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April 3, 2006

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

etrials, Inc.
4000 Aerial Center Parkway
Morrisville, NC 27560
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RE: Docket Number 2006D-0044

In response to the FDA's Guidance for Industry titled, "**Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims**" released February 2006, **etrials, Inc.**, an eClinical software and services company offering pharmaceutical, biotechnology and contract research organizations worldwide a suite of technology-based tools including electronic data capture, electronic patient diaries and interactive voice response, respectfully submits the following comments and suggestions.

Line: 43

Comment: How will reliability and validity be measured?

Line: 161

Comment: Does the FDA plan on formally evaluating the PRO instrument upon protocol development or upon completion of the study?

Line: 178-179

Comment: When does the FDA plan to conduct this evaluation: at protocol development or upon completion of the study?

Line: 180-181

Comment: Should this refer to the instrument developer or the license holder of the instrument?

Line: 190

Comment: If the process of creating the electronic representation of the instrument is interpreted to be just step "iv. Modify instrument" (mode of administration) then what supporting documentation is generally expected by the FDA? Who is responsible to provide this supporting documentation?

Line: 374-378

Comment: Are cognitive debriefing reports required for modifications that include transferring an instrument from paper to an electronic format? Who will be the responsible party to determine when these cognitive debriefing reports are required: the FDA, the developer or license holder? What if the instrument is in the public domain?

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- Line:** 396
Comment: We feel that it is important to identify what party/parties are accountable for the validation of PRO instruments and at what stage of approval this validation is to be presented. In addition, etrials would ask that the FDA clarify the process it plans to implement to review the choice of PRO instruments used for each study. For example, does the FDA plan on formally evaluating the PRO instrument upon protocol development or upon completion of the study?
- Line:** 581 and 635
Comment: etrials would suggest additional guidance on the validation of electronic PRO devices to include who is responsible for the validation.
- Line:** 582-583, 591
Comment: How will the "extent of additional validation" be guided? For example, what level of validation would the FDA expect for each of the six modification examples given in Section D?
- Line:** 831
Comment: Is the investigator considered to have 'direct control over the source data' if they have 24x7 access to all patient data residing on a remote server, provided this data is exactly what was input by the patient via an electronic diary device or computer? Also, it is the opinion of etrials that the investigator have sole control over who can modify the data and be able to determine when, why, what and by whom it was modified.
- Line:** 968
Comment: Who should be responsible for creating the rules to govern the statistical weight assigned to missing data?
- Line:** Other
Comment: It is also the stance of etrials that the information collected in relation to source document verification in clinical trials would be of interest to the PRO guidance. This is especially true as PRO captured without a paper source (such as using interactive voice response technology or electronic patient diaries) is subject to guidance in both areas.

etrials would like to thank the FDA for the release of this draft guidance and their continued dedication to support of safe and effective clinical research.

Sincerely,

Richard Piazza, PharmD.
Vice President, Product Strategy
etrials, Inc.