



QT Prolongation Risk Assessment

The ICHS7B and E14 documents provide guidance on the assessment of risk of QT prolongation and cardiac arrhythmias by compounds undergoing preclinical and clinical development. Since the introduction of the EMEA CPMP “Points to Consider” document on this subject in 1998, the industry has been adopting testing paradigms to screen out, where possible, compounds with implicit potential to cause QT prolongation. However, from experience of testing large numbers of compounds from varied structural classes, 70% of the compounds screened for hERG channel blocking activity were positive. Although concentrations tested may be well in excess of the intended therapeutic concentrations, this has meant that some compounds are being taken into formal preclinical development and subsequently clinical development carrying a positive hERG signal. The E14 guidance requires that a thorough QT study is conducted that will detect a mean increase in corrected QT interval of 10 ms or around 2-3%. This study cannot be conducted until the therapeutic concentrations are well understood and therefore what they are likely to be during Phase II clinical trials.

A good understanding of risk of QT prolongation in the development candidate is highly desirable from both a time and economic point-of-view.

Aptuit consultants, with over 20 years of experience in assessing new compounds for the risk of QT prolongation, can help you in the following areas:

- review of preclinical data and interpretation of results
- development of an integrated risk assessment plan
- identification of plasma concentrations at which QT prolongation may be expected
- review and analysis of ECGs from Phase I clinical studies, and
- design and execution of a ‘thorough QT study’

Specialist consulting areas include:

- **Strategic** – Drug development strategy and management services
- **CMC** – Drug substance/drug product development; pharmaceutical sciences
- **Preclinical** – Safety assessment, metabolism/PK, and discovery support
- **Clinical** – Clinical studies to achieve evaluation of safety/proof of concept; clinical trial supply logistics
- **Regulatory** – Regulatory strategy and submissions

Additional Aptuit Capabilities

Aptuit offers a comprehensive suite of drug development services that range from candidate selection through to market, including consultancy services, API development and manufacture, preclinical and clinical technologies, pharmaceutical services, large and small scale manufacturing, IVRS, and clinical packaging and logistics, across a wide range of compounds, dosage forms and delivery systems.

For information about Aptuit consulting services, please call one of our offices or email:

+1 781 778 0418 North America

+44 1506 813333 Europe

email: consultinginfo@aptuit.com

or visit our website: www.apptuitconsulting.com

Engineering a better drug development process.