Model Name
Cardiovascular, QTc Interval

Item Number
516350

Introduction
The hERG potassium channel is a major molecular component of the delayed rectifier current (IKr) underlying cardiac repolarization. Decreased hERG activity prolongs the QT interval and can lead to the potentially lethal ventricular arrhythmia Torsades de pointes. As the QT interval has an inverse relationship to heart rate, the measured QT intervals are generally corrected for heart rate (QTc) in order to determine whether they are prolonged relative to baseline. Various correction formulae have been suggested, of which Bazett's and Fridericia's corrections are the most widely used. Because the best correction approach is a subject of controversy, uncorrected QT and RR interval data, heart rate data, as well as QTc are reported.

Procedure Summary
Groups of 5 male guinea pigs weighing 350 - 400 gm are employed. The animals are anesthetized with urethane (1500 mg/kg, i. v. bolus injection in a volume of 5 ml/kg) and allowed to breathe spontaneously. Lead II ECG is obtained with subdermal needle electrodes and ECG signal conditioner (20-4615-64, Gould). Heart rate (HR) is measured with a pulse rate tachometer (13-G4615-66, Gould). The carotid artery is cannulated with a catheter connected to a pressure transducer (20-4615-50, Gould) and a processor (20-4615-526611, Gould) for recording arterial blood pressure (BP). The parameters evaluated (QT Interval, QTc, HR, BP) are recorded and analyzed by a data acquisition and analysis system (PO-NE-MA, U.S.A.). QTc values are calculated according to Bazett's and Fridericia's equations. Test compound is dissolved in 0.9% NaCl and administered intravenously (1 ml/kg at a rate of 1ml/min). All recorded parameters are monitored for 20 minutes: time 0 (immediately before injection) as well as 1, 3, 5, 10 and 20 minutes following each intravenous injection. QTc prolongation serves as a marker for potential cardiac arrhythmias. Changes in QTc at each recorded time interval relative to 0 time is calculated. A ≥5% lengthening of the QTc interval in any of the test animals is considered a significant response.

Suggested Testing
• n=5/group (study design dependent)
• Cardiotoxic effects assessed at an initial dose of 10 mg/kg
• Dosing volume at 10 mL/kg

Turnaround Time(s)
• Acute Assay: In-Life completion in 2-4 weeks from sample receipt
• For Subacute Assays: 6 weeks to 3 months

Literature

Related Assay(s)  (Item # - Assay Name - Species)
265910* - Potassium Channel hERG, [3H]Dofetilide – Human
265900* - Potassium Channel hERG – Human
*provided by partner lab Eurofins Pharma Discovery Services

Modified Protocols
We will readily accommodate client-specified alterations.
Laboratory
These assays are performed at our AAALAC accredited laboratory in Taipei.

Animal Welfare
All aspects of this work is performed in general accordance with the Guide for the Care and Use of laboratory animals (National Academy Press, Washington, DC, 2011). The study protocol was approved by the Pharmacology Discovery Services IACUC and is performed with the oversight of veterinarians to assure the humane treatment of laboratory animals.

Reference Compound(s)
Erythromycin, Quinidine, Terfenadine, Verapamil, Dofetilide, * Sotalol, Astemizole, E-4031

Graph(s)

For current details about our Company address and contact information, please reference our website
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