Integrating Cardiovascular Endpoints into toxicology studies: Preliminary Results from An Industry Survey

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Agenda

- Introduction
- Webinar survey
- Preliminary results from an Industry Survey
- Expert panel presentations
  - Pros: Marc Bailie (Michigan State University)
  - Cons: Mike Engwall (Amgen)
  - Regulatory perspective: John E Koerner (FDA)
- Open discussions
- Closing remarks
Introduction: Methodologies

- Technologies for Cardiovascular Investigations in Toxicology Studies
Webinar Poll

Is the assessment of Cardiovascular endpoints in a toxicology study rather than a stand alone safety pharmacology study suitable to support IND studies in the majority of cases?
Preliminary Industry Survey Results

Total of 361 participants

Please indicate if you are a member of any of the following organizations (check all that apply):
Preliminary Industry Survey Results

Total of 361 participants

What is your geographical location?

- 71.4% North America
- 19.4% Europe
- 9.1% Asia
If you have added safety pharmacology endpoints to **investigative (non-regulatory)** toxicology studies what species have you used?

- **Mouse**: 18
- **Rat**: 57
- **Canine**: 121
- **Nonhuman primate**: 109
- **Mini-pig**: 29

**Categories:**
- CV
- CNS
- Respiratory
- GI
- Renal
If you have conducted cardiovascular safety pharmacology investigations with New Chemical Entities by adding endpoints to regulatory toxicology studies what technique have you used?

- ECG in restrained animals
- ECG implanted telemetry
- ECG jacketed animals
- Arterial pressure with indirect measurement (cuff including HDO)
- Arterial pressure with implanted telemetry

Options:
- Mouse
- Rat
- Canine
- Nonhuman primate
- Mini-pig
If you have conducted cardiovascular safety pharmacology investigations with **BIOLOGICAL AGENTS** by adding endpoints to regulatory toxicology studies what technique have you used?

- **ECG in restrained animals**: 60
- **ECG implanted telemetry**: 42
- **ECG jacketed animals**: 58
- **Arterial pressure with indirect measurement (cuff including HDO)**: 37
- **Arterial pressure with implanted telemetry**: 41

- Mouse
- Rat
- Canine
- Nonhuman primate
- Mini-pig

**WEBINAR**
If you have received regulatory feedback, what did it indicate?

- **ECG in restrained animals**
- **ECG implanted telemetry**
- **ECG jacketed animals**
- **Arterial pressure with indirect measurement (cuff)**
- **Arterial pressure with implanted catheter e.g. ear artery**
- **Arterial pressure with implanted telemetry device**

- This methodology was considered acceptable by the agency
- This methodology was NOT considered acceptable by the agency
- The agency suggested modification(s) to the design
Slides of expert panel members
Questions for open discussions

- Based on your opinion, S7A safety pharmacology endpoints in regulatory toxicology studies are generally appropriate for:
  - CV safety pharmacology for small molecules?
  - CV safety pharmacology for large molecules?
  - As a standalone study?
Questions for open discussions

- In your organization, has the ability to add safety pharmacology endpoints onto regulatory toxicology studies had any of the following consequences?
  - Allowed you to manage safety risk more effectively?
  - Data contributed to the halting the progression of a compound?
  - Data addressed a specific concern and supported the continuation of a compound?
Questions for open discussions

- Based on your experience, please state any **disadvantages** of safety pharmacology investigations in toxicology studies?

- Based on your experience, please state any **advantages** of safety pharmacology investigations in toxicology studies?
Questions for open discussions

- Have you received **regulatory feedback** on inclusion of cardiovascular safety pharmacology in toxicology studies?
Thank you for your time and participation!

Looking forward to see you in Phoenix for the 2012 Annual SPS meeting.