Applying Preclinical Data from Adult Devices to Pediatric Device Development

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Disclosure Statement of Financial Interest

I DO NOT have a financial interest, arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

What is the problem?

- Unmet clinical need for size 15, 17mm valves for pediatric patients
- Historically, a lack of development in this area due to several barriers, such as:
  - Uncertain regulatory pathway
  - Length of time required to collect the data necessary to support regulatory approval
  - Lack of financial incentive for device industry

How do we identify a solution?

- AdvaMed Pediatric Heart Valve Workshop on January 12, 2010
- Collaboration between academic, industry, and regulatory communities to address these issues
- Primary goal – Leverage existing adult data to the extent possible and encourage a global approach to future product development

Building Off What We Already Know

- Existing paradigm for adult valves based on HV Guidance Document and ISO 5840
- Pathway for pediatric valves hinges on a couple of key points:
  - Scaling down of approved adult heart valves
  - Same materials as approved valves
- Total Product Life Cycle (TPLC) approach

Preclinical Testing Paradigm

- Take an approach similar to adult-sized valves
  - Start with a risk analysis
  - Worst-case test conditions should be applied
  - In some cases, a justification may be adequate
  - In others, new testing will be necessary
- Engineering Testing
  - Test conditions based on clinical input
- Animal Studies
  - New testing should not be necessary, as long as same materials and design

Hydrodynamic Testing

- New testing will be needed in several areas
  - Steady forward flow
  - Steady backflow leakage
  - Pulsatile flow pressure drop
  - Pulsatile flow regurgitation
  - Flow Visualization
- Justification* may be sufficient for others
  - Cavitation Potential
  - Verification of Bernoulli relationship

*Based on loading and/or fluid mechanics and computational fluid dynamics (CFD)

Structural Performance Testing

- Accelerated wear
  - 15-year equivalent for mechanical valves
  - 5-year equivalent for tissue valves
  - Test smallest size only
- Fatigue
  - Finite element analysis (FEA) used to identify test parameters
  - Life analysis performed on worst-case size**
- Dynamic failure mode
  - Test worst-case size** only
- Sewing ring integrity
  - Test all new sizes

**Worst-case for entire adult/pediatric size range

Biocompatibility/Sterilization

- Leverage existing data for these tests, based on same materials and design
  - Sterilization validation
  - Shelf life
  - Biocompatibility
  - Bioburden
  - Bacterial Endotoxin

Clinical Testing Paradigm

- Again, a similar approach to that used for adult-sized valves
  - 15 patients per size per position
  - Effectiveness based primarily on hemodynamic data
  - Safety based on key adverse events

Postapproval Study Paradigm

- Postmarket data will play a major role
  - Limited premarket clinical data
  - Questions regarding device durability in this patient population
- Industry collaboration to develop registry

Summary & Next Steps

- Maintaining a high bar for preclinical testing
- Streamlined clinical study requirement
- Postapproval study data will be critical
- White paper from AdvaMed Heart Valve Working Group forthcoming
- This model could be utilized for other pediatric medical device areas as well

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