



# KENYA MEDICAL RESEARCH INSTITUTE

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**KEMRI/RES/7/3/1**

**March 15, 2018**

**TO: PROF. FEIKO TER KUILE, DR. TITUS KWAMABAI AND DR. SIMON KARIUKI,  
PRINCIPAL INVESTIGATORS.**

**THRO: THE DIRECTOR, CGHR,  
KISUMU.**

Dear Sir (s),

**RE: SSC 2965 (AMENDMENT 3): MALARIA CHEMOPREVENTION WITH MONTHLY TREATMENT WITH DIHYDROARTEMISIN-PIPERAQUINE FOR THE POST DISCHARGE MANAGEMENT OF SEVERE ANAEMIA IN CHILDREN AGED LESS THAN 5 YEARS IN UGANDA AND KENYA: A 3-YEAR, MULTI-CENTER PARALLEL-GROUP, TWO ARM RANDOMIZED PLACEBO CONTROLLED SUPERIORITY TRIAL.**

This is to inform you that at the 273<sup>rd</sup> Committee A meeting of the KEMRI Scientific and Ethics Review Unit (SERU) held on **March 13 2018**, the request for amendment for the above referenced research proposal was discussed.

The SERU Committee acknowledges receipt of the following documents:

1. PMC 2965 SERU Amendment form v4.0 dated 6<sup>th</sup> February 2018
2. PMC protocol V4.0 dated 06 Feb 2018 clean and tracked version showing changes in BOLD relative to v3.0 dated 28<sup>th</sup> October 2016

The Committee noted the following amendment;

1. Page 10: Target sample size Revised to 1040 from original: 2212.
2. Page 15: **Narrative protocol summary Sample size:**  
Sample size revised from 1106 to 520 children per arm and 2212 to 1040 for total children.
3. Page 22: **Design and methodology** -Overview study design  
Sample size revised from 2212 to 1040 children; the number per study arm changed from 1106 to 520 less than 5 years of age who have been admitted for all cause severe anaemia and have completed the standard in-hospital treatment.

**4. Page 41: Sample Size**

The following text has been added

*8.8.1.1. Sample size re-estimation*

*Following recommendations from the DMEC and TSC, a blinded interim sample size re-estimation was conducted to take the lower than expected rate of loss to follow-up into account and the higher than expected pooled event rate of the composite primary endpoint (death or All-cause readmission) across both arms. This was favor (I over an*

*interim analysis, because the available funding did not allow an extension: 1' the recruitment period, even if the results of any Interim analysis would suggest this was required.*

*The revised sample size calculations were conducted in PASS (v15) software using a test for the ratio of two Poisson rates. A total sample size of 1040 children (520 per arm) is required to detect a 25% reduction in the incidence of the composite primary outcome from 1,152 per 1000 child years (530 events per 1000 children during the 24 weeks from randomization at 2 weeks to the end of follow-up at 26 weeks) in the control arm to 864 per 1000 child years (398 per 1000 children over 24 weeks) in the intervention arm (power 80%,  $\alpha=0.05$ ), allowing for 10% loss to follow-up. The same sample size would also provide 90% power to detect a 28.7% reduction in the primary endpoint from 1,152 to 822 events per 1000 children years*

The Committee concluded that the amendments are justified and do not alter the risk/benefit status of the study and are therefore **granted approval** for implementation. You are also required to submit any further requests for changes to the approved protocol to SERU prior to initiation.

Yours faithfully,



**THE HEAD,  
KEMRI SCIENTIFIC AND ETHICS REVIEW UNIT.**