Appendix 3: Ratings of Importance of Proposed Requirements

Table 1. Amended Requirements- Frequency of assigned value of importance by the key informants [9 Key Informants] (Essential =2; Important =1; Not important=0)

Amended Requirement	Frequency of Essential Value	Frequency of Important Value	Frequency of Not Important Value	Mean Rating of Importance
A. The study is conducted by investigators with the resources and skills to complete it successfully.	9	0	0	2.0
B. A written plan describes the schedule for completion of key study milestones.	5	4	0	1.6
C. The rationale for the study is supported by scientific evidence and study results are expected to fill the specified knowledge gap.	9	0	0	2.0
D. CMS and investigators agree on an evidentiary threshold for the study as needed to demonstrate clinically meaningful differences in key outcome(s) with adequate precision.	8	1	0	1.9
E. The study's protocol is publicly posted on the CMS website and describes, at a minimum, the data source(s), key outcome(s), and study design.	7	2	0	1.8
F. The protocol describes the information governance and data protection requirements that have been established.	8	1	0	1.9
G. The data are generated or selected with attention to completeness, accuracy, sufficiency of duration of observation, and size as required by the question.	8	1	0	1.9
H. Data for the study comes from patients treated in the usual sites of care delivery for the product..	4	5	0	1.4
I. The key outcome(s) for the study are those that are important to patients. A surrogate outcome that reliably predicts these outcomes may be appropriate for some questions.	7	2	0	1.8
J. The study population reflects the demographic and clinical complexity among the Medicare beneficiaries who are the intended users of the product.	3	6	0	1.3

Amended Requirement	Frequency of Essential Value	Frequency of Important Value	Frequency of Not Important Value	Mean Rating of Importance
K. When using secondary data, investigators provide information about the performance of the algorithms used for measurement of key exposures and outcomes.	6	3	0	1.7
L. The study design is selected to efficiently generate valid evidence. If a contemporaneous comparison group is not included, this choice must be justified.	9	0	0	2.0
M. The investigators minimize the impact of confounding and biases on inferences with appropriate statistical techniques, in addition to rigorous design.	7	2	0	1.8
N. In the protocol, the investigators describe considerations for analyzing demographic subpopulations as well as clinically-relevant subgroups as motivated by existing evidence.	3	6	0	1.3
O. The investigators demonstrate robustness of results by conducting alternative analyses and/or using other data sources.	6	3	0	1.7
P. The results and analytic code are submitted for peer review using a reporting guideline appropriate for the study design and structured to enable replication.	6	3	0	1.7
Q. The investigators commit to sharing de-identified data, methods, and analytic code with CMS or with a trusted third party. Other sharing is to follow the rules of the funder and the institutional review board.	6	3	0	1.7
R. The study is not designed to exclusively test toxicity unless the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.	4	5	0	1.4
S. The research study complies with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration, it is also in compliance with 21 CFR Parts 50 and 56.	9	0	0	2.0

Figure 1. Amended Requirements- Frequency of assigned value of importance by the key informants [9 Key Informants]