

Substantial amendment: **YES** or **NO** or "it depends"

Yes = Generally, the change must be submitted as a substantial amendment. EC approval is required before the change can be implemented.

In some cases, e.g. for some HRO category A research projects, the EC can decide that the submitted change is not a substantial amendment and inform the applicant accordingly, in a short time.

No = If not indicated otherwise, non-substantial changes must be notified to the ethics committee in the annual safety report (KlinO Art. 29). Non-substantial changes of HRO research projects must be notified to the ethics committee as per HRO Art. 18.

| Changes | ClinO | HRO | ClinO/HRO, GCP, comments |
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| Study Protocol / Investigator's Brochure (IB) / CRF | | | |
| Change in the inclusion/exclusion criteria. | Yes | Yes | Art. 29 3b ClinO, Art. 18 3b HRO. |
| Change in methods and procedures (e.g. additional MRI, a CT is dropped, number of study subjects is increased) | Yes | Yes | Art. 29 3b ClinO, Art. 18 3b HRO. |
| Change in goals (e.g. in addition to efficacy also safety parameters should be evaluated or additional correlations). | Yes | Yes | Art. 29 3b ClinO, Art. 18 3b HRO. |
| Changes in the statistic plan in the study protocol. | Yes | Yes | Art. 29 3b ClinO, Art. 18 3b HRO. <i>It changes the scientific value of the research project, e.g. increase or reduction of the n° of subjects.</i> |
| Modifications to the study protocol and/or ICF requested by Swissmedic. | Yes | n.a. | Art. 29 3b, ClinO. |
| Need to combine study with persons (HRO or ClinO) with data from medical records (further use) | Yes | Yes | Art. 29 3b ClinO, Art. 18 3b HRO. |
| Change in experimental set-up (e.g. addition of a control population, or addition of a different set of study subjects). | Yes | Yes | Art. 29 3b, ClinO, Art. 18 3b HRO. |

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| Changes in the CRF not directly related to changes in the study protocol (e.g. additional instructions for the researcher, changes to the format, etc.) | No | No | |
| Switch from paper-CRF to e-CRF (or the other way round) | No | No | |
| Change/new contracts (e.g. change in financing, change in publishing rules, etc.) | Yes | Yes | Art. 25, 29 3 ClinO/ Art. 18 3 HRO. |
| New version of IB <u>not</u> resulting in new ICF/study protocol. | No | n.a. | 'Yes' if there is a higher risk for the study subjects. |
| New versions of IB and/or study protocol after Swissmedic approval. | Yes No | n.a. | Art. 29 3b ClinO. 'Yes' for the study plan; 'No' for the IB. |
| Study period extension. | Yes | Yes | Here 'study period extension' means a prolonged participation of the individual participants in the study. For example, a prolonged period of treatment, addition of hospital visits for the participants, ... This change requires an amendment to the protocol. This change might require a change to the insurance (extension of the period covered, ...). |
| Extension of the recruitment period | No | No | This change might require a change to the insurance (extension of the period covered). |
| Study period remains the same but the start date is moved months / a year into the future. | No | No | This change might require a change to the insurance (extension of the period covered). |
| Patient Information / Informed Consent (ICF) | | | |
| Additional ICF for further use of data/material (related to study) | Yes | Yes | Art. 29 (3), ClinO, Art. 18 (3) HRO. |
| Additional ICF for further use of data/material (unrelated to the approved research project). New research projects are not defined yet. E.g. for an institutional biobank | on a voluntary basis | on a voluntary basis | The EC can review the additional ICF as an offer of service. |
| Formal and administrative changes in the ICF (addresses, spelling, etc.) | No | No | |
| Change of content in the ICF (e.g. additional MRI, new side effects) | Yes | Yes | Art. 29 3a, ClinO, Art. 18 3a HRO. |

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| Approved ICF translated in another Swiss national language | Yes It depends | Yes It depends | A translated ICF is considered a substantial amendment, when it is submitted with the notification of a new site (in a multicentric study) in a new linguistic region that was not part of the initial submission. The Lead EC must approve it before the translated ICF can be used. If there are no ECs located in the linguistic region of the language of the translated ICF, the Lead EC will acknowledge the reception of the translated ICF only. In all cases, the translated ICF needs to be sent to the EC immediately and can't be used till the EC has either approved it or acknowledge it. |
| Approved ICF translated in a non-Swiss national language | No | No | The Lead EC will acknowledge the reception of the translated ICF only. The translated ICF needs to be sent to the EC immediately and can't be used till the EC has acknowledge it. |
| Study set up | | | |
| New address of the investigational site: Minor changes: academic title, address, phone number/email. | No | No | |
| New address of the investigational site: Infrastructure has completely changed, e.g. the clinic has moved. | Yes | Yes | Art. 29 3c, ClinO; Art. 18 3c, HRO. |
| New institution but still the same PI (e.g. PI works now at the CHUV instead of USZ). | Yes | Yes | Art. 29 3c, ClinO; Art. 18 3c, HRO. |
| Change of PI at an investigational site (e.g. Prof. Müller instead of retiring Prof. Meier) | Yes | Yes | Art. 29 3d, ClinO, Art. 18 3d HRO. |
| Temporarily leave of PI | Yes No | Yes No | See document on swissethics.ch (What if an Investigator of an ongoing clinical trial is absent for an extended period of time? How should this be handled?) |
| Change of coordinating PI (e.g. Dr. Dupont CHUV instead of Dr. Müller USZ) | Yes | Yes | Art. 29 3d, ClinO, Art. 18 3c HRO. In principle, the Lead EC should not change. |
| Replacement of a study staff member mentioned by name in the study protocol (e.g. blood will now be drawn by Mr Müller or by "a nurse" instead of Ms Meier). | No | No | |
| Additional investigational site | Yes | Yes | Art. 29 3c, ClinO, Art. 18 3c HRO. |
| Change of Sponsor (e.g. due to an acquisition, new contract but same conditions) | Yes | Yes | Art. 29 3d, ClinO, Art. 18 3c HRO. |
| Change of the Sponsor's local (Swiss) representative | Yes | Yes | Art. 29 3d, ClinO, Art. 18 3c HRO. |

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| Change in CRO | No | No | Art. 29 3d, ClinO, Art. 18 3d HRO. However, the EC should be informed immediately and not only with the annual study report. |
| Change in Monitor (e.g. a new institution will make the monitoring) | No | n.a. | |
| Safety | | | |
| Change of risk category (higher or lower). | Yes | Yes | Art. 29 3a, ClinO; Art. 18 3a, HRO. |
| Change in safety measures (harder because of higher risks or lower because the risks seem lower than expected). | Yes | Yes | Art. 29 3a, ClinO; Art. 18 3a, HRO. |
| Study subjects' recruitment | | | |
| Change in recruiting method, e.g. from face-to-face consultations in the clinic to distribution of flyers. | Yes No | Yes No | Art. 25, 29 3 ClinO/ Art. 18 3 HRO. Yes if the text changes or if the recruiting method is described in the protocol. No, if it is only a change of media with the same text (e.g. flyer). |
| New recruiting material, like flyers (new text, new versions) for the patients (i.e. the patients are addressed directly) | Yes | Yes | Art. 25, 29 3 ClinO/ Art. 18 3 HRO. |
| New recruiting material, like flyers, letters, study synopsis (new text, new versions) for referring physicians (i.e. the patients are <u>not</u> addressed directly) | No | No | |
| Extension of the recruitment period | No | No | This change might require a change to the insurance (extension of the period covered). |
| Other changes / other documents | | | |
| New logo, new corporate design for all the documents. | No | No | |
| New/changes in sponsor's / investigational site's SOPs, working instructions, etc. | No | No | |
| Changes relevant for Swissmedic (e.g. GMP related) but not in the scope of ECs' responsibility. No changes to any EC-relevant documents. | No | n.a. | |
| Changes relevant to the FOPH, radiation-protection, which would require a new BAG permit. | Yes | Yes | |

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| Main changes in monitoring plan. | Yes | n.a. | Art. 29 3a ClinO. |
| Increasing and /or expanding the scope of the monitoring. | No | n.a. | Art. 29 3a ClinO. Increase of monitoring is not a substantial amendment by itself. However, the reason for the increase might need to be notified as substantial amendment (e.g. safety reasons). |
| Changes to the insurance policy (e.g. change of the cover ratio, ...) | Yes | Yes | Art. 13, 14, ClinO; Art. 13, HRO. |
| Renewal of the insurance policy (extension of the insurance) | No | No | Art. 13, 14, ClinO; Art. 13, HRO. The EC can issue objections |
| Change in compensation to the study subjects (more/less money) | Yes | Yes | Art. 14, HRA. |
| Additional informational material for the study subjects | No | No | |
| Additional questionnaire(s) for the study subjects | Yes | Yes | |
| Correcting spelling errors in any document. | No | No | |
| Lay summary of study results | No | No | The lay summary of study results must comply with the provisions set up in the Code of Conduct of the Pharmaceutical Industry in Switzerland (Swiss Pharma Code, Pharmakodex, Code pharmaceutique) published on www.scienceindustries.ch |