01 January 2025
European Medicines Agency

Questions and Answers about the SEND proof-of-concept for industry

Scope, terms of participation and data submission process

EMA has launched a proof-of-concept (PoC) study to evaluate the added value of using SEND datasets in the evaluation of new Marketing Authorisation Applications. Applicants are encouraged to submit their SEND datasets, in addition to the eCTD format, as part of their MAA submission. Detailed instructions are available on the e-submission website (eSubmission: Projects (europa.eu)).

What is SEND?

SEND, also referred to as "Standard for Exchange of Nonclinical Data" provides the structures and implementation rules for the submission of data from single- and repeat-dose toxicity studies, safety pharmacology studies, developmental and reproductive toxicity studies, and carcinogenicity studies.

SEND has been created by the Clinical Data Interchange Standards Consortium (CDISC) in 2002 to execute on the Study Data Tabulation Model (SDTM) for the submission of non-clinical studies (SEND | CDISC). A SEND package contains the SEND datasets (.xpt files), the Nonclinical Study Data Reviewer's Guide (nsdrg.pdf), and the Define XML Document (define.xml).

Why a proof-of concept?

Standardisation of data presentation has been shown to significantly reduce the time regulators require for reviewing non-clinical data packages. The PoC study aims to evaluate whether using SEND datasets in the assessment of the non-clinical dossier will lead to improved and more consistent quality of assessments, fewer data-driven questions to Applicants, and to faster completion of the non-clinical dossier assessment.

Any questions? Email us at send@ema.europa.eu

1. General questions about the SEND Proof of Concept

1.1. Why is the SEND PoC performed?

The PoC study will be conducted to investigate the benefits of visualising and assessing raw non-clinical data to support the scientific assessment of medicinal products. The PoC study will provide valuable insights for future assessments by capturing the practical implications, such as the operational, resource and technological requirements, and soliciting feedback from all the parties involved, such as their perceptions of the benefits and challenges of the new process. This will include feedback from the Rapporteurs' assessment team, the Agency, and the Applicant or MAH of the regulatory procedures concerned by the PoC phase. The aim of the PoC is to generate learnings that will be translated into recommendations to the European Medicines Regulatory Network whether access to non-clinical raw data could support future regulatory assessments.

How will relevant stakeholders be consulted on the PoC design and how they be consulted on its execution?

EMA has informed relevant stakeholders via presentations at various fora, information on the e-submission website and personal communications to Applicants.

1.2. When has the PoC started and how long will it run?

The PoC has been launched in January 2024. It is envisaged that the PoC runs until it includes at least 10 centralised applications submitted to EMA that contain SEND data-packages. EMA has not defined a submission deadline for the inclusion of procedures in the PoC.

1.3. Which regulatory procedures are in scope for the PoC?

Initial Marketing Authorisation Applications (iMAAs) submitted centrally to EMA are in scope for the PoC.

1.4. Are decentralised procedures or referral procedures in scope for the PoC?

No, decentralised procedures or referral procedures are not in scope for the PoC.

1.5. Are procedures concerning Advanced Therapy Medicinal Products (ATMPs) eligible to be included in the PoC?

Yes, procedures concerning ATMPs are eligible to be included in the PoC.

1.6. Are procedures with accelerated assessment eligible to be included in the PoC?

Yes, procedures with an accelerated assessment are eligible for inclusion in the PoC.

1.7. Is it mandatory for applicants/marketing authorisation holders to participate in the PoC?

Applicants/MAHs submitting an iMAA to EMA that falls within the scope of the PoC (see Question 1.4) are encouraged to participate. Participation allows the applicant/MAH to share feedback on their experience and support the European Medicines Regulatory Network in evaluating relevant lessons learned about the future role of access to non-clinical raw data to support the regulatory assessment (see Question 1.1). A procedure will only be included in the PoC if Applicant/MAH has submitted their

SEND datasets with their eCTD submission (or following a request from the NCA) and the NCA participates in the PoC.

1.8. How will the raw data analysis results be used?

The SEND data analyses will include re-analyses, additional analyses, and visualisations. No cross-product analyses will be performed as part of the PoC. The decision as to which analyses are performed will be driven by the Rapporteur teams' needs and individual to each submission. The focus will be on additional analyses that are deemed of relevance by the Rapporteur teams in the context of reviewing the dossier. Since, without pilot participation, the applicant/MAH likewise would have been asked to provide the additional analyses, it is per se not expected that pilot participation will increase the number of questions to the applicant/MAH. So, SEND data will only be used as a supplement to the benefit-risk assessment of the regulatory procedure.

1.9. Will the applicant/MAH be informed about which analysis has been done?

The applicant/MAH will not be consulted prior to running the analysis, however, information about the analysis method and the results will be shared allowing the applicant/MAH to respond (see Question 2.8). Furthermore, the results from the Agency may be included in the Assessment Report (AR) and the European Public Assessment Report (EPAR). The appointed Rapporteurs' teams and the CHMP will decide whether certain analyses will be included in the AR and the EPAR. In general, those will be results considered relevant to the scientific assessment of the dossier.

1.10. Who is going to analyse the SEND data submitted for the PoC?

For each regulatory procedure, SEND data analysis will be performed by the CHMP Rapporteur and/or co-rapporteur teams at the NCAs or by EMA staff.

1.11. How will learnings from the PoC be shared with the public?

The Agency will organise a workshop with external stakeholders towards the end of the PoC to present and discuss lessons learned. A summary of the pilot's outcomes will also be published, acknowledging commercially confidential information. This summary will include information about which procedures were included in the pilot as well as high-level aggregate information on most relevant outcomes such as the regulatory benefit of access to SEND data in support of the regulatory assessment and decision-making.

1.12. Does the Agency plan to request raw data for all future applications following the PoC?

No decision has been taken on the future scope of requests for SEND data by the Agency. The objective of the PoC is to gather information and provide recommendations to the European Medicines Regulatory Network on the role of SEND data in future regulatory submissions. Therefore, this is one of the key questions that the PoC will help to answer.

2. Questions on the terms of participation

2.1. How can applicants/MAHs ask questions about the PoC pilot?

Applicants/MAHs can contact EMA via send@ema.europa.eu to ask questions about the PoC.

2.2. How and when can applicants/MAHs express interest to participate in the PoC?

The process of volunteering for PoC participation involves three possibilities: (1) submission of SEND data package to initial MAA (2) provide SEND data package in a subsequent filing and (3) submission of SEND data package after follow-up request from the Rapporteur. In order to express interest in PoC participation, applicants/MAHs are encouraged to contact the EMA via SEND@ema.europa.eu. Alternatively, interest may also be expressed via one of the existing communication channels such as during pre-submission interactions.

2.3. Will participation in the PoC pilot cause a delay to the adoption of the opinion by the CHMP?

Participation in the PoC pilot will not delay the adoption of the scientific opinion by the CHMP. The Agency shall ensure that the opinion is adopted within the legal timeframes as laid out in Article 6 of Regulation (EC) No 726/2004 for iMAAs.

2.4. Can an applicant/MAH withdraw their participation in the PoC pilot?

Once an applicant/MAH has submitted their SEND dataset, the applicant or MAH cannot withdraw participation for this procedure.

2.5. How will the applicant/MAH communicate with the Agency and the Rapporteurs on proof-of-concept related aspects?

In general, existing regulatory channels shall be used to discuss questions related to the proof-of-concept participation. However, the Agency will follow a flexible approach to allow for sufficient dialogue with the applicant/MAH.

- Before submission: The pre-submission interactions can be used to discuss which non-clinical studies shall be submitted as SEND data package.
- At the time of submission: Applicant/MAH is expected to submit the SEND data packages as part of their iMAA submission package.
- During the assessment: Applicant/MAH can submit (additional) SEND data packages on their own initiative or following a request from the Rapporteurs' team. Analysis results that are considered relevant for the benefit-risk assessment will be discussed in the assessment report and shared with the applicant/MAH.
- After the issuance of an opinion by the CHMP: The applicant/MAH is encouraged to provide feedback to the Agency on their proof-of-concept participation.

2.6. How long will the SEND data files be stored by EMA?

The retention period for the raw data files is the same as for the rest of the dossier which is submitted to the Agency. According to EMA's existing records policies, the SEND data files will be retained up to 30 years after the withdrawal of the product from the market.

3. Questions on the data package to be submitted.

3.1. Are data packages as prepared for other international regulators suitable to be submitted to the Agency for the PoC?

SEND data packages prepared for other international regulators may be submitted to the Agency for the proof-of-concept study, provided they meet the mandatory criteria listed in Question 3.3.

Accordingly, all versions of Standard for Exchange of Nonclinical Data Implementation Guide (SENDIG) that make use of SDTM model 1.5 or higher, as supported by other international regulators, are permissible for the proof-of-concept. The overview or summary should state which level of compliance is used.

3.2. Does the data package need to contain raw data for all non-clinical studies included in the application or only for certain non-clinical studies?

The expectation is that the applicant submits the SEND data packages for all non-clinical safety pharmacology and toxicology studies for which SEND data has been generated, based on requirements of other international regulators.

3.3. Which files are mandatory to be included in the data package?

The data package should as a minimum contain the following data files as well as ancillary files: the SEND datasets (.xpt files), the Nonclinical Study Data Reviewer's Guide (nsdrg.pdf), and the Define XML Document (define.xml).

3.4. Are there any requirements on naming convention for the files?

Applicants/MAHs are asked to use the naming conventions already specified by the data standards and agreed upon by other international regulators.

3.5. Could issues with the data formats/standards or missing files impact the start of the procedure?

Technical issues with the data format/standard or missing files will not impact the start of the procedure since the Agency will not invalidate submissions for these reasons. However, a delayed submission of the required files or of the data in the required format/standard might lead to the procedure being excluded from the proof-of-concept study.

Who should be contacted regarding questions on the required data to be submitted?

Questions concerning the requirements on the datasets should be sent to send@ema.europa.eu

4. Technical questions on the submission of the raw data

4.1. How can datasets be submitted to the EMA?

The files as specified in Section 3 should be submitted via the eSubmission Gateway: ***eSubmission: Projects (europa.eu)***

The SEND package must be provided outside the eCTD, inside the working documents folder to avoid eCTD technical validation failure.

An updated version of the eSubmission Gateway XML delivery file user interface is available that introduces in the delivery file for Human submissions the option to specify if there is a "SEND Data package Included".