INTRODUCTION:

Recommendations of the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use concerning cardiovascular adverse effects are focused on HERG channel assay and QT prolongation. However, it is important to notice that QT shortening may lead to the occurrence of severe arrhythmias such as supraventricular and ventricular fibrillations. Thus, the aim of the present study was to demonstrate that both rabbit Purkinje fibre's action potentials and guinea-pig isolated perfused heart are useful to detect the decrease in action potential duration (APD), and extend the QT shortening associated with $K_{ap}$ channels opening.

RESULTS

Pinacidil concentration-dependently decreases action potential durations at both frequencies without affecting resting potential, amplitude and maximal upstroke velocity.

Conclusion: The two presented models are useful for the preclinical evaluation of APD/QT shortening, which can be at the origin of severe ventricular arrhythmias.