

Standard Clinical Trial Agreement

This Clinical Trial Agreement (“Agreement”), dated as of 200601] is made by and between;

Institution:

[Name]

[Street]

[City, Country]

(hereinafter jointly called “Institution”)

Represented by

[Name of National Coordinator]

(hereinafter called National Coordinator)

[Name of National Coordinator], an employee at [Name of Institution] will be responsible for the performance of the Study in [Country] on behalf of the Institution as National Coordinator

and

Sponsor:

Rigshospitalet

Blegdamsvej 9

2100 Copenhagen

Business Registration No.: 29190623

(hereinafter called "Sponsor")

The Institution and Sponsor are hereinafter each individually referred to as a “Party” and collectively referred to as the “Parties”.

Preamble

WHEREAS Sponsor is the regulatory Sponsor of the clinical multi-centre study regarding **Hydrocortisone**, (hereinafter defined as “the Study Drug”) as defined in the protocol entitled **Low dose hydrocortisone in patients with COVID-19 and severe hypoxia – the COVID STEROID trial**, with the version no. 1.9 dated 06 04 2020 a copy of which is incorporated herein by reference as Appendix A, (hereinafter defined as “the Study”) and wishes to enter into an agreement with Institution; and has requested National Coordinator to conduct the Study according to this Agreement and it’s Appendices, the Protocol including subsequent Protocol amendments.

WHEREAS, National Coordinator is equipped and authorized to undertake the Study as National Coordinator, and National Coordinator have agreed to perform the Study on the terms and conditions hereinafter set forth.

NOW THEREFORE in consideration of the premises and the mutual promises and covenants expressed herein, the Parties agree as follows:

1. Obligations of the Parties

1.1 Authorizations

1.1.1 The Sponsor shall be responsible for obtaining and maintaining approvals from the Danish Medicines Agency and Data Protection Agency for the conduct of the Clinical Trial. The [Country] National Coordinator is responsible to obtain and maintain approvals from the [Country] medical products agency and the Swedish ethics committee. National Coordinator shall obtain all necessary approvals from the Ethics Committee, hereunder but not limited to the Protocol and its amendments and informed consent form, and relevant regulatory authorities, with assistance from Sponsor.

1.1.2 In the event that EC requires amendments in the Protocol or informed consent form, such amendments shall be agreed upon by both by the National Coordinator and Sponsor and be documented in writing.

1.2 Conduct of Study

1.2.1 The Parties shall conduct the Study in accordance with the Protocol and its amendments, the terms of this Agreement, and the terms and conditions of the approval of relevant authorities. National Coordinator shall adhere to separate manuals and specific procedures provided by Sponsor applicable for conducting the Study.

1.2.2 National Coordinator shall be fully informed of the Protocol and the Study Product. Sponsor shall provide all relevant clinical pharmacology and toxicology information and advice to National Coordinator, which are required for the proper planning and conduct of the Study. Such information will include the Investigator’s Brochure (IB) and information on Suspected Unexpected Serious Adverse Events (SUSARs) for unlicensed products or the Summary of Product Characteristics (SPC) for licensed products. National Coordinator shall attend, or ensure a delegate attends, all Investigators’ meetings for the Study from time to time as reasonably required by Sponsor.

1.2.3 National Coordinator shall perform and act with reasonable care and shall use her/his best effort and shall possess an sufficient working knowledge to fulfil her obligations in the Agreement. National Coordinator undertakes the responsibility of performing of the Study in [Country] in collaboration with Sponsor. National Coordinator will do her/his best effort to include the number of patients in the Study agreed with Sponsor by including other Sites in [Country] after mutual written agreement between the Parties.

1.2.3 National Coordinator shall ensure that Sites and Investigators who are involved in the Study fully understands and adhere to the Protocol and the obligations set forth in this Agreement. Sites and Investigators agreement are attached as Appendix B.

1.3 Data and Safety

1.3.1 National Coordinator shall on request submit written reports, in accordance with all laws, regulations and guidelines including the Ethics Committee standards, to Sponsor and the EC regarding the Study being conducted at the Institution.

1.3.2 Required Systems: National Coordinator and Investigators agrees to implement and use any electronic system that Sponsor may specify for use in the reporting and monitoring of the Study and Study findings at Sponsor's expense.

1.3.3 National Coordinator and Investigator agrees to report to Sponsor and local authorities immediately if applicable but not later than twenty-four (24) hours after learning of any serious adverse events and other important medical events, as identified in the Protocol, affecting any Study subject in the Study. National Coordinator further agrees to follow up such report with detailed, written reports in compliance with all applicable legal and regulatory requirements. National Coordinator shall record and evaluate all Adverse Events experienced by the Study subjects in accordance with the Protocol.

1.4 Record Management

1.4.1 Investigator will retain in a safe and secure location, one (1) copy of all printed and electronic data and reports resulting from the Study for such longer period as required by regulatory requirements. Sponsor will provide instructions for the retention or destruction of documentation.

1.4.2 If Sponsor agree, National Coordinator and Institution may store Study documents at a mutually agreed third party site at their own expense. If they want to move the Study documents to another location, the Sponsor must be notified in writing.

1.4.3 National Coordinator shall ensure that the Investigators maintain accurate data collection and up-to-date records of all Study subjects.

1.5 Informed Consent

1.5.1 National Coordinator must ensure that the Investigator undertakes to use the patient information sheet according to local Laws and as approved by the Ethics Committee and to obtain written informed consent from each Study subject prior to inclusion or initiation of any Study specific procedures for screening according to the Protocol.

1.6 Study subject Enrolment

1.6.1 National Coordinator shall make reasonable efforts to ensure that the recruitment target of eligible subjects in accordance with the Protocol is met timely, and that data from all eligible Study subjects are available for Sponsor and that data is entered when data are available for each Study subjects and not later than before the expiration of the Study. If, after using its best endeavours, the Institution is unable to recruit the requisite number of trial subjects for the Study as specified in this Agreement and/or the Protocol, such inability shall not be deemed by Sponsor as a breach from the National Coordinator of the Agreement.

1.6.2 Institutions may enrol Study subjects in mutual competition with other participating sites. Sponsor reserves the right to end Study subject enrolment under this Agreement when the desired number of Study subjects for all sites has been reached. Further, National Coordinator must inform Institutions that continued screening or randomisation of subjects must not take place after Study Subject enrolment has been ended by Sponsor and notice hereof has been given to National Coordinator by Sponsor. National Coordinator must inform the Investigator immediately if enrolment has been ended by Sponsor.

1.7 Monitoring and Audit

1.7.1 Sponsor shall provide reasonable supervision, training and monitoring during the conduct of the Study.

1.7.2 National Coordinator shall inform Institutions, that Institutions shall - on reasonable prior written notice and at an agreed upon time, during the Study - permit authorized personnel of Sponsor to access the sites during normal business hours in order to conduct monitoring and audits. Any review by Sponsor of source documents shall be performed with due regard for Study subject confidentiality.

2. Compensation

2.1 Compensation in the Study shall be due and payable in accordance with Appendix C for each Site. As the Study is financed by grant, it is acknowledged by the Parties, that fully compensation is not possible.

3. Confidentiality

Any information acquired by National Coordinator from Sponsor concerning existing (or contemplated) products, services, processes, techniques, know-how or data (hereinafter "Confidential Information") shall be maintained in confidence by National Coordinator. Confidential Information shall not be used by National Coordinator without Sponsor's written consent - which shall not be unreasonably withheld – except as necessary to perform the

activities described in this Agreement or until the lapse of three (3) years from the date of expiration or cancellation of the Agreement.

The following information is not considered Confidential Information:

- Information that is already known at the time of its revelation or later is made public through no fault of the National Coordinator or;
- Information that the National Coordinator at the time of its revelation can show was already known by the National Coordinator or;
- Information that National Coordinator has received in good faith from a third party or;
- Information that can be demonstrated as independently developed or acquired by the National Coordinator without reference to or reliance upon information disclosed by Company or;
- Information that is required to be disclosed by law.

National Coordinator is obligated to inform Investigator of this obligation.

4. Publication

4.1 The Parties recognize that local law places an obligation on hospitals carrying out health and social care research to publish their work.

The Parties agree that this Section 4 should be interpreted in light of such obligation.

4.2 Following completion of the entire Study at all sites, Sponsor shall use all reasonable endeavors to ensure the appropriate publication or other dissemination of the conclusions of the Study, and National Coordinator must ensure that Investigators for such Study will not publish data/results derived from the individual institution site until the combined results from the entire Study has been published in a joint, multi-centre publication. National Coordinator and Institution is aware that this is a multi-center Study with participating Sites from Denmark and other countries. If such a multi-centre publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after the Sponsor confirms there will be no multi-centre clinical trial publication, the Investigators may publish the data/results from the Institution individually in accordance with this Section 5.

4.3 If the Investigators wish to publish data/results from the Study, a copy of the manuscript must be provided to the Sponsor for review at least thirty (30) days prior to submission for publication, presentation or release. The Sponsor and the Investigator will arrange expedited reviews for abstracts, poster presentations or other materials. Within this 30-day period, the Sponsor shall review such proposed publication or presentation or release to determine whether it contains any Confidential Information of Sponsor (as defined in Section 3), or whether Sponsor desires to file patent applications on subject matter contained therein. Upon receiving any notification from Sponsor requesting deletion of Confidential Information of Sponsor, or requesting a delay in publication to allow the filing of patent applications before publication or release, Investigator shall take the requested action; provided however, that any delay in publication shall not exceed ninety (90) days from the date on which Sponsor received the draft manuscript for review.

5. Publicity

None of the Parties shall use the name of any other Party for marketing or promotional purposes without the prior written consent of the Party whose name is proposed to be used, nor shall either Party disclose the existence or substance of this Agreement except as required by law or otherwise provided for in this Agreement.

6. Ownership of Data

6.1 National Coordinator must ensure, that all data/results generated by Investigators in the direct course of conducting the Study ("Data") will be transferred to Sponsor, which may utilize the Data in any way it deems appropriate, subject to and in accordance with applicable privacy and security laws and regulations and the terms of this Agreement.

6.2 Investigators retains the right to use Data for further research, education and treatment purposes.

7. Ownership of Inventions

7.1 Any inventions/improvements within the field of research, as resulting directly from the Study shall be owned by Sponsor ("Inventions"). National Coordinator must inform the Investigators of this obligation. Sponsor shall be entitled to file in its own name relevant patent applications or in other ways protect the Inventions, and the said Inventions will become and remain the property of Sponsor solely.

7.2 National Coordinator and Institution shall promptly disclose and assign to Sponsor all Inventions generated by National Coordinator and/or Institution pursuant to this Agreement.

9. Liability and Insurance

9.1 Institution must retain or have appropriate insurance or is self-insured as a public body according to local law to cover any liability assumed by Institution and/or National Coordinator and Investigators under this Agreement.

9.2 Sponsor as a public Danish body is self-insured according to Danish law. Sponsor's assets are sufficient to cover any contemplated self-insured liability assumed by Sponsor under this Agreement. Sponsor shall not be liable for any direct or indirect losses, consequential damages, operational losses, loss of profit or other consequential financial losses, including claims for damages from a third party.

10. Term and Termination

10.1 This Agreement shall be considered fully executed on the latest date that a Party executes the same Agreement, and will remain in effect until completion of the Study, close-out of Institution or completion of the obligations of the Parties under this Agreement or earlier termination in accordance with this Section 10 whichever occurs first.

- 10.2 This Agreement may be terminated by either Party at any time in the exercise of its sole discretion upon thirty (30) calendar days prior written notice to the other Party, if i) a material breach of this Agreement occurs, including failure to comply with the Protocol and applicable laws and regulations, ii) receipt of safety information makes it advisable to do so.
- 10.3 Notwithstanding the above, Sponsor may immediately terminate the Study if, within its sole judgment, such immediate termination is necessary based upon considerations of subject safety or upon receipt of data suggesting lack of sufficient efficacy. Upon receipt of notice of termination, National Coordinator agrees to promptly inform the Investigators of terminating of the Study to the extent medically permissible for any individual who participates in the Study.
- 10.4 Notwithstanding the above, Institution may terminate this Agreement upon 30 calendar days written notice to Sponsor, if the National Coordinator becomes unavailable due to death, disability or other reasons beyond the control of Institution and not attributable to Institution's own acts or omissions. However, Institution agrees to first use its best efforts to identify a replacement National Coordinator acceptable to Sponsor
- 10.5 In the event of termination hereunder, other than as a result of a material breach by National Coordinator or Investigator, the total sums payable by Sponsor pursuant to this Agreement shall be equitably prorated for actual work performed to the date of termination including any reasonably non-cancellable costs and start-up costs, with any unexpended funds previously paid by Sponsor to Institution being refunded to Sponsor.
- 10.6 National Coordinator and Investigator shall immediately deliver to Sponsor all Data generated as a direct result of the Study and shall, at Sponsor's expense, return to Sponsor or destroy upon instructions of the Sponsor, all unused Study Product, all documents, materials and equipment provided by Sponsor and all Sponsor Confidential Information, as defined in Section 3, at the earlier of the conclusion of the Study or termination of this Agreement. This provision does not apply to those documents that should be maintained and retained by National Coordinator and/or Investigator as defined in the Protocol and as requested by applicable laws and regulations.
- 10.7 The rights and obligations of the Parties which by intent or meaning have validity beyond termination as set forth above, including, but not limited to, rights with respect to patent rights, ownership of Inventions, confidentiality, liability limitations, indemnification and insurance, and publication shall survive five (5) years after the termination or expiration of this Agreement.

11. Applicable Law and Regulations

- 11.1 The Parties shall comply with all applicable national and international laws, regulations and guidelines, especially those governing the conduct of clinical trials, dealings in medicinal products, responsibilities of clinical investigators and National Coordinator, informed consents, protection and privacy of personal data and storage of data and records, including, without limitation, the ICH Guidelines and the European Guidelines on Good Clinical Practice (hereinafter referred to as "ICH-GCP"), Good Laboratory Practice, the revised versions of the Declaration of Helsinki, the Regulation (EU) 2016/679 (General Data Protection Regulation)

and Directive 2001/20/EC of the European Parliament and of the Council, and professional industry association regulations. Insofar, and if any, Personal Data is to be processed during the performance of the Study, the regulations regarding the processing must abide by the General Data Protection Regulation 2016/679 (GDPR) and any other applicable law and must be agreed on in a separate written agreement between the Parties.

- 11.2 The Parties agree that the collection, processing and disclosure of personal data and medical information related to the Study subject, and personal data related to National Coordinator and Investigators and any investigational staff (e.g., name, hospital or clinic address and phone number, curriculum vitae) is subject to compliance with applicable personal data protection and security laws and regulations. National Coordinator or Investigators shall not disclose to the Sponsor the identity of the subjects or information from which the identity of the subject can be deduced without prior written consent of the subject.
- 11.3 National Coordinator and Investigators agrees to inform the investigational staff that their personal data may be collected. Sponsor will apply adequate privacy safeguards to protect such personal data. Personal data may also be disclosed as required by individual regulatory agencies or applicable law, such as to report serious adverse events.
- 11.4 The National Coordinator confirms that neither she/him, and - to the best of her/his knowledge - nor any of the Investigators or of Investigators', employees, agents or other personnel providing services for the Study pursuant to this Agreement, has ever been debarred, disqualified, or banned by the competent authority or any equivalent regulatory authority.

12. Law and Venue

- 12.1 In the event of any dispute arising between the Parties in relation to the terms of this Agreement, the Parties shall use their best endeavours to resolve the matter on an amicable basis. Any legal action, claim or other legal proceeding commenced by one party against another party, arising out of this Agreement, shall be commenced in the courts of the jurisdiction in which the responding party is situated; and for the purposes of such proceeding, this Agreement shall be governed by, and shall be interpreted, construed and enforced, in accordance with the laws of that same jurisdiction.

13. Miscellaneous

- 13.1 Sponsor shall have the right to assign this Agreement to an affiliate of Sponsor upon prior written notice to National Coordinator. In all other instances, neither Party shall assign its rights or duties under this Agreement to another without prior written consent of the other Party. Subject to the foregoing, this Agreement shall bind and inure to the benefit of the respective Parties and their successors and assigns.
- 13.2 Except as set forth in this Agreement, no Party, or its employees, agents, or subcontractors, has any right or authority to bind or act on behalf of another Party.

- 13.3 National Coordinator confirms that there is no conflict of interest that will inhibit or affect the National Coordinator's performance under this Agreement and confirm that the performance under this Agreement does not violate any other agreement with third parties. For the avoidance of doubt, National Coordinator is free to enter into any other agreement with any third parties as long as this does not prevent National Coordinator from fulfilling the obligations according to this Agreement.
- 13.4 This Agreement may not be altered, amended or modified except by written document signed by the Parties.
- 13.5 If any of the provisions of this Agreement conflicts with any provision of the Protocol or any other relevant document, this Agreement shall take precedence.
- 13.6 This Agreement constitutes the entire agreement of the Parties with respect to the subject matter hereof. It expressly supersedes any prior or contemporaneous oral or written representations or agreements. The Appendices form an integral part of the Agreement. If any part of this Agreement is found to be unenforceable, the rest of this Agreement will remain in effect.

14 [Name of National Coordinator] is the national coordinator for the COVID STEROID trial in [Country].

Signatures:

Acknowledged and agreed:

For [Institution]:

For and on behalf of **Sponsor:**

Rigshospitalet

Date:

Date:

[Name]

Per Jørgensen

[Title]

Deputy Director

Read and acknowledged:

As National Coordinator:

On behalf of Sponsor:

Date:

Date:

[Name of National Coordinator]

Anders Perner

National Coordinator:

I hereby acknowledge that I have read and agree with the terms of this Agreement, and that I will act and perform my duties in the study in accordance with the content of this Agreement and the details outlined in the Appendices.

*Signatures for Site and Investigator in Appendix B
Budget in Appendix C.*

If electronic signatures are applied to this contract only signatures from those stated above will actually be signing the contract. Additional electronic signatures from persons not mentioned above may be from persons considered important for the signature process, i.e. legal advisors, secretariats.

Appendix A – Protocol

Version [1.9] [06-04-2020]

Protocol can be downloaded from <http://www.cric.nu/covid-steroid-trial-protocol/>

Appendix B – Site and Investigator agreement:

This Site and Investigator agreement is entered with:

Site:

Represented by (Investigator):

Signatures:

Acknowledged and agreed:

Acknowledged and read:

Date:

Date:

Signatures:

Signatures:

Name

For Investigator:

I hereby acknowledge that I have read and agree with the terms of this Agreement, and that I will act and perform my duties in the study in accordance with the content of this Agreement and the details outlined in the Appendices.

Appendix C – Budget: