Medicines & Healthcare products Regulatory Agency

The International Council for Harmonisation (ICH) M15 Model-Informed Drug Development (MIDD) Guideline

Please note that these comments and the identity of the responder may be published unless a specific justified objection is received.
When completed, this form should be uploaded into the MHRA consultation portal, in Excel® format.

For more details on how to use this template please refer to the tab "Instructions for Responder".

Line from* (line Number or 0 for general comment)	Line to* (line Number or 0 for general comment)	Section number	Comment and rationale (to go to next line within the same cell use Alt + Enter)	Proposed changes / recommendation (if applicable - to be used if you want to propose specific text changes)	Category of comment (drop-down list - see definitions in instructions tab)
72	74	2.1	Regarding the context of use, the description of the model is mentioned, including data to build the model. However, with current developments regarding the use of foundational or general-purpose models, such models and their rationale for using or fine-tuning them could be considered.		Major
72	74	2.1	The context of use considers data to use the model; however, data to evaluating the performance of the model could also be added	Consider adding language to include evaluating the performance of the model.	Minor
72	74	2	Human input may be needed to build or train a model; for instance, a user may select or disregard suggestions by the model for various iterations, upon which the model will learn and refine the approach. These human factors can contribute to model risks and are relevant for the model result. Hence, the description should include that human interaction elements are foreseen.		Major
78	79	2	Guidance on what constitutes a low, medium or high risk may be helpful to provide context and consistency in the approach. For example, risk to the patient and/or development could be described. Alternatively the guidance could recommend that the categorization should follow procedures as established internally by the organization to avoid subjectivity.		Major
128	133	3	The impact of human factors, including an assessment of the usability and potential risk mitigation measures to address risks in human factors and the impact of human-in-the-loop in the decision-making and model-tuning, may influence the validation activities and therefore should be considered as part of those activities.		Major
147	150	3	The guidance refers to data selection, transformation and imputation; however, data may be also fully synthesized, which may be mentioned as an additional option. Expectations on the description of the modeling approach deriving and using such synthetic data could be described.		Major
157	158	3	Overfitting is mentioned as issue for consideration of model validation and applicability; however, other considerationss such as underfitting or lack of robustness to variations or noise in data input could be mentioned as well.		Minor