Investigator-Initiated Clinical TRIAL agreement

Regarding the trial entitled: “***Low-dose hydrocortisone in patients with COVID-19 and severe hypoxia – the COVID STEROID Trial***, (hereinafter the “Trial”)

This Investigator-initiated Clinical Trial Agreement (“Agreement”) is entered into by and between:

 Rigshospitalet

 Department of Intensive Care

 Blegdamsvej 9, 2100 København Ø

 CVR 29190623

 (Hereinafter “Sponsor-Investigator”)

Senior Staff Specialist and Professor in Intensive Care, Anders Perner (Principal Investigator) shall be responsible for the performance of the Trial on behalf of Sponsor-Investigator (“Principal Investigator”)

And

[Indsæt navn på Site]

[Indsæt afdeling på Site]

[Indsæt adresse på Site]

[Indsæt CVR-nr på Site]

(Hereinafter “Site”)

[Insæt navn på Investigator fra Site] shall be responsible for the performance of the Trial on behalf of Site (“Site-Investigator”)

In the following Sponsor-Investigator and Site are also referred to as “Party” and collectively as “Parties”

1. Performance of the Trial

1.1 Site shall conduct the Trial in accordance with the Protocol entitled “***Low-dose hydrocortisone in patients with COVID-19 and severe hypoxia – the COVID STEROID Trial***“,, version 1.6, dated 29/03/2020, attached as Appendix 1 (hereinafter “Protocol”) and all ethical regulations, applicable laws, guidelines, rules and regulatory requirements.

1.2 Site shall not begin the Trial until all of the required approvals of the competent authorities are obtained. Sponsor-Investigator will obtain the required approvals, including approvals of any required amendments to the Protocol, from the competent authorities including the Danish Medicines Agency and the Ethics Committee.

1.3 Site shall be responsible for its own recruitment of patients (“**Subjects**”) to the Trial. Such recruitment shall be carried out in accordance with the time schedule, selection procedures and criteria set out in the Protocol or appendixes. Site shall ensure that prior to enrolment of a Subject in the Trial a signed and dated written informed consent form (ICF) is obtained from the Subject or from the Subject’s legally acceptable representative in accordance with any requirement set forth in applicable law including; authorizing direct access to the Subject’s original medical records by the auditor(s) including Sponsor-Investigator, Sponsor-Investigator’s representative, The Danish Medicines Agency, the Ethics Committee and the Monitor for verification of clinical procedures and/or data, without violating the confidentiality of the Subject, to the extent permitted by the applicable laws and regulations.

1.4 Inclusion period is ending when the total expected number of 1000 Subjects in the Trial has been enrolled by all participating sites. As there are more than one Site in the Trial, there will be competitive enrollment of Subjects at the Sites. Sponsor-Investigator reserves the right to end Subject enrolment, once the desired number of Subjects has been reached. If deemed necessary, extension of the inclusion period may be applied for. If Site is unable to recruit the requisite number of Subjects for the Trial as specified in this Agreement and/or the Protocol, such inability shall not be deemed by Sponsor-Investigator as a breach of the Agreement.

1. Personal Data

2.1 The Parties agree to comply with applicable data protection laws and regulations.

2.2 Insofar, and if any, Personal Data is to be processed during the performance of the Trial, 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.

1. Documentation

3.1 Each Site shall archive all documents from the Trial in accordance with applicable law.

1. Financial support

4.1 Sponsor-Investigator has received a grant (hereinafter “Grant”) for the Trial from the Novo Nordisk Foundation, as attached in Appendix 2.

4.2 It is the responsibility of Sponsor-Investigator to inform Site of the terms and conditions set forth in the Grant. Site shall ensure that Site-Investigator and other relevant personnel shall conduct the Trial in accordance with the Grant.

4.3 In case of conflict between the Grant and the Agreement, the Agreement will be amended accordingly.

1. Payment

5.1 Sponsor-Investigator will reimburse Site for costs and expenses according to Appendix 3.

1. Confidentiality

6.1 Site agrees to treat as confidential, information (a) disclosed to it by Sponsor-Investigator in connection with the Trial and (b) generated during the conduct of the Trial (”Confidential Information”). Site undertakes not to disclose the Confidential Informationor permit it to be disclosed to any third party except for the purposes of and to the extent to which disclosure is necessary to enable the Site to fulfill its obligations under this Agreement. Site and Site-Investigator further undertake not to use the Confidential Information for any other purpose than the purposes of this Agreement. Site shall ensure that the Confidential Information is maintained in a manner which assures its confidentiality, and which permits immediate access and/or disposal upon written request from the Sponsor-Investigator or regulatory authorities.

6.2 The above obligations of confidentiality and non-use shall not apply to Confidential Information:

1. which can be shown to have been known by Site prior to receipt of such information from Sponsor-Investigator and which has not been acquired from Sponsor-Investigator, directly or indirectly;
2. which is in the public domain or lawfully becomes generally available to the public through no fault of Site;
3. which is lawfully acquired by the Site from third parties, provided any such third party is not bound by an obligation of confidentiality with respect to such information at the time of disclosure; or
4. which by written agreement of Sponsor-Investigator is released from confidential status
5. is independently developed by Site without the use of or benefit of any Confidential Information; or

6.3 Site may disclose the Confidential Information to the extent such disclosure is required by law; provided that Site provides prompt written notice to Sponsor-Investigator of such requirement.

6.4 This Section 6 does not limit Site’s rights according to Section 7.2 (research rights) and Section 9 (Publication rights).

1. data and results

7.1 All data and non-patentable results provided and/or generated under the Agreement shall be owned by Sponsor-Investigator, excluding Site’s patient medical records and Site-Investigator’s personal notes.

7.2 Notwithstanding the foregoing, Site shall be entitled to conduct further research using own data and non-patentable results, after conclusion of the Trial and publication of the Trial results according to Section 9 without further agreement between the Parties.

1. Intelectual property

8.1 All existing information, which a Party brings into the Trial, shall remain the property of that Party.

8.2 Each Party shall own the results created by the Party during the conduct of the Trial to extent such results can be protected by patent legislation.

8.3 Results created jointly by the Parties shall be jointly owned by the Parties pro rata to their intellectual contribution to the extent such results can be protected by patent legislation. If the respective contributions of the Parties cannot be documented, such results shall be owned by the Parties in equal shares.

8.4 All disposal of jointly owned patentable results shall require agreement between the Parties.

1. Publication

9.1 Results generated in connection with the Trial, positive as well as negative, will be published by Sponsor-Investigator.

9.2 Publication and authorship will be decided in accordance with the Vancouver guidelines.

9.3 After the Trial is completed, which means completion of the Trial at all sites, and once the main publication has been submitted, each of the Parties shall have the individual right to publish the results or otherwise make public any data resulting from the Trial under the Agreement.

9.4 The Parties agree that any external funding provided shall be acknowledged in any publication.

1. Insurance

10.1 Each Party as public Danish bodies are self-insured.

10.2 All Trial Subjects are covered by Danish mandatory law: ”Lov om Klage- og erstatningsadgang inden for sundhedsvæsenet, (LBK nr. 995 af 14. juni 2018)” as amended from time to time.

10.3 The Parties shall not be liable for any indirect losses, consequential damages, operating losses, loss of profits or other consequential financial losses, including claims for damages from a third party.

1. Effective Date and Term

11.1 This Agreement will become effective on the date of last signature to the Agreement and will continue in effect until completion of the Trial or until the earlier termination of this Agreement pursuant to the termination clause of this Agreement.

1. Termination

12.1 Each Party shall have the right to terminate the Agreement at any time for good reason upon thirty (30) days written notice.

12.2 Sponsor-Investigator shall be entitled to terminate the Agreement with immediate effect in the event of the following:

* If the Grant is terminated.

12.3 Either Party shall be entitled to terminate the Agreement or suspend its obligations with immediate effect in the event of the following:

* any material breach of or failure to comply with any of the terms or conditions of the Agreement or Protocol by one Party, which breach or failure, if capable of remedy, is not remedied within thirty (30) days after notice from the aggrieved Party demanding such remedy;
* if one Party breaches the Agreement or Protocol to such an extent that such breach cannot be remedied or if it be of such nature that the one Party cannot reasonably expect or demand the other Party to perform;
* if Site-Investigator is no longer available to perform the Trial at Site and a mutually agreed successor cannot be found;
* if Trial related harmful events occur, which exceed the bounds considered justifiable in the light of knowledge available in medical science;
* if the continuation of the Trial is unacceptable on medical or ethical grounds and ECs withdraws its approval to continue the Trial

12.4 Immediately upon receipt of – or as the case may be given - a notice of termination, Site shall stop entering Subjects into the Trial and shall cease conducting procedures, to the extent medically permissible on Subjects already entered in the Trial.

12.5 In the event of termination, the sum payable under this Agreement shall be limited to prorated fees based on the actual work performed. Any reimbursement not due to the performance under this Agreement by Site shall be returned to Sponsor-Investigator.

12.6 Termination of the Agreement will be without prejudice to the rights and obligations of the Parties accrued prior to termination, and which, from the context thereof, are intended to survive termination or expiration of the Agreement.

1. Law and Jurisdiction

13.1 This Agreement shall be governed by, and construed in accordance with, the substantive laws of the country where Site is established without regard to the conflict of law provisions thereof. For the purpose of any dispute which cannot be resolved amicably, the Parties submit to the exclusive jurisdiction of the ordinary courts of the country where Site is established.

1. Entire Agreement

14.1 This Agreement reflects the entire Agreement between the Parties related to the subject matter hereof, and supersedes all prior communications, understandings and agreements.

1. Invalidity

15.1 If any provision of this Agreement is held by any court or other competent authority to be illegal, invalid or unenforceable in whole or in part, this Agreement shall continue to be valid as to its other provisions, and if possible, the affected provision should be modified to the minimum extent necessary to make it valid, legal and enforceable.

1. Conflict with Attachments

16.1 To the extent that terms or provisions of this Agreement conflict with the terms and provisions of the Protocol, the terms and provisions of this Agreement will control as to legal and business matters, and the terms and provisions of the Protocol will control as to technical research and scientific matters unless expressly agreed in writing between the Parties. If any of the provisions of the Grant conflicts with any provisions of this Agreement or Protocol, the Grant shall take precedence.

1. Amendments

17.1 Any amendment or modification to this Agreement must be in writing and signed by authorized representatives of each Party.

**IN WITNESS WHEREOF**, the Parties hereto have executed this Agreement by proper persons thereunto duly authorized and this Agreement shall be effective as of the Effective Date.

**For the Capital Region in Denmark:**

Acknowledged and agreed on behalf of Rigshospitalet as Sponsor and for the Capital Regions Hospitals:

Date:

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Name: Jens Gordon Claussen

Title: Executive Vice President of the Capital Region in Denmark

Acknowledged and read on behalf of Principal Investigator:

Date:

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Name: Anders Perner

Title: Professor, Senior Staff Specialist.

**For Site:**

Acknowledged and agreed on behalf of Site:

Date:

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Name

Title:

Acknowledged and read on behalf of Sites Investigator:

Date:

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Name:

Title:

**For Site:**

Acknowledged and agreed on behalf of Sites Investigator:

Date:

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Name:

Title:

**Appendix 1**

**Protocol (Only by reference)**

Appendix 2

**Grant**

**(Only by reference)**

**Appendix 3**

**Trial Budget and Payment Details:**

Sponsor will pay the Site for Trial related work (handling of the data in accordance with the Protocol) performed by scholar-students or other personnel employed by the Site (together referred to as “Site Personnel”) at Site, DKK 10.000 pr. Site, excluding VAT, if applicable, Personnel per month for full time Site Personnel. Alternatively, at Site’s option, Sponsor-Investigator will point out scholar-students employed with Sponsor-Investigator to perform the Trial related work at the Site. The number of Site Personnel that Site will be reimbursed for with DKK 10.000 per month depends on the number of Trial Subjects at each Site. The maximum amount of scholar-students at each Site will be 5. The amount (or alternative one scholar-student/Site Personal) will cover Study related work from approximately 23 numbers of Patients.

Payment is subject to receipt by Sponsor-Investigator of a specified invoice. Invoices will be sent to Sponsor-Investigator every third month (Quarterly). The cost set forth are inclusive of any Institutional overhead, but exclusive of any Value added tax (VAT) and should be added to the budget at the relevant if applicable.

Invoices shall be addressed to:

EAN: 5798 001 023 399

Rigshospitalet

Intensivafdeling 4131

Blegdamsvej 9

2100 København Ø

Tlf. +45 3545 7237

E-mail: covid-steroid@cric.nu

Insert Sites bank details: