Development of a Unique Tool for Assessing the Feasibility of an External Control Arm Study

HTA109

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Background

External control arms (ECAs) are used to generate comparative evidence (e.g., effectiveness) when only a single-arm trial has been conducted during the drug development process. However, key stakeholders often face substantial delays in determining the feasibility of an ECA; a responsive tool could streamline this process in a structured, rigorous manner.

Methods

- A comprehensive review was performed to identify ECA guidelines and reflection papers from relevant agencies such as the US Food and Drug Administration (FDA)[1] and the European Medicines Agency (EMA)[2] as well as other literature describing best practices for the conduct of an ECA.
- A structured questionnaire was first developed to assess general topics, data feasibility and design feasibility. Questions were coded with skip logic when appropriate.
- A checklist indicating positive (i.e., supportive of the ECA feasibility) and negative (i.e., challenges to the ECA feasibility) responses was created to allow the user to easily identify potential gaps at the strategic planning stage.
- A report summarizing the responses and recommended advice per question based on expertise from relevant literature was generated.
- The ECA Questionnaire Tool was developed as an interactive web application using a modern JavaScript framework for the frontend, enabling dynamic question logic, progress tracking, and automated report generation. User responses are transmitted via a RESTful API to a C# backend, where they are securely stored in a SQL database. This architecture supports structured data collection, real-time feedback, and seamless integration of feasibility checklists and reporting features.

Results

ECA Feasibility Questionnaire: A total of 24 questions including 2 general questions, 13 data feasibility questions, and 9 design feasibility questions were developed. Sample questions from the general domain (**Figure 1**) and the design feasibility domain (**Figure 2**) are provided below.

Figure 1: Example General Question from ECA Questionnaire

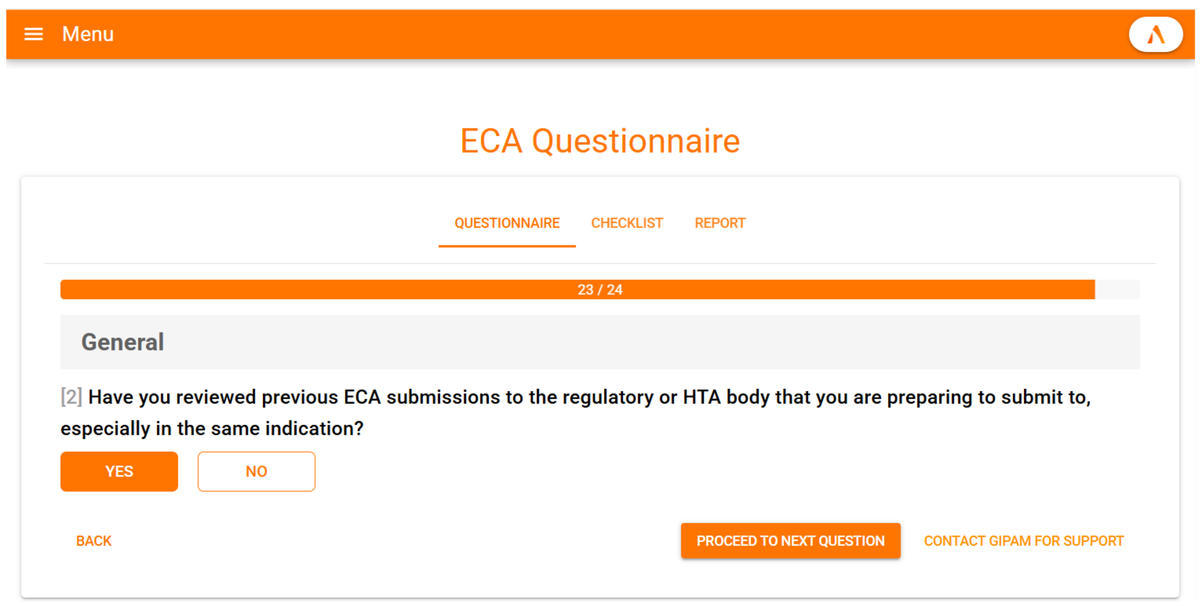
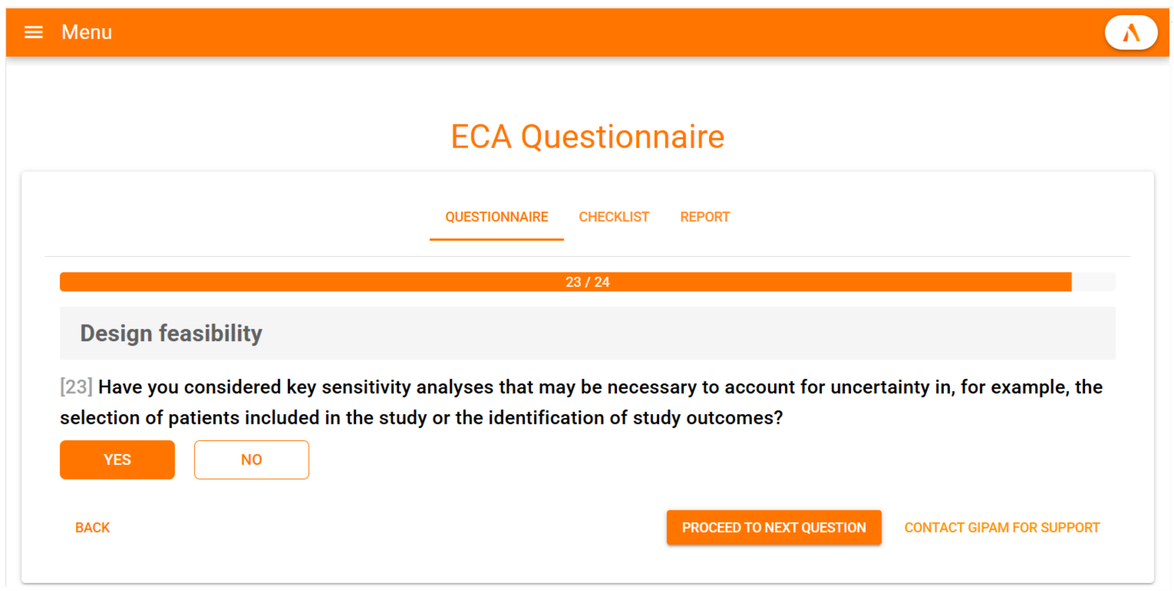
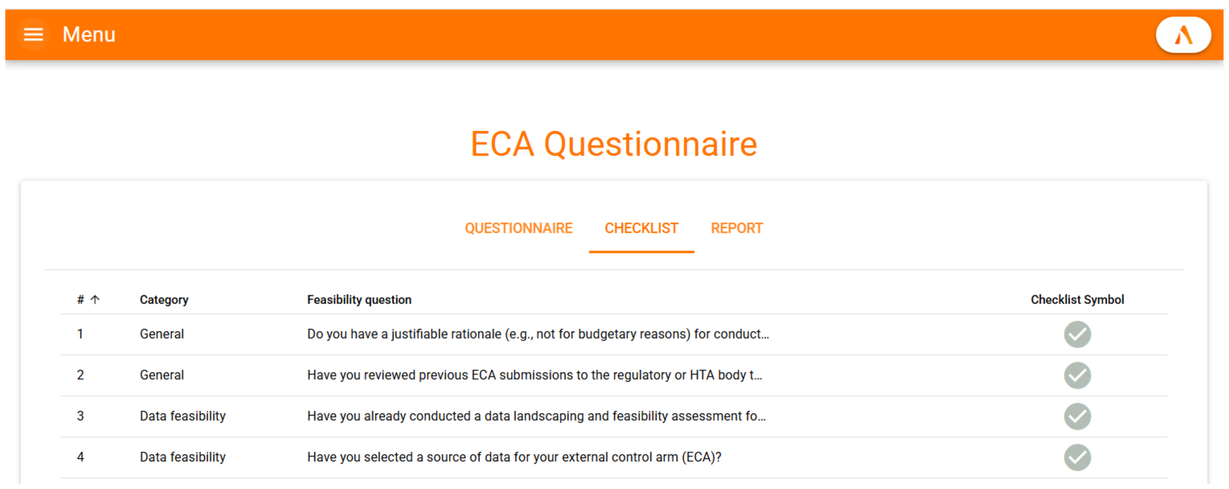


Figure 2: Example Design Feasibility Question from ECA Questionnaire



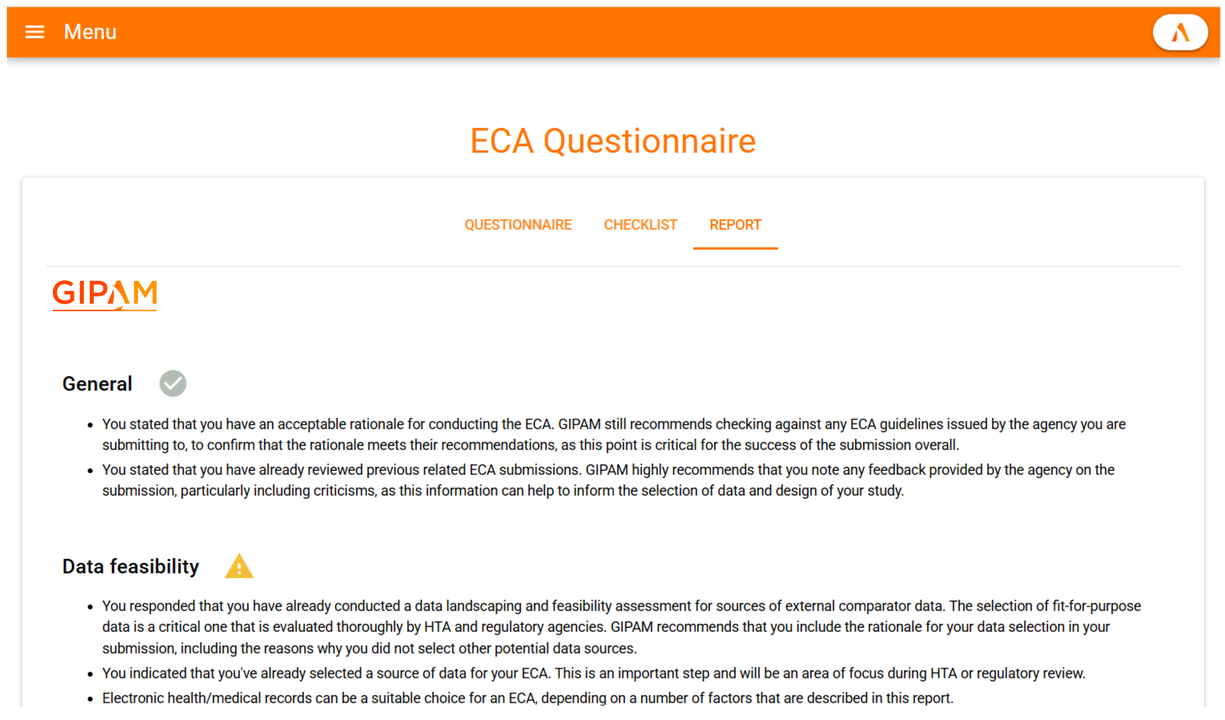
Checklist: Following the questionnaire, the completion status of all feasibility questions is summarized for user review (**Figure 3**).

Figure 3: Selected Output from ECA Questionnaire Checklist



Report: A comprehensive explanation of all responses along with associated guidance is then generated (**Figure 4**).

Figure 4: Selected Output from ECA Questionnaire Report



Conclusion

- A user-friendly electronic tool to assess the feasibility of an ECA across multiple domains can de-risk the evidence generation process, saving time and financial resources; the tool is available in GIPAM's EVIGATOR platform or independently.
- The use of a feasibility tool does not replace required analyses of patient-level data. However, a structured, rapid assessment can quickly identify gaps for focus during a full feasibility analysis.

Disclosure statement and Acknowledgements

No disclosures other than those related to the listed affiliations need to be reported.

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References

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[2] European Medicines Agency. Reflection paper on establishing efficacy based on single-arm trials submitted as pivotal evidence in a marketing authorisation application. 2024 Sept. Accessed at: https://www.ema.europa.eu/en/establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing-authorisation

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