

**Information sheet**  
**Performance studies of IVD**

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## List of contents

|          |   |           |
|----------|---|-----------|
| <b>1</b> | <b>Objective</b> .....  | <b>3</b>  |
| <b>2</b> | <b>Introduction</b> .....   | <b>3</b>  |
| <b>3</b> | <b>Legal basis, standards, and guidances</b> .....  | <b>4</b>  |
| 3.1      | Legal texts .....   | 4         |
| 3.2      | Guidance documents, templates, international conventions .....  | 4         |
| <b>4</b> | <b>ISO 20916 standard</b> .....   | <b>5</b>  |
| <b>5</b> | <b>Approval of performance studies of IVD</b> .....   | <b>5</b>  |
| 5.1      | Study categories and responsible authorities.....   | 5         |
| 5.2      | Applications to Swissmedic for the approval of category C interventional performance studies (pre-market) ..... | 8         |
| 5.2.1    | First submission to Swissmedic of an approval application .....   | 8         |
| 5.2.2    | Validation.....   | 9         |
| 5.2.3    | Review and approval .....   | 9         |
| 5.2.4    | Rejection, restrictions, conditions .....   | 9         |
| 5.2.5    | Fees .....  | 10        |
| 5.3      | Submissions to Swissmedic for combined studies .....  | 10        |
| 5.4      | Radioactive substances, ionising radiation, radiation protection .....  | 11        |
| <b>6</b> | <b>Review and surveillance activities by Swissmedic</b> .....   | <b>11</b> |
| 6.1      | Frequent objections .....   | 11        |
| 6.2      | Inspections .....   | 12        |
| <b>7</b> | <b>Submissions during performance studies (reporting duties, notification duties, approvals)</b> .....          | <b>12</b> |
| 7.1      | Category A performance studies .....  | 12        |
| 7.1.1    | Reporting duties to Swissmedic.....   | 12        |
| 7.1.2    | Reporting duties to ethics committees .....   | 13        |
| 7.2      | Category C interventional performance studies .....   | 13        |
| 7.2.1    | Modifications (amendments).....   | 14        |
| 7.2.2    | Safety (risks and safety measures).....   | 16        |
| 7.2.3    | Serious adverse events (SAEs) and device deficiencies.....  | 16        |
| 7.2.4    | Annual report.....  | 19        |
| 7.2.5    | End, premature termination, interruption of the study .....   | 20        |
| <b>8</b> | <b>Data retention requirements</b> .....  | <b>20</b> |
| <b>9</b> | <b>Databases used in Switzerland</b> .....  | <b>20</b> |

|   |   |           |
|---|---|-----------|
| <b>10</b>   | <b>Sponsors with registered offices abroad, submissions by third parties.....</b> | <b>20</b> |
| <b>11</b>   | <b>Liability in the case of damage, coverage in the form of insurance .....</b>   | <b>21</b> |
| <b>12</b>   | <b>Penal provisions.....</b>  | <b>21</b> |
| <b>ANNEXES .....</b>  |   | <b>22</b> |
| <b>A1: Recording of adverse events and device deficiencies .....</b>              |   | <b>22</b> |
| <b>A2: Risk mitigation measures .....</b>   |   | <b>26</b> |
| <b>A3: Patients lost to follow-up, mortality, permanent impairment.....</b>       |   | <b>26</b> |
| <b>A4: Inclusion and exclusion criteria, particularly vulnerable persons.....</b> |   | <b>27</b> |
| <b>A5: Reflection period when consenting for invasive procedures .....</b>        |   | <b>29</b> |
| <b>A6: How to make a submission .....</b>   |   | <b>29</b> |
| <b>A7: Special groups of products .....</b>                                       |   | <b>30</b> |
| <b>Contacts in case of questions .....</b>  |   | <b>31</b> |

## 1 Objective

In vitro diagnostic medical devices and accessories for such devices are referred to as 'IVD' in this information sheet. This information sheet is valid under the new regulation that comes/came into force on 26 Mai 2022 and it is intended for sponsors of performance studies of IVD, contract research organisations (CROs), and investigators. It provides guidance on the approval process, reporting requirements of sponsors, and the surveillance by the Swiss Agency for Therapeutic Products, Swissmedic.

This document does not cover clinical investigations of medical devices that are not IVD. For clinical investigations, please refer to information sheet [BW600 00 0015e MB](#).

For submissions regarding a combined study, where an interventional performance study of an IVD and a clinical trial of a medicinal product/ATMP<sup>1</sup> are conducted in parallel, please also refer to information sheet [BW600 00 017e MB](#).

## 2 Introduction

The Swiss Human Research Act (HRA, SR 810.30) regulates biomedical research on human subjects and is based on internationally recognised principles. It shall in particular ensure that

- the investigational medical device must demonstrate a sufficient stage of development for its intended use on humans.
- the investigation must satisfy scientific and ethical criteria
- the dignity, personality and health of human subjects must be protected.

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<sup>1</sup> Advanced therapy medicinal products (ATMP) include, for example, gene therapy products, somatic cell therapy products, tissue engineered products, RNA products.

IVD include, for example, reagents, calibrators, control material, kits, instruments, apparatus, equipment, software and systems.

### 3 Legal basis, standards, and guidances

The information in this document is in summarised form. For that reason, please consult the valid legal texts, standards and guidelines in order to appraise a specific situation.

#### 3.1 Legal texts

The following legal texts describe requirements applicable to performance studies of IVD in Switzerland:

- HRA: Swiss Federal Act on Research involving Human Beings (Human Research Act; SR 810.30)
- TPA: Swiss Federal Act on Medicinal Products and Medical Devices (Therapeutic Products Act; SR 812.21)
- ClinO-MD: Swiss Ordinance on Clinical Trials of Medical Devices (SR 810.306).
- HRO: Ordinance on human research with the exception of clinical trials (SR 810.301)

These texts extensively refer to European requirements [Regulation (EU) 2017/746 (the European in-vitro-diagnostic device regulation, IVDR)] and implementing regulations (such as implementing regulation 2022/1107 on common specifications for certain class D in vitro diagnostic medical devices).

For selected aspects they also refer to requirements of the Swiss Ordinance on Clinical Trials in Human Research (ClinO; SR 810.305), the Swiss Ordinance on Organisational Aspects of the Human Research Act (HRA Organisation Ordinance, OrgO-HRA; SR 810.308), and the Swiss Ordinance on In vitro Diagnostic Medical Devices (IvDO, SR 812.219).

You can find Swiss legal texts in German, French and Italian together with English translations at [www.fedlex.ch](http://www.fedlex.ch). As English is not an official language of the Swiss Confederation, English translations of legal texts are for information purposes only and have no legal force.

#### 3.2 Guidance documents, templates, international conventions

- Swiss documents
  - Guidance and templates published by Swissmedic: [www.swissmedic.ch/ci](http://www.swissmedic.ch/ci).
  - Guidance and templates published by cantonal ethics committees: [www.swissethics.ch](http://www.swissethics.ch).
- European documents: Guidance under the IVDR is published at [ec.europa.eu/health/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance\\_en](https://ec.europa.eu/health/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en).
- Standards:
  - ISO 20916, In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice

- Other standards that reflect the status of science and technology with regard to the development and manufacturing of IVD
- International conventions: Declaration of Helsinki, Biomedicine Convention, *Additional Protocol* by the Council of Europe to the Biomedicine Convention, CIOMs Guidelines, etc.

## 4 ISO 20916 standard

*Art. 3 to 5 ClinO-MD, Chapters 2 and 4 ClinO-MD; Art. 67, Annexes XIII and XIV of Regulation (EU) 2017/746*

Standard ISO 20916 describes principles relevant to clinical performance studies of IVD using specimens from human subjects. It defines internationally recognised terms, describes the content of the documents necessary and the obligations of involved persons. The standards describes ethical considerations, study planning, site initiation, conduct, close-out and auditing.

For clinical trials involving particularly low risks, certain deviations are possible, particularly for post-market trials. However, the protection of the participants and data quality and security must not be affected by such deviations.

The sponsor is required to address compliance to the standard and disclose any deviations from the standard in the following documents: Clinical Performance Study Plan (CPSP)<sup>2</sup>, 'list of standards'<sup>3</sup>, Swissmedic approval application form.

## 5 Approval of performance studies of IVD

### 5.1 Study categories and responsible authorities

*Art. 2-2a, 6-7, 16-18, 33-34, 38-39, 42, and Annex 1 ClinO-MD*

a) Terms and definitions:

- 'Clinical trial' in Swiss legal texts is an umbrella term used for clinical investigations of medical devices, performance studies of IVD, clinical trials of medicinal products, and clinical trials of other interventions (e.g. surgical interventions, other therapies).
- A 'performance study' is a study undertaken to establish or confirm the analytical or clinical performance of an IVD.
- An 'interventional performance study' is a performance study where the test results may influence patient management decisions and/or may be used to guide treatment

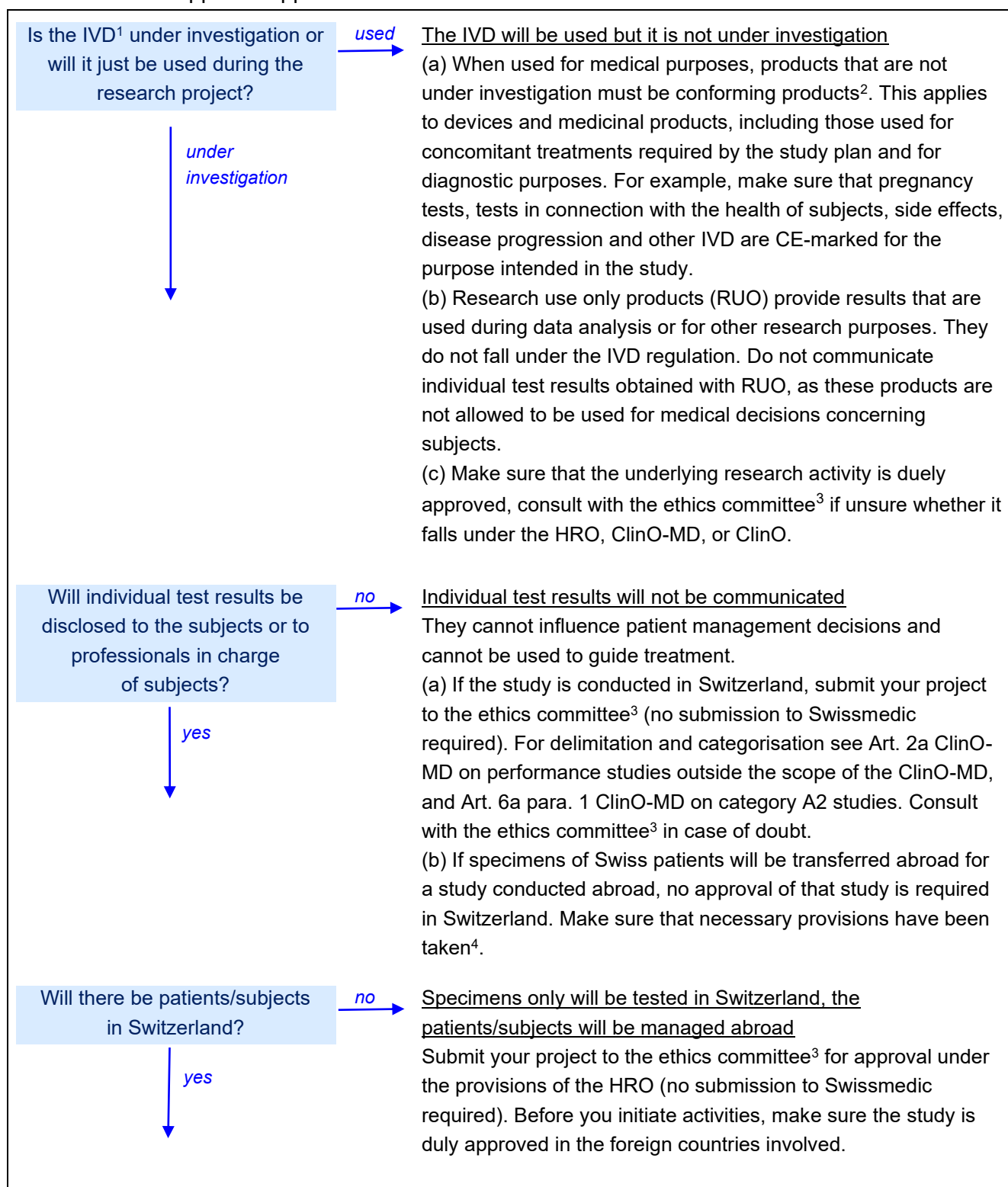
b) Applicable procedures for performance studies

The Swiss legislation distinguishes between different types of research. Below, you can find a decision tree showing the type of research and to which institution you have to file an approval application. In case of doubt, contact the cantonal ethics committee, which in Switzerland is the responsible entity for the delimitation and categorisation of research projects.

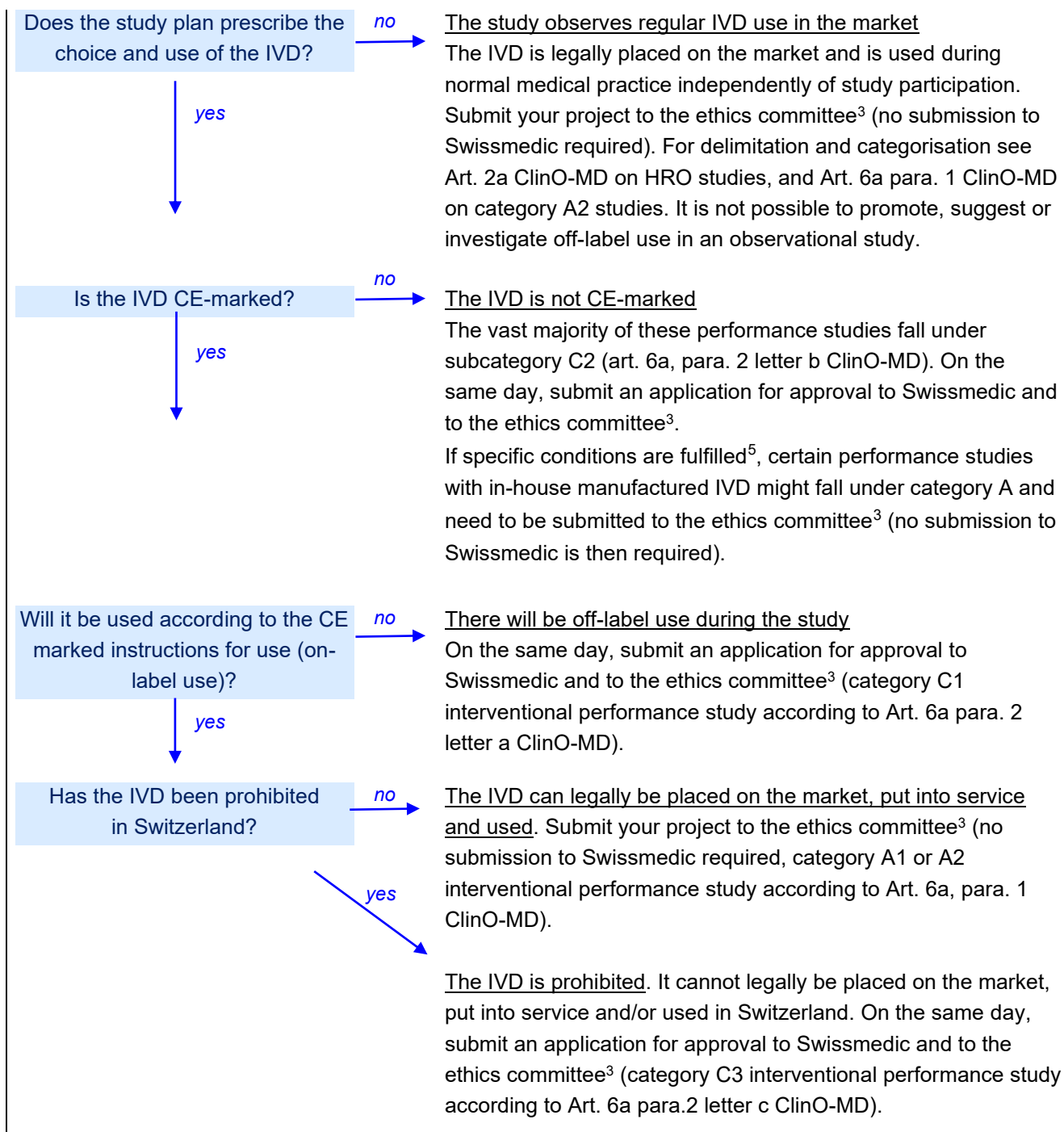
<sup>2</sup> Expected contents of a CPSP are listed in Annex XIII of the IVDR, and in the Annex to ISO 20916.

<sup>3</sup> A template for the list of standards is available at [www.swissmedic.ch/ci](http://www.swissmedic.ch/ci).

Decision tree for approval applications







<sup>1</sup> The IVD can be used alone, or used as part of a system, including software (e.g. an app). Refer to the IVDO for definitions and exceptions. Consult information sheet BW630\_30\_007e\_MB (Medical Device Software) and the European guidance document MDCG 2019-11 in order to determine whether a software is an IVD.

<sup>2</sup> See annex A7 of this information sheet (BE600\_00\_016e\_MB) for guidance on interventional performance studies of IVD manufactured and used in the same healthcare institution.

<sup>3</sup> The application for the clinical trial is submitted to the ethics committee responsible for the investigator. In a multicentric clinical trial the application is submitted to the lead ethics committee responsible for the coordinating investigator. The coordinating investigator is the individual with responsibility in Switzerland for coordinating the investigators responsible for the various trial sites in Switzerland. The list of ethics commissions that details the cantons for which they are responsible can be found here: [www.swissethics.ch/en/ethikkommissionen](http://www.swissethics.ch/en/ethikkommissionen).

<sup>4</sup> You can find templates for material transfer agreements on the website of the [Swiss Biobanking Platform](http://www.swissbiobankingplatform.ch). On the website of [swissethics](http://www.swissethics.ch) you can find a template for a general consent for specimens taken in the clinical

routine, and a template for a study specific informed consent form for specimens taken specifically for the study ([www.swissethics.ch](http://www.swissethics.ch) > Templates > Patient information and Declaration of consent). Please contact the cantonal ethics committee in case of doubt.

<sup>5</sup> See annex A7 of this information sheet (BW600\_00\_016e\_MB) for guidance on interventional performance studies of IVD manufactured and used in the same healthcare institution.

## 5.2 Applications to Swissmedic for the approval of category C interventional performance studies (pre-market)

*Arts. 16-20 and Annex 1 ClinO-MD; Art. 54 TPA; FeeO-Swissmedic*

### 5.2.1 First submission to Swissmedic of an approval application

|  |
|--|
| First submission of an approval application  |
| Use the form <a href="#">BW610_10_024e_FO</a> . The form also contains a list of required documents. See annex A6 for instructions on how to create an eDok and submit an application. |

#### *EMDN code for medical devices:*

In the approval application form, you are required to enter the European Medical Device Nomenclature (EMDN) code applicable to the devices. The EMDN has been published by the European commission and is available free of charge at <https://webgate.ec.europa.eu>. You can also consult a questions and answers document on EMDN published by the European commission (*md\_q-a\_emdn\_en\_0.pdf*).

#### *Simplified review:*

Under the conditions listed in Art. 17 para. 2 ClinO-MD, you may ask Swissmedic to perform a simplified review of your submission:

1. The performance study falls under category C1 or C2 and concerns the investigation of an IVD classified as risk class A or B according to Art. 14 IvDO<sup>4</sup>.
2. The use of the investigational IVD is at most associated with minimal risks to the subjects.
3. The investigators have agreed in written form to inform the Sponsor without delay of all serious adverse events or other (new) circumstances that could threaten the safety of subjects or device users according to Art. 32 ClinO-MD (see also sections 7.2.2 and 7.2.3 of this information sheet).
4. The Sponsor has a risk management system in place to monitor safety.

To check if your project meets these conditions and to apply for a simplified review, please complete and submit the form [BW610\\_10\\_025e\\_FO](#) in addition to the form [BW610\\_10\\_024e\\_FO](#) (active pdf format, some questions will pop up as you fill in the fields).

In case Swissmedic deems the application for a simplified review to be unsubstantiated or unjustified, you will receive a preliminary letter from Swissmedic (explaining that a rejection of the application for simplified review is foreseen, including the reasons). Upon receipt of the preliminary letter, you will have the opportunity to clarify any misunderstandings, submit corrections and missing information.

<sup>4</sup> Consult the latest revision of [MDCG 2020-16](#) for guidance of classification of IVD.



You will also have the option to withdraw the application for simplified review and switch to a regular review of the submission (fees for regular reviews will then be applicable, see below) or the option to withdraw the application for the performance study altogether. Swissmedic will initiate a regular review only after you have submitted a request for a regular review.

#### *Incomplete submissions:*

In case of incomplete requests, stringent deadlines apply for the end of the application. Please make sure you or your deputy will be available for handling requests after the submission.

While the following documents are essential, they are regularly missing in applications, leading to delays. Please make sure you submit the following documents, they need to show the name of the investigational device and identification of exact models and versions that are foreseen in the performance study:

- List of applicable standards, includes information on applicable EU common specifications<sup>5</sup>, and the GSPR information. A template for the list of standards and GSPR information is available at [www.swissmedic.ch/cj](http://www.swissmedic.ch/cj) > EN > Forms and templates.
- The statement of the manufacturer according to Annex XIV point 4.1 of the IVDR, and declaration for access of Swissmedic to additional technical documents during 10 years (dated and signed by the manufacturer).
- For category C performance studies of IVD emitting ionising radiation, please also submit the permit(s) of SFOPH according section 5.4 of this information sheet or a copy of your application.

### **5.2.2 Validation**

A formal check of every new application will be carried out within 10 days to ensure that the performance study falls under the competence of Swissmedic and that documents have been provided as required. Submissions that fail the validation step are considered to be incomplete and will not be processed by Swissmedic. In such cases, Swissmedic requests you to complete the information/documentation within 10 days. If needed, you may request an extension of up to 20 days. Swissmedic will acknowledge the successful validation in writing, with confirmation that the application is proceeding to the content review stage.

Always send additional submissions to Swissmedic and to the ethics committee (on the same day).

### **5.2.3 Review and approval**

During and/or after the content review, Swissmedic can ask for additional information. If a positive assessment is possible on the basis of the documentation submitted, Swissmedic will inform you and wait for the decision of the cantonal ethics committee. Swissmedic is only allowed to approve a performance study after ethics committee approval.

### **5.2.4 Rejection, restrictions, conditions**

If a positive assessment is not possible, you will receive a preliminary decision within 45 days of the validation acknowledgment of the application. The review of the contents by Swissmedic may, in

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<sup>5</sup> The EU implementing regulation 2022/1107 introduced common specifications for certain class D IVD. Please regularly check if other common specifications have been published.

certain cases, take up to 65 days (for first-in-man investigations or manufacturing using a new procedure). The cantonal ethics committee carries out its review independently. Swissmedic and the ethics committee will therefore send separate letters to you.

The two preliminary decision letters (of Swissmedic and of the ethics committee) will list the findings leading to rejection, restrictions or conditions, any missing information that must be provided, references to the current requirements.

Based on the two letters, you can clarify any misunderstandings, submit any missing information, and will also be allowed to correct application documents and resubmit these to Swissmedic and the cantonal ethics committee within approximately 30 calendar days. Please make sure you submit the same information and updated document versions on the same day to both institutions.

You may contact Swissmedic, if necessary, to ask questions regarding the identified shortcomings and discuss required changes. If issues cannot be addressed in due time, you can either request Swissmedic and the ethics committee for an extension of the deadline, or retract the application. After a retraction or a rejection, a new submission with corrected documents is possible at any later point in time.

At the end of the approval procedure, you will receive letters of decision.

### 5.2.5 Fees

The flat rate fee for handling an application for the approval of an interventional performance study is CHF 5000.- for a regular review, CHF 1500.- for a simplified review and CHF 1000.- for a substantial modification (FeeO-Swissmedic). The fee will be invoiced by Swissmedic. Relevant additional workload will be invoiced at a rate of CHF 200.- per hour, for example in case of shortcomings and corrections.

Academic sponsors may apply for an 80% reduction of the flat rate fee. To be eligible for the fee reduction, the sponsor must confirm that it does not receive financial support for the conduct of the clinical trial (or parts thereof) from commercial "for profit" sources. Sponsors who receive financial support from non-commercial funding sources, such as university funds, the Swiss National Science Foundation, foundations or Innosuisse, may still apply for a fee reduction.

To apply for the reduction please complete the following documents:

- [BW610\\_10\\_029e FO Application fee reduction.pdf](#) and
- [BW610\\_10\\_030e VL Appliation fee reduction selfdeclaration.docx](#)

Place both documents in folder 00.00\_Swissmedic\_forms of your submission eDok as described in Annex A6.

## 5.3 Submissions to Swissmedic for combined studies

In a combined study, a performance study of an IVD and a clinical trial of a medicinal product or ATMP are conducted in parallel. The application procedure for combined studies is described in information sheet BW600\_00\_017e\_MB.

## 5.4 Radioactive substances, ionising radiation, radiation protection

For performance studies of IVD emitting ionising radiation, requirements of the Swiss Radiological Protection Ordinance (RPO, RS 814.501) are mandatory for involved personnel and a permit of the Federal Office of Public Health (SFOPH) is required for imports and laboratories in Switzerland. A permit can be requested and additional information are available at

[www.bag.admin.ch/bag/en/home/gesetze-und-bewilligungen/gesuche-bewilligungen/bewilligungen-aufsicht-im-strahlenschutz.html](https://www.bag.admin.ch/bag/en/home/gesetze-und-bewilligungen/gesuche-bewilligungen/bewilligungen-aufsicht-im-strahlenschutz.html)<sup>6</sup>. Questions can be sent to the Radiation Protection Division of SFOPH (str@bag.admin.ch).

According to Annex 1 number 4 ClinO-MD, the permit has to be submitted to Swissmedic for approval of a category C interventional performance study. Submit either the permit or a copy of your approval application form to SFOPH.

Other information listed in annex 1 numbers 4 and 5 ClinO-MD: Other information are usually not applicable to performance studies and need not be submitted, except if ionising radiation is applied to the subjects.

## 6 Review and surveillance activities by Swissmedic

*Art. 54, 54b and 66 TPA; Art. 3 para 1 section f and Art. 17 ClinO-MD; Arts. 46-48 ClinO*

In order to approve category C interventional performance studies, Swissmedic checks the status of the fulfilment of General Safety and Performance Requirements (Annex I of Regulation (EU) 2017/746), if the product risks are duly considered in the performance study, and if the product data is in line with current scientific knowledge and correctly indicated in the protocol.

It is mandatory for sponsors of interventional performance studies to operate an appropriate quality assurance system and check the following (not a complete list):

- whether all duties have been assigned to specific persons,
- whether written procedures are available and up to date,
- whether the reporting duties, notification duties and approval requirements for Switzerland are correctly implemented in the written procedures,
- whether the job descriptions of personnel are complete and up to date,
- whether written contracts are available with external parties,
- the appropriateness of the basic and advanced training of involved personnel.

### 6.1 Frequent objections

In category C clinical trials the following aspects have recurrently led to objections. Additional information regarding each of these aspects can be found in the annex:

- CRF for documentation of adverse events and device deficiencies
- Risk reduction measures
- Handling of mortality, disabilities, patients lost to follow-up
- Inclusion and exclusion criteria, particularly vulnerable persons

<sup>6</sup> <https://www.bag.admin.ch/bag/de/home/gesetze-und-bewilligungen/gesuche-bewilligungen/bewilligungen-aufsicht-im-strahlenschutz.html>

- Reflection period when consenting for invasive procedures

## 6.2 Inspections

Like other authorities in Europe, Swissmedic may carry out inspections. Performance studies of all ClinO-MD categories, compliance with all requirements, and all companies, institutions and persons involved may be inspected. If necessary, Swissmedic may withdraw or suspend an approval that has been granted, or make the continuation of a study dependent on additional conditions.

## 7 Submissions during performance studies (reporting duties, notification duties, approvals)

Sponsors must send spontaneously and without solicitation information to Swissmedic and the ethics committee. The following sections describe duties of the sponsor in regard to Swissmedic.

Requirements in regard to cantonal ethics committees are not addressed in this information sheet; please follow the instructions of the cantonal ethics committees.

Fulfilment of statutory reporting duties needs to be organised as part of the sponsor's quality assurance system (see chapter 6 of this information sheet).

### 7.1 Category A performance studies

*Art. 32-39 ClinO-MD; Art. 59 para. 4 IvDO; Art. 60 para 2 IvDO*

#### 7.1.1 Reporting duties to Swissmedic

- Materiovigilance reporting to Swissmedic is mandatory for category A performance studies if devices are CE-marked.
- If the sponsor is the manufacturer of the investigational device or Swiss representative of the manufacturer: According to Art. 59 para. 1 to 3 IvDO, the sponsor has to send reportable incidents to Swissmedic. Use the form available at [www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas/hersteller---inverkehrbringer.html](http://www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas/hersteller---inverkehrbringer.html) and send it to [materiovigilance@swissmedic.ch](mailto:materiovigilance@swissmedic.ch).
- 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 subject to materiovigilance reporting duties for users (Art. 59 para. 4 IvDO). Use the guidance [MU680 20 008e WL](#) for checking reporting duties. If the performance study is conducted in a hospital, you can also ask the materiovigilance contact person of the hospital (Art. 60 para. 2 IvDO). The sponsor has to ensure that reportable incidents are sent to Swissmedic. Use the form [MU680 20 015d FO](#) and send it to [materiovigilance@swissmedic.ch](mailto:materiovigilance@swissmedic.ch). The guidance and the form are available at [www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas/users---operators.html](http://www.swissmedic.ch/swissmedic/en/home/medical-devices/reporting-incidents---fscas/users---operators.html). Additionally, please note that users are legally obliged to inform the suppliers of the devices about serious incidents (Art. 59 para. 4 IvDO).

### 7.1.2 Reporting duties to ethics committees

- Consult information at [www.swissethics.ch](http://www.swissethics.ch) for preparing and sending reports to the ethics committee.
- Consult Art. 33 ClinO-MD for correct reporting of serious adverse events and device deficiencies with an SAE potential to the ethics committee. Art. 33 para. 1 describes reporting in category A2 performance studies, Art. 33 para. 6 in category A2 performance studies. Use the form [BW610 20 024e FO](#).
- For safety and protective measures, annual reports and final reports, refer to Art. 35 to 37 and Art. 39 ClinO-MD.

### 7.2 Category C interventional performance studies

Table: Overview of submissions after initial approval of a pre-market interventional performance study.

| Type of submission  | Deadlines   |
|---|---|
| Modifications (Art. 15 and 20 ClinO-MD) <ul style="list-style-type: none"> <li>- requiring approval</li> <li>- requiring notification</li> </ul>  | Substantial modifications can be submitted anytime.<br>Note: If safety and protective measures are necessary, such as a temporary suspension of product use, they must be taken immediately and notified to Swissmedic and the ethics committee. Modifications can be submitted later on.<br><br>Submit non-substantial modifications to Swissmedic asap.<br>Submit to the ethics committee either together with the next annual report or asap according to the document ' <i>Substantial modifications to clinical investigations of medical devices</i> ' <sup>1</sup> |
| Reportable SAE and device deficiencies (Art. 33 ClinO-MD)   | 7 days  |
| Safety and protective measures (Art. 34, 36 and 38 ClinO-MD) <ul style="list-style-type: none"> <li>- temporary halt or premature termination on safety grounds (Art. 36 and 38 ClinO-MD)</li> <li>- other measures (Art. 34 ClinO-MD)</li> </ul> | 24 hours<br><br>2 days  |
| Annual report (Art. 35 and 38 ClinO-MD)   | Not later than 1 year after the date of approval / the last annual report   |
| Interruption and premature termination (Art. 36 and 38 ClinO-MD) <ul style="list-style-type: none"> <li>- on safety grounds</li> </ul>  | 24 hours <sup>2</sup>   |

|  |   |
|--|---|
| - not on safety grounds  | 15 days <sup>2</sup>  |
| End of the performance study in Switzerland <sup>3</sup><br>(Art. 36 ClinO-MD)   | 15 days   |
| Final report and summary for lay persons (Art. 37 and 38 ClinO-MD)<br>- after regular study end<br>- after interruption or premature termination | Within 1 year, exceptions are possible if motivated by scientific reasons <sup>4</sup><br>Within 3 months |
| Radiation incident (Art. 39 ClinO-MD, the permissible dose guide value has been exceeded in a subject)   | 7 days  |

1 Available at [www.swissethics.ch](http://www.swissethics.ch)

2: In case of multiple Swiss centres, send the information to all ethics committees involved.

3: Last patient last visit, except if defined otherwise in the CIP

4: The scientific reasons and the deadline need to be described in the CIP

### 7.2.1 Modifications (amendments)

*Art. 15, 20 and 48 ClinO-MD; FeeO-Swissmedic*

Modifications require Swissmedic approval/notification as well as ethics committee approval/notification. Before submitting a modification, please check which documents and what information has already been provided to Swissmedic, which of these are affected by modifications, and if the modifications must be considered substantial. You only need to submit documents that are new or have been modified.

For modifications, you need to submit the following documents to Swissmedic:

- A cover letter explaining the reason for the modification.
- Documents affected by the modification, with all modifications compared to the earlier version highlighted in the text. Please only submit the versions with the modifications highlighted/track-changed in the text; clean versions are not required.

a) Modifications that must be submitted for approval (substantial modifications)

|   |
|---|
| Submission of modifications requiring approval  |
| Use the form <a href="#">BW610 20 021e FO</a> . See annex A6 for instructions on how to create an eDok and submit an application. |

Modifications that are likely to have a substantial impact on the safety, health or rights of the subjects or on the robustness or reliability of the clinical data generated in the performance study must be approved by the ethics committee and Swissmedic before they can be implemented. Substantial modifications notably include the following: Design modifications and modifications of product administration or use; modification of safety procedures, additional interim analyses, modification of inclusion criteria, exclusion criteria or subject numbers foreseen; new Swiss sites or new principal investigators; changes to a primary or secondary endpoint, mode of



measurement of endpoints or other aspects of the performance study design with a possible impact on results; changes in the subject information and consent forms; etc.

Submit the application to Swissmedic and to the ethics committee on the same day. Once a complete documentation has been submitted, it will be reviewed within 38 days. Within 10 days of your submission, you will receive a confirmation of receipt of complete documentation or a request to provide any missing documents. Swissmedic may extend its review period by 7 days if needed.

b) Change of sponsor, issuing of a letter of approval for the new sponsor

|                                   |
|-----------------------------------|
| Submission of a change of sponsor |
|-----------------------------------|

|   |
|---|
| Use the form <a href="#">BW610_20_021e_FO</a> . See annex A6 for instructions on how to create an eDok and submit an application. |
|---|

Submit documents at least 38 days before the scheduled date of the change.

The following documents should be submitted:

- Cover letter signed by the previous sponsor, date when its activities in the study end, explanations about the changes.
- The completed form BW610\_10\_021e\_FO, with all the details of the new sponsor.
- Amended study documents in “Track changes” mode.

c) Modifications subject to notification only

|  |
|--|
| Submission of modifications requiring notification |
|--|

|   |
|---|
| Use the form <a href="#">BW610_20_021e_FO</a> . See annex A6 for instructions on how to create an eDok and submit an application. |
|---|

Modifications that do neither fall under a) nor b) must be notified to Swissmedic and will normally lead to no further correspondence. Please be aware that Swissmedic does not issue manual acknowledgements of receipt. Immediately after a submission, you can find two automatic acknowledgements in eMessage (for successful upload and technical validation). See annex A6 for additional information.

If modifications are found that are subject to approval (instead of notification), Swissmedic will contact you. If this is the case, you will need to stop implementation of the modifications in the study and wait for approval. In case of gross errors or repetition, Swissmedic may open surveillance activities and asks you to check your quality assurance system and implement corrective and preventive action (CAPA) to improve submissions.

Fees: The flat rate fee for handling modifications that are subject to approval amounts to CHF 1000.-<sup>7</sup> and is invoiced by Swissmedic. Relevant additional workload caused by shortcomings regarding the documentation and corrections will be invoiced at an hourly rate of CHF 200.-.

<sup>7</sup> Reduced fees are available for certain academic clinical trials, see section 5.2.5.

In case of withdrawal of a modification before review has started, the flat rate fee is not applicable. In this particular case, the work performed until withdrawal will be invoiced at a rate of CHF 200.- per hour. Likewise, in case of change of sponsor requiring approval the provided work will be charged to the hourly rate of CHF 200.-.

### 7.2.2 Safety (risks and safety measures)

*Arts. 12 and 15 HRA; Art. 34 and 36.4 ClinO-MD*

Submission of new circumstances that could threaten the safety of the subjects, and the corresponding safety and protective measures

Use the form [BW610 20 022e FO](#). See annex A6 for instructions on how to create an eDok and submit an application.

A risk mitigation responsibility lies with the sponsor and the clinical investigator. The sponsor and the investigator themselves must take all necessary measures without delay in order to protect the subjects from immediate danger. Expedited reporting to Swissmedic lies in the responsibility of the sponsor.

The reporting deadline is 2 days for measures concerning ongoing investigation, 24 hours for a temporary halt or premature termination on safety grounds. The following situations in particular must be reported:

- device deficiencies requiring measures.
- previously underestimated risks, safety-related measures or modifications of the CPSP in Switzerland or abroad (includes modifications agreed upon with foreign authorities or ethics committees or those imposed by them).
- temporary halt or premature termination on safety grounds in Switzerland or abroad.

### 7.2.3 Serious adverse events (SAEs) and device deficiencies

*Art. 4, 12 and 15 HRA; Art. 4, 32 and 33 ClinO-MD; Articles 2(60), 2(61), 76 and Annex XIV chapter II letter 1 of the IVDR; Annex G of standard ISO 20916*

#### a) General considerations

- Sponsors have to fully record adverse events and device deficiencies described in Art. 32 ClinO-MD (or Art. 76 of the IVDR) and have a duty of diligence. Notably, they need to be able to quickly identify unexpected situations during category C interventional performance studies, including higher than expected frequency or severity of harm, and unexpected types of harm, in order to take appropriate measures and stop undue risks. The sponsor needs to be in a position to temporarily stop product use in the sites and/or take other measures. Swissmedic and ethics committees can request records according Art. 32 ClinO-MD at any time.
- For adverse events and serious adverse events, in spite of similar terminology, different sets of criteria must be used in performance studies of IVD versus clinical investigations of medical devices or clinical trials of medicinal products.

Study personnel must be trained accordingly and use correct criteria in performance studies of

IVD; members of events committees or safety monitoring boards also need to be trained in order to use correct criteria for performance studies of IVD.

- Adverse events (AE) and device deficiencies must be recorded by the investigator on the case report forms (CRFs). For all SAE and for all device deficiencies with an SAE potential<sup>8</sup>, please make sure that all data necessary for timely fulfilment of the reporting duty with Swissmedic are collected on the CRFs. You can find examples of templates in annex 1 of this information sheet.
- For pre-market interventional performance studies (category C), CRF concerning SAE and device deficiencies must be sent to the sponsor rapidly, normally within 24 hours to 3 days, and malfunctioning IVD should normally be returned for examination.
- The information needs to be monitored continuously by the sponsor. Queries for incomplete or non-plausible entries need to be issued rapidly. For unexpected SAEs (with regard to type, severity or frequency of harm) and device deficiencies, it may be necessary to take precautionary measures. Typically, use may need to be temporarily suspended by the investigator and/or the sponsor. During suspension, the sponsor can carry out necessary investigations, check the design of the device, hypotheses for the study, or adequateness of investigation procedures, and if necessary prepare and file amendments. See also section 7.2.2 (measures for safety reasons) and 7.2.1 (amendments).

The following events must be reported to Swissmedic within 7 days:

- Any serious adverse event in Switzerland or abroad that has a causal relationship with the IVD for performance study, the comparator or study procedures or where such causal relationship is reasonably possible (i.e. serious and not obviously unrelated to the study);
- any device deficiency with an SAE potential noted in Switzerland or abroad;
- any new finding in relation to events above.

To assess whether sending a report is mandatory, it is therefore necessary to clarify whether the issue is serious, and whether causality with the IVD for performance study, or comparator, or a study procedure can be excluded.

In case of a device deficiency that causes a SAE, a report for the device deficiency and a report for the SAE need to be sent to Swissmedic. If a device deficiency causes several SAE, each SAE needs to be reported and followed-up separately.

- b) Is the event an adverse event, is it serious, what is the causal relationship between the event and the devices or study procedures, has a device deficiency a potential for causing SAE?<sup>9</sup>

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

Seriousness criteria for adverse events in performance studies of IVD:

<sup>8</sup> A device deficiency with an SAE potential is a 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

<sup>9</sup> Art. 2(60), 2(61), 2(62) and 76.1.c of the IVDR

- 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,
- death
- 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
  - life-threatening illness or injury
  - permanent impairment of a body structure or a body function
  - hospitalisation or prolongation of patient hospitalisation
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
  - chronic disease
  - foetal distress, foetal death or a congenital physical or mental impairment or birth defect

A planned hospitalisation for a pre-existing condition or a procedure required by the CPSP without a serious deterioration in health is not considered to be a serious adverse event.

While continuation of a pre-existing condition is not an 'event', increased severity or clinically relevant progression of a pre-existing disease in a patient need to be documented as adverse events (e.g. increased severity of migraine, clinically relevant worsening of arrhythmia, clinically relevant progression of renal disease, etc.).

The causal relationship of each SAE with investigational devices, comparators and study procedures has to be assessed by the investigator and also by the sponsor. For the attribution, the sponsor must take into account the complete data that are available (including the technical documentation, literature, all study sites involved). Four levels of causality are used in Europe in order to correctly described the causal relationship:

- not related
- possible
- probable
- causal relationship

Also consult [MDCG 2024-4](#) for correct causality attribution. Unknown causes (e.g. insufficient data available) must be adjudicated as possibly related.

Causality cannot be ruled out and you must not describe an event as "not related" if for example

- there are insufficient information for causality assessment,
- no other clear cause can be identified, and there is a correlation in time or with the bodily part concerned,
- the investigational device or a procedure could affect the bodily part concerned,
- similar events have already been recorded as side effects or complications with other, similar devices and procedures, or
- user errors are involved, e.g. in case of an injury due to an operating error.

c) Timelines and forms for the reporting of sponsors to Swissmedic, forms for sponsors

For multi-centre studies, reportable SAEs and device deficiencies with an SAE potential must be reported to Swissmedic within 7 days:

|   |
|---|
| Tabular summary reporting of serious adverse events and device deficiencies that occur in all centres (worldwide) |
|---|

|   |
|---|
| Use the Excel table <a href="#">MDCG 2024-4 Appendix</a> , fill in the data according to the guidance document <a href="#">MDCG 2024-4</a> , and send the table via eMail to <a href="mailto:clinicaltrials.devices@swissmedic.ch">clinicaltrials.devices@swissmedic.ch</a> . |
|---|

The Excel table is filled in cumulatively over the course of the study, highlight all changes compared with the previous version. Always submit the Excel file to Swissmedic (not a pdf file), Swissmedic must be able to search and edit the table.

If a reportable SAE or a device deficiency with an SAE potential takes place in a Swiss centre, please also fill in and submit the following form that contains more detailed information:

|   |
|---|
| Reporting of serious adverse events and device deficiencies that occur in Swiss centres |
|---|

|   |
|---|
| Use the form <a href="#">BW610 20 024e FO</a> . See annex A6 for instructions on how to create an eDok and submit the report. |
|---|

#### 7.2.4 Annual report

*Art. 35 and 38 ClinO-MD*

|                                 |
|---------------------------------|
| Submission of the annual report |
|---------------------------------|

|   |
|---|
| Use the form <a href="#">BW610 20 021e FO</a> . See annex A6 for instructions on how to create an eDok and submit an application. |
|---|

From the date of approval of the performance study, a report must be submitted annually to the cantonal ethics committee and Swissmedic. A typical report includes the following information:

- Data cut-off date up to which study data has been considered in the report, and the reporting period
- Status of recruitments: Current number of subjects worldwide and in Switzerland, duration of the currently existing follow-up observations
- Status of the performance study abroad (countries involved, any study interruptions or premature terminations)
- Anticipated serious adverse events: Description, occurrence in the trial arm versus control arm and medical literature, evaluation by the sponsor
- Unanticipated serious adverse events and any device deficiencies: causality of SUAEE with the IVD for performance study or a procedure, possible causes, problems related to the use of the investigational devices at the centres
- Safety-relevant measures taken by the sponsor or imposed by ethics committees or authorities anywhere in the world
- Results from other performance studies of the IVD (if applicable)
- Sponsor's conclusions regarding the safety of the subjects and the continuation of the investigation

- Annex with the cumulative list per cut-off date of reportable serious adverse events and device deficiencies

The report must be up to date, a cut-off date older than 2 months is generally not considered adequate for pre-market performance studies. You are allowed to submit annual reports to Swissmedic before the specified deadline, which especially in multinational studies allows to write and submit a joint annual report for all authorities and ethics committees involved.

### 7.2.5 End, premature termination, interruption of the study

*Art. 36 to 39 ClinO-MD*

Notification of end, premature termination or temporary halt for reasons not related to safety  
 Use the form [BW610 20 021e FO](#). See annex A6 for instructions on how to create an eDok and submit an application.

The sponsor must notify Swissmedic of the end of a performance study within 15 days (as of last patient, last visit). A premature termination or an interruption of the study for reasons not related to safety, and the reasons for this, must also be notified within 15 days.

The final report, with contents in accordance with Annex XIII and Art. 73 of the IVDR ("performance study report" and summary presented in terms understandable to the intended user) must generally be submitted within one year of the end of the study. Additional information concerning contents of the report are available in ISO 20916. In case of a temporary halt or premature termination, the report is due within 3 months.

## 8 Data retention requirements

*Art. 40 ClinO-MD*

An archiving period of at least 10 years after the end of the study is required and is applicable to sponsors and investigators.

## 9 Databases used in Switzerland

Availability of a module for studies in the European database (new EUDAMED IT system) under the IVDR is expected in 2023. However, the access of Swissmedic to that database might be postponed. Until further notice, the sponsor has the obligation to submit requests and reports via the Swissmedic portal eMessage, including information about different CPSP versions used abroad, or safety measures taken abroad such as study interruptions and premature terminations on safety grounds. In annex A6, you can find information explaining how to make a submission to Swissmedic. BASEC must be used for submissions to cantonal ethics committees.

## 10 Sponsors with registered offices abroad, submissions by third parties

*Art. 4 para 3 und Annex 1 Section 2.1 ClinO-MD*



Sponsors headquartered in another country must specify an agent that is domiciled or has a place of business in Switzerland as an address for correspondence. Preliminary decisions, official decisions and invoices from Swissmedic are sent to the agent. Legal and natural persons domiciled or headquartered in Switzerland can be specified as agents, e.g. distribution companies, a lawyer or the investigator.

Swissmedic accepts submissions made by

- the sponsor,
- a third party acting on behalf of the sponsor, for example a clinical research organisation. When submitting an approval application, list third parties in the application form.

## 11 Liability in the case of damage, coverage in the form of insurance

*Arts. 19-20 HRA; Arts. 13-14 ClinO; Art. 15 Insurance Oversight Act (Versicherungsaufsichtsgesetz, VAG, SR 961.01) and implementing provisions in the Oversight Ordinance*

An insurance company headquartered in Switzerland or with a branch office in Switzerland can be considered to offer an acceptable coverage as the subjects are able to assert their legal right of direct claim and the associated legal enforcement claims within Switzerland.

The cantonal ethics committee will review the fulfilment of the liability and coverage obligations.

Cantonal ethics committees have published information on insurance coverage requirements including templates for insurance policies (see [www.swissethics.ch](http://www.swissethics.ch) > [Templates/Checklists](#)).

## 12 Penal provisions

Penal provisions in the case of offences and infringements are described in the HRA and the TPA (*Arts. 62-64 HRA; Arts. 86-90 TPA*).

## ANNEXES

### A1: Recording of adverse events and device deficiencies

Art. 12 and 15 HRA; Article 10 ClinO-MD and statement of the manufacturer according to Annex XIV Chapter I Sections 1.17 and 4.1 of Regulation (EU) 2017/746; Art. 32-33 ClinO-MD; MDCG 2024-4; Annex G of standard ISO 20916

The sponsor needs to prepare adequate case report forms (CRF). He receives CRF filled in by the centres and must satisfy risk management requirements and reporting requirements in respect of adverse events and device deficiencies. Boxes 1 to 3 show typical examples of CRF for category C interventional performance studies of IVD.

#### Box 1: Documentation of occurrence of adverse events and device deficiencies

Texts need to be integrated in the following CRF: procedure CRF, CRF for follow-up visits, unscheduled visits, contacts by phone.

*Have there been any adverse events?*

- Yes, please fill in an "Adverse events" form.       No

*Have any device deficiencies been noted (e.g. malfunctions, use errors, inadequate labelling)?*

- Yes, please fill in a "Device deficiency" form.       No

#### Box 2: Adverse events form

*Study title*

*Name of sponsor*

*Study site: .....*

*Subject ID code: .....*

*Age of the patient on date of event onset: .....*

*Patient gender: .....*

*Date the centre became aware of event:*

*Date of surgically invasive sample taking: .....*

*Date of IVD use: .....*

*Date of event onset: .....*

*Current location of the device: .....*

*Type of information*

- new event  
 follow-up information

*Criteria for seriousness*

- 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

- death
- 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
  - serious life-threatening illness or injury
  - permanent impairment to a body structure or a body function
  - in-patient hospitalisation or prolongation of existing hospitalisation
  - a medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
  - chronic disease
- foetal distress, foetal death or a congenital abnormality or birth defect

*Description of event*

[blank space for extensive descriptions]

.....

.....

.....

.....

.....

.....

.....

*Action/treatment/patient outcome*

[blank space for extensive descriptions]

.....

.....

.....

.....

.....

.....

.....

*Relationship to procedure*

- not related
- possible / unknown
- probable
- causal relationship

*Relationship to device*

- not related*
- possible / unknown*
- probable*
- causal relationship*

*Expectedness*

- Anticipated*     *Unanticipated*

*Investigation arm*

- Investigation arm*     *Comparator arm*

*Outcome*

- ongoing, medical condition is not stable, please provide updates on a regular basis*
- resolved without sequelae, date of event resolution: .....*
- resolved with sequelae, medical condition is stable, date of event resolution: .....*

[Version number]

[pagination]

**Box 3: Device deficiency form (malfunction, use error, inadequate labelling)**

*Study title*

*Name of sponsor*

*Study site: .....*

*Subject ID code: .....*

*Date the centre became aware of event:*

*Date of IVD use: .....*

*Date of event: .....*

*Current location of the device: .....*

*Type of information*

- new deficiency*
- follow-up information*

*Nature of the problem (tick all that apply)*

- Malfunction*
- Use error*
- Inadequate labelling*
- Other: .....*

*SAE potential*

- Led to a serious adverse event. Please complete an Adverse Event CRF.*
- Is a Device deficiency that did not lead to an adverse event but could have led to a medical occurrence*  
a) *if appropriate action had not been taken*

- b) *intervention had not occurred, or*
- c) *circumstances had been less fortunate*

*None*

*Description of the deficiency (occurrence, measures taken, outcome of investigation):*

*[blank space for extensive descriptions]*

.....

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*[Version number]*

*[Pagination]*

## A2: Risk mitigation measures

In line with the stage of clinical development, innovation and the risk potential, the sponsor is obliged to implement risk mitigation measures. Box 5 shows safety measures that need to be considered and, where necessary, included in the clinical performance study plan for pre-market interventional performance studies. The aim is to avoid problems, or identify them at an early stage, so that the subjects are not exposed to unnecessary risk. Additional measures may be necessary, depending on the specific project. For additional information, see also information on risk mitigation in guidance document MDCG 2024-3.

### Box 4: Safety measures for pre-market interventional performance studies

- a) Procedures for the installation of devices and instruction/ training of users.
- b) Procedures for correct sample taking, especially if surgically invasive: Define necessary qualifications, foresee training and if necessary assistance with imaging or other techniques.
- c) In early phases of research, enroll a narrow study population with more favorable benefit-risk profile.
- d) Monitoring: Foresee frequent visits to the sites and ensure compliance with the PSP, accurate recording of AE and DD, as well as compliance with reporting deadlines.
- e) Risk-adapted recruitment, interim analyses: Do not expose an unnecessarily large number of subjects. Define phases, e.g. feasibility phase/ pivotal phase. Before each new phase, carry out an interim analysis. Define the data needed for the interim analysis, incl. the minimum required follow-up of subjects who have already been treated. For interim analysis, 100% source data verification and resolution of queries (AE, SAE, device deficiencies, missing data) normally needs to be foreseen.
- f) Handling of CRF: Foresee short deadlines for submission of safety relevant data to the sponsor. Readily verify the clarity of descriptions and attributes (serious/not serious, anticipated/unanticipated, relatedness to devices and procedures, device deficiencies with/without an SAE potential), rapidly issue queries. Maintain the list of AE/SAE/device deficiencies as requested by law. Retrain the sites if you see repetitive errors in CRF. Immediately evaluate measures in case of unexpected nature, severity or frequency of problems. If necessary, suspend device use until measures are completed.
- g) Safety committees, e.g. data monitoring committees (DMC), data safety monitoring boards (DSMB) or data safety monitoring committees (DSMC): In double-blind randomised investigations with relevant risks, unblinded data need to be assessed periodically. The committees oversee seriousness and causality attributions made by investigators, recognise unexpected types, severities and frequencies of harm, may evaluate unblinded data, and are expected to make independent evaluations; investigators should therefore not be part of the committees. Make sure members have been trained on the European seriousness criteria and causality assessment criteria that are applicable specifically to interventional performance studies (consult art. 2(61) IVDR and the guideline [MDCG 2024-4](#)).
- h) Stopping criteria: Define the type and number of incidents that will lead to the suspension of further use.
- i) Systematic return and examination of devices in case of problems.
- j) Sufficient duration of follow-up of subjects to fulfil the goals of the study and to ensure patient safety.
- k) Contact persons, retrieval of information on serious incidents: Procedures to be followed before subjects are declared lost to follow-up should be determined in a risk-based approach. They should be timely, effective and in line with the data analysis that is planned. For details see annex 3.

## A3: Patients lost to follow-up, mortality, permanent impairment

*Art. 4, 5, 10, 12 and 15 HRA; Art. 4, 32 and 33 ClinO-MD; Annex XIII chapter II sections 2.3.2(i) and 4.1 and chapter III MDR; points 5.3(o) and B.8.1(c) of standard ISO 20916*



Studies must be planned in such a way that the endpoints foreseen by the sponsor can be recorded correctly. The course of various diseases and different interventions can lead to mortality, and to physical or mental disability. Such events are often foreseen as endpoints and need to be retrieved. During pre-market studies with relevant risks, the events must be monitored continuously by the sponsor. It is the duty of the sponsor to rapidly identify and avert excessive risks. Deficient study planning and missing data can moreover threaten the validity of the results. Important aspects can be found in Boxes 5 and 6.

**Box 5: Organisational aspects for studies with a mortality endpoint or endpoints that lead to a loss of independence**

- a) Informed consent form: The form should include the consent for the sharing of medical information with a contact person, e.g. that the investigator may clarify the state of health with the subject's general practitioner and/or named individuals.
- b) Clinical performance study plan:
  - Procedures for follow-up visits: If a subject can no longer be traced, its address and state of health should quickly be clarified by the investigator with the contact person.
  - Monitoring plan: If a subject can no longer be traced, the monitor should check with the centre on the appropriateness of attempts made to contact the subject and his contact person.
  - Missing data and statistical considerations: If the occurrence of a death or other endpoints cannot be established, sensitivity analyses should usually be provided for (analyses on the effect of the missing data on the results).
- c) Reports: The number of patients lost to follow-up and the results of the sensitivity analyses should be included in final reports and publications.

**Box 6: Examples of inadequate study planning in the case of studies with a mortality endpoint or endpoints that lead to a loss of independence**

- a) Clinical performance study plans that describe no measures for patients lost to follow-up.
- b) Insufficient measures e.g.
  - failing to obtain the written consent of the subject with regard to obtaining health information from third parties.
  - no sensitivity analysis (failure to take into consideration that subjects lost to follow-up may have experienced a fatal outcome or severe disabilities).

## **A4: Inclusion and exclusion criteria, particularly vulnerable persons**

*Arts. 11 and 21-31 HRA; Arts. 15-17 ClinO; Arts. 60-64 IVDR*

A research project involving particularly vulnerable persons may only be carried out if equivalent findings cannot be obtained in any other way. Particularly vulnerable persons are, for example, minors (children, adolescents), adults lacking the capacity in the consent procedure, patients in emergency situations, pregnant women or embryos / fetuses. Investigations with own employees are considered as problematic due to financial dependence.

For that reason, please check the wording of the inclusion and exclusion criteria. If particularly vulnerable groups of persons are not explicitly excluded from the study, the necessary justifications must be in the documentation. Information texts and consent forms are needed for all persons taking part in the study, as is a written description of the procedure for enrolment / consent / post hoc consent.

Flow charts or diagrams, for example, may also be appropriate as a written description. These should show which person, at which point, using which documents, carries out which activities that lead to inclusion in the study and, if in case of enrolment in an emergency situation, to obtain a correct post hoc consent.

In practice, studies under mixed conditions present particular difficulties, and especially if both vulnerable and non-vulnerable subjects are to be enrolled or if a temporary, particular vulnerability exists. In such cases, please pay particular attention to correct study planning. Considerations and examples can be found in Box 7.

### **Box 7: Considerations regarding performance studies on both vulnerable and non-vulnerable subjects**

#### Example 1, mixed populations

The IVD can in principle be used for elective interventions and for emergency patients. According to inclusion and exclusion criteria, emergency patients are not excluded from the study:

- Are you sure the study should involve emergency patients?
- Does the documentation state which research question can only be investigated using the emergency patients, and why?
- Has the necessary number of emergency patients, that is needed to investigate these particular research questions, been calculated?
- For enrolment, how do you make sure that the correct number of emergency patients and elective patients will be included (stratification)?

#### Example 2, emergency situation at the beginning of a study

An IVD is used for emergency patients, and the study is then continued with a follow-up under regular clinical conditions.

- Who clarifies the emergency patient's capacity to consent, and how?
- When and how are the patients themselves and / or their representatives involved?
- At what point is the independent doctor involved?
- When and how, after implantation, does the post hoc consent and the consent to continue taking part in the performance study take place (now administered with the appropriate reflection period)?
- Is the written description of the whole consenting procedure available?
- Are the necessary documents for the various steps available (information and consent forms for use under emergency conditions, documented decision of the independent doctor, post-hoc information and consent forms for use of previously collected data and continued participation in the study)?

Specific provisions also apply regarding research involving prisoners (*Art. 28 HRA*).

## A5: Reflection period when consenting for invasive procedures

### Art. 16 HRA

The subject must be given an appropriate reflection period. For procedures that can be planned, the question of the time required arises in particular in the case of additional surgical sample taking and additional invasive procedures with relevant risks are performed for the purpose of the study.

Guidance and case descriptions are available on the subject:

- Swissethics: „Leitfaden Bedenkfrist“ (available at [www.swissethics.ch](http://www.swissethics.ch)).
- Decisions of the Federal Supreme Court: As a result of legal disputes, the Federal Supreme Court has commented on aspects regarding consent to invasive procedure in daily clinical practice (considerations available e.g. in the judgement of the Federal Supreme Court no. 4P.265/2002, free of charge at [www.bger.ch](http://www.bger.ch)).

## A6: How to make a submission

You can find information on the eGovernment Service eMessage in various languages at

- [www.swissmedic.ch/ci](http://www.swissmedic.ch/ci) and [www.swissmedic.ch/performance-studies-en](http://www.swissmedic.ch/performance-studies-en) > [How to submit](#)
- [OS000\\_00\\_005e\\_MB eMessage functions](#)

The following items can be sent by email to [clinicaltrials.devices@swissmedic.ch](mailto:clinicaltrials.devices@swissmedic.ch):

- Tabular listings of reportable serious adverse events and device deficiencies according to European reporting formats.
- Communications during an ongoing procedure with no documents attached, e.g. for extension of deadlines, other coordination needs, questions concerning the procedure.

In all other cases, you must follow the eGovernment submission procedures. In order for your submission to be handled correctly, standardised forms and a standardised folder structure are necessary and must always be used.

Electronic submissions consist of three steps

#### 1. *Prepare the standardised form and download the standardised folder structure*

To prepare a submission, go to [www.swissmedic.ch/ci](http://www.swissmedic.ch/ci) > EN > Forms and templates, choose and fill in the correct form. Go to [www.swissmedic.ch/performance-studies-en](http://www.swissmedic.ch/performance-studies-en) > “How to submit” > “eDok electronic folder structure (ZIP)”, and download the standardised folder structure.

#### *Generate an eDok*

Copy the form, an accompanying letter if needed and every document into the correct folder. Your files should be in pdf or Excel format. Zip the whole structure (the standardised folders with all your files). This file is called an “eDok”. One eDok includes one entire submission. In rare cases of errors due to size overload, or in case of confidentiality issues, you can split the documents (two eDoks for one submission). Explain the split in your cover letter.

#### *Submit the eDok*

Send eDoks for clinical trials of devices to Swissmedic via the Swissmedic Portal eMessage ([www.swissmedic.ch/emessage-en](http://www.swissmedic.ch/emessage-en)). Swissmedic also runs the platform eSubmissions, which cannot be used for devices.

In order to create an eGovernment account, you need an email-address and a mobile phone. Immediately after the registration step, you can submit to Swissmedic. A two-way identification procedure will be carried out for safety reasons each time you access the portal, with a code that is sent to your mobile phone.

For a submission, answer the questions on the screen, select your eDok, select the “Upload” button and confirm. You will receive two automatic communications. The first one shows whether the 'submit' step was successful ('delivery confirmation'). Immediately afterwards, a second communication will show whether your files passed the automatic technical validation ('acceptance of delivery' or 'acceptance of delivery denied'). Confirmations and error messages will be stored in eMessage for you. Always check the messages you receive.

You should not store files in the portal. Instead, download correspondence from Swissmedic and store your submissions and the correspondence in your trial master file, so that all authorised persons can access these during the clinical trial and the mandatory archiving period.

Trouble shooting: The error message 'acceptance of delivery denied' mostly occurs when the eDok format is not respected.

- Always provide your files in the standardised folder structure and accompanied by the corresponding Swissmedic form.
- In your eDok, include pdf and Excel files only (xlsx, xls, ods). Files from digital sources are preferred. When scanning documents you must use the OCR standard in order for the documents to be machine readable.
- If the file name is too long or contains unforeseen characters, the system will not be able to process your submission. The maximum recommended length is 60 characters with the file extension. File names can include 'A' to 'Z', 'a' to 'z', '0' to '9', '.', '-', and '\_'. You may not use a blank space at the beginning or end of a file name, and you should not use the following characters: « \* : < > ? / \ | ~ # % & " { }.
- If you do not see messages from Swissmedic, adapt the filter option in eMessage to see unread messages only (default setting), or all messages. Please be aware that you will only see messages and other correspondence made under your ID, not correspondence concerning the same clinical trial sent to other users that have used a different ID.

If you are unable to register or to submit, you can contact [eSubmission@swissmedic.ch](mailto:eSubmission@swissmedic.ch) for help.

## A7: Special groups of products

- a) **In-house devices:** Manufacture and use of non CE-marked IVD in healthcare institutions  
 Art. 9 IVDDO together with art. 5(5) of the IVDR describe the conditions allowing a healthcare institution to manufacture and use certain IVD within its own premises and without the need of a notified body and CE-marking in order to address the specific needs of target patient groups which

cannot be met, or cannot be met at the appropriate level of performance, by an equivalent CE-marked device available on the market.

For information on the conditions that must be fulfilled, please consult the Swissmedic information available at [www.swissmedic.ch](http://www.swissmedic.ch) > EN > Medical devices > Frequently asked questions > Devices manufactured and used in healthcare institutions.

Swiss healthcare institutions must notify the devices to Swissmedic before they are put into service. Notification forms are available at [www.swissmedic.ch](http://www.swissmedic.ch) > EN > Medical devices > Market access > Notification of IVD.

It is acceptable for the manufacturing healthcare institution to use these IVD in a category A clinical investigation. In the study plan, disclose that the IVD is not CE-marked and describe fulfilment of The General Safety and Performance requirements and of each condition listed in art. 5(5) of the IVDR. These cases are rare.

If an applicable General Safety and Performance Requirement (Annex I of the IVDR) is not fulfilled, or if a condition listed in art. 5(5) of the IVDR is not fulfilled: An application for approval of a category C2 clinical investigation must be submitted to Swissmedic and to the ethics committee. Example: There is a CE-marked device with an appropriate performance on the market, the conditions are therefore not fulfilled.

- b) **Software as an IVD:** Consult the Swissmedic information sheet BW630\_30\_007d\_MB (Medical Device Software) and the European guidance document MDCG 2019-11 in order to determine whether a software is an IVD and to determine its risk classification.

## Contacts in case of questions

- General questions: [questions.devices@swissmedic.ch](mailto:questions.devices@swissmedic.ch).
- Questions concerning an ongoing procedure or an approved clinical trial: Contact the person that is mentioned on Swissmedic correspondence or [clinicaltrials.devices@swissmedic.ch](mailto:clinicaltrials.devices@swissmedic.ch)
- Questions concerning the Swissmedic eMessage portal: [eSubmission@swissmedic.ch](mailto:eSubmission@swissmedic.ch)

Further information from Swissmedic on clinical investigations of medical devices can be found on the Internet: [www.swissmedic.ch/ci](http://www.swissmedic.ch/ci)

## Change history

| Version | Change   | Sig     |
|---------|--|---------|
| 5.1     | Box 4 in Annex A2: Information added on enrolling a narrow study population with more favorable benefit-risk profile.<br>The federal revision of Human research act ordinances resulted in some updated terminology (authorisation/approval, clinical trial with/clinical trial of, etc.).   | sci     |
| 5.0     | A new information sheet dedicated to submissions for combined studies has been published by Swissmedic. Corresponding contents in sections 1, 5.3 and Annex A7 have been replaced by references to the new information sheet.  | sci     |
| 4.0     | New contents available in section 5.2.5 concerning reduced fees for academic sponsors.   | sci     |
| 3.5     | Contents relating to MDCG guidance documents have been updated: MDCG 2020-10 replaced by MDCG 2024-4, Annex A2 has been updated according to MDCG 2024-3.  | sci     |
| 3.4     | New layout.<br>Appendix A7, in-house manufacturing in healthcare institutions: New references added (link to new Swissmedic information available on the topic, link to the notification form for in-house manufactured devices).<br>Appendix A7, combined trials: Update on sending CIOMS forms for SUSAR to Swissmedic.  | hem/sci |
| 3.3     | Updated contents in section 5.1 (updated decision tree for authorisation applications), section 5.2.5 (flat fee for simplified reviews), section 5.2.1 (EU common specifications for certain class D IVD are now available), and annex A7 concerning in-house manufactured IVD, combined trials (MDCG 2022-10 on combined trials is now available, submissions for combined trials in Switzerland, fees for combined trials, reporting of SUSAR in combined trials, submissions when non conforming products are added to previously authorised trials). | sci     |
| 3.2     | Section 7.2.4: Clarification, the list of reportable SAE and DD needs to be a cumulative list.<br>Section 10: Use of the term 'agent' for a clearer distinction between agents for foreign sponsors and legal representatives of manufacturers or study subjects.  | sci     |
| 3.1     | Updated links and references throughout the document. New format for the decision tree in chapter 5.1. Regulatory references updated and reporting form included in chapter 7.1.2.   | sci     |
| 3.0     | Doc newly created owing to revision of IVD regulatory provisions   | sci     |