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Guidance for applicants: Pre-CTA advice pilot

ACT EU priority action on consolidated advice

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1. What is the Pre-CTA advice pilot? - *updated*

The Accelerating Clinical Trials in the EU (ACT EU) initiative launched two advice pilots on 10 June 2024, aimed at enhancing the coordination within the European Medicines Regulatory Network (EMRN). The pilots provide sponsors/applicants with harmonized advice on how to enhance the quality of their applications for marketing and/or clinical trial authorization(s). The initiative aims at establishing an early dialogue between sponsors/applicants and regulators, on scientific and regulatory matters, to facilitate the development of safe and effective medicine for human use in Europe.

The Pre-CTA advice pilot provides guidance to sponsors/applicants planning to submit a Clinical Trial Application (CTA) to the Clinical Trial Information System (CTIS) under European Regulation (EU) No 536/2014.

The Pre-CTA advice will involve coordination between assessors from the National Competent Authorities (NCAs) of EU Member States (MS) on the regulatory and technical aspects of clinical trials (CT).

The pilot project is coordinated by the Clinical Trial Coordination Group (CTCG).

2. How does this pilot fit within the landscape of all EU advice activities? - *updated*

There are several ways to seek advice within the EMRN (please refer to the mapped information available on the ACT-EU webpage). The Pre-CTA offers a new opportunity but will not replace the existing procedures provided by EU regulators for Medicines for Human Use. This pilot provides consolidated technical and regulatory advice on a CTA dossier from the Member States concerned (MSCs) before it is submitted to the CTIS for assessment. The initiative aims to foster early interaction between clinical trial sponsors/applicants and regulators, addressing regulatory and technical questions related to the CTA. By doing so, it will help improve the quality of the CTA and reduce the risk of divergent views among the Member States concerned due to differing national approaches

For the Pre-CTA pilot, the forum for exchange and communication between assessors from the NCAs of the MSCs is the weekly Assessors Round Table (ART). This forum was established by the CTCG to facilitate discussions on specific topics among assessors from different NCAs. The final advice letter will be issued to the MSCs involved in the outcome of the Pre-CTA advice.

ACT EU priority action on consolidated advice has updated the **mapped information** on voluntary procedures available within the European medicines regulatory network: Advice on medicines for Human use in the EU medicines regulatory network (europa.eu)

3. What are the criteria to apply for the Pre-CTA advice pilot?

Essential criteria

These criteria will need to be satisfied in order to be considered as a possible pilot case:

- Only (up to 5) regulatory and technical questions are allowed for each Pre-CTA advice request.
- The applicant should already have an almost mature protocol.
- The applicant should know the proposed Reporting MS for the future CT application in CTIS.

Scope of the Pre-CTA advice

The following topics fall within the scope of the Pre-CTA advice. The list is not exhaustive.

- CT within scope of the Clinical Trial Regulation (Y/N).
- Low Intervention Clinical Trial.
- Combination products / combined CTs (MDR/IVDR).
- Operational aspects of the submission of the CTA in CTIS (Complex CT, transition of CT).
- Regulatory request on Good Laboratory Practice (GLP) guideline.
- Regulatory request on Auxiliary Medicinal Product (AxMP) guideline.
- Decentralized elements in CTs.
- Risk based trial performance (e.g. reduced safety reporting).
- Open questions before re-submission of updated dossier.
- Other regulatory and technical aspects of the CTA.

Out of scope of Pre-CTA advice pilot

- Requests on scientific aspects of clinical trials are out of scope and better suited for other advice procedures: Advice on medicines for Human use in the EU medicines regulatory network (europa.eu).
- Preassessment of CTA is out of scope.

4. How do I apply for Pre-CTA advice pilot procedure? - *updated*

- For the Pre-CTA advice pilot, you can apply through the Specific National Scientific Advice (SNSA) entry point via a dedicated email address SNSA@fagg-afmps.be.
- Please use the application form available on HMA and ACT EU websites, ticking the box indicating that the request refers to a Pre-CTA advice.
- Please add the following information:
  - Request to be admitted to the Pre-CTA advice pilot.
  - The proposed reporting member state (RMS) for the application. Where applicable provide the Trial reference number.
  - The proposed MSCs for the application.

Finally, it is considered useful to submit a cover letter containing as much information as possible about the advice request sent.

- Sponsors/applicants are recommended to review the list of MS participating and their roles. Please ensure that the proposed RMS can take the role of Lead-MS in the Pre-CTA advice. The validation phase takes a maximum 7 calendar days, and it is aimed at assessing whether the

questions do fall within the scope of the Pre-CTA and to select the Lead-MS. Applicants will be informed of the receipt of the request by the SNSA coordination unit, which indicates the start of the validation phase.

- Sponsors/applicants will also receive a notification at the end of the validation phase indicating that the request will or will not continue with the assessment phase, the Lead MS and the timetable. The assessment phase takes a maximum 30 calendar days.
- A Pre-CTA application may be declined if the request is not related to technical/regulatory matters and therefore does not fall within the scope of the pilot or if the proposed RMS and/or none of the MSCs apply for the Lead-MS role.

For any further information please write an email to the following address: prectaadvice@ema.europa.eu.

5. What fees will I have to pay if my request is accepted into the pilot? - *updated*

For the Pre-CTA pilot, only the Lead-MS might require a fee according to national requirements and following national procedures. Different approaches might exist for commercial and non-commercial sponsor/applicants depending on the national requirements. There is no published list of national fees for Pre-CTA advice, it is therefore necessary to communicate with single MS for detailed information.

6. How many pilot procedures are foreseen?

During the initial pilot phase, a series of **5 Pre-CTA advice procedures** will be followed by an evaluation step leading to procedural optimization. During this phase the pilot can continue. Some flexibility on cases is anticipated, based on the capacity.

7. What is the process?

For high level details of the process flow see annex 1.

8. What is the outcome of a pilot procedure?

The outcome of a pilot procedure will be a Pre-CTA advice letter.

As for other standard European advice, the Pre-CTA advice will not be legally-binding, but applicants should justify divergence with the advice received when submitting the formal CTA.

The Pre-CTA advice does not represent a pre-assessment of the data for CTA.

9. How can I be assured that the information is kept confidential?

As for standard European advice procedures, normal principles of confidentiality and handling of conflicts of interest apply.

10. Pilot – Deliverables and measure of success - *updated*

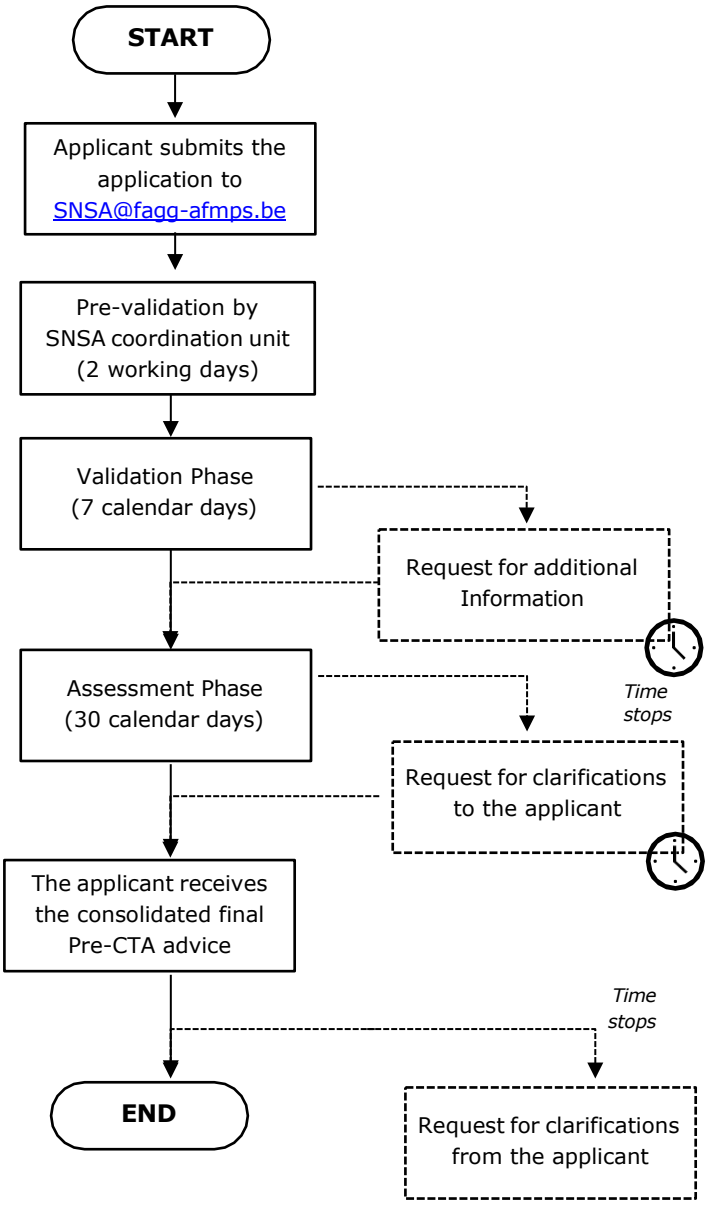
The aim of a Pre-CTA is to provide a single consolidated opinion, thus promoting harmonisation of regulatory expectations between different MSC, with the possibility of achieving greater consistency in the interpretation and application of technical and regulatory requirements.

The sponsors/applicants admitted to the Pre-CTA advice pilot will receive a questionnaire upon completion of the pilot procedure regarding the more immediate efficiency and benefits of the procedure, and of the perceived downstream benefits. This feedback will help the evaluation of the pilot. Interim analyses will be provided to monitor progress of projects and identify potential issues during the course. Long-term feedback on the outcome of the CTA will be also requested.

List of annexes

Annex 1 Process flow for Pre-CTA pilot.

Annex 1


START
Applicant submits the application to SNSA@fagg-afmps.be
Pre-validation by SNSA coordination unit (2 working days)
Validation Phase (7 calendar days)
Request for additional Information
Time stops
Assessment Phase (30 calendar days)
Request for clarifications to the applicant
The applicant receives the consolidated final Pre-CTA advice
Time stops
END
Request for clarifications from the applicant