

Cardiac Safety Screening Services

Reliably evaluate the proarrhythmic and
cardiotoxic liabilities of your compounds



Reliably evaluate the proarrhythmic and cardiotoxic liabilities of your compounds

Our specialist team has extensive experience in developing cardiac safety assays. The cardiac safety screening assays we offer include:

Non-GLP hERG screening to eliminate cardiac risk liability

Due to its link to life threatening drug-induced arrhythmias, such as *Torsades de Pointes*, the hERG potassium channel represents a significant off-target liability. This risk liability is exacerbated by reports that up to 30% of compounds inhibit the hERG channel. Therefore, assessing novel compounds against hERG early in the drug discovery process is essential for eliminating drug-induced proarrhythmic liability.

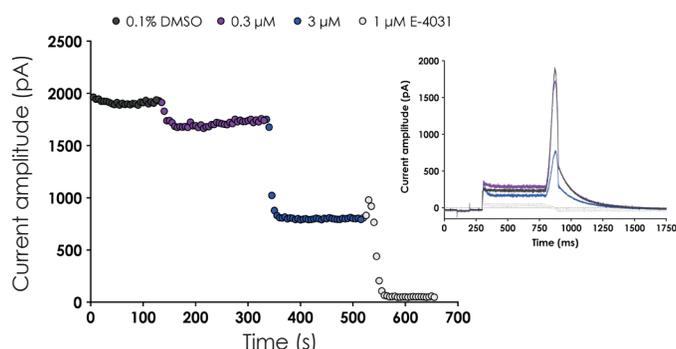


Figure 1. Peak hERG tail current (recorded at 37 °C) plotted against time for a representative cell treated with 0.3 and 3 μM ondansetron followed by 1 μM E-4031. Inset: representative current traces in 0.1% DMSO, ondansetron and E-4031.

Comprehensive *in vitro* proarrhythmia assay

Metrion has been an active participant in the CiPA ion channel working group and a member of the Health and Environmental Sciences Institute (HESI) cardiac committee.

Table 1. Assays for a wide range of different human cardiac ion channels.

Ion Channel Panel	Target	Platform		
		Manual Patch	QPatch 48	Qube
CiPA	hERG	✓	✓	✓
	hNav1.5	✓	✓	✓
	hCa _v 1.2	✓	✓	✓
	hK _r 2.1	✓	✓	-
	hK _v 4.3_KChIP	✓	✓	-
CiPA+	Dynamic hERG	✓	✓	-
	Late Nav1.5	✓	✓	-
Other	hHCN4	✓	✓	-
	hK _v 1.5	✓	✓	✓

hiPSC-derived cardiomyocyte model for early cardiac derisking

Our clinically translatable cardiomyocyte model utilises the VOLTA platform and provides early decision-making data on the potential cardiac risks of novel early-stage discovery compounds, thereby, significantly reducing the reliance on costly animal studies.

This high-throughput model:

- Provides comprehensive safety pharmacology and toxicology data from acute and chronic (24 h or greater) exposure of compounds
- Is a cost effective 96-well plate-based assay, that accurately assesses changes in action potential morphology
- Aligns with current ICH S7B guidelines and adheres to the principles of the FDA Modernization Act 2.0

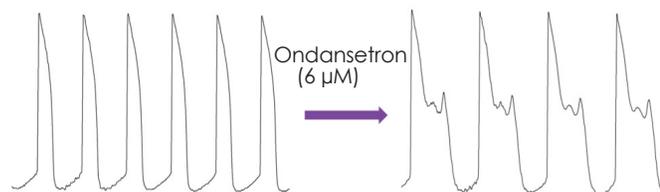


Figure 2. Assessing the effect of compounds on the ventricular action potential waveform in a high-throughput hiPSC-derived cardiomyocyte model.

Evaluate the effect of compounds on action potentials recorded from hiPSC-derived cardiomyocytes using manual patch screening

Successfully detect differences between compounds with low, medium and high proarrhythmic risk profiles, by evaluating the effect of compounds on action potentials recorded from hiPSC-derived cardiomyocytes using conventional manual patch-clamp methodology.

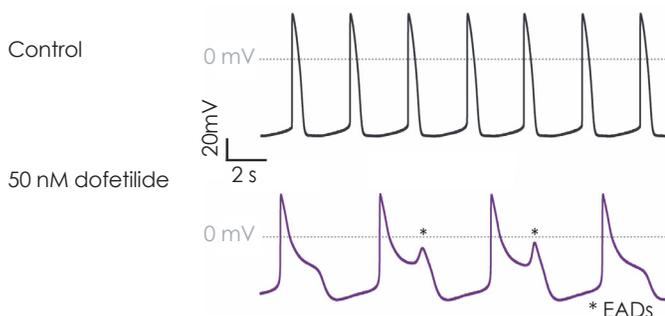


Figure 3. Action potentials recorded from hiPSC-derived cardiomyocytes showing the effect of 50 nM dofetilide on the action potential profile.

Chronic cardiotoxicity assay: hiPSC-derived cardiomyocytes to measure the cardiotoxic potential of test compounds

Base impedance, an indicator of cell viability, can be used to non-invasively identify structural and functional cardiotoxicity over a chronic time course. Metrion has developed a chronic cardiotoxicity assay using hiPSC-derived cardiomyocytes, which has been validated with several cardiotoxicants.

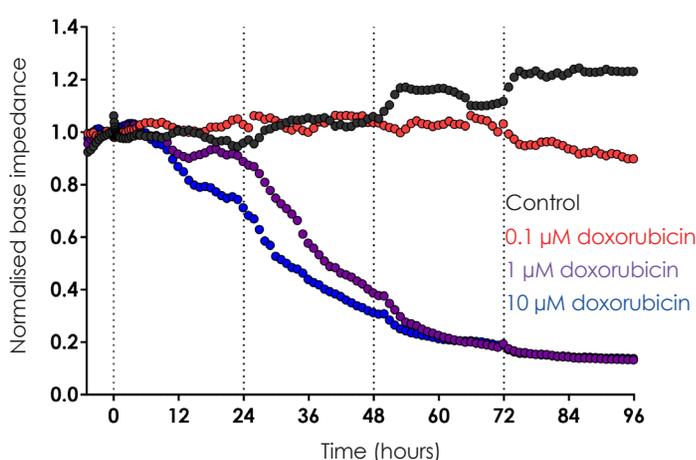


Figure 4. Representative traces showing the effect of doxorubicin on the base impedance signal recorded using hiPSC-derived cardiomyocytes.

High-quality, cost effective and rapid turnaround GLP testing against hERG

We provide specialist GLP hERG testing services using the conventional whole-cell patch-clamp technique.

For most IND filings, GLP compliant hERG testing is included under the ICH S7B guidelines. Metrion is a member of the UK GLP Compliance Monitoring Programme and provides screening services against hERG in accordance with the best practice guidelines provided by the Food and Drug Administration (FDA).

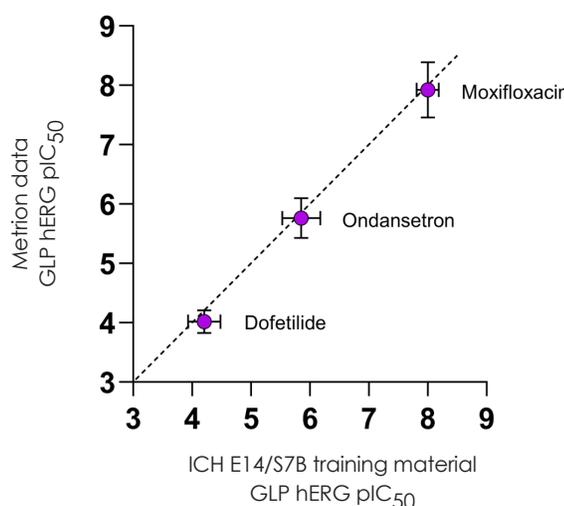


Figure 5. Graph showing the excellent correlation between Metrion's GLP hERG pIC₅₀ data and the published ICH E14/S7B training material data.

Supporting an integrated QTc risk assessment using the hERG margin distributions for three positive control agents derived from multiple laboratories and on multiple occasions

Derek J. Leishman, Jessica Brimecombe, William Crumb, Simon Hebeisen, Steve Jenkinson, Peter J. Kilfoil, Hiroshi Matsukawa, Karim Melliti, Yusheng Qu.
Journal of Pharmacological and Toxicological Methods. (2024), **128**, 107524.

GLP hERG data generated by Metrion were included in a multi-laboratory study published in the *Journal of Pharmacological and Toxicological Methods* (2024). The analysis demonstrated high intra- and inter-laboratory concordance in hERG IC₅₀ values when data are generated using ICH best practices, supporting the use of robust hERG safety margins within integrated QTc risk assessments. The findings support continued use of established hERG margin thresholds, including a 30-fold margin, within an integrated risk-based framework.

Specialist Preclinical Drug Discovery CRO

Metrion is a sector-leading CRO specialising in preclinical ion channel drug discovery, cardiac safety and neuroscience research services.

We deliver comprehensive drug discovery outsourcing solutions to pharmaceutical and bioscience customers worldwide; all from our state-of-the-art research hub.

Priding ourselves on delivering high quality data, our team use their extensive experience to:

- Complete laboratory studies on time and on budget.
- Carefully interpret the experimental findings.
- Communicate the results.
- Provide strategic recommendations.
- Support your decision making to best inform your screening strategy.



1,700+ projects completed globally



170+ different customers in the last 5 years



87% of science and senior team hold a Master's degree or higher, with 65% trained to PhD level



250 years combined experience managing ion channel research programmes

Testimonials

"We recognize this type of study is very difficult and the cells we provided posed technical challenges. We also appreciate the timeliness of the study execution and the detailed report you provided."

Top 10 pharma
Global

"Attention to detail with executing the study and the quality of reports is the best we have ever seen. By far the most accurate and well interpreted data. Explanations clear for a non-expert to understand."

Biotech
USA

"Aligos values the consistency and convenience of working with Metrion. The data is always correct and in a format that imports directly into our systems, making it so quick and easy for our team to review across individual projects. Metrion are always on top of the regulations as they change - they were incredibly helpful in supporting us navigate the ICH changes."

Dr Dinah Misner, VP,
Aligos Therapeutics, USA

"I've been pleased with the efficiency of the Metrion team, especially with their scientific expertise / practical ion channel knowledge."

It's not every ephys CRO that can make intellectual contributions towards the assay design and troubleshooting, and I've definitely appreciated that."

Dr John Gilchrist, Principal Scientist,
Latigo Biotherapeutics Inc., USA

