Annex 1: Clinical trial Application Form

REQUEST FOR AUTHORISATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

To be filled in by the applicant
The questions in this form for the request for authorisation from the Competent Authority are also relevant for the opinion from an Ethics Committee (it represents module 1 of the form for applying to an ethics committee) and can be used as part of that application. Please indicate the relevant purpose in a box below.

REQUEST FOR AUTHORISATION TO THE COMPETENT AUTHORITY: **Yes ●**
REQUEST FOR OPINION OF THE ETHICS COMMITTEE: **No ●**

A. TRIAL IDENTIFICATION

A.1	Member State in which the submission is being made:	**Denmark - DHMA**
A.2	EudraCT number:	**2017-000632-34**
A.3	Full title of the trial:	
	English	**Handling oxygenation targets in adults with acute hypoxaemic respiratory failure in the intensive care unit: A randomised clinical trial of a lower versus a higher oxygenation target**
A.3.1	Title of the trial for lay people, in easily understood, i.e. non-technical, language:	
	English	**Oxygen supplementation in patients with acute pulmonary failure admitted to the intensive care unit: A clinical trial of two seperate levels of oxygen supplementation during treatment in the intensive care unit**
	Danish	**Ilttilskud til kritisk syge voksne patienter som indlægges på en intensiv afdeling med akut lungesvigt: Et multicenter og internationalt randomiseret klinisk forsøg, hvor to niveauer af iltindhold i blodet under behandlingen undersøges**
A.3.2	Name or abbreviated title of the trial where available:	
	English	**Handling Oxygenation Targets in the Intensive Care Unit (HOT-ICU)**
A.4	Sponsor's protocol code number, version and date[1]:	
A.4.1	Sponsor's protocol code number:	**AAUH-ICU-01**
A.4.2	Sponsor's protocol version:	**1.2**
A.4.3	Sponsor's protocol date:	**2017-05-24**
A.5	Additional international study identifiers (e.g. WHO, ISRCTN[2] , US NCT Number[3]) if available	
A.5.1	ISRCTN number:	
A.5.2	US NCT number:	
A.5.3	WHO Universal Trial Number (UTN):	
A.5.4	Other Identifier:	
A.6	Is this a resubmission?	**No ●**
	If 'Yes', indicate the resubmission letter[4]:	**First Submission**
A.7	Is the trial part of an agreed Paediatric Investigation Plan?	**No ●**
A.8	EMA Decision number of Paediatric Investigation Plan:	

B. IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

B.1	**SPONSOR**	
B.1.1	Name of organisation:	**Department of Anaesthesia and Intensive Care Medicine, Aalborg University Hospital**
B.1.2	Name of the person to contact:	
B.1.2.1	Given name	**Bodil**
B.1.2.2	Middle name	**Steen**
B.1.2.3	Family name	**Rasmussen**
B.1.3	Address:	
B.1.3.1	Street address	**Hobrovej 18-22**
B.1.3.2	Town/city	**Aalborg**
B.1.3.3	Post code	**9000**
B.1.3.4	Country	**Denmark**
B.1.4	Telephone number:	**+45 97661864**
B.1.5	Fax number:	
B.1.6	E-mail:	**bodil.steen.rasmussen@rn.dk**

B.2	**LEGAL REPRESENTATIVE[5] OF THE SPONSOR IN THE COMMUNITY FOR THE PURPOSE OF THIS TRIAL** (if different from the sponsor)
B.2.1	Name of organisation:
B.2.2	Name of person to contact:
B.2.2.1	Given name
B.2.2.2	Middle name
B.2.2.3	Family name
B.2.3	Address:
B.2.3.1	Street address
B.2.3.2	Town/city
B.2.3.3	Post code
B.2.3.4	Country
B.2.4	Telephone number:
B.2.5	Fax number:
B.2.6	E-mail:

B.3	**STATUS OF THE SPONSOR:**	
B.3.1	Commercial:	**No •**
B.3.2	Non commercial:	**Yes •**

B.4	**Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**	
B.4.1	Name of organisation:	**Innovation Fund Denmark**
B.4.2	Country:	**Denmark**

B.4	**Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**	
B.4.1	Name of organisation:	**Danish Society of Anaesthesia and Intensive Care Medicine (DASAIM)**
B.4.2	Country:	**Denmark**

B.4	**Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**	
B.4.1	Name of organisation:	**Obel Family Foundation**
B.4.2	Country:	**Denmark**

B.4	**Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**	
B.4.1	Name of organisation:	**Regionernes Medicinpulje**
B.4.2	Country:	**Denmark**

B.5	Contact point[6] designated by the sponsor for further information on the trial	
B.5.1	Name of organisation:	**Department of Anaesthesia and intensive Care Medicine, Aalborg University Hospital**
B.5.2	Functional name of contact point (e.g. "Clinical Trial Information Desk"):	**Bodil Steen Rasmussen**
B.5.3	Address:	
B.5.3.1	Street address	**Hobrovej 18-22**
B.5.3.2	Town/city	**Aalborg**
B.5.3.3	Post code	**9000**
B.5.3.4	Country	**Denmark**
B.5.4	Telephone number:	**+45 97661864**
B.5.5	Fax number:	
B.5.6	E-mail: (use a functional e-mail address rather than a personal one)	**bodil.steen.rasmussen@rn.dk**

C. APPLICANT IDENTIFICATION, (please tick the appropriate box)

C.1	REQUEST FOR THE COMPETENT AUTHORITY	
C.1.1	Sponsor	**Yes •**
C.1.2	Legal representative of the sponsor	
C.1.3	Person or organisation authorised by the sponsor to make the application	
C.1.4	Complete the details of the applicant below even if they are provided elsewhere on the form:	
C.1.4.1	Name of Organisation:	**Department of Anaesthesia and Intensive Care Medicine, Aalborg University Hospital**
C.1.4.2	Name of contact person:	
C.1.4.2.1	Given name	**Bodil**
C.1.4.2.2	Middle name	**Steen**
C.1.4.2.3	Family name	**Rasmussen**
C.1.4.3	Address:	
C.1.4.3.1	Street address	**Hobrovej 18-22**
C.1.4.3.2	Town/city	**Aalborg**
C.1.4.3.3	Post code	**9000**
C.1.4.3.4	Country	**Denmark**
C.1.4.4	Telephone number:	**+45 97661864**
C.1.4.5	Fax number:	
C.1.4.6	E-mail:	**bodil.steen.rasmussen@rn.dk**
C.1.5	Request to receive a copy of CTA data as XML:	
C.1.5.1	Do you want a copy of the CTA form data saved on EudraCT as an XML file?	**No •**
C.1.5.1.1	If Yes provide the e-mail address(es) to which it should be sent (up to 5 addresses):	
C.1.5.1.2	Do you want to receive this via password protected link(s)[7]?	**No •**

If you answer No to question C.1.5.1.2 the .xml file will be transmitted by less secure e-mail link(s)

D. INFORMATION ON EACH IMP

Information on each 'bulk product' before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator and each placebo, if applicable. ***For placebo go directly to D.8****. If the trial is performed with several products use extra pages and give each product a sequential number in D.1.1. If the product is a combination product, information should be given for each active substance.*

D.1	**IMP IDENTIFICATION**	
Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial (assign numbers from 1-n):		
D.1.1	This refers to the IMP number:	**PR1**
D.1.2	IMP being tested	**Yes •**
D.1.3	IMP used as a comparator	**No •**

D.2	**STATUS OF THE IMP**	
D.2.1	Has the IMP to be used in the trial a marketing authorisation?	**Yes •**
If the IMP has a marketing authorisation in the Member State concerned by this application, but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2.		
D.2.1.1	If 'Yes', specify the product to be used in the clinical trial:	
D.2.1.1.1	Trade name	
D.2.1.1.1.1	EV Product Code (where applicable)	
D.2.1.1.2	Name of the Marketing Authorisation Holder:	
D.2.1.1.3	Marketing Authorisation number (if Marketing Authorisation granted by a Member State):	
D.2.1.1.4	Is the IMP modified in relation to its Marketing Authorisation?	**No •**
D.2.1.1.4.1	If 'Yes', please specify:	
D.2.1.2	The country that granted the Marketing Authorisation	**Denmark**
D.2.1.2.1	Is this the Member State concerned with this application?	**Yes •**

D.2.2	Situations where an IMP to be used in the CT has a Marketing Authorisation in the Member State concerned, but the protocol allows that any brand of the IMP with a Marketing Authorisation in that Member State be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start	
D.2.2.1	In the protocol, is treatment defined only by active substance?	**No •**
D.2.2.1.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.2	In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?	**No •**
D.2.2.2.1	If 'Yes', give active substance in D.3.8 or D.3.9	
D.2.2.3	The products to be administered as IMPs are defined as belonging to an ATC group[9]	**Yes •**
D.2.2.3.1	If 'Yes', give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4	Other:	**No •**
D.2.2.4.1	If 'Yes', please specify:	

D.2.3	IMPD submitted:	
D.2.3.1	Full IMPD:	**No •**
D.2.3.2	Simplified IMPD:	**No •**
D.2.3.3	Summary of product characteristics (SmPC) only:	**Yes •**
D.2.4	Has the use of the IMP been previously authorised in a	**No •**

	clinical trial conducted by the sponsor in the Community?	
D.2.4.1	If 'Yes' specify which Member States:	
D.2.5	Has the IMP been designated in this indication as an orphan drug in the Community?	**No •**
D.2.5.1	If 'Yes', give the orphan drug designation number[10]**:**	

D.2.6	Has the IMP been the subject of scientific advice related to this clinical trial?	**No •**
D.2.6.1	If 'Yes' to D.2.6, please indicate source of advice and provide a copy in the CTA request:	
D.2.6.1.1	CHMP[11]?	**No •**
D.2.6.1.2	National Competent Authority?	**No •**

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable[12]:	
D.3.2	Product code where applicable[13]:	
D.3.3	ATC codes, if officially registered[14]:	**V 03 AN 01**
D.3.4	Pharmaceutical form (use standard terms):	**Medicinal gas, cryogenic**
D.3.4.1	Is this a specific paediatric formulation?	**No •**
D.3.5	Maximum duration of treatment of a subject according to the protocol: **90 days**	
D.3.6	Dose allowed:	
D.3.6.1	For first trial only:	
	Specify per day or total	**Not Answered •**
	Specify total dose (number and unit):	
	Route of administration (relevant to the first dose):	
D.3.6.2	For all trials	
	Specify per day or total	**Per day •**
	Specify total dose (number and unit):	**100 % (V/V) percent volume/volume**
	Route of administration (relevant to the maximum dose):	**Inhalation use**
D.3.7	Routes of administration (use standard terms):	**Inhalation use**

D.3.8	Name of each active substance (INN or proposed INN if available):
D.3.9	Other available name for each active substance (provide all available):
D.3.9.1	CAS[15] number
D.3.9.2	Current sponsor code
D.3.9.3	Other descriptive name
D.3.9.4	EV Substance code
D.3.9.5	Full Molecular formula
D.3.9.6	Chemical/biological description of the Active Substance
D.3.10	Strength (specify all strengths to be used):
D.3.10.1	Concentration unit:
D.3.10.2	Concentration type ("exact number", "range", "more than" or "up to"):
D.3.10.3	Concentration (number).

D.3.11	Type of IMP	
Does the IMP contain an active substance:		
D.3.11.1	Of chemical origin?	**Yes •**
D.3.11.2	Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP)?	**No •**
Is this a:		
D.3.11.3	Advanced Therapy IMP (ATIMP)?	**No •**
D.3.11.3.1	Somatic cell therapy medicinal product[16]?	**No •**

D.3.11.3.2	Gene therapy medicinal product[17]?	**No** •
D.3.11.3.3	Tissue Engineered Product[18]?	**No** •
D.3.11.3.4	Combination ATIMP (i.e. one involving a medical device[19])?	**No** •
D.3.11.3.5	Has the Committee on Advanced Therapies issued a classification for this product?	**No** •
D.3.11.3.5.1	If 'Yes' please provide that classification and its reference number:	
D.3.11.4	Combination product that includes a device, but does not involve an Advanced Therapy?	**No** •
D.3.11.5	Radiopharmaceutical medicinal product?	**No** •
D.3.11.6	Immunological medicinal product (such as vaccine, allergen, immune serum)?	**No** •
D.3.11.7	Plasma derived medicinal product?	**No** •
D.3.11.8	Extractive medicinal product?	**No** •
D.3.11.9	Recombinant medicinal product?	**No** •
D.3.11.10	Medicinal product containing genetically modified organisms?	**No** •
D.3.11.10.1	Has the authorisation for contained use or release been granted?	**No** •
D.3.11.10.2	Is it pending?	**No** •
D.3.11.11	Herbal medicinal product?	**No** •
D.3.11.12	Homeopathic medicinal product?	**No** •
D.3.11.13	Another type of medicinal product?	**No** •
D.3.11.13.1	If 'another type of medicinal product' specify the type of medicinal product:	
D.3.12	Mode of action (*free text*[20]) **Oxygen is essential in the oxidative phosphorylation within the mitochondria of all humans. Oxidative phosphorylation is the principal energy source of the body, sustaining vital functions of all organs.**	
D.3.13	Is it an IMP to be used in a first-in-human clinical trial?	**No** •
D.3.13.1	If 'Yes', are there risk factors identified, according to the guidance FIH?[21]	

D.4	**SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)**	
D.4.1	Origin of cells	
D.4.1.1	Autologous	**No** •
D.4.1.2	Allogeneic	**No** •
D.4.1.3	Xenogeneic	**No** •
D.4.1.3.1	If 'Yes', specify the species of origin:	
D.4.2	Type of cells	
D.4.2.1	Stem cells	**No** •
D.4.2.2	Differentiated cells	**No** •
D.4.2.2.1	If 'Yes', specify the type (e.g. keratinocytes, fibroblasts, chondrocytes…):	
D.4.2.3	Others:	**No** •
D.4.2.3.1	If others, specify:	

D.5	**GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**	
D.5.1	Gene(s) of interest:	
D.5.2	In vivo gene therapy:	**No** •
D.5.3	Ex vivo gene therapy:	**No** •
D.5.4	Type of gene transfer product	
D.5.4.1	Nucleic acid (e.g. plasmid): If 'Yes', specify if:	**No** •
D.5.4.1.1	Naked:	**No** •
D.5.4.1.2	Complexed	**No** •
D.5.4.2	Viral vector:	**No** •

D.5.4.2.1	If 'Yes', specify the type: adenovirus, retrovirus, AAV, …:	
D.5.4.3	Others	**No •**
D.5.4.3.1	If others, specify:	
D.5.5	Genetically modified somatic cells:	**No •**
If 'Yes', specify the origin of the cells:		
D.5.5.1	Autologous:	**No •**
D.5.5.2	Allogeneic:	**No •**
D.5.5.3	Xenogeneic:	**No •**
D.5.5.3.1	If 'Yes', specify the species of origin:	
D.5.5.4	Specify type of cells (hematopoietic stem cells…):	

D.6	**TISSUE ENGINEERED PRODUCT**	
The indication which determines that this is a Tissue Engineered Product as opposed to a Cell Therapy product is given in section E.1.1.		
D.6.1	Origin of cells	
D.6.1.1	Autologous	**No •**
D.6.1.2	Allogeneic	**No •**
D.6.1.3	Xenogeneic	**No •**
D.6.1.3.1	If 'Yes', specify the species of origin:	
D.6.2	Type of cells	
D.6.2.1	Stem cells	**No •**
D.6.2.2	Differentiated cells	**No •**
D.6.2.2.1	If 'Yes', specify the type of cells(e.g. keratinocytes, fibroblasts, chondrocytes, …):	
D.6.2.3	Others:	**No •**
D.6.2.3.1	If others, specify:	

D.7	**PRODUCTS CONTAINING DEVICES (i.e. MEDICAL DEVICES, SCAFFOLDS ETC.)**	
D.7.1	Give a brief description of the device:	
D.7.2	What is the name of the device?	
D.7.3	Is the device implantable?	**No •**
D.7.4	Does this product contain:	
D.7.4.1	A medical device?	**No •**
D.7.4.1.1	Does this medical device have a CE mark?	**No •**
D.7.4.1.1.1	The notified body is:	
D.7.4.2	Bio-materials?	**No •**
D.7.4.3	Scaffolds?	**No •**
D.7.4.4	Matrices?	**No •**
D.7.4.5	Other?	**No •**
D.7.4.5.1	If other, specify:	

D.8 INFORMATION ON PLACEBO (if relevant; repeat as necessary)

D.8.1	Is there a placebo:	**No •**

D.8.2	This refers to placebo number:
D.8.3	Pharmaceutical form:
D.8.4	Route of administration:

D.8.5	Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1	
D.8.5.1	Composition, apart from the active substance(s):	
D.8.5.2	Is it otherwise identical to the IMP?	**Yes ? No ? Not Answered ?**
D.8.5.2.1	If not, specify major ingredients:	

D.9 SITE(S) WHERE THE QUALIFIED PERSON CERTIFIES BATCH RELEASE[22]

*This section is dedicated to **finished** IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. If there is more than one site or more than one IMP is certified, use extra pages and give each IMP its number from section D.1.1 or D.8.2 In the case of multiple sites indicate the product certified by each site*

D.9.1	Do not fill in section D.9.2 for an IMP that: *Has a MA in the EU **and*** *Is sourced from the EU market **and*** *Is used in the trial without modification(e.g. not overencapsulated) **and*** *The packaging and labelling is carried out for local use only as per article 9.2. of the Directive 2005/28/EC (GCP Directive)* If all these conditions are met tick ● and list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2 to which this applies **PR1**

D.9.2	**Who is responsible in the Community for the certification of the finished IMPs?** This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2): please tick the appropriate box:	
D.9.2.1	Manufacturer	**?**
D.9.2.2	Importer	**?**
D.9.2.3	Name of the organisation:	
D.9.2.4	Address:	
D.9.2.4.1	Street Address	
D.9.2.4.2	Town/City	
D.9.2.4.3	Post Code	
D.9.2.4.4	Country	
D.9.2.5	Give the manufacturing authorisation number:	
D.9.2.5.1	If No authorisation, give the reasons:	

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.9.2 above.

E. GENERAL INFORMATION ON THE TRIAL

This section should be used to provide information about the aims, scope and design of the trial. When the protocol includes a sub-study in the MS concerned section E.2.3 should be completed providing information about the sub-study. To identify it check the sub-study box in the 'Objective of the trial' question below.

E.1	**MEDICAL CONDITION OR DISEASE UNDER INVESTIGATION**	
E.1.1	Specify the medical condition(s) to be investigated[23] (free text):	
	English	**Acute hypoxaemic respiratory failure in patients admitted to the intensive care unit**
E.1.1.1	Medical condition in easily understood language	
	English	**Patients with acute pulmonary failure and inadequate oxygenation of the blood, admitted to an intensive care unit**
	Danish	**Patienter indlagt akut på en intensiv afdeling med lungesvigt**
E.1.1.2	Therapeutic area	
	Diseases [C] - Respiratory Tract Diseases [C08]	

E.1.2 MedDRA version, system organ class, level, term and classification code[24]:

Version	System Organ Class	Classification Code	Term	Level
20.0	**10038738 - Respiratory, thoracic and mediastinal disorders**	**10001053**	**Acute respiratory failure**	**PT**
20.0	**10042613 - Surgical and medical procedures**	**10022519**	**Intensive care**	**PT**

E.1.3 Is any of the conditions being studied a rare disease[25]? **No •**

E.2	**OBJECTIVE OF THE TRIAL**	
E.2.1	Main objective:	
	English	**To assess the benefits and harms of two targets of partial pressure of oxygen in arterial blood in guiding the oxygen administration in acutely ill adults with hypoxaemic respiratory failure at ICU admission.**
	Danish	**At belyse fordele og ulemper ved at tilstræbe to forskellige niveauer af iltindhold i blodet, målt ved standard målemetoden på intensiv afdeling, som er ilttrykket i pulsårerne, hos kritisk syge voksne patienter, som indlægges akut på en intensiv afdeling med lungesvigt**
E.2.2	Secondary objectives:	
	English	**To asses health economic implications of two targets of partial pressure of oxygen in arterial blood in guiding the oxygen administration in acutely ill adults with hypoxaemic respiratory failure at ICU admission. Conducted through a health economic analysis at one year follow-up of the last enrolled patient.**
	Danish	**At vurdere de sundhedsøkonomiske omkostninger/besparelser ved at tilstræbe to forskellige niveauer af iltindhold i blodet hos kritisk syge voksne patienter, som indlægges akut på en intensiv afdeling med lungesvigt. Dette planlagt når der er lavet et års opfølgning af den sidste inkluderede patient.**

E.2.3 Is there a sub-study? **No •**

E.2.3.1 If 'Yes', give the full title, date and version of each sub-study and their related objectives:

E.3	**PRINCIPAL INCLUSION CRITERIA *(list the most important)***	
	English	**- Acutely admitted to the intensive care unit AND**

		- Aged ≥ 18 years AND **- Receive supplemental oxygen with a flow of at least 10 L per minute in an open system or at least an fraction of inspired oxygen of 0.50 in a closed system, including invasive ventilation, non-invasive ventilation or continuous positive airway pressure AND** **- Are expected to receive oxygen administration for at least 24 hours in the ICU AND** **- Have an arterial line in place**
	Danish	**- Akut indlagt på intensiv afdeling OG** **- Alder ≥ 18 år OG** **- Får et ilttilskud på mindst 10 liter per minut via iltkateter i næse eller gennem ansigtsmaske, eller er tilkoblet en respirator med et ilttilskud på mindst 50% OG** **- Forventes at skulle have behov for ilttilskud på den intensive afdeling i mindst 24 timer OG** **- Har et fungerende kateter anlagt i en pulsåre (arterie-kanyle)**

E.4	**PRINCIPAL EXCLUSION CRITERIA *(list the most important)***	
	English	**- Cannot be randomised within twelve hours after present ICU admission** **- Chronic mechanical ventilation for any reason** **- Use of home oxygen** **- Previous treatment with bleomycin** **- Organ transplant during current hospital admission** **- Withdrawal from active therapy or brain death deemed imminent** **- Fertile woman with positive urine human gonadotropin (hCG) or plasma-hCG** **- Carbon monoxide poisoning** **- Cyanide poisoning** **- Methaemoglobinaemia** **- Paraquat poisoning** **- Any condition expected to involve the use of hyperbaric oxygen (HBO)** **- Sickle cell disease** **- Consent not obtainable according to national regulations** **- Previously randomised into the HOT-ICU trial**
	Danish	**- Inklusion til studiet kan ikke foretages indenfor de første 12 timer efter indlæggelsen på intensiv afdeling** **- Har hjemme-respirator** **- Får ilt i hjemmet** **- Er tidligere behandlet med bleomycin** **- Der er planlagt/har været foretaget en organtransplantation under indeværende indlæggelse.** **- Aktiv behandling vurderet udsigtsløs eller patienten er nært forestående hjernedød** **- Er gravid** **- Er forgiftet med kulmonooxid, cyanid eller paraquat** **- Har methæmoglobin i blodet** **- Har en tilstand, som kræver behandling med ilt under overtryk (hyperbar iltbehandling)** **- Har seglcelle sygdom** **- Det er ikke muligt at indhente informeret samtykke** **- Tidligere inkluderet i HOT-ICU forsøget**

E.5	**END POINT(S):**	
E.5.1	Primary End Point (repeat as necessary)[26]	
	English	**Mortality**

	Danish	**Dødelighed**
E.5.1.1	Timepoint(s) of evaluation of this end point	
	English	**90 days post-randomisation**
	Danish	**90 dage efter lodtrækning**
E.5.2	Secondary End Point (repeat as necessary)	
	English	**- Number of patients with one or more SAEs in the ICU after randomisation; SAEs are defined as new episode of shock and new episodes of ischemic events including myocardial or intestinal ischaemia or ischemic stroke in the 90-day period** **- Days alive without the use of respiratory support, renal replacement therapy or circulatory support in the 90-day period** **- Days alive out of the hospital in the 90-day period** **- Mortality 1-year after randomisation** **- Health related quality of life (Euroqual, EQ-5D-5L) 1-year after randomisation.** **- Cognitive function 1-year after randomisation as assessed using RBANS score in selected sites** **- A health economic analysis based on the result of the trial and specified (cost-effectiveness versus cost-minimisation analyses)**
	Danish	**- Nyopståede tilfælde af kredsløbssvigt, nyopståede tegn på vævskade i hjerte, hjerne og tarm i 90 dage efter lodtrækningen** **- Dage i live uden behandling med respirator, dialyse eller kredsløbsstimulerende medicin i 90 dage efter lodtrækningen** **- Dage i live og udskrevet fra hospitalet i 90 dage efter lodtrækningen** **- Dødelighed et år efter lodtrækningen** **- Vurdering af livskvalitet og kognitiv funktion (selekterede sites) efter et år efter lodtrækningen** **- Overordnede sundhedsøkonomiske analyser et år efter lodtrækningen af den sidste inkluderede patient.**
E.5.2.1	Timepoint(s) of evaluation of this end point	
	English	**See description in E.5.2**
	Danish	**Se beskrivelse i E.5.2**

E.6	**SCOPE OF THE TRIAL – Tick all boxes where applicable**	
E.6.1	Diagnosis	**No •**
E.6.2	Prophylaxis	**No •**
E.6.3	Therapy	**Yes •**
E.6.4	Safety	**No •**
E.6.5	Efficacy	**No •**
E.6.6	Pharmacokinetic	**No •**
E.6.7	Pharmacodynamic	**No •**
E.6.8	Bioequivalence	**No •**
E.6.9	Dose Response	**No •**
E.6.10	Pharmacogenetic	**No •**
E.6.11	Pharmacogenomic	**No •**
E.6.12	Pharmacoeconomic	**Yes •**
E.6.13	Others	**No •**
E.6.13.1	If others, specify:	

E.7	**TRIAL TYPE AND PHASE[27]**	
E.7.1 Is it:	Human pharmacology (Phase I)	**No •**
E.7.1.1	First administration to humans	**No •**

E.7.1.2	Bioequivalence study	**No •**
E.7.1.3	Other:	**No •**
E.7.1.3.1	If other, please specify:	
E.7.2	Therapeutic exploratory (Phase II)	**No •**
E.7.3	Therapeutic confirmatory (Phase III)	**No •**
E.7.4	Therapeutic use(Phase IV)	**Yes •**

E.8	**DESIGN OF THE TRIAL**	
E.8.1	Controlled	**Yes •**
	If 'Yes', specify:	
E.8.1.1	Randomised:	**Yes •**
E.8.1.2	Open:	**Yes •**
E.8.1.3	Single blind:	**No •**
E.8.1.4	Double blind:	**No •**
E.8.1.5	Parallel group:	**Yes •**
E.8.1.6	Cross over:	**No •**
E.8.1.7	Other:	**No •**
E.8.1.7.1	If other specify:	
E.8.2	If controlled, specify the comparator:	
E.8.2.1	Other medicinal product(s)	**No •**
E.8.2.2	Placebo	**No •**
E.8.2.3	Other	**Yes •**
E.8.2.3.1	If 'Yes' to other, specify :	
	Danish	**Forskellig dosering af ilt. Komperatoren er det højeste oxygeneringsmål.**
	English	**Different dosage of oxygen. The comparator is the highest oxygenation target.**
E.8.2.4	Number of treatment arms in the trial	**2**

E.8.3	Single site in the Member State concerned (see also section G):	**No •**
E.8.4	Multiple sites in the Member State concerned(see also section G):	**Yes •**
E.8.4.1	Number of sites anticipated in Member State concerned	**21**
E.8.5	Multiple Member States:	**Yes •**
E.8.5.1	Number of sites anticipated in the EEA:	**50**
E.8.6	Trial involving sites outside the EEA:	
E.8.6.1	Trial being conducted both within and outside the EEA:	**Yes •**
E.8.6.2	Trial being conducted completely outside of the EEA:	**No •**
E.8.6.3	If E.8.6.1 or E.8.6.2 are Yes, specify the regions in which trial sites are planned:	
	Denmark **Finland** **Iceland** **Netherlands** **Norway** **Sweden** **Switzerland** **United Kingdom**	
E.8.6.4	If E.8.6.1 or E.8.6.2 are Yes, specify the number of sites anticipated outside of the EEA:	**2**
E.8.7	Trial having an independent data monitoring committee:	**Yes •**

E.8.8	Definition of the end of trial: If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition:	
	English	**Trial allocation is planned to end when 2 x 1464 (2928) patients have been randomised (April 2019) and 90-days follow-up has been completed (July 2019).** **The patients will be contacted one year after randomisation (last patient contacted April 2020) to conduct follow-up on health related quality of life and cognitive function (selected sites).**
	Danish	**Forsøgsallokeringen er planlagt til at stoppe når 2 x 1464 (2928) patienter er blevet randomiseret (april 2019) og 90 dages opfølgning er færdiggjort (juli 2019).**

		Patienterne vil blive kontaktet et år efter randomiseringen (sidste patient forventes kontaktet i april 2020) for at lave vurdering af livskvalitet og kognitiv funktion (selekterede sites).
E.8.9	Initial estimate of the duration of the trial[28] (years, months and days)	
E.8.9.1	In the Member State concerned	**3 years 0 months 0 days**
E.8.9.2	In all countries concerned by the trial	**3 years 0 months 0 days**
E.8.10	Proposed date of start of recruitment	
E.8.10.1	In the Member State concerned	**2017-05-01**
E.8.10.2	In any country	**2017-05-01**

F. POPULATION OF TRIAL SUBJECTS

F.1	AGE RANGE		
F.1.1	Are the trial subjects under 18? If 'Yes', specify the estimated number of subjects planned in each age range for the whole trial:	Approx. No. of patients[29]	**No •**
F.1.1.1	In utero	()	**No •**
F.1.1.2	Preterm newborn infants (up to gestational age < 37 weeks)	()	**No •**
F.1.1.3	Newborns (0-27 days)	()	**No •**
F.1.1.4	Infants and toddlers (28 days - 23 months)	()	**No •**
F.1.1.5	Children (2-11 years)	()	**No •**
F.1.1.6	Adolescents (12-17 years)	()	**No •**
F.1.2	Adults (18-64 years)	(**1312**)	**Yes •**
F.1.3	Elderly (>= 65 years)	(**1616**)	**Yes •**

F.2	GENDER	
F.2.1	Female	**Yes •**
F.2.2	Male	**Yes •**

F.3	GROUP OF TRIAL SUBJECTS	
F.3.1	Healthy volunteers	**No •**
F.3.2	Patients	**Yes •**
F.3.3	Specific vulnerable populations	**Yes •**
F.3.3.1	Women of child bearing potential not using contraception	**Yes •**
F.3.3.2	Women of child bearing potential using contraception	**Yes •**
F.3.3.3	Pregnant women	**No •**
F.3.3.4	Nursing women	**Yes •**
F.3.3.5	Emergency situation	**Yes •**
F.3.3.6	Subjects incapable of giving consent personally	**Yes •**
F.3.3.6.1	If 'Yes', specify:	
	English	**The trial will enroll critically ill patients (emergency situations) who will be temporarily incompetent due to the severety of illness or as a consequence of the treatment (sedation and analgesics).**
	Danish	**Forsøget inkluderer kritisk syge patienter i akutte situationer, disse patienter vil være midlertidigt uden handleevne grundet sygdomssværhedsgraden og/eller behandlingen med bedøvelsesmidler og smertestillende medicin.**
F.3.3.7	Others:	**No •**
F.3.3.7.1	If 'Yes', specify:	

F.4	PLANNED NUMBER OF SUBJECTS TO BE INCLUDED:	
F.4.1	In the member state	**1500**
F.4.2	For a multinational trial**:**	
F.4.2.1	In the EEA	**2488**
F.4.2.2	In the whole clinical trial	**2928**

F.5	PLANS FOR TREATMENT OR CARE AFTER THE SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. **please specify** (free text):	
	English	**None**

G. CLINICAL TRIAL SITES/INVESTIGATORS IN THE MEMBER STATE CONCERNED BY THIS REQUEST

G.1	**CO-ORDINATING INVESTIGATOR (for multicentre trial) and principal investigator (for single centre trial)**	
G.1.1	Given name:	**Olav**
G.1.2	Middle name, if applicable:	**Lilleholt**
G.1.3	Family name:	**Schjørring**
G.1.4	Qualification (MD…….)	**MD**
G.1.5	Professional address:	
G.1.5	Institution name	**Aalborg University Hospital**
G.1.5	Institution department	**Department of Anaesthesia and Intensive Care Medicine**
G.1.5.1	Street address	**Hobrovej 18-22**
G.1.5.2	Town/city	**Aalborg**
G.1.5.3	Post code	**9000**
G.1.5.4	Country	**Denmark**
G.1.6	Telephone number:	**+45 97661921**
G.1.7	Fax number:	
G.1.8	E-mail:	**o.schjoerring@rn.dk**

G.2	**PRINCIPAL INVESTIGATORS *(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Christian**
G.2.2	Middle name, if applicable:	**S.**
G.2.3	Family name:	**Meyhoff**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Bispebjerg Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS *(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Morten**
G.2.2	Middle name, if applicable:	**Heiberg**
G.2.3	Family name:	**Bestle**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Hillerød Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Hans-Henrik**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Bülow**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Holbæk Sygehus**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Ulf**
G.2.2	Middle name, if applicable:	**Gøttrup**
G.2.3	Family name:	**Pedersen**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Hvidovre Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Thorbjørn**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Grøfte**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Randers Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Bjørn**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Brand**

G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Copenhagen University Hospital Rigshospitalet**
G.2.5	Institution department	**Department of Intensive Care, 4131**
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Thomas**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Hildebrandt**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Roskilde Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Helle**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Nibro**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Aarhus University Hospital, NBG**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Steffen**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Christensen**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Aarhus University Hospital, Skejby**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	

G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Hans**
G.2.2	Middle name, if applicable:	**Michael**
G.2.3	Family name:	**Betsch**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Aarhus University Hospital, THG**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Lone**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Buus**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Horsens Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Robert**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Winding**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Herning Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Nilanjan**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Dey**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Holstebro Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Susanne**
G.2.2	Middle name, if applicable:	**Andi**
G.2.3	Family name:	**Iversen**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Slagelse Sygehus**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Christoffer**
G.2.2	Middle name, if applicable:	**Grant**
G.2.3	Family name:	**Sølling**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Viborg Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Valerij**
G.2.2	Middle name, if applicable:	

G.2.3	Family name:	**Khridin**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Zealand University Hospital, Køge**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Jane**
G.2.2	Middle name, if applicable:	**Stab**
G.2.3	Family name:	**Nielsen**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Kolding Sygehus**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Andrei**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Ciubotariu**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Hjørring Regional Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	
G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.2	**PRINCIPAL INVESTIGATORS** ***(for multicentre trial ; where necessary, use additional forms)***	
G.2.1	Given name:	**Henrik**
G.2.2	Middle name, if applicable:	
G.2.3	Family name:	**Christensen**
G.2.4	Qualification (MD…….)	
G.2.5	Professional address:	
G.2.5	Institution name	**Herlev Hospital**
G.2.5	Institution department	
G.2.5.1	Street address	

G.2.5.2	Town/city	
G.2.5.3	Post code	
G.2.5.4	Country	**Denmark**
G.2.6	Telephone number:	
G.2.7	Fax number:	
G.2.8	E-mail:	

G.3	**CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL** **Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised** (repeat as needed for multiple organisations).	
G.3.1	Name of organisation:	
G.3.2	Department	
G.3.3	Name of contact person:	
G.3.3.1	Given name	
G.3.3.2	Middle name	
G.3.3.3	Family name	
G.3.4	Address:	
G.3.4.1	Street address	
G.3.4.2	Town/city	
G.3.4.3	Post code	
G.3.4.4	Country	
G.3.5	Telephone number:	
G.3.6	Fax number:	
G.3.7	E-mail:	
G.3.8	Enter the details of any duties subcontracted to this central technical facility in this trial	
G.3.8.1	Routine clinical pathology testing	**Yes ? No ? Not Answered ?**
G.3.8.2	Clinical chemistry	**Yes ? No ? Not Answered ?**
G.3.8.3	Clinical haematology	**Yes ? No ? Not Answered ?**
G.3.8.4	Clinical microbiology	**Yes ? No ? Not Answered ?**
G.3.8.5	Histopathology	**Yes ? No ? Not Answered ?**
G.3.8.6	Serology/ endocrinology	**Yes ? No ? Not Answered ?**
G.3.8.7	Analytical chemistry	**Yes ? No ? Not Answered ?**
G.3.8.8	ECG analysis/ review	**Yes ? No ? Not Answered ?**
G.3.8.9	Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	**Yes ? No ? Not Answered ?**
G.3.8.10	Primary/ surrogate endpoint test	**Yes ? No ? Not Answered ?**
G.3.8.11	Other Duties subcontracted?	**Yes ? No ? Not Answered ?**
G.3.8.11.1	If 'Yes', specify the other duties	

G.4	**NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)**	
G.4.1	Name of organisation:	**Scandinavian Critical Care Trials Group**
G.4.2	Name of contact person:	
G.4.2.1	Given name	**Anders**
G.4.2.2	Middle name	
G.4.2.3	Family name	**Perner**
G.4.3	Address:	
G.4.3.1	Street address	**Blegdamsvej 9**
G.4.3.2	Town/city	**Copenhagen**
G.4.3.3	Post code	**2100**
G.4.3.4	Country	**Denmark**
G.4.4	Telephone number:	
G.4.5	Fax number:	
G.4.6	E-mail:	**anders.perner@regionh.dk**
G.4.7	Activities carried out by the network:	

G.4	NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)	
G.4.1	Name of organisation:	**Centre for Research in Intensive Care (CRIC)**
G.4.2	Name of contact person:	
G.4.2.1	Given name	**Anders**
G.4.2.2	Middle name	
G.4.2.3	Family name	**Perner**
G.4.3	Address:	
G.4.3.1	Street address	**Blegdamsvej 9**
G.4.3.2	Town/city	**Copenhagen**
G.4.3.3	Post code	**2100**
G.4.3.4	Country	**Denmark**
G.4.4	Telephone number:	
G.4.5	Fax number:	
G.4.6	E-mail:	**anders.perner@regionh.dk**
G.4.7	Activities carried out by the network:	

G.4	NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)	
G.4.1	Name of organisation:	**Copenhagen Trial Unit (CTU)**
G.4.2	Name of contact person:	
G.4.2.1	Given name	**Jørn**
G.4.2.2	Middle name	
G.4.2.3	Family name	**Wetterslev**
G.4.3	Address:	
G.4.3.1	Street address	**Blegdamsvej 9**
G.4.3.2	Town/city	**Copenhagen**
G.4.3.3	Post code	**2900**
G.4.3.4	Country	**Denmark**
G.4.4	Telephone number:	
G.4.5	Fax number:	
G.4.6	E-mail:	**wetterslev@ctu.dk**
G.4.7	Activities carried out by the network:	

G.5	ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS	
G.5.1	**Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?**	**Yes •**

Repeat as necessary for multiple organisations:

G.5.1.1	Organisation name:	**GCP-unit**
G.5.1.2	Organisation department	**Aalborg and Aarhus University Hospitals**
G.5.1.3	Name of contact person :	
G.5.1.3.1	Given name	**Annette**
G.5.1.3.2	Middle name	
G.5.1.3.3	Family name	**Jørgensen**
G.5.1.4	Address:	
G.5.1.4.1	Street address	**Olof Palmes Alle 15**
G.5.1.4.2	Town/city	**Aarhus N**
G.5.1.4.3	Post code	**8200**
G.5.1.4.4	Country	**Denmark**
G.5.1.5	Telephone number:	**+45 78413950**
G.5.1.6	Fax number:	
G.5.1.7	E-mail:	**anjor@clin.au.dk**
G.5.1.8	All tasks of the sponsor	**No •**
G.5.1.9	Monitoring	**Yes •**

G.5.1.10	Regulatory (e.g. preparation of applications to CA and ethics committee)	**No** •
G.5.1.11	Investigator recruitment	**No** •
G.5.1.12	IVRS[30] – treatment randomisation	**No** •
G.5.1.13	Data management	**No** •
G.5.1.14	E-data capture	**No** •
G.5.1.15	SUSAR reporting	**No** •
G.5.1.16	Quality assurance auditing	**No** •
G.5.1.17	Statistical analysis	**No** •
G.5.1.18	Medical writing	**No** •
G.5.1.19	Other duties subcontracted?	**No** •
G.5.1.19.1	If 'Yes' to other, please specify:	

H. COMPETENT AUTHORITY / ETHICS COMMITTEE IN THE MEMBER STATE CONCERNED BY THIS REQUEST

H.1	**TYPE OF APPLICATION**	
If this application is addressed to the Competent Authority, please tick the Ethics Committee box and give information on the Ethics committee concerned. If this application is addressed to the Ethics Committee, please tick the Competent Authority box and give the information on the Competent Authority concerned.		
H.1.1	Competent Authority	**No ●**
H.1.2	Ethics Committee	**Yes ●**

H.2	**INFORMATION ON ETHICS COMMITTEE**	
H.2.1	Name:	**The Commitee on Health Research Ethics of the North Denmark Region**
H.2.2	Address	
H.2.2.1	Street address	**Niels Bohrs Vej 30**
H.2.2.2	Town/city	**Aalborg Øst**
H.2.2.3	Post code	**9220**
H.2.2.4	Country	**Denmark**
H.2.3	Date of submission:	**2017-01-30**

H.3	**OPINION**	
H.3.1	To be requested	**No ●**
H.3.2	Pending	**Yes ●**
H.3.3	Given	**No ●**
	If 'Given', specify:	
H.3.3.1	Date of opinion:	
H.3.3.2	Opinion favourable	**No ●**
H.3.3.3	Opinion not favourable	**No ●**
	If not favourable, give:	
H.3.3.3.1	The reasons	
H.3.3.3.2	The eventual anticipated date of resubmission:	

I. SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

I.1	I hereby confirm that /confirm on behalf of the sponsor (delete which is not applicable) that: • the information provided is complete; • the attached documents contain an accurate account of the information available; • the clinical trial will be conducted in accordance with the protocol; and • the clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

I.2	**APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY** (as stated in section C.1):
I.2.1	Date:
I.2.2	Signature[31]:
I.2.3	Print name:

I.3	**APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section C.2):
I.3.1	Date:
I.3.2	Signature[32]:
I.3.3	Print name:

ENDNOTES

[1] Any translation of the protocol should be assigned the same date and version as those in the original document.
[2] International Standard Randomised Controlled Trial Number. Sponsors may wish to use an International Standardised Random Controlled Trial Number (ISRCTN) to identify their trial in addition to the EudraCT number; for instance if their trial is part of a multinational trial with sites outside the Community. They can obtain the number and guidance from the Current Controlled Trials website http://www.controlled-trials.com/isrctn to which there is a link from the EudraCT database website http://eudract.ema.europa.eu. When available they should provide it in Section A.6 of the application form.
[3] US National Clinical Trial (NCT) Numbers required on the FDA clinical trial application form.
[4] For a resubmission following previous withdrawal of an application or unfavourable opinion of an ethics committee, or previous withdrawal of an application or refusal of a request by the competent authority, enter a letter in the sequence, A for first resubmission, B for second, C for third et seq.
[5] In accordance with Article 19 of Directive 2001/20/EC.
[6] The contact point should give functional information rather than details of one "person", in order to avoid the need for update and maintenance of these contact details.
[7] This requires a EudraLink account. (See https://eudract.ema.europa.eu/document.html for details)
[8] According to national legislation.
[9] Available from the Summary of Product Characteristics (SmPC)
[10] According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000): http://ec.europa.eu/enterprise/pharmaceuticals/register/index.htm
[11] Committee for Medicinal Products for Human Use of the European Medicines Agency
[12] To be provided only when there is No trade name. This is the name routinely used by a sponsor to identify the IMP in the CT documentation (protocol, IB…).
[13] To be provided only when there is No trade name. This is a code designated by the sponsor which represents the name routinely used by the sponsor to identify the product in the CT documentation. For example, a code may be used for combinations of drugs or drugs and devices.
[14] Available from the Summary of Product Characteristics (SmPC).
[15] Chemical Abstracts Service.
[16] Complete also section D.4 Cell therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[17] Complete also section D.5 Gene Therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[18] Complete also section D.6 - Tissue Engineered Product as defined in Article 2(1)(b) of Regulation1394/2007/EC.
[19] Complete also section D.7
[20] The mode of action should briefly describe the chemical, biochemical, immunological or biological means the IMP uses to effect its pharmaceutical action.
[21] Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007 19 July 2007
[22] In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medical Products in the European Union.
[23] In the case of healthy volunteer trials, the intended indication for the product under development should be provided.
[24] Applicants are encouraged to provide the MedDRA lower level term if applicable and classification code. These can be accessed from the EMEA EudraCT website (http://eudract.ema.europa.eu/).
[25] Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation: COM/436/01 (http://www.ema.europa.eu/htms/human/orphans/intro.htm).
[26] The protocol will usually identify a single primary end point but there may be a co-primary end point in some cases and/or a number of secondary end points.
[27] The descriptions of the trial types provided are those recommended in preference to Phases. See page 5 of Community guideline CPMP/ICH/291/95. The development of a new indication after initial approval of a medicine should be considered as a new development plan.
[28] From the first inclusion until the last visit of the last subject.
[29] These numbers will be initial estimates. Applicants will not be required to update this information nor do they constitute an authorisation or restriction on the inclusion of these numbers of patients in the trial. The numbers of subjects whose inclusion is authorised are those set out in the authorised version of the protocol, or subsequent authorised amendments.
[30] Interactive Voice Response System: commonly used for randomisation of treatment and controlling the shipment of stock of product.
[31] On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.

[32] On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.