

Statistical Analysis Issues for PROs: Response

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FDA Guidance re: Statistical Issues

- important – “appropriate statistical methods” is one of the 7 requirements for an “adequate and well-controlled study”
- controversial - the area that generated the most comments
 - advancing science vs. “reification” of principles and/or methods on which the jury is still out?

Challenges :: Solutions

Convincing the FDA :: Ensure a Scientifically Rigorous Evidence Base/Analysis Plan

- getting FDA approval for a labelling claim :: engage FDA at the outset to discuss analysis plans (best predictor of first cycle approval)
- rigorous endpoint analysis :: have a SAP and stick to it
- asking the right question :: match the analysis to study objectives
 - same approach as for any other endpoint used in drug development

Challenges :: Solutions

Convincing the FDA :: Ensure a Scientifically Rigorous Evidence Base/Analysis Plan

- multiple endpoints :: gatekeeper/fix sequence methods, Bonferroni, Hochberg, O'Brien
- missing data (an outcome by itself) :: AVCF, LVCF, MVCF, ZVCF, OA
- analysis of longitudinal data :: ? over time from baseline, group differences at a point (or area under curve), differences in ? from baseline
 - sensitivity analyses!!

General Considerations: Statistics and Psychometrics

- get to know your statistician
- get psychometric expertise
- statistical-psychometric collaborations – educating each other
 - ? Cronbach's alpha, IRT, generalizability theory, conceptual models
 - ? splines, sensitivity/specificity, ROC curves
 - ? item weighting
 - ? scales of measurement (the interval-ordinal debate)