4 June 2024
EMA/251446/2024

Guidance for applicants on Simultaneous National Scientific Advice (SNSA) – phase 2 pilot – Optimized process

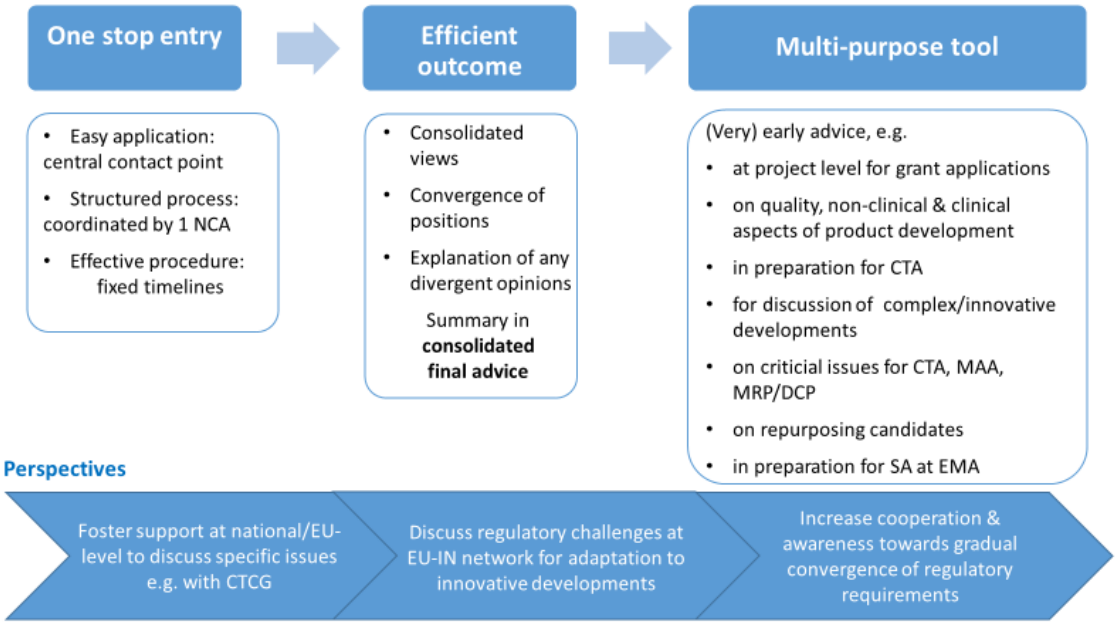
1. Background

Developers of medicinal products regularly seek national scientific advice to prospectively optimise their development programme. Scientific and / or regulatory advice can be received nationally by national competent authorities (NCAs), or centrally coordinated by EMA and these advice procedures are intended to complement each other. Developers may choose to obtain national scientific advice or EMA scientific advice at different stages of development for various reasons. National scientific advice is often sought in earlier stages of development (e.g. relating to clinical trials to be performed in a limited number of MSs) or relating to matters falling within the remit of national competent authorities whereas EMA scientific advice may be sought in advance of multinational pivotal clinical trials expected to generate data to support a future centralised marketing authorisation application. Experience has shown that when national advice is sought it is often requested in parallel from more than one NCA.

In order to optimize resources on both sides and improve the regulatory support, the Simultaneous National Scientific Advice (SNSA) approach has been developed. The objective of the concept is to establish a more efficient procedure for applicants who wish to seek advice on the same set of questions and data package from different NCAs.

Following a positive evaluation of the first pilot phase from 2020 to early 2022 during which more than 33 pilot requests were received across different therapeutic areas covering a broad range of medicinal products, the HMA endorsed a second pilot phase to run for a two-year period (i.e. from dec 2022 – end of 2024). The second phase of the pilot incorporates an optimised process which will include commonly agreed predictive timelines, the use of one common application form, reduced administrative burden for applicants and competent authorities, increased efficiency and transparency as well as the participation of additional NCAs in the pilot. In addition, the optimised SNSA process also allows the option for other NCAs to participate as observer in the SNSA procedure if adequately justified by the Applicant. The SNSA process will continue to complement and provide a bridge between purely national scientific advice and centralised EMA scientific advice as well as supporting the aims of the ACT-EU initiative related to clinical trials.

The second phase of the pilot will continue to explore the opportunities and interest in the concept for especially developers of innovative medicines. For the regulators the focus will be on identifying the different needs of the applicants to enhance innovation, support clinical research and applications under the new clinical trial regulation, facilitate and speed up regulatory approval across the entire product development cycle whereas avoiding gaps in early regulatory support.



2. Scope, participating NCAs, target groups and procedure

2.1 Scope

The scope of the SNSA is in general identical to single national scientific and regulatory advice procedures offered by NCAs. At current, the scope for SNSA pilot requests is limited to medicinal products for human and veterinary use as well as drug-device combination products for as far as these combination products fall within the remit of the NCA's participating in the SNSA pilots and their scientific-regulatory advice services. SNSA requests related to stand-alone medical devices are currently excluded from the scope of this guidance document; applications of borderline products will be decided case by case depending on the principal mode of action.

In principle SNSA requests can be submitted throughout the entire product life cycle (i.e. pre- and post-marketing authorization stage, with the main focus of the SNSA pilots currently lying on facilitating the early clinical development stages (e.g. Phase 1 – 2) and in particular multinational clinical trials in the context of the new Clinical Trial Regulation (EC 536/2014). In addition, applications at pre-grant stage, prior to applying for funding grants as well for repurposing of authorised medicinal products are possible as well.

The question(s) raised by the Applicant should address specific scientific and/or technical-regulatory issues. The aim of an SNSA request is to advise the Applicant in a targeted way on the specific questions that are being raised and not to perform a pre-assessment of the complete formal application(s) to which the SNSA request. EMA scientific advice should continue to be used for scientific advice related to the suitability of the proposed clinical development to support a centralized marketing authorisation application.

Where during the SNSA the involved NCAs agree that the questions raised would benefit from discussions at the Clinical Trial Coordination Group (CTCG) level, it is also possible to obtain CTCG-coordinated clinical trial expert feedback as part of the SNSA procedure. When sufficiently justified by the Applicant, participation of a CTCG representative and/or an Ethic Committee representative in the SNSA meeting can also be requested by the applicant. (In the latter case, an Ethic Committee representative will be proposed in concertation with the CTCG). In addition, in justified cases, e.g. where the request relates to a clinical trial to be performed in more than 2 MSs, the involvement of additional MSs in a single SNSA procedure will be considered subject to the agreement of the NCAs.

Applicants are also strongly being recommended to seek SNSA in an agile, iterative manner in the course of the product development cycle through follow-up SNSA requests in a stepwise approach to leave room to discuss in detail each developmental step – in case of doubt the scope of the SNSA can be clarified when drafting the application.

Questions on quality, non-clinical and clinical aspects

- of medicinal products
- of drug device combination products at NCAs with the corresponding remit
- at any stage of product development

Restrictions

- HTA and reimbursement aspects are currently excluded; restrictions may be lifted along the future development of the pilot project
- SNSA is limited to the scope and questions raised in the briefing document

2.2 Participating NCAs

- the concept has been developed to optimize use of resources on both sides to improve scientific and regulatory support. National scientific and/or regulatory advice can be requested with two or more NCAs simultaneously in one single step. In special cases, when sufficiently justified by the Applicant, participation of a CTCG representative and/or an Ethic Committee representative in an SNSA request can be considered.
- NCAs will participate on an opting-in basis for individual SNSA procedures based on the established best-practice model and following the new optimized procedure.

2.3 Target Groups

• No restrictions are foreseen, all types of applicants can apply for an SNSA pilot

• Special support for academia and SMEs to prepare SNSA, especially for requests of innovative/complex developments, e.g. clarification of issues by phone possible

For SNSA requests/inquiries the contact details at NCA level (cfr. List of NCA's participating in the SNSA pilot phase 2) can be used in addition to the central contact point snsa@fagg-afmps.be.

2.4 Procedure

The key features of the optimized SNSA procedure to be used as of 1st December 2022 onwards in Phase 2 of the pilot project are described below:

Request for SNSA

1. Select one NCA as lead NCA and one or more NCAs from the list of participating NCAs. Add also alternative NCA to replace the lead NCA or participating NCA in case their respective participation is not possible (1).

2. The Applicant can also select another NCA as Observer (See below for knowing more about the Observer's role)

3. Send the request to the central contact point called "Coordinating Unit" (PEI, AEMPS and FAGG-AFMPS) using the following email address: (snsa@fagg-afmps.be):

- using the common SNSA application form, indicating the selected NCAs
- adding the list of questions you seek SNSA for. Please bear in mind that only very minor updates could be included in a later stage (*)
- giving a brief outline of the scope of the SNSA request(*)

(*) For more details please refer to the Guidance for applicants on SNSA briefing book format and content.

The Coordinating unit is composed by PEI, FAGG-AFMPS and AEMPS so any of this NCA could contact the Applicant after the submission of the application.

If the proposed NCA(s) are not able to accept the SNSA, it is possible to:

- continue the SNSA procedure with alternative lead/participating NCAs (see above)
- change the procedure to a standard national scientific advice request or
- withdraw the whole SNSA application

At some point, see the "Flow chart" of the procedure, the Lead NCA will take over the procedure. Information will be disseminated to the Applicant by the Coordinating unit or by the Lead NCA as contact points for the SNSA procedure. The participating NCA will only contact the Applicant for the fees.

The procedural timeline of the SNSA will be mutually agreed on by the participating NCAs, respecting as far as possible the preferred dates proposed by the Applicant as stated in the submitted application form. The date of the meeting will be communicated by the Coordinating Unit.

Apart from some limited member-state specific aspects (eg. follow-up on the scientific advice fee payments to the NCA's or any fee reduction/exemptions provided by the respective NCA's) it is the role of the lead NCA to act as single point of contact towards the Applicant during the course of the SNSA procedure. The NCA contact emails of the involved NCAs will be sent to the Applicant.

Observer NCA role

The observer NCA will attend to the preparatory meeting between NCAs (if occurs) and attend the formal SNSA meeting with the Applicant but it will not contribute to the formal SNSA meeting with the Applicant nor to the review of the meeting minutes and a note will be included within the final advice report stating that the Observer NCA did not evaluate the application in detail due to its observer role. The Observer NCA will review the minutes only to check the participants list and include only information about national legal requirements, if needed.

SNSA procedural steps

1. At the time of initiating the SNSA submission request:

The following documents should be provided by the Applicant to the SNSA coordination unit at the time of initiating the SNSA submission request:

- Application form.
- Draft List of Questions for which SNSA is being requested to allow the involved NCAs to start designating the most appropriate experts for addressing the SNSA request.
- Brief outline of the scope of the SNSA request (e.g. including short description of the drug product characteristics, manufacturing process for e.g. ATMP, background of the intended (pre) clinical development project, etc.

2. At the time of the formal start of the procedure:

- According to the Flow Chart published together with this guidance document. Send the briefing documents at Day 0. However, to allow some flexibility, the Applicant is allowed to send in an updated version of the briefing package until Day 20 of the procedure as long as it concerns only minor updates which would not require additional experts to be involved in the SNSA.
- At the beginning of the application add a cover letter and a detailed list of questions stating a clear position to each question (for more details please refer to the Guidance for Applicants on SNSA Briefing book format and content).

- The briefing document will be subject to validation. During formal validation of received SNSA requests, a request for additional information, clarification or resubmission could follow.
- After successful validation of the briefing documents the SNSA procedure will formally start.
- The SNSA meeting will be scheduled at the latest 55 days after the formal start of the procedure.

Please note:

- Meetings will normally be arranged virtually. However, if justified, a hybrid meeting format can be provided on mutual agreement.
- Information about the details to join the meeting will be sent out by day 50 at the latest.
- NCAs will be represented by national experts based on the scope and questions of the advice.
- The lead NCA will also take the lead for moderating the meeting.
- There is no possibility to change or add new questions or data in the course of the SNSA procedure nor during the meeting.
- If during the course of the SNSA procedure the lead NCA and participating NCAs consider that the SNSA could be satisfactory resolved in writing instead of by teleconference it would be notified to the Applicant.

Post Meeting

- After the meeting the lead NCA will ask the Applicant to draft the meeting minutes of the formal SNSA meeting, using the template provided which should be sent to the lead and participating NCAs within 10 days after the meeting.
- According to the Flow Chart the consolidated final advice incorporating the positions of each of the participating NCAs will normally be finalised and disseminated to the Applicant by day 90.

Please note:

- A request for clarification is possible after receipt of the formal advice report and will be handled in agreement between the NCAs and in compliance with their respective procedures.
- New questions from the applicant would be dealt with in a follow-up advice request.
- The fees for a SNSA procedure will be based on the national fees of each of the involved NCAs (except for the Observer NCA) and will be payable individually to each NCA.

- As feedback is very important to us to further improve the procedure a questionnaire on the SNSA meeting will be sent by the lead NCA to the Applicant to be completed and returned within four weeks.

2.5 Implementation and evaluation of the pilot

- This second pilot phase is running for a two-year period till end 2024. New SNSA requests submitted under pilot phase 2 can be submitted until end of 2024.
- At the end of this period a further evaluation will be performed to analyse the experiences of the optimised SNSA procedure both from NCA's and Applicant's perspective. The outcome of that evaluation will inform the next steps in relation to the SNSA concept to be agreed with HMA. Based on the demand for SNSA , the available NCA resources and the positive evaluation of the pilot, steps to continue with this consolidated advice format will be taken in the near future procedure.
- In order to facilitate the evaluation of the pilot, applicants are strongly encouraged to use the SNSA procedure during the pilot particularly in scenarios where they are considering seeking national scientific advice from more than one NCA in parallel.
- Applicants are also requested to complete the questionnaire which will be sent to them at the end of each procedure to facilitate the evaluation of the pilot.