

# Advancing HIV Prevention Research in Pregnant and Lactating Populations (PLP): Priority Advocacy Objectives and Next Steps

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## Background

- Growing consensus around the ethical and public health imperative for the responsible inclusion of PLP in HIV research has gained critical momentum.
- Milestones include Ethics Guidance from the PHASES Working Group<sup>1</sup> and the 2021 WHO/IMPAACT/IAS Call to Action<sup>2</sup> to accelerate the study of new HIV drugs for pregnant and lactating populations, though much work to realize equitable study for PLP remains.
- To this end, AVAC, as part of the Coalition to Accelerate and Support Prevention Research (CASPR), and the PHASES Project convened a think tank in April 2022 to identify priority advocacy objectives, informed by consensus recommendations, and develop an action plan to accelerate HIV prevention research with PLP.

## Think Tank Approach

- Significant stakeholder engagement guided the development of the think tank, in alignment with the Good Participatory Practice Guidelines (GPP) – including consultations with key stakeholders and a pre-meeting (co-convened with Pangaea Zimbabwe Aids Trust) with civil society advocates and former trial participants.
- 63 global stakeholders, including researchers, product developers, former trial participants, civil society, regulators, and funders attended a half-day virtual workshop which utilized facilitated planning sessions to identify advocacy and action priorities.
- Following the workshop, the planning team distilled draft priority goals from the discussion using the following criteria: 1) represents major theme identified as a priority by numerous participants; 2) goal adds to without replicating other ongoing efforts; and 3) perception that attainment of the goal would significantly advance the field.
- Objectives and action steps were informed by the think tank workshop, subsequent discussions with and feedback from think tank participants, and application of the Reproductive Justice framework to relevant emerging issues.
- Feedback and revisions to the Action Plan from think tank participants is ongoing in an iterative process.

## Action Plan

### Priority Goal 1: Advance responsible HIV prevention research in pregnant and lactating people (PLP) using a Reproductive Justice framework.

Reproductive Justice is the human right to maintain personal bodily autonomy, have children, not have children, and parent children in safe and healthy communities. Developed by a Black women's collective in 1994, Reproductive Justice elevates and centers needs, voices, lived experiences, and leadership of African and other Black and Brown women, trans and gender diverse people, and youth. Rooted in the human rights framework and the core principles of justice and dignity, Reproductive Justice emphasizes importance of access to evidence-based, comprehensive sexual and reproductive health care.<sup>3</sup>

#### ➤ Center PLP in all efforts to set and advance a HIV prevention research agenda responsive to their needs.

##### Action Steps:

- Organizations responsible for setting HIV prevention research priorities, including the World Health Organization (WHO), funders, product developers and HIV prevention research organizations, should meaningfully engage and center PLP and the organizations that work with and for ensuring the rights of these populations in setting HIV prevention research priorities and elevate the importance of evidence on maternal and fetal safety, dosing, access, feasibility and acceptability for PLP.
- Civil society, researchers & advocates, with support of funders, should identify, co-develop and disseminate resources and tools to strengthen, inform, and support the meaningful participation of PLP, as well as organizations that work with and for ensuring their rights, in HIV prevention research agenda setting, and should advocate for their meaningful engagement in the process.
- Understanding that evidence gaps surrounding HIV prevention in pregnancy are further magnified for certain marginalized groups including adolescents and trans and gender non-binary people, these populations and the organizations that work with and for them should be intentionally engaged and actively supported to participate in setting a HIV prevention research agenda responsive to the needs of these marginalized groups.

#### ➤ Join together with key allies addressing intersecting oppressions and identify and develop shared goals to advance equity and reproductive justice.

##### Action steps:

- Researchers, civil society, and advocates should engage with other stakeholder groups addressing intersecting oppressions to advance the goals of this action plan and develop HIV prevention research with PLP that is responsive to these issues.
- Researchers, civil society and advocates committed to promoting the health and wellbeing of PLP should join allies, amplifying efforts to address intersecting issues including racial and gender-based disparities as well as other diseases (e.g., malaria, cancer, tuberculosis) that differentially impact these populations.

*"Without being able to bring in an intersectional approach, without being able to think of all these different lived experiences combined with the changes in how we engage with community...we wouldn't be having this conversation quite frankly... there has to be an emphasis on centering blackness in this conversation." - Think tank participant*

#### ➤ Identify potential challenges to and solutions for advancing equitable clinical research with PLP in restrictive reproductive health policy environments.

##### Action steps:

- Researchers and civil society, with the support of funders and in partnership with other key stakeholders and allies, should conduct legal, ethical and policy analyses to characterize potential implications of rescinding the US constitutional right to abortion on conduct of global HIV prevention research with PLP and identify approaches to advance timely research in this context.
- Researchers, civil society and advocates should widely disseminate these findings across stakeholder groups and support the implementation of recommendations.

#### ➤ Ensure that contraception requirements for pre-licensure trials are sensitive to actual fetal risk, as set out in the WHO/IMPAACT/IAS Call to Action<sup>2</sup>, and incorporate evidence-based contraceptive counseling when indicated.

##### Action Steps:

- Product developers should remove contraception requirements in pre-licensure trials once non-clinical reproductive toxicity data are available with no negative signals, and dosing for non-pregnant people is determined, as set out in the WHO/IMPAACT/IAS Call to Action.
- When contraception requirements are indicated, product developers should provide evidence-based contraceptive counseling.
- HIV prevention trial sites should actively facilitate and strongly consider providing access to sexual and reproductive health services that promote women's health and autonomy, including contraceptive counseling, even when contraception requirements are not warranted.

### Priority Goal 2: Engage stakeholders in an early, sustained, and meaningful way in the design and conduct of biomedical HIV prevention trials tailored to the distinctive complexities of research with PLP.

Early, sustained, and meaningful stakeholder engagement and participatory practices are critical to success and help shape ethical research responsive to community needs. Pregnancy introduces unique cultural, social, ethical and scientific complexities to HIV prevention research, necessitating approaches that specifically attend to these complexities.

## Priority Goal 2, continued

### ➤ Develop and disseminate Good Participatory Practice (GPP) best practices specific to biomedical HIV prevention research with PLP in all their diversities.

#### Action steps:

- AVAC will lead collaborative development of GPP best practices tailored to biomedical HIV prevention trials with PLP, which should include an emphasis on:
  - Developing research literacy specific to biomedical HIV prevention studies that include PLP among PLP, their communities, extended family members, and other influential stakeholders.
  - Early, meaningful and sustained community engagement and participatory practices, with attention to the involvement of PLP, their extended family members, and other influential stakeholders in trial advisory mechanisms.
- Stakeholder groups, including sexual and reproductive health and HIV advocates, WHO, and researchers, should leverage existing platforms and networks for wide dissemination of GPP best practices specific to PLP and integrate them into existing GPP trainings.

*I think one of the priority issues is improving literacy around pregnant and breastfeeding populations in research. And this literacy is two pronged – firstly, targeting the pregnant and breastfeeding populations themselves and targeting their influencers... (W)hen a person is pregnant, especially in our African context, every family member has a stake in what you do. - Think tank participant*

### ➤ Robust implementation of GPP best practices specific to biomedical HIV prevention research with PLP.

#### Action steps:

- Funders, sponsors and implementers of HIV biomedical research robustly implement GPP best practices in the design and conduct of biomedical HIV prevention trials with PLP, including:
  - Research literacy specific to biomedical HIV prevention studies that include PLP is developed among PLP, their communities, extended family members, and other influential stakeholders.
  - Communities are meaningfully engaged throughout the design and conduct of trials utilizing approaches that attend to the distinctive complexities of biomedical HIV prevention research with PLP. This engagement will include the involvement of PLP, their extended family members, and other influential stakeholders in trial advisory mechanisms.

### Priority Goal 3: Develop and harmonize regulatory frameworks and processes that promote the responsible generation of data specific to PLP for new therapeutics.

Regulatory frameworks across jurisdictions that are harmonized to protect PLP through responsible research have the potential to be pivotal catalysts for advancing the evidence base. The global evolution of regulations around pediatric-specific evidence for drug development holds important lessons and examples of successful approaches to generating needed data for a historically excluded group.

### ➤ Incentivize and/or require the generation of data specific to PLP for approval of new therapeutics.

#### Action steps

- Advocates should identify and coordinate with key stakeholders to encourage national governments, especially in areas with high HIV burden and/or outsized global influence, to bolster the ability of drug regulatory agencies to incentivize and/or require the generation of data specific to PLP as a component of applications for approval of new therapeutics.

*"Industry is highly regulated, and if there is a clear protocol, clear guidance, it makes it a lot easier for sponsors to innovate by following guidance." - Think tank participant*

### ➤ Accelerate the ethical inclusion of PLP in research and generate PLP-specific data as early as possible in product development, as set out in the PHASES Guidance<sup>1</sup> and the WHO/IMPAACT/IAS Call to Action framework<sup>2</sup> through harmonized regulatory approaches.

#### Action steps

- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), African Medicines Regulatory Harmonisation (AMRH), and other drug regulatory harmonization organizations should be encouraged to develop guidelines for the responsible inclusion of PLP in pre-licensure drug development trials.
- WHO should utilize their convening power to advance the adoption of harmonized regulatory frameworks by regulatory agencies, with particular attention to promoting the inclusive involvement of national and regional regulatory bodies in areas with high HIV burden.

### Priority Goal 4: Ensure sound ethics review processes that promote the responsible inclusion of PLP, including adolescent girls and young women, in biomedical HIV prevention research.

Ethics review of protocols is intended to ensure that principles and practices for responsible human participants research are followed. However, this process is not without considerable challenges – e.g., guidelines may be conflicting or unclear; and the broad scope of research IRB/RECs are often asked to review may make it challenging to have familiarity with all applicable guidelines for any specific context, including around the inclusion of PLP.

### ➤ Create and disseminate resources to support investigators to develop protocols that facilitate the responsible inclusion of PLP in biomedical HIV prevention research.

#### Action Steps:

- The HIV AIDS Vaccines Ethics Group (HAVEG, UKZN) will collate the current ethics recommendations for PLP inclusion, as set out in leading international ethics guidelines.
- HAVEG, AVAC/CASPR and PHASES will convene a PLP ethics review working group including IRB/REC members, researchers, ethicists and PLP to consider the implications for researchers drafting protocols and to develop a user-friendly tool to help them proactively incorporate ethics recommendations in protocol development. The tool will be reviewed and updated on an ongoing basis.
- The working group, stakeholders and allies will widely disseminate the tool through existing platforms, networks, and listservs.

*"Clinical trials compete for attention with other studies, and .. pregnant person enrollment likely competes for attention with other ethics issues. A tool might help both parties affirm that protocols resonate with current ethics recommendations." - Think tank participant*

### ➤ Develop and disseminate resources to support REC/IRB members to review protocols and assess if proposed approaches resonate with current ethics standards for the inclusion of PLP in biomedical HIV prevention research.

#### Action Steps:

- The PLP ethics review working group will consider the implications of current leading ethics recommendations around PLP inclusion for RECs/IRBs reviewing protocols and develop a user-friendly tool to assist REC/IRB members in conducting reviews and developing constructive, guidance-informed responses. The tool will be reviewed and updated on an ongoing basis.
- Working group members, stakeholders and allies will widely disseminate the tool through existing platforms, networks, and listservs.

## Next Steps

- Further feedback from think tank participants is being solicited and integrated.
- Final Action Plan will be broadly disseminated through think tank participants' networks and to key allies addressing intersecting oppressions.
- AVAC and PHASES will engage think tank participants and other stakeholders to implement action steps.
- AVAC will establish a process to monitor and support action plan implementation and ongoing engagement.

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<sup>1</sup>Lyerly AD, Beigi R, Bekker L-G, et al. Ending the evidence gap for pregnancy, HIV and co-infections: ethics guidance from the PHASES project. J Int AIDS Soc. 2021;24(12):e25846.

<sup>2</sup>Research for informed choices: Accelerating the study of new drugs for HIV in pregnant and breastfeeding women. A call to action. WHO, IMPAACT, & IAS. December 2021.

<sup>3</sup>Ross, L., & Solinger, R. (2017). Reproductive justice: An introduction, University of California Press.

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