

* Automated detection of drug-induced delayed ventricular repolarization (QT-prolongation):

- assay based on primary cardiac myocytes
- parallel recording on 96 channels
- high throughput
- 21 CFR Part 11 software compliance

* QT-Screen supervises your experiment:

- online signal quality check
- automated analysis
- compound saving strategy
- automated generation of concentration series

* Direct data export to database:

- QT-interval duration
- multiparameter analysis
- sample traces
- arrhythmogenic activity
- concentration-response curve
- environmental parameters

* Throughput:

hands-on time per run	5 min
time per run	45 min
compounds per day	100
data points per day	up to 8.000
cost per datapoint	0,16 USD

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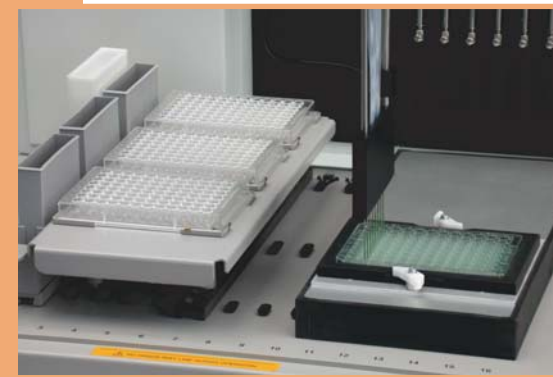
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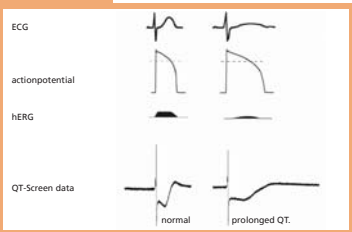
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QT-Screen*

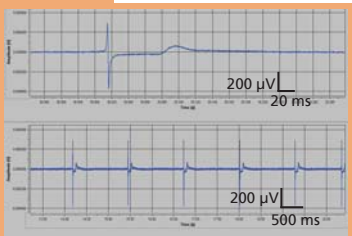
Automated Cardiac Electrophysiology
for
Drug Profiling and Safety Screening



Field potentials are measured by extracellular microelectrodes. This allows the recording of the composite cardiac action potential, because all components of the action potential are reflected in the field potential. The interpretation is very similar to the electrocardiogram. Whereas the QRS complex in the ECG reflects ventricular depolarization, the opening of sodium channels in ventricular cardiomyocytes is revealed as a rapid upstroke. The repolarization is visible as a "T-Wave" in both cases.



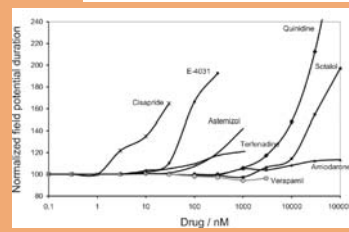
In the figure, data recorded from ECG, intracellular recording of action potential, and voltage-clamp assay of hERG channels, under control conditions and conditions inducing prolonged QT, are aligned with data recorded from QT-Screen under similar conditions.



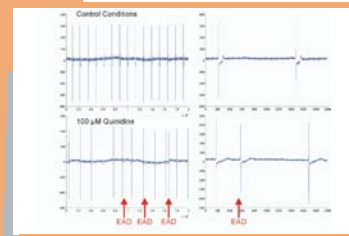
In the upper panel the signal display window of the QT-Screen software shows the shape of a single cardiac action potential (recorded as field potential). In the lower panel the same channel is displayed on a compressed timescale. Each recorded channel can be displayed in this window with a simple mouseclick. The scaling of both axes can be adjusted. The signals displayed show the typical time course of ECG recordings: rapid depolarisation, sustained plateau and a repolarisation wave.

A variety of drugs known to prolong the QT interval in the ECG, along with appropriate negative controls, have been tested with the QT-Screen. The results are in agreement with results obtained by classical repolarization assays or patch-clamp studies. All known positives also yield positive results in the QT-Screen; all negative controls yield negative results. Tested drugs include:

- Cisapride
- E-4031
- Sotalol
- Quinidine
- Astemizol
- Terfenadine
- Amiodarone
- Verapamil



For all drugs tested, the effects are in agreement with the published data recorded with various standard assay systems. Verapamil is particularly interesting, because it yields a false positive in assays based on hERG-transfected cells. Because the QT-Screen is based on cardiac myocytes, Verapamil yields no effect.



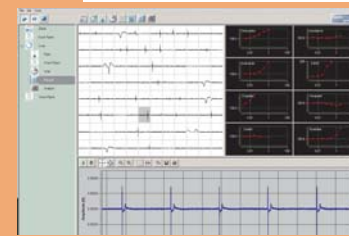
Unlike assays based on transfected cells, the QT-Screen, employing cardiac myocytes, directly measures the arrhythmogenic activity of tested compounds. In the lower figure, early afterdepolarization evoked action potentials appear as a result of the Quinidine-induced AP prolongation. The upper panel displays similar recordings under control conditions; the right panels display the data on an expanded time scale.



QT-Screen is the world's first fully automated system for high-throughput QT prolongation screening and combines the advantages of superior extracellular recording and reliable data acquisition technology with standardized-liquid handler technology. Concentration series are generated automatically from 96 well compound plates. Starting with the lowest concentration, 8 to 10 concentrations of 8 different compounds are tested in parallel and in replicates of 12.



Cardiac myocytes are easily plated directly into disposable 96 well QT-plates. After 2-3 days in culture, the cell cultures begin to beat spontaneously. Each well includes a recording, reference, and stimulating electrode. All materials are tested for excellent biocompatibility. The low cost of consumables insures low operating costs.



With the user-friendly, flexible graphical user interface, designing recording sequences, and implementing custom quality checks and compound saving strategies are easy. Fluid delivery, real-time monitoring, and online dose response analysis are all computer-controlled. The wide range of analytical tools available include algorithms for calculating corrected QT intervals and identifying tachycardia and bradycardia. Results are entered automatically into a standard database.