

Final Concept Paper
**S7B: The Non-clinical Evaluation of the Potential for Delayed Ventricular
Repolarization (QT Interval Prolongation) by Human Pharmaceuticals**
dated 8 November 2000

Endorsed by the Steering Committee on 24 May 2001

Issue

Non-clinical Approaches for predicting Torsade de Pointes

Proposal

To outline currently available nonclinical methodologies that can be used for assessment for potential ventricular tachyarrhythmia, and to discuss the advantages and disadvantages of the models. See outline below.

Resources

Representation from ICH six parties (Expert Working Group S7A).

E-mail and video-conference

Two to three EWG meetings; anticipated to reach step 4 approximately 2 years

Guidance Outline

Current state of guidance

CPMP „Points to Consider“ document, Publications

Systems

Heterologous expression systems

- Models available:
- Advantages and Limitations of each model

Disaggregated cells

- Models available:
- Advantages and Limitations of each model

Isolated tissue

- Models available:
- Advantages and Limitations of each model

Isolated intact heart (Langendorff)

- Models available:
- Advantages and Limitations of each model

Intact animal (e.g., Guinea pig, rabbit, dog, pig)

- Models available:
- Advantages and Limitations of each model

On-going assessment of approaches

Review of existing industry practices and research

Recommendations

No scientific consensus on approaches and no international consensus on regulatory recommendations, resulting from inadequate information about predictivity of the models for human risk

Currently, individual cases are being dealt with on a case-by-case basis.