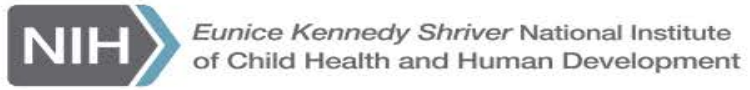
Working Group #2: Regulatory Report
August 23, 2019

Co-Chairs: Shelli Avenevoli and Karin Bok



Working Group 2: Regulatory

- Co-chairs: Shelli Avenevoli (NIMH) and Karin Bok (NIAID/VRC)
- Members: Melissa Gorman (Shriners Hospital), Robert Ternik (Eli Lilly), Dorothy Fink (OWH/HHS)
- *Ad hoc* Members: Michael Greene (Harvard), Rahul Gupta (March of Dimes), Susan McCune (FDA), Melissa Tassinari (Mother-to-Baby), Susan Wood (GWU), Anne Zajicek (NIH)
- NICHD Staff: Lisa Kaeser

Regulatory Recommendations

- 1. Include and integrate pregnant women and lactating women in the clinical research agenda.
- 4. Remove regulatory barriers to research in pregnant women.
- 7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

1. Include and integrate pregnant women and lactating women in the clinical research agenda.

Has any part of the recommendation been implemented to date?

- Pregnant women removed as an example of vulnerable population only (implemented)
- FDA is currently harmonizing their guidance with the common rule (12/13/19)

1. Include and integrate pregnant women and lactating women in the clinical research agenda.

What are the key factors needed to implement the recommendation?

- Investigate and learn from pediatric precedent
- Highlight benefits of determination of proper dosing
- Streamline and implement opportunistic data gathering
- Delineate specific needs for integrating PRGLAC women into research
- Consider optimal entity to lead and coordinate implementation across relevant agencies– e.g., creation of a separate office/team within HHS
  - Requires additional resources, relevant expertise, separate funding stream
- Professional organizations could lobby for action (e.g., funding)
- Consider creating business case to incentivize industry

1. Include and integrate pregnant women and lactating women in the clinical research agenda.

Are there any major obstacles that could prevent implementation?

- Liability
- Consideration of risk of not treating pregnant women vs risk of being exposed to drug

1. Include and integrate pregnant women and lactating women in the clinical research agenda.

What additional information or expertise do you need to complete your work?

- Kweder, Sandra. FDA/EMA representative. Historical perspective
- Liability attorneys

4. Remove regulatory barriers to research in pregnant women.

Has any part of the recommendation been implemented to date?

- No

4. Remove regulatory barriers to research in pregnant women.

What are the key factors needed to implement the recommendation?

- Discussion on minor increase over minimal risk
- Research on the impact of 46.204(e) as it stands. What is the impact of requiring both consents vs mother consent alone?
- Survey IRBs on impact of regulation; educate and encourage including OB expertise
- Research on impact of adding “minor increase to minimal risk” for pregnant women; consider for lactation
- Develop models/correlates to predict concentration of drug in milk. Should this information be required prior to licensing?
- Consider leveraging IMI-Conception

4. Remove regulatory barriers to research in pregnant women.

Are there any major obstacles that could prevent implementation?

- Could become politically or socially charged

4. Remove regulatory barriers to research in pregnant women.

What additional information or expertise do you need to complete your work?

HHS, OHRP representative

Jonathan Greene at NIH- centralized IRB

Maggie Little

Ethicist

7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

Has any part of the recommendation been implemented to date?

- No

7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

What are the key factors needed to implement the recommendation?

- Leverage and apply experience in vaccine compensation and pediatrics
- Influence culture change
- Concentrate liability tampering efforts on a subset of options, keeping in mind feasibility of research studies
- Review pregnant study plan as potential option
- Survey FDA authority and review what information is required
- Consider FDA authority to require relevant data – e.g., PK/PD and placenta-crossing
- Consider ethics of not doing the research

7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

Are there any major obstacles that could prevent implementation?

- Inability to implement a no-fault compensation program because there is a baseline of adverse outcomes in pregnancy even without any intervention

7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

What additional information or expertise do you need to complete your work?

- Insurance representatives
- Industry attorneys
- Liability program-government attorneys/experts
- VCP representative

Questions?