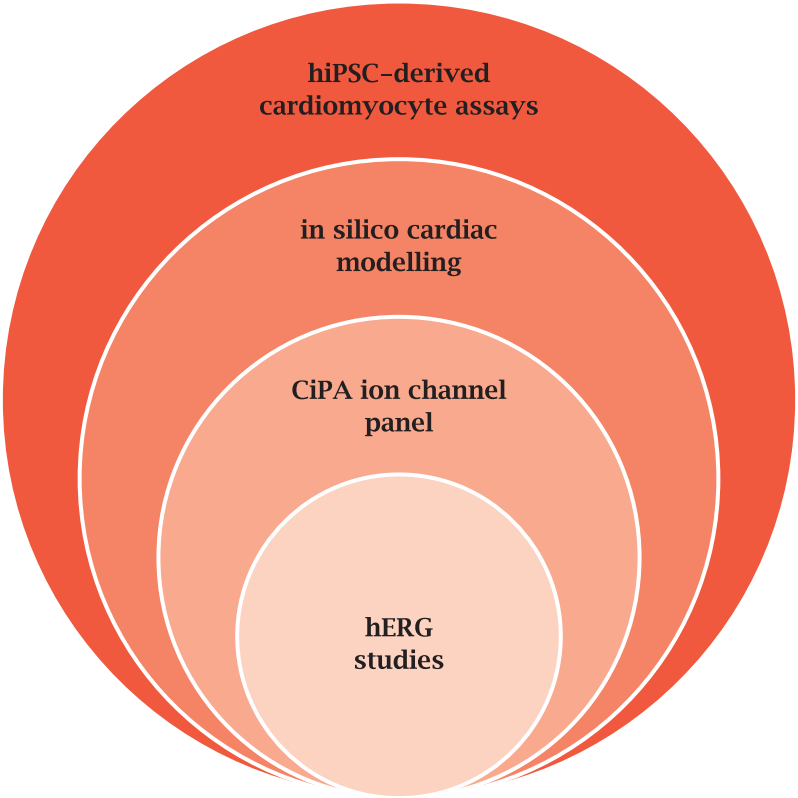
Predict cardiac safety early with

APCONIX

a better decision



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Cardiac Safety Doesn't Stop with hERG

Verapamil is a widely prescribed drug. It blocks hERG, but its simultaneous action on calcium channels means that it has low Torsades de Pointes (TdP) risk.

However, cardiomyocyte assays identified that verapamil acts on calcium ion channels causing slower cardiac contractility, which could lead to potential safety issues.

When it comes to cardiac safety, you need an integrated approach

At ApconiX, we offer comprehensive cardiac safety assessment to support you in making better informed project decisions.

Why is it important to do hERG testing?

Blocking the hERG ion channel can lead to QT interval prolongation and fatal arrhythmias (like TdP). hERG safety testing is a regulatory guideline if you are developing a new small molecule pharmaceutical or chemical entity for human clinical trials. Testing compounds for cardiac liability early during the drug discovery and lead optimisation phases saves time and money.

Why test hERG using electrophysiology?

Patch clamp electrophysiology is the gold standard for drug safety. Electrophysiology measures functional activity, providing data which can inform next steps including IC_{50}. This can then be used to determine compound safety margins. Automated patch clamp returns results quickly. ApconiX has a four day turnaround for hERG testing.

Why do a CiPA ion channel panel?

The Comprehensive in vitro Proarrhythmia Assay (CiPA) ion channel panel tests not only hERG, but a wide range of human cardiac ion channels, including: $Na_V1.5$ peak, $Na_V1.5$ late, $Ca_V1.2$, K_VLQT1 (Iks current), $K_V4.3$ (Ito current), hKir 2.1. Since blocking one ion channel can offset the action of another, this multichannel approach better assesses clinical risk.

What are the benefits of in silico modelling for cardiac safety?

In silico cardiac safety modelling uses advanced computer simulations to assess cardiac liability risk quickly and cost effectively. In silico modelling is a core pillar of CiPA, allowing drug developers to identify potential cardiac toxicity before beginning clinical trials.

Why do a cardiomyocyte MEA assay?

A hiPSC derived cardiomyocyte MEA assay shows how the drug affects the entire human cardiac cell. This includes the testing of action potential duration, signs of arrythmia and disruptions in electrophysiology, contractility, cell viability, and beating rate. Testing the whole cell response in this way is not possible by assessing drug action on ion channels alone.

Key facts

90% of new drugs fail to reach clinical trial. *Clinical failure rates have not shown sustained improvement since the 1960s, and the* ***failure rate for new drugs between 2000 and 2010 was 91%*** *(Filipova, 2026).*

Adverse drug reactions in the cardiac field are responsible for almost 10% of market withdrawals (Destere, 2023).

Key definitions

HERG

Automated patch clamp: uses robotic fluidics and microchip plates to record ion channel activity of many cells simultaneously.

hERG: a key potassium channel in the heart responsible for the repolarisation of the cardiac action potential. It is encoded by the KCNH2 gene.

hERG block: inhibition of the hERG channel by a drug may cause QT prolongation.

IC_{50}: the half maximal inhibitory concentration, which is the concentration of a drug needed to block 50% of ion channel activity.

Safety margin: the ratio between the concentration of a drug that causes adverse cardiac electrophysiology and the unbound maximum plasma concentration (Cmax, free) in humans. Redfern et al (2003) established that a >30-fold margin between hERG IC_{50} and therapeutic (Cmax, free) would avoid QT prolongation and TdP.

QT prolongation: a delay in the ventricular repolarisation phase of the cardiac cycle. QT prolongation may lead to TdP.

Torsades de Pointes (TdP): a potentially lethal cardiac ventricular arrhythmia.

CiPA

CiPA: comprehensive in vitro Proarrhythmia Assay.

The CiPA four pillars: 7 ion channel panel, in silico action potential modelling, human stem cell derived cardiomyocytes and early clinical human ECGs.

CiPA ion channel panel: is made up of hERG, $Ca_v1.2$, Na_v 1.5 (peak and late current), $K_v7.1$ (Iks current), $K_v4.3$ (Ito current) and Kir2.1.

In silico

Action potential: a brief change in a cell's membrane voltage, caused by ions moving across its membrane. In heart muscle cells, it triggers contraction.

APD: action potential duration. The time from the start of an action potential until the cell's voltage returns towards its resting level. APD_{90} measures this time to 90% recovery.

EAD: early afterdepolarisation. An abnormal voltage rise before a heart cell has finished recovering from its action potential, which can trigger an abnormal heartbeat.

qNet: the net electrical charge carried by selected ion currents during a simulated heartbeat, used to assess the risk of dangerous heart rhythms.

Cardiomyocyte

hiPSC: human induced pluripotent stem cells. These types of cells can be specifically grown to form cardiomyocytes hiPSC.

MEA: microelectrode (or multielectrode) array is used to simultaneously record or stimulate electrical activity in excitable cells such as neurons and heart cells.

Contractility: refers to the ability of heart muscle cells (cardiomyocytes) to shorten and generate force during a contraction. Evaluating contractility ensures that a drug does not weaken the heart's pumping power.

Impedance: a measure of the physical beating and structural health of a cardiomyocyte cell. Impedance is used to measure contractility and cytotoxicity.