



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

<Date>

Request for advice from the Expert Panels on the clinical development strategy or clinical data required for the clinical evaluation pursuant to MDCG 2024-10¹ guidance, for a device previously designated as orphan

¹ [MDCG 2024-10 Clinical evaluation of orphan medical devices](#)



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Guidance text

Guidance text is in green italics. You may print a copy of this template with the drafting note, then delete them all in one go:

Click on Ctrl-Alt-Shift-S to view the "styles" window. Select "Drafting notes (Agency)" and click on the icon on the right, chose "Select all XXX instances", press the "Delete" key on the keyboard.

Do not change or delete the titles and the numbering style. (Add "Not applicable" if necessary)

Suggested font: Verdana 9.

Paragraph tab: alignment: left, outline level: body text, indentation: 0, spacing before: 0pt and after: 7pt; line spacing: at least, at: 14pt.

I – General Information

1. Administrative Information

1.1. Information on the requester

Name:

Position:

Email:

Phone:

1.2. Information on the manufacturer

Name of the company:

Address:

Country:

[For EU/EEA manufacturers]

SME status*: Yes /No

*https://single-market-economy.ec.europa.eu/smes/sme-definition_en

1.3. Information on the authorised representative

[Mandatory for manufacturers outside of the EU/EEA and Turkey]

Name of the company:

Address:

Country:

1.4. Information on the notified body

[Only for late stage advice]

Name of the notified body:

Address:

Country:

Notified body number:

2. Information on the device

2.1. Device name, risk class, risk class justification, EMDN level, clinical area

Reference is made to the briefing document for the orphan device status request.

2.2. Development history and regulatory status

[Please provide an updated brief overview of the device development. Describe the worldwide regulatory status of the device. Indicate if scientific advice has been previously requested from other regulatory authorities.]

3. Type of advice

- Early scientific advice (prior to clinical evaluation and/or investigation)
- Late stage scientific advice (clinical evaluation is in an advanced stage or completed)

[For late stage advice]

- The manufacturer and notified body confirm that they are in agreement for the consultation procedure.
- The manufacturer and notified body confirm that the expert panel consultation does not interfere with the notified body's assessment.
- The notified body confirms that the expert panel advice will be awaited before the file is submitted for Clinical Evaluation Consultation Procedure (CECP), if applicable, and commits to reflecting in the CEAR how the advice was considered.

4. Brief outcome from the orphan device status confirmation

[Add the conclusion and a summary of the rationale from the orphan device status procedure for reference, and append the orphan designation letter.]

II - Application – Request for scientific advice

1. Overview of device development

[This section should give a comprehensive scientific overview of the device clinical development strategy, providing relevant systematic information in sufficient detail, together with a critical discussion. Cross-references to annexes can be included only when additional details are needed to support the argument. The use of tabulated overviews and graphs is encouraged.]

The orphan device status will influence the expected level of pre-market clinical evidence, notably the justification for limitations in the pre-market clinical evidence and acceptable level of pre-market clinical uncertainty. In order to seek clinical advice on an orphan medical device, it is important that the clinical development strategy and proposals for clinical investigation are described in detail, including the foreseen limitations in the pre-market clinical evidence, as well as the proposed way to address these post-marketing, i.e. via a detailed Post-Market Clinical Follow-up (PMCF) plan. The following items should be part of the briefing document, the level of detail might depend on the stage of development:

- summary of any identified limitations in clinical data and residual risks, including a description of how these were identified;*
- intended limitations in clinical data and residual risks, and acceptability thereof;*
- justification why it is not feasible or proportionate to generate further clinical data within an acceptable timeframe in the pre-market setting;*
- proposed PMCF plan that, once executed, will generate clinical data in an appropriate timeframe that will fully address the remaining limitations in clinical data.*

Devices that are intended by the manufacturer to be used for orphan populations or indications, as well as in non-orphan populations, may have clinical data from use of the device in the 'other population/indication'. In some circumstances, it may be appropriate to extrapolate these clinical data from other population(s)/indication(s), for the purposes of clinical evaluation of the intended use in the orphan population/indication. In case such extrapolation of data is proposed, the appropriateness thereof needs to be justified, based on:

- the relevance of the data, including the similarity of characteristics between the proposed orphan subpopulations/indications, and the other(s) from which the data were collected;*
- the quality of the data in terms of scientific validity and suitability; and*
- the extent to which the data can provide sufficient clinical evidence to assess the safety, performance and expected clinical benefit for the orphan indication.]*

1.1. Clinical background information

[A tabular overview of all relevant studies including study number (if available), main design features, patient number and characteristics, number of investigator sites by geographical region, as well as current study status (completed, ongoing, planned) etc. could be informative, if not provided elsewhere. Include any additional information that might be relevant (e.g., pre-clinical information directly relevant for the clinical development strategy).]

For early advice (on clinical development strategy): if advice is requested for (a) particular clinical investigation(s), a schematic of the clinical study(ies) for which advice is requested should be included.

For late advice (on clinical data required for the clinical evaluation): if (a) clinical investigation is (are) ongoing, detailed information on the current status of the study(ies) should be provided, including the number of patients currently enrolled, date of first patient enrolment, anticipated date of last patient enrolment and number of investigator sites currently participating by geographical region.

Whilst the focus should be kept on the intended purpose(s), the development in future indications could be briefly summarised, where relevant.]

1.2. Clinical performance

[A general overview of the clinical performance profile of the device should be based on a comprehensive discussion of e.g., the main clinical results so far, exploratory studies, special populations, supportive and pivotal clinical studies, and any analyses performed across the studies (pooled and meta-analysis). The discussion should identify the most important findings and challenges in the clinical development strategy, and its compliance with legal requirements, relevant guidelines, previous scientific advice, etc.]

1.3. Clinical safety

[A general overview of the safety profile of the device should be based on a comprehensive discussion of the safety database of the device and predecessor versions (if applicable) including the incidents observed, previous field safety corrective actions, specific safety findings, safety in special populations, etc.]

2. Questions to the expert panel and applicant's positions

*[Questions should conform to the **scope** of this advice, i.e., **clinical domain only**. It is recommended that questions are phrased in a way to allow for an unambiguous understanding of the question. The scope should be carefully considered in order to avoid too broad or too narrow questions.*

The wording of the questions should be clear and concise, starting with e.g. "Does the Expert Panel agree that/with ...?".

The presentation of the proposal as well as the justification for it is to be presented in the Applicant's position.

IMPORTANT INFORMATION

Each question should be followed by a corresponding, separate Applicant's position including a comprehensive justification for the chosen approach.

All key information about the topic should be sufficiently discussed, so that the Applicant's position can function as a 'stand-alone' argument. Issues to be covered could include the following: context and proposal, other options (potentially) considered together with a critical discussion on the relative merits and drawbacks of the various approaches, possible consequences and eventual measures to mitigate these. In general, 1 to 3 pages for each Applicant position is recommended.

Cross-references to the relevant parts of the briefing document or annexes can be included if additional detail is needed to support the argument.

For late stage development advice, a manufacturer should only request advice from an expert panel if it will be able to update its clinical evaluation report taking into consideration the expert panel's views, before the notified body assesses it, to avoid any overlap with the technical documentation assessment by the notified body. The manufacturer's clinical evaluation plan or its draft clinical evaluation report could be suitable documents to be submitted with the request. The manufacturer should inform the notified body about the request and about any advice provided by the expert panel, for example, in its application for conformity assessment. The manufacturer should make the expert panel advice available to the notified body, for example as an annex to the clinical evaluation report.

If the manufacturer intends to request advice from an expert panel after it has already lodged an application to a notified body, the manufacturer and notified body should agree that the expert panel consultation does not interfere with the notified body's assessment, and the notified body should confirm that the expert panel advice will be awaited before the file is submitted for Clinical Evaluation Consultation Procedure (CECP), if applicable, and should commit to reflecting in the CEAR how the advice was considered. If this cannot be ensured, a consultation of the expert panel should be left to the notified body pursuant to Article 106(11) MDR.

Expert Panels members address each question independently, taking into consideration the information provided in the applicant's position.

No preassessment of the data is performed; only the strategy and the possibility of it providing the results needed is advised on.]

2.1. Question {X}

Applicant's position {X}

{Expert panel position}

2.2. Question {Y}

Applicant's position {Y}

{Expert panel position}

IIIa - List of Abbreviations

[Please provide a list of abbreviations used in this document, if applicable]

IIIb - List of Annexes

1. Orphan designation letter for the medical device in scope