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Safety Monitoring in Immunization in Pregnancy Efforts at NIH

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Objective: Review safety monitoring in maternal immunization studies sponsored by DMID/NIH, and how these efforts may align with the tools developed by the GAIA consortium.

Abstract: Key knowledge gaps identified during DMID sponsored studies were addressed by subject matter experts during consensus-building conferences. The output from these discussions were toxicity grading tables for laboratory tests, and adverse events grading tables of pregnancy and neonatal outcomes.

Although overlapping in the topics of interest, DMID and GAIA efforts differ in the scope. DMID Tables do not provide ontology of terms and definitions, or the assessment of diagnostic certainty, that is especially relevant for studies in MLICs. Standardized definitions and tools to evaluate and report 21 most critical adverse events in pregnancy and neonatal period are provided by the GAIA consortium. Thus, GAIA and NIH efforts are complementary and if combined could improve quality of data generated in clinical trials, harmonize reporting and facilitate meta-analyses across multiple studies.

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NVAC Initiatives

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Objective: Discuss updates on recent National Vaccine Advisory Committee (NVAC) initiatives regarding maternal immunization

Abstract: NVAC is working to identify barriers to and opportunities for developing vaccines for pregnant women and make recommendations to overcome these barriers. There are several current scientific and structural barriers for developing vaccines and countermeasures for pregnant women.¹

One barrier is a lack of a broadly accepted ethical framework for guiding clinical research in pregnancy. Therefore, IRBs often resort to categorizing most intervention research in pregnancy as high risk, often without a balanced consideration of the risks of not performing the research. Hence, there is a need for development and articulation of a pregnancy specific ethical framework that can offer guidance to investigators and IRBs.

Pregnancy is a physiologically dynamic state. The immune profile of a pregnant woman is responsive to the changing levels of sex hormones, and evolves through the course of pregnancy.² However, the current knowledge base for vaccine response draws from observational studies mostly conducted in the latter part of pregnancy, with limited data available from the first and early second trimester. On the other hand, clinical, practical and public health considerations require that vaccine use not be restricted to advanced gestational age.

Robust safety evaluation is a cornerstone of any vaccine development and deployment program. While there has been increased attention on evaluation of safety of immunization in pregnancy, barriers remain. For example, a review commissioned by the WHO highlighted that there is a lack of standard definitions of outcomes, and standards for measurement of these outcomes, relevant to evaluation of vaccines in pregnancy.³ This lack of standardization poses a challenge for conduct of clinical trials, generalizability of safety data, and the merging of large safety datasets. This last point is critical because large multi-location datasets would optimize the evaluation of rare but clinically important outcomes, such as microcephaly.

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Maternal Immunization: Perspective of PATH

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Objective: Discuss opportunities and challenges in the implementation of maternal immunization programs in limited-resource settings.

Abstract: The greatest burden of severe influenza and pertussis in children occurs during the first few months of life, yet vaccines against these diseases are not effective at that age. Immunization of pregnant women against both influenza and pertussis, however, has been shown to be effective in protecting infants.¹⁻² These interventions have therefore been recommended by global policy makers³⁻⁴, yet their adoption in most countries has been slow, particularly in low-resource settings. Major reasons for this include a lack of quality data regarding disease burden and the impact of the intervention, uncertainties regarding the programmatic feasibility, regulatory and legal constraints, and low levels of awareness. This presentation will discuss many of the opportunities and challenges for implementing maternal immunization programs in low-income countries, and current efforts to address them.

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