Understanding the social and ethical implications of Human Infection Studies in Kenya: A programme of work for the KWTRP

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Outline

• Background
• Aims and objectives
• Approach and Overall strategy
• Ongoing social science sub-study and preliminary emerging issues
• Future areas of focus in upcoming studies
• Collaborators/networks and acknowledgements

Understanding the social and ethical implications of HIS in Kenya
Background: Features of HIS/CHIMS

- **Deliberate infection** of healthy volunteers

- **Well-characterised** strain of infectious agent or disease-causing micro-organism at a **controlled** dose and environment, and by a **specific** route (Gordon et al. 2017)

- Insight into **disease pathogenesis** & **potential** to rapidly test clinical **proof-of-concept** of vaccine candidates (Giersing et al. 2019)

- Controlled Human Malaria Infection (CHMI studies) are important and **potentially cost-effective tool** in the control and elimination of malaria (Coffeng et al 2017; Collins et al 2018)
Background: some key ethical issues in HIS (Bambery et al. 2015; Emerson 2018; Gordon et al. 2017)

• **Complex study to explain**- may attract those with higher education

• Inadequate guidance on **compensation mechanisms**

• **Social value** of the research – current guidelines inadequate, should this be more immediate?

• Involvement of **paediatrics in HIS**
Background: HIS in Kenya

• Malaria and shigella infection remain public health problems in Kenya and other LMICs, disproportionately affecting children.

• The KEMRI-Wellcome Trust Research Programme (KWTRP) has developed a platform of malaria HIS, aiming to accelerate potential vaccine and drug development.

• Need to develop evidence to strengthen HIS ethical review and regulatory capacity; and generate ethical discourse and understanding of HIS across different stakeholders - in Kenya and other LMICs.

• A number of HIS are ongoing or planned at the KWTRP in Kilifi.
The current malaria challenge study at KWTRP

- **Initial feasibility study** conducted in Nairobi in 2012; (Hodgson et al. 2014)

- Current study on Semi-Immune Kenyan Adults (CHMI SIKA) - to assess human immunity to *Plasmodium falciparum* via DVI of sporozoites (Kapulu et al. 2018)

- **Social science study** embedded in some earlier phases (*Njue et al. 2018; and Jao et al. – manuscript submitted; Chi et al. – data analysis ongoing*)

- Ongoing community engagement activities have characterized the implemented malaria HIS.
Understanding the social and ethical implications of HIS in Kenya
# Background: Ongoing and anticipated studies

<table>
<thead>
<tr>
<th>Study features</th>
<th>CHMI-SIKA*</th>
<th>CHMI-Transmod</th>
<th>CHMI-Vac</th>
<th>Shigella HIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment sites</td>
<td>Kilifi &amp; Ahero</td>
<td>Kilifi &amp; Ahero</td>
<td>Kilifi</td>
<td>Kilifi</td>
</tr>
<tr>
<td>Number of participants</td>
<td>200</td>
<td>104</td>
<td>64</td>
<td>120</td>
</tr>
<tr>
<td>Dose of Challenge agent</td>
<td>3,200 (DVI)</td>
<td>6,400; 12,800, and 25,600 (DVI)</td>
<td>3,200 (DVI) or 22,500 (ID)</td>
<td>Dose escalation (oral)</td>
</tr>
<tr>
<td>Procedures</td>
<td>Injection of sporozoites</td>
<td>Dose escalation and verification, Sporozoite injection, sub-curative anti-malarial, &amp; mosquito feeding</td>
<td>Vaccination followed by malaria challenge</td>
<td>Dose finding &amp; verification, &amp; vaccine efficacy studies</td>
</tr>
<tr>
<td>Maximum length of in-patient stay</td>
<td>25 days</td>
<td>45 days</td>
<td>25 days</td>
<td>15 days</td>
</tr>
<tr>
<td>Means of infection</td>
<td>DVI</td>
<td>DVI</td>
<td>DVI or Intradermal</td>
<td>Oral</td>
</tr>
<tr>
<td>Direct therapeutic benefit</td>
<td>N/A</td>
<td>N/A</td>
<td>Possibility if vaccine(s) work</td>
<td>Possibility if vaccine(s) work</td>
</tr>
</tbody>
</table>

*Kapulu et al. 2018*
Aims and objectives

• Explore and analyse the social and ethical implications of HIS among stakeholders and to develop a framework for understanding social and ethical issues for HIS in LMICs

Specific Objectives:

1. Explore understanding, attitudes and experiences of a range of HIS stakeholders towards research based on a CHIM model

2. Describe practical and ethical issues raised by ethics review committees, policy makers, and relevant regulatory authorities in the review, approval and monitoring of CHIM studies

3. Identify and critically analyse social and ethical issues arising from conducting HIS at KWTRP (based on 1 & 2 above and research ethics literature (incl. ethics guidelines and guidance)
Approach: Methods and study participants

• **Empirical ethics** approach, using mixed methods in social science (cross-sectional surveys, observations, document review, individual and group interviews etc.) to understand ground realities and drawing on ethics literature and guidance to support analysis.

• **Target study participants**: HIS participants, HIS research teams, and RECs, RAs, community representatives and members, policy makers, health providers, engagement professionals etc.

• **Implementation plan**: For each HIS, a mini *study-specific* proposal will be developed from the main study proposal, taking into consideration the study design and implementation strategy.
Overall strategy

Within and across these varying HIS studies, using social science/mixed methods to explore multiple grounded perspectives around key issues over time to inform **practice and/or policy** AND **ethical analysis**

- Where compensation models differ, how is this perceived and what implications (for whom) in practice?
- Where differing periods of required residency involved, what difference does this make to experienced benefits, burdens and acceptability of the study?

For these questions, what are the implications in our and other similar settings for:
  - Understanding and balancing the nature of ethical issues
  - Policy/planning/implementation of HIS
Ongoing social science sub-study: CHMI-SIKA

Research questions

1. What are HIS participants’ experiences about participating and how has that shaped their perception about malaria HIS and HIS in general?

2. What is the impact of participation in HIS on participants’ significant others?

3. How was community engagement undertaken in the context of the malaria HIS and what lessons could be learned for future HIS?

- Based on 1 - 3 above and the research ethics literature (including ethics guidelines), to identify and critically analyse social and ethical issues arising from conducting HIS at the KWTRP

Social and ethical issues to explore:

- Deliberate infection in HIS
- Undue inducement, fair benefits (compensation)
- Understanding, consent, and autonomy
- Trust in the context of HIS
- Limit of risks to healthy participants in HIS
- Right to withdraw (RTW)
- Burdens/unintended outcomes in HIS
- Fair participant selection
Preliminary coding framework from ongoing study

- Understanding CHMI SIKA
- Deciding to participate (reasons/influences)
- Valuing ‘payment’ / Wanting to be in the study (extent to which payment was critical to participants motivation to join)
- Experiencing and understanding screening
- Being in study (experiences during and outside residential period)
- Since participation (Life after the study)
- Going forward/Improving participants experience
Issues of focus in upcoming HIS?

• Appropriate **models of compensation** for highly burdensome HIS

• **Markers of undue inducement**, and how can they be assessed in the context of HIS

• The **upper limit of risks and burdens** that participants in HIS should be exposed to

• Possible situations where a small probability of irreversible or long-term harm be acceptable in the context of HIS participation. How to weigh such risks against benefits.
Acknowledgements & Collaborators/networking

Collaborators/networks

• Global Health Bioethics Network (Univ. Of Oxford)
• HIC-Vac network –funded as part of 4 AAPs conducting/considering HIS (MORU, OUCRU, MLW and KWTRP)
• WHO framework on ethical considerations for HIS in LMIC – group lead by Katherine Littler, Seema Shah/Monash team/WT etc

Acknowledgments

• Study participants
• Participating communities
• HIS research team at KWTRP
• The community engagement team at KWTRP
• Colleagues - Dpt. of HSRE at KWTRP
• Ahero Clinical Trial Unit (ACTU)
• The Wellcome Trust