Six steps to the definitive QTc study

1) Concept and QTc Study Design

Expert advice on study concept and protocol design, is available to clients.

Our unique collaboration with the renowned Department of Cardiac and Vascular Sciences at St George's University of London, provides access to world leading Cardiologist Professor AJ Camm and his colleagues for consultation on your QTc study.

2) Clinical Conduct

Richmond Pharmacology has extensive experience in the clinical conduct of highly intensive thorough QTc studies. All study procedures including ECG recordings are performed to very accurate and precise ('to-the-minute') study schedules by trained and highly experienced staff. Due to the complexity of such trials, we have a dedicated team of nurses, doctors and technicians specialised in the conduct of thorough QTc studies within an efficient and safe hospital setting.

Prior to recording the nurses and technicians will ensure that all pre-requisites for high a quality resting ECG are satisfied. Our skilled staff will make sure that the same standards in skin preparation, lead placement and subject position are consistently adhered to throughout.

The recordings are taken and immediately transmitted to the MUSE server within a busy but quiet and orderly environment with no distractions to the study subjects. As they arrive at the MUSE database, the recorded ECGs are reviewed by a research physician on an ongoing basis and signed off electronically.

The review performed by the research physician includes a cardiac safety review and checking the trace quality. Signed-off ECGs will be printed from the MUSE and filed in the subject's Case Report Form (CRF).

3) ECG Data Management

Prior to commencement of the study, all ECG machines used for that particular project are configured to ensure that every ECG data file contains the exact and correct information in a standardised format as per client and protocol requirements. The configruation of an ECG machine is validated which includes acquisition and transfer of test ECGs from the machine's simulator. The entire configuration and validation process is fully documented.

During the study, Richmond Pharmacology's ECG data management team tracks all the acquired ECGs and applies stringent quality control checks to ensure that all planned and unscheduled ECGs are accounted for, and that the time points, subjects' identifiers and demographic data are properly recorded. This process is done on an ongoing basis during the clincal conduct of the study which allows for the clean ECG data to be available for the analysis almost immediately as the last subject completes the trial.

After the study is completed, our experienced data managers can provide the collected ECG files in any format the clients require including .ecg, XML, SAS or ASCII format.

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4) QTc Measurement and Analysis

As standard, all ECGs are recorded in triplicate at each protocol time point from which the best quality recording is selected by a cardiologist for analysis.

In partnership with Richmond Pharmacology St George's University of London offers client's two main approaches in QT interval measurement and analysis:

1) Manual over-read by cardiologists
2) Semi-automated method with cardiologist verification

1) Manual over-read

In full manual over-read the QT interval is measured by a highly trained and experienced cardiologist using electronic callipers (MUSE CV® Interval Editor, GE Marquette Medical Systems) with sufficient magnification allowing the measurement precision equal to the storage frequency of 500 MHz, i.e. ±1 ms.

Details of the analysis can be discussed and agreed with our clients at the study design stage as a matter of routine.

In every ECG a minimum of five consecutive QRS-T complexes that are least noise polluted are selected. For each of them the QT interval is measured in all 12 leads. The median QT interval of the 12 leads is determined for each beat and then the medians are averaged across the selected beats. The resultant QT interval is taken as representative.

2) Semi-automated

Alternatively, if this better suits client's needs we also offer regulatory compliant semi-automated QT interval measurements. In this method, interval markers derived by MUSE CV® Interval Editor are assessed for accuracy by an experienced and fully trained cardiologist. The degree of cardiologist input may vary to meet the client needs.

In line with the current regulatory requirements and at least every six months, all cardiologists at St George's University of London undertake intra- and inter-reader variability tests under blinded conditions to ensure that our measurements are as accurate and reproducible as possible. Furthermore, systematic in–process QC checks are performed by a senior cardiologist during a specific study analysis. All QC checks and any corrective actions are reconciled and fully documented.

The measured and verified QT intervals are corrected for heart rate using conventional population-derived formulae (e.g. Bazett, Fridericia) or an individually derived formula – or both. The QT/QTc interval data are then subjected to a statistical analysis in accordance with the current regulatory guidelines which also includes input and interpretation of the results from experienced cardiological scientists.

5) Report

We will present your data and results of the QTc analysis effectively and in a timely manner both as a 'stand-alone' report and incorporated in the integrated study report, as required. These reports are written by our professional, full time, in-house medical writers with senior cardiologist review and input. Your final, summarised data will be presented on paper as well as electronically.

6) Regulatory Acceptance

We undertake all regulatory matters on behalf of our clients depending on your regulatory requirements. We write and present the ethics submission and CTA application to gain regulatory approval I for clinical studies from the relevant Ethics Committee and the MHRA. We attend ethics meetings and present all protocols to facilitate the efficient progression of your application through the regulatory progress.