



## **Oral Comments for Meeting of the Task Force on Research Specific to Pregnant and Lactating Women**

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The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network is a global collaboration of investigators, institutions, community representatives and other partners organized for the purpose of evaluating interventions to treat and prevent HIV infection and its consequences in pregnant/postpartum women, infants, children, and adolescents through the conduct of high quality clinical trials. The Network is funded by the National Institute of Allergy and Infectious Diseases (NIAID), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH).

The Network's mission is population-oriented and focused specifically on pregnant and postpartum women, infants, children and youth. Our research agenda includes evaluation of:

- new and existing anti-HIV drugs and formulations;
- novel approaches for addressing tuberculosis (TB) in HIV-infected or at-risk populations;
- therapeutic interventions for achieving HIV "cure" (sustained viral remission);
- biomedical and behavioral interventions to prevent HIV acquisition and transmission;
- immunogenicity, safety and efficacy of high priority vaccines; and
- methods to prevent and manage comorbidities and complications of HIV infection and its treatment.

The Network has over two decades of experience conducting clinical trials in pregnant and postpartum women and a strong US domestic and international presence. We currently work with 52 NIAID- and NICHD-funded sites located in US (22) and 13 other countries (30). These sites bring extensive clinical trials capacity and a wealth of experience for implementation of the Network's scientific agenda. The IMPAACT Network has an excellent track record of productivity, with data from our studies informing and shaping public health policy and guidelines in the US and worldwide. Our research agenda draws upon the expertise and experience of leading scientists and investigators from around the world and benefits from strong collaborative partnerships with other research organizations, private industry and other groups. In pursuit of the highest priority science for our key populations, we invite investigators from inside and outside of the network to submit new study proposals at any time, and our work is guided and supported by a strong and active Community Advisory Board.

While the network is well known for studying how to prevent mother-to-child transmission (PMTCT) of HIV, our research agenda and expertise stretch far beyond PMTCT. We are experienced clinical researchers with a passion for solving problems in our specific populations of interest. We have learned from our experiences in these studies that, when properly informed, pregnant and breast-feeding women are more than willing to participate clinical research and can successfully be enrolled and followed in studies with a range of designs.

An example of the Network's contributions is our master study for evaluation of pharmacokinetics (PK) and safety of licensed ARVs for HIV and TB drugs in pregnant and postpartum women. This trial has evaluated over 15 agents to date and provided essential and previously non-existent information on appropriate dosing of these therapies across the trimesters and post-partum. Incorrect dosing of TB therapies during pregnancy puts both mothers and infants at risk of dying from TB, hence the evaluation of these drugs as well. This unique trial also includes the opportunity to study the "wash-out" and post-delivery PK of these HIV and TB therapies in newborn infants, recognizing that both mothers and infants are persons in their own right - not simply extensions of each other. This templated study, led by experts in obstetrics, pharmacokinetics and pharmacodynamics, has broad applicability to other licensed treatments that are commonly used in pregnant/postpartum women despite the absence of PK data and knowledge of appropriate dosing levels in these populations.

We also have enormous strength in emerging infections. For example, at the height of the H1N1 epidemic, our Network developed, fielded and completely enrolled a study of a novel H1N1 vaccine in HIV+ pregnant women within three months. This study evaluated both a novel type and dose of influenza vaccine and demonstrated both safety and immunogenicity, making it the reference for all new influenza vaccines in pregnant (and HIV+) women.

The Network knows when to challenge 'status quo' as seen with our nearly completed study of isoniazid (INH) in pregnant women at high risk for TB. The existing guidelines recommend administering a standard adult dose of INH to pregnant women at risk for TB, despite a paucity of data on safety and effectiveness of this approach in this population. To address this gap, the IMPAACT Network developed a study into which over 900 pregnant women at risk for TB were rapidly enrolled (ahead of schedule). The results will be presented soon after the study and analysis are completed next year.

Investigators, funding agencies and even ethics committees/institutional review boards must let go of the mind-set that pregnant women or even women who could become pregnant should automatically be excluded from studies of novel therapies. The IMPAACT Network's track record demonstrates that such studies - designed specifically for pregnant and postpartum women - can be implemented in a safe, timely and effective manner.

The IMPAACT Network is an existing, unique and valuable resource for which funding should be continued. In fact, our expertise and infrastructure for studies in pregnant and postpartum women and their children can and should be utilized to study other pathogens in these important but often neglected populations.