accordingly.

All applications submitted to the Ethics Committee should address the issue of **sex and gender** (unless totally irrelevant). Based on the recommendations “sex and gender in research involving humans according to the HRA” (swissethics.ch / topics / sex and gender equitable research), a set of instructions has been elaborated by a group of experts to guide researchers in the writing of their research documentation, including a grid inspired by the SAGER guidelines. Researchers need to know that the check-up grid provided in the instructions are used by ethics committees’ members to review all protocols and related documents.

Instructions are indicated in *blue italics* and they need to be deleted.

Chapters and sections headings and template text formatted in regular type (black) should be included in the CPSP as provided in the template.

Header and footer should contain the following information (on all pages): [Study ID], [CPSP version number, CPSP version date DD/MM/YYYY], [Page x of xx].

In places where the information is redundant, it is acceptable to reference to another chapter or section, to document or to state its redundancy but the chapter or section should not be deleted.

The CPSP must be submitted via BASEC in an Optical Character Recognition (OCR) PDF format, i.e. in a searchable PDF format.

The CPSP has to be signed by the Principal Investigator, the Sponsor (if applicable) and in case of a multicentric project by the Principal Investigators of each participating research center as well.

Electronic signatures of the CPSP are accepted under the following conditions: The service provider used for the electronic signature process must have a system that verifies that the electronic signature is correct and genuine and properly embedded in the document. Copy-paste of scanned signatures are not accepted. If the protocol is signed by hand, the scans of the wet-ink signed signature pages are uploaded to BASEC separately

Refer questions regarding the use of this CPSP template to swissethics, info@swissethics.ch, phone: +41 31 306 93 95, www.swissethics.ch.

The content of the CPSP has to be consistent with the content of the application form «RESEARCH PROJECT APPLICATION FORM FOR MEDICAL DEVICES AND IVD DEVICES» in BASEC. You can refer to the CPSP in the application form in BASEC to avoid redundancies but not vice versa.

Change history

Version Nr	Version date	Modified without version change	Description, comments	Control
1.0	27.06.2022		Initial version	PG
		X	Chapter 2.3.1 and 2.4.1: Added notes for the submission to the ethics committee and to Swissmedic of the summary of the final report in lay language and other reporting requirements	PG
		X	Added instructions on sex and gender-equitable research and references to MDCG 2024-4 Safety reporting in performance studies of in vitro diagnostic medical devices under Regulation (EU) 2017/746	PG
2.0	16.09.2024		New version adapted to the amended ClinO-MD, status as of November 1, 2024	PG
		X	Added reference to Clinicaltrials.gov in chapter 2.1, and reference to art. 5 ClinO-MD in chapter 2.8. Confidentiality	PG

✂ **Remove the ‘General information and instructions’, and the table ‘Change history’** ✂

Clinical Performance Study Plan (CPSP)

INSERT TITLE OF THE PERFORMANCE STUDY

[Descriptive title identifying the design of the performance study (e.g., randomised, sham controlled, etc.), population (if relevant), target disease(s), the in vitro diagnostic (IVD) device, and, if the study is multi-centre (-country)]

SHORT TITLE and / or acronym / or translation (if relevant; title used in the informed consent)

Type of clinical trial:	*In vitro diagnostic (IVD) device clinical performance study* *In vitro diagnostic (IVD) post-market performance follow-up study*
Categorisation:	*Category according to Art. 6a ClinO-MD (A1, A2, C1, C2 or C3).*
Registration:	*Name of the primary registry (if not yet registered name the intended registry) and the registration number.* *Swiss National Clinical Trials Portal (SNCTP): SNCTP-Number (this number is not available when the performance study is initially submitted to the Competent ethics committee (CEC). It should be added once available).* *If applicable: EUDAMED-number, names of other registries, and the registrations numbers*
Identifier:	*Clinical trial ID (e.g., institutional or Sponsor CPSP identifier) [this must correspond to the clinical trial ID in the footer]*
Principal Investigator and Sponsor, or Sponsor-Investigator:	*Name of Principal Investigator (PI) and of the Sponsor, and addresses, if the roles are separated, add their full contact details.* *Name of Sponsor-Investigator, and address, if the PI and the Sponsor are the same person, add his/her full contact details.* *Indicate the coordinating Investigator if the study is multicentric, add his/her full contact details.*
Sponsor representative (if the Sponsor is not located in Switzerland)	*Name address of the Sponsor representative in Switzerland.*
IVD device:	*Identification of the IVD device, including name, model/type, software version and accessories, if any, to permit full identification.* *If available: Unique Device Identifier (UDI, the UDI system is detailed in Part C of Annex VI IVDR).*
Manufacturer of the IVD device	*Name of the manufacturer of the IVD device, address and full contact details.*
CPSP Version and Date:	*CPSP Version number and version date [these must correspond to the version number and version date in the footer].* *In case of changes to the CPSP, Amendment number, from (date), replaces version number from (date) here and in the footer. Track the changes in the table "summary of the revision history in case of amendments".*

CONFIDENTIAL

Add, if applicable, an institutional confidentiality statement here respecting that it is not in conflict with applicable transparency rules.

e.g. "The information contained in this document is confidential and the property of the xx (or "Sponsor"). The information may not - in full or in part - be transmitted, reproduced, published, or disclosed to others than the applicable Competent Ethics Committee(s) and Regulatory Authority(ies) without prior written

authorisation from the Sponsor except to the extent necessary to obtain informed consent from those who will participate in the investigation.

SUMMARY OF THE REVISION HISTORY IN CASE OF AMENDMENTS

Version Nr, Version Date	Chapter	Description of change	Reason for the change

Signature Page(s)

Complete the signature pages with name and title of the person(s) authorised to sign the CPSP and the CPSP amendment(s): Sponsor, medical expert, Principal Investigator responsible for conducting the performance study, Statistician.

Add more lines, functions and pages as needed.

ID number of the performance study:	*Performance study ID* *Registry and registration number (to be filled in once available, in any case before the start of the study).*
Title:	*Full title as written on title page*

The Sponsor, the Principal Investigator and the Statistician have approved the CPSP version [x (dated DD.MM.YYYY), make sure this corresponds to the CPSP version and date in the footer], and confirm hereby to conduct the investigation according to the CPSP, the current version of the World Medical Association Declaration of Helsinki and the recognized ethical principle for medical research involving humans, ISO 20916 norm, ICH-GCP when applicable, and the local legally applicable requirements.

The Investigator has received the ICF and consider it appropriate for use.

Sponsor: If the Sponsor and PI are the same person, replace both lines with Sponsor-Investigator

Place/Date	Signature

Principal Investigator: *If the Sponsor and PI are the same person, replace both lines with Sponsor-Investigator*

Place/Date	Signature

Statistician

Place/Date	Signature

Principal Investigator at the local study site*:

I have read and understood this CPSP version [x (dated DD.MM.YYYY), make sure this corresponds to the CPSP version and date in the footer], and agree to conduct the investigation according to the CPSP, the current version of the World Medical Association Declaration of Helsinki and the recognized ethical principle for medical research involving humans, ISO 20916 norm, ICH-GCP when applicable, and the local legally applicable requirements.

I have received the ICF and consider it appropriate for use.

Site:	*Name and address of study site*
Principal Investigator at the local study site:	*Printed name of Principal Investigator*

Place/Date	Signature

**Note: In multicentre investigations, this page must be individually signed by all participating Local Principal Investigators.*

Table of Contents

SYNOPSIS

A summary or overview of the clinical performance study shall include all the relevant information regarding the study, such as study design, study objective(s) and outcome(s)/endpoint(s) inclusion/exclusion criteria, number of specimens, description of the study population, duration of the study, etc.

Title:	*Full title of the CPSP.*
Short title / Study ID:	*Short title of the CPSP, Study acronyms, if applicable, and study ID.* *For performance study conducted in EU, the study ID is the single identification number as referred to in Art. 66(1) IVDR*
CPSP, version and date:	*The version number and the date of the valid CPSP. Make sure they correspond to the version number and version date in the footer, on the first page and on the signature pages.*
Registration:	*Name of the primary registry (if not yet registered name the intended registry) and the registration number. SNCTP-Number (this number is not available when the performance study is initially submitted to the CEC. It should be added once available). If applicable: EUDAMED-number, names of other registries, and the registrations numbers.*
Sponsor / Sponsor-Investigator	*Name of Sponsor / Sponsor-Investigator.*
Category and its rationale:	*Provide the investigation category determined by Art. 6a ClinO-MD with the rational/justification for this category.*
Intervention:	*Indicate if the performance study is interventional.* *"Interventional clinical performance study" means a performance study where the test results may influence patient management decisions and/or may be used to guide treatment (Art. 2 ClinO-MD, Art. 2(46) IVDR).*
Name of the IVD device, Unique Device Identification (UDI), name of the manufacturer	*Provide name of the IVD device, model/type, including software version and accessories, if any, to permit full identification. If available, provide the Unique Device Identification (UDI). The UDI is mandatory for category A investigations. The UDI system is detailed in Part C of Annex VI IVDR.* *Name of the manufacturer, address and full contact details, and the SRN number (Art. 28 IVDR), when available:).*
Stage of development:	*Indicate the development phase of the IVD device (establishment resp. confirmation of the analytical evidence, resp. clinical evidence, post-market surveillance, vigilance and market surveillance).* *Indicate if the performance study is conducted for a conformity assessment purpose.*
Background and rationale:	*Provide a short background and the rationale for the performance study, this includes the health condition studied.* *Are "sex and gender" dimensions relevant to the topic of the study (specifying genetic/biological or social mechanisms at play)? To address this question, refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research). If it is considered that "sex and gender" dimensions are not relevant, provide a justification.*
Objective(s):	*Brief statement of primary objective and the main secondary objectives.*
Outcome(s) / endpoint(s)	*Brief statement of primary outcome and the main secondary outcome measures. Brief description of the principal (primary) and secondary outcome(s)/endpoint(s) used in the performance study to assess the performance of the IVD device*

Design:	*Design attributes such as observational, cross-sectional (single time-point design), longitudinal, retrospective and prospective, interventional).*
Inclusion / exclusion criteria:	*Brief description of the population under investigation, the key inclusion and exclusion criteria and if applicable, the reasons for inclusion of vulnerable participants.* *Are "sex and gender" dimensions relevant to the topic of the study? To address this question, refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research).*
Measurements and procedures:	*Brief description of the measurements and procedures (methodology, procedures, sampling, …).*
Control (if applicable):	*Describe the control group/the comparator(s), when applicable.*
Number of participants:	*Number of participants projected/needed for the entire performance study (all study sites combined). Give the total and the numbers for each study group.*
Overall study duration and duration for the individual participants:	*Estimated duration for the performance study (e.g., from first participant's specimens collected to study close-out).* *When applicable, estimate the duration of each participant's participation.*
Performance study schedule:	*Planned study starting date: Month Year of First- participant-In (planned).* *Expected study termination date: Month Year of Last- participant-Out (planned).*
Investigator(s):	*Name(s) of Investigator(s); Full contact details.*
Study Site(s):	*Single- or multicentric performance study. If multicentric give the number of projected study sites to be involved. Indicate also the countries if the investigation is multi-national.*
Statistical considerations, incl. rational for sample size.	*A very brief description of the main elements of the statistical methodology to be used in the performance study. Give the rational for the number of participants and for the number of specimens.*
Compliance statement:	This performance study will be conducted in compliance with the CPSP, the current version of the Declaration of Helsinki, standard ISO 20916 *(indicate version/year)*, ICH-GCP (as far as applicable) as well as all national legal and regulatory requirements.

ABBREVIATIONS

Provide a list of abbreviations used in the CPSP – complete and adapt the list as appropriate.

AE	Adverse Event
ADE	Adverse Device Effect
ASADE	Anticipated Serious Adverse Device Effect
CA	Competent Authority (e.g., Swissmedic)
CEC	Competent Ethics Committee
ClinO-MD	Ordinance on Clinical Trials with Medical Devices *(in German: KlinV-Mep, in French: OClin-Dim, in Italian: OSRUm-Dmed)*
CPSP	Clinical performance study plan
CPSR	Clinical performance study report
CRF	Case Report Form (pCRF paper CRF; eCRF electronic CRF)
DD	Device Deficiency
DMC / DSMC	Data Monitoring Committee, Data Safety Monitoring Committee
Ho, H1	Null hypothesis, Alternative hypothesis
HRA	Federal Act on Research involving Human Beings *(in German: HFG, in French: LRH, in Italian: LRUm)*
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH-GCP	International Council for Harmonisation – guidelines of Good Clinical Practice
IFU	Instructions For Use
ISF	Investigator Site File
ISO	International Organisation for Standardisation
ITT	Intention to treat
IVD	In Vitro Diagnostic
IVDR	In Vitro Diagnostic Device Regulation (EU) 2017/746 of 5 April 2017
MedDO	Medical Devices Ordinance *(in German: MepV, in French: ODim, in Italian: ODmed)*
PI	Principal Investigator
PMPF	Post-Market Performance Follow-up
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDV	Source Data Verification
SNCTP	Swiss National Clinical Trials Portal
SOP	Standard Operating Procedure
USADE	Unanticipated Serious Adverse Device Effect

INVESTIGATION SCHEDULE

Insert a flow chart (graphic) or tabular listing of schedule of events and assessments and procedures of the performance study (an example is provided below, amend and expand according to the specific study). To be repeated in chapter 9.1). E.g.:

Study Periods	*Participant information*	*Consent (ICF) Screening*	*Study visits.*			
Visit	*0*	*1*	*2*	*3*	*4*	*5*
Time (hour, day, week)	*-10*	*-7*	*0*	*1*	*8+/-1d*	*22*
Participant Information	*X*					
Participant consent (ICF)		*X*				
Demographics		*X*				
Medical History		*X*				
In- /Exclusion Criteria		*X*	*x*			
Physical Examination		*X*				*x*
Vital Signs		*X*	*x*	*x*	*x*	*x*
Laboratory Tests		*X*	*x*	*x*	*x*	*x*
Pregnancy Test		*X*				*(x)*
Randomisation			*x*			
Other examinations, tests…		*X*	*x*	*x*		*x*
Specimens collection			*x*	*x*	*x*	*x*
(Serious) Adverse Events			*x*	*x*	*x*	*X*
Device Deficiencies			*x*	*x*	*x*	*x*

1. INVESTIGATION ADMINISTRATIVE STRUCTURE

Provide complete contact details (address, phone, e-mail) of all individuals or groups/committees and their composition, roles, and responsibilities overseeing the performance study (e.g., Sponsor, PI, statistician, monitor, coordinator, data management team, and other individuals or groups, laboratories if applicable).

Provide complete contact details of any committee(s) involved in the clinical trial (e.g., Data Monitoring Committee, Data Safety Monitoring Committee, etc.).

If critical personnel involved in the clinical trial is not determined at the moment of writing the CPSP, refer to other documents, e.g., staff list.

Note: Refer to Art. 4 ClinO-MD for the general obligation of the Sponsor and PI.

1.1 Sponsor, Sponsor-Investigator

Identification of the Sponsor, including the name, address of the registered place of business and contact details of the Sponsor and, if applicable, the name, address of the registered place of business and contact details of its contact person or legal representative in Switzerland pursuant to Art. 2 ClinO-MD

1.2 Principal Investigator(s)

Information on the PI or PIs, qualifications, contact details, and investigation site or sites, such as number, qualification, contact details:

a) Name, title, address, and professional position of the PI(s) at each study site

b) Name and address of the study site(s) in which the clinical performance study will be conducted.

Note: The Sponsor shall maintain an updated list of PI(s), study sites, and institutions. This list can be kept separately from the CPSP. The final list shall be provided with the clinical performance study report.

Note: Required professional qualifications of the PI and other persons conducting the clinical performance study is given in Art. 5 ClinO-MD.

1.3 Statistician ("Biostatistician")

Name, title, address, of the qualified statistician(s) involved in the performance study.

1.4 Laboratory

If applicable: Name(s) and address(es) of the laboratory(ies) involved in the clinical performance study.

1.5 Monitoring institution

Name and address of the institution that monitors the performance study.

1.6 Data Safety Monitoring Committee

If applicable this should comprise the composition of data safety monitoring committee (DSMC); summary of its role and reporting structure; statement of whether it is independent from the Sponsor and competing interests; and reference to where further details about its charter can be found, if not in the /CPSP. Alternatively, provide an explanation of why a DSMC is not needed.

1.7 Any other relevant Committee, Person, Organisation, Institution

If applicable e.g., coordination, data management, etc. Alternatively, write "not applicable".

2. ETHICAL AND REGULATORY ASPECTS

Describe here the ethical considerations relating to the performance study:

Refer to the ethical requirements in clinical research of E. Emanuel (Emanuel E et al., What makes clinical research ethical? JAMA 2000; 283:2701-2711): 1. Value, 2. Scientific validity, 3. Fair participant selection, 4. Favourable risk-benefit ratio, 5. Independent review, 6. Informed consent, 7. Respect for enrolled participants.

Describe and evaluate the ethical implications for individuals and the society as a whole. Make a careful risk benefit evaluation.

Before the performance study is conducted, the CPSP, the ICF as well as other study specific documents must be submitted to a properly constituted Competent Ethics Committee (CEC) and to the competent regulatory authorities (name the authority, e.g., Swissmedic / FOPH / foreign competent authorities.), in agreement with the national laws and requirements, for formal approval. Any substantial amendment to the CPSP must as well be approved by the competent CEC and regulatory authorities.

The Sponsor must obtain the final written positive decision from the CEC *and from the CA* before the performance study can start (adapt the sentence for category C clinical trials: in Switzerland the national approval is issued by Swissmedic and includes the approval of the CEC). The Sponsor ensure that additional requirements set by the regulatory authorities are implemented.

2.1 Registration of the investigation

The performance study must be registered in a primary registry recognized by the WHO (International Clinical Trials Registry Platform: https://www.who.int/clinical-trials-registry-platform), or in the registry of the U.S. National Library of Medicine (https://clinicaltrials.gov). In addition, registration in SNCTP (via BASEC) in the national languages of Switzerland in which recruitment is intended is required for clinical trials conducted in Switzerland (Art. 41 ClinO-MD, Art. 56 HRA).

Note: The data of the performance study entered in BASEC will be automatically published in SNCTP no later than six months after the performance study has been granted approval by the CEC and CA.

Provide a statement of registration of the performance study. Indicate in which primary register the performance study is registered (or will be registered)? Include the registry identification number and registration date; include details of registration(s) in other registries, when applicable.

2.2 Categorisation of the investigation

Indicate the performance study category and the rationale for the categorisation (Art. 6a ClinO-MD).

2.3 Competent Ethics Committee (CEC)

For category A performance study: The Sponsor *(or The Sponsor-Investigator, as applicable)* submits the performance study to the CEC and obtain ethical committee approval before the start of the performance study. The PI *(for multicenter investigations: 'Each PI at each participating study site')* ensures that copy of the final CEC approval letter is received from the Sponsor. Copy of the final approval letter and filed in the Investigator's file before the performance study starts.

For category C performance study [to streamline the approval process and prevent receiving a letter of deficiencies during the formal review, it is strongly advised to submit the performance study to the CEC and to the CA (Swissmedic) the same day]: The Sponsor *(or The Sponsor-Investigator, as applicable)* submits the performance study to the CEC and obtain ethical committee approval. The study only starts after the Sponsor has obtain the positive national decision issued by Swissmedic (see chapter 2.4). The PI *(for multicenter investigations: 'Each PI at each participating study site')* ensures that CEC approval and the positive national decision issued by Swissmedic is received from the Sponsor. Copy of the approval letter is filed in the Investigator's file before the performance study starts.

2.3.1 Reporting duties to the Competent Ethics Committee (CEC)

Mention the reporting duties and the legal time frame for the reporting (amendments to the CPSP and changes to the approved documents, including the reporting duties in case of planned or premature termination of the performance study, and the final report). No changes to the CPSP are implemented without prior Sponsor and CEC approval, except where necessary to eliminate apparent immediate hazards to participants. Refer to chapter 10 for safety reporting.

Amendments are reported according to Art. 15 ClinO-MD (see chapter 2.10 for details).

Safety reporting is done according to Art. 33-35 ClinO-MD and is described in chapter 10. *Do not repeat in this chapter again safety reporting duties to the CEC.*

The regular or premature termination of the performance study, as well as the suspension of the performance study is reported to the CEC within 15 days. The suspension or premature termination of the performance study is reported to the CEC within 24 hours if due to safety reasons The reasons for the study suspension or premature termination must be given (Art. 36 ClinO-MD).

A final report is submitted to the CEC within one year after the regular end of the performance study and within 3 months after a premature termination of the performance study A summary in easily

understandable terms must be included with the final report (Art. 37 ClinO-MD). *A guidance document on how to prepare, write, and translate, summaries of clinical trial results in lay language is given here. The lay summary is **not** the study report synopsis.*

Add other requirements in case of international investigations.

2.4 Competent Authorities (CA)

CA approval is required for performance studies category C (C1, C2, C3).

The Sponsor *(or The Sponsor-Investigator, as applicable)* submits the performance study to the CA and obtains national approval before the start of the performance study. The PI *(for multicentric investigations: 'Each PI at each participating study site')* ensures that approval from the CA is obtained and filed in the Investigator's file before the first participant is informed and recruited for the performance study.

To streamline the approval process and prevent receiving a letter of deficiencies during the formal review, it is strongly advised to submit the performance study to the CEC and to the CA (Swissmedic) the same day.

2.4.1 Reporting duties to the competent authorities

Mention the reporting duties and allowed time frame for the reporting to the CA including the reporting duties in case of planned or premature termination of the performance study and the final report. Reporting duties and timelines are the same as for CEC, except of non-substantial amendments that shall be reported as soon as possible (Art. 20 ClinO-MD).

Amendments are reported according to Art. 20 ClinO-MD (see chapter 2.10 for details).

Safety reporting is done according to Art. 33-35 ClinO-MD and is described in chapter 10. *Do not repeat in this chapter again safety reporting duties to the CA.*

The regular or premature termination of the performance study, as well as the suspension of the performance study is reported to the CA within 15 days. The suspension or premature termination of the performance study is reported to the CA within 24 hours if due to safety reasons The reasons for the study suspension or premature termination must be given (Art. 38, resp. 36, ClinO-MD).

A final report is submitted to the CA within one year after the regular end of the performance study and within 3 months after a premature termination of the performance study A summary in easily understandable terms must be included with the final report (Art. 38, resp. 37 ClinO-MD). *A guidance document on how to prepare, write, and translate, summaries of clinical trial results in lay language is given here. The lay summary is **not** the study report synopsis.*

Add other requirements in case of international clinical trials.

2.5 Ethical Conduct of the Investigation

The performance study will be carried out according to the CPSP and with principles enunciated in the current version of the Declaration of Helsinki, standard ISO 20916, ICH-GCP as far as applicable, the Swiss Human Research Act (HRA) and its Ordinances, and Swiss regulatory authority's requirements.

Add other national/local requirements, as applicable.

2.6 Declaration of interests

The PI and the Investigators shall declare any conflict of interest, if applicable, or provide a statement of no conflict of interest (independence, intellectual, financial, proprietary etc.).

A conflict of interest /competing interest is defined as "a set of conditions in which professional judgment concerning a primary interest (such as patients' welfare or the validity of research) tends to be unduly influenced by a secondary interest" (DF Thompson, NEJM, 1993).

2.7 Patient Information and Informed Consent

swissethics strongly recommends to exclusively use the swissethics templates for writing the patient information documents and informed consent forms (ICF). They meet the legal requirements of Switzerland. The templates can be downloaded in German, French and Italian from swissethics.ch/templates and checklists/patient information and declaration of consent.

A Guidance document on "How to write comprehensible patient information and consent forms for research" and a "Glossary for medical terms and abbreviations" are available on

swissethics.ch/templates/patient information and declaration of consent. swissethics strongly recommends to read the guidance document before writing the ICF.

If the sponsor or investigator plan to develop an electronic ICF for the study, swissethics strongly recommends to refer to the Guidance document on the development and use of an Electronic Informed Consent (eIC), published on swissethics.ch/topics/position papers, to meet international and national requirements.

Explain that participants will be informed about the study (what, how, by whom) and that consent is obtained from each participant; include the mention of compensation if any. Describe the process specific to the study (see also HRA and Art. 7-9 ClinO), including processes for vulnerable participants (e.g. children assent) or participant lacking capacity of judgment, if applicable.

Check that the layout of the information respects the epicene language, or is it written in an inclusive format. Make sure that the information covers the study's aspect related to "sex and gender" appropriately. If applicable, ensure that the issue of contraception and pregnancy are fully and clearly presented. If applicable, ensure that the issue of contraception and pregnancy are fully and clearly presented.

The PI explains to each participant the nature of the performance study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each participant is informed that the participation in the performance study is voluntary and that he/she may withdraw from the performance study at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment. The participants are informed that he/she can ask any question, and consult with family members, friends, their treating physicians or other experts before deciding about their participation in the performance study. Enough time for reflection is given to the participants. *Important note: Enough time needs to be given to the participant to give an informed consent. The time depends on the specificities of the performance study, the risks, and other factors (see the guidance document "Guideline of swissethics for the time for consideration between information and consent" published on swissethics.ch/topics/position papers, available in German and French). If necessary, specify the time-frame given (give the details in chapter 7.2)).*

The participants are informed that authorised individuals other than their treating physician may examine his/her medical records.

All participants a given a study information sheet and a consent form describing the performance study and providing sufficient information for the participants to make an informed decision about their participation in the performance study.

The formal consent of a participant, using the consent form approved by the CEC, is obtained before the participant is submitted to any study procedure.

The participant should read, understand, and voluntarily agree before signing and dating the informed consent form and is given a copy of the signed document. The consent form is signed and dated by the participant and the PI (or her/his designee, when applicable).

The participants are informed, with their approval, that their personal physicians are informed about the participants' participation in the performance study, when applicable.

The signed consent form it is retained as part of the performance study documents. The participant's medical records are clearly marked to indicate that the participant is enrolled in the performance study.

The participant is provided with well-defined procedures for possible emergency situations related to the performance study. The PI makes the necessary arrangements for emergency treatment. If the clinical performance study involves a blinding/masking technique: *chapter 6.9 gives the procedures for breaking the blinding/masking code in emergency situations and describes under which circumstances unblinding/unmasking is permissible.*

In case prenatal and presymptomatic genetic tests are provided for in the protocol, the ICF must comply with the provisions of Art. 7e ClinO. That is, the study participants must be informed that incidental findings are to be expected as a result of the genetic tests. the following aspects should be addressed and described:

- *Describe how genetic counselling is provided to study participants, when prenatal or presymptomatic genetic testing is performed as part of the study. Describe how study participants will be informed of any incidental genetic findings that directly affect their health.*

Additionally, if applicable, in case of non-genetic incidental findings are expected in the study (e.g., radiological findings) that directly affect the study participants health care provided to the study participants, describe how they will be informed.

In case of in case of vulnerable population the following aspects should be addressed and described:

- *Describe how the legal representative is informed regarding the procedures of the performance study and how his or her consent is obtained;*
- *In the event that the minor and / or participant under tutelage is capable of judgment, describe how their consent is collected in addition to the consent of their legal representative;*
- *In the event of a participant lacking capacity of judgment, mention that signs and symptoms showing that the participant is unwilling to participate in the performance study will result in the participant being excluded from participation.*

Additionally, for performance studies in emergency situations, the following aspects should be addressed and described (a guidance document and templates for writing informed consent forms for clinical trials in emergency situations are available on swissethics.ch/topics/research in an emergency situation, weblink):

- *How the will of the participant can be elucidated without unjustified delay (e.g., patient's provision);*
- *Mention that signs and symptoms showing that the participant is unwilling to participate in the performance study will result in the participant being excluded from participation;*
- *The guarantee that a physician not participating in the performance study, safeguards participant interest and insures proper medical care;*
- *How to get an informed consent for the use of the data from the participants after regaining capacity of judgement;*
- *How to obtain an informed consent from the legal representative of participants that are permanently lacking capacity of judgement, minors or participants under tutelage.*

2.8 Participant privacy and confidentiality

The Sponsor and the PI affirm and uphold the principle of the participants' right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

The investigator has appropriate knowledge and skills in the areas of data security and data protection or is able to ensure compliance by calling in appropriate expertise (Art. 5, ClinO-MD).

Individual participant medical information obtained as a result of this performance study is considered confidential and disclosure to third parties is prohibited.

Specify here how the participants' confidentiality is guaranteed (for example: the assignment to each participant of a unique participant identification number ensures participant confidentiality. Describe how the unique identification number is generated.

Specify in the CPSP that the PI(s)/institution(s) will permit study-related monitoring, audits, CEC study reviews, and regulatory inspection(s), providing direct access to source data / and other study documents.

For data verification purposes, authorised representatives of the Sponsor, the CA or a CEC may require direct access to parts of the medical records relevant to the performance study, including participants' medical history.

2.9 Premature termination or suspension of the performance study

Describe the "stopping rules" of the entire performance study or of the performance study at one or more study sites, and provide a statement that the Sponsor (the CEC and CA) may suspend or terminate the performance study prematurely according to certain circumstances (name the reasons).

The Sponsor may terminate the performance study prematurely, or at a particular study site or suspend the PI, according to following circumstances, *(the following is given as example only, adapt to the specificities of the performance study)*:

- *ethical concerns;*
- *insufficient participant recruitment;*
- *when the safety of the participants is doubtful or at risk, respectively;*
- *when monitoring or auditing identifies serious or repeated deviations on the part of a PI;*
- *alterations in accepted clinical practice that make the continuation of the performance study*

unwise;

- *early evidence of benefit or harm.*

When suspension or premature termination occurs, the Sponsor justifies its decision in writing and promptly inform the other parties with whom it is in direct communication.

When, for any reason, the Sponsor suspends or prematurely terminates the performance study at an individual study site, the Sponsor ensures that the CEC *and CA (applicable for category C performance studies)* is notified. Moreover, when the suspension or premature termination was in the interest of safety, the Sponsor informs all other participating PIs.

The PI, CEC, *or CA (applicable for category C performance studies)* can suspend or prematurely terminate participation in a performance study at the study sites for which they are responsible. The PI and Sponsor keep each other informed of any communication received from either the CEC *or CA (applicable for category C performance studies)*.

When suspension or premature termination occurs, the PI or authorized designee promptly inform the enrolled participants at his/her study site, when applicable. The method and the timing of this communication will depend on the circumstances and the perceived risks.

Procedure for resuming the performance study after termination

In case of the performance study is suspended, detail the processes and requirements needed to restart the suspended study.

If suspension occurred without safety concerns: If the Sponsor, after an analysis of the reason(s) for the suspension and implementation of the necessary corrective actions, decides to lift the suspension, it informs the PI(s), CEC *and CA (applicable for category C performance studies),* of the rationale and provide them with the relevant data supporting its decision.

If suspension occurred on safety grounds: The Sponsor submits new safety information and any modified documents to the CEC *and CA (applicable for category C performance studies)*. The performance study can resume upon reception of CEC *and CA (applicable for category C performance studies)* approval. *(Note: In EU countries, substantial chances are notified with a 38-day holding period before the changes can be implemented. EU CA do conduct a review, but some CA only provide a written statement if there are questions or if there is disagreement).*

The PI or authorized designee inform the participants of the reasons for study resumption.

2.10 Clinical performance study plan amendments

State, who is allowed to amend the CPSP or to provide suggestions for a CPSP amendment. Provide plans for communicating important CPSP modifications (e.g., changes to eligibility criteria, tests and analyses) to e.g., PIs, CEC, CA, study participants, registries, journals, etc.

For category A performance study:

Substantial amendments are implemented only after approval by the CEC (Art. 15 ClinO-MD) The use of waivers from the CPSP is prohibited (Annex XIII, Part A, Art. 2.3.2(r) IVDR).

Under emergency circumstances, deviations from the CPSP to protect the rights, safety and well-being of the participants may proceed without prior approval by the Sponsor and the CEC. Such deviations shall be documented and reported to the Sponsor within 2 days (Art. 34 ClinO-MD).

All non-substantial amendments are communicated to the CEC annually together with the safety report / general progress report of the performance study (Art. 15 ClinO-MD). The report will include any deviations from the CPSP that may have affected the rights, safety or well-being of the participant or the scientific integrity of the clinical trial (ISO 20916).

For category C performance study:

Substantial amendments are implemented only after approval by the CEC (Art. 15 ClinO-MD) and the CA (Art. 20 ClinO-MD). The use of waivers from the CPSP is prohibited (Annex XIII, Part A, Art. 2.3.2(r) IVDR).

Under emergency circumstances, deviations from the CPSP to protect the rights, safety and well-being of the participants may proceed without prior approval by the Sponsor, the CEC and the CA. Such deviations shall be documented and reported to the Sponsor, the CEC, and to the CA within 2 days (Art. 34 ClinO-MD).

All non-substantial amendments are communicated to the CEC annually together with the safety report / general progress report of the performance study (Art. 15 ClinO-MD). The report will include any deviations from the CPSP that may have affected the rights, safety or well-being of the participant or the scientific integrity of the clinical trial (ISO 20916). Non-substantial amendments concerning application documents submitted to the CA must be communicated to the CA as soon as possible (Art. 20 ClinO-MD).

2.11 Deviation from the Clinical Performance Study Plan

Write a statement that the Investigator is not allowed to deviate from the CPSP, except as specified in chapter 2.10.

Describe the procedure for recording, reporting and analysing CPSP deviations.

Describe corrective and preventive actions.

Describe procedures for corrective and preventive actions for repeated and/and or major CPSP deviations, and Investigator disqualification criteria.

If applicable, describe the notification requirements to CA / CEC, and the time frames.

The use of waivers from the CPSP is prohibited (Annex XIII, Part A, Art. 2.3.2(r) IVDR).

Deviations from the approved CPSP that occur during the course of the performance study are documented and explained. Corrective and preventive actions to prevent further deviations are defined.

3. BACKGROUND AND RATIONALE

3.1 Background and Rationale for the clinical performance study

Describe the relevance of the performance study in the context of the state of the art of clinical/diagnostic practice and the proposed benefits of the IVD device under investigation. Set the context by providing a clear explanation of its purpose.

Justify the rationale for the choice of the type and design of clinical performance study (interventional study design or the need for specimens primarily collected for the study which pose additional risks for the participant) to be performed in relation to the intended use of the IVD device under investigation.

Describe the research question, including summary of relevant performance studies (published and unpublished) examining benefits and harms for the intervention / assessment; including disease background, e.g., epidemiology and current standard of care (if relevant).

Any statement that relies on existing knowledge or published information shall be adequately referenced.

Refer to chapter 6.5 and chapter 6.6 for analytical and clinical evidence, resp.

3.2 Risk evaluation (Risk-to-Benefits rationale)

Note: before conducting a performance study, the Sponsor shall undertake and document an assessment of the risks associated with the participation in and/or conduct of the study (risk analysis report). The risk analysis should include or refer to an objective review of published and, when available, unpublished medical or scientific data.

Describe the anticipated adverse device effects.

Describe the anticipated adverse events associated with the study other than those associated with the IVD device, e.g., during specimen collection.

Give the residual risks associated with the performance study, as identified in the risk analysis report.

Describe and discuss measures to control or mitigate the risks (give the reference to the risk analysis report) and how post performance study participants' care is organised.

Indicate the anticipated clinical benefit, as well as the risk-benefit rationale. This shall include an analysis of adverse device effects and any history of modification or recall in relation to safety and clinical performance in relation to both the IVD device under investigation and, when applicable, the comparator(s).

Include harm caused directly by the IVD device, invasive procedures carried out for using the devices, medical consequences of device deficiencies and side effects, wrong diagnostic output (false positive or false negative results), delaying correct screening/ diagnosis/ treatment in participants.

Include harm caused by any additional study procedure (invasive procedure and other procedures which

are not caused by the IVD device, by its use, …) carried out on the participants for research purposes.

For performance studies without immediate benefit to the participants, a rationale should be provided stating how the results of the performance study could be beneficial for future participants due to e.g., earlier and more accurate diagnosis, a better understanding of the disease and improved treatment options, etc.

Note: The risk management process, which includes risk analysis, risk-to-benefit assessment and risk control is described in the standard ISO 14971.

3.3 Justification of the choice of the study population

Describe the choice of the study population and the rationale for it.

Provide information on the representativeness of the investigation population in relation to the target population (Annex XII, art 2.3.2(m) IVDR).

Ensure that the criteria for selecting the persons intended to participate and the trial design allow an appropriate representation of the groups of persons who are relevant for answering the scientific question; in particular, they must take into account the distribution of genders and age groups. The exclusion or intended underrepresentation of relevant groups of persons must be stated and justified (Art. 4a ClinO).

Describe how recruitment of the participants is conducted to ensure sex and gender balance is achieved, or give an explanation why this would not be possible and how this imbalance would impact the scientific validity of the clinical trial result. Refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research) to address "sex and gender" issues in this chapter. If it is considered that "sex and gender" dimensions are not relevant, provide a justification.

For vulnerable participants (e.g., minors, participants' incapable of judgment or participants under tutelage), the following aspects need to be addressed in the CPSP: Rationale for the inclusion of vulnerable participants (i.e., reasons why comparable results / findings cannot be obtained from adults capable of judgment, Art. 11 HRA).

If both vulnerable and non-vulnerable participants are foreseen for recruitment: Describe the aspects of the research question that are specific to the vulnerable participants. Describe in chapter 11, the numbers needed to evaluate those aspects and the sample size calculation, the stratification process for recruitment of the correct number of vulnerable and non-vulnerable participants.

4. OBJECTIVES OF THE PERFORMANCE STUDY

Provide a clear, simple statement describing the overall purpose(s) of the performance study, explaining why the performance study is performed (you can refer to chapter 3.1).

Describe the overall, primary and secondary objective(s) of the performance study in a clear and simple form. The primary objective should be clearly marked as such.

4.1 Primary Objective

Provide one clear, simple statement describing the primary objective of the performance study.

4.2 Secondary Objective(s)

Provide a clear, simple statement describing the secondary objective(s) of the performance study trial.

4.3 Safety Objective(s)

Provide a clear, simple statement describing the safety objective(s) of the performance study.

5. PERFORMANCE STUDY OUTCOMES (ENDPOINTS)

Indicate the claims and the intended performance of the IVD medical device under investigation that are to be evaluated.

Indicate the risks and anticipated adverse devices effects that are to be assessed.

In case of feasibility study, indicate the data needed for further steps of development. Special reasoning and sample sizes may apply for feasibility studies; describe these in chapter 11.

Describe the primary, secondary, and other outcomes (or endpoints), in the corresponding chapters below, including the specific measurements and variables (e.g., blood sugar levels), analysis metrics (e.g., change from baseline, final value, time to event, any evaluation criteria), time point for each outcome etc.

Explain the relevance of the chosen efficacy and safety outcomes.

5.1 Primary Outcome

The primary outcome is the main result that is measured to assess the performance of the IVD device under investigation, or in feasibility studies to guide further steps of development.

Provide a short description of the primary outcome variable and with regard to the performance of the IVD device. Give the rationale for the choice of the outcome.

There is only one primary performance outcome and one primary safety outcome. Separate sample size calculations are carried out for both parameters (performance and safety), the higher n needs to be taken.

Other endpoints are listed under 'secondary endpoint(s)' or under 'other outcomes of interest', as applicable (chapter 5.2 and 5.3, resp.).

Note: The statistical analysis needs to be carried out on each specific population separately. A detailed description of the statistical analysis must be given in chapter 11.

5.2 Secondary Outcome(s)

Provide a short description of the secondary outcome variables and the rationale for the choice of outcomes.

5.3 Other Outcomes of Interest

Provide a short description of other outcome variables of interest. If applicable, describe how 'other outcomes of interest' are assessed in chapter 9.2. If statistical analysis is done, describe it in chapter 11.

5.4 Safety Outcome(s)

Provide a short description of the safety outcome variables referring to e.g., specific adverse events, expected adverse device effects, etc.

6. DESIGN OF THE PERFORMANCE STUDY

6.1 General

Give the rationale for the choice of the type and design of performance study (e.g., blinded, randomized, controlled (comparator), parallel design, etc.), allocation ratio and framework (e.g., superiority, equivalence, non-inferiority, exploratory) to be performed in relation to the intended use of the IVD device under investigation.

Justify the need for an interventional study design or the need for specimens primarily collected for the study which pose additional risks for the participant.

Provide a discussion of the known or potential problems and limitations of the study design.

Describe the measures to be taken to avoid bias (considerations of bias from, for instance, population, test protocol, reference measurement procedure, interpretation and analysis), including when applicable randomization and blinding/masking.

6.2 Concomitant Interventions

When applicable, describe any specific or relevant concomitant care and interventions that are permitted (additional treatments) during the performance study. Their use should be recorded in the CRF. Describe their potential impact on the objectives of the performance study, if any.

6.3 Control (comparator(s), standards, routine

Justify the use and the choice of the control group(s). Describe the control group(s)

Give the scientific and ethical justification for the use and the choice of the comparator(s).

When used, list and describe the comparator(s).

When the comparator is a commercial IVD device, include name and manufacturer, and when applicable, the version or catalogue number. When the comparator is a reference method or "gold standard", provide adequate published references supporting the methodology.

If the use of the comparator deviates from the commercial product. Give the rational and describe all the deviations.

Include a description of the necessary training and experience needed for the use of the comparator(s) use.

6.4 Specimens

Describe the choice of the specimens and the rationale for it.

Describe the specimens' type(s) (e.g., «plasma collected using concentration xyz of the anticoagulant abc »).

Important note: Only specimen types that have been proven to lead to an acceptable analytical performance of the IVD device (validated specimen types) can be foreseen for interventional performance studies. Those foreseen in the CE-marked Instructions for Use (IFU) should be used when the IVD device is CE-marked.

State whether the planned specimen types are foreseen in the CE marked-IFU. In this case do not describe how specimen types have been validated but refer to the IFU (chapter 18)

In case of deviation from the CE-marked IFU, or when the IVD device is not CE-marked, describe how specimen types have been validated.

Describe the method of specimens' collection, when applicable.

When applicable, indicate if left-over specimens are used. Indicate information on use of data out of left-over specimens' banks, genetic or tissue banks, patient or disease registries etc. with description of reliability and representativeness and the statistical analysis approach (you can refer to chapter 11); Give the relevant method for determining the true clinical status of patient specimens.

Describe availability and accessibility of specimens (e.g., left-over specimens ….), when applicable.

Describe the specimen storage conditions (e.g., specimens can't be frozen), handling, processing, transport, and disposal.

Give the volume, quantity of the specimens to be collected and number of participants providing specimens required to be included in the performance study.

Note: a standardized method of capturing and securing the information for each specimen used in the performance study shall be implemented. Study sites shall record required information for all the specimens in the study, e.g., in the 'study sample log'.

Provide information necessary to characterise the specimens (e.g., status of other analytes, concomitant medications, …).

Indicate the necessary training and experience required for the specimens' collection, processing, disposal, as applicable.

No participant's personally identifiable information is included within the Sponsor's records.

6.5 Analytical performance

Describe the analytical performance characteristics such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross reactions (Annex I, Art. 9.1(a) IVDR), with justification for any omission.

You can refer to the analytical performance report and annex it to the CPSP, chapter 18.

6.6 Clinical Performance

Describe the parameters of clinical performance, such as sensitivity, specificity, positive predictive value, negative predictive value, reference intervals, cut-off (Annex I, Art. 9.1(a) IVDR), with justification for any omission.

With the exception of studies using left-over samples, specify the clinical outcomes/endpoints (primary/secondary) used with a justification and the potential implications for individual health and/or public health management decisions.

You can refer to the clinical performance report and annex it to the CPSP, chapter 18.

6.7 Methods for minimising bias

Describe measures to be taken in order to minimise or avoid bias; if applicable describe randomisation, blinding and other measures (e.g., the use of validated questionnaires). You can refer to other chapters in the CPSP, as appropriate.

6.8 Blinding, masking procedures

If the clinical performance study involves a blinding/masking technique describe how this is done.

Indicate the level and method of blinding/masking (e.g., double-blind, open, blinded evaluators and unblinded participants and/or PI(s), care providers, outcome assessors, data analysts, …),

Describe how blinding/masking is guaranteed throughout the performance study.

6.9 Unblinding, unmasking procedures (code break)

If the clinical performance study involves a blinding/masking technique, describe under which circumstances unblinding/unmasking is permissible. Give the criteria for accessing to and breaking the blinding/masking code and the unblinding procedures.

in the case of suspension or premature termination of the clinical performance study, give the criteria for accessing to and breaking the blinding/masking code.

7. PARTICIPANTS PROVIDING SPECIMENS

Describe in the subchapters below the performance study population (participants' providing specimens): information on the performance study population: specifications of the participants, selection criteria, size of performance study population, representativeness of target population and, if applicable, information on vulnerable participants involved, such as children, pregnant women, immuno-compromised or elderly participants (you can refer to chapter 3.3.).

Give an estimated time needed to enrol the needed number of participants (i.e., estimate the enrolment period) and provide plan of actions to be taken if the enrolment goals are not met (chapter 7.2).

Include here a description of the trial settings if relevant (e.g., out-patients, community clinic, academic hospital) and list of study sites/countries where data and specimens will be collected (or reference to where list of study sites can be obtained).

7.1 Inclusion and exclusion criteria for participants providing specimens

Describe in detail the inclusion and exclusion criteria for the participants' eligibility to the performance study. Create a list of criteria and be as specific as possible.

Participants fulfilling all of the following **inclusion criteria** are eligible for the performance study:

- *Informed Consent signed by the participant;*
- *Documented diagnosis of xyz, with genetic testing abc;*
- *Etc. adapt the list and continue as applicable for this performance study.*

The presence of any one of the following **exclusion criteria** will lead to the exclusion of the participant *(following list is given as an example only. Please indicate here the exclusion criteria applicable to the performance study)*:

- *Contraindications and limitations of the IVD device as described in the instructions for use.*

- *Contraindications to the class of IVD device under investigation. Do not merely write a generic sentence here, but clearly state the names of the substances that have a known potential for allergies, include the trade-names where applicable. For example: "Patients with known iodine allergy, including previous reactions to Betadine™ or other iodine-based disinfectants".*
- *Participants lacking capacity to provide informed consent.*
- *Clinically significant concomitant disease states (e.g., renal failure, hepatic dysfunction, cardiovascular disease, etc.),*
- *Known or suspected non-compliance to the study visits' schedule, inability to follow the procedures of the performance study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant,*
- *Drug or alcohol abuse,*
- *Participation in a clinical trial with an investigational drug within the 30 days preceding and during the present investigation,*
- *Previous enrolment into the current performance study,*
- *Enrolment of the PI, his/her family members, employees and other dependent persons,*
- *Etc. adapt the list and continue as applicable for this performance study.*

Note: In line with the recommendations of the EU GCP Inspector's Working Party (web-Link) the inclusion and exclusion criteria must all be mapped individually in the CRF. An overall statement regarding a participant's eligibility in the trial such as 'Did the participant satisfy all study entry criteria?' is not accepted.

The PI or a qualified and authorized designee must assess each individual eligibility criteria and take the final decision to include the participant in the performance study (ICH GCP 4.3.1). This decision is to be documented.

Refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research) to address "sex and gender" issues in this chapter, if relevant.

7.2 Recruitment and screening

Describe how, where and by whom participants are screened / recruited for the performance study.

Note: participants must be given enough time to consider and to council with relatives and experts before they agree to participate in the performance study (see the guidance document "Guideline of swissethics for the time for consideration between information and consent" published on swissethics.ch / topics / position papers).

Indicate the expected duration of the recruitment period.

Provide plan of actions to be taken if the enrolment goals are not met.

Mention details in case of advertisement; describe any screening requirements (e.g., laboratory or diagnostic tests), if the clinical trial foresees a screening visit.

7.3 Randomisation, assignment to trial groups,

Describe the exact randomisation method: unit, allocation ratio, number generation mechanisms, block randomisation, stratification, how this is provided to the study site (central telephone; sequentially numbered, opaque, sealed envelopes) and how concealment of the randomization/assignment list is guaranteed throughout the randomization process.

7.4 Participant compliance with clinical investigation intervention

If the IVD device is used or operated by the participants themselves (for example at their homeplace), describe the procedures for monitoring participants' compliance and the strategies to improve adherence to the performance study, and any procedures for monitoring adherence.

Define non-compliance and how cases of non-compliance should be handled.

7.5 Criteria and procedure for participant withdrawal or discontinuation

Describe the criteria, reasons (e.g., voluntary withdrawal, non-compliance to the study procedures, …)

and procedures when and how participants are withdrawn from the performance study and if and under which circumstances participants will be replaced.

Refer to chapter 9.4 for description of follow-up procedures (e.g., due to withdrawal of informed consent, non-compliance, safety, etc.).

7.6 Accounting for participants

All participants enrolled in the performance study (including those withdrawn from the performance study or lost to follow-up) shall be accounted for and documented. Describe how this is done and documented.

When a participant withdraws from the performance study, the reason(s) shall be recorded; the PI shall make all reasonable efforts to ascertain the reason(s) for a participant's premature withdrawal from the performance study while fully respecting the participant's rights.

Describe efforts taken in case of lost to follow-up. European Considerations are available for ISO 14155 and can be taken by analogy for IVD devices. Reference MEDDEV 2.7/2 rev.2, chapter 7.2 Annex A.7, link.

When applicable (e.g., due to an early performance study withdrawal due to serious adverse event (SAE)), the PI shall ask for the participant's permission to follow his/her status outside the performance study. Describe how this is done and documented.

8. IDENTIFICATION AND DESCRIPTION OF THE IVD DEVICE UNDER INVESTIGATION

8.1 IVD device under investigation

Identify the IVD device, including name, model/type, including software version and accessories, if any, to permit full identification.

If available: Unique Device Identifier (UDI, the UDI system is detailed in Part C of Annex VI IVDR.

Give a statement concerning the regulatory classification of the IVD device under investigation and any accessories and system components that are needed.

Describe the IVD device under investigation and its intended use, clinical test purpose (including description of the analyte(s) and/or marker(s)), and all its components (software, decision algorithms, and accessories) along with supporting scientific literature.

Describe the technical and functional features of the device indicating the features that are covered by the performance study. Describe the metrological traceability of the IVD device.

Describe the target population and intended user.

Describe the intended performance characteristics, when applicable.

Summarise the available clinical experience with relevance to the performance study (published or available unpublished data that should be based on or referred to a systematic review). This shall include an analysis of adverse device effects, benefits, and any history of modification or recall. If none is available, include a statement that there is no available clinical experience to date on the IVD. Also include postmarked experience if applicable.

Indicate the name of the manufacturer, address and full contact details, and the SRN number (Art. 28 IVDR).

8.2 Mode of use of the IVD device under investigation

Give manufacturer's instructions for installation, when applicable.

Describe how the IVD device is used, give the specific medical or surgical procedures involved in the use of the IVD device, and when applicable, any deviation from the commercially available IVD device.

Indicate the necessary training and experience required for the use of the IVD device under investigation and the medical and/or surgical procedures involved in the use of the IVD.

Describe the storage and handling requirements, preparation for use, any pre-use safety or performance checks and any precautions to be taken after use (e.g., disposal, decontamination), when relevant.

If the Manufacturer's instructions for installation and use is a stand-alone document or integrated in the Investigator's Brochure, annex it to the CPSP, chapter 18.

8.3 Labelling, supply (re-supply) and storage conditions

Describe how the IVD device under investigation and the comparator, if applicable, are labelled and are provided to the study site. When applicable, describe logistics of re-supply.

Note: for an IVD device that is not commercially available in the country in which it is being studied, the labelling shall indicate that the IVD device under investigation is exclusively for use in a performance study (ISO 20916). For commercially available IVD devices, a study specific labelling is not required.

Describe how the IVD device under investigation and the comparator, if applicable, are stored (e.g., temperature range, exposure to light, sterile environment, etc.). IVD devices must be kept in a secure, limited access storage area under the recommended storage conditions.

For commercially available IVD devices, "supply, "storage", "return or destruction" are according to standard procedures and may be simply mentioned in the CPSP without specific details.

8.4 Accountability of IVD device (under investigation and comparator)

Describe the procedures for the accountability of IVD device under investigation, including procedures to ensure that access to IVD devices shall be controlled and these devices shall be used only in the performance study and according to the CPSP.

Describe the process for returning unused, expired or malfunctioning IVD devices.

Describe the process for returning IVD devise at performance study termination, when applicable.

The Sponsor keeps records to document the physical location of all IVD devices from shipment to the study site(s) until return or disposal.

The PI or an authorized designee keep records documenting the receipt, use, return and disposal of the IVD medical devices, which include: (when applicable),

a) the date of receipt,

b) the identification of each IVD device (e.g., batch number, serial number or unique code),

c) the expiry date,

d) the date or dates of use,

e) the date on which the IVD devices were returned or disposed of, when applicable, and

f) the date of return of unused, expired or malfunctioning IVD devices, when applicable.

The accountability includes the accountability of the comparator(s).

8.5 Return, Analysis or Destruction of the IVD Device

Provide a statement if the IVD devices are shipped back to the Sponsor disposed/destructed at the hospital at the end of the performance study. Add procedures for preparation and shipment of used IVD devices at the end of the performance study.

For IVD devices already in use at the hospital "return or disposed/destructed" are according to standard procedures and mentioning this in the CPSP is enough (no details needed).

When applicable: In case of IVD device deficiency(ies), including malfunction, usability issues, or inadequacy in the information supplied by the manufacturer including labelling, the IVD devices will be returned to the Sponsor for root-cause analysis of the deficiency(ies).

Add procedures for documenting IVD device deficiencies by the study site and for providing them to the Sponsor.

9. PROCEDURES

Describe all performance study related medical and non-medical procedures participants will undergo during the performance study (Annex XIII, Art. 2.3.2(h) IVDR).

Indicate the medical procedure that deviate from normal clinical practice.

Describe all study related procedures the specimens will undergo during the performance study.

Describe how the participants are trained on the proper use, handling, storage and return of the IVD device under investigation, when it is used or operated by the participants.

*Describe how the participants are informed of any **new significant findings** occurring during the*

performance study, including the need for additional medical care that might be required.

*When applicable, describe procedure for determine when and how **incidental findings** should be reported to the PI and to the participants.*

9.1 Performance study flow chart(s) / table of procedures and assessments

Provide a detailed graph, chart or table of flow of the performance study and for the participant ("assessment schedule") with what is measured and how, grouped according to primary and/or secondary endpoints. Include the allowed time frames for each visit. The flow chart should comprise all procedures during the whole course of the performance study, not only the assessed endpoints.

Give the total expected duration of the clinical performance study.

When applicable, give the expected duration of each participant's participation.

9.2 Assessments of outcomes

In not already described under chapter 5: Describe for each endpoint (performance and safety, as applicable) what variables will be measured / assessed / observed and detail how it will be done.

Describe processes to guarantee data quality (e.g., duplicate measurements, training of assessors; arrangements for device maintenance and calibration).

Provide the rationale or justification to use certain methods and not others etc.

Define the time windows allowed for the assessments.

9.2.1 Adverse events

Recording of adverse event (AE) information, what information needs to be collected: time of onset, duration, resolution, action to be taken, assessment of intensity, relationship with the IVD device and with the procedures of the performance study, expectedness, seriousness. Define specific process to ask the participant at the visits about adverse events, collection of spontaneous reports. You can refer to chapter 10.

Refer to chapter 10 for AE definition and to chapter 10.4 and 10.5 for reporting procedures to CA and CEC.

9.2.2 Laboratory parameters

When applicable, specify laboratory parameters to be assessed; define time-points of assessment; describe sampling if deviating from hospital routine; specify tests to be used (e.g., for pregnancy: blood, urine; urinalysis); describe analysis of specimens: local or abroad, if abroad, describe procedure for shipment, storage until shipment; if not yet known, refer to instruction to be written for the study site staff and to be included in the Laboratory Manual.

Define when abnormal laboratory parameters are considered as adverse events in chapter 10. Refer to chapter 10.4 and 10.5 for reporting procedures to CA and CEC.

9.2.3 Vital signs

When applicable, describe how and when they will be assessed (e.g., heartbeat, blood pressure, body temperature, ECG) (e.g., in supine position after 5 minutes resting).

9.2.4 Assessments in participants who withdrew/drop out from the investigation prematurely

Describe the type and timing of data to be collected for withdrawn participants.

Note: If a participant withdraws and gives the reason(s), this/these shall be recorded. If such withdrawal is due to problems related to the IVD safety or performance, the PI shall ask for the participants' permission to follow his/her status/condition outside the performance study.

Describe follow-up procedures and assessments in participants who withdrew/drop out from the performance study prematurely (e.g., recording of AEs, physical examination, laboratory parameters, vital signs). The information provided here should not contradict the information provided under chapter 9.4.

Define the follow-up period.

Indicate if and how the collected data of participants withdrawing their consent during the course of the performance study is used and analysed. Indicate what happens to the data after the analysis. The details given here must match the information given in the ICF.

In case of withdrawal, after the evaluation the data will be a) anonymised (if possible) or b) not anonymised (i.e., the data remains coded). Please specify which one. The biological material will be anonymised (if possible) or destroyed after evaluation.

The medical follow-up of withdrawn participants, or of participants that drop out from the investigation prematurely is described in chapter 9.4.

9.3 Procedures at each visit

Describe the procedures at each visit: e.g., screening, baseline, visits during intervention, close-out visit, follow-up visits. Include additional tasks as scheduling of next visit, time windows permitted, etc.

Split into subtitles by type of visit, e.g.;

- Screening visit, Day (e.g., -10 to 0): List all exams/tests and other actions to be performed.

- Visit 1, Baseline (Day e.g., 1): List all exams/tests, actions to be performed according to flow chart (chapter 9.1) including also e.g., specimens' collection, scheduling of next visit.

- Visit 2-5 (± indicate the window), if they are identical, otherwise describe each visit separately. Final visit, safety follow-up visits 7-9 (± indicate the window).

9.4 Follow-up of the participants after the termination of the performance study

If applicable, describe the arrangements for the follow-up of the participants after their participation in the performance study has ended.

Describe what medical care or other care (e.g., counselling, …), if any, will be provided for participants after the performance study has been completed, and where it differs from that normally expected for the medical condition in question.

Describe the medical care or other care of withdrawn participants, or of participants that drop out from the investigation prematurely.

Describe the follow-up of participants terminating the performance study (either regularly or prematurely) with reported ongoing SAE, or any ongoing AEs of laboratory values or of vital signs. Describe how and what is done to follow-up on ongoing SAE and AEs, and what is documented.

Note: the Sponsor remains responsible for providing resources to fulfil the obligations from the CPSP and existing agreements for following up the participants enrolled in the performance study

10. SAFETY

Describe plans for collecting, documenting, assessing, reporting, and managing solicited and spontaneously reported AE, adverse device effects (ADE) and other unintended effects of the IVD device under investigation, or of the conduct of the performance study.

Both participant and operator can be exposed to AE. A failure or malfunction of an IVD medical device can lead to indirect or direct harms:

- *Indirect harms occur when inaccurate test results from an IVD medical device (e.g., false positive, false negative) lead to inappropriate patient management decisions, impacting the participant. In the context of a performance study, this would apply, for example, when in an interventional study, the inaccurate test result leads to inappropriate stratification of treatment groups leading to harm.*
- *Direct harms occur when failure or malfunction of an IVD medical device injures a user or other person. In addition, in the context of a performance study, direct harms can also occur when additional specimen material is collected primarily for the purpose of the study, and results in harm to the participant.*

10.1 Terms and definition

In alphabetical order:

Adverse Device Effect (ADE) (ISO 20916)

Adverse event related to the use of an IVD medical device under investigation.

This includes any adverse event resulting from insufficient or inadequate instructions for use, installation,

operation, or any malfunction of the IVD medical device. It also includes any event resulting from use error or from intentional misuse of the IVD medical device.

Adverse Event (AE) (Art. 2(60) IVDR)

Any untoward medical occurrence, inappropriate patient management decision, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in participants, users or other persons, in the context of a performance study, whether or not related to the device for performance study.

This includes events related to the IVD device under investigation or the comparator and to the procedures involved. For users or other persons this is restricted to events related to the IVD device.

Device Deficiency (DD) (Art. 2 Abs 62 MDR)

Inadequacy of a medical device related to its inadequacy in the identity, quality, durability, reliability, safety or performance of a device for performance study, including malfunction, use errors or inadequacy in information supplied by the manufacturer.

The definition includes deficiencies related to the IVD device under investigation or the IVD device used as comparator.

Device Deficiency with Serious Adverse Event (SAE) potential (Art. 76 IVDR; ISO 20916)

Any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.

Malfunction (ISO 20916)

Failure of an IVD medical device under investigation to perform in accordance with its intended use when used in accordance with the instructions for use or CPSP

Serious Adverse Device Effect (SADE) (ISO 20916)

Adverse device effect (ADE) that has resulted in any of the consequences characteristic of a serious adverse event.

Serious Adverse Event (SAE) (Art. 2(61) IVDR)

Any adverse event that led to any of the following:

(a) a patient management decision resulting in death or an imminent life-threatening situation for the individual being tested, or in the death of the individual's offspring,
(b) death,
(c) serious deterioration in the health of the individual being tested or the recipient of tested donations or materials, that resulted in any of the following:
  (i) life-threatening illness or injury,
  (ii) permanent impairment of a body structure or a body function,
  (iii) hospitalisation or prolongation of patient hospitalisation,
  (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
  (v) chronic disease,
(c) foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

Note: planned hospitalization for pre-existing condition, or a procedure required by the CPSP, without a serious deterioration of the health status of the participant, is not considered an SAE

Serious Incident (Art 2(68) IVDR)

Any incident that directly or indirectly led, might have led or might lead to any of the following:

(a) the death of a patient, user or other person,
(b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
(c) a serious public health threat.

Serious public health threat (Art 2(69) IVDR)

Aa event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time.

Unanticipated Serious Adverse Device Effect (USADE) (ISO 20916)

Serious adverse device effect (SADE) which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

10.2 Assessment and categorization of (Serious) Adverse Events and other safety related events

10.2.1 Causal Relationship of SAE

A causal relationship towards the medical device or the procedure of the investigation should be rated by the PI and the Sponsor as follows (MDCG 2024-4):

- **Not related:** The relationship to the device or procedures can be excluded.
- **Possible:** The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible. Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- **Probable:** The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause.
- **Causal relationship:** The serious event is associated with the investigational device or with procedures beyond reasonable doubt.

10.2.2 Adverse events categorization

The adverse events are categorized by the PI and the Sponsor using the following algorithm:

- Does the AE meet the seriousness criteria?
  - No, it is not serious: AE
  - Yes, it is serous: SAE
- If AE, is it device related?
  - No: non-related AE
  - Yes, related AE: ADE
- If SAE, is it device related?
  - No, non-related SAE
  - Yes, it is a possibly, probably, or causally related SAE: SADE
- If SADE, is it anticipated (within expected type, severity and frequency of the complications)?
  - No: unanticipated SADE: USADE
  - Yes: anticipated SADE: ASADE

10.3 Documentation and reporting obligations to the Sponsor

Adapt this chapter to other local requirements in case of international investigations.

10.3.1 Documentation

The PI records every AE and observed DD, together with an assessment as to whether the IVD device or sampling procedure were a cause of the event (ISO 20916)

The documentation of AEs (including SAEs) by the PI includes information about the participant, diagnosis or symptoms, start and stop dates of event, event treatment, event resolution, the PI's assessment of seriousness, causal relationship to IVD device and/or study procedures, and expectedness.

The documentation of DDs includes description of event, start date, IVD device information, action taken with regard to the IVD device under investigation, the PI's assessment whether the DD is a DD with SAE potential, whether the DD led to an AE, the location of the device involved in a DD.

Describe how the information on AEs is systematically collected (e.g., by clinical safety assessment and/or safety lab at the regular visits, as applicable and clinically justified in the context of the specific CPSP).

Specify the follow-up period (also in case of premature withdrawal of the participant from the investigation) and justify if no safety follow-up is needed.

Foreseeable risks:

List here foreseeable AEs, SAEs and anticipated ADEs, together with their likely incidence, mitigation or treatment.

The AEs, SAEs and ADEs, together with their likely incidence, can be presented in a tabular form.

10.3.2 Reporting of safety events and device deficiencies to the Sponsor

Indicate the emergency contact details for reporting safety events and DD to the Sponsor, when applicable.

Describe how, by whom and in what time frame the serious and other reportable AE (health hazards, laboratory abnormalities, pregnancies if applicable, etc.) are reported.

Describe the reporting responsibilities of the PI to the Sponsor in case of a multicentre investigation, when the Sponsor and the PI are not the same person. Similarly, define the reporting roles and responsibilities to the manufacturer when the Sponsor and the PI are the same person.

Describe if there are exceptions for the reporting.

Details the time period in which the PI shall record and report all adverse events and DDs to the Sponsor. For SAEs and DDs, reporting deadlines to the Sponsor normally vary between 24h to 3 days, depending on stage of development and severity of possible consequences (MDCG 2024-4).

The following events are to be reported to the Sponsor by the PI (or authorized designee) without delay, but not later than 3 days, after becoming aware of the event:

- *All SAEs,*
- *Health hazards that require measures,*
- Device deficiencies with SAE potential.

The Sponsor shall define the timelines for reporting of non-serious AEs and DDs without SAE potential, to the Sponsor.

The sponsor shall review the investigator's assessment of adverse events and determine and document in writing the seriousness and relationship to the investigational device and procedures required by the CPSP (ISO 20916). The Sponsor shall evaluate AEs and SAEs with regard to causality and seriousness. Device deficiencies are also assessed regarding their potential to lead to an SAE (DD with SAE potential) (Art 32. ClinO-MD, ISO 20916).

Pregnancies:

Note: Depending of the performance study, reporting of pregnancies may not be necessary.

If reporting is needed, e.g., the pregnancy is due to error/malfunction of the IVD device under investigation, include in the CPSP how pregnancies is reported (usually within 24 hours to the Sponsor), and how occurrence of pregnancy will be handled in the performance study (patient is withdrawn, outcome of the pregnancy should be followed-up, etc.

10.4 Reporting to the Competent Ethics Committee and to Swissmedic for Category C performance studies

Adapt this chapter to other local requirements in case of international investigations.

The Sponsor reports the following events to the CEC and CA within 7 days of awareness (whether that occurred in Switzerland or abroad or 2 days for SAE requiring prompt action for the safety of other study participants, in line with European guidance document MDCG 2024-4:

a. any SAE that has a possible, probable or causal relationship with the investigational device, the comparator device or a test procedure;
b. any DD that could have resulted in SAE under less propitious circumstances or if appropriate action or an intervention had not taken place;
c. any new findings relating to a reported incident as specified in letters a and b.

In order to ensure reporting is not delayed, the Sponsor may provisionally submit an incomplete report (Art. 33 ClinO-MD).

If safety and health hazards that require measures must be taken immediately during the conduct of the investigation, the Sponsor notifies the CEC and Swissmedic within 2 days of these measures and the circumstances which made them necessary (Art. 34 ClinO-MD).

When applicable: For performance studies that are also being conducted or are also due to be conducted in EU or EEA states, the Sponsor notifies the CEC and the CA within 2 days of all prescribed or voluntary safety and protective measures that are being implemented in EU or EEA states and the circumstances that necessitated them (Art. 34 ClinO-MD).

If the performance study is terminated or interrupted for reasons of safety, the report must be submitted to the CEC and Swissmedic within 24 hours. (Art 36, Art. 38 ClinO-MD).

When applicable: For performance studies that are also being conducted in EU or EEA states, the

Sponsor also reports any termination or interruption of the trial in EU or EEA states to the CEC within 24 hours if the termination or interruption was for reasons of safety. (Art 36, Art. 38 ClinO-MD).

The Sponsor provides the CA and the CEC with the documentation specified in chapter 10.3.2 at their request (Art. 32 ClinO-MD).

Periodic safety reporting (Art. 35 ClinO-MD)**:**

Once a year, the Sponsor submits to the CEC and Swissmedic a list of all SAEs and DDs and provides a report on their severity, causal relationship with the device and/or procedure, as well as on the safety of the participants (outcome, event status). The Sponsor informs the CEC and Swissmedic annually about the general progress and status of recruitment of the performance study. Any safety-relevant measures taken by the sponsor or imposed by ethics committees *or authorities anywhere in the world as well as results from other clinical investigations with the investigational device (if applicable)* shall be described. Based on the data presented in the report, the sponsor will draw his/her conclusions regarding the safety of the participants and the continuation of the investigation.

When applicable: For performance studies that are also being conducted in, or are also due to be conducted in, EU or EEA states, the report must include the status of the clinical trial in the states in question and the safety events that occurred abroad.

The cumulative list of reportable serious adverse events and device deficiencies (MDCG 2024-4 Appendix) per cut-off date is submitted in parallel.

10.5 Reporting to the Competent Ethics Committee and to Swissmedic for Category A performance studies

Adapt this chapter to other local requirements in case of international investigations.

For **sub-category A2** performance studies the following events are to be reported to the CEC without delay (Art. 33 ClinO-MD):

a. any SAE that has a causal relationship with the investigational device, the comparator device or a test procedure or where a causal relationship appears entirely possible;
b. any DD that could have resulted in SAE under less propitious circumstances or if appropriate action or an intervention had not taken place;
c. any new findings relating to a reported incident as specified in letters a and b.

In order to ensure reporting is not delayed, the Sponsor may provisionally submit an incomplete report (Art. 33 ClinO-MD).

For **sub-category A1** performance studies, the Sponsor is responsible for ensuring that the CEC is informed, without delay of any SAE for which a causal relationship between the event and the test procedure used in the performance study has been ascertained (Art. 33 ClinO-MD).

For all category A (sub-category A1 and A2) performance studies:

If safety and health hazards that require measures must be taken immediately during the conduct of the investigation, the Sponsor notifies the CEC and Swissmedic within 2 days of these measures and the circumstances which made them necessary (Art. 34 ClinO-MD).

When applicable: For performance studies that are also being conducted or are also due to be conducted in EU or EEA states, the Sponsor notifies the CEC within 2 days of all prescribed or voluntary safety and protective measures that are being implemented in EU or EEA states and the circumstances that necessitated them (Art. 34 ClinO-MD).

If the performance study is terminated or interrupted for reasons of safety, the report must be submitted to the CEC within 24 hours. (Art 36, Art. 38 ClinO-MD).

When applicable: For performance studies that are also being conducted in EU or EEA states, the Sponsor also reports any termination or interruption of the trial in EU or EEA states to the CEC within 24 hours if the termination or interruption was for reasons of safety. (Art 36, Art. 38 ClinO-MD).

The Sponsor provides the CA and the CEC with the documentation specified in chapter 10.3.2 at their request (Art. 32 ClinO-MD).

Materiovigilance reporting to Swissmedic:

The Sponsor is responsible for ensuring that Swissmedic is informed of serious incidents in accordance with Art. 66 MedDO and Art. 59 IvDO.

Materiovigilance reports are not sent to the CEC.

If the Sponsor is the manufacturer of the investigational device or Swiss representative of the

manufacturer:

- *the Sponsor has to send reportable incidents to Swissmedic (materiovigilance@swissmedic.ch) with the form available at www.swissmedic.ch/md-materiovigilance-manufacturers (Art. 66 para. 1 to 2bis MedDO; Art. 59 para. 1-3 IvDO).*

If the Sponsor is not the manufacturer of the investigational device or Swiss representative of the manufacturer:

- *In case of incidents, check whether the event is participant to materiovigilance reporting duties for users acc. to Art. 66, para. 4 MedDO / Art. 59, para. 4 IvDO (using guidance MU680_20_008e_WL). If the clinical investigation/performance study is conducted in a hospital, the materiovigilance contact person of the hospital may also be contacted (Art. 67 para. 2 MedDO / Art. 60 para. 2 IvDO)*
- *The Sponsor has to ensure that reportable incidents are sent to Swissmedic with the form MU680_20_015d_FO (materiovigilance@swissmedic.ch). Guidance and forms are available at www.swissmedic.ch/md-materiovigilance-users.*
- *Users are legally obliged to inform the suppliers of the devices about serious incidents (Art. 66, para 4 MedDO/ Art. 59, para. 4 IvDO).*

Periodic safety reporting (Art. 35 ClinO-MD):

Once a year, the Sponsor submits to the CEC a list of SAEs and DDs and provides a report on their severity, causal relationship with the device and procedure, as well as on the safety of the participants. The Sponsor informs the CEC about the general progress of the performance study, annually. *The safety report and the general progress report can be merged in one single report.*

10.6 Assessment, notification and reporting on the use of radiation sources

In performance studies involving therapeutic or IVD devices capable of emitting ionising radiation and/or medical exams that use ionizing radiation (X-rays, CT scans, PET scans, fluoroscopy, …), the Sponsor shall assess compliance with the dose guidance value in accordance with Art. 45 of the Radiological Protection Ordinance of 26 April 2017. The dose guidance values for investigations without expected direct benefit for the participants is 5 mSv effective dose per year.

If the permitted dose guidance value is exceeded at any time, the Sponsor or the PI notifies the CEC within 7 working days after becoming aware of the event (Art. 39 ClinO-MD).

When applicable, in the case of Category C performance study with IVDs that emit ionising radiation: If the permitted dose guidance value is exceeded at any time, the Sponsor or the PI notifies the CA within 7 working days after becoming aware of the event (Art. 39 ClinO-MD).

Within one year of the completion or discontinuation of the performance study, the Sponsor sends to the CEC *(and for category C add: and to the CA)* a final report containing all information relevant to radiation protection, in particular an estimate of the doses to which the participants were exposed (Art. 39 ClinO-MD).

11. STATISTICAL METHODS

This chapter can be replaced by a detailed statistical analysis plan. The statistical analysis plan must be annexed to chapter 18 of the CPSP.

Describe the statistical considerations done for the performance study, with justification, including power calculation for the sample size, the statistical methods to be employed, the level of statistical significance that will be used, including timing of any planned interim analysis(es) (chapter 11.4.3).

Describe the pass/fail criteria to be applied to the results of the performance study.

Special reasoning and sample sizes may apply for early performance studies [e.g., feasibility studies (ISO 20916)].

Describe the procedures to ensure that all the data is taken into account.

11.1 Hypothesis

If a Null Hypothesis is tested, state explicitly both Null and Alternative Hypotheses in terms of the primary endpoint(s) and justify them in regard of the participant population and specimens.

The stated safety and benefit hypotheses have to be used in the determination of sample size. Relate these hypotheses to the objectives of the performance study.

If hypothesis testing is not used, then discuss how the approach used (e.g., Bayesian methods) will address the objectives.

11.2 Determination of Sample Size

Provide the number of participants planned to be enrolled and the number of specimens, as applicable. Reason for choice of sample size with justification, including a power calculation for the sample size.

If "sex and gender" dimension is of primary interest, does the sample size estimation integrate this aspect?e Are the statistical analyses appropriate?

Provide the estimated number of participants for each study site and investigation arm (if applicable) needed to meet the safety and study objective, how it was determined, including the assumptions made to support the sample size calculations, the power of the investigation, the type I error (one- or two-sided) and the related risk, the clinical justification.

11.3 Statistical criteria of termination of the performance study

When applicable, describe the statistical criteria for the termination of the performance study.

When applicable, describe the 'stopping/go' rules for the suspension of the performance study.

11.4 Planned Analyses

Describe all analyses planned for the performance study. Describe the methods, types and variables and data sets used. When applicable, specify when interim analysis(ses) is(are) done.

Include a statement that analyses of gender differences are planned. If such an analysis is not possible, please state the reasons.

This chapter can be replaced by a detailed statistical analysis plan and referenced in chapter 18 of the CPSP.

11.4.1 Primary and secondary analysis

Describe the datasets to be used for the primary and secondary analyses (i.e., the selection of participants to be included in the analyses (e.g., all eligible participants, all specimens). This applies to all endpoints / outcomes.

Describe the intended primary and secondary analysis, when, how and who does them.

Indicate the pass and fail criteria to be applied to the results of the performance study.

11.4.2 Subgroup analyses

Describe the datasets to be used for the subgroups analyses.

When applicable, describe the intended subgroup analyses, when, how and who does them. Give the hypothesis for each subgroup.

Indicate the pass and fail criteria.

11.4.3 Interim analyses

When applicable, describe the intended interim analysis that will be done, why, when and how and by whom it will be done, taking into consideration their purpose, frequency, timing, scope, statistical procedures, Data Monitoring Committee involvement, and stopping rules (refer to chapter 11.3).

Explain the methods that will be used to adjust for interim analyses, or give a rationale for why adjustment is not necessary.

11.5 Deviation(s) from the original statistical plan

Describe the procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in the CPSP and/or in the final report, as appropriate).

11.6 Treatment of missing, spurious or unused data and drop-outs

When applicable, estimate and give the expected drop-out rate, and number of missing data.

Describe how missing data will be handled (e.g., multiple imputation, last observation carried forward, complete case analysis, consider primary and secondary outcomes…).

Describe how spurious data will be handled.

When applicable, describe how and how often lost-to-follow-up participants are being contacted.

When applicable, describe if dropouts are replaced. All participants/specimens shall be accounted for and documented, including participants withdrawn from the performance study or lost to follow-up. Do not describe here again the efforts taken in case of lost to follow-up but refer to chapter 7.6.

When applicable, describe which data will remain unused and how unused data will be handled (stored, archived, destroyed, …).

12. QUALITY ASSURANCE AND CONTROL

Describe how quality is assured and controlled. The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs and Working Instructions, at all study sites in case of multicentric investigations. Indicate the software used.

The PI is responsible that all people participating in the study are properly trained.

The PI ensures that experience and scientific or clinical knowledge is guaranteed and documented for all members of the study team at the study site to adequately conduct the performance study, including specific training, as applicable to each role. All members of the study team receive specific training on the performance study and such training is documented in the Study Site File.

12.1 Study documentation

Note: Due to the specific nature of IVD medical devices, in order to demonstrate good clinical performance study practices, distinct and separate sets of documentation to that required for other medical devices (such as that described in ISO 14155) are required.

ISO 20916 Annex H describes the type of documentation that should be compiled and maintained in the Investigator's file and Sponsor's file in order to demonstrate good clinical performance study practices. The type of documentation differs according to the type of performance study.

- *studies using left-over / archived specimens or studies where specimens are primarily collected for the purposes of the study and for which the collection procedure pose no additional risks to the participant.*
- *interventional studies or studies where the specimens are primarily collected for the purposes of the study and for which the collection procedure poses additional risks to the participant.*

Describe how the documentation is handled throughout the course of the performance study and at study termination.

For any of the documents, source documents should be maintained throughout the duration of the performance study.

12.1.1 Source data and source documents

Note: Source data is all information in original records, certified copies of original records of clinical findings, observations, device results or other activities in the performance study, necessary for the traceability and evaluation of the clinical performance study (Art 3.45, ISO 20916).

Note: Source document is a printed or electronic document or other media containing source data (example: Hospital records, laboratory notes, test results, patient's surveys, device accountability records, photographic evidence, records kept at the study site, at the laboratories and at the medico-technical departments involved in the clinical performance study (Art. 3.46, ISO 20916).

Describe precisely what is considered the source documents in the performance study and specify what is the source document for each data collected in the CRF, e.g., Hospital records, laboratory notes, test results, patient's surveys, device accountability records, photographic evidence, records kept at the study site, at the laboratories and at the medico-technical departments involved in the clinical performance study.

In case of electronic source data (e.g., from Apps or from automatic recording devices), describe how the data is handled, transferred, stored and accessed by the PI and authorised staff.

Identify data that are directly recorded in the CRF, which is also be considered being source data.

Indicate where source data are kept at the study site.

You can also refer to a separate document ('source data description and source data location') in

chapter 18.

12.1.2 Case Report Forms

Case report forms (CRFs) shall be developed to capture the data for each enrolled participant/specimen as required by the CPSP. The CRFs shall include information on each participant/specimen at commencement, and during the course of the clinical performance study, use of the IVD device and any other relevant information.

Describe how the study data is recorded, e.g., with paper or electronic CRF (p-/e-CRF).

If paper-CRF is used, describe how data is entered into an electronic database for analysis (e.g., double data entry).

No participant's personally identifiable information shall be included within the CRF.

Describe the coding used for the performance study, e.g., participant number in combination with year of birth (see the guidance document published on swissethics.ch "coding of trial participant accepted by swissethics and secure storage of participant identification list").

Note: The person(s) authorized by the PI to enter the data in the CRF must be listed on the delegation log.

If applicable, describe which study data is not recorded in the CRF but recorded by other means (e.g., instrument printouts, etc.).

When it is necessary to amend the CPSP, the Sponsor shall review the CRFs to determine if an amendment of these forms is also necessary.

The CRF is annexed to the CPSP chapter 18.

12.1.3 Storage of biological material and related health data

In the event the participants' personal data of the performance study is stored in a data-registry: add here that the coded data of the participants who consented for the further use of their data (independently of the study specific consent) will be stored in a registry for an undetermined length of time, and the data could be re-used for other research projects (provided previous approval by the CEC).

If applicable, describe for how long and where the specimens and personal data are stored, or state that specimens are destroyed, and data anonymised after the end of the storage period. You can refer to chapter 12.3. In any case, the information provided here must match the information given in chapters 9.2.4 and 12.3.

In the event the specimens are stored in a Biobank, confirm that coded specimens and associated personal data are stored only if the participants' consent for further use has been obtained. This consent is given (or withheld) independently of the participation in the investigation (Art. 17. ClinO).

12.1.4 Archiving of essential clinical investigation documents

All the documents of the performance study must be archived for a minimum of 10 years after regular or premature termination of the performance study.

Describe Sponsor (Art. 40 Abs 1 ClinO-MD) and PI (Art. 40 Abs 2 ClinO-MD) responsibilities.

Indicate location and process for archiving, secure access, etc.

You can refer to Sponsor / study site written Standard Operating Procedures.

12.2 Monitoring and monitoring plan

Give a detailed plan to be followed for monitoring the performance study, including access to source data, list of data and documents to be monitored (e.g., confirmation of quality control results, calibration, etc.) and the extent to which source data will be verified.

Indicate which organisation or person does the monitoring; specify monitor qualification and training. Describe procedure to review the monitoring visit reports, follow-up on monitoring findings and corrective actions.

Alternatively, the extent and nature of monitoring activities and all the details described in the above paragraph, based on the objective and design of the investigation, can be written in a Monitoring Plan. The Monitoring Plan must be annexed to the CPSP chapter 18 (Annex XIII, art. 2.3.2, IVDR).

Provide a statement that the source data/documents are accessible to monitors and questions are answered during monitoring by the PI and the study site staff.

12.3 Data management

Give procedures used for data review, database cleaning, and issuing and resolving data queries.

Give Procedures for verification, validation, and securing of electronic clinical data systems, when applicable.

Give procedures for data retention.

Describe in which form the data is retained after the termination of the performance study (e.g., retained in coded form). If the data is anonymised, describe the procedure of anonymization of the data.

Specify data retention period.

Specify other aspects of quality assurance, as appropriate.

When electronic databases or remote electronic data systems are used, implement written procedures to:

a) establish and document requirements for the electronic data system to receive, transfer and process data – information/data transferred to the Sponsor shall be without personal individual identifiers,

b) verify and validate that the requirements for the electronic data system can be consistently met,

c) ensure traceability, completeness, reliability, consistency and logic of data entered,

d) ensure accuracy of reports,

e) ensure that data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail),

f) maintain a security system that prevents unauthorized access to the data, both internally and externally,

g) maintain a list of individuals who have access to the electronic data system as well as the dates of access and privileges granted to each user,

h) ensure that all completed documents are signed by the Principal Investigator or authorized designee,

i) maintain adequate backup, retention and retrievability of the data, and

j) provide documented training of users on proper use of the system.

It is possible to provide a detailed plan for data management separate from the CPSP. The plan for data management must be annexed to the CPSP chapter 18 (Annex XIII, art. 2.3.3, IVDR).

12.4 Audits and Inspections

The PI or institution support the Sponsor to perform auditing activities and when relevant, ethics committee review and RA inspections.

The PI or institution provide direct access to source data during and after the performance study for Sponsor audits, ethics committee review and RA inspections.

As required, the PI or institution obtain permission for direct access to source documents from the participant and/or hospital administration before starting the performance study.

Describe the frequency and procedures for auditing the investigation, if any, and whether the process will be independent from the PI and the Sponsor. All involved parties must keep the participant data strictly confidential.

13. CONFIDENTIALITY, DATA PROTECTION

The Sponsor and the PI affirm and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals. Individual participant medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited.

Specify here how the participants' confidentiality is guaranteed (for example: the assignment to each participant of a unique participant identification number ensures participant confidentiality).

Describe how the unique identification number is generated.

For data verification purposes (monitoring) the PI or institution provide direct access to source data during and after the performance study to the Sponsor's personnel, or to other personnel designated and authorized by the Sponsor.

The PI or institution provide direct access to source data during and after the performance study for Sponsor audits, CEC review and RA inspections.

Refer to chapter 12.1.1 for description of source data and source documents.

Refer to chapter 14 for publication and communication policy of the results of the study.

14. PUBLICATION AND COMMUNICATION POLICY

Give the publication policy of the results of the performance study, if not addressed in a separate agreement, according to Art. 41 and 42 ClinO-MD and Annex XIII Art. 2.3.2(y,x) IVDR.

Describe plans to communicate the results of the performance study to the participants, healthcare professionals, the public, and other relevant groups (e.g., via a summary in lay language, publication, reporting in results databases, or other data sharing arrangements); anticipate for authorship eligibility guidelines and any intended use of professional writers and, if any plans for granting public access to the full CPSP, participant-level dataset, and statistical code, including who will have ultimate authority over any of the activities.

Mention the protection of trade secrets, if applicable.

Confirm that if gender effects are observed, they will be published in the Clinical Performance Study Report (CPSR). If an analysis is performed but no gender effects are observed, this should also be published.

The Sponsor will enter and publish a summary of the results of the clinical investigation in a public recognized register (as specified in Art. 64 Abs. 1 lit a or b ClinO) *(complete the paragraph as appropriate)*:

a) immediately after submitting the final report *(for completed clinical trials with devices that already bear a conformity marking and were used in accordance with the instructions, or in the event of an early termination or interruption of a clinical trial: in accordance with Article 37)*

or b) at the latest before the device is placed on the market or one year after submitting the final report if the device has not been placed on the market by this point in time. *(for all other completed clinical trials, in accordance with Article 37).*

The Sponsor also ensures that a lay summary of the results is entered in BASEC within the period specified in the paragraph above. The entry is made at least in the national languages of Switzerland in which the study participants were recruited.

If publication of the results is not possible within the specified period for scientific reasons, the sponsor will explain this in the application documents and indicate when publication will take place. Adapt this paragraph accordingly.

The investigator will provide each participant with the lay summary of the results of the clinical investigation at the end of the study, directly. *The investigator should ensure that participants are adequately informed about this in the patient information document and also that they are informed where the lay summary of the results of the clinical investigation will be published online.*

15. FUNDING AND SUPPORT

15.1 Funding

Provide statement of sources and types of financial support for the PI / study site and/or Institution.

If applicable, reference to written agreements or contracts where this information is captured.

15.2 Other Support

Provide brief statement of any other type of support received to conduct the performance study (IVD device, comparator, investigation material, software's, …).

If applicable, reference to written agreements or contracts where this information is captured.

16. INSURANCE

Give proof of insurance cover or indemnification of participants in case of injury, pursuant to Art. 3 ClinO-MD. E.g., "Insurance is provided by the Sponsor and fulfils the legal provision of art. 3 ClinO_MD. A copy of the insurance certificate is filed in Investigator's file and in the Sponsor's file."

Note: Category A1 performance studies involving measures for sampling of biological material or collection of health-related personal data which entail only minimal risks and burden are exempt from liability coverage requirements (ClinO Art. 12). Categories A2 and C performance studies need to document the guarantee of liability (insurance certificate or equivalent guarantee) (ClinO Art. 13).

The insurance must cover damages occurring up to 20 years after the end of the clinical performance study.

The policy value shall be set in accordance with ClinO Annex 2.

It can be referred here to another place where the document is found, e.g., chapter 18 or elsewhere.

17. REFERENCES

Provide a list of the references pertaining and cited in the CPSP.

1. Declaration of Helsinki, Version October 2013 (http://www.wma.net)
2. Federal Act on Research involving Human Beings (Human Research Act, HRA) of 30 September 2011 / Humanforschungsgesetz, HFG Bundesgesetz über die Forschung am Menschen (Bundesgesetz über die Forschung am Menschen, HFG) vom 30. September 2011/ Loi fédérale relative à la recherche sur l'être humain (loi relative à la recherche sur l'être humain, LRH) du 30 septembre 2011 / Legge federale concernente la ricerca sull'essere umano (Legge sulla ricerca umana, LRUm) del 30 settembre 2011
3. Ordinance on Clinical Trials with Medical Devices (ClinO-MD) of 1 July 2020 / Verordnung über klinische Versuche mit Medizinprodukten (KlinV-Mep) vom 1. Juli 2020 / Ordonnance sur les essais cliniques de dispositifs médicaux (OClin-Dim) du 1er juillet 2020 /. Ordinanza sulle sperimentazioni cliniche con dispositivi medici (OSRUm-Dmed) del 1 luglio 2020
4. Verordnung über klinische Versuche mit Ausnahme klinischer Versuche mit Medizinprodukten (Verordnung über klinische Versuche, KlinV) vom 20. September 2013 / Ordonnance sur les essais cliniques hors essais cliniques de dispositifs médicaux (Ordonnance sur les essais cliniques, OClin) du 20 septembre 2013. Ordinanza sulle sperimentazioni cliniche ad eccezione delle sperimentazioni cliniche con dispositivi medici
5. In vitro Devices Ordinance (IvDO) of 4 May 2022 / Verordnung über In-vitro-Diagnostika (IvDV) vom 4. Mai 2024 / Ordonnance sur les dispositifs médicaux de diagnostic in vitro (ODiv) du 4 mai 2022 / Ordinanza relativa ai dispositivi medico-diagnostici in vitro (ODIV) del 4 maggio 2022
6. Medical Devices Ordinance (MedDO) of 1 July 2020 / Medizinprodukteverordnung (MepV) vom 1 Juli 2020 / Ordonnance sur les dispositifs médicaux (ODim) du 1er Juillet 2020 / Ordinanza relativa ai dispositivi medici (ODmed) del 1 luglio 2020
7. Medical Device Regulation (EU) 2017/745 of 5 April 2017 (MDR)
8. In Vitro Diagnostic Medical Device Regulation (EU) 2017/746 of 5 April 2017 (IVDR)
9. MDCG 2024-4 Safety reporting in performance studies of in vitro diagnostic medical devices under Regulation (EU) 2017/746
10. ISO 20916: In vitro diagnostic medical devices — Clinical performance studies using specimens from human participants — Good study practice (www.iso.org)
11. ISO 10993: Biological evaluation of medical devices (www.iso.org)
12. ISO 14971: Application of risk management to medical devices (www.iso.org)
13. WHO, International Clinical Trials Registry Platform (ICTRP)
14. Strahlenschutzverordnung (StSV) vom 26. April 2017 / Ordonnance sur la radioprotection (ORaP) du 26 avril 2017 / Ordinanza sulla radioprotezione (ORaP) del 26 aprile 2017.
15. International Conference on Harmonization (ICH) Guideline for Good Clinical Practice E6(R2).
16. Zz
17. Yy

18. APPENDICES

NOTE: Further relevant information can be found in ISO 20916, chapter 5.5, Annex A and Annex B

Clinical Performance Study Plan (CPSP)

Documents that do frequently change during the course of the investigation can be referenced as «documents provided separately» and listed here.

The section headings can be renamed accordingly.

1. *Investigator's Brochure*
2. *Manufacturer's instructions for installation and use*
3. *Analytical performance report*
4. *Clinical performance report*
5. *General Insurance Conditions, insurance certificate*
6. *List of norms*
7. *List of study sites / PIs (List of countries or centres where data will be collected)*
8. *Case Report Form*
9. *Monitoring Plan*
10. *Statistical Plan*
11. *Other material handed over to the participants*