

# **Task Force on Research Specific to Pregnant and Lactating Women**

Summary and Discussion of Meetings 1&2&3





## TF3: Communication Strategies



# Report Components and Strategy

TF 3	(1) A plan to identify and address gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women, including the development of such therapies;
	(2) Ethical issues surrounding the inclusion of pregnant women and lactating women in clinical research;
	(3) Effective communication strategies with health care providers and the public on information relevant to pregnant women and lactating women;
	(4) Identification of Federal activities, including: <ul style="list-style-type: none"><li>(a) The state of research on pregnancy and lactation;</li><li>(b) Recommendations for the coordination of, and collaboration on research related to pregnant women and lactating women;</li><li>(c) Dissemination of research findings and information relevant to pregnant women and lactating women to providers and the public; and</li><li>(d) Existing Federal efforts and programs to improve the scientific understanding of the health impacts on pregnant women, lactating women, and related birth and pediatric outcomes, including with respect to pharmacokinetics, pharmacodynamics, and toxicities; and</li></ul>
TF 4	(5) Recommendations to improve the development of safe and effective therapies for pregnant women and lactating women.



# Communication Strategies

- Variety of communication strategies / multiple platforms
- Identify audiences – tailor to target group across demographics
  - Strategies for engagement
- Engage stakeholders
- Coalition based approach
  - across research, policy and health care delivery spectrum
- Need to improve communication on importance of research and evidence and reporting into registries
- Analytics / metrics of communication strategies
- Consistent messaging



# Communication Strategies With Health Care Providers

- Pharmaceutical industry adapting field-based employees to adjust to changing healthcare ecosystem that may include population health, medical liaison specialists, account executives and sales representatives to create value in the systems.
- Variety of communication strategies / multiple platforms – tailor to target group
  - Emails vs Facebook vs Twitter depending on age/demographic of HCP
  - CME/CNE for health care providers
  - Physicians: Maintenance of Certification articles/ABOG
  - Can it be streamlined, to limit 5 messages on same things from different groups
- Utilization of electronic medical records point of contact/alerts



# Communication Strategies With Public

- Social media: Digital media, websites, Facebook, webinars, smartphone apps, emailed newsletters, books, blogs, podcasts, twitter, hashtags, online chats, TED talks, text messages/text for baby
  - Creative insight: font/colors change the message
- Internet advertising
- Influence the influencer: information often from friends, family
- Screening questions when seen by HCPs
- Informational posters
- Education to dads/partners
- Shifting/changing beliefs – need multifaceted approach
- Art of transmitting content, putting a face to the message



**TF3:** A plan to identify and address gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women, including the development of such therapies



# Report Components and Strategy

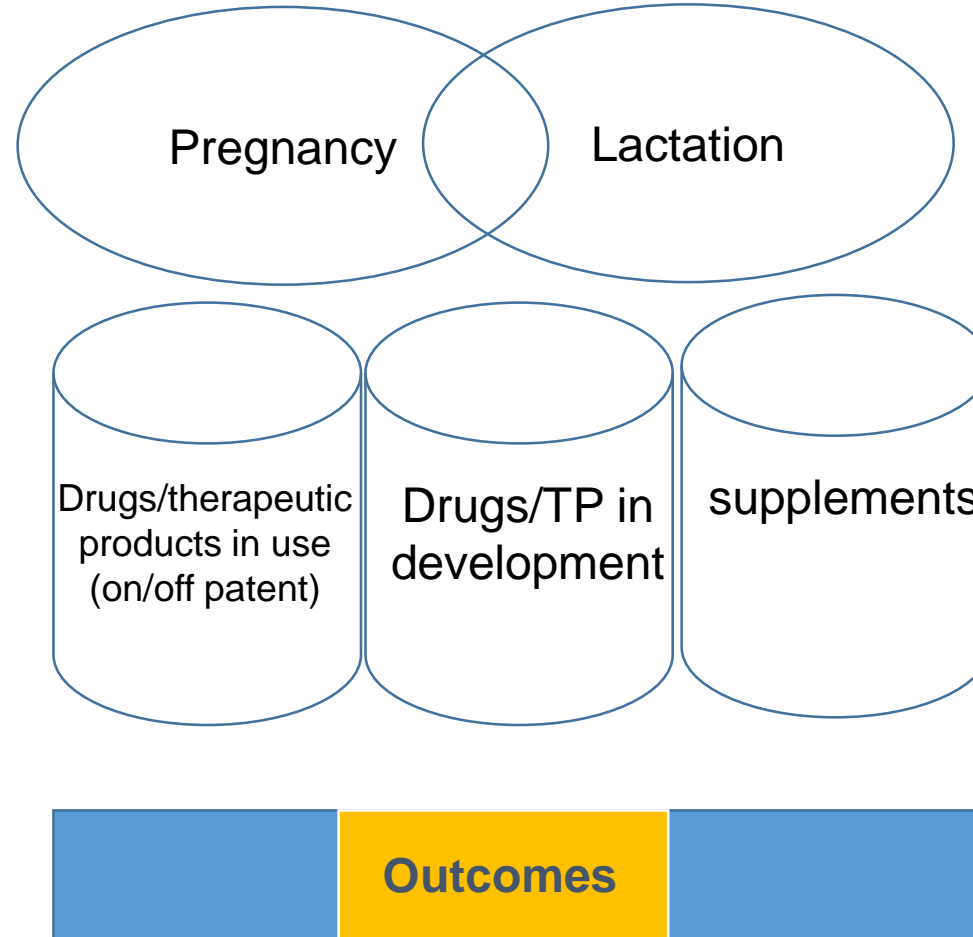
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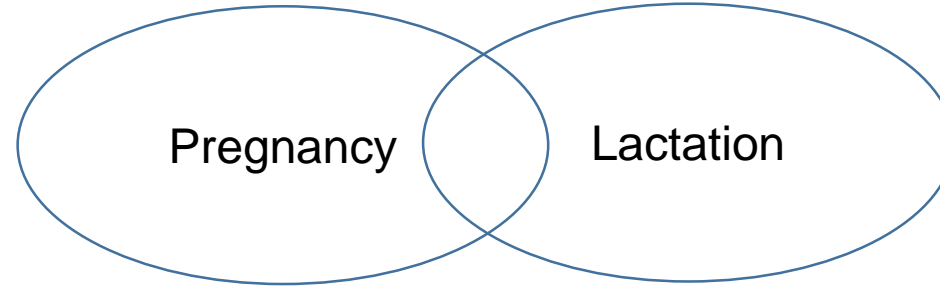




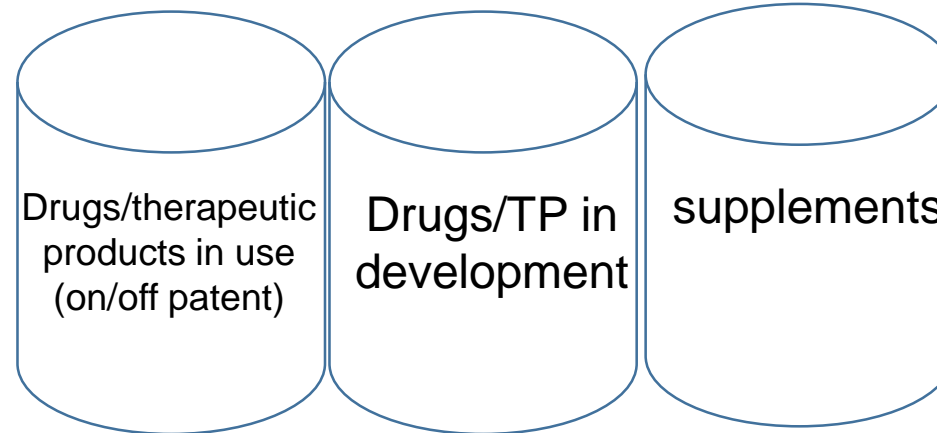
## The “Plan”

- Need separate plans/tracks for therapeutic products in use vs therapeutic products in development vs supplements
- Separate plans/tracks are needed for lactation and pregnancy
- Is a separate plan needed for supplements?





- **Specific to P&L**
- **Used in P&L**



**Outcomes:  
mom & baby**

- Identify constraints and consider new ways to operationalize
- Prioritization
  - Need
  - Value
  - Gaps in knowledge / Ability to execute
    - Resources
  - Ability to succeed
    - Sustainability
    - Funding
- For those being used need to consider Indication/use to prioritize

Risk of not lactating and not taking medications need to be included



## Plan: Vision / Goal

Women and providers will have an evidence base on which to guide informed decisions on the use of therapeutic products during pregnancy and lactation in order to improve health outcomes for mother, child and family



## Plan: Objectives

- Increase the availability of clinically meaningful information for pregnant women and mothers and babies in Pregnancy & Lactation (P&L) in approved product labels
- Increase amount and dissemination of information on therapeutic products in P&L
- Increase participation of pregnant and lactating women in research
- Stimulation of research in P&L
- Increase expertise in obstetrical / lactation pharmacology
- Prioritization process developed
- Enhanced collaboration among stakeholders (public, industry, government, etc)
- Improve maternal and pediatric health outcomes



# Plan: Metrics

- Increase the availability of clinically meaningful information for pregnant women and mothers and babies in P&L in approved product labels
  - # Therapeutic products labeled for P&L
  - Clinical guidelines
  - Fewer “I do not know”
  - Timeliness
- Increase amount and dissemination of information
  - Deliver right message to target groups
  - Ensure the data is accessible to women/providers/families
  - Change in practice / clinical guidelines
  - Consistency of message
- Increase participation of pregnant and lactating women in research
  - # women in trials



## Plan: Metrics (2)

- Stimulation of research in P&L
  - Augment infrastructure for research in P&L women
  - Funding levels
  - Industry involvement
  - # grants/PIs
  - Collection of consistent data / Common data elements
  - Capture P&L in large datasets
- Increase expertise in obstetrical / lactation pharmacology
  - # PIs, # ob/lactation pharmacologists
- Prioritization process developed
- Enhanced collaboration among stakeholders (public, industry, government, etc)
- Clinical outcomes
  - maternal and child short term and long term health, birth outcomes



# Prioritization

- Need to focus on need / unmet need
  - Common conditions / vaccines that have high impact and result in morbidity/mortality
  - Lactation – milk supply research
  - Emerging threats
  - What is not being used due to fear
  - Attributable risk
  - Impact on preventive health
  - Important to work on both short and long term impact
- Ability to execute – where can you have the biggest win – common meds, need data on dosing, levels, transfer to breastmilk
- Collect information on what patients/providers need
- Scientific opportunity - developmental pipeline – e.g. Hepatitis C new class of drugs without information in pregnancy
- Opportunity to facilitate translation to product label rapidly – that will translate to clinical guidelines, practice
- Standards of care where evidence is limited / not uniform





# Training

- Don't reinvent research wheel – sustained infrastructure needed
- Consider developing certificates and/or fellowships of obstetric/lactation pharmacology for ObGyn, Peds, Nursing, and health care practitioners
  - Leverage other groups vested in this training
- Pharmacometrics and modeling, pharmacogenomics and pharmacoepidemiologists training needed
  - Resources needed
- Training of pharmacology in obstetric and lactation work
- Contractual process of building a public private partnership
- Consortia approach
- Training needed – across every sector – woefully low in expertise to support modeling/simulation/dosing
  - industry, academia, clinical pharmacology
- Target education and training to enhance infrastructure in support
- Training for reporting adverse events and registries
- Members of IRBs, ethics committees on P&L and P&L research



## Infrastructure

- Leverage ongoing efforts of pharmacology trials, networks, studies, centers
- Have laboratories with expertise in PK/PD partner with networks/studies
- Develop a platform in collaboration with networks already in place with industry
- Change construct of how to retain women who become pregnant in studies



# Leverage Efforts & Develop New Efforts

- Networks & infrastructure
  - Existing data collections – eg PRAMS at CDC, OTIS, NBDPS
- Attract pharmacologists into P&L
- Big data
  - Caution re confounders, statistical interpretation, cannot capture that women may stop taking medications, quality of database
  - Can be hypothesis generating
  - Key standard for vaccine use after the license in pregnancy: H1N1 vaccine
  - Need ability to verify findings from big data
  - Natural language processing – done in VA, can give qualitative information
  - Common data elements important
  - Multiple health systems



## Leverage Efforts & Develop New Efforts (2)

- Pediatric training
- Optimize registries
  - Innovative options – pharmacoepidemiologist to assist
  - Health care provider practices, patients able to register themselves
  - Required vs voluntary registries
  - Design by sponsor – may not be able to combine
  - Obstacles as opportunities
  - Leverage those coming – All of Us, PregSource, etc
  - Common data elements
  - Specifically designed registries – trained abstractors for outcomes enrolling all patients at a site
  - Access to data and transparency of information important
  - Can electronic medical records facilitate input into registries



## Basic Science

- Models in obstetrics limited, how to study the placental longitudinally, need more animal models
  - Animal models have limited utility
    - Useful for mechanistic studies, etc
  - Novel models - placenta on a chip
  - Understanding the predictability of animal models
- Model based on opportunistic sampling in neonatology to understand physiologic changes
  - Neonatal developmental spectrum; physiologic state in P&L
- Pharmacogenomics critical in P&L



## Outcomes: Mom & Baby

- Risk for taking vs not taking the therapy
- Long term outcomes important for mom and baby
  - Ability to execute hinders long term outcome
- Benefit : Risk analysis - How balance risk (ability to execute)
- Patient reported outcomes – and sex as a biologic variable

\*Outcomes for family/partner are important too\*



# Key Players

- Engage pregnant and lactating women, partner, family, community
- Preconceptional women / reproductive age women
- Health care providers, pharmacists and pharmacies, allied health care providers
- Electronic health records, insurance claims datasets – opportunity
- Professional societies
- Patient advocacy organizations
- Health care professional training organizations
- Industry
- Federal participants: FDA, NIH, CDC, HRSA, DoD, VA, SAMSA
- Academia
- Large health care systems (eg Kaiser, Geisinger, VA)
- Legal system
- Ethics committees, IRBs
- Communication science
- Existing effective networks



## Draft Recommendations



# Draft Recommendations



## \*\*\*Important Notes\*\*\*

- These are ***draft*** based on discussions to date
- Aiming for reaction and refinement
- May meeting focused on recommendations



# Workforce Recommendations

- Prioritize and support the development and training of pharmacologists and research scientists who understand pregnancy and lactation
- Prioritize and support the development and ob/gyn and pediatrics who understand pharmacology for studies in P&L
- Prioritize and support the development of investigators with obstetrical, lactation, and pharmacology expertise for industry, academics, and the federal workspace
- Facilitate a multidisciplinary approach to research teams including expertise in obstetrics, quantitative clinical pharmacology, clinical trial, behavioral/social sciences and regulatory sciences



## Infrastructure Recommendations

- Leverage established networks to expand capacity and training.
- Provide support and incentives to established and develop new multicenter infrastructures that capitalize on standard of care procedures (opportunistic studies), innovative designs, with rigorous methodology.
- Studies should account for the physiologic complexity throughout pregnancy and lactation. Note also that these may be impacted by other health conditions, environmental conditions, social determinants
- Leverage advances in sampling techniques, bioanalytical techniques, multiplex assays, quantification of drug concentrations developed for work in pregnancy and lactation studies.



## Recommendations for Data

- Require studies to include plans for incident pregnancies to capture outcomes and add to available data
- Develop requirements and provide support for disease focused registries with mandates that facilitate input of pertinent data with easy, transparent access to obtain information in real time
- Recommend enhanced access and sharing of available data to provide information for pregnant and lactating women. Examples of available data include VA clinical database, DoD clinical database, federally funded studies, milk banks.
- Add P&L status to clinical trials, studies, data collections



# Recommendations to Increase Opportunities

- Encourage the use of numerous and innovative trial designs
- Facilitate longer award periods given needed duration for follow-up.
- Use PK/PD modeling and simulation to design protocols – identify dosage selection.
- Ensure trials are designed to appropriately capture the time dependency of physiologic changes in P&L, ideally having patients serving as own controls.



# Recommendations to Increase Opportunities

- Develop scalable programs for evidence-based therapies
- Recommend use of new methods to do research and disseminate information – crowd sourcing, digital / internet
- Prioritize the development of new tools and methods to assay medications in breastmilk targeted to utilize small volumes and are sensitive to detect minute quantities



## Regulatory/Legal and Policy Recommendations

- Rework the components of subpart B, although useful to assess the risk ratio they are vague and burdensome for the investigator
- Modify subpart B: Given the recognized autonomy of a pregnant woman, given the evolution of family structure, given that for a child only one parental signature is required for research to benefit the child (align with pediatric consenting), *46.204(e) in subpart B should be changed to maternal consent alone*
- Add in the option of “Minor increase over minimal risk” from subpart D to 36.046



# Regulatory/Legal and Policy Recommendations

- Develop incentives to engage industry and agencies and to facilitate collaboration, development of public private partnerships. Develop incentives for drug development for both on and off patent therapeutics and P&L exclusivity incentives for drug sponsors.
- Create a regulatory framework for evaluating medication use in pregnant and lactating women.
- Limit the legal liability and ethical challenges for physician scientists, researchers, and industry for P&L research
- Create the presumption of inclusion of pregnant and lactating women in clinical research. Removing pregnant women as an example of a vulnerable population in the common rule *shifts to a presumption of inclusion*. Investigators must justify exclusion in their study design
- Require that lactation status be collected as part of every study design
- Facilitate the ability for investigators to work in P&L therapeutic studies; facilitate regulatory issues, funding, IRB review





# Regulatory/Legal and Policy Recommendations

Need things to happen before can address these fully

Need  
liability  
dealt with  
for these

- Recommend P&L studies to be performed for new molecular entities if relevant to the P&L communities
- Recommend that for all new product development, pregnant and lactating women should not be post-market evaluation
- Develop best practices in interpretation of benefit for investigators; provide examples to allow them to cite an interpretation benefit
- Develop best practices in interpretation of risk for investigators; provide examples to allow them to cite an interpretation of risk



## Recommendations to Increase Awareness

- Highlight the importance of research on therapies in pregnancy and lactation including impact of not taking the medication during pregnancy and lactation as well as the impact of not breastfeeding on mother and child
- Develop evidence based tools for public to understand risk, evidence, and lack of evidence



# Feedback and Input

- Format
- Corrections / additions / suggestions?
- Anything missing?

Work in progress – finalized document ~September 2018



# Incentives Discussion

- Funding for investigators to do this work
- Increasing feasibility of what needs to be done
- Disease specific registries
- Pregnancy:
  - Industry: reduce risk liability
    - Example vaccination compensation program
  - Clinician liability
  - Patent exclusivity (6 month extension) in peds – not likely to be a value in obstetrical studies –
    - has to be of public health benefit for children, needs to be completed and fairly respond to the written request
  - Written request for P&L is different between peds indications and P&L
    - Written request for pregnancy specific diseases
  - Liability concern is different for new entities vs drugs in use
  - Do we need to get the label changed? Would this limit industry liability?
- Lactation