

Appendix 6 : Protocol Revision History

Version Number	Summary of Revisions Made	Version Date
1.0	n/a	July 11, 2017
2.0	<ul style="list-style-type: none"> • Addition of the Clinical trials.gov registration number • Correction of typos and wording • Update of the list of abbreviations • Precision regarding one exclusion criteria (fixed <u>bilateral</u> dilated pupils) • Modification to the size of permuted blocks for randomization (4 and 6 instead of 2 and 4) • Update of the list of participating sites and anticipated recruitment rate • Modification of the interim analysis (one analysis at 50% enrolment instead of 2 analyses at one third and two thirds) • Modification of the time frame to report protocol violations at the Coordinating Centre (72 hours instead of 96 hours) 	Nov 22, 2017
3.0	<ul style="list-style-type: none"> • Increase in sample size • Addition of Withdrawal of Life-Sustaining Therapies as a trigger to stop applying the intervention • Addition of the PACT as a collaborative research network • Minor corrections to the text and references • Clarification of secondary and tertiary objectives • Addition of patient minimum age • Clarification of potential protocol violation definitions and management • Precision regarding the start and end of treatment strategy • Modification of the list of participating centres • Increase in recruitment period • Precision on required imaging results • Deletion of one secondary outcome (return to work) • One secondary outcome changed to tertiary outcome (complications related to transfusion) • Modification of the statistical and analytic plan for the primary outcome, of subgroup and sensitivity analyses • Modification to how follow-ups are organized • Update of References • Update of Steering Committee members and Knowledge users 	May 17, 2022