**REQUEST FOR EVALUATION**

**OF RELEVANT AMENDMENT OF CLINICAL TRIAL**

The sponsor is responsible for determining the relevance of the amendment.

**Relevant amendment:** An amendment is relevant when it has a significant impact on the **physical or mental safety or integrity of participants** or on the **scientific value of the study.**

* Examples: Changes in IB such as new toxicological or pharmacological data, any change in the Patient information sheet, amendment in recruitment material.

**Non-relevant amendment:** An amendment is considered not relevant if it does not meet the relevant amendment criteria; these amendments must be reported to the CREC as notifications.

* Examples: Typographical corrections, minor clarifications to the protocol, CRF changes, CRO changes.

**Note - Economic report:** CEIm evaluation is only necessary for amendments that involve changes in participant and investigator compensation submitted in the initial economic report. If submitted, redline changes to previous version.

**DOCUMENTATION TO SUBMIT ACCORDING TO TYPE OF AMENDMENT**

**Remember** that documents must be named as described in Appendix I of the AEMPS (Agencia Española de Medicamentos y Productos Sanitarios [Spanish Agency of Medicines and Medical Devices]) instruction document. **Never** indicate a concept that is not “OTHER” as the type of document in the platform.

1. **Relevant amendment to documents:**
2. **Cover letter** requesting the amendment:

* **Protocol code + EudraCT No. + Title**
* Contact person (name, telephone and email)
* **Identification** of the substantial amendment: name and date
* **Part** affected by changes.
* Date of submission to AEMPS.
* **Brief description** of the amendment.
* **Index** of documentation: indicate documents with version, date and how they must be described in the amendment resolution.
* Must be submitted in a format that allows information to be copied.

For the specific case of the following amendments, please consider:

* **Amendments only affecting the Investigator’s Brochure:** If a relevant amendment to the investigator’s brochure is submitted that only affects part I, include justification of the reason no change is required in the trial PIS-IC. This will be included in the request for clarification if not provided.
* **Amendments including recruitment material and posters:** include justification of how this material will be used and, if they are aimed at patients, who will provide them with the material. This will be included in the request for clarification if not provided.

1. **Appendix 1C** (European application form for the relevant amendment for clinical trials with medication) in a format that allows information to be copied.

Filled out via the “Clinical trial management portal” of the **Ministry of Health and Social Policy:** <https://ecm.aemps.es/ecm/paginaPresentacion.do>**.**

1. If the amendment involves a change in **Appendix 1A**  (European application form for clinical trials with medication), include the redlined document and submit it in a format that allows information to be copied.
2. **Summary and justification of changes:** A maximum of 1200 words containing a summary of changes made and reasons behind them.
3. **Redlined documents:** Include a clean and redlined version for each document to be evaluated if the documents are not new.
4. **Consequences of the amendment**: Include (a) an updated overall benefit/risk assessment, (b) possible consequences for subjects already included in the study, and (c) possible repercussions on result evaluation.
5. **Proof of CEIm fee payment:** PDF of the invoice request email sent to the foundation economic management department ([facturacion@vhir.org](mailto:facturacion@vhir.org)) indicating invoicing details.

***Note - In the case of an independent sponsor*** (academic sponsor, non-profit organisation, or investigators from HUVH or any of its Departments), exemption from fees may be requested by sending the following document: [**Request for exemption from fees**](#exención)

If exemption from fees was granted in the initial study request you need not request exemption again for each amendment.

1. **Adding site/s:**
2. Cover letter
3. Appendix 1C
4. Appendix 1A updated and redlined
5. Proof of CEIm fee payment
6. Suitability of investigators document in digital format signed by the sponsor (Appendix II of the AEMPS instruction document) with the new site and PI.
7. CV of the principal investigator for the site in digital format, including training in good clinical practice, professional experience in clinical trials and patient care. As well as any other circumstance that may influence impartiality of investigators (no reference will be understood as there being no such circumstance).

\*Training in good clinical practices can be included in the CV or as a separate document.

1. [Suitability of site](#Instal) in digital format (form attached on page 5 of this document, also included in the AEMPS instruction document; the logo of each site need not be included). Indicate the name and position of the person signing the document.
2. Proof of insurance coverage or financial guarantee covering the new site:
3. In the case of trials approved under RD 1090/2015, submit the *Insurance certificate form* for a clinical trial with medication and commercial sponsor (appendix IV of the AEMPS instruction document).
4. In the case of trials approved under RD 223/2004, please remember that the insurance policy must be submitted with reference to the new RD 1090/2015 and list exclusions.
5. And in the case of a clinical trial with a low level of intervention, provide the site/organisation representative certificate form (appendix VI of the AEMPS instruction document) for each participating site.
6. **Change of Principal Investigator (PI) for a site:**
7. Cover letter

1. Appendix 1C
2. Appendix 1A updated and redlined
3. Proof of CEIm fee payment
4. Suitability of investigators document in digital format signed by the sponsor (Appendix III of the AEMPS instruction document) with the new PI.
5. CV of the new principal investigator for the site in digital format, including training in good clinical practice, professional experience in clinical trials and patient care. As well as any other circumstance that may influence impartiality of investigators (no reference will be understood as there being no such circumstance).

\*Training in good clinical practices can be included in the CV or as a separate document.

1. Proof of insurance coverage or financial guarantee covering the new PI:
2. In the case of trials already approved under RD 1090/2015, submit the *Insurance certificate form* for a clinical trial with medication and commercial sponsor (appendix IV of the AEMPS instruction document).

In the case of trials approved under RD 223/2004, please remember that the insurance policy must be submitted with reference to the new RD 1090/2015 and list exclusions.

1. **Change of trial title:**
2. Remember to submit Appendix 1A, redlined.
3. Include a clear notice in the cover letter.
4. Submit all trial documents with the title changed and also redlined versions.
5. Submit the insurance policy certificate with the updated title.

**AMENDMENT DOCUMENTATION FORMAT**

Documentation for *amendments* and for **clinical trial with medications** must be submitted electronically via the clinical trial Management Portal of the Ministry of Health and Public Policy ([https://ceic.msssi.es/siccceic/index.jsf](https://ecm.aemps.es/ecm/paginaPresentacion.do))

**SIMULTANEOUS SUBMISSION OF TWO RELEVANT AMENDMENTS:**

Two relevant amendments may be submitted simultaneously if one only affects part II of the trial and is not related to part I: adding sites or PI changes, for example.

In the case of adding sites or PI changes, remember that if amendments to part I+II are included, these changes will follow the schedule for processing together. Therefore, if they are urgent, the amendments can be submitted separately.

## VALIDATION, CORRECTION AND CALENDAR FOR RELEVANT AMENDMENT TO A CLINICAL TRIAL WITH MEDICATION

* **Validation**: The deadlines established in RD1090/2015 will apply: 6 calendar days.
* **Corrections:** If a correction is requested, it will be sent by email to the contact person indicated in the letter of presentation. Documentation to be corrected may be sent via the Clinical Trial Management Portal of the Ministry of Health and Social Policy (<https://ecm.aemps.es/ecm/paginaPresentacion.do>**)** or by mail.

The corrected documentation must be submitted within 10 calendar days from receipt of the email. The evaluation schedule will not start until documentation is complete, so we recommend not sending amendments with missing documentation.

* Once validated, the status will change from “validation” to “evaluation” on the portal and the applicant will receive an email from the system.
* In the case of amendments affecting part I or part I+II, AEMPS will send the evaluation schedule.

**EVALUATION**

The CEIm will distribute and organise validated amendments at the meeting deemed appropriate according to total entries received, and always according to the evaluation calendar provided in RD 1090/2015. An amendment being evaluated sooner or later will depend on evaluator availability, therefore, we cannot indicate the exact date the amendment will be evaluated once validated.

There is normally one meeting a week (Friday). The updated schedule can be found on our website.

## RESOLUTION OF PART II:

* The CEIm will issue the resolution for part II within the deadlines established in RD1090/2015 and in accordance with the validation calendar issued by the AEMPS.
* The resolution will **only** include lists of documents evaluated by the Committee with relevant amendments.
* **Documents not listed in the resolution**: non-relevant amendments, amendments that can only be evaluated by the AEMPS (such as the IMPD) and other documents the Committee does not evaluate (patient diary or card, calendars, etc.).
* If requesting **clarifications for part II**, the **resolution will always be sent by email** to the applicant. And documentation responding to clarifications will be sent by email.
* In the case of clinical trial with medications, the **favourable resolution** for part II will be sent **via the Clinical Trial Management Portal of the Ministry of Health and Social Policy.**
* **Appendix II** will only be included for amendments that add sites or change PI, and only added sites or changes in sites will be listed.

## SUBMISSION OF RESPONSE TO CLARIFICATIONS TO THE CEIM (IF REQUESTED):

* For a clinical trial with medication, the sponsor has **12 calendar days** to send a response to the CEIm and non-commercial sponsors will have 30 calendar days to send it.

The period starts from date the resolution is received.

* The response to relevant amendment clarifications will be submitted **by email** to [ceic@vhir.org](mailto:ceic@vhir.org).
* **Documentation to be submitted:** A document responding to the clarifications and amended documents must be submitted. In the case of the latter, submit a clean and redlined version, updating version and date. And new versions must be listed in the email/letter of response to clarifications, as they appear in the resolution.
* In the case of a clinical trial with medication: In the case of a request for clarification to part I and II, we recommend including the responses to the clarifications requested by the AEMPS to part I and those requested by the CEIm to part II at the same time

**AUTHORISATION FOR RELEVANT AMENDMENT BY THE AEMPS:**

* Substantial amendments involving changes in ***part I and in part II*** will be considered authorised due to failure to respond 5 calendar days following notification by the sponsor to the AEMPS of the favourable resolution of the CEIm to part II, or after the evaluation deadline for part I (whichever date is later).
* Substantial amendments that only involve changes in ***part I*** will be considered authorised due to failure to respond if the applicant indicates that the sponsor has not received the authorisation resolution within 5 calendar days following the evaluation deadline.
* Amendments with ***part I*** only are also evaluated by the CEIm, but **no resolution will be issued**. We will send our report to the AEMPS and they will issue a joint resolution. Therefore, an amendment can be considered approved if authorisation is received from the AEMPS for an amendment with part I only.

**QUERIES:**

Send any queries to:

CEIm Support Unit

[ceic@vhir.org](file:///e:\36520918t\Escritorio\SOL.LICITUDS%20AC-EPA\AC\ceic%40vhir.org)

Telephone: +34 93 489 40 10

##### REQUEST FOR EXEMPTION FROM FEES

**STUDY CODE TO BE FILLED IN BY THE CEIm SECRETARY’S OFFICE**

**REQUEST DATE:**

Study details

Study code:

EudraCT:

Sponsor:

CRO:

Type of evaluation

First evaluation

Relevant amendment

Has approval from a REC or CEIm in Spain:

YES

NO

**Reasons** for requesting exemption (explain briefly in 3-5 lines)

The sponsor/CRO/PI undertakes to notify any change in study funding.

**RESOLUTION:** *(To be filled in by the site*)

Accepted Signature:

Denied

The fee for non-commercial sponsors with funding will be paid.

**Send this request to:** [ceic@vhir.org](mailto:ceic@vhir.org)