Reviewer's report

Title: A Perfect Correlate Does Not A Surrogate Make

Version: 1 Date: 12 August 2003

Reviewer: David DeMets

Reviewer's report:

General

Discretionary Revisions (which the author can choose to ignore)

1. This is a nice illustrative example for being cautious in using surrogate measures.
2. Fleming & DeMets indeed agree that a high correlation between a potential surrogate and a clinical outcome is not sufficient - rather the flaw is that a treatment may have other negative effects not captured by the potential surrogate. This is the point the authors make on page 7 (before the Conclusion section).
3. Because of issues raised in #2 (above), it is not clear that any meta-analysis could ever justify a surrogate.
4. Another point of extreme importance, even if a surrogate could be validated for one treatment, it does not validate the surrogate for another treatment of the same class (not all statistics are beneficial) and not for treatments in different classes.

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
NONE

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
NONE

Advice on publication: Accept after discretionary revisions

Level of interest: A paper of considerable merit and interest in its field

Quality of written English: Acceptable

Declaration of competing interests:
I consult with government, academia and industry, all of whom are affected by the surrogate issue in their design of clinical trials.