

Working Group #1: Research and Training Report August 23, 2019

Co-Chairs: Andrew Bremer and Victoria Pemberton





Working Group 1: Research/Training

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Research and Training Recommendations

- 2. Increase the quantity, quality, and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women.
- 3. Expand the workforce of clinicians and research investigators with expertise in obstetric and lactation pharmacology and therapeutics.
- 8. Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the NIH BPCA as a model.
- 11. Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women.



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2. Increase research quantity, quality, and timeliness

Some Factors to Consider in Implementation

- Wide variety and large number of stakeholders
- Detailed knowledge and sophisticated knowledge of context needed to help agencies, industry, academic researchers become more comfortable with research on pregnant women and lactating women
 - Understand impact of untreated disease on mother and fetus
 - At every level – regulator, industry, researcher, clinician – understand that without knowledge, all the risk and responsibility rests with the patient
 - Understand context in which medication will be used
- Full arc of research needed – mechanistic, PK/PD, dosing, formulation, clinical trials and more
- Identify, encourage champions



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Increase funding for pregnancy and lactation research
- Develop framework to prioritize recommendations
 - What types of research might be cheaper and quicker to do (lactation)
 - What types of research is most lacking (lactation)
 - Return on investment
 - Difficulty of research
- Increase data sharing – allow others researchers to use data gathered within networks, including biospecimens.
 - Sub-studies of current trials
 - Standardization, archiving, data quality can be expensive
 - May be best done prospectively



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Support public-private partnerships with industry, to provide industry funding for studies within research networks
- Bring in philanthropic organizations as partners – BMGF, e.g.
- Leverage research results for quality improvement efforts within health systems, and thus incentivize clinical centers to enroll patients in research to decrease costs. Collaborate with CMS
- Collaborate, interact with European agencies and industry partners
- Facilitate access to clinical research networks so a wider variety of researchers, including junior investigators and industry partners, can work with the established networks



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Consider mechanisms to fund and facilitate innovative strategies and alternative study designs (including, but not limited to, clinical trials)
 - Comparative effectiveness research
 - Multi-site and/or multi-country trials with surrogate endpoints that would ultimately be combined into a prospective meta-analysis for the definitive outcome
 - Pragmatic trial designs
 - Harmonizing methods, common data elements, outcome measures across studies
 - Other methods (to be further discussed later)
- Because pregnant women are already taking prescription drugs, opportunistic studies will be important
- Improve incentives for clinical staff and health systems to participate in clinical research recruitment



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Collaborate with researchers, EHR companies, data warehouse companies, and other purveyors of big data
 - to add people to clinical registries by pulling data from the EHR
 - to identify people eligible for research studies
 - to develop best practices for EHR-based studies
- Advocate and incentivize the CTSA's to include pregnancy research and develop mentorship in pregnancy- and lactation-related research



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Improve the IND process for pregnancy-related research
 - Requirements for long neonatal follow-up can be a barrier
 - Accept Bayesian, adaptive research designs, and other alternative approaches
 - Pregnancy-related studies may face more difficulty in getting approval
 - PERC review committee within FDA has been helpful in getting consistency in regulatory input in pediatrics
 - Clarify when placebo comparison is required (sometimes guidance for specific diseases specifies placebo even if off-label is standard of care)



2. Increase research quantity, quality, and timeliness

Potential elements of an implementation plan

- Institutions with strong regulatory infrastructure support mechanisms tend to be more successful in moving studies forward
- Improve regulatory support for researchers by:
 - Educating IRBs about research on pregnant and lactating women
 - Exploring industry-academic partnerships
- Regulatory support is needed through the entire life cycle of the product
- This working group could outline a model for what are the key components of these support mechanisms, and identify best practices for both initial regulatory steps and through approval and post-marketing processes



3. Expand the Workforce

Existing Resources to Build On

- Most existing resources include, but do not focus on, MFM
- Clinical pharmacology certification programs to help people w clinical expertise and/or pharmacology get training, without as large a time commitment as traditional training
- Dual fellowship program through NIH T32, leads to a K23 application
- Current NIH training and career development programs—expand?
 - T32
 - Individual K, including K99/R00
 - CTSA training
 - K12
- Working closely with ACCP (P=Pharmacology) should be helpful
- Industry partners may also provide short-term fellowship opportunities (one example involved 50-50 salary sharing)



3. Expand the workforce

Barriers to Implementation

- Salary limitations, protected times, and malpractice insurance costs that are needed to support individual K awardees can be a barrier for institutional support for Ks – institutions lose money on K awards.
- It does not help to train people if they do not have a solid well-supported career path and ability to do the clinical trials after they are done with training
- The first few years of establishing a career are very difficult
- Availability of patient populations can be a challenge
- Research funding stream may not be as reliable in perinatal or pediatric compared to other research areas, so people may be diverted to other areas
- Resources need to be patched together to support training and to support young scientists after training



3. Expand the workforce

Potential elements of an implementation plan

- Adapt training and career development programs to the needs of the field
 - Consider K99/R00 targeted to pregnancy and lactation research
 - Allow OB-GYNs on K23s (clinical Ks) and K12s to move to 50 percent protected time, like surgeons have been allowed to do in the past
 - Consider new training mechanisms that are structured to meet the needs of the field – lower protected time requirements, assistance with malpractice insurance, etc.
- Consider providing dedicate training support within centers of excellence and current networks (MFMU, NRN, OPRU, IMPAACT, PHN, CTSA, GN, etc.)
- Expand MERIT awards and T32s for pregnancy- and lactation-related research
- Loan repayment programs targeted at obstetric and perinatal research could be helpful
- Shorter-term internships within clinical centers and networks, CTSA, FDA, and industry



3. Expand the workforce

Potential elements of an implementation plan

- Collaborate with industry to bring in industry mentors for trainees
- Support for mentors – via R37, K24, existing clinical networks
- Support to help mentees identify potential mentors – a “college of mentors”
- Reconsider criteria for successful T32 grants, including acknowledging value of quality improvement and other research
- Improve incentives for clinical staff to participate in clinical research recruitment
- Provide more training for mentors and trainees on FDA processes
 - Expand FDA IPAs for ob-gyns, perinatologists, clinical pharmacologists to work at FDA during their research careers
 - Expand FDA and NIH clinical investigator in-person workshops and/or webinars for ob-gyn researchers



3. Expand the workforce

Potential elements of an implementation plan

- Work with accreditation bodies, credentialing groups, professional societies, board certification organizations, hospital groups, payers, and continuing education organizations to recommend changes to requirements to help train health professionals about clinical research and pharmacology related to pregnancy and lactation.
- Create incentives by providing easy, online training opportunities.



Questions?