**IMMEDIATELY APPLICABLE AMENDMENT - URGENT SAFETY MEASURES:**

Any new development related to conducting the trial or the evolution of the investigational product that may affect the safety of trial subjects, the sponsor or investigator will take the relevant urgent safety measures to protect trial subjects from immediate danger. The sponsor will notify these new developments and the measures adopted simultaneously to AEMPS (Agencia Española de Medicamentos y Productos Sanitarios [Spanish Agency of Medicines and Medical Devices])  
 and the mREC via the ECM portal without delay.

Examples of urgent measures for trial subject safety include temporary suspension of the trial or implementation of other supervision measures.

Urgent safety measures can be taken without prior notification but the AEMPS and mREC must be notified of the measures taken and plans via the ECM portal as soon as possible.

Then subsequently:

* Submit the relevant amendments (requirements are available on the website, in the section “*EC amendment evaluation request*”).
* Notify if the trial is terminated early, within15 days.
* Notify adverse events or serious adverse reactions within the legally established deadlines.

**TEMPORARY TRIAL HALT**

1. A trial halt is a temporary stoppage that was not envisaged in the approved protocol and the intention is to resume the trial.
2. It may be due to a relevant amendment; or be an urgent safety measure (in this case, the trial halt must be notified immediately and, at the latest, within 15 days for early trial termination).
3. The reasons and scope will be clearly explained —for example, suspension of inclusion of participants or interruption of treatment for subjects already included— in the notification (for a relevant amendment) or in the subsequent information (in case of urgent safety measures).
4. **Restart of the trial** may be treated like a relevant amendment, submitting proof that it is safe to resume (requirements for submitting the amendment are available on the website, in the section “*EC amendment evaluation request*”). If the documents were already submitted and approved for a prior relevant amendment, restarting will be notified as a notification sent to the mREC and the AEMPS.
5. If the sponsor decides to not resume a halted trial, they will notify the AEMPS and the mREC of their decision within 15 days.