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| **SCIENTIFIC ASSESSMENT REPORT** |

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| ***Scientific Board Secretariat*** | ***Day 1***  ***(first Monday of each month)*** |

**PROJECT ID CODE: 2016-07-EOB 01/08/2016**

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| ***Coordinating EuCo*** | ***Day 0***  ***(within the end of each month)*** |

**STUDY PROTOCOL SUBMISSION SUBMITTED ON 08/07/2016**

**PROJECT FULL TITLE: Simple Intensive Care Unit Study (SICS) pack**

**PROJECT ACRONYM:** **SICS**

**PRINCIPAL INVESTIGATOR:**

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**SCIENTIFIC BOARD PRELIMINARY CHECK**

**Week 1**

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| ***Scientific Board Secretariat*** | ***Day 7*** |

**SCIENTIFIC BOARD PRELIMINARY CHECK EXPECTED ON 07/08/2016**

**CirculateD on 08/07/2016**

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| ***Scientific Board Secretariat*** | ***Day 7*** |

**Referee(S) agreed. Protocol circulated on** **13/07/2016**

**Protocol circulated to the SCIENTIFIC BOARD on****21/07/2016**

**Referees’ comments and recommendations**

**Weeks 2-3**

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| ***Methodological reviewer*** | ***Day 21*** |

**Assessment report EXPECTED ON 22/08/2016 CirculateD on 28/07/2016**

**Deleted**

**ScIENTIFIC BOARD’s comments and recommendations**

**Weeks 2-3**

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| ***Scientific Board members*** | ***Day 21*** |

**Comments EXPECTED ON 22/08/2016 CirculateD on 29/07/2016**

**Deleted**

**Scientific Board recommendations**

**Week 4**

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| ***Scientific Board Secretariat*** | ***Day 28*** |

**SCIENTIFIC BOARD advice EXPECTED ON 29/08/2016 Released on 02/08/2016**

**Background**

This project is an interesting proposal, which consists of a registry to conduct both a complete assessment based on a cohort study design and randomised clinical trials. All patients admitted to the participating Intensive Care units will be eligible for inclusion in the observation cohort study, which is expected to be as inclusive as possible. Part of the patient population will participate in nested RCTs addressing questions generated by and relying on the collected data.

The system is designed as an ongoing multinational multicenter infrastructure, encompassing different modules, with all variables to be collected for both the observational study and the trial(s). Several trials and different observational designs may be based on this infrastructure. In fact, there is already a proposal for a randomised trial currently under evaluation in ECRIN.

The synopsis includes a discussion on the pros and cons of observational studies and RCTs, and the potential benefit for the combination of both approaches in this infrastructure.

The information is structured in several modules. Not all centres will participate in all modules, depending on the feasibility to provide the specific data. An introduction, a research question, description of variables and references are provided for each pre-planned module, that are as follows:

• Module 1: Core Module. All-cause mortality and SAE

• Module 2: Secondary Outcomes. All outcomes are graded according to the patient’s perspective following GRADE. For large trials in critically ill patients these outcomes are “standard” set of core outcomes which will be more or less the same for future trials.

• Module 3: Genetics and epigenetics

• Module 4: Prognostication. Prognostic variables

• Module 5: Cardiovascular pathophysiology including advanced imaging

• Module 6: Chronic long-term kidney function

• Module 7: Patient and relatives satisfaction.

The sample size for the observational study is driven by the numbers of patients needed for genetic association studies, which is around 25000.

**Comments on the proposal**

Overall, this synopsis describes an interesting project However, the CIs may wish to consider the following recommendations and advice:

IT and data management (DM): IT and DM aspects are not addressed. These aspects may not be critical at this stage, but should be dealt with in detail for the future studies. It is stated that the project is on-going. Therefore, it is expected that all the aspects related to IT and DM have already been or are being addressed. To this aim, the investigators may wish to take into consideration some key references of direct application to IT-DM issues for the clinical investigations (see References).

Sample size: while the intended sample size (i.e. 25000 patients) appears reasonable, the assumptions on which it is based should be provided. It is also recommended to calculate what effect size might be estimated with that sample in the future. The objective is to provide unquestionable data to the H2020 reviewers on the minimum detectable effect in a range of reasonable scenarios.

“Scalability”: Some references have been given to the “scalability” regarding the participation to the different modules. This is an important aspect which should be addressed not only in terms of addition of new modules, but also of potential inclusion of new centers after the initial phase.

For the preparation of their final protocol the CIs are advised to:

* follow the relevant sections of the SPIRIT statement ([www.spirit-statement.org/](http://www.spirit-statement.org/))
* adopt the ECRIN transparency rules (<http://www.ecrin.org/images/pdf/Check_List_for_submission_to_the_ECRIN_Scientific_board_SOP_03_ECRIN_V2_2015_10_15.pdf> )
* describe plans for sharing data after the trial and in what format and where they will be placed
* follow the STROBE statement on the reporting of observational studies (<http://www.strobe-statement.org/index.php?id=strobe-home> ).

Conclusion

The rationale for the study is relevant. Despite some discrepancies among methodologists regarding the respective role and implications of observational studies and RCTs, it is unquestionable that the conduction of both designs may help support both the definition of efficacy/safety profile of experimental interventions and the actual role of the variables under study. Some recommendations have been provided for future steps, which are not necessarily relevant at the current stage.

**References**

Ohmann C, Kuchinke W, Canham S, Lauritsen J, Salas N, Schade-Brittinger C, Wittenberg M, McPherson G, McCourt J, Gueyffier F, Lorimer A, Torres F; ECRIN Working Group on Data Centres. Standard requirements for GCP-compliant data management in multinational clinical trials. Trials. 2011 Mar 22;12:85. doi: 10.1186/1745-6215-12-85.

2 Revising the ECRIN standard requirements for information technology and data management in clinical trials. Ohmann C, Canham S, Cornu C, Dreß J, Gueyffier F, Kuchinke W, Nicolis EB, Wittenberg M. Revising the ECRIN standard requirements for information technology and data management in clinical trials. Trials. 2013 Apr 5;14:97. doi: 10.1186/1745-6215-14-97.