

**Harmonised approach to Early Feasibility Studies for Medical
Devices in the European Union (HEU-EFS)**

**WP2 Research and analysis on
regulatory framework, and
institutional and organizational
characteristics of EU competent
authorities**

DELIVERABLE 2.2

Professional and organizational characteristics of
competent authorities

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Project Acronym	HEU-EFS
Project Title	Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union
Project Coordinator	Giuditta Callea giuditta.callea@unibocconi.it
Grant Agreement Number	101112185
Project Duration	October 2023 – October 2027 (48 months)
Deliverable Number	2.2
Work Package	2
Task	2.3
Lead Beneficiary	TCD
Status	Final
Dissemination Level	PU
Type	R – Document, report
Due Date of Deliverable	28 February 2025
Actual Submission Date	26 February 2025
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File History

Version	Date	Status	Author	Review
1.0	28-01-2025	V1.0	Tom Melvin, Majella Geraghty (TCD), Francesco Malandrini, Giuditta Callea (UB), Nicolas Martelli, Ornella Tangila Kayembe, Tess Martin (APHP), Sebastian Kuhn, Marlen Peseke, Ilja Michaelis (UMR)	Federico Facciolo, Francesco Malandrini, Giuditta Callea, Maria Luisa Buzelli (UB), National Competent Authorities (NCAs), Laura Sampietro-Colom (HCB), Adrián Valledor (FCRB), Yasemin Zeisl (EPF), Karen Fricke, Fanny van der Loo (Edwards Lifesciences), Marta Kerstan-Huber, Sebastiaan de Jongh (MEDTRONIC), Benedetta Brancadoro (GEMELLI), Martha Bragagnolo (GHH)

TABLE OF CONTENTS

TABLE OF FIGURES	6
ABBREVIATIONS.....	7
EXECUTIVE SUMMARY.....	8
1. Introduction	10
2. Methods	12
2.1. Development of an on-line survey of National Competent Authorities.....	12
2.2. Workshop with National Competent Authorities	14
3. Results	17
3.1 Experience with pre-market exploratory clinical investigations of medical devices at the pilot stage of clinical development	18
3.2. Resources, recruitment and training needs related to the assessment of applications to conduct Early Feasibility Studies	32
3.3 Other findings: Deficiencies, Information Requests, and Approval Timelines.....	35
4. Discussion.....	45
5. Conclusion	47
References	48
Appendix 1 – Survey Questions.....	49
Appendix 2 – Workshop Questions	68

TABLE OF FIGURES

Figure 1. Participation rate of NCAs in survey and workshop	17
Figure 2. Do you document/record the clinical development stage (for example pilot stage/pivotal stage) for the CIs.....	18
Figure 3. Number of CI applications received in 2023 - All medical devices risk classes	20
Figure 4. Number of CI applications received in 2023 - All medical devices risk classes	21
Figure 5. Volume of all CI applications received in 2023	22
Figure 6. Numbers of EFS applications received in 2023	23
Figure 7. Number of EFS applications/total no. of CI	23
Figure 8. Dialogue between NCAs and sponsors	24
Figure 9. NCA dialogue processes at key time points.....	25
Figure 10. National Competent Authority dialogue processes at key time points	25
Figure 11. Types of advice sponsors typically seek.....	27
Figure 12. Correlation between sponsor size and likelihood of seeking NCA dialogue	28
Figure 13. Does sponsor dialogue improve CI application quality?.....	29
Figure 14. Do you provide guidance for pre-market CIs?.....	30
Figure 15. Key focus areas in Pre-Market CI guidance.....	31
Figure 16. Mechanisms for dialogue with patients/patient organisations.....	31
Figure 17. Number of internal or external assessors/area of expertise	33
Figure 18. Challenges in the recruitment of experts in key competency areas.....	34
Figure 19. Main challenges faced in the recruitment of and retaining assessors	34
Figure 20. Training programs for staff on medical devices and digital health advancements	35
Figure 21. Documents with the highest frequency of deficiencies identified by NCAs.....	36
Figure 22. Most likely cause of deficiencies.....	36
Figure 23. Common reasons for requesting additional information from sponsors during application assessment.....	37
Figure 24. Average time (days) from initial application to study authorization in 2023 for investigational devices (excluding class I and non-invasive class IIa/IIb).....	40
Figure 25. How many of those applications required the use of the 20-day period for consulting with experts?.....	41
Figure 26. Timeline for REC approval.....	42

ABBREVIATIONS

AI	Artificial Intelligence
AIeMD	AI-enabled Medical Devices
CI	Clinical Investigation
CIE Working Group	Clinical Investigation and Evaluation Working Group
CIRCA-BC	Communication and Information Resource Centre for Administrations, Businesses and Citizens
CSV	Comma-Separated Value
DHT	Digital Health Technology
EFS	Early Feasibility Study
EU	European Union
FIH	First in Human
GDPR	General Data Protection Regulation
HEU-EFS	Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union
IHI	Innovative Health Initiative
ISO	International Standards Organization
MDCG	Medical Device Coordination Group
MDR	Medical Device Regulation (2017/745)
NB	Notified Body
NCA	National Competent Authority
No/n	Number
REC	Research Ethics Committee
WG	Working Group
WP	Work Package

EXECUTIVE SUMMARY

National Competent Authorities (NCAs) play a vital role in assessing applications to conduct pre-market Clinical Investigations (CIs) of medical devices (MDs) and as such, NCAs will play a central part in any future program for Early Feasibility Studies (EFS) in the European Union (EU). To gain insight into the perspectives and experiences of NCAs regarding the assessment of CIs, particularly EFS and/or EFS-like studies^a, we conducted a survey and workshop with NCAs. This report represents the first thorough examination of NCA practice and perspectives in the context of CI and EFS assessments.

The survey included various closed-ended questions, along with spaces for additional comments in free-text format. An open-ended discussion was conducted during the workshop. Thirty-one (31) countries participate in the Medical Device Regulation (MDR) regulatory framework, consisting of EU Member States and European Economic Area and European Free Trade Area members.

The survey response rate was 61% (19/31). The workshop participation rate was also 61% (19/31), with 27 assessors participating. Twenty six percent (8/31) of countries did not either respond to the survey or participate in the workshop. The total participation rate for both the survey and the workshop was 74% (23/31). Additionally, the Commission Chair of the Clinical Investigation and Evaluation (CIE) Working Group (WG)¹ also participated in the workshop.

The key themes explored in the survey and workshop were:

- The experience and challenges of NCAs in assessing pre-market exploratory CIs of MDs at the pilot stage of clinical development.
- The opportunity for dialogue and communication with sponsors and patients.
- The value of patient and clinician perspectives in MD development.
- The resources, recruitment and training needs amongst NCAs.
- Co-ordinated CI assessments for multi-state studies.

Other themes explored included experience with digital health technologies (DHT) and artificial intelligence (AI) systems, and the expectations for a future EFS program.

^a EFS-like studies were defined as studies explicitly identified as EFS in their titles or summaries, or any other open-label, non-comparative interventional study with an estimated sample size of 30 or fewer patients.

NCA respondents noted that a total of 1,298 applications for CI in 2023, with responses received from 19 (19/31) countries that are active in the MDR framework. Six (6) countries record if the study was an EFS when recording the clinical development stage.

The results of the survey revealed that advice and dialogue structures are available from eleven (11/19, 58%) respondents, however, the timing, type of advice and costs associated with this are variable. Findings from the workshop indicated that NCAs have different perspectives on how to manage the need for additional pre-clinical testing, with some NCAs allowing it in the context of an application, with other NCAs rejecting the application when further testing is needed. For EFS, NCAs prioritised the importance of demonstrating the sufficiency of pre-clinical testing, and the importance of being able to understand the likelihood that non-clinical test methods will correlate with clinical outcomes.

The majority of NCAs (14/19, 75%) have training programmes for assessors relating to advancements in MDs and DHTs, however they are limited in scope. NCAs highlighted regulatory uncertainties around AleMDs, such as distinguishing prospective data-gathering from formal CIs, justifying the need for early-stage clinical exposure when robust *in-silico* testing exists, and overseeing continuously learning algorithms. NCAs also provided information concerning the types of deficiencies observed in pre-market CI applications and the likely causes. The inclusion of patient perspectives was valued by NCAs, and the inclusion of summaries of this activity by sponsors in the application was noted to be potentially of value to the assessment by the NCAs.

1. Introduction

EFS are limited clinical investigations (CIs), early in the development of a MD to evaluate the device design concept and understand initial safety and performance². National Competent Authorities (NCAs) play a vital role in assessing applications to conduct pre-market CIs of medical devices (MDs). Consequently, active engagement to understand the perspectives of NCAs with respect to the objectives and outcomes of the Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is essential.

The Medical Device Regulation 745/2017 (MDR),³ in Article 101 concerning Member State responsibilities in the regulatory framework, mandates that:

The Member States shall designate the competent authority or authorities responsible for the implementation of this Regulation. They shall entrust their authorities with the powers, resources, equipment, and knowledge necessary for the proper performance of their tasks pursuant to this Regulation.

To assess the current professional and organizational capacities of NCAs, as well as their perspectives on EFS, a mixed-method approach was applied, combining a web-based survey with an interactive workshop.

This report evaluates key factors, including workforce composition, workforce size, expertise, reliance on external assessors, and experience with pre-market CIs, particularly EFS. It provides a comprehensive analysis of the resources and knowledge currently available within the NCAs. Furthermore, the report explores the number of pre-market CIs processed by NCAs in 2023, providing valuable insights into the current state of play of EFS within the European Union.

This report is organised into three main sections:

- **Methods:** This section will detail the approach used to create the survey and the workshop activities with the NCAs. It provides an overview on the management of the survey and workshop process, and the methodology used to analyse the data.
- **Results:** This section will present the results of the survey and workshop and the analyses that was performed on the data.
- **Discussion and Conclusion:** This section will interpret and analyse the findings presented in the results section and will address the implications of the findings and explore their

significance. This section will also address limitations of the research and assess how these limitations might affect the interpretation of results.

The findings from these activities will serve to complement Work Package (WP)1, Task 1.1 which concerns a systematic review of characteristics and impact of pre-market programs for MDs in the EU and other relevant jurisdictions.

The findings will also support the activities of the following work packages:

- **WP3:** Rationale, processes, and procedures to develop and validate a sound, widely applicable, and harmonized EU EFS Program, compliant with EU regulations.
- **WP4:** Evidence requirements, data, and statistical tools to develop a standard protocol for conducting EFS studies in the EU.
- **WP6:** Ethical and legal aspects in support of the EFS Program.
- **WP7:** Testing the methodology: Pilot use cases.

2. Methods

The methodology of this report comprises two interconnected research components aimed at exploring the professional and organisational capacity, and the perspectives and experience of NCAs in the assessment of EFS. This includes:

- Development of an on-line survey of NCAs.
- Development of a workshop to further elicit NCA experience and perspectives.

2.1. Development of an on-line survey of National Competent Authorities

WP2 developed a draft survey, which was iteratively refined based on feedback from consortium members and the NCA members of the Advisory Board of the HEU-EFS project.

The survey covered the following thematic areas in three sections:

- **Section 1:** Experience with pre-market exploratory CIs of MDs, including EFS and EFS-like studies;
- **Section 2:** Dialogue, communication and patient perspectives;
- **Section 3:** Resources, recruitment and training needs related to the assessment of applications to conduct EFS and EFS-like studies.

The survey consisted of 28 closed-ended questions, of which 20 questions included an opportunity for respondents to provide additional information in a free-text manner. The complete survey questions are presented in [Appendix 1](#).

A consultation was undertaken with the Commission Chair of the CIE WG to discuss the survey, the optimal format for gathering responses, the plan for circulation and management of responses.

A web-based survey hosted on the Qualtrics^{XM} platform was selected as this is a secure platform, complying with applicable data privacy laws, and accessible to the HEU-EFS project coordinator (Bocconi University). Access to the survey was provided through an anonymous link to Qualtrics^{XM} and an anonymous quick-response (QR) code. The link was distributed by the CIE WG chair, through the CIE WG's mailing list to ensure it reached all relevant countries, totalling 31 in number

(comprising the 27 EU Member States and the European Economic Area/European Free Trade Association countries: Norway, Iceland, and Liechtenstein and Turkey).

The survey was circulated amongst the membership of the CIE WG on 9 December 2024 with a deadline of 21 December 2024. In order to increase the participation in the survey, a series of reminders were issued to the mail-list. In order to allow for any further responses, the Qualtrics^{XM} survey remained open until 29 January 2025 to facilitate any final responses.

In order to facilitate NCAs in completing the survey, a separate document (information pack) was prepared detailing background information, information concerning informed consent and data privacy, and the survey questions that were uploaded in the Qualtrics^{XM} platform. This allowed NCAs to consult internally and to gather any necessary information in advance of completing the on-line survey.

NCAs were offered the opportunity to enter “Prefer not to answer / No opinion” for each question, in order to facilitate NCAs to provide only the information that is within the remit of their organisation, and to ensure that NCAs are comfortable with responding to the survey.

2.1.1. Ethical considerations

The survey and workshop received research ethics committee (REC) approval from both the Bocconi University (request n. EA000790) and Trinity College Dublin (Reference no. 240910) and informed consent was achieved prior to completing the survey. EU General Data Protection Regulation (GDPR) data protection measures were applied.

2.1.2. Data analysis

The data collected in Qualtrics^{XM} was downloaded in Microsoft Excel format. In order to ensure maximum response rates, and the provision of detailed responses from individual NCAs, all responses have been anonymised, and survey responses have been analysed in aggregate. Data was stored securely and accessible only to the research team in WP2. A preliminary analysis was prepared to present initial findings to the NCA workshop on 14 January 2025. Following the presentation of preliminary results, individual country responses were extracted and shared directly with individual countries for the purpose of validation of responses. The complete analysis is presented in the results section.

For the free text responses provided, these were assessed to identify any new or unanticipated information, and this is detailed in the results section. Both the closed-ended and open-ended free

text responses were analyzed prior to the workshop with NCAs to identify any additional focus areas for the workshop discussion.

2.2 Workshop with National Competent Authorities

To supplement the data generated from the surveys, and to allow for a more open-ended discussion of NCA perspectives, a workshop was arranged with NCAs, regardless of survey completion. This workshop was held on 14 January 2025.

The workshop utilised a semi-structured interview approach, with lead thematic questions and further back-up questions. These questions were developed in WP2 and informed by the preliminary survey analysis. A consultation was undertaken with WP3 to identify thematic areas relevant to that activity. To complement the survey, the workshop consisted of predominantly open-ended questions, to allow NCAs to share their experience of EFS and CIs in an open manner. The questions were arranged thematically in two sections:

- **Section 1:** Experience and challenges with EFS assessments; coordinated CI assessments (multi-state studies); the opportunity to discuss an EFS application with sponsors or developers.
- **Section 2:** Experience with DHTs and AI systems and AI-enabled Medical Devices (AIeMD); expectations for a future EFS program; the value of patient and clinician perspectives in MD development.

The final question was open-ended to allow for NCAs to share any additional perspectives that may not have been covered in the survey or workshop and asked: “Are there any other topics or activities that you see as important to support better coordination of Early Feasibility Study assessments in future?”

Microsoft Teams was used for the purpose of the workshop and the instant polls function was utilised to gather live data for relevant thematic questions. These instant polls did not record any names and the results were automatically presented and instantly shared with attendees in order to launch the discussion. An information pack was prepared for NCAs participating in the workshop. This included the logistic details (dial-in link and agenda), rules of engagement and the thematic questions that were utilised during the workshop. The thematic questions are presented in [Appendix 2](#), demonstrating the lead and back-up questions, in addition to the questions that were presented in the instant polls.

The transcription function of Microsoft Teams was used to generate a record of all contributions. The transcript of the Teams recording underwent a review to verify its accuracy, completeness, and fidelity. This transcription was stored locally in Trinity College Dublin (TCD) and was anonymised to ensure confidentiality. To ensure full and frank discussions, ‘Chatham House’ rules were applied to the workshop, meaning that any statements made in the workshop are not attributed to any individual or Member State.

Given the diversity of MD technologies that may undertake an EFS, participation by multiple assessors from NCAs was encouraged. Attendees from the HEU-EFS project at the workshop consisted of members from Bocconi University as overall project lead and members of WP2, WP2 members TCD, APHP, Marburg University and the WP3 lead NIPH.

2.2.1. Ethical Considerations

The workshop received research ethics committee (REC) approval from both the Bocconi University (request n. EA000790) and Trinity College Dublin (Reference no. 240910) EU GDPR data protection measures were applied. Ethical approval for the survey was valid for the workshop.

2.2.2. Data Analysis

The data from the workshop consisted of:

- A transcript of the workshop recording.
- Data from the instant polls.
- Additional comments provided in the chat function of Microsoft Teams.

The transcript was downloaded and all personally identifiable information relating to attendees was anonymized by TCD. The non-anonymized transcript was then deleted, and the anonymized version was securely stored in TCD and accessible only to the WP2 lead (TCD).

2.2.3. Synthesis of findings from both the survey and workshop

The findings from both the survey and workshop are presented together in the results section, organised with respect to the following key topic areas:^b

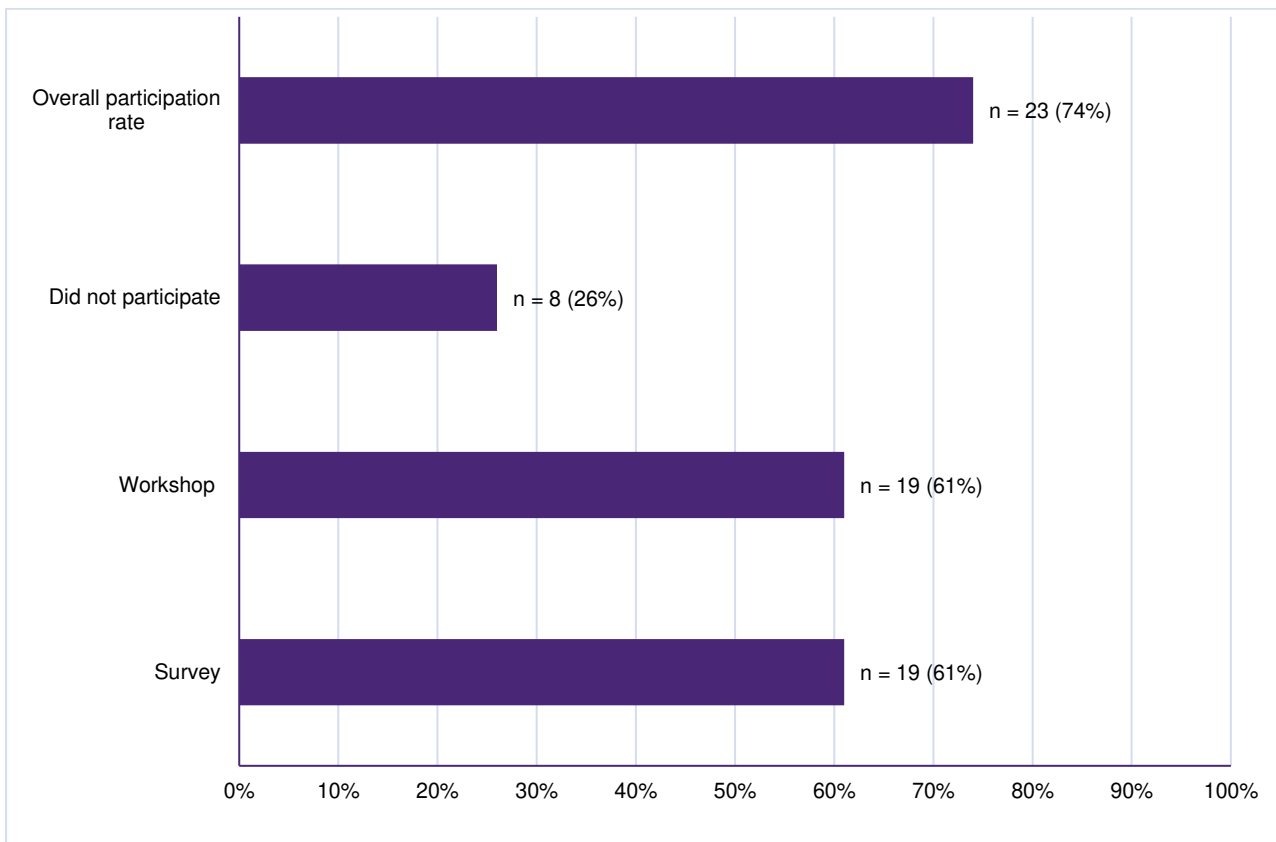
^b With the exception of ‘other findings’, these are the same as the thematic groupings used for the survey.

- Experience with pre-market exploratory CIs of MDs at the pilot stage of clinical development, for example first-in-human (FIH) CIs, early feasibility CIs and traditional feasibility CIs;
- Dialogue, communication and patient perspectives;
- Resources, recruitment and training needs related to the assessment of applications to conduct EFS;
- Other key findings.

3. Results

Of the 31 target countries, 61% (19/31) provided survey results, and 61% (19/31) participated in the workshop, with 27 assessors in attendance. Since some countries took part in either the survey or the workshop but not both, the overall participation rate across one or both activities was 74% ([Figure 1](#))

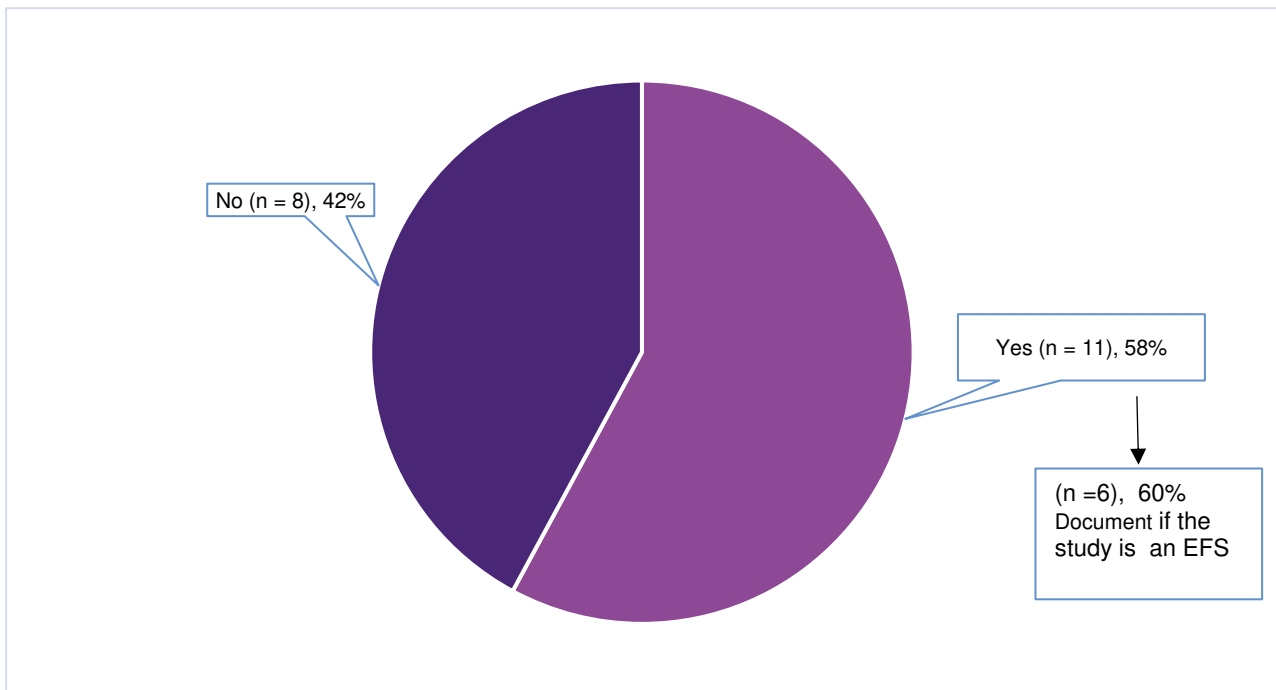
Figure 1. Participation rate of NCAs in Survey and Workshop



3.1 Experience with pre-market exploratory clinical investigations of medical devices at the pilot stage of clinical development

All of the 19 (100%) NCAs who participated in the survey responded to the question “Do you document/record the clinical development stage (for example pilot stage/pivotal stage) for the CIs” of which 58% responded “yes” (Figure 2). From the “yes” sample, 60% recorded if the study was an EFS. The terms “proof of concept” and EFS are used by NCAs to describe the study stage.

Figure 2. Do you document/record the clinical development stage (for example pilot stage/pivotal stage) for the CIs



3.1.1. Assessor Experience

Of the NCAs who joined the workshop and responded to the instant poll, 11 out of 16 had assessed an EFS in their practice.[°] When asked about the challenges that assessors face in assessing these applications, the key challenges identified were:

- The assessment of risks and risk management for novel devices.
- The assessment of whether sufficient pre-clinical work has been undertaken to justify an early clinical use.
- The assessment of data from animal studies, understanding when an animal test protocol is sufficient and assessing later clinical outcomes in the context of the knowledge derived from animal testing.
- The assessment of deviations from standards in the context of pre-clinical evaluation.
- The assessment of the investigational device in the context of alternative available treatment options.
- The assessment of the investigational device in the context of a 'loss of chance' for patients if the investigational device is not made available.
- Assessing the overall benefit/risk.
- Assessing heterogenous study designs in the absence of standards or guidance that demonstrate what a good study design for a pilot stage should look like.
- Finding the best balance between clinical outcomes and surrogate outcomes.

Key Quote from the Workshop



There's a degree of guesswork and a degree of extrapolation that might not always be accurate when you're trying to evaluate risks, so that'll be one of the main issues that I would see with early feasibility studies is how the risk assessment is done.



[°] Microsoft instant poll during the workshop.

One common theme in discussing the above factors is the ‘gap’ between pre-clinical testing and the knowledge that needs to be generated by means of EFS and pilot stage. This was exemplified by the following comment:

Key Quote from the Workshop



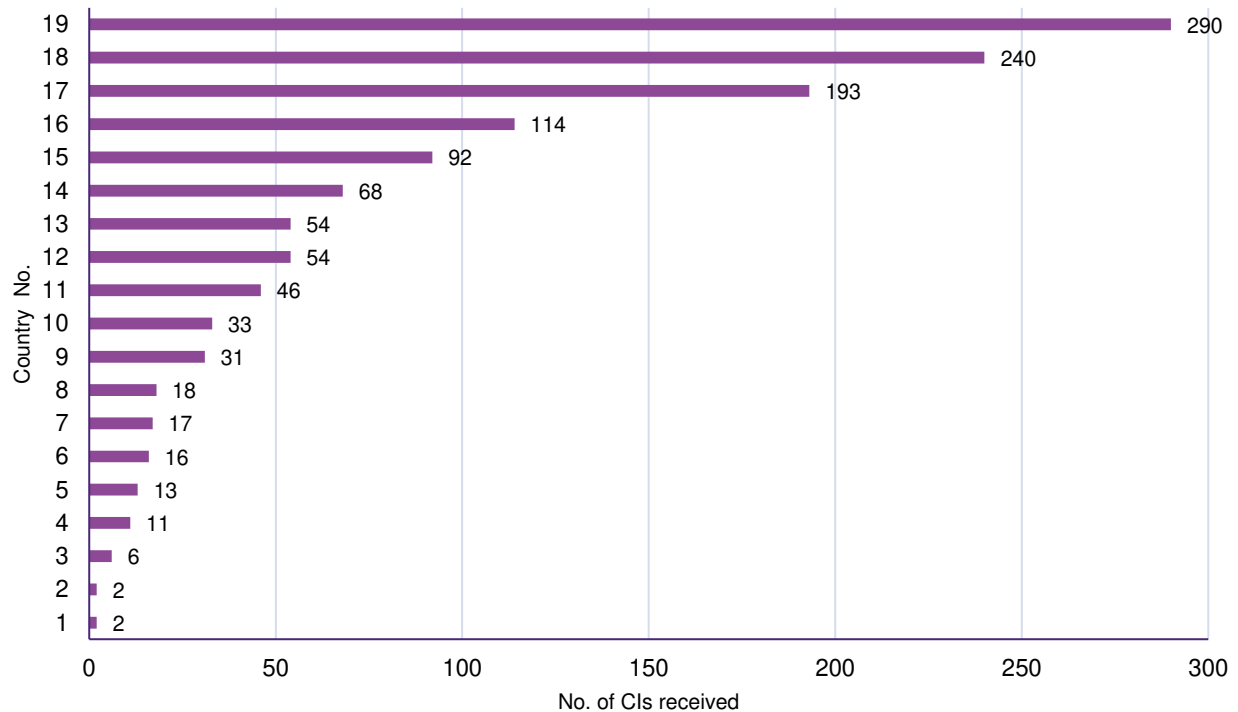
Fundamentally for me when I look at assessing these, I want to be able to understand that it's reasonable that the amount of preclinical testing that has been done for animal studies or simulation testing, that they've done what they can and feasibly they can't really do anything more in order for them to progress in the level of knowledge they have to proceed to human studies.



3.1.2. National Competent Authority Experience

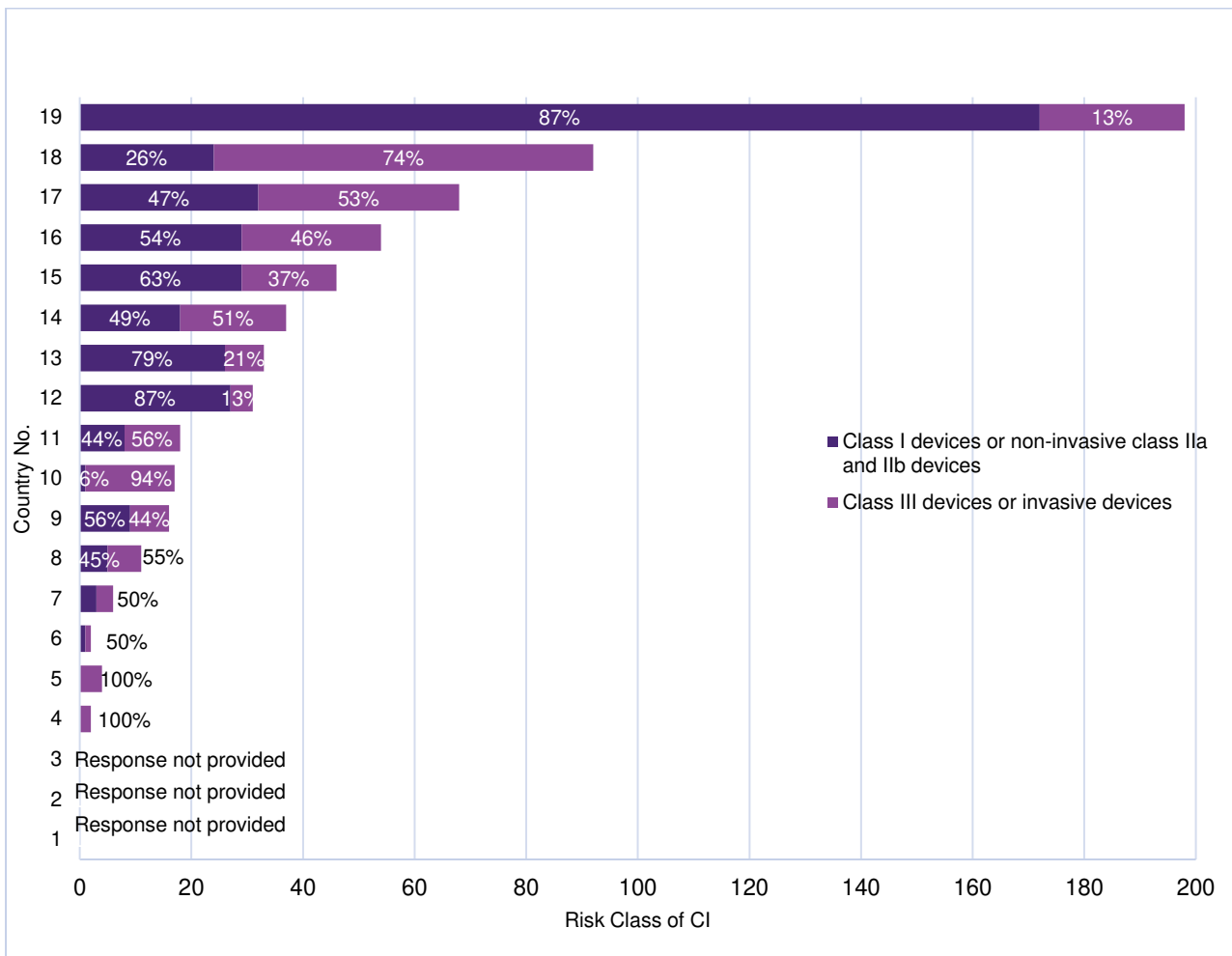
All NCAs participating in the survey provided data on the number of applications to conduct a CI that were received in 2023. From these 19 countries, 1,298 applications were received. There was a wide variation across countries ranging from 2 to 290 application ([Figure 3](#)).

Figure 3. Number of CI applications received in 2023 - All medical devices risk classes



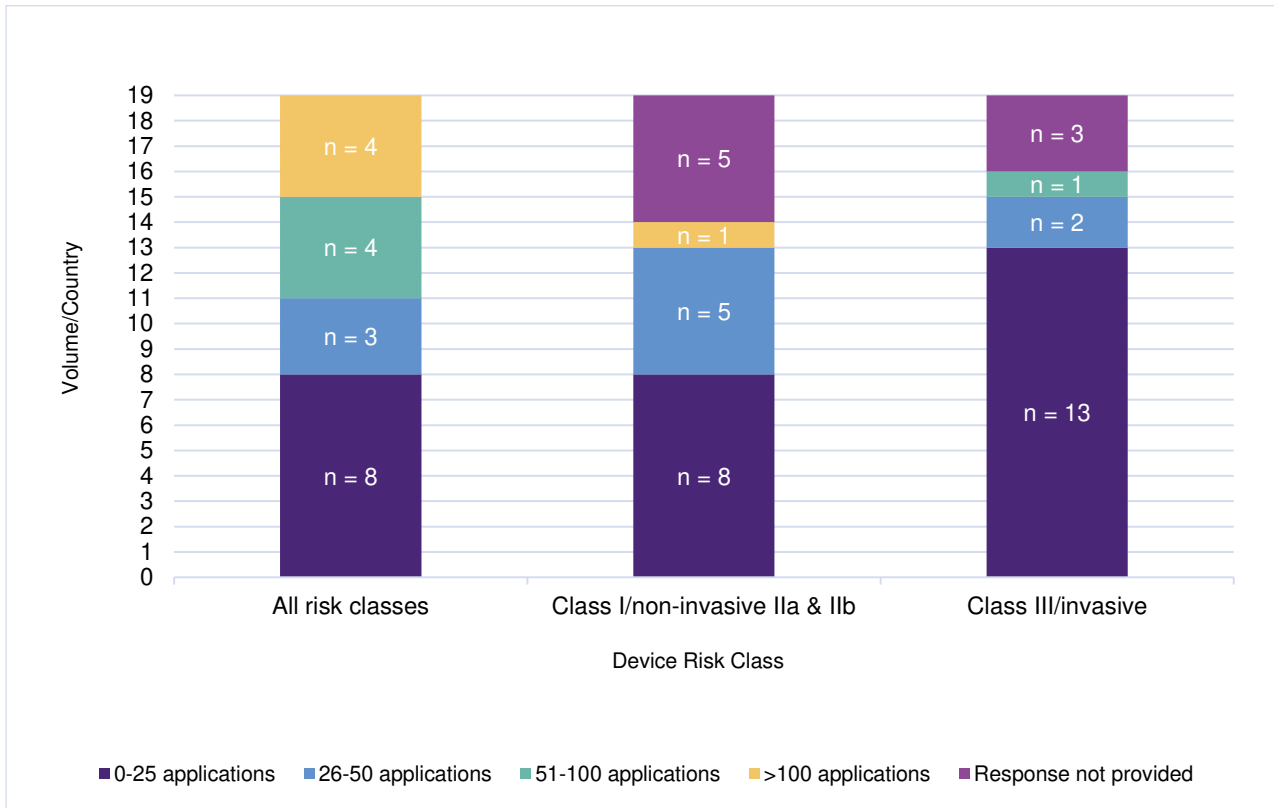
When analysing the number of CIs categorized by risk classes, the number of respondents was smaller ([Figure 4](#)). Five (5) countries did not provide data for class I or non-invasive class IIa and IIb devices, while three (3) countries did not report data on higher-risk devices, resulting in a total of 635 studies. This reduced number of studies may be attributed to incomplete reporting in the survey. Additionally, some NCAs may not assess lower-risk devices, as the MDR permits national laws to determine whether a study can proceed immediately after validation or requires an assessment by the NCA.

Figure 4. Number of CI applications received in 2023 - All medical devices risk classes



NCAs see different volumes of applications, this is demonstrated in [Figure 5](#).

Figure 5. Volume of all CI applications received in 2023

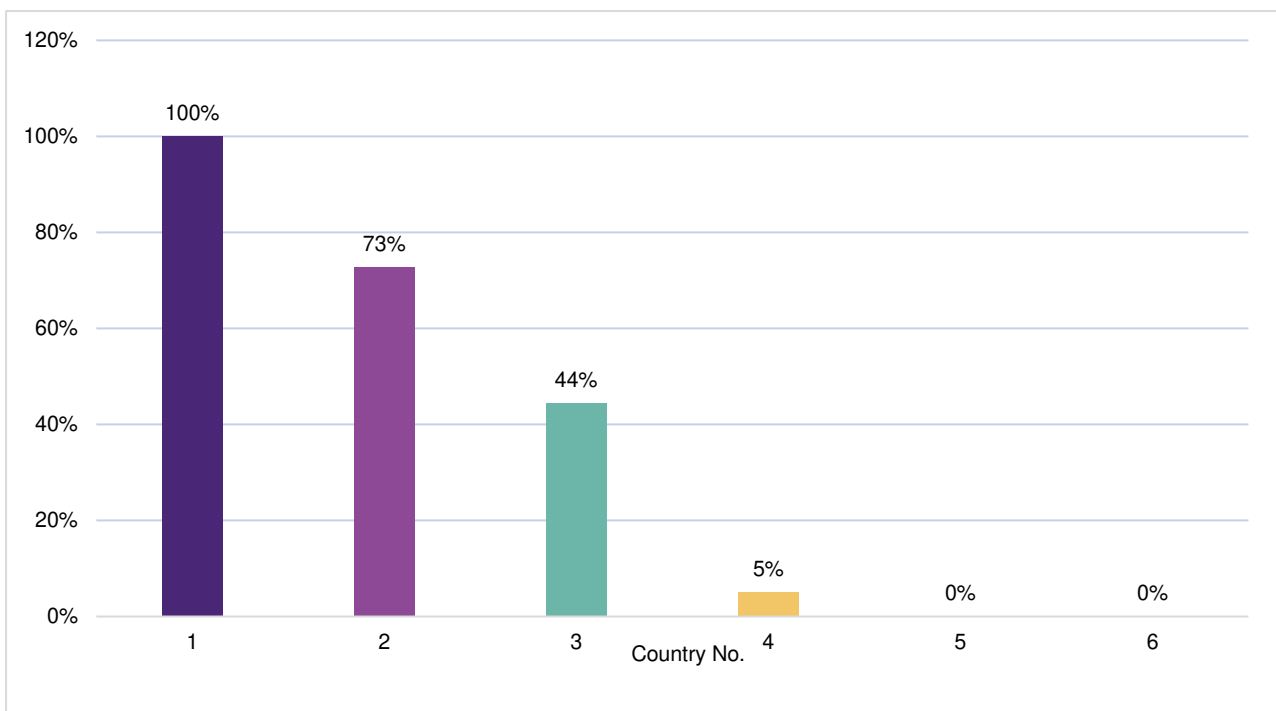


With respect to the number of EFS applications specifically, for all risk classes, data was provided from 6 (26%) NCAs ([Figure 6](#)). The total number of EFS identified was 46, with 21 (46%) studies related to class I devices or non-invasive class IIa and IIb devices, 18 (39%) related to class III devices or invasive devices and 7 (15%) related to DHTs. The range of studies received varied from 0 to 13/country for class I devices or non-invasive class IIa and IIb devices; 0 to 11/country for class III/invasive devices. The range was lower for DHTs from 0 to 6/country. From the 6 respondents, the number of EFS applications as a proportion of the total CI applications was assessed ([Figure 7](#)). There was a wide variation range of EFS applications/CI reported from 0% for 2 countries to 100% for 1 country.

Figure 6. Numbers of EFS applications received in 2023



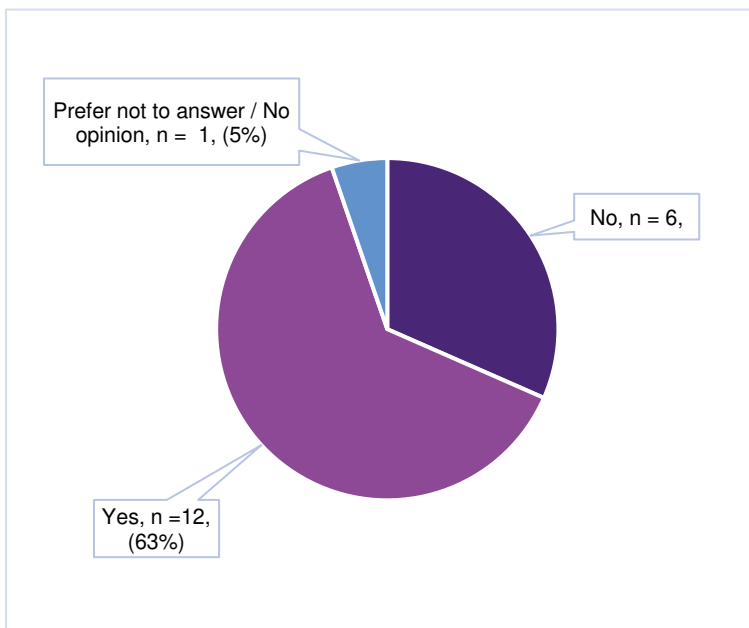
Figure 7. Number of EFS applications/total no. of CI



3.1.3. Dialogue, Communication and Patient Perspectives

The majority of respondents (12/19 equal to 63%) identified the possibility for dialogue between the sponsor and NCA ([Figure 8](#)). For the NCAs that do not offer a formal dialogue process, it was noted that *ad hoc* contacts with sponsors were possible, typically by e-mail or sometimes by teleconference. Some NCAs do not have a process for this activity and do not have the opportunity to offer scientific advice.

Figure 8. Dialogue between NCAs and sponsors



For the NCAs that do offer meetings, 'pre-submission' or 'innovation' meetings were highlighted. Scientific advice is possible in some NCAs, and this is associated with a fee in some cases. Dialogue may occur at different key time-points of a CI, either before a submission, during an assessment or after the assessment has been completed.

In [Figure 9](#) the number of NCAs that offer meetings at these different time-points is identified and [Figure 10](#) highlights those who engage in dialogue at multiple points (e.g., before and during application/assessment or before, during, and after application/assessment).

Figure 9. NCA dialogue processes at key time points

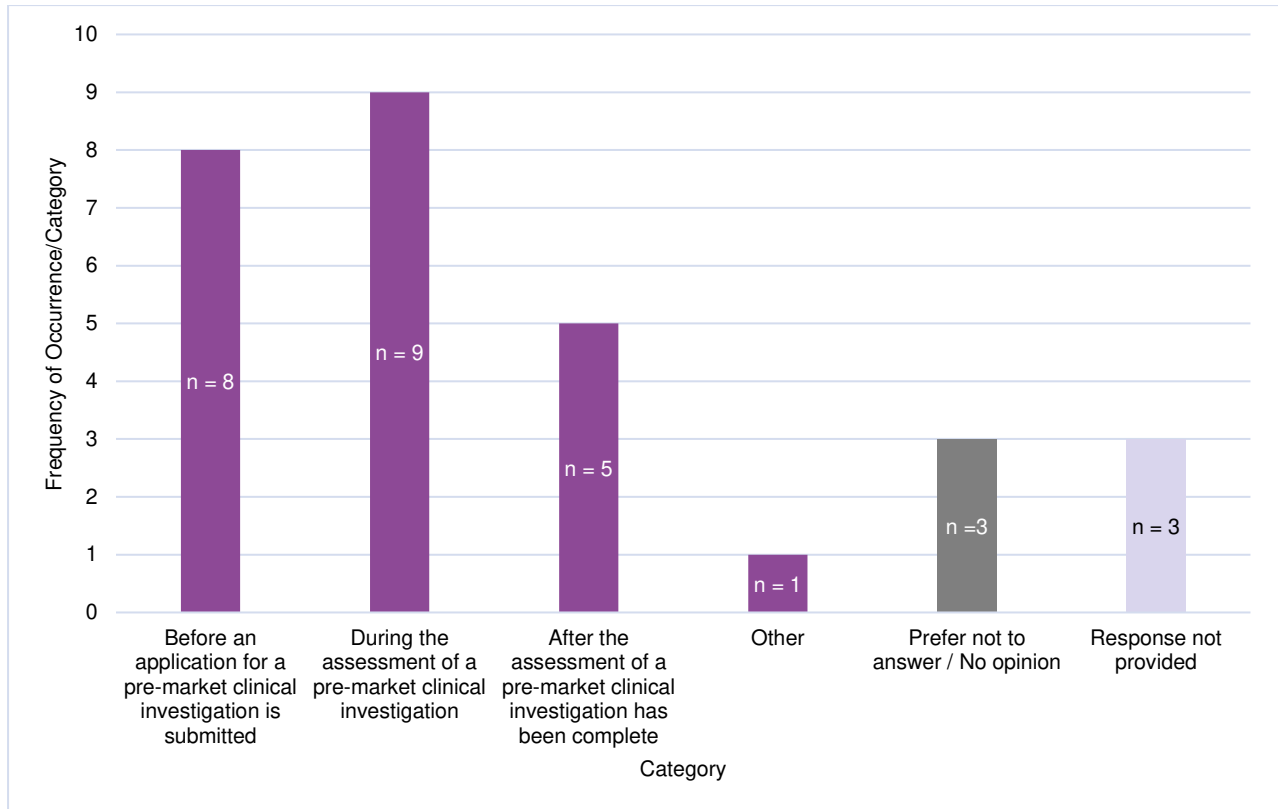
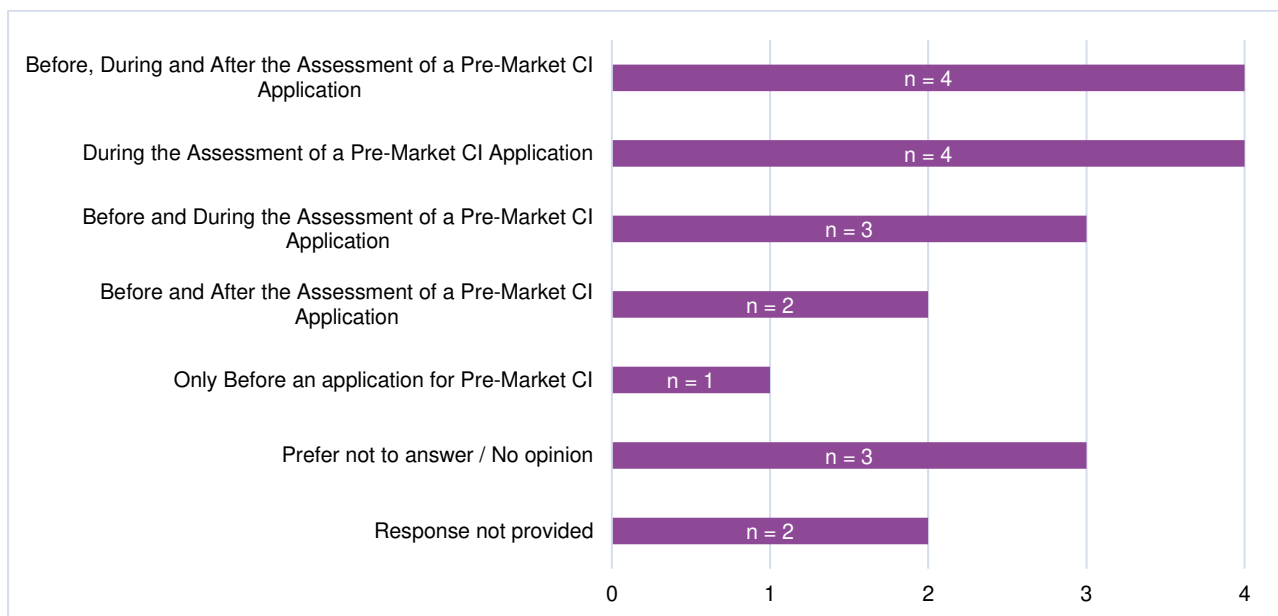


Figure 10. National Competent Authority dialogue processes at key time points



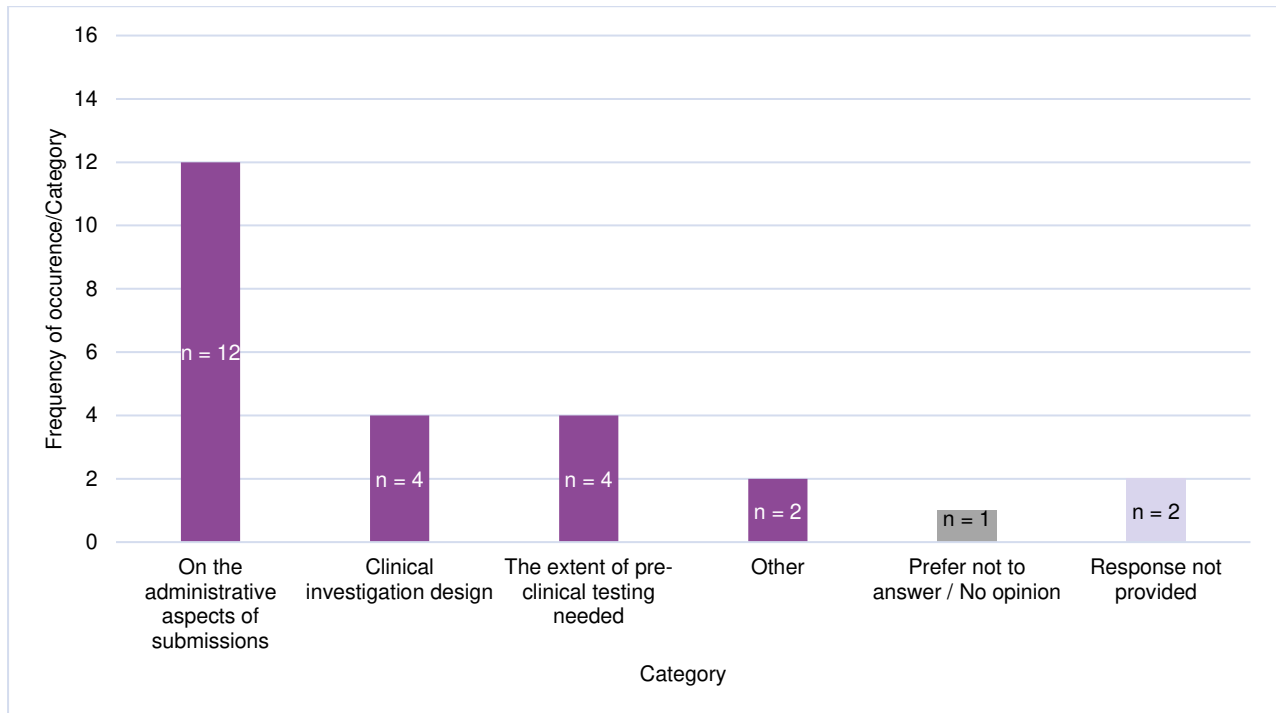
In the free-text responses, NCAs noted that in some cases the process is official, and in some cases, it is *ad hoc* or sporadic. One NCA noted that the purpose of these meetings is to identify ‘potential showstoppers for applications with innovative aspects. Scientific advice is possible from some NCAs, however there are legal constraints in the provision of scientific advice amongst other NCAs. When an application is under assessment, NCAs cannot offer scientific advice, however there can be a possibility to have a meeting between the sponsor and NCA to discuss procedure-specific questions.

In the workshop, one NCA noted that the topics that are explored in pre-submission versus during an assessment are typically different. In a meeting during the CI assessment, the discussion is typically focussed on specific issues that have been identified, whereas a pre-submission meeting is to understand the technology and CI design.

3.1.4. Types of advice that sponsors typically seek

Dialogue between sponsors and NCAs often relates to administrative aspects of submissions, and it can sometimes concern the extent of pre-clinical testing or advice on study design ([Figure 11](#)).

Figure 11. Types of advice sponsors typically seek



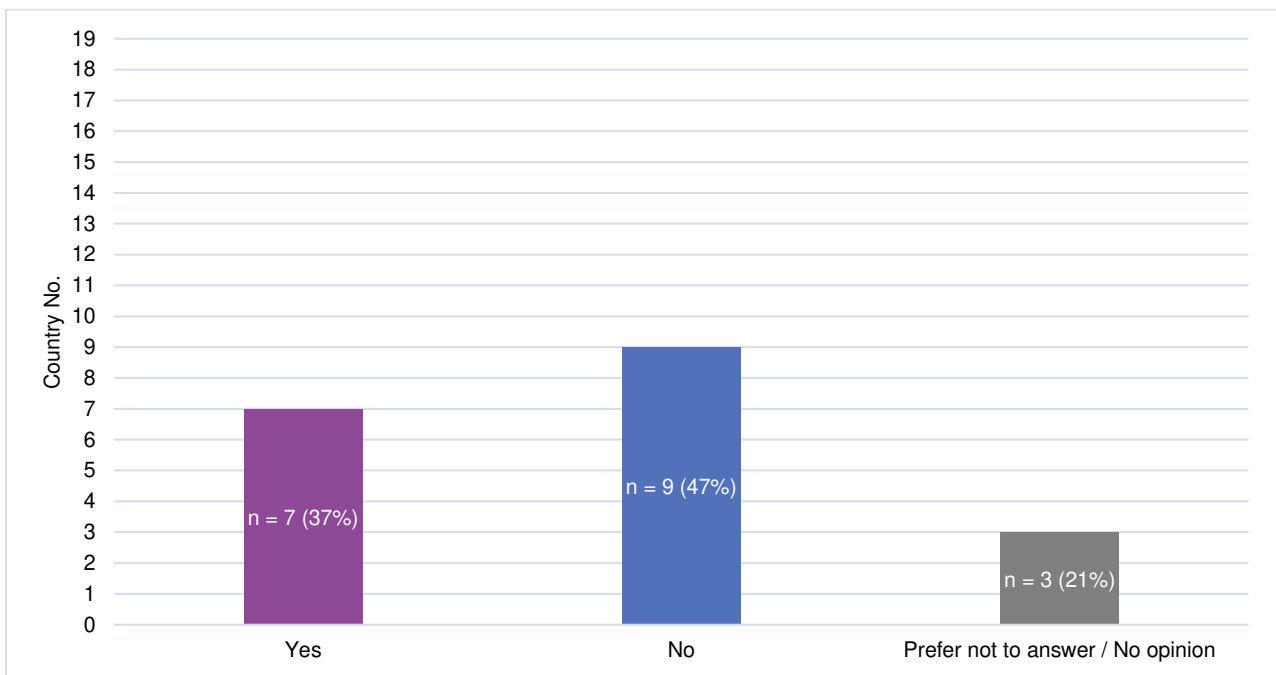
In the free-text responses, one NCA noted that advice on study design is outside the remit of the NCA, and that questions on these aspects may be more suitable for the notified body (NB) rather than NCA. One NCA noted that questions on study design do arise, but they are less common. One NCA noted that a question that can sometimes arise is whether the data that will be generated will be sufficient for CE-marking, and it was noted that this is a question for the NBs.

With respect to the 'other' types of advice that may be given, the following aspects were noted:

- Regulatory aspects in general, in preliminary phase of development.
- Advice on the application and documents needed.
- Study device test requirements (biocompatibility, electric safety, etc.), investigations with CE-marked MD and the need of an investigator's brochure, Declaration of Conformity etc.
- The general need to apply to the NCA.

Seven out of 19 (37%) NCAs noted a correlation between the sponsor size and the likelihood of seeking a dialogue with the NCA (Figure 12). In the free-text responses provided, it was noted that smaller sponsors⁴ tend to be more active in seeking dialogue, with this particularly being the case for SMEs and academic sponsors. One NCA noted particular challenges with inexperienced sponsors of low-risk device studies. As a corollary, one NCA noted that “*smart agile small companies with experienced experts are sometimes more efficient and easier to communicate with.*” A common theme amongst NCAs was the experience of the sponsor with CIs.

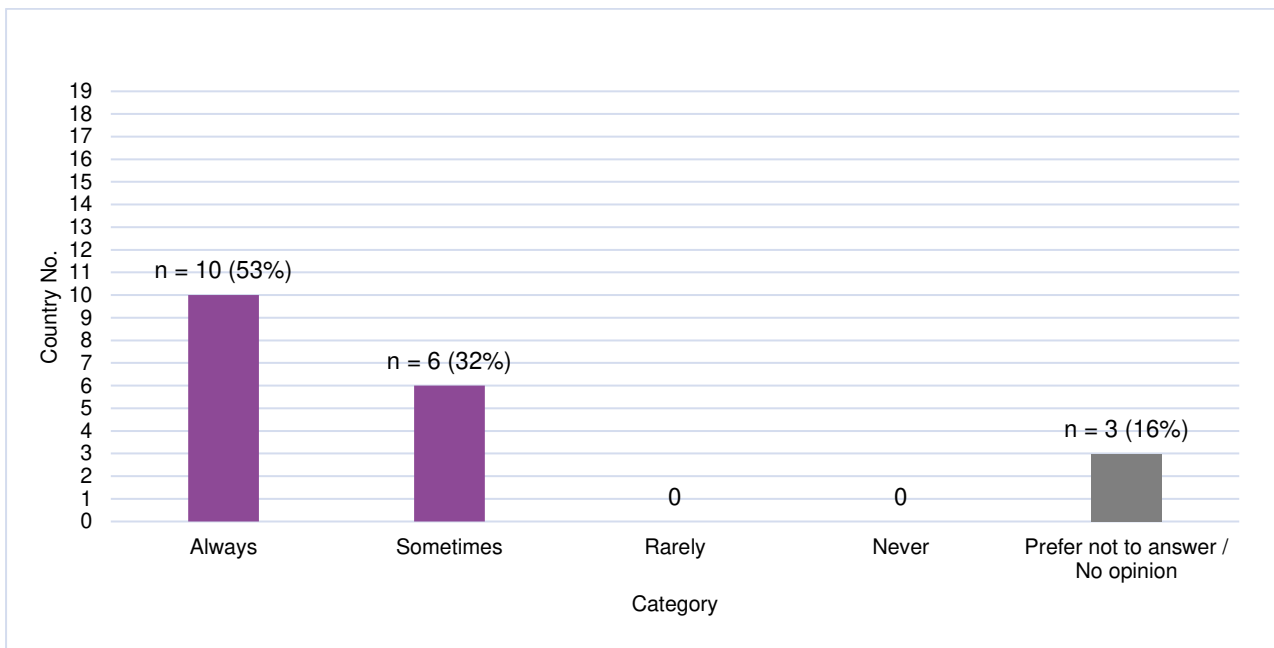
Figure 12. Correlation between sponsor size and likelihood of seeking NCA dialogue



3.1.5. Does sponsor dialogue improve clinical investigation application quality?

NCA's reported positive experience of dialogue processes when considering the subsequent quality of applications, with 10/19 reporting that it always improves quality and 6/19 noting that it sometimes improves quality (Figure 13). In the free-text responses, one NCA noted that they do not have a dialogue process, however they expect that it would improve submission quality.

Figure 13. Does sponsor dialogue improve CI application quality?



Key Quote from the Workshop



In general, the applicant benefits from getting to know the authority's expectations in advance. On the other hand, it is often also helpful for the authority to have already familiarised itself with the investigational device

However, a key condition is that sponsor has certain level of experience, willingness to co-operate and honesty.



3.1.6. Technologies or device classes requiring more frequent/in-depth dialogue

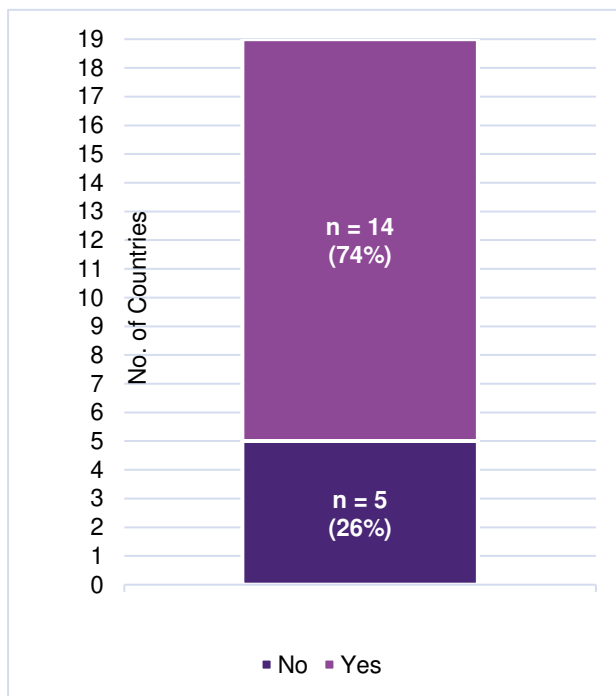
NCA highlighted the following factors as relevant to the need for dialogue:

- For lower-risk categories, such as class I, discussions are necessary to address gaps in information regarding the informed consent process.
- As the technological aspects of the field and the class of the device increases, the need for dialogue increases.
- Software, combined products (regardless of the class of the devices).
- All high risk FIH studies require dialogue - namely for the safety of patients.

Dialogue for software-based MDs was prominent in the free-text responses.

3.1.7. NCA Communication

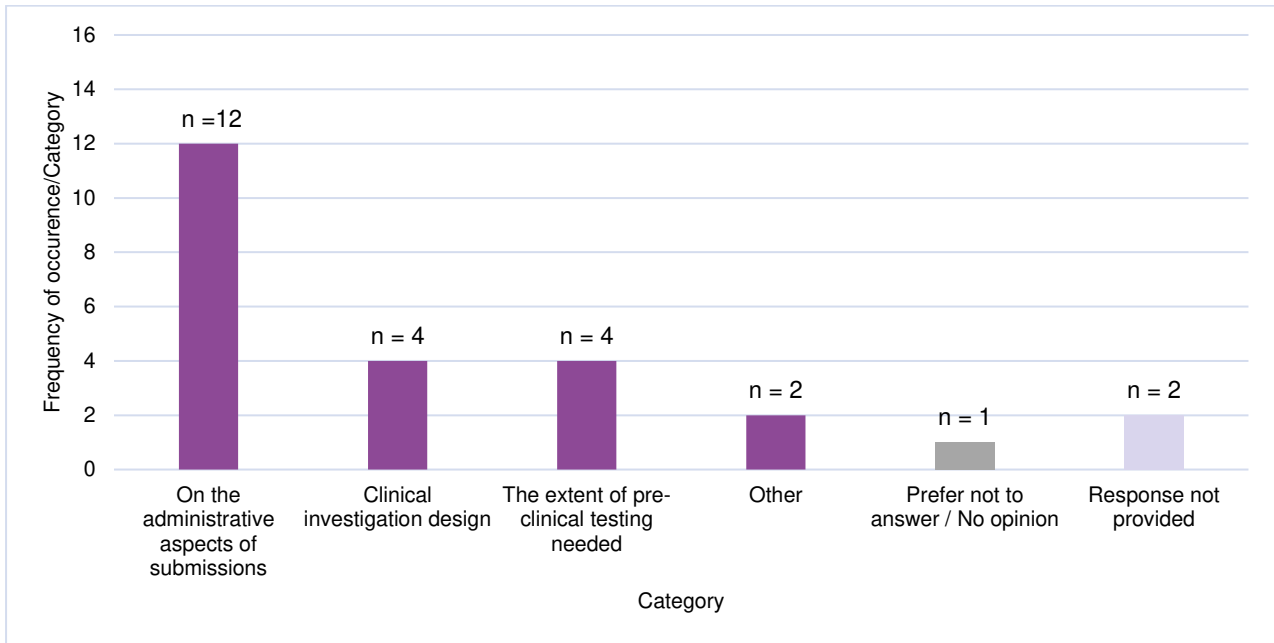
Figure 14. Do you provide guidance for pre-market CIs?



Overall, 14 (74%) NCAs provide guidance on pre-market CIs (Figure 14). The key focus areas are described in Figure 15. Other topics referenced in NCA guidance include classification and the difference between CI, performance studies (testing of in-vitro diagnostic devices) and other study types.

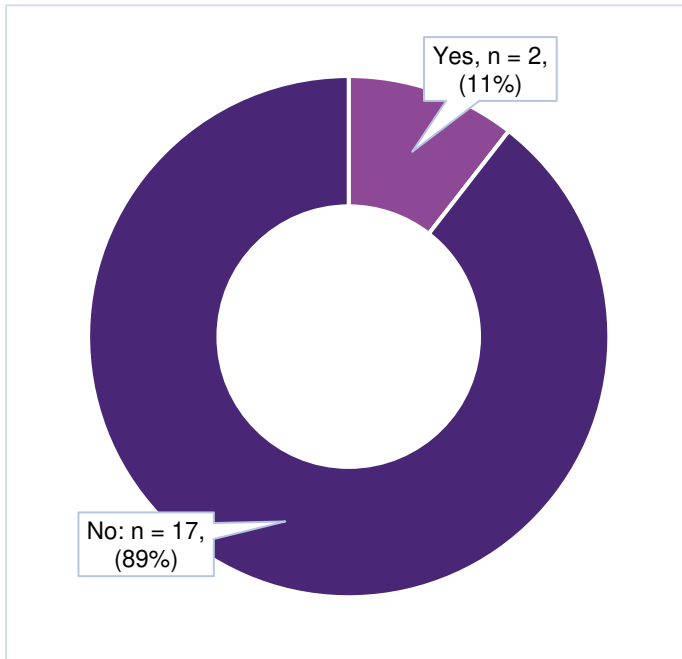
One NCA noted that they typically refer sponsors to international standards and guidance documents such as ISO 14155:2021², MDCG 2024-3⁵, and MDCG 2024-5.⁶

Figure 15. Key focus areas in pre-market CI guidance



3.1.8. Dialogue with patients or patient organisations on clinical investigations

Figure 16. Mechanisms for dialogue with patients/patient organisations



Out of 19 NCAs, 2 (11%) have established mechanisms for dialogue with patients or patient organisations (Figure 16). During the workshop, it was highlighted that these patient interactions do not occur within the framework of individual CI assessments.

NCAs noted the potential benefit of incorporating patient perspectives into the technical documentation supporting the submission for a CI. To assist the application, NCAs noted that an explanation of how patient feedback was taken on board by the product developer would be helpful.

Key Quote from the Workshop



In terms of the assessment of individual studies, it could be useful if the sponsors articulate how they have taken the patients point of view on board. Ideally for early feasibility studies, it could become the default. This might help us with the acceptability of the study design conduct and oversight

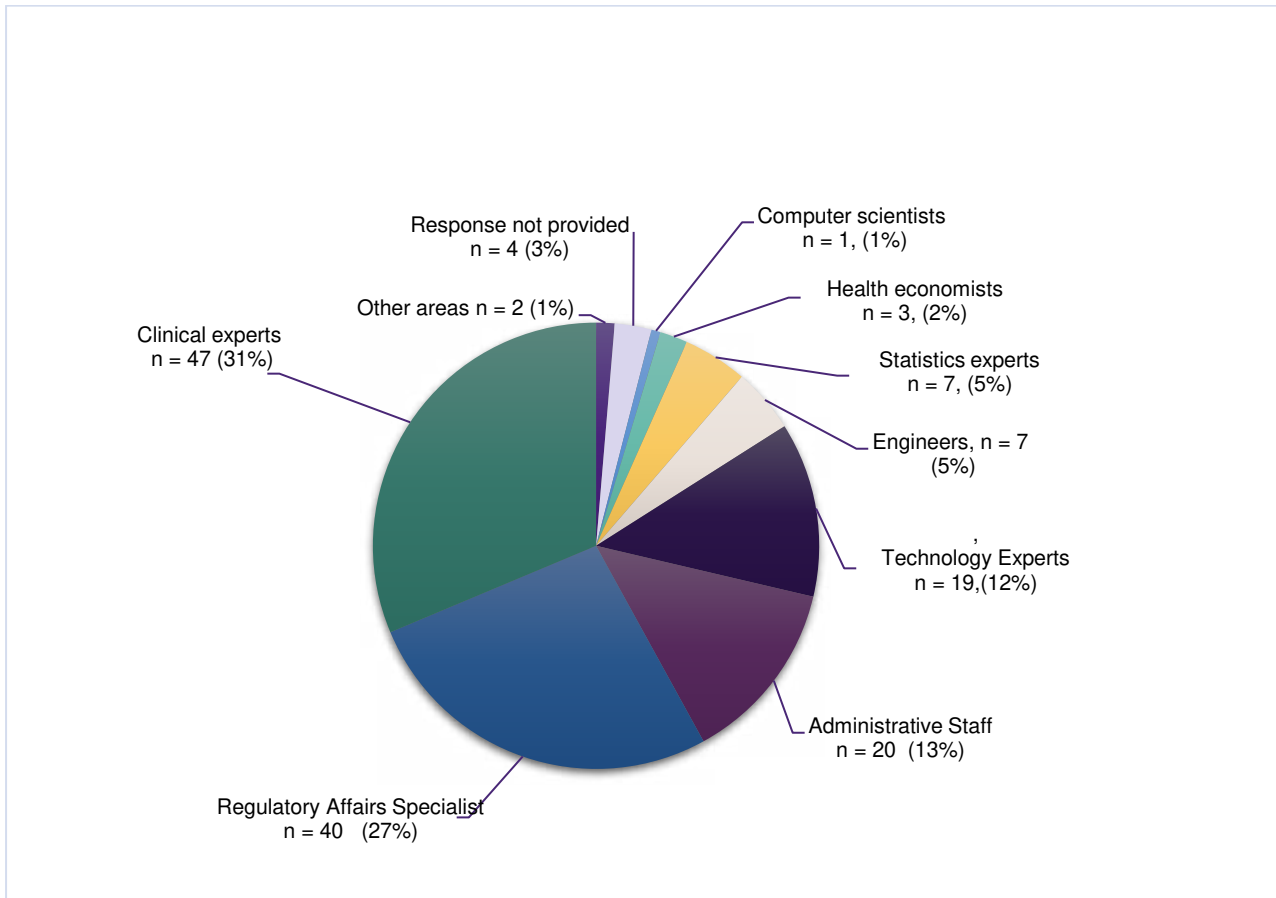


3.2. Resources, recruitment and training needs related to the assessment of applications to conduct Early Feasibility Studies

3.2.1. Resources

We examined the number and expertise of internal and external assessors involved in reviewing the CI application. Based on responses from 19 countries, a total of 150 assessors were identified. The most common specialism was clinical experts (47/150, 31%), followed by regulatory affairs specialists (40/150, 27%), and those with technology expertise (19/150, 12%) We explored the number and expertise of internal and external assessors involved in reviewing the CI application ([Figure 17](#)).

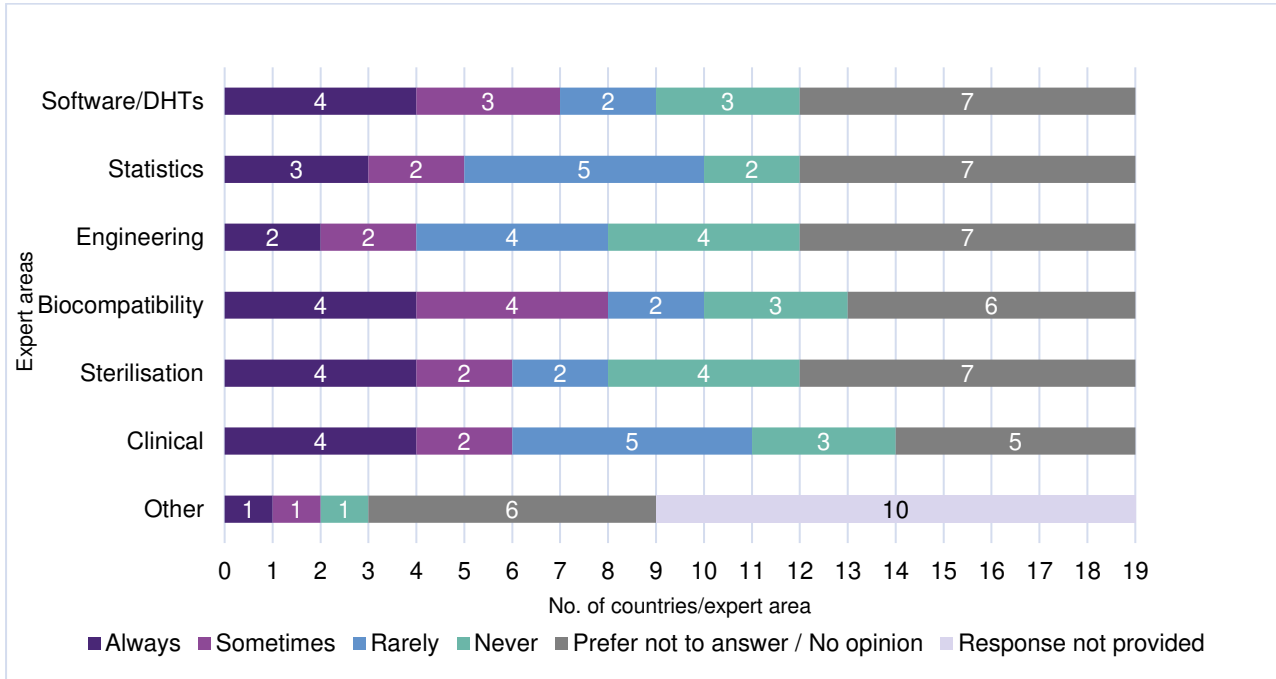
Figure 17. Number of internal or external assessors/area of expertise



3.2.2. Challenges in the recruitment and retention of assessors

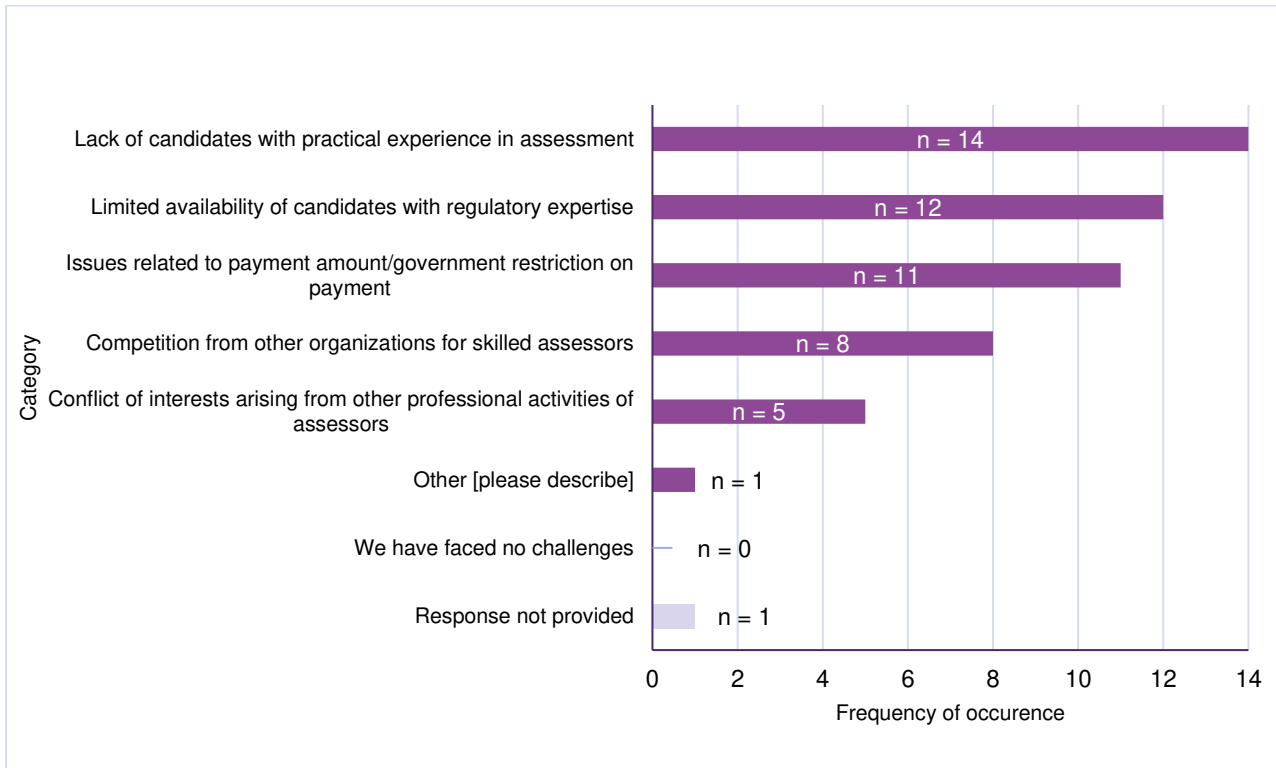
NCA reported challenges in recruiting experts in a variety of key domains ([Figure 18](#)). In free-text responses, NCAs noted constraints in public recruiting of internal assessors, in addition to challenges arising from conflicts of interest. The recruitment of assessors with digital health and software backgrounds were noted to be challenging for specialisms such as artificial intelligence, cybersecurity and data privacy.

Figure 18. Challenges in the recruitment of experts in key competency areas



With respect to both recruiting and retaining assessors, NCAs identified a variety of challenges (Figure 19).

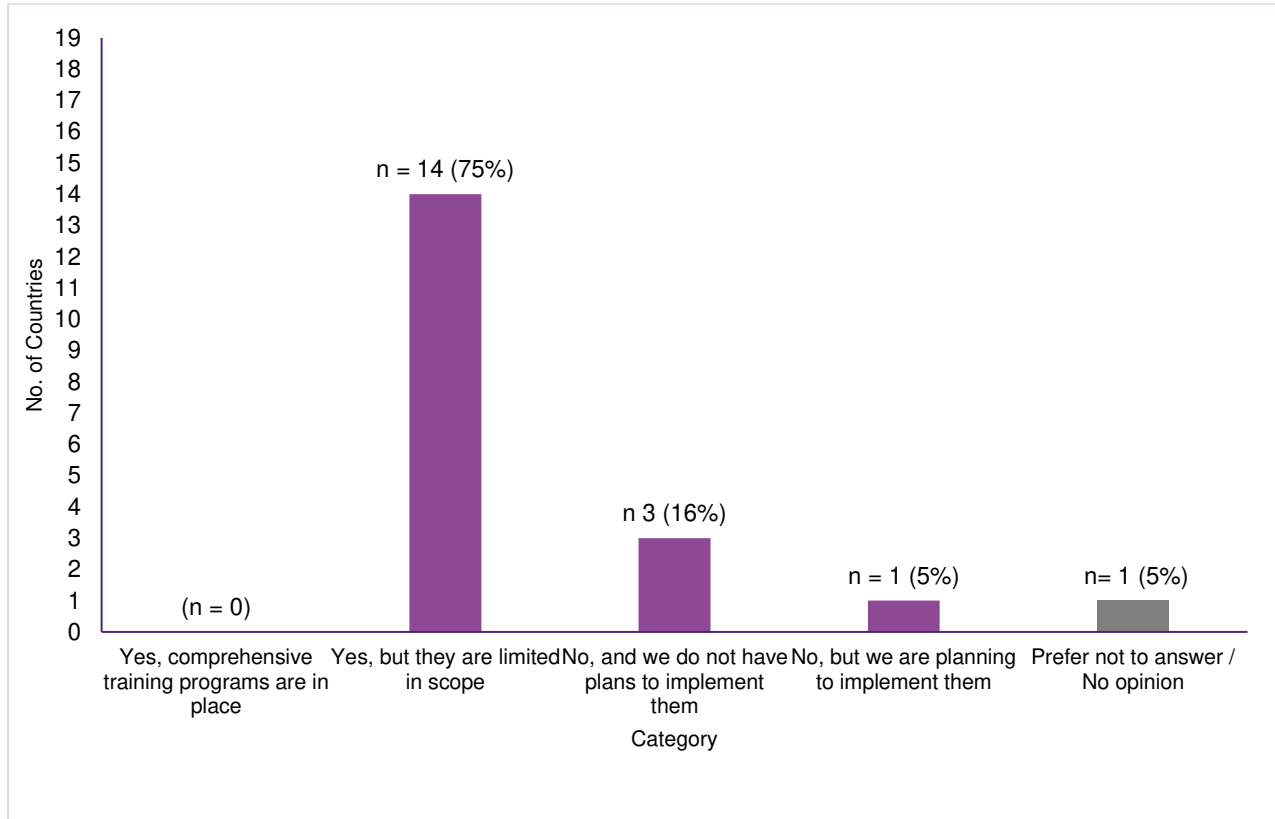
Figure 19. Main challenges faced in the recruitment of and retaining assessors



3.2.3. Training programs for staff on medical devices and digital health advancements and challenges in the recruitment and retention of assessors

The majority of NCAs (14/19, 75%) have training programmes for assessors relating to advancements in MDs and DHTs, however they are limited in scope ([Figure 20](#)).

Figure 20. Training programs for staff on medical devices and digital health advancements



3.3 Other findings: Deficiencies, Information Requests, and Approval Timelines

3.3.1. Common deficiencies and likely cause

The documents most frequently identified by NCAs as having the highest number of deficiencies during the assessment of CIs were the investigator's brochure, the CI plan, and the risk management file ([Figure 21](#)). The type of deficiency and frequency of occurrence are described in [Figure 22](#). The free text responses provided additional perspectives into the causes of these deficiencies, and these included, price of standards, a lack of understanding of the CI process and applicable MDCG guidance documents.

Figure 21. Documents with the highest frequency of deficiencies identified by NCAs

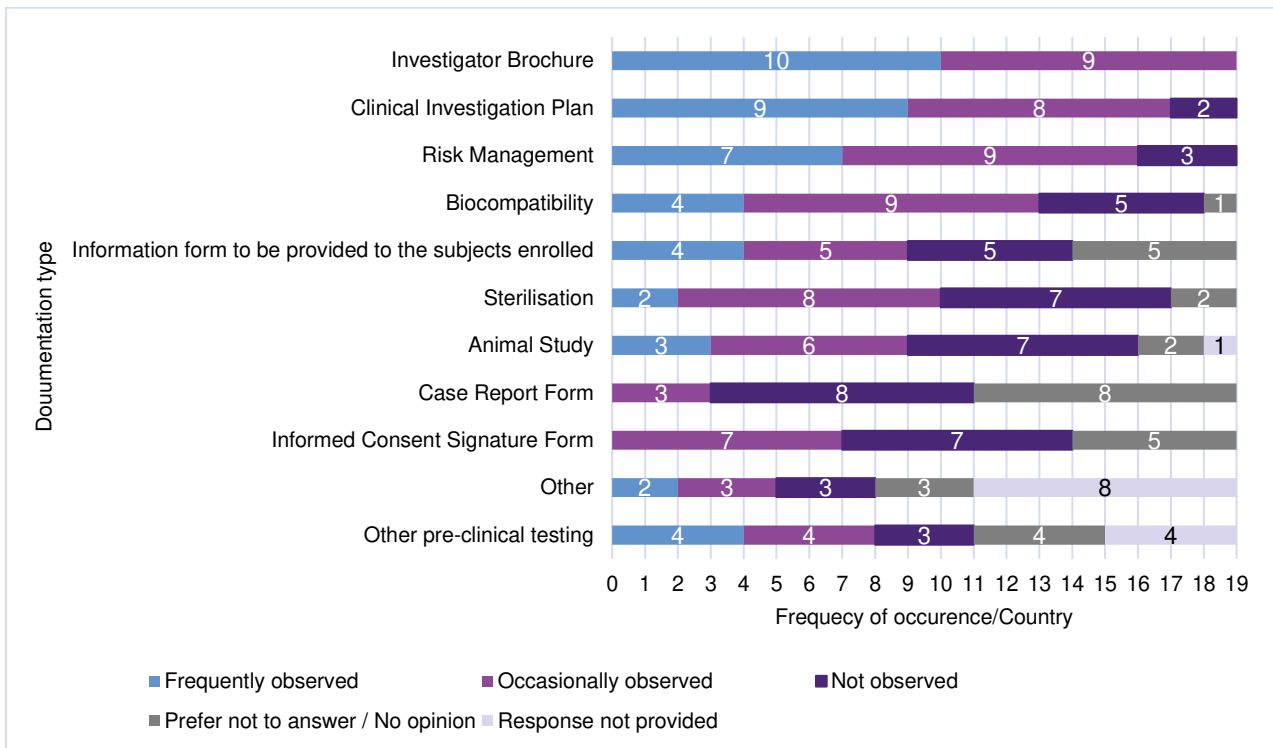
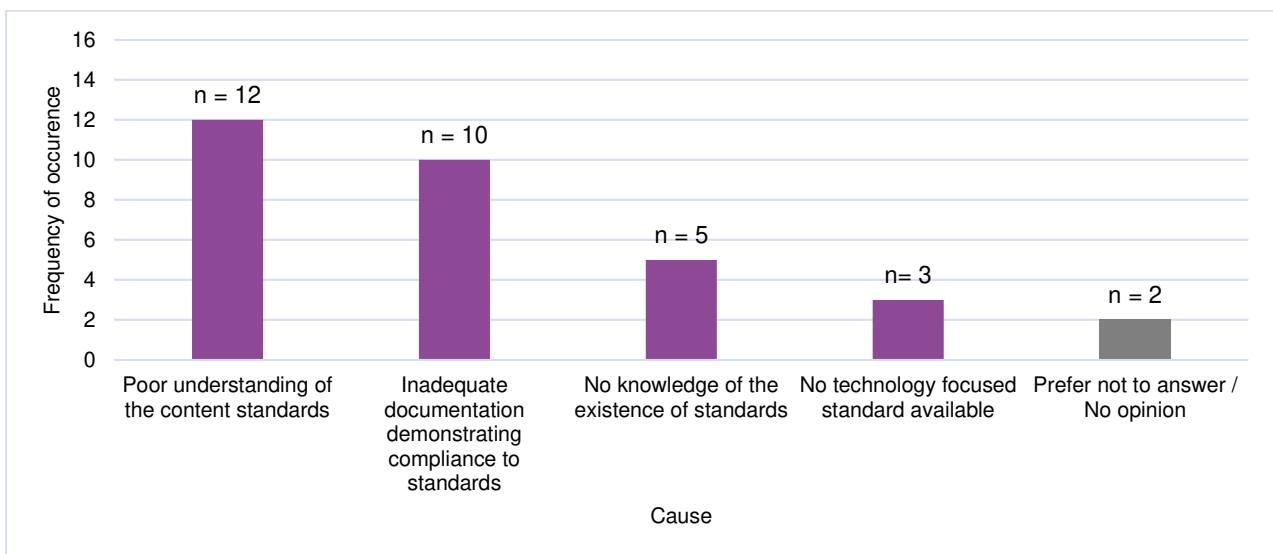


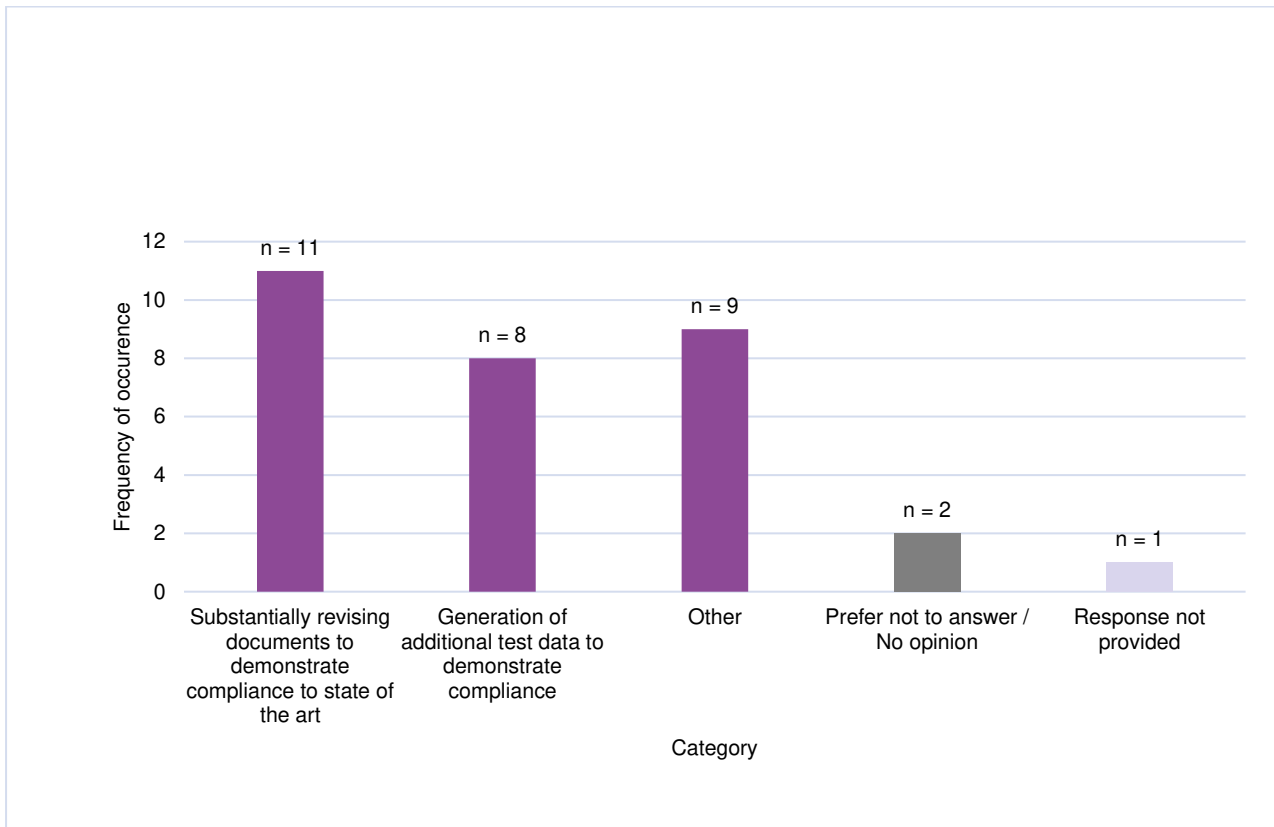
Figure 22. Most likely cause of deficiencies



3.3.2. Reasons for requesting additional information

The most common reasons for requesting additional information related to either substantially revising documents to demonstrate compliance to the state of the art, or the generation of additional test data (Figure 23).

Figure 23. Common reasons for requesting additional information from sponsors during application assessment



Requests for additional preclinical test data to be generated are variable across the countries surveyed. In some NCAs, further data is requested, however in other NCAs, if additional testing is needed, the application is refused. In some NCAs, the generation of additional data is possible within the context of an application. Some NCAs never or rarely ask for additional data.

'Other' factors were prominent in the responses, and these were described in the free-text responses summarised below, arranged by thematic area:

CI design

- Exploratory trial: provide a critical analysis of compassionate clinical cases or early trials conducted in other countries, or if the trial has started in other countries, first available data.

- Confirmatory trial: provide an analysis of clinical safety and performance data from previous trials.
- For highly innovative MDs subject to FIH studies: patient selection criteria with potential loss of chance compared with existing treatments (comparing the investigational device to alternative available treatment options).
- Incomplete non-inclusion criteria with absence of contraindications to the use of the MD listed in the investigator's brochure and instructions for use.
- Insufficient follow-up time for study subjects, particularly with regard to implantation test results.
- Intermediate analysis: no alpha risk control method, no associated decision rules.
- No management of missing data.
- No sensitivity analysis.
- Request for addition of futility analysis and/or “stopping rules” with a phased, step-by-step enrolment of subjects (particularly for FIH, innovative MDs).

Generation of additional test data to demonstrate compliance

- Lack of justification for the transposability of the results of pre-clinical tests carried out on a version of the MD that does not correspond to the one used in the CI.
- Lack of justification for not performing biocompatibility studies required by ISO 10993-1.⁷
- Implantation test in progress and interim report failing to demonstrate complete degradation of the MD or achievement of a steady state – for example in the case of a FIH.
- CI with an implantable and resorbable MD (e.g. biodegradable reconstruction membrane or tissue reinforcement).

Regulatory requirements

- Reporting of serious adverse event data not in line with MDCG 2020-10.⁸
- Not providing the documentation required by the Regulation (EU) 2017/745

3.3.3. Co-Ordinated CI Assessments

Article 78 of MDR provides for a single assessment of a multi-state CI, the CIE WG launched a pilot “call for applications” on February 6, 2025. In the workshop, we explored this emerging policy area. The CIRCA-BC (Communication and Information Resource Centre for Administrations, Businesses and Citizens) platform of the European Commission will be used for applications, and the templates provided for in MDCG 2021-8⁹ will be used.

Dialogue between the sponsor and NCAs, or the coordinating NCA is being considered at the CIE WG currently and is technically possible for the pilot. For the pilots, NCAs may focus on larger multi-state studies, which are typically at the pivotal phase of clinical development, however EFS applications under this pilot are possible and will be explored later this year in the context of the HEU-EFS project.

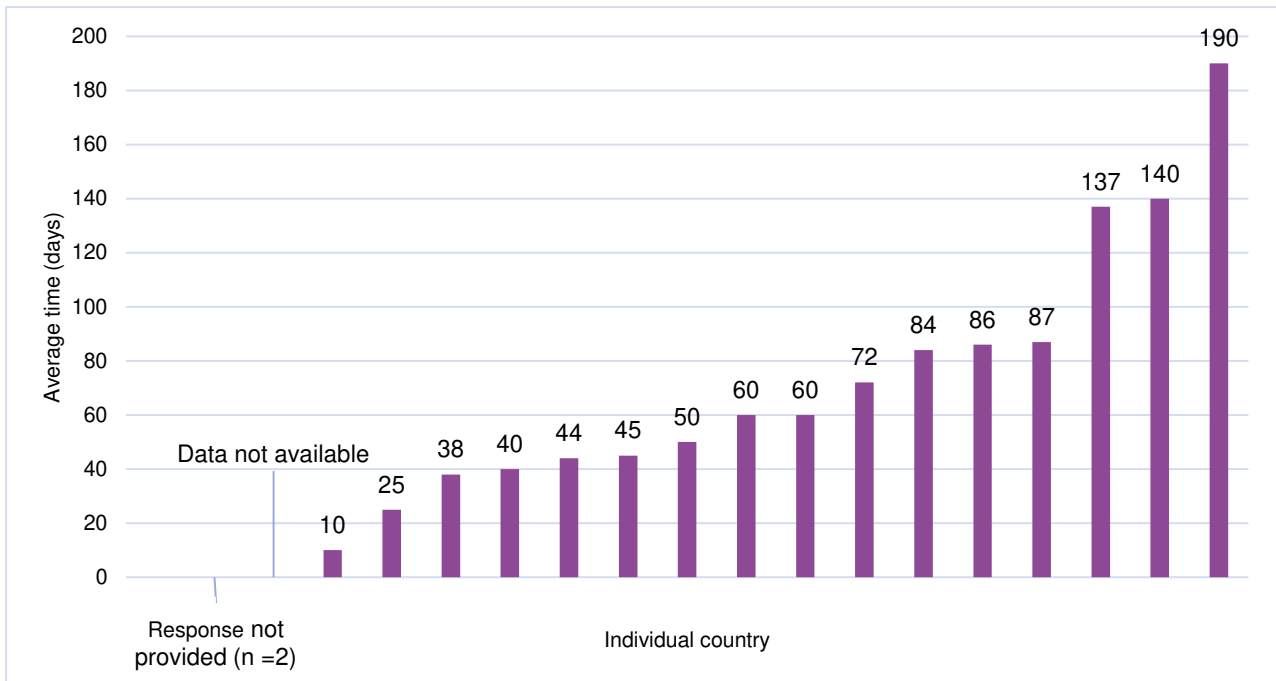
3.3.4. NCA Timeline from Application to Authorization

The majority of NCAs (16/19, 84%) provided data on the average time from initial application to authorisation for higher risk MDs ([Figure 24](#)). These devices were selected as all NCAs subject these studies to a complete assessment, rather than ‘validation only’ approach. There is a wide variance in the average timelines reported, ranging from 25 days to 190 days.

This variance may be accounted for due to the following differences across NCAs:

- The use of ‘stop-clocks’ to allow for the generation of additional test data.
- The use of additional time to consult with external experts.
- Resource constraints within NCAs to complete the assessment.

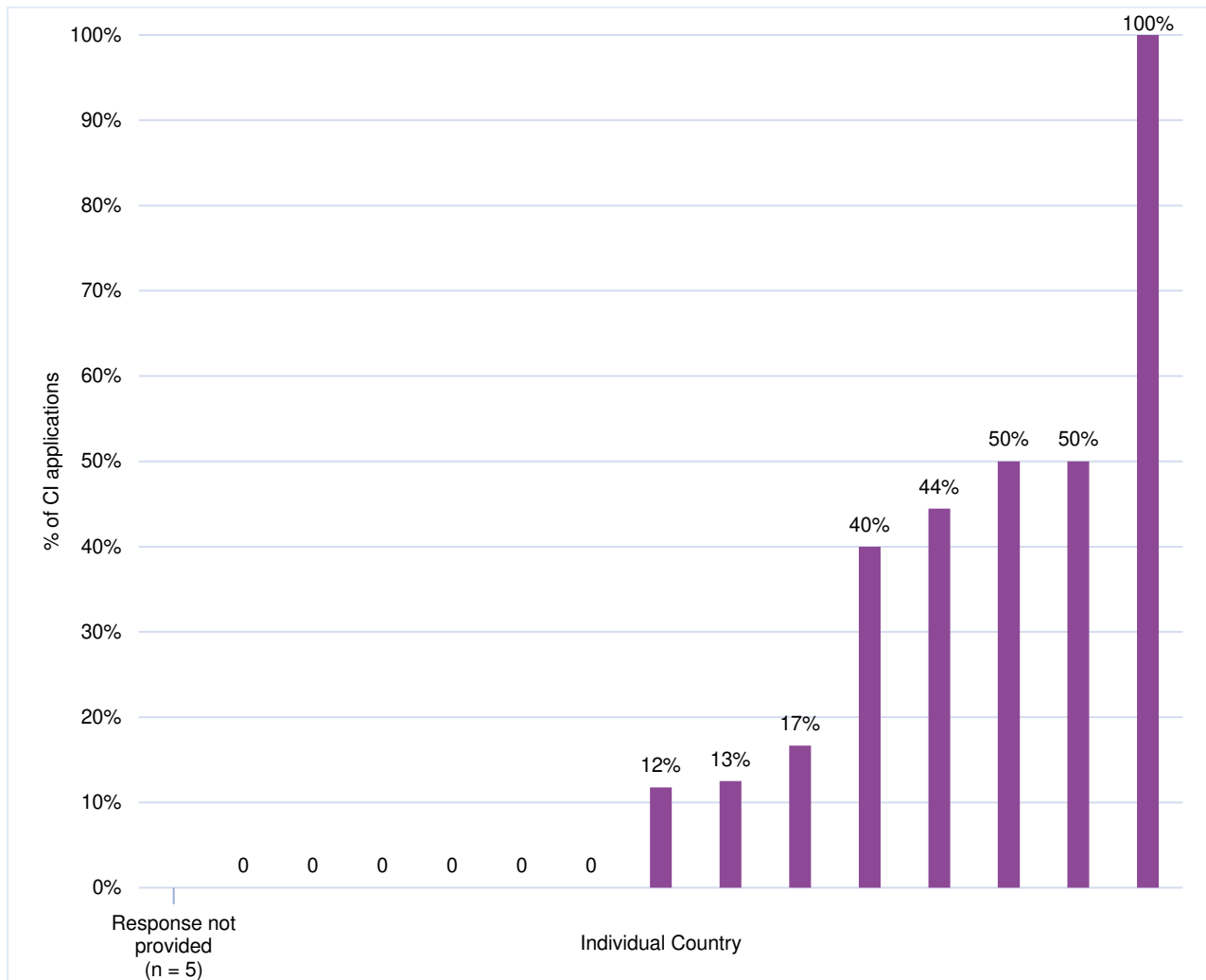
Figure 24. Average time (days) from initial application to study authorization in 2023 for investigational devices (excluding class I and non-invasive class IIa/IIb)



In the free-text responses, one NCA noted that “pre-submission dialogue helps to shorten the assessment timeline”.

The utilisation of additional assessment time to consult with external experts is variable across NCAs. One NCA uses external experts in all cases, 8 NCAs use external experts in some cases and 6 NCAs do not use additional time to consult with experts ([Figure 25](#)).

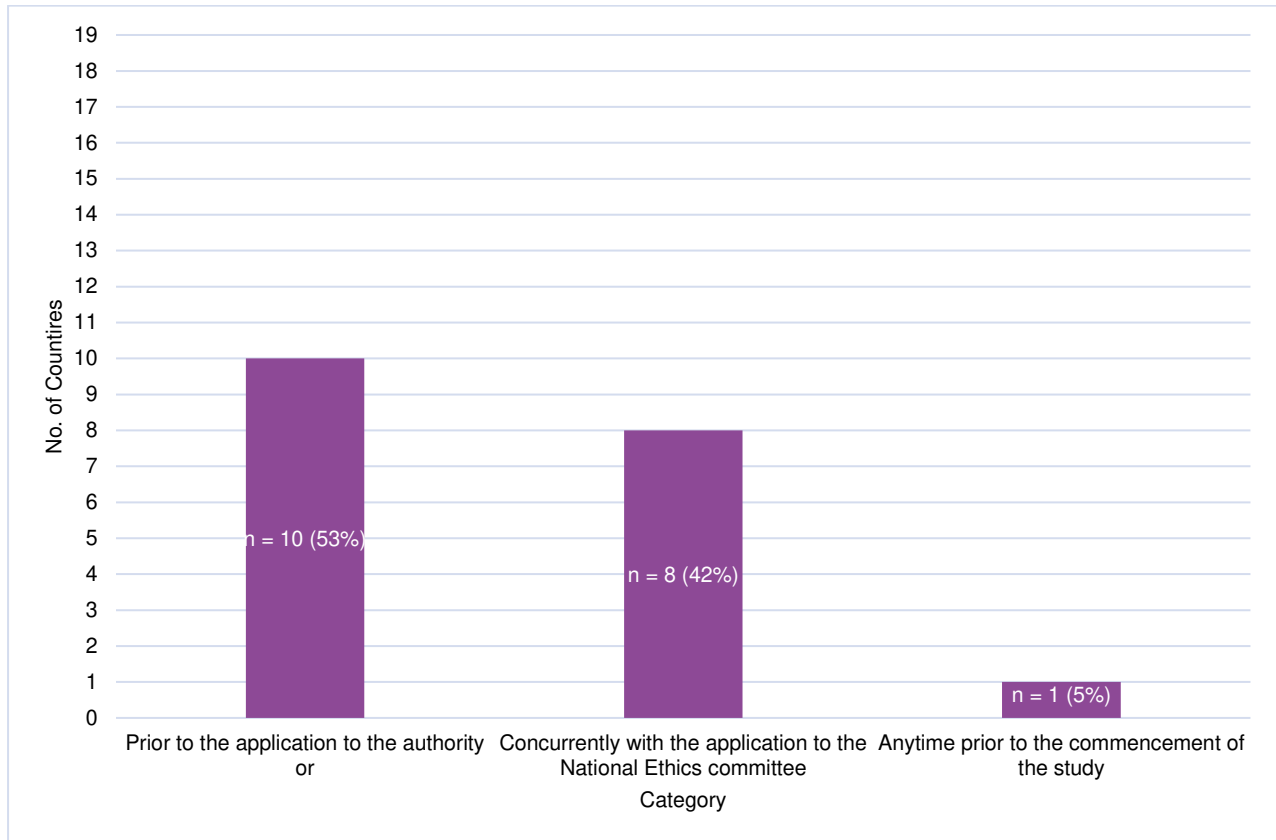
Figure 25. How many of those applications required the use of the 20-day period for consulting with experts?



3.3.5. Timeline for Research Ethics Committee Approval

CI's require both NCA and REC approval. Depending on national implementing law, the order of applications for NCA and REC may be sequential or in parallel. The majority of NCAs (10, 53%) require REC approval prior to making the application to the NCA whereas other NCAs allow parallel assessments or applications at any time prior to commencement of the study (Figure 26). This is important for sponsors to prepare as part of project planning, especially in the context of future coordinated (MDR, Article 78) applications.

Figure 26. Timeline for REC approval



3.3.6. Clinical investigations of artificial intelligence and digital health technologies

NCA's noted a variety of challenges in the assessment of AIeMD. These are described in the thematic areas described below.

Challenges in Assessing AI-Enabled Medical Devices

In the workshop, one NCA noted a variety of challenges in the assessment of AIeMD. These challenges arise especially during early-stage development, when sponsors often need to generate data for training or tuning AI algorithms. In some cases, such data collection presents no or minimal risk to subjects, particularly if the AI outputs do not influence patient management. Sponsors may wish to avoid formal CI applications in these instances, viewing them akin to retrospective data gathering. However, because data collection may be prospective, there is regulatory uncertainty as to whether this constitutes a CI or a form of pre-clinical validation. The NCA thus emphasize the

need for clear European-level policy to distinguish when data-gathering activities qualify as a regulated CI and when they do not.

EFS and *In-silico* Testing

EFS for DHT represent a unique situation. EFS traditionally requires that the device cannot be adequately evaluated by non-clinical methods. Yet many AI-based solutions can undergo extensive *in-silico* testing, making it more difficult to justify why human exposure is necessary early on. Sponsors must therefore demonstrate why *in-silico* methods are insufficient before proceeding with an EFS involving human subjects.

Adaptive Designs and Multiple Prototypes

To address uncertainties in prototype performance, sponsors may propose adaptive study designs that allow testing multiple versions under one CI. Such designs can reduce the number of separate studies, which is especially beneficial for low-risk devices. One NCA expressed willingness in the workshop to consider these adaptive approaches, recognizing that iterative development and learning are common in AI.

Continuously Learning AI

Another open question involves software or AI that continues learning after market approval. Because such devices can fundamentally change over time through ongoing data inputs, further clarity is needed regarding how these updates are monitored, documented, and potentially re-approved.

3.3.7. Adaptive clinical investigation designs

In the workshop, one theme that emerged is the sample size for pilot stage studies. NCAs have seen experience of studies described as FIH enrolling 10-20 subjects, and this overlaps with the typical subject size for EFS studies. NCAs noted the possibility to submit an adaptive CI, although experience with these types of studies has been limited amongst workshop participants. An adaptive clinical study design is defined as a design that allows modifications to the trial and/or statistical procedures of the trial after its initiation without undermining its validity and integrity.¹⁰

For MDs, this could allow for a larger sample size initially, with the potential for an interim analysis prior to further recruitment. This could allow for progression of clinical development in a phased approach, to potentially expand to pivotal studies with sample sizes such as 150 patients. Adaptive trial designs could also take iterations to the device into account, if these are introduced during the

trial. NCAs noted that adaptive study designs have been incorporated in the MDCG guidance on orphan devices.¹¹

4. Discussion

This report represents the first thorough examination of NCA practice and perspectives in the context of CI and EFS assessments. NCAs have variable experience of both CIs and EFS due to the number of CI applications that are received on an annual basis.

For EFS, NCAs prioritised the importance of demonstrating the sufficiency of pre-clinical testing, and the extent to which this can justify first clinical use. NCAs also prioritised the importance of being able to understand the likelihood that non-clinical test methods will correlate with clinical outcomes. Opportunities for dialogue and scientific advice are available in many NCAs, however the timing, nature of advice and costs associated with these processes are variable.

For some NCAs, it is possible to pause an assessment in order to generate additional test data, however in other NCAs this will result in a rejection of the application. Sponsors will need to be aware of the need to achieve research ethics committee approval prior to making an application to an NCA in some cases. NCAs typically offer training to assessors on advancements in MDs and DHTs, however these are limited in scope.

DHTs and AleMDs often require real-world clinical data for training or refinement, creating regulatory uncertainty when this data collection poses no risk to patients but is conducted prospectively. While such activities may resemble retrospective research, some can still be classified as clinical investigations, necessitating clearer guidance on when this distinction applies.

Some EFS for DHTs and AleMDs may face challenges in justification, as robust *in-silico* testing is often available. Sponsors must demonstrate why clinical evidence generation is necessary, given that EFS are only warranted when preclinical methods cannot provide answers.

Additionally, adaptive study designs could help streamline development for low-risk devices by allowing multiple prototypes or iterative refinements within a single investigation. Current practices often rely on successive studies, increasing the burden on both sponsors and regulators. A further challenge lies with continuously learning AI systems, which evolve post-approval based on new data. These changes raise concerns about whether the device remains within its originally approved specifications, highlighting the need for harmonized guidance on regulating adaptive AI technologies and clarifying ongoing monitoring requirements.

NCAs support the inclusion of patient perspectives in technical documentation for CI applications and there was no strong consensus expressed as to the optimal place to document this in the submission.

The timeline for assessments is variable across NCAs and this may be accounted for by a variety of factors such as the use of ‘stop-clocks’ to allow for the generation of additional testing, the use of external experts or resource constraints in the NCA. A pilot of the co-ordinated CI assessments for multi-state studies has launched and will allow for the sharing of experience amongst NCAs to support increased harmonisation of assessments. The CIE WG has also established a ‘clinical roundtable’ to allow NCA assessors to share experience in the context of challenging assessments.

Limitations of this work relate to an incomplete number of NCAs who participated to the survey or workshop, which limits the validity of findings. The survey and workshop were conducted in English, which may limit some countries from fully engaging in the activity.

5. Conclusion

The goal for this deliverable was to investigate the professional and organizational aspects of NCAs engaged in CI and EFS assessments. We would like to sincerely thank NCAs for their active participation and engagement in this activity. The development of a harmonized framework for EFS in the EU will need to integrate with NCA practices and procedures for assessment. Many of the building blocks for this framework are already in place within NCAs, where dialogue and advice structures are often available.

EFS applications to NCAs are assessed under the same framework, and typically the same procedure (Article 62 of the MDR), however there are also heterogenous approaches amongst NCAs with respect to dialogue, advice and assessment activities. This will need to be taken into account when preparing recommendations for an EU EFS Program.

References

1. European Commission. Medical Device Coordination Group Working Groups, Clinical investigation and evaluation (CIE). Available from: https://health.ec.europa.eu/medical-devices-dialogue-between-interested-parties/medical-device-coordination-group-working-groups_en#three
2. European Committee for Standardization. ISO 14155:2020 Clinical investigation of medical devices for human subjects - Good clinical practice [Internet]. 2020. Available from: <https://www.iso.org/standard/71690.html>
3. Regulation (EU) 2017/745 European Parliament. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.) [Internet]. OJ L Apr 5, 2017. Available from: <http://data.europa.eu/eli/reg/2017/745/oj/eng>
4. European Commission. SME definition. Available from: https://single-market-economy.ec.europa.eu/smes/sme-fundamentals/sme-definition_en
5. Medical Device Coordination Group Document. MDCG 2024-3 Guidance on content of the Clinical Investigation Plan for clinical investigations of medical devices 2024
6. Medical Device Coordination Group Document. MDCG 2024-5 Guidance on content of the Investigator's Brochure for clinical investigations of medical devices 2024
7. European Committee for Standardization. ISO 10993-1:2018, Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process. Available from <https://www.iso.org/standard/68936.html>
8. Medical Device Coordination Group. MDCG 2020-10/1 Rev 1 Safety reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745. 2022.
9. Medical Device Coordination Group. MDCG 2021-8 Clinical investigation application/notification documents 2021
10. Chow SC, Chang M, Pong A. Statistical consideration of adaptive methods in clinical development. J Biopharm Stat. 2005;15:575–91. doi: 10.1081/BIP-200062277
11. Medical Device Coordination Group. MDCG 2024-10 Clinical evaluation of orphan medical devices, June 2024. Section A.2.5.2. Adaptive and sequential designs

Appendix 1 – Survey Questions

Background Information

Name of National Competent Authority (Mandatory)

Name and Surname of the contact (Optional)

E-mail of the contact (Optional)

Q1 Section 1: Experience with pre-market exploratory clinical investigations of medical devices at the pilot stage of clinical development, for example first-in-human clinical investigations, early feasibility clinical investigations and traditional feasibility clinical investigations
Here you can find the list of [Abbreviations](#).

Do you document/record the clinical development stage (for example pilot stage/pivotal stage) for the clinical investigation (CI) applications that you receive? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- Yes _____
- No _____
- Prefer not to answer / No opinion _____
-

Q2 Do you record if the study is an Early Feasibility Study (EFS)? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- Yes _____
- No _____
- Prefer not to answer / No opinion _____
-

Q3 What was the number of CI applications received in 2023 for the following
[Please insert number of clinical investigations in the text box below]

- EFS related to class I devices or non-invasive class IIa and IIb devices

 - EFS related to class III devices or invasive devices

 - EFS related to Medical Device - Digital Health Technologies

 - Please add any additional information that you consider relevant

-

Q4 What was the total number of CI applications received in 2023 for the following:
[Please insert number of clinical investigations in the text box below]

- All medical devices _____
 - Class I devices or non-invasive class IIa and IIb devices

 - Class III devices or invasive devices

 - Please add any additional information that you consider relevant

-

Q5 Have you observed any common deficiencies in documentation supporting pre-market CIs in terms of their compliance with the standards in the following areas:

(For each item below, please rate the level of frequency)

Not observed	Occasionally observed	Frequently observed	Prefer not to answer / No opinion	
Clinical Investigation Plan (CIP)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Information form to be provided to the subjects enrolled in the CI (e.g. patient information and informed consent)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Investigator Brochure	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Informed Consent Signature Form	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Case Report Form	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Risk Management	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Biocompatibility	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Animal Study	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sterilisation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other pre-clinical testing [please describe]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other [please describe]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please add any additional information that you consider relevant

Q6 In your opinion, what is the most likely cause of these deficiencies [*Please select all that apply*]

- No knowledge of the existence of standards
- Poor understanding of the content standards
- Inadequate documentation demonstrating compliance to standards
- No technology focused standard available
- Other [Please describe]_____
- Prefer not to answer / No opinion

Q7 Does your national system require ethical approval to be obtained: *[Tick which ones apply] (If you have any additional comments, please use the text box provided next to your answer)*

- Prior to the application to the authority or

- Concurrently with the application to the National Ethics committee.

- Anytime prior to the commencement of the study

- Prefer not to answer / No opinion

Q8 In the case of investigational devices OTHER THAN investigational class I devices or non-invasive class IIa and class IIb devices.

[Please insert number of clinical investigations in the text box below]

- For the year 2023 what was the average time (days) from initial application to the authorization for the start of the study

- How many of those applications required the use of the 20-day period for consulting with experts? _____

Q9 What are the reasons that your Authority might request additional information from the sponsor during the application assessment period *[Please select all that apply]*
(If you have any additional comments, please use the text box provided next to your answer)

Generation of additional test data to demonstrate compliance

Substantially revising documents to demonstrate compliance to state of the art

Other [please describe]

Prefer not to answer / No opinion

Q10 Do you provide guidance for pre-market clinical investigations? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

Yes (please provide the link to the guidelines in the box below, if available)

No _____

Prefer not to answer / No opinion _____

Q11 Does this guidance for pre-market clinical investigations contain substantial information on:
[Please select all that apply]

(If you have any additional comments, please use the text box provided next to your answer)

- Clinical investigation design _____
- The extent of pre-clinical testing needed _____
- On the administrative aspects of submissions _____
- Other [Please describe] _____
- Prefer not to answer / No opinion _____

Q12 Does the National Competent Authority have a process to engage in dialogue with sponsors who are preparing a pre-market CI? *[Tick which ones apply]*

(If you have any additional comments, please use the text box provided next to your answer)

- Yes _____
- No _____
- Prefer not to answer / No opinion _____

Q13 Does the National Competent Authority have a process to engage in dialogue with sponsors at the following time points: *[Please select all that apply]*

(If you have any additional comments, please use the text box provided next to your answer)

- Before an application for a pre-market clinical investigation is submitted
- During the assessment of a pre-market clinical investigation
- After the assessment of a pre-market clinical investigation has been complete
- Other [Please describe]
- Prefer not to answer / No opinion

Q14 What kind of advice do the sponsors typically look for? *[Please select all that apply]*

(If you have any additional comments, please use the text box provided next to your answer)

- Advice on clinical investigation design
- Advice related to the extent of pre-clinical testing needed
- Advice related to administrative aspects of submissions
- Other [Please describe]

Q15 In your opinion, is there a correlation between the size of the sponsors organisation and the likelihood of engaging in/seeking dialogue with the NCA? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- Yes _____
 - No _____
 - Prefer not to answer / No opinion _____
-

Q16 In your opinion, does the quality of the CI application improve as a result of dialogue with the sponsor? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- Never _____
 - Rarely _____
 - Sometimes _____
 - Always _____
 - Prefer not to answer / No opinion _____
-

Q17 In your experience, are there particular technologies (such as orthopaedics, software) or class of device (Class 1, IIa, IIb etc) that require more frequent and in-depth dialogue than others? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- Yes _____
 - No _____
 - Prefer not to answer / No opinion _____
-

Q18 Do you have a mechanism for engaging in dialogue with patients or patient organisations regarding CIs (e.g. patient forums)? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

Yes _____

No _____

Prefer not to answer / No opinion _____

Please add any additional information that you consider relevant

Section 2: Resources, recruitment and training needs related to the assessment of clinical investigation (CI) applications to conduct pre-market clinical investigations

Here you can find the list of [Abbreviations](#).

Q19 Please indicate the number of internal / external assessors involved in medical devices CIs for each area of expertise listed below:

- Regulatory affairs specialists _____
- Clinical experts _____
- Technology experts _____
- Statistics experts _____
- Administrative staff _____
- Computer scientists _____
- Engineers _____
- Health economists _____
- Other areas _____
- Prefer not to answer _____

Q20 Have you encountered challenges in recruiting candidates with knowledge and expertise in the following areas:

(For each item below, please rate the level of frequency)

	Always	Sometimes	Rarely	Never	Prefer not to answer / No opinion
Clinical	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sterilisation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Biocompatibility	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Engineering	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Statistics	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Software / digital health technologies	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other [Please describe]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q21 What are the main challenges your organization faces in recruiting/retaining assessors?
[Please select all that apply]
(If you have any additional comments, please use the text box provided next to your answer)

Lack of candidates with practical experience in assessment

Competition from other organizations for skilled assessors

Limited availability of candidates with regulatory expertise

Conflict of interests arising from other professional activities of assessors

Issues related to payment amount/government restriction on payment

We have faced no challenges

Other [please describe]

Q22 Do you have training and development programs in place to keep your staff updated on the latest technological advancements in medical devices and/or digital health technologies? *[Tick which ones apply]*

(If you have any additional comments, please use the text box provided next to your answer)

Yes, comprehensive training programs are in place

Yes, but they are limited in scope

No, but we are planning to implement them

No, and we do not have plans to implement them

Prefer not to answer / No opinion

Please add any additional information that you consider relevant

Section 3: Allocation of Resources

Here you can find the list of [Abbreviations](#).

Q23 For the assessment of the clinical investigation (CI) application, does your Authority assign?

[Tick which ones apply]

(If you have any additional comments, please use the text box provided next to your answer)

- Single assessor _____
- More than one assessor _____
- Other [please describe] _____
- Prefer not to answer / No opinion _____

Q24 For the CI assessment, where relevant, how often do you assign assessors with the following competencies:

(For each item below, please rate the level of frequency)

	Always	Sometimes	Rarely	Never	Prefer not to answer / No opinion
Clinical	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sterilization	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Biocompatibility	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Engineering	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Statistics	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Software engineers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other (please describe)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q25 How do you assign assessors for the CI?
(For each item below, please rate the level of frequency)

	Always	Sometimes	Rarely	Never	Prefer not to answer / No opinion
Based on their expertise in the specific therapeutic area	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
By their experience with similar types of investigations	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Through a random selection process	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
According to availability and workload distribution	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other [please describe]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q26 Do you engage external assessors or experts to assist with the evaluation of the pre-market CI applications? *[Tick which ones apply]*
(If you have any additional comments, please use the text box provided next to your answer)

- We do not engage external experts _____
- Rarely _____
- Sometimes _____
- Always _____
- Prefer not to answer / No opinion _____

Q27 Do you engage external assessors or experts to assist with evaluating pre-market CIs applications for the following reasons: *[Tick which ones apply]*

- Lack of internal resources
- Lack of internal expertise
- Prefer not to answer / No opinion

Q28 What areas do you engage external assessors or experts to assist with when evaluating pre-market CI applications?

(For each item below, please rate the level of frequency)

	Always	Sometimes	Rarely	Never	Prefer not to answer / No opinion
Clinical	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sterilisation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Biocompatibility	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Engineering	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Biostatistics	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Software / digital health technologies	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other (please describe)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please add any additional information that you consider relevant

If you are happy to submit please tick the yes box.

- Yes
- No

Appendix 2 – Workshop Questions

Part 1

Experience with EFS assessments

Have you assessed an application to conduct an early feasibility study of a medical device in your practice? This will be presented as an instant poll in Microsoft Teams.

If yes, what challenges have you experienced?

Follow-on questions to explore the challenges identified.

Co-ordinated clinical investigation assessments (multi-state studies)

Do you see co-ordinated clinical investigation assessments as a useful way to harmonise the assessment of multi-state early feasibility studies? This will be presented as an instant poll in Microsoft Teams.

Will there be an opportunity to engage in a co-ordinated meeting with developers in advance of an application?

Could you provide information on the application format – will a central application be possible in future?

The opportunity to discuss an EFS application with sponsors or developers

Discussions between the National Competent Authority and developer can happen at an early stage (i.e. when the device is under development), a pre-submission stage (i.e. when the protocol and clinical investigation documents are near-final) and during the clinical investigation (when substantial modifications may be required).

Do you offer meetings:

- ***To developers at an early stage of development (preliminary meetings)?***
- ***To developers planning to submit a clinical investigation application for an EFS (pre-submission meetings)?***
- ***To developers who are conducting a clinical investigation (continuous dialogue)?***

This will be presented as an instant poll in Microsoft Teams.

For the Authorities who offer these meetings - are these meetings helpful for the subsequent assessment of applications? In what way are they most valuable?

For the Authorities who do not offer some of these meetings – do you see value in providing this in future?

Part 2

Experience with digital health technologies and artificial intelligence systems

Do you have experience in assessing early-stage clinical studies of digital health technologies and/or artificial intelligence systems? This will be presented as an instant poll in Microsoft Teams.

What challenges have you experienced in assessing early-stage clinical studies of these technologies?

Are there specific regulatory aspects (such as risk management or clinical investigation planning), that have been challenging?

How do you manage the need for multiple substantial modifications, based on the iterative nature of digital health technologies or Artificial Intelligence Systems?

Do you feel that the current regulatory guidelines adequately cover EFS for digital health technologies, or are there areas that lack clarity?

For AI System developers, what are the most important aspects of the AI Act that will need to be considered by developers in making an application for a clinical investigation?

For example, how should plans to reduce bias, support explainability of the algorithm or to meet the transparency requirements about how the algorithm works?

Do you see potential benefits or challenges from the EU AI Act that could influence the way digital health technologies are developed and assessed in early feasibility stages?

Expectations for a future EFS program

What would best support your work to assess applications to conduct an EFS? For example, would secretariat (i.e. administrative support), technical (i.e. engineering or scientific support) or clinical (for example from expert panels) support be helpful?

The value of patient and clinician perspectives in medical device development

Do you believe there is value in manufacturers or sponsors engaging with clinicians or patients during the product development process?

If yes, how should this be documented – for example in the clinical investigators brochure?

Open question

Are there any other topics or activities that you see as important to support better coordination of Early Feasibility Study assessments in future?



Co-funded by
the European Union

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is supported by the Innovative Health Initiative Joint Undertaking (JU) under grant agreement No 101112185. The JU receives support from the European Union's Horizon Europe research and innovation programme and life science industries represented by MedTech Europe, COCIR, EFPIA, Vaccines Europe and EuropaBio.



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