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
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. It changes the scientific value of the research project, e.g. increase or reduction of the nº of subjects.
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.

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 not 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	
Study period remains the same but the start date is moved months / a year into the future.	No	No	
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.
Approved ICF translated in another Swiss national language	Yes / It de-pends	Yes / It de-pends	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.
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 not addressed directly)	No	No	
Other changes			
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 (e.g. change of CT device -> new BAG permit).	Yes	Yes	Yes if the device is the object of the study and if there is a higher risk for the patients.
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 (e.g. handout with information about handling a device)	No	No	
Additional questionnaire(s) for the study subjects	Yes	Yes	
Correcting spelling errors in any document.	No	No	