

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.