

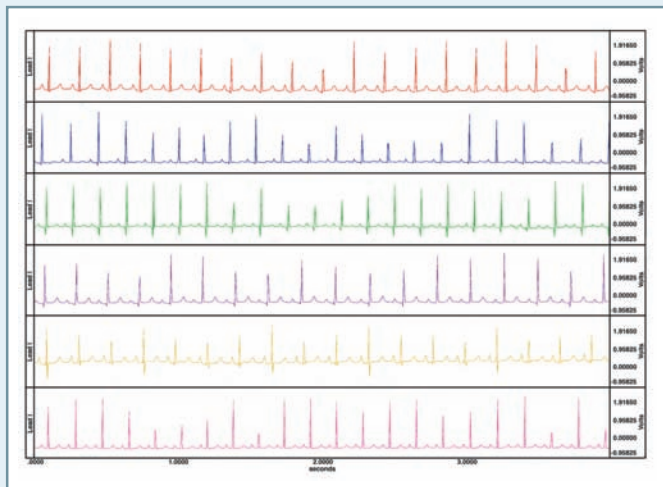
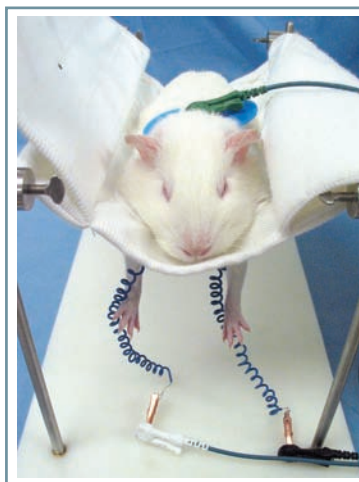
Conscious Preparations

Canine, Rabbit or Guinea Pig

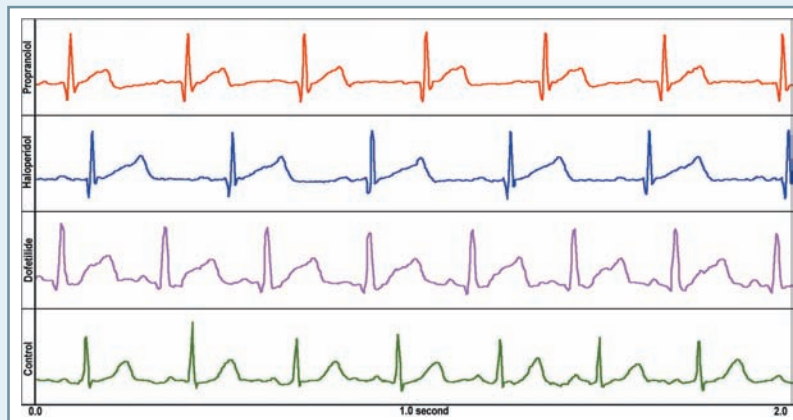
Conscious Preparations - Quality repeat sampling

- Intact preparation
- Integrity of autonomic nervous system and metabolism
- No obfuscation by anesthetics
- Measure vascular and cardiac parameters
- Evaluate baroreceptor function
- Rapid turn-around time
- Validated acquisition and analysis systems
- GLP compliant

Animals resting in a padded sling allow for collection of ECG, arterial pressure and baroreceptor response to escalating doses of test article, monitored continuously.

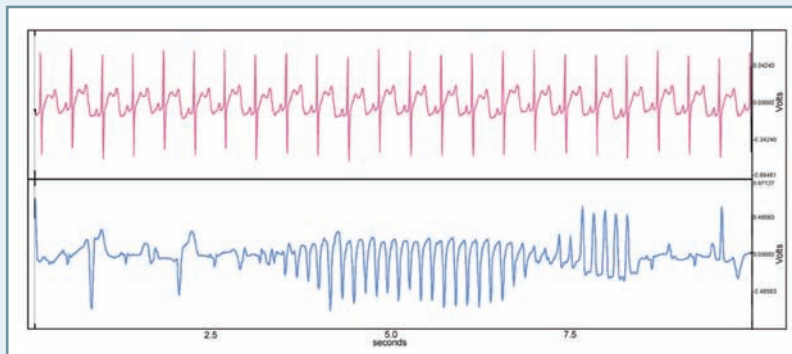
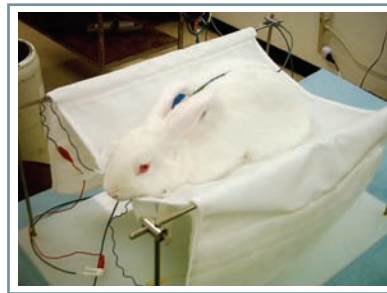


Examples of bipolar, transthoracic ECGs obtained simultaneously from 6 conscious guinea pigs. Notice the high-quality tracings without artifact.

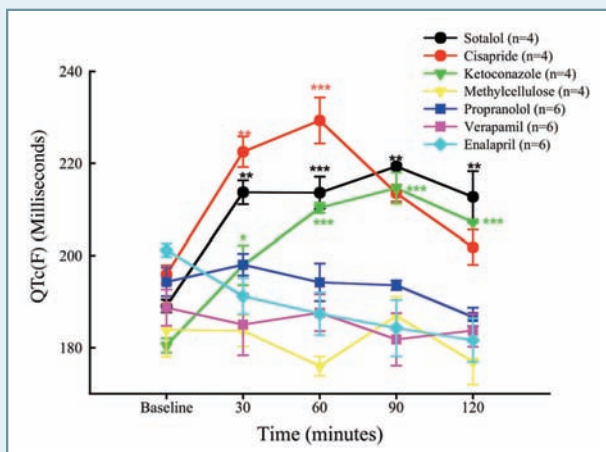


Representative bipolar, transthoracic ECGs from four conscious rabbits receiving two torsadogenic compounds (haloperidol and dofetilide), and one non-torsadogen (propranolol), and a control.

- Animals may be dosed intravenously, parenterally or orally
- Blood samples may be obtained for pharmacokinetic studies
- ECGs, LVP and arterial pressure may be recorded
- Animals remain quiet in the slings for repeated sampling and high quality, artifact free recordings



ECGs from normal (top trace) and heart failure (bottom trace) rabbits exposed to dofetilide. Bottom trace showing torsade de pointes from a rabbit in heart failure. Notice the sensitivity of the rabbit in heart failure to develop torsade.



Plots of QTc(F) versus time after oral dosing, in awake guinea pigs, of 3 test articles known to lengthen QTc in man (cisapride, sotalol, ketoconazole), 3 test articles thought not to lengthen QTc in man (verapamil, propranolol, enalapril) and vehicle methylcellulose.

