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.