

**Title:**

Advanced Cardiac Safety: De-Risking Drug Candidates in Early Clinical Development and Preventing Late Stage Failures

**Abstract:**

Approximately 10% of late stage compounds (Phase IIb – Phase III) experience failure in the FDA-mandated TQT studies to conclusively characterize drug's effect on cardiac repolarization. These failures lead to delays in development programs, mounting costs, loss of revenue and in some cases may lead to termination of the drug in development. This problem stems from very well known limitations of the conventional cardiac safety approaches, i.e., high rate of false-positives and negatives and very high cost of the precise measurements with conventional analysis techniques. A significant opportunity exists to cost-effectively and significantly reduce late stage cardiac safety risks in early clinical development. This opportunity is often overlooked in development programs, causing downstream issues ranging from false positives to un-interpretable QT study results. By applying advanced, validated and FDA-accepted ECG analyses, a number of critical cardiac safety questions can be answered in small studies (FIH/SAD/MAD) and help drug developers avoid costly downstream problems. By applying advanced techniques and proactive cardiac safety assessment strategies, drug developers can prevent the catastrophic late stage failures, reduce the total cost of the cardiac safety assessment programs and in some cases, avoid TQT studies in the late stages of development.