CDI

Context of Use for Regulatory Applications
Context of use for CDI cells

• **What would it replace?: Safety profile**
  – Currently generate ion channel data
  – Dissociated animal cells
  – In vivo telemetry

• **What would be the context of use?**
  – Justification on the basis of mechanism
  – QT prolongation
  – pro-arrhythmia
  – cardiotoxicity
What would be the endpoints in that system for the given context of use?

• Impedance pattern
• Beat rate
• Amplitude of the wave
Test compounds needed to establish if endpoints have been reached

- QT prolongation set
- pro-arrhythmia set
- cardiotoxicity set
Could this data predict clinical response or predict safety profile in Phase 1?

• Comparative data with known human set of compounds.
• Submit these data to support conclusions from other tests.
• Knowledge about the target.
For use in predicting general toxicity.

• Does compound have any toxicity at all? YES
• What are the levels of tox if present? YES
• Can it be used to establish mechanisms for known/unknown drug toxicity? NO
How should we look at genetic diversity with these systems?

- There is an ongoing study which is currently assessing the impact of genetic diversity on the performance of these cells.