



Preclinical Technologies

FACTSHEET



Assessment of Potential to Prolong QT Interval

The ICH S7B guidelines highlight the importance of understanding the consequences for development of a drug candidate with a potential to prolong QT interval. Cardiovascular assessment *in vivo* along with *in vitro* assessment at the HERG channel is recommended. If results from these two tests are equivocal then further investigation in other models are advised. Aptuit provide a fully comprehensive package of studies to cover ICH S7B regulatory requirements, which can be monitored for GLP compliance.

Cloned Human Potassium Channel

Whole-cell patch-clamp measurement of HERG channel current recorded from HEK 293 cells. Studies on cloned cardiac sodium channels are also available.

ECG by Telemetry

Radio-telemetry devices are used for continuous measurement of blood pressure and lead II ECG in conscious guinea-pigs, dogs or primates. In addition to analysis of haemodynamic and ECG variables at selected time points, recordings can be scanned for incidences of arrhythmias.

Cardiac Action Potential *In Vitro*

Intracellular recordings from canine or rabbit cardiac Purkinje fibers or guinea-pig papillary muscles. Measurement of range of action potential parameters to detect cardiac ion channel interactions. Examination of multiple frequencies to determine use-dependent effects.

ECG and MAPD in the Isolated Heart

Langendorff-perfused isolated hearts (rabbit or guinea-pig) are used to investigate the effects of test substances on QT interval, QRS complex, monophasic action potential duration (MAPD) and coronary perfusion. Recordings are scanned for arrhythmias. Cardiac contractility may also be measured.

ECG and MAPD in Anaesthetized Guinea-Pigs

This model allows MAPD and ECG to be recorded from the left ventricle using a suction electrode during atrial pacing in pentobarbitone-anaesthetized, vagotomized and β -adrenoreceptor blocked male guinea-pigs. The atrioventricular conduction time is also recorded.

QT Intervals in Anaesthetized Dogs

Haemodynamics (including LV pressures, blood flow and multi-lead ECG) in closed chest, *a*-chloralose anaesthetized and ventilated dogs. QT interval analysis performed during sinus rhythm and during intraluminal right atrial pacing. Studies also can be performed in primates.

Support Services

- Analytical method transfer/validation.
- Measurement of test substance levels in perfusate and recording chamber for *in vitro* studies.
- Assessment of plasma levels for *in vivo* studies.

Additional Aptuit Capabilities

Aptuit offers a comprehensive suite of drug development services that range from candidate selection through to market, including consultancy services, API development and manufacture, preclinical and clinical technologies, pharmaceutical services, large and small scale manufacturing, IVRS, and clinical packaging and logistics, across a wide range of compounds, dosage forms and delivery systems.

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Engineering a better drug development process.