



Thorough QT Studies

b i o m e d i c a l s y s t e m s

Cardiac Safety Concerns In Drug Development

Over the past several years cardiac safety concerns have been the primary reason for the FDA to call for the withdrawal of a drug from the market, limit a drug's indication, or deny pharmaceutical companies the approval to market a drug. One of the major issues of concern is a drug induced delay in cardiac repolarization. For that reason, the FDA and other international regulatory organizations have requested pharmaceutical companies and biotechnology companies to conduct more intensive testing for cardiac safety related issues with protocol designs now known as Thorough QT studies.

What Are Thorough QT Studies?

FDA guidelines indicate the need for additional cardiac safety testing when a positive signal for QT prolongation is found in pre-clinical development of a compound. Thorough QT Studies use precise methodologies to detect and evaluate the QT interval prolongation of small magnitudes to better assure a new drug's cardiac safety.

Thorough QT Studies Requirements

Per the ICH E14 Document, a protocol for a Thorough QT Study recommends:



- Conducting the trial early in a drug's development, though not as the initial first-in-man study.
- Recruiting healthy volunteers.
- Acquiring ECGs that have:
 - Triplicate measurements
 - Time matched timepoints
 - Timepoints around the Cmax
- Using a Positive Control (a compound that has already been proven to prolong the QT interval but at clinically insignificant amounts) to establish assay sensitivity.

Global Capabilities

- Participating in trials in over 75 countries, 11,000 clinical sites
- Offices in North America, Europe & Asia
- Multilingual staff fluent in 20 languages to facilitate communication with sites
- Phase I through Phase IV studies
- Single Project Manager assigned per study
- Web-based Sponsor access to data and reports

TQT

Methods To Collect ECG Data

Device	Advantages	Challenges
	<ul style="list-style-type: none"> • Well characterized • Immediate feedback 	<ul style="list-style-type: none"> • Personnel intensive • Missed timepoints • Cost per ECG at CPU
	<ul style="list-style-type: none"> • Not personnel intensive • Minimize risk of missing timepoints • Ability to retrospectively review data 	<ul style="list-style-type: none"> • Susceptible to artifact • Different lead system • No immediate feedback • Still require safety ECGs

The two most common methods to collect cardiac safety data for TQT studies is with a standard 12-lead ECG machine or with a 12-lead digital Holter. Each system has advantages and challenges associated with acquisition. Study design should take into account both pieces of equipment prior to making a final decision.

Biomedical Systems offers sponsors equipment options for both formats. If you require a standard 12-lead ECG machine, Biomedical Systems has the MAC 1200, ELI 150, ELI 250 and our proprietary BEAMS PC System. For 12-lead digital Holter, both the Mortara H12+ and the BMS1200 are available for use.

For more information or to schedule a presentation, please contact a Biomedical Systems' Representative at 800-877-6334 in North America or 32-2-661-20-70 in Europe. Or access our website at www.biomedsys.com.



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