



April 4, 2006

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Guidance for Industry – Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims [Docket No. 2006D-0044]

Dear Captain Burke,

We appreciate the opportunity to comment on the proposed FDA Guidance for Industry – Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims.

Mapi Values is an international health research organization, a member of the Adelphi and Mapi Groups, and an affiliate of the Mapi Research Trust.

Mapi Values' main interest is in the development and interpretation of patient-reported outcomes (PRO) and Health Economic arguments to facilitate access to the market and optimize medical intervention.

Over the years, Mapi Values has developed partnerships with regulatory bodies and academic experts to assist in the advancement of world-wide standards for these processes. As part of this ongoing goal for improvement and to continue open-discussion relationships, we have provided herein a document that outlines our principal opinions and concerns regarding the PRO draft guidance.

Overall comments

The FDA PRO draft guidance is a clearly written document that provides a comprehensive and up-to-date set of guiding principles to assist in the development, validation, implementation, and analysis of PRO questionnaires in clinical research. All these principles have already been implemented by outcomes researchers such as Mapi Values. With this document, clinical researchers now have a structured understanding of FDA strategies and standards for integrating PRO effectiveness endpoints in clinical trials, particularly to support future labeling claims.

The guidance describes how the FDA evaluates PRO instruments in the assessment of a product's claimed treatment benefits. The guidance emphasizes that assessment of treatment effectiveness, as determined by a PRO instrument, includes an assessment of the ability of the PRO instrument to measure the claimed benefit. Sufficient evidence and controls are recommended and explicitly listed in the document. Effectiveness claims using a PRO instrument are also specific to the intended population and to the characteristics of the condition or disease. It is recommended that broad claims related to improvements in a patient's ability to function or psychological state include evidence of improvements in PRO domains constitutive of the claim.



Although this guidance document will no doubt improve the standards of the PRO field, and will be extremely useful for clinical researchers, several important issues merit further review.

- The standards suggested by the guidance for questionnaire development may be very difficult to achieve for every instrument, particularly those developed and validated in the nineties. These standards also seem above and beyond some of the standards required for clinical endpoints accepted by the FDA.
- The strict categorization of modified instruments as 'new' instruments. Minor modifications or translations of instruments need not be considered as completely new and therefore should not require complete re-validation.
- Currently the guidance suggests that determination of the MID is key in the analysis of an instrument's performance. Yet, practical and consistent methodologies for calculating the MID are not clarified or reviewed for their validity. The MID is not the only method for interpreting the meaningfulness of results. Moreover the definition proposed for the MID based on the "between" group difference, is different from the usual meaning of the term in the literature which relates to the minimum meaningful change within a group.

Finally, given the above mentioned concerns, we would strongly recommend the FDA add a statement to emphasize that the guidance reflects ideal requirements but evidence will be evaluated in light of methodological and practical issues.

We would also encourage the FDA to consider including a section on clinician-reported instruments that are well-established in clinical research and the standards for evaluating their appropriateness to support label claims.

By plainly stating our main opinions and concerns, we hope to improve endpoint discussions with FDA during the product development process and provide optimal information about the patient's perspective of treatment benefit at the time of product approval.

Thank you for your consideration. If you have any questions regarding our comments, please contact Patrick Marquis, MD, MBA, Executive Director, Mapi Values at info.usa@mapivalues.com

Sincerely,

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