Impact of CiPA on Drug Discovery and Development

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Assumptions

- Successful completion of validation studies
- Specific proposal for use
- Acceptance of paradigm by individual regulatory agencies
- Acceptance of paradigm by ICH

Impact on drug development

- Replacement of TQT study as the second-best indicator of proarrhythmic potential
- New product labeling based on CiPA results
- Revision of older labeling

Impact on FDA/CDER

- Revamp “QT team”
- Preserve culture of
  - Organizing, mining of existing data
  - Improving model and practices, facilitating sponsors’ decision-making processes

Impact on drug discovery

- Either a lot or a little
  - Many sponsors do something more than hERG + TQT now. CiPA design was intended to enable better decision-making earlier in development, through leveraging high throughput technologies for voltage clamp and cardiomyocyte studies
  - Opportunity to reassess previously shelved compounds
  - No one has to do anything.

Impact on the environment

- Getting better
  - High throughput instrumentation
  - Cell model
  - Cardiomyocytes
    - Won't need overexpression systems for long
- Other mechanistic assays for cardiotoxicity, based on human biology

When?

- In the first public discussion of the CiPA initiative in July 2013, I predicted:
  - Abandon E14 by July 2015
  - Revise S7B by July 2016

  …so who am I to guess?
- CiPA development team has done and is doing what it can
  - To develop protocols
  - To organize a complex set of validation studies
  - To anticipate agency and ICH review


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