Date: March 14th, 2018

Professor Ibrahim Al Janahi - Executive Director of Research, Medical Research Center
Dr. Mohammed Hammoudeh - Chair of Hamad Medical Corporation IRB
Dr. Mohd. Abdel Daem Mohd. Yassin - Principal Investigator

This letter is in reference to the clinical trial entitled **"The Efficacy and Safety of Ferriprox® for the Treatment of Transfusional Iron Overload in Patients with Sickle Cell Disease or Other Anemias"**, submitted on February 15th, 2018 by Hamad Medical Corporation.

The study is sponsored by ApoPharma Inc.

Research proposal	Documents initially reviewed
17151/17	1) 17151_IRB Approval letter_11Feb18 2) 17151_Assent_Age12_V2.0_Ara_30Apr17_07Pages 3) 17151_Assent_Age12_V2.0_Eng_30Apr17_08Pages 4) 17151_Assent_Age12-17_V2.0_Ara_29Aug17_08Pages 5) 17151_Assent_Age12-17_V2.0_Eng_29Aug17_08Pages 6) 17151_AssentAgeLessThan12_V2.0_Ara_30Apr17_06Pages 7) 17151_AssentAgeLessThan12_V2.0_Eng_30Apr17_06Pages 8) 17151_CaseBookReport_V5.3_Eng_193Pages 9) 17151_CHQ-CF87Questionnaire_Baseline_V1.0_Ara_07Pages 10) 17151_CHQ-CF87Questionnaire_Baseline_V2.0_Eng_06Pages 11) 17151_CHQ-CF87Questionnaire_EOS_V1.0_Ara_07Pages 12) 17151_CHQ-CF87Questionnaire_EOS_V2.0_Eng_06Pages 13) 17151_CHQ-CF87Questionnaire_Semi-Annual_V1.0_Ara_07Pages 14) 17151_CHQ-CF87Questionnaire_Semi-Annual_V2.0_Eng_06Pages 15) 17151_CHQ-PF50Questionnaire_Baseline_Ara_05Pages 16) 17151_CHQ-PF50Questionnaire_Baseline_Eng_05Pages 17) 17151_CHQ-PF50Questionnaire_EOS_Ara_05Pages 18) 17151_CHQ-PF50Questionnaire_EOS_Eng_05Pages 19) 17151_CHQ-PF50Questionnaire_Semi-Annual_Ara_05Pages 20) 17151_CHQ-PF50Questionnaire_Semi-Annual_Eng_05Pages 21) 17151_DFOPatientEmergencyCard_V4.0_Ara_27Jan14_01Page 22) 17151_DFOPatientEmergencyCard_V4.0_Eng_27Jan14_01Page 23) 17151_DFPPatientEmergencyCard_V4.0_Ara_27Jan14_01Page 24) 17151_DFPPatientEmergencyCard_V4.0_Eng_27Jan14_01Page 25) 17151_DiaryDFO_V2.0_Ara_12Dec13_11Pages 26) 17151_DiaryDFO_V2.0_Eng_12Dec13_11Pages 27) 17151_DiaryDFPLiquid_V2.0_Ara_12Dec13_12Pages

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Research proposal	Documents initially reviewed
17151/17	28) 17151_DiaryDFPLiquid_V2.0_Eng_12Dec13_12Pages 29) 17151_DiaryDFPLiquid_Wk1-4_V2.0_Ara_12Dec13_12Pages 30) 17151_DiaryDFPLiquid_Wk1-4_V2.0_Eng_12Dec13_12Pages 31) 17151_DiaryDFPTablet_Ara_V2.0_12Dec13_12Pages 32) 17151_DiaryDFPTablet_Eng_V2.0_12Dec13_12Pages 33) 17151_DiaryDFPTablet_Wk1-4_V2.0_Ara_12Dec13_12Pages 34) 17151_DiaryDFPTablet_Wk1-4_V2.0_Eng_12Dec13_12Pages 35) 17151_HospiraDFOSmPC_Eng_08Pages 36) 17151_InformedConsent_Adults_V2.0_Ara_30Apr17_13Pages 37) 17151_InformedConsent_Adults_V2.0_Eng_30Apr17_15Pages 38) 17151_InformedConsent_GeneticTesting_V2.0_Ara_30Apr17_03Pages 39) 17151_InformedConsent_GeneticTesting_V2.0_Eng_30Apr17_04Pages 40) 17151_InformedConsent_Parents_V2.0_Ara_29Aug2017_14Pages 41) 17151_InformedConsent_Parents_V2.0_Eng_29Aug2017_16Pages 42) 17151_InformedConsent_Spouse_V1.0_Ara_29Aug2017_14Pages 43) 17151_InformedConsent_Spouse_V1.0_Eng_29Aug2017_15Pages 44) 17151_InformedConsentforParent_GeneticTesting_V2.0_Ara_30Apr17_04Pages 45) 17151_InformedConsentforParent_GeneticTesting_V2.0_Eng_30Apr17_05Pages 46) 17151_InitialApplication_Eng_30Apr17_08Pages 47) 17151_InstructionsReconstitution-Deferoxamine_V3.0_Ara_24Jun14_05Pages 48) 17151_InstructionsReconstitution-Deferoxamine_V3.0_Eng_24Jun14_05Pages 49) 17151_InvestigatorBrochure_Edition11.0_30Mar17_115Pages 50) 17151_Protocol_V7.0_Eng_12Aug14_99Pages 51) 17151_SchemeOfDelegation_04Pages 52) 17151_SF-36_Qatar_V2.0_Ara_06Pages 53) 17151_ShortInstructionCronoSuperPID-USA_VAug04_Ara_02Pages 54) 17151_ShortInstructionCronoSuperPID-USA_VAug04_Eng_02Pages 55) 17151_SignedAgreementToProtocol_Eng_01Page 56) 17151_UserGuideSuperPID-USA_Ara_Nov2013_43Pages 57) 17151_UserGuideSuperPID-USA_Eng_Nov2013_43Pages

Upon review of the submitted documents, the Ministry of Public Health (MoPH) supports the conduct of this clinical trial. Please be noted that it is the institution, sponsor and the Principal Investigator (PI)'s responsibility, to ensure that this clinical trial is conducted in compliance with MoPH regulations and the principles of International Conference on Harmonization (ICH) - Good Clinical Practice (GCP), and to ensure the below responsibilities are fulfilled:

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1. The safety and wellbeing of participants are protected

2. Research involving human subjects begins only after IRB review and approval

3. The research is conducted in accordance with the local IRB-approved protocol, including the approved recruitment and consent procedures

4. When informed consent is required, it is obtained and documented before research participation begins

5. All unanticipated problems, including adverse event(s) are reported in accordance with the IRB's policy on reporting unanticipated problems including adverse events

6. The protocol's amendments (e.g., protocol, recruitment materials, consent form, status of the study, etc.) are submitted to the IRB for review and approval prior to initiation of the change(s), except where necessary to eliminate hazards to the subject(s). Changes made to eliminate apparent immediate hazards to subjects must be reported to the IRB as unanticipated problem

7. All investigators and study staff listed on the project are informed of changes and unanticipated problems, including adverse events, involving risks to subjects or others

8. The continuing review submission to the IRB should be submitted with sufficient time to allow for IRB review and approval and provide an opportunity for response by the Principal Investigator to any stipulations of the local registered IRB

9. When the research protocol ends, a final report is submitted to the IRB

10. Adequate and accurate research records are kept and retained

11. The confidentiality of data is maintained at all times

12. Upon request for monitoring and oversight of the research, research records are made available to MoPH and HMC Monitor

13. All drug logistic is maintained and recorded

14. When supervising the conduct of the research, the PI ensures that study personnel:

- are qualified by training and experience, and credentialed if necessary, to perform study-related tasks that have been assigned to them
- are aware of regulatory and policy requirements and standards for the conduct of human subjects research

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- have a complete understanding of the details of the protocol relevant to the tasks they will be performing
- Follow the IRB-approved protocol
- are informed of any pertinent changes to the protocol during the conduct of the study and are educated or given additional training, as appropriate

It is ApoPharma, HMC and HMC-IRB's responsibility to:

1. Monitor the safety and wellbeing of research participants
2. Ensure that informed consents are in place
3. Provide enough support to the PI to fulfill his above mentioned responsibilities
4. Protect the privacy and confidentiality of participants
5. Provide one to one training to involved research staff
6. Conduct periodic reviews throughout the trial's duration
7. Conduct continuous monitoring during the conduct of the trials
8. Report all unanticipated problems including adverse events to the MoPH
9. Keep IRB meeting minutes, trial recordkeeping, etc. for inspection purposes

It is the Independent Data and Safety Monitoring Board responsibility to:

1. Review the trial prior its implementation
2. Periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy
3. Make recommendations concerning the continuation, modification, or termination of the trial
4. Ensure that the timeliness, completeness, and accuracy of the data submitted to them for review are sufficient for evaluation of the safety and welfare of study participants
5. Report adverse events to HMC-IRB, the sponsor, and MoPH

For any enquiries, please contact the Research Division at MoPH via: irb@moph.gov.qa

Sincerely yours,

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