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Guidance for applicants on Simultaneous National Scientific Advice (SNSA) phase 2 pilot (from October 2022) – Optimized process

1. Background

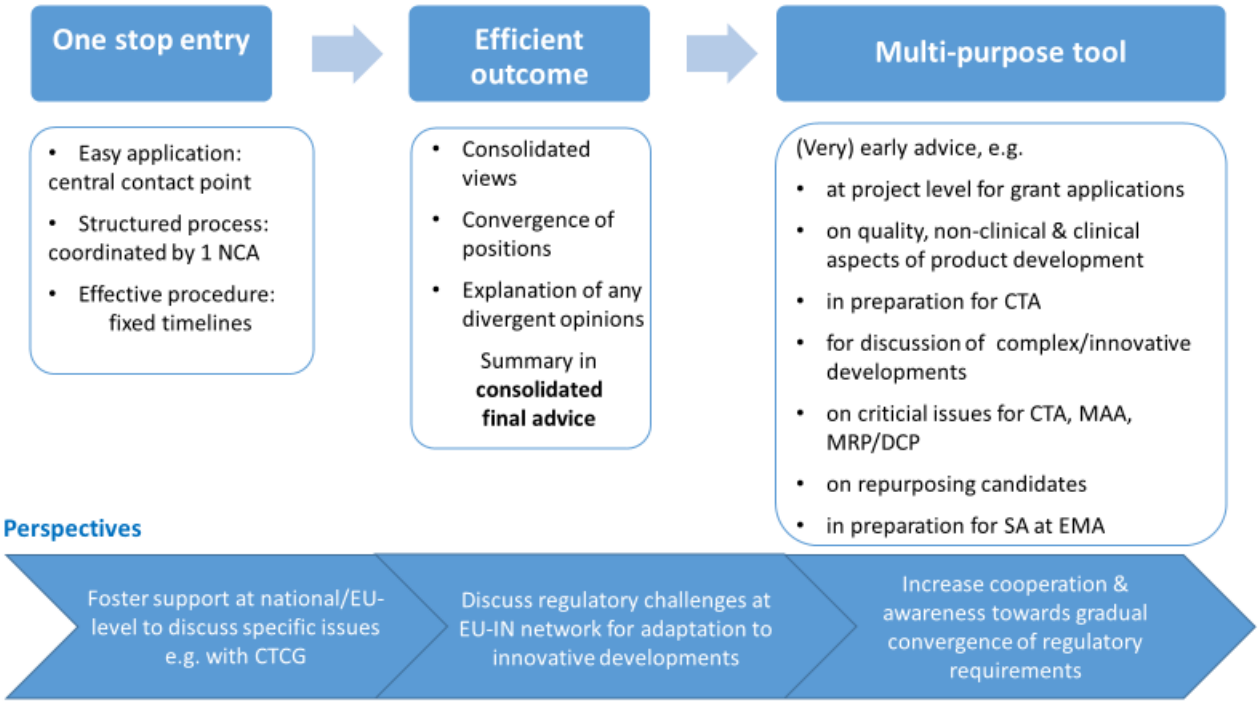
Developers of medicinal products regularly seek national scientific advice to prospectively optimise their development programme. Scientific and / or regulatory advice can be received nationally by national competent authorities (NCAs), or centrally coordinated by EMA and these advice procedures are 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. 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 a third NCA to participate as observer in the SNSA procedure. 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.

The SNSA approach is to provide concise advice embedded in an efficiently structured consistent procedure which aims to optimise resources for both the applicants and NCAs. The key success criteria build on different levels, starting with the guided advice process from the stage of initial SNSA application, reaching over follow-up support beyond the scope of the initial SNSA request until addressing crucial issues at EMA/HMA level (e.g. CTCG, EU IN, SAWP, etc) to improve exchange of knowledge and support for innovative developments across the product development life cycle and finally to strengthen regulatory science.



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 as observer in the SNSA meeting can also be requested by the applicant. 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, safety and efficacy

- 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 regulatory support, national scientific and/or regulatory advice can be requested with two NCAs simultaneously or even in special cases including a third NCA as observer in one single step.
- NCAs will participate on an opt-in basis for individual SNSA procedures based on the established best-practice model and following the new optimized procedure.

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@pei.de.

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

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 in below:

Request for SNSA

1. Select two NCAs from the list of participating NCAs and if applicable add an alternative NCA to replace NCA 1 or 2 in case the respective participation is not possible(1)
2. Send the request to the central contact point **SNSA@pei.de**:
   - using the common SNSA application form, indicating the selected NCAs
   - adding a draft list of questions you seek SNSA for(*)
   - 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.

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

- continue the SNSA procedure with an alternative second NCA (see above)
- change the procedure to a standard national scientific advice request or
- withdraw the whole application

By mutual agreement of both NCAs, one NCA will take over the lead of the procedure. Information will be disseminated by the coordinating agency as the main contact point for the SNSA procedure.

The timeline of the SNSA will be mutually agreed on by both NCAs, respecting the preferred dates for the SNSA stated in the application form as far as possible.
The date will be communicated by the coordinating agency.

(1) At the time of initiating the SNSA submission request the Applicant can also propose a 3rd NCA to join the SNSA pilot as an observer, in addition to the 2 NCAs being proposed to take the role of either coordinating or participating NCA. However, it is up to the NCA's internally to decide on which NCA will take the lead in the overall coordination and communication throughout the procedure as "coordinating NCA" towards the Applicant and the other involved NCA(s).
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 coordinating NCA to act as single point of contact towards the Applicant during the course of the SNSA procedure.

SNSA process

- Send the briefing documents at least 25 days before the meeting date to the coordinating NCA.
- 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 documents will be subject to validation.
  Alternatively, a request for 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 60 days after the formal start of the procedure.

Please note:

- Meetings will normally be arranged virtually.
- 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 coordinating 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 in the meeting.

Post Meeting

- After the meeting the coordinating NCA will ask for a first draft of meeting minutes report drafted by the applicant using the template provided.
- The consolidated final advice incorporating the positions of each of the participating NCAs will be finalised and disseminated by day 90 at the latest.
- In case of any doubt a request for clarification is possible at the coordinating NCA within two weeks after receipt of the consolidated final advice.

Please note:

- Requests for clarification 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 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 coordinating agency to be completed and returned within four weeks.

2.5 Implementation and evaluation of the pilot

- This second pilot phase will run from a two-year period. 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. In the event that the pilot is successful options could include further optimisation of the SNSA procedure including the participation of additional NCAs in each 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.