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CONSIDERATIONS FOR PEDIATRIC DEVICE DEVELOPMENT JANUARY 2014

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Speaking on behalf of AdvaMed

BRINGING INNOVATION TO PATIENT CARE WORLDWIDE

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Topics

- Current state
- Proposals to reduce barriers
  - Flexible regulatory models
  - Alternative valid scientific evidence
  - HUD/HDE program clarifications
  - Enhanced FDA communication/collaboration
  - Custom device guidance
- Progress

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Disclaimer

Mr. Morton is an employee of Medtronic, Inc., a manufacturer of medical devices for both adult and pediatric patients.

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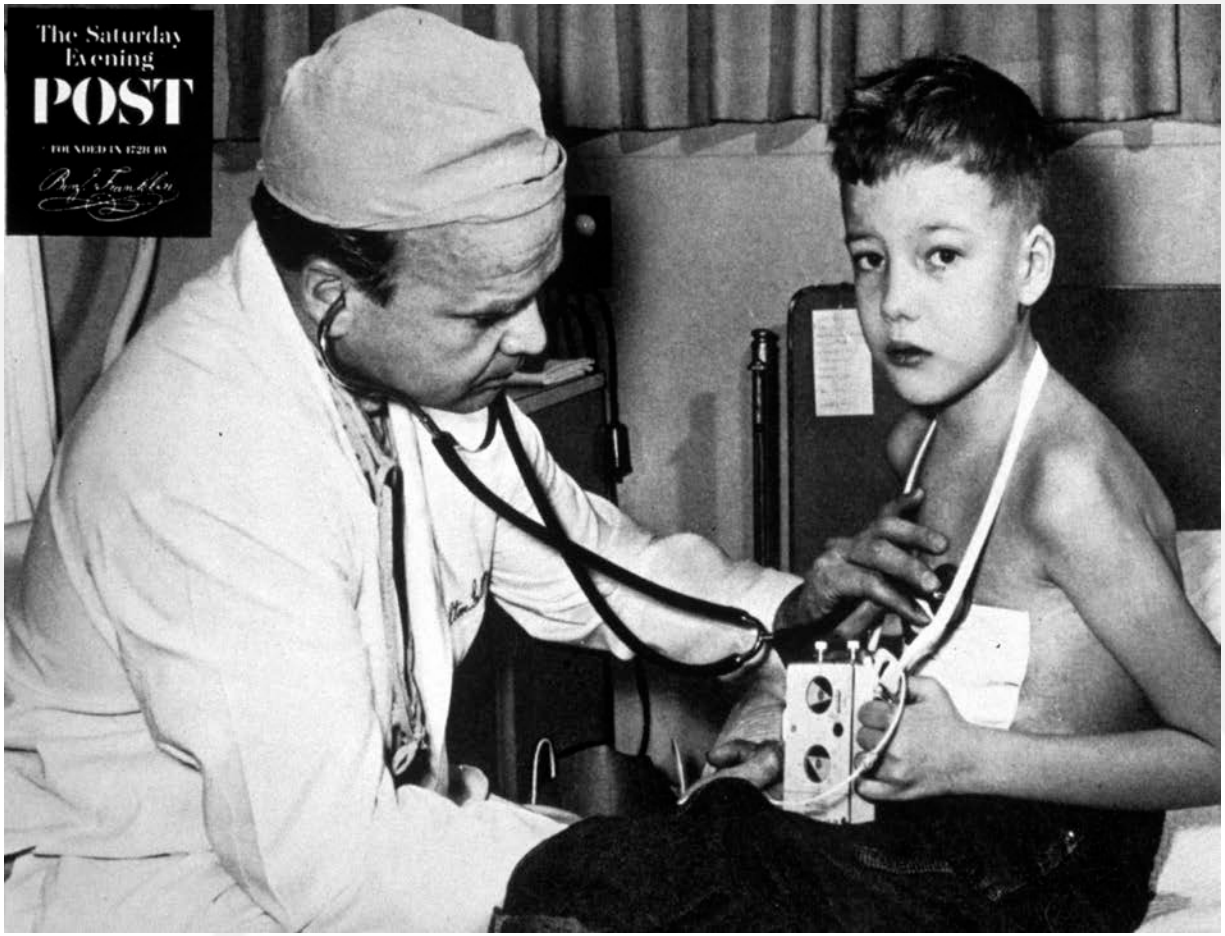

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Current State

- Unmet needs
- Off label use of adult devices
- Jury rigging of adult devices
- Lack of data on long-term effects of devices used for pediatrics

Unique Clinical Challenges with Pediatric Devices

- Small populations, widely dispersed
  - Difficult to accrue sufficient numbers
  - Reasonable timeframe
  - Manageable number of sites
- Off label use of an adult device may have become the standard of care
  - May not be accepted as a control for a pediatric study

Unique Challenges, continued

- Difficulties in informed consent
  - Emotional factor of parent-child
  - Higher standard for pediatric studies by some IRB's
- Less invasive procedures vs. a surgical control

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Pediatric Treatment Carries Emotional Baggage

Proposals to Address Challenges to Developing Devices for Rare Diseases - Current Framework

Existing regulatory tools can improve patient access to medical devices for rare diseases

- Flexible regulatory models
- Alternative valid scientific evidence
- HUD/HDE program clarifications
- Enhanced FDA communication/collaboration
- Custom device guidance

Flexible Regulatory Models

- FDA is authorized to use valid scientific evidence other than well-controlled trials to demonstrate "reasonable assurance of safety and efficacy"
  - FDCA §513(a)(3); 21 CFR 860.7
- Consider small patient population and benefit/risk in determining data required to show probable benefit (HDE) or reasonable assurance of safety and efficacy (PMA)
- Appropriate use of all forms of valid scientific evidence can help mitigate issues associated with orphan populations

Alternative Valid Scientific Evidence

- Use objective performance criteria, historical controls or well-documented case histories in lieu of randomized, controlled study
  - Literature, HDE/off-label experience, registries, retrospective consecutive case series with/or without long-term post-market registries
- Use non-clinical data to support device variants or changes
- Extrapolate predicates/data from another population, e.g., apply adult data to pediatric population
- Smaller pre-market studies with long-term post-market registries

HUD/HDE Program Clarifications

- Clarify type and level of data that demonstrates safety and probable benefit for HDE
  - RCT generally not required
  - Non-clinical data, literature, historical data, patient records, surrogate endpoints, experience with similar devices
  - Innovative statistical methods

Enhanced FDA Communication/Collaboration

- Facilitate FDA access to specific rare disease expertise within or outside of agency
- Dedicated orphan/pediatric ombudsman in CDRH
- Predictable requirements applied with flexibility recognizing orphan population challenges
- Early agreement on innovative approaches to achieve full PMA approval for HDE devices
- Promote Expedited PMA/PMA-S Review

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Custom Device Guidelines

- FDA guidance on application of custom device provisions to unique devices for very small orphan or pediatric populations

- Reduce need for clinician to “jury-rig” existing devices

Progress!

- HDE's
  - Lifted profit cap
  - Q&A clarifies "approval"
- A new paradigm of obtaining marketing approval for pediatric-sized prosthetic heart valves
  - J Thoracic Cardiovascular Surgery, OCT 2013

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Conclusions

- Unmet needs for pediatric devices
- Some of the challenges are emotional
- Existing regulatory tools can be used to promote development of devices for pediatric and rare diseases
- Significant progress has been made