# Analyzing Thorough QT Study 1 & 2 in the Telemetric and Holter ECG Warehouse (THEW) using Hannover ECG System: A Validation Study

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Following the ICH E14 guideline, the measurement of QT/QTc prolongation has become the standard surrogate biomarker for cardiac drug safety evaluation. The focus is on reliability and precision of the evaluation, as the low threshold level of just about five to ten milliseconds may decide on the faith of a drug development. Attempts to automate ECG evaluation meet concerns that algorithms might fail under challenging conditions. Therefore, validation of automated ECG algorithms is needed to build trust in their reliability and precision. Hannover ECG System (HES) is one of the well-renowned and well-reputed ECG analysis and interpretation programs worldwide. In this work we demonstrate the ability of HES to assess drug effects by detecting QT/QTc prolongation as mentioned, using THEW database studies Thorough QT (TQT) 1 and 2. For the assessment of drug effect, calculation of double delta parameters was performed for RR, QT/QTc changes from the baseline in both studies. Baseline was considered from start of recording to the time of drug administration and was characterized by the median of parameters. The single delta differences are calculated by baseline subtraction from all time segments. Furthermore, double delta difference was built by subtracting placebo single delta from Moxifloxacin single delta for each study subject. Finally, double delta differences were characterized by mean, median, SEM and 95% CI per hour. For brevity only results from TQT1 and the maximum effects are reported here. Results: double delta difference means [ms] (SEM [ms]; maximum effect time[h]); QT: 12.0 (2.56; 3 to $<$4); QTcB: 14.0 (1.88; 2 to $<$3); QTcF: 12.9 (1.68; 3 to $<$4) and QTcI: 12.3 (1.88; 3 to $<$4). Similar results have been reported from comparable studies. We conclude that HES algorithm is capable to evaluate TQT studies according to the requirements specified by ICH E14 guideline.