HUTH Sponsor Oversight Group (SOG): Terms of Reference September 2019

1. BACKGROUND

The Sponsor Oversight Group (SOG) is being established in response to the routine MHRA GCP inspection conducted in March 2018. The SOG remit will currently focus on HUTH Sponsored CTIMPs only. Future expansion of the Terms of Reference may occur in line with a requirement to provide formal oversight structures for high-risk HUTH Sponsored non-CTIMPs.

The role of this SOG will be to provide expertise to ensure the documented oversight of these studies, monitor the conduct and progress of these trials, ensure that the protocol is adhered to, take appropriate action to safeguard participants and ensure the quality of the trial data. Furthermore, the SOG will act as decision making body and escalation route for the Trust (as Sponsor) whilst documenting, assessing and reviewing the ongoing risk assessment of all HUTH Sponsored CTIMPs.

2. TERMS OF REFERENCE

- To evaluate, consider and provide approval decisions for the Trust to act as Sponsor for CTIMPs. To consider instances where the Trust would not be in a position to act as a study Sponsor. To support the decision to withdraw Sponsorship if required.
- To receive and contribute to the Sponsor's ongoing risk assessment of each trial. To ensure this is documented and appropriate corresponding action is taken by the Trust.
- To review and approve the Sponsor Quality Systems (SOPs, Policies, working instructions etc.). To co-opt expertise as required.
- To assess and review ongoing 3rd party vendor risk assessments conducted by the Sponsor (i.e. UoH labs and CTUs – including vendor QA systems). Endorsing 3rd party vendors and highlighting and escalating any issues with these vendors as they arise.
- To escalate any delivery, management, oversight and non-compliance issues of concern to the Sponsor, specifically where the issue could compromise patient safety or the integrity of the trial or quality of the trial data.
- To monitor patient safety in order to protect the rights, safety and well-being of trial patients.
- To assess the safety and efficacy of the interventions during the trials.
- To monitor and ensure the quality of the trial data (including ongoing validation of computer systems used).
- To monitor the conduct of the clinical trials (CTIMPs), in particular the timely progress of the trial and adherence to the protocol. To provide a general interim review of the trial's progress (tailored to the needs of the trial and information supplied – i.e. toxicity data, SAEs, recruitment figures, protocol deviations, monitoring reports, external data).
- To review at regular intervals relevant information from other sources (e.g. related trials).
- To provide clinical and professional advice relating to trial design, where relevant.

- To advise on and approve substantial amendments to the trial design during the course of the trial, where relevant (document and agree Sponsor substantiality decisions).
- To provide a robust audit trail of decisions to escalate issues in HUTH-sponsored studies (as per past MHRA Inspection recommendations) including but not exhaustively:
    - Dose escalation in HUTH CTIMP Studies
    - Protocol Deviations
    - Safety Issues
    - QA Department capacity issues
- To ensure that the results of the trials are adequately disseminated (SOG to receive reports) and that due consideration is given to the implementation of the results into clinical practice.
- To agree to any relevant statistical analysis plans (e.g. DMC plans, interim analysis plans).
- To consider interim safety and efficacy data (if deemed appropriate) from interim analyses and relevant information from other sources. Any recommendations relating to patient safety may be subject to expedited reporting to the MHRA and Ethics Committee.
- To review safety data to look for any emerging trends, including increases in severity or frequency of expected Serious Adverse Reactions/Events such that they would require expedited reporting to the MHRA and Ethics Committee.
- To aid the implementation of the Trust's MHRA GCP Inspection Action Plan (where applicable)
- To agree Sponsor monitoring plans and receive subsequent escalation actions.
- To agree an audit programme (3rd party vendors and independent assessment of Trust QA) and receive subsequent escalation actions.
- Specifically the SOG will be responsible for:
    - Pharmacovigilance compliance and safety reporting/trend analysis oversight.
    - Monitoring of screening, recruitment, consent, treatment and follow-up procedures, safety, data quality and compliance with UK Clinical Trials Regulations and GCP.
    - Identifying and addressing concerns about the safety or efficacy of one or more of the treatment arms.
    - Informing the Sponsor of the trial where the results show;
        - a benefit of one treatment arm over another that is so large, and precise, that it is likely to convince a broad range of clinicians to change practice or
        - it is evident that if the trial continued it would fail to show a clear benefit for any treatment arm or
        - where accrual is so low that it is unlikely that a sufficient number of patients would be recruited to provide meaningful results.
- To produce minutes of each SOG meeting with points discussed and actions decided, to review the minutes of at the next meeting and to file a copy in the Trial Master File.

3. MEMBERSHIP

Membership of the SOG should reflect the disciplines and clinical specialties necessary to interpret the data from the clinical study and to fully evaluate subject safety. It should include representatives from the following groups/directorates:

- SOG Chair (Director of R&D not involved in HUTH Sponsored CTIMPs)
- Deputy Chair
- Sponsor representative (R&D Manager, QA Manager or Clinical Trial Monitor)
- UoH and HHTU representative(s)
- Chief Investigators (UoH Academic Lead and NHS Lead)
- Clinical Trials Pharmacy representative(s)
- Clinical Trial Co-ordinator / Trial Manager
- A statistician (if applicable)
- Research Nurse (if applicable)
- Lay member(s)
- Other support services co-opted as required.
- IT Support and representation co-opted as required.

4. QUORUM

Four members on the SOG including the Chair or Deputy Chair, a representative from the Sponsor (R&D) and a Chief Investigator.

5. FREQUENCY OF MEETINGS

It is proposed that the SOG meets every 2 months with the provision for extraordinary meetings to be called at short notice as required. Escalation of Sponsorship decisions, oversight and GCP non-compliance issues to the SOG to happened virtually via email group as required.

6. REPORTING ARRANGEMENTS

Reports to R&D Committee (minutes to be sent).

7. EFFECTIVENESS

The effectiveness of the terms of reference will be assessed annually by the SOG.

8. ACTION

- Circulate this ToR to all relevant personnel requesting any feedback be sent to the R&D Manager.

9. RECOMMENDATION

The SOG are asked to endorse the outlined SOG Terms of Reference.