


White Paper

Preliminary summary of the
February 22, 2005 session: A
critique of long term trial design



*"If it ain't broke don't fix
it"*

Samuel L Goldwyn



Long term clinical trials

THEY ARE BROKE



*Concepts where there
were consensus*



One size does not fit all!

*Although key concepts may apply to
the development of long term trials,
different syndromes will require
different trial designs*



Who are the stakeholders?

- ✧ Patients
- ✧ Clinicians
- ✧ Academics
- ✧ Industry and the stock market
- ✧ Society
- ✧ Regulators and their governing agencies
- ✧ Journal Editors



Who will make up the sample?

- ❖ Do we take “all comers”?
- ❖ Are certain subsets of patients more informative?
- ❖ How do we keep these subjects in the trial over time?



Attrition

- ❖ Huge problem;
- ❖ Effects efficacy outcomes
- ❖ Safety outcomes
- ❖ We need to engage our subjects as active collaborators in the trial
- ❖ We need to consider why there is attrition. How different is it from “real world” practice?



Outcomes

- ✧ What are more accurate ways to measure the success of a trials?
 - ✧ Symptom measures as surrogates for syndromes
 - ✧ Global definitions of remission
 - ✧ Cumulative, summary measures of wellness
 - ✧ Biological and psychological surrogate markers



Placebo: a complex subject

- ❖ Placebo is not “no treatment”
- ❖ Is a placebo intervention always less effective than.....
- ❖ Placebo discontinuation designs may not be truly informative designs to assess the long term effects of treatment



The Problem of Heterogeneity

- ✧ Sample
- ✧ Measures
- ✧ Training
- ✧ Sites
- ✧ Trial designs
- ✧ Agencies



Regulatory Agencies

- ✧ Gorillas of varying sizes
- ✧ The tribes do not talk (a lot)
- ✧ Different philosophies about the goals of long term trials
- ✧ Regulatory agencies have had a disproportionate effect on long term trial design



Catch 22

- ✧ The regulatory agencies contend that they are guided by advances in the field and the consensus of leaders of field.
- ✧ The majority of large trials are industry sponsored and so they are designed to comply with the guidance from the agencies.



There is a consensus that

*We need to break this
detrimental cycle!*



Consider alternatives

- ❖ Other Designs: Add-on, Long-term extended placebo or active comparator trials
- ❖ Other statistical approaches
- ❖ Other types of outcomes



Should we consider

- ✧ The development of trial networks similar to cardiology or cancer?
- ✧ Should we consider developing larger simple trials as has been done with the statins?



*We need to think outside
the box*

*We need to develop common principles
to guide the development of new long
term trial designs*



We need to consider

- ❖ Different trial designs for different syndromes
- ❖ Data about the long term course of the syndrome to inform trial design
- ❖ The development of consistency of design and measures within syndromes
- ❖ Developing trials that assess efficacy and safety in an ecologically sound manner



OK, Where do we go from here?

List servers?

Working groups?

Publications?

Follow-up Meetings?