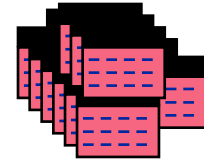


ECG QT WAREHOUSE

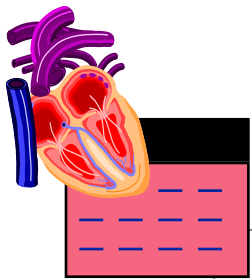


STRUCTURE, ACQUISITION, VETTING, AND USE

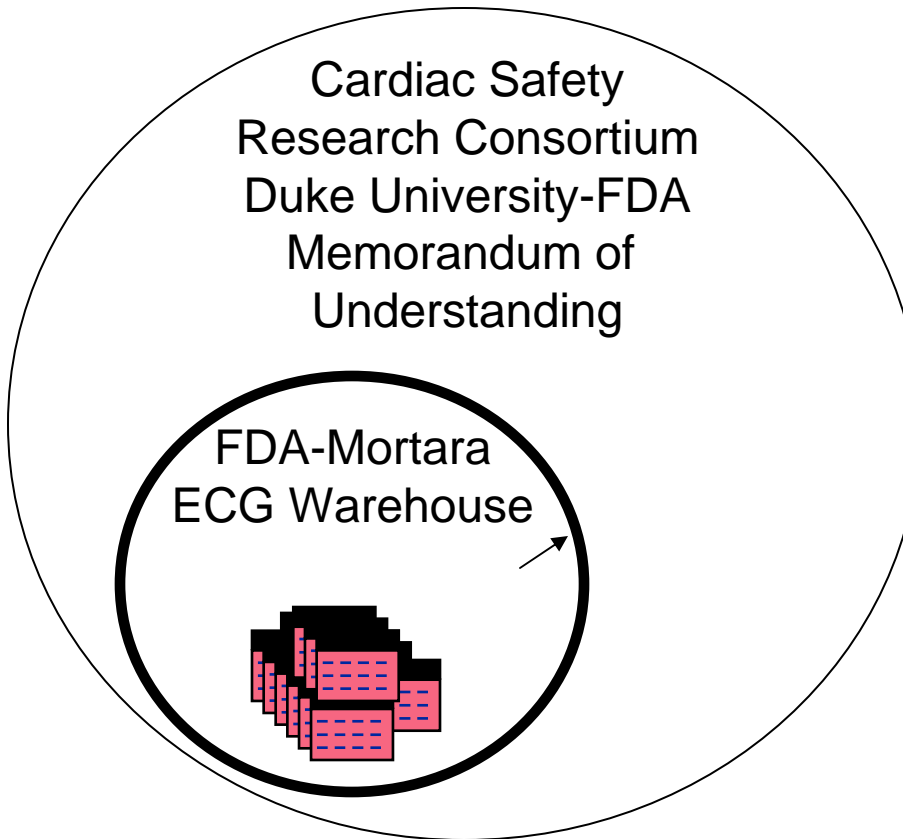
Paul Kligfield, MD
CSRC Bethesda,
October 29-30, 2009

Cindy Green, PhD
Norman Stockbridge, MD
Mike Li, MS
Justin Mortara, PhD

CSRC-SOC CHALLENGES



Critical Path Initiative

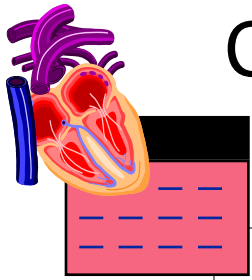


Project Management

Intellectual Property

Ownership of ECG data within the ECG warehouse resides with the sponsors

CSRC ALGORITHM DATASET PROCESS



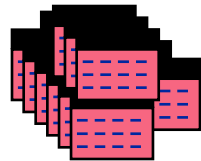
Critical Path Initiative

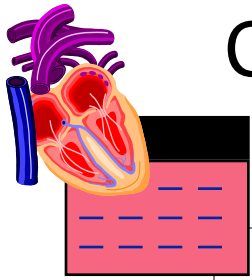


Cardiac Safety
Research Consortium
Duke University-FDA
Memorandum of
Understanding

FDA-Mortara
ECG Warehouse
(Sponsor Release)

Algorithm
datasets



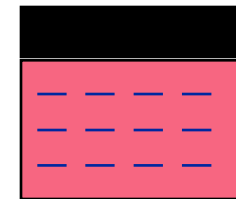
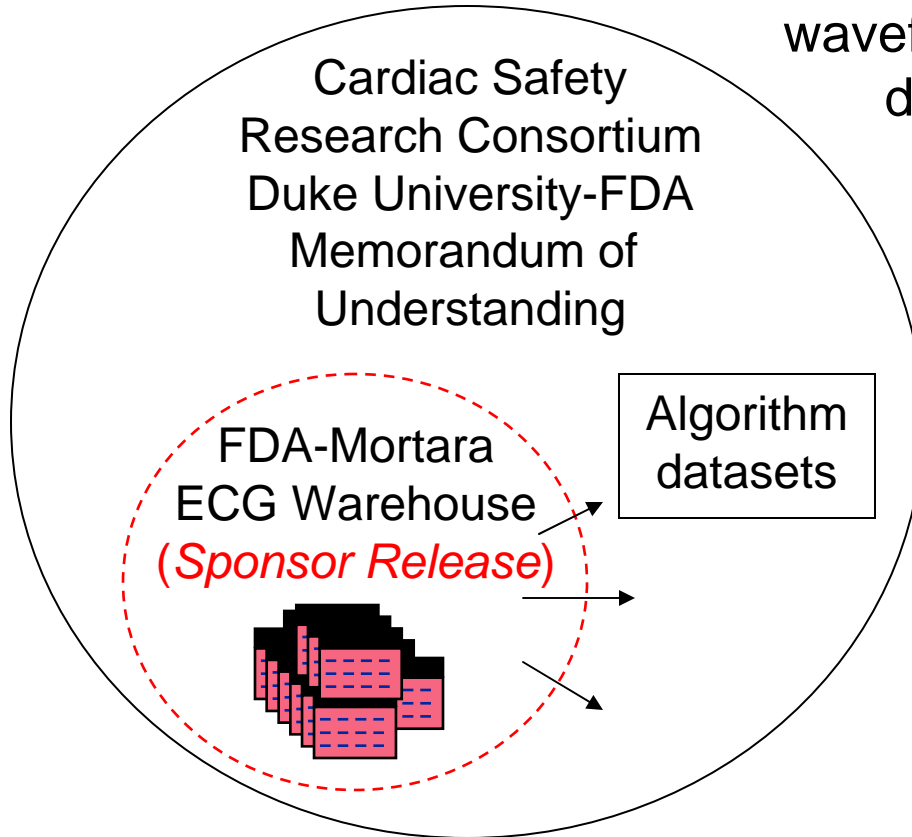


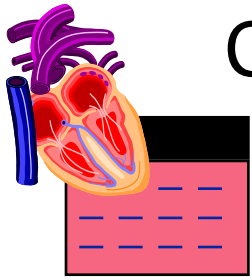
CSRC ALGORITHM DATASET PROCESS

Critical Path Initiative

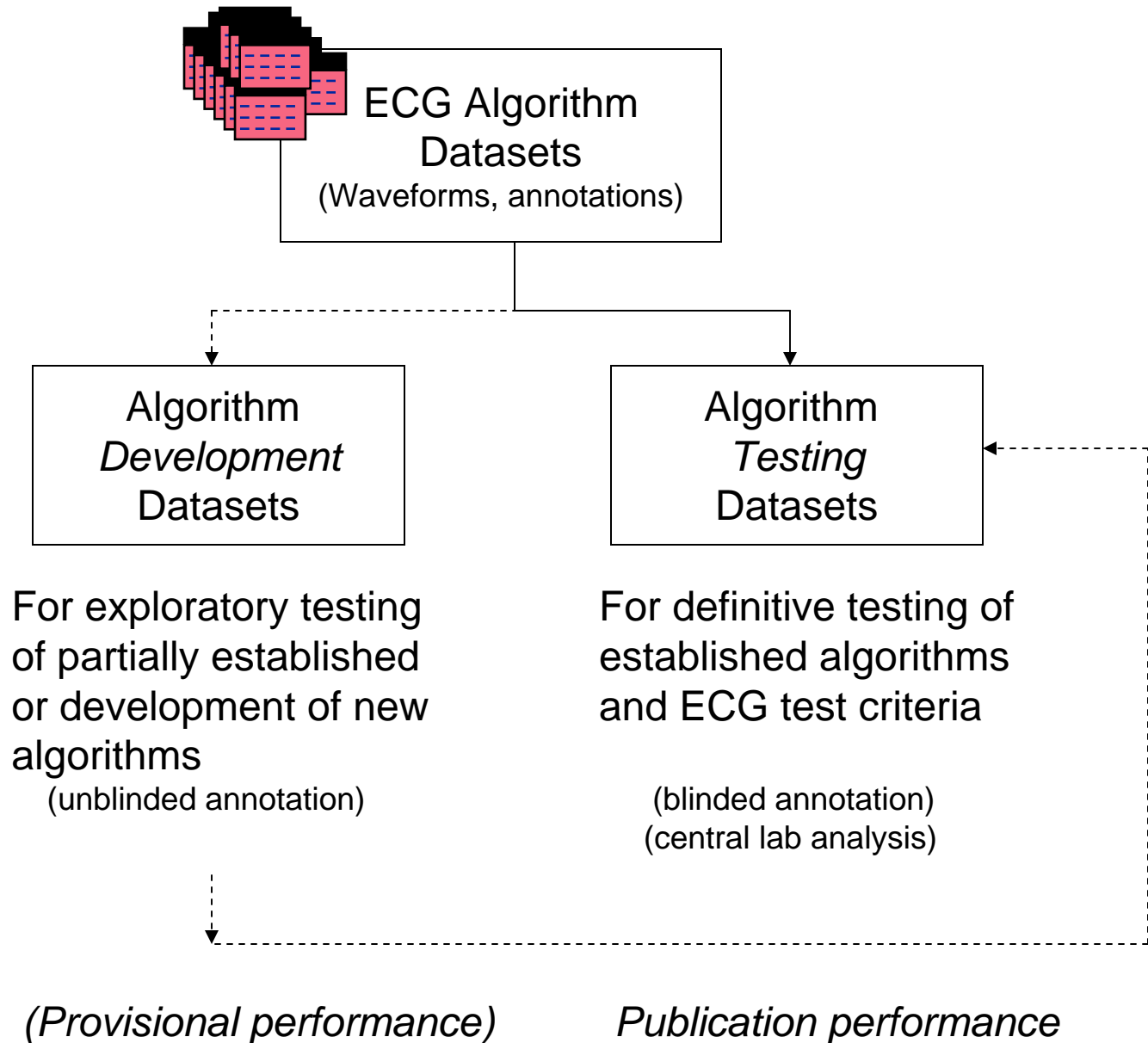


Sponsors: Release of waveforms and clinical data assembly are critical and rate-limiting steps

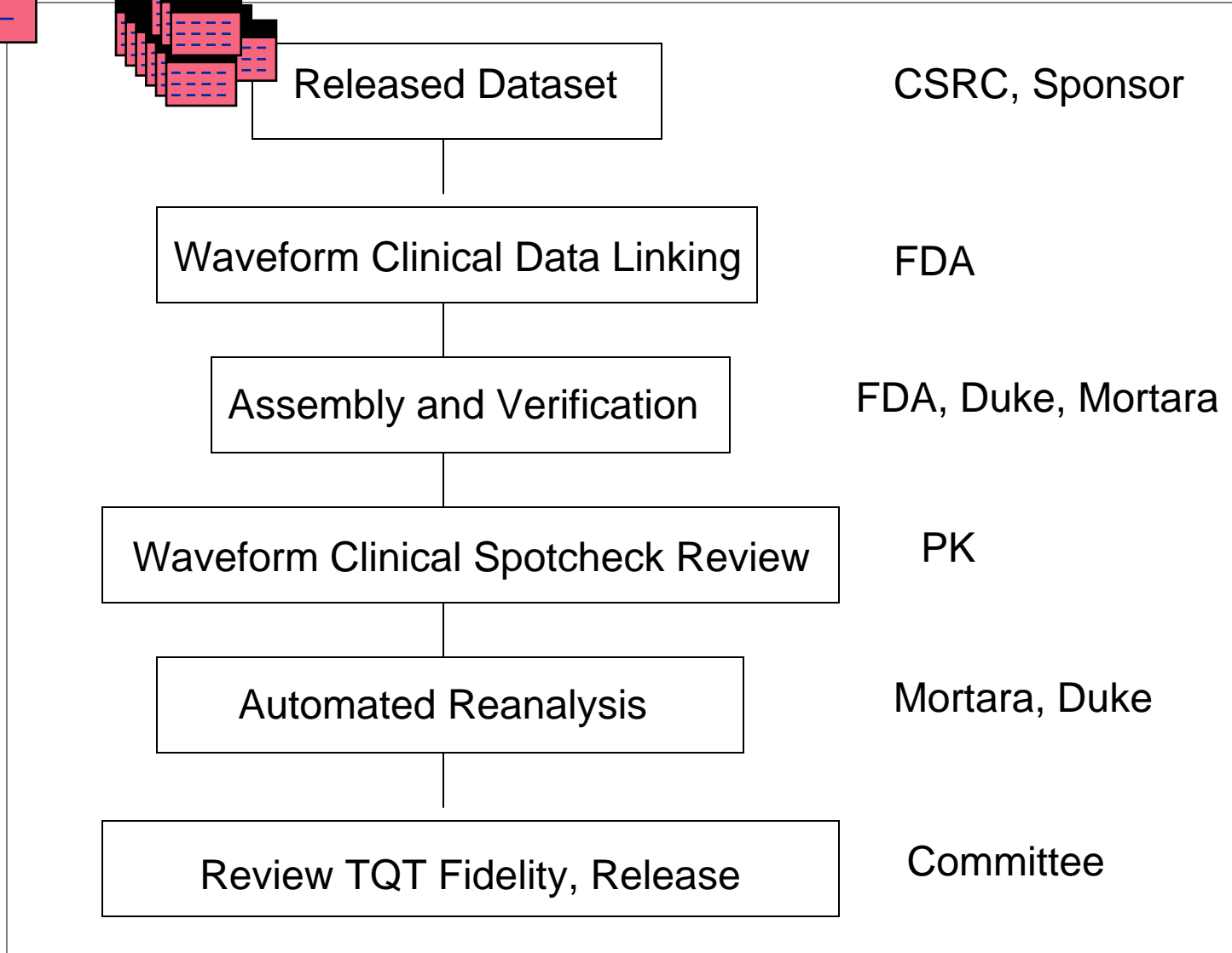
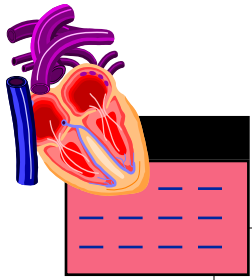


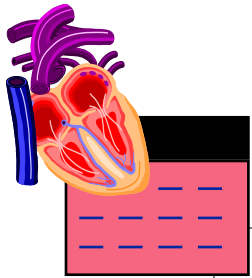


CSRC ALGORITHM DATASET PROCESS



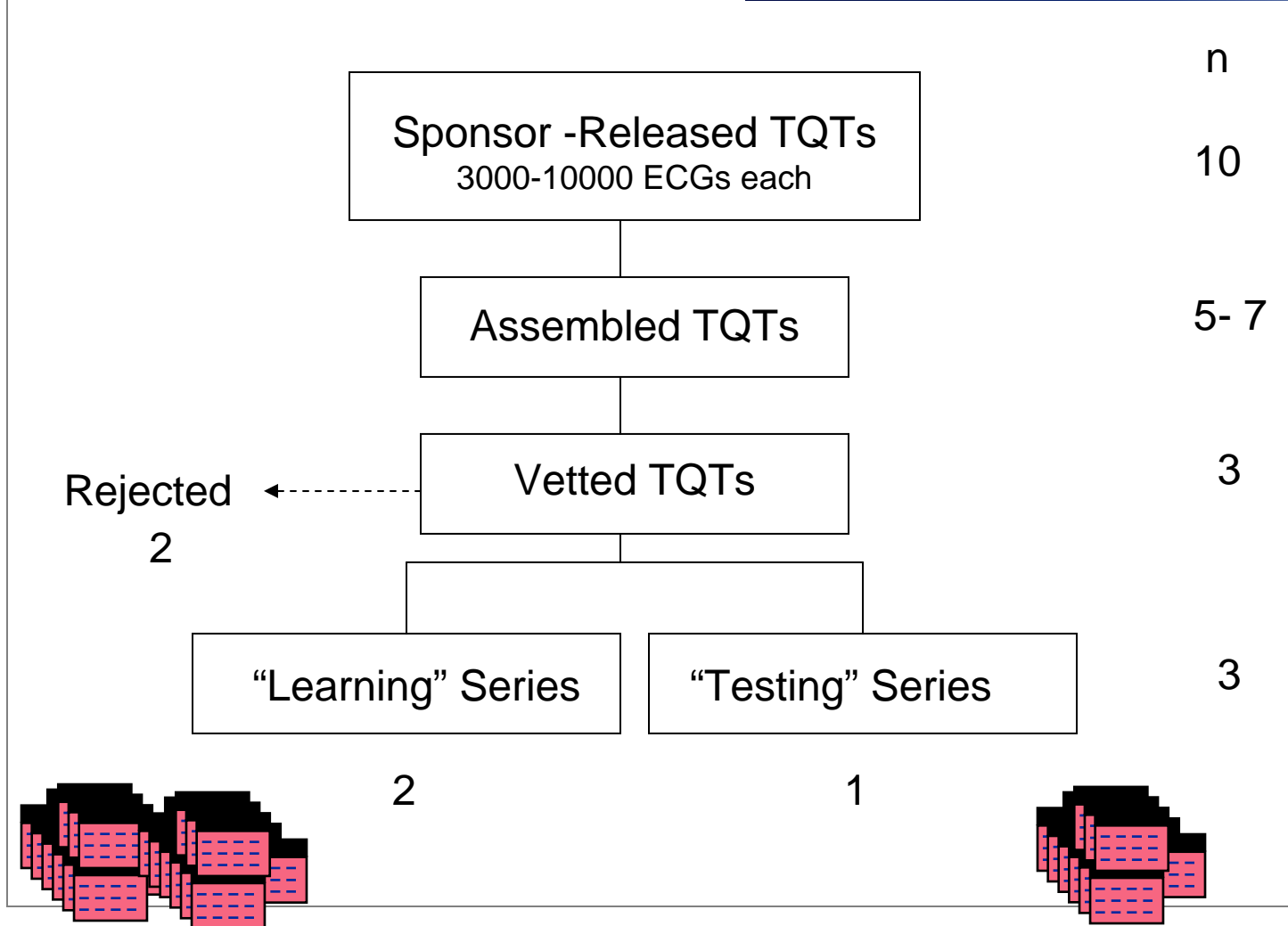
CSRC ALGORITHM VETTING PROCESS



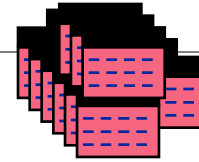
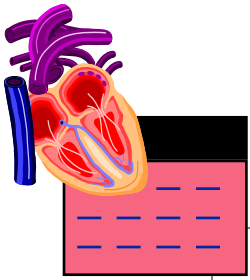


CSRC ALGORITHM DATASETS

10/29/09



AUTOMATED REANALYSIS



Example: Released TQT Study 4

Moxifloxacin/placebo arms of study

10,379 12-lead ECGs in 73 subjects

1000 samples/sec

0.05-300 Hz bandwidth

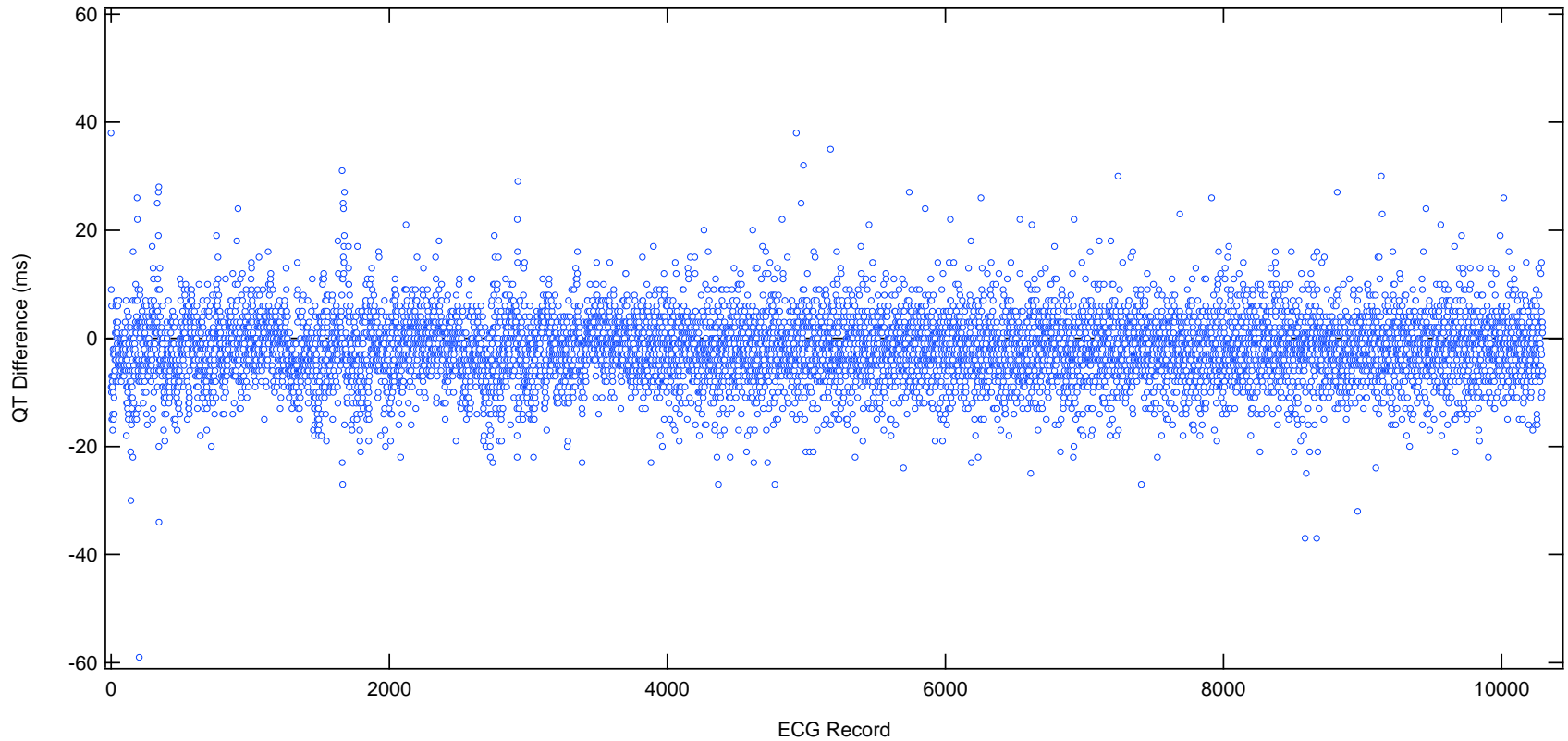
Single lead raw data analyzed by core lab
(lead II)

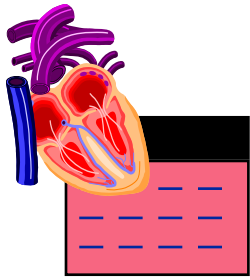
Automated QT reanalysis

*(Reanalysis potential and value relates
to entire waveform data, not just QT)*

QT DIFFERENCES: AUTOMATED REANALYSIS vs SPONSOR CORE LAB MEASUREMENTS

CSRC Waveform Learning Set #1

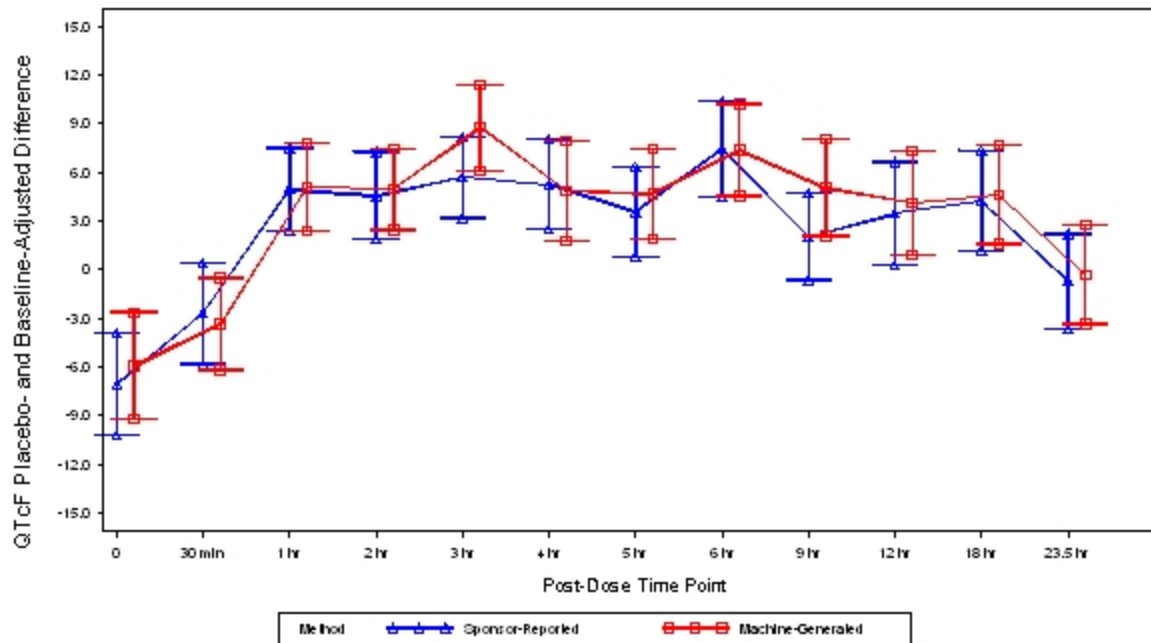


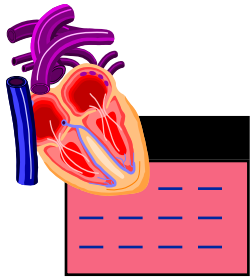


AUTOMATED REANALYSIS

Sample automated reanalysis (in red) compared with sponsor submission (in blue) of Dataset 4: Moxifloxacin vs Placebo double delta (Learning set #1, released)

Figure 1.1
QToF Placebo- and Baseline-Adjusted 90% Confidence Intervals by Time Point





CSRC ALGORITHM DATASET USE

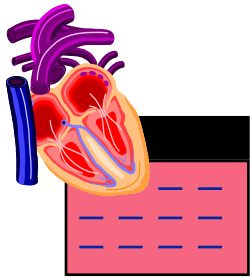
Rules of Engagement

- Project approval by SOC, endorsed by CSRC EC
- Specification of either “learning” or “testing” dataset project
- Agreement to protect dataset from unauthorized use
- Agreement not to publish or present “learning” dataset performance for newly developed algorithm as established “test” performance
- Encouragement, but not requirement, to evaluate newly developed algorithm in subsequent blinded “testing” dataset

ECG Warehouse partitioning

ECG Warehouse access

Publication/dissemination of algorithm performance



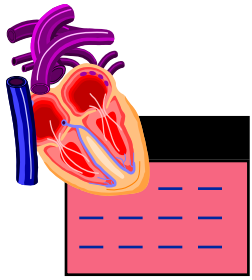
CSRC ALGORITHM DATASET USE

Rules of Engagement

ECG Warehouse partitioning:

CSRC will maintain a partition between publicly released waveform and descriptor data (“unblinded” data) and waveforms released without descriptor data (“blinded” data). Unblinded data may be used for sponsors to train/develop algorithms, or to use for other preliminary testing steps and strategies. All reporting of outputs using unblinded data will be clearly identified as unblinded “training” results.

Algorithm performance will only be reported from assessments of unique, independent blinded testing dataset cohorts scored by the CSRC.



CSRC ALGORITHM DATASET USE

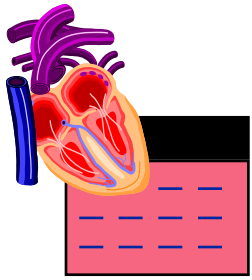
Rules of Engagement

ECG Warehouse access:

ECG waveforms from the warehouse will be made available for sponsors of SOC approved projects. Waveform release has been designed so that algorithm developers can execute their own algorithms without needing to release proprietary measurement strategies.

For blinded test dataset performance evaluation, such as moxifloxacin signal detection, algorithm measurements from blinded data ECG waveforms will be submitted to the CSRC statistics group where they will be matched to descriptors including treatment assignments (placebo vs. moxifloxacin), and scores will be returned to sponsors. The statistical analyses plan will be submitted to the CSRC before release of the blinded data sets.

The CSRC expects to charge a fee for use of the blinded data set to cover the CSRC costs associated with the maintenance of the ECG dataset and the algorithm scoring of the blinded data set.



CSRC ALGORITHM DATASET USE

Rules of Engagement

Publication/dissemination of algorithm performance:

Publication or dissemination of algorithm performance will be expected from those sponsors using the blinded data set(s). Commitments to public domain information release at the time of SOC approval will be expected to be delivered by sponsors in the form of such reports in the public domain.

Sponsors will agree that any publication/dissemination of results from unblinded study cohorts will clearly indicate that performance results represent only unblinded training data.

For any questions, please contact cardiacsafety@mc.duke.edu