Comments of Monebo Technologies, Inc
on
"E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs"

Docket Nos. 2004D-0377

Summary

The automatic analysis of ECG strips developed as a result of thorough clinical trials, with high accuracy and precision, is realistic and achievable. Combining this capability with continuous ambulatory monitoring will significantly improve the consistency and accuracy of QT/QT_c prolongation data.

General

The current draft (Draft 4) contains several items of significant interest to Monebo Technologies. In particular these are:

- The use of automated techniques for analysis
- The use of ambulatory monitoring

As will become apparent, increased utilization of the first, provides a pathway to increased utilization of the second which may improve the consistency and accuracy of the results.

Draft 4 considers the use of automated techniques for measurement and analysis of the QT interval given that certain accuracies can be measured. It appears from the draft that 5 millisecond accuracy is contemplated as a minimum requirement for automated analysis. In our opinion this level of accuracy is achievable on a consistent basis.

We would like to comment on the measurement accuracy related to the threshold mean change of around 5 ms (the last paragraph on page 6 of Draft 4) and the upper limit of the confidence interval 8.0 ms (the first paragraph on page 7).

It is difficult to maintain the 5 ms threshold on a large volume of ECGs using manual measurements because the end of T wave is often ill defined. Advances in signal processing techniques open an opportunity for automated QT measurement providing overall more consistent and accurate results related to the 5 ms threshold for a **large volume** of data points.

In many circles, the "gold standard" for ECG analysis is that conducted by humans. However, in general, machines do repetitive tasks with greater accuracy and significantly faster than humans. The problem in this case is the differing morphology of the

waveforms. In fact, advances in adaptive filter design and signal analysis are overcoming that barrier.

The concept of continuous ambulatory monitoring opens a window into greater understanding. In normal practice, a 10 second ECG strip is taken at 15 minute intervals. In a 24 hour period, this results in 96 strips, or approximately 960 data points, assuming a "normal" heart rate. If continuous monitoring were utilized, that same time period could conceivably result in approximately 86,400 data points.

The resulting data set exceeds the ability of consistent human analysis. But, using fully automated techniques the analysis is trivial and can be obtained efficiently and economically.

Further development and implementation of automated methods depends on commonly accepted criteria of validation and verification of such techniques. These criteria may be a manual annotated database similar to databases developed by AHA, MIT, and ESC for evaluation of ECG analysis and interpretation algorithms. The database should contain short and long ECG strips, fiducial marks, and manually verified QT measurement values.

However, until such validation and verification methods are available, the FDA should encourage the use of fully automated analysis techniques with careful consideration of the rationale and data characterization.

Monebo Technologies, Inc is an Austin, Texas development stage company that develops technology which monitors, assesses, and predicts heart electrical activity. Monebo is a member of the Austin Technology Incubator, a part of the IC^2 Institute at the University of Texas in Austin.

Contact Information:

Dale Misczynski
President and CEO
Monebo Technologies, Inc
1800 Barton Creek Blvd
Austin, Texas 78735-1606
Telephone: 512.732.0235
Facsimile: 512.732.0285
Email: dale.misczynski@monebo.com
Website: www.monebo.com