

**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**

*For official use:*

Date of receiving the request:	Date of request for additional information:	Grounds for non acceptance / negative opinion :
Date of request for information to make it valid:		Give date:
Date of valid application :	Date of receipt of additional / amended information :	Authorisation / positive opinion:
Date of start of procedure :		Give date:
Competent authority registration number :		Withdrawal of application :
Ethics Committee registration number :		Give date :

**A: Trial identification**

**A1. National Competent Authority:**

UK - MHRA

**A2. European Clinical Trials Database (EudraCT) number:**

2020-001113-21

**A3. Full title of the trial:**

Randomised Evaluation of COVID-19 Therapy (RECOVERY)

**A3-1. Title of the trial for lay people, in easily understood, i.e. non-technical, language**

RANDOMISED EVALUATION OF COVID-19 THERAPY (RECOVERY)

**A3-2. Name or abbreviated title of the trial where available:**

RECOVERY trial

**A4. Sponsor's protocol:**

Number: NDPHRECOVERY

Version: 27.0

Date: 13/09/2023

**A5-1. ISRCTN number, if available :**

ISRCTN50189673

**A5-2. US NCT number:**

NCT04381936

**A5-3. Who Universal Trial Reference Number (UTRN)****A5-4. Other Identifiers:**

Name	Identifier

**A6. Is this a resubmission?**
☐ Yes ☒ No
**A7. Is the trial part of a Paediatric Investigation Plan?**
☐ Yes ☒ No ☐ Not Answered
**B: Identification of the sponsor responsible for the request****B1. Sponsor****SP1****Contact person**

Name of organisation	University of Oxford
Given name	NA
Family name	NA
Address	Clinical Trials & Research Governance, 1st Floor, Boundary Brook House, Old Road, Headington
Town/city	OXFORD
Post code	OX3 7GB
Country	United Kingdom
Telephone	00000
Fax	00000
E-mail	rgea.sponsor@admin.ox.ac.uk

**B2. Legal Representative for the purpose of this CTIMP.**

*A legal representative must be appointed for a clinical trial of an investigational medicinal product (CTIMP) if the sponsor is not established in the UK or on the MHRA approved country list (please refer to question specific guidance).*

**Legal Representative 1****Contact person**

Name of organisation

Given name  
Family name  
Address  
Town/city  
Post code  
Country  
Telephone  
Fax  
E-mail

**B3. Status of the sponsor:** Non-Commercial

**B.4 Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):**

**B.5 Contact point designated by the sponsor for further information on the trial:**

Name of organisation  
Functional name of contact point  
Street Address  
Town/city  
Post code  
Country  
Telephone  
Fax  
E-mail

## C: Applicant identification

### C1. Request for the competent authority

#### C1-1. Who is responsible for the Clinical Trial Authorisation Application?

Sponsor

#### C1-4. Complete the details of the applicant below even if they are provided elsewhere on the form:

##### Contact person

Person or organisation name: University of Oxford

Contact person Given name **Ferdousi**

Contact person Family name **Chowdhury**

Address Research Governance, Ethics & Assurance, First Floor, Boundary Brook House

Town/city	Headington, Oxford
Post code	OX3 7GB
Country	United Kingdom
Telephone	00000
Fax	00000
E-mail	rgea.sponsor@admin.ox.ac.uk

**C1-5. Do you want a xml file copy of the CTA form data saved on EudraCT?**

☐ Yes ☒ No ☐ Not Answered

**C2.Request for ethics committee**

**C2-1. Who is responsible for the Clinical Trial Authorisation Application?**

.....

**C2-5. Complete the details of the applicant below even if they are provided elsewhere on the form**

Person or organisation name: .....

Title: .....

Forename/Initials: .....

Surname: .....

Middlename: .....

Address: .....

Town/city: .....

Post code: .....

Country: .....

Telephone: .....

Fax: .....

E-mail: .....

## Part D: Investigational Medicinal Products

### D: Information on the IMPs

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, if applicable. If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance.

Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question D7 using the navigation screen.

### D. Investigational medicinal products

PR7 [Hydrocortisone](#)

PR8 [RoActemra](#)

PR16 [Kineret](#)

PR17 [Dexamethasone](#)

PR19 [Prednisolone](#)

PR21 [Empagliflozin](#)

PR22 [Oseltamivir](#)

PR23 [Baloxavir](#)

PR24 [Sotrovimab](#)

PR25 [Molnupiravir](#)

PR26 [Nirmatrelvir/ritonavir](#)

### D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR7**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** 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

### D2-1. Does the IMP to be used in the trial have a marketing authorisation?

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

### D2-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

### D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

### D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

### D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

### D3. Description of IMP

**D3-1.**

D.3.1 Product name where applicable Hydrocortisone

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered H02AB09

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 1600 mg

D.3.6.2 Specify per day or total ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 1600 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

**D.3.7 Routes of administration for this IMP**

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Hydrocortisone

CAS number:

Current sponsor code:  
 Other descriptive name:  
 Full Molecular formula  
 Chemical/biological description  
 of the Active Substance  
*Strength*

Concentration unit:

Concentration type:

Concentration number (only  
 use both fields for range):

### D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

*Is this a:*

Advanced Therapy IMP (ATIMP) <sup>(1)</sup>

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.*

Immunomodulatory

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007



DRAFT

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR8**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☒ Yes ☐ No ☐ Not Answered

Trade name:

RoActemra

EV Product Code

Name of the MA holder:

Roche

MA number (if MA granted by a Member State):

EU/1/08/492/001

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

☒ Yes ☐ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

## Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

## Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable      RoActemra

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered      L04AC07

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation?      ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

1600 mg

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

1600

mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

**D.3.7 Routes of administration for this IMP**

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Tocilizumab

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

**Strength**

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 20

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

*Is this a:*

Advanced Therapy IMP (ATIMP) <sup>(1)</sup> ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☒ Yes ☐ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-interleukin 6 receptor antagonist*

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR16**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☒ Yes ☐ No ☐ Not Answered

Trade name:

Kineret

EV Product Code

Name of the MA holder:

Swedish Orphan Biovitrum Ltd

MA number (if MA granted by a Member State):

EU/1/02/203/005

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Sweden

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

## Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

## Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable

Kineret

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

L04AC03

D.3.4 Pharmaceutical form (use standard terms)

Solution for injection

D.3.4.1 Is this a specific paediatric formulation?

☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

2 mg/kg for 7 days

D.3.6.2 Specify per day or total

☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

2 mg/kg  
milligram(s)/kilogram

D.3.6.2 Route of administration (relevant to the maximum dose): Subcutaneous use

**D.3.7 Routes of administration for this IMP**

Intravenous use

Subcutaneous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Anakinra

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

*Strength*

Concentration unit: mg/ml milligram(s)/millilitre

Concentration type: equal

Concentration number (only use both fields for range): 150

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☐ Yes ☒ No ☐ Not Answered



- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) <sup>(1)</sup> ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☒ Yes ☐ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* Human interleukin-1 receptor antagonist to reduce inflammation in PIMS-TS.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR17**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☒ No ☐ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☒ Yes ☐ No ☐ Not Answered

Specify which Member States:

AUSTRIA	<input type="checkbox"/>	BELGIUM	<input type="checkbox"/>	BULGARIA	<input type="checkbox"/>
CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>

FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable      Dexamethasone

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered      H02AB02

D.3.4 Pharmaceutical form (use standard terms)      Concentrate for solution for infusion

D.3.4.1 Is this a specific paediatric formulation?      ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol      3 days

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

59.4 mg

D.3.6.2 Specify per day or total

☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

59.4 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

**D.3.7 Routes of administration for this IMP**

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Dexamethasone

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

*Strength*

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 5

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) <sup>(1)</sup>

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Immune response modulation*

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR19**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☒ No ☐ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☒ Yes ☐ No ☐ Not Answered

Specify which Member States:

AUSTRIA

☐

BELGIUM

☐

BULGARIA

☐

CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable      Prednisolone

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered      H02AB06

D.3.4 Pharmaceutical form (use standard terms)      Tablet

D.3.4.1 Is this a specific paediatric formulation?      ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol      10 days

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

975 mg over 10 days

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

975 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

**D.3.7 Routes of administration for this IMP**

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Prednisolone

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description  
of the Active Substance*Strength*

Concentration unit:

Concentration type:

Concentration number (only  
use both fields for range):**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered



Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

*Is this a:*

Advanced Therapy IMP (ATIMP) <sup>(1)</sup> ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.*

Immunomodulatory

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR21**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable

Empagliflozin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

A10BK03

D.3.4 Pharmaceutical form (use standard terms)

Film-coated tablet

D.3.4.1 Is this a specific paediatric formulation?

☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

Duration of admission (average 15 days)

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☒ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

10 mg  
milligram(s)

D.3.6.1 Route of administration (relevant to the first dose):

Oral use

D.3.6.2 Maximum dose allowed

10 mg once daily

D.3.6.2 Specify per day or total

☒ per day ☐ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 10 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

### D.3.7 Routes of administration for this IMP

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

## D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

### Active Substance 1

Name of active substance (INN or proposed INN if available): Empagliflozin

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

*Strength*

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

## D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered

*Is this a:*

Advanced Therapy IMP (ATIMP) <sup>(1)</sup> ☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered

- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-inflammatory; anti-oxidant; haemodynamic*

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR22**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☒ No ☐ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable

Oseltamivir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

J05AH02

D.3.4 Pharmaceutical form (use standard terms)

Capsule, hard

D.3.4.1 Is this a specific paediatric formulation?

☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

10 days

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☒ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

1500 mg

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

1500 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

**D.3.7 Routes of administration for this IMP**

Oral use

Nasogastric use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Oseltamivir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

*Strength*

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) <sup>(1)</sup>☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered



Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Antiviral therapy*

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR23**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable Baloxavir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J05AX25

D.3.4 Pharmaceutical form (use standard terms) Film-coated tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Two doses: day 1 and day 4

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: ☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 160 mg

D.3.6.2 Specify per day or total ☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit) 160 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

**D.3.7 Routes of administration for this IMP**

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Baloxavir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) <sup>(1)</sup>

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-viral.*

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable*

*(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended*

*(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC*

*(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

**D1. Indicate which of the following is described below then repeat as necessary for each:**

This refers to the IMP number: **PR24**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☒ Yes ☐ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☐ Yes ☒ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable

Sotrovimab

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

D.3.4 Pharmaceutical form (use standard terms)

Solution for infusion

D.3.4.1 Is this a specific paediatric formulation?

☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

Single dose only

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day ☐ total ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

1000 mg

D.3.6.2 Specify per day or total

☐ per day ☒ total ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

1000 mg  
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

**D.3.7 Routes of administration for this IMP**

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Sotrovimab

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance: Monoclonal antibody against SARS-CoV-2 spike protein.

**Strength**

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 500

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☐ Yes ☒ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) <sup>(1)</sup>

☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☒ Yes ☐ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered



Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-SARS-CoV-2 spike protein human monoclonal IgG antibody*

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**This refers to the IMP number: **PR25**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☒ No ☐ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☒ Yes ☐ No ☐ Not Answered

Specify which Member States:

AUSTRIA	<input type="checkbox"/>	BELGIUM	<input type="checkbox"/>	BULGARIA	<input type="checkbox"/>
CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>

HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable Molnupiravir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 5 days

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed 8000 mg	
D.3.6.2 Specify per day or total	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	8000 mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose): Oral use	

**D.3.7 Routes of administration for this IMP**

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Molnupiravir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

*Strength*

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 200

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) <sup>(1)</sup> ☐ Yes ☒ No ☐ Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not Answered
- Radiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not Answered
- Plasma derived medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Extractive medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Recombinant medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Medicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not Answered
- Herbal medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Homeopathic medicinal product? ☐ Yes ☒ No ☐ Not Answered
- Another type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product  
*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.* Molnupiravir is a prodrug that is metabolised to the ribonucleoside analogue N-hydroxycytidine (NHC) which distributes into cells where it is phosphorylated to form the pharmacologically active ribonucleoside triphosphate (NHC-TP). NHCTP acts by a mechanism known as viral error catastrophe. NHC-TP incorporation into viral RNA by the viral RNA polymerase, results in an accumulation of errors in the viral genome leading to inhibition of replication.

Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered

<sup>(1,2,3,4,5)</sup> Complete sections D.4, D.5, D.6. and D.7, as applicable

<sup>(2,3)</sup> As defined in Annex 1 part IV of Directive 2001/83/EC as amended

<sup>(4)</sup> As defined in Article 2(1)(b) of Regulation 1394/2007/EC

<sup>(6)</sup> Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D1. Indicate which of the following is described below then repeat as necessary for each:**This refers to the IMP number: **PR26**

Investigational medicinal product category:

Test IMP

**D2. Status of the IMP** *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*

**D2-1. Does the IMP to be used in the trial have a marketing authorisation?**

☐ Yes ☒ No ☐ Not Answered

**D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start**

In the protocol, is treatment defined only by active substance?

☒ Yes ☐ No ☐ Not Answered

*If 'Yes', give active substance in D.3.8 or D.3.9*

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?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☒ Yes ☐ No ☐ Not Answered

*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.3.1*

Other :

☐ Yes ☐ No ☒ Not Answered

**D2-3. IMPD submitted:**

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

*Provide justification for using simplified dossier in the covering letter*

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

**D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?**

☒ Yes ☐ No ☐ Not Answered

Specify which Member States:

AUSTRIA

☐

BELGIUM

☐

BULGARIA

☐

CROATIA

☐

CYPRUS

☐

CZECH REPUBLIC

☐

DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

**D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?**

☐ Yes ☒ No ☐ Not Answered

**D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?**

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

*CHMP = Committee for Medicinal Products for Human Use*

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3. Description of IMP****D3-1.**

D.3.1 Product name where applicable Nirmatrelvir/ritonavir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

D.3.4 Pharmaceutical form (use standard terms) Film-coated tablet

D.3.4.1 Is this a specific paediatric formulation? ☐ Yes ☒ No ☐ Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 5 days

**D.3.6 Dose allowed**

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total:

☐ per day
 ☐ total
 ☐ Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed

3000 mg Nirmatrelvir

1000 mg Ritonavir

D.3.6.2 Specify per day or total

☐ per day
 ☒ total
 ☐ Not Answered

D.3.6.2 Specify total dose (number and unit)

D.3.6.2 Route of administration (relevant to the maximum dose):

**D.3.7 Routes of administration for this IMP**

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

**D3-8. Active substances**

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

**Active Substance 1**

Name of active substance (INN or proposed INN if available): Nirmatrelvir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

**Strength**

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 150

**Active Substance 2**

Name of active substance (INN or proposed INN if available): Ritonavir

CAS number: 155213-67-5

Current sponsor code:

Other descriptive name:



Full Molecular formula C37H48N6O5S2

Chemical/biological description of the Active Substance

*Strength*

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 100

**D3-11. Type of IMP**

Does the IMP contain an active substance:

Of chemical origin?

☒ Yes ☐ No ☐ Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP))

☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) <sup>(1)</sup>☐ Yes ☒ No ☐ Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy

☐ Yes ☒ No ☐ Not Answered

Radiopharmaceutical medicinal product?

☐ Yes ☒ No ☐ Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)?

☐ Yes ☒ No ☐ Not Answered

Plasma derived medicinal product?

☐ Yes ☒ No ☐ Not Answered

Extractive medicinal product?

☐ Yes ☒ No ☐ Not Answered

Recombinant medicinal product?

☐ Yes ☒ No ☐ Not Answered

Medicinal product containing genetically modified organisms?

☐ Yes ☒ No ☐ Not Answered

Herbal medicinal product?

☐ Yes ☒ No ☐ Not Answered

Homeopathic medicinal product?

☐ Yes ☒ No ☐ Not Answered

Another type of medicinal product?

☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Nirmatrelvir is a 3-chymotrypsin-like protease inhibitor which inhibits cleavage of polyproteins involved in viral replication. It is co-formulated with ritonavir which inhibits its CYP3A-dependent metabolism and hence increases the plasma concentration of nirmatrelvir.*

Is it an IMP to be used in a first-in-human clinical trial?

☐ Yes ☒ No ☐ Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

**D8. Information on placebo (if relevant; repeat as necessary)****D8. Is there a placebo:**

☐ Yes ☒ No ☐ Not Answered

**D9. Sites responsible for final QP release for distribution to investigators.****D9-1. IMPs and placebos for which no responsible site needs to be identified.**

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

*If all the conditions above are met, then select below the IMPs and placebos to which this applies.*

Finished IMP  
PR7

Finished IMP  
PR8

Finished IMP  
PR16

Finished IMP  
PR17

Finished IMP  
PR19

Finished IMP  
PR21

Finished IMP  
PR22

Finished IMP  
PR25

**Index of Sites where the qualified person certifies batch release**

*In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medicinal Products in the European Union*

**D9-2. Who is responsible in the Community for the certification of the finished IMP or placebo?**

*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 D1 or D7. In the case of multiple sites indicate the product certified by each site.*

RS6

## Manufacturer

Name of the organisation: Fisher Clinical Services  
Address Langhurst Wood Road  
Town/city Horsham  
Post code RH12 4QD  
Country United Kingdom

Give the manufacturing authorisation number  
MIA - 18693

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP  
PR24

## RS8

## Importer

Name of the organisation: Roche Pharma AG  
Address Emil Barell-Strasse 1  
Town/city Grenzach-Whylen  
Post code 79639  
Country Germany

Give the manufacturing authorisation number  
DE\_BW\_01\_MIA\_2020\_0096

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP  
PR23

## RS9

## Importer

Name of the organisation: Roche Product Limited  
Address 6 Falcon Way, Shire Park  
Town/city Welwyn Garden City  
Post code AL7 1TW

Country United Kingdom

Give the manufacturing authorisation number

MIA(IMP)31

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP  
PR23**E: Design of the Trial.****E.1 Medical Condition or Disease under Investigation****E1-1. Medical condition or disease under investigation <sup>(1)</sup>**Specify the medical condition(s) to be investigated (free text) :  
COVID-19 (infection with SARS-CoV-2 virus) or influenza pneumonia

Medical condition in easily understood language

Covid-19 or flu

Identify the therapeutic area

Diseases [C] - Virus Diseases [C02]

*<sup>(1)</sup> In the case of healthy volunteer trials, the intended indication for the product under development should be provided.***E1-2. MedDRA information <sup>(2)</sup>****MR1**

Version	21.1
Level	PT
Classification Code	10035737
Term	Pneumonia viral
SOC	10021881 - Infections and infestations

**MR2**

Version	21.1
Level	PT
Classification Code	10061982
Term	Severe acute respiratory syndrome
SOC	10021881 - Infections and infestations

*<sup>(2)</sup> Applicants are encouraged to provide the MedDRA lower level term (LLT) if applicable and classification code.***E1-3. Is any of the conditions being studied a rare disease? <sup>(3)</sup>**
☐ Yes
 ☒ No
 ☐ Not Answered

(3) Refer to "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/docs/en\\_GB/document\\_library/Regulatory\\_and\\_procedural\\_guideline/2009/09/WC500003773.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/09/WC500003773.pdf)

## E2. Objective of the trial

### E2-1. What is the principal research question/objective? Please put this in language comprehensible to a lay person.

The primary objective is to provide reliable estimates of the effect of study treatments on death within 28 days of randomisation (with subsidiary analyses of cause of death).

### E2-2. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.

The secondary objectives are to assess the effects of study treatments on duration of hospital stay and on need for (and duration of) ventilation or renal replacement therapy.

### E2-3. Is there a sub-study?

☐ Yes ☒ No ☐ Not Answered

## E3. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Patients are eligible for the study if all of the following are true:

- (i) Hospitalised
- (ii) Viral pneumonia
- (iii) Confirmed SARS-CoV-2 or influenza infection
- (iv) No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial

In addition, if the attending clinician believes that there is a specific contra-indication (see Appendix 2; section 8.2) to one of the active drug treatment arms, then the patient will not be excluded from randomisation to that arm.

## E4. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Participants may be excluded from receiving one or more of the possible randomised options if their medical history suggests that a treatment may be contraindicated.

Corticosteroid

Contraindications:

- Known contra-indication to short-term corticosteroid.

Endemic infections may be screened for as required by local practice. Patients in the UK with SARS-CoV-2 infection are not eligible for the low-dose dexamethasone comparison for influenza infection because of the proven benefits of dexamethasone in COVID-19.

Tocilizumab

Contraindications:

- Known hypersensitivity to tocilizumab.
  - Evidence of active TB infection
  - Clear evidence of active bacterial, fungal, viral, or other infection (besides COVID-19)
- (Note: Pregnancy and breastfeeding are not exclusion criteria.)

Anakinra

Contraindications:

- Known hypersensitivity to anakinra
- Neutrophil count  $<1.5 \times 10^9$  cells/L
- Pregnancy

Empagliflozin

Contraindications:

- Type 1 diabetes mellitus (or post-pancreatectomy diabetes)
- Pregnancy and breast-feeding
- History of ketoacidosis
- Other patients with diabetes: blood ketones  $\geq 1.5$  mmol/L (or urine ketones  $\geq 2+$  if near-patient testing for blood ketones unavailable). Such patients are eligible once their ketosis has resolved.

Cautions:

- Participants with diabetes allocated empagliflozin should have regular checks of blood ketones (or urine ketones if blood ketone testing is unavailable). Blood ketones should be checked twice daily or urine ketones daily (or if clinical concern). If blood ketones rise  $\geq 1.5$  mmol/L (or urine ketones  $\geq 2+$ ), clinicians should:
  - o Ensure adequate fluid and calorific intake
  - o Consider increasing insulin dose (if on insulin)
  - o Inform local diabetes team (if available) and treat ketosis using local protocols
  - o Consider discontinuing empagliflozin until ketosis resolves
- Clinicians should consider temporarily discontinuing empagliflozin in participants with diabetes mellitus who cannot maintain oral calorific intake (until nutrition is restored)
- Clinicians should be aware of "euglycaemic ketoacidosis" which occurs with empagliflozin and should check ketones (ideally blood) if this is suspected (e.g. unexplained metabolic acidosis)
- Empagliflozin does not cause hypoglycaemia alone, but may do so in combination with insulin or insulin secretagogues. Doses of these other medications may need to be temporarily modified while the participant is taking empagliflozin
- Empagliflozin causes an osmotic diuresis so careful fluid balance assessment is required
- Empagliflozin increases the risk of mycotic genital infections (e.g. candidiasis) which are usually easily treated with topical therapy. It is unclear whether it causes Fournier's gangrene (a very rare genital infection), but clinicians should be aware.

Baloxavir Marboxil

Contraindications:

- Weight  $<40$ kg
- Known hypersensitivity to baloxavir marboxil or the drug product excipients
- Participants who have received baloxavir marboxil for the current influenza infection

Oseltamivir

Contraindications:

- Known hypersensitivity to oseltamivir or the drug product excipients
- Participants who have received oseltamivir for the current influenza infection

Cautions:

- Dose should be reduced in presence of renal impairment
  - o eGFR  $\geq 30$  mL/min/1.73m<sup>2</sup>: dose as in normal renal function (75 mg twice daily)
  - o eGFR  $\geq 10$   $<30$  mL/min/1.73m<sup>2</sup>: 75 mg once daily
  - o eGFR  $<10$  mL/min/1.73m<sup>2</sup>: 75 mg as a single dose on day 1

Sotrovimab

Contraindications:

- Weight  $<40$ kg (regardless of age)
- Known hypersensitivity to sotrovimab or the drug product excipients

Cautions: no dose adjustment for kidney or liver function is required.

Molnupiravir

Contraindications:

- Age  $<18$  years
- Pregnancy or breast-feeding

- Known hypersensitivity to molnupiravir or its excipients
- Prior treatment with molnupiravir during the index illness

Cautions: no dose adjustment for kidney or liver function is required.

#### E5-1. What is the primary outcome measure for the study?(max 5000 characters)

All-cause mortality within 28 days of randomisation.

##### Timepoint(s) of evaluation of this end point (max 800 characters)

28 days after randomisation.

*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.*

#### E5-2. Secondary end point(s) (max 5000 characters)

Duration of hospitalisation

Use of ventilation

##### Timepoint(s) of evaluation of this end point (max 800 characters)

28 days

#### E6. What is the scope of the trial?

- |                  |                                      |                                     |                                    |
|------------------|--------------------------------------|-------------------------------------|------------------------------------|
| Diagnosis        | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Prophylaxis      | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Therapy          | <input checked="" type="radio"/> Yes | <input type="radio"/> No            | <input type="radio"/> Not Answered |
| Safety           | <input checked="" type="radio"/> Yes | <input type="radio"/> No            | <input type="radio"/> Not Answered |
| Efficacy         | <input checked="" type="radio"/> Yes | <input type="radio"/> No            | <input type="radio"/> Not Answered |
| Pharmacokinetic  | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacodynamic  | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Bioequivalence   | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Dose Response    | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacogenetic  | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacogenomic  | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacoeconomic | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Others           | <input type="radio"/> Yes            | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |

Specify:

#### E7-1. Trial type and phase <sup>(1)</sup>

Human pharmacology (Phase I)

☐ Yes ☒ No ☐ Not Answered

Therapeutic exploratory (Phase II)

☒ Yes ☐ No ☐ Not Answered

Therapeutic confirmatory (Phase III)

☒ Yes ☐ No ☐ Not Answered

Therapeutic use (Phase IV)

☒ Yes ☐ No ☐ Not Answered

*(1) 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.*

## E8. Design of the Trial.

### E8-1. Is the trial design controlled?

☒ Yes ☐ No ☐ Not Answered

Specify:

Randomised ☒ Yes ☐ No ☐ Not AnsweredOpen ☒ Yes ☐ No ☐ Not AnsweredSingle blind ☐ Yes ☒ No ☐ Not AnsweredDouble blind ☐ Yes ☒ No ☐ Not AnsweredParallel group ☒ Yes ☐ No ☐ Not AnsweredCross over ☐ Yes ☒ No ☐ Not AnsweredOther ☐ Yes ☒ No ☐ Not Answered

### E8-2. If controlled, specify the comparator:

Other medicinal product(s) ☒ Yes ☐ No ☐ Not AnsweredPlacebo ☐ Yes ☒ No ☐ Not AnsweredOther ☒ Yes ☐ No ☐ Not Answered

Specify the comparator

Standard care

Number of treatment arms in the trial

7

### E8-3. Single site in the Member State concerned (see also section G):

☐ Yes ☒ No ☐ Not Answered

### E8-4. Multiple sites in the Member State concerned (see also section G):

☒ Yes ☐ No ☐ Not Answered

Number of sites anticipated in Member State concerned

175

### E8-5. Multiple Member States



☐ Yes ☒ No ☐ Not Answered

Number of sites anticipated in the Community.

**E8-6. Trial being conducted both within and outside the EEA**

☒ Yes ☐ No ☐ Not Answered

Trial conducted completely outside EEA

☐ Yes ☒ No ☐ Not Answered

Specify the countries in which trial sites are planned

Vietnam

Indonesia

Nepal

Ghana

South Africa

Sri Lanka

Pakistan

Specify the number of sites anticipated outside of the EEA

20

**E8-7. Will a data monitoring committee (DMC) be convened?**

☒ Yes ☐ No ☐ Not Answered

**E8-8.**

**Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial.**

*If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition.*

All randomised participants are to be followed up until death, discharge from hospital or 28 days post-randomisation (whichever is sooner). Longer term follow-up will be sought through linkage to electronic healthcare records and medical databases including those held by NHS Digital, Public Health England and equivalent bodies. The end of the study is the date of the final data extraction from NHS Digital (anticipated to be 10 years after the last patient is enrolled).

**E8-9. How long do you expect the study to last? <sup>(1)</sup>**

In all countries concerned by the trial

Years: 11 Months: 6 Days: 11

In the MS concerned

Years: 11 Months: 6 Days: 11

*(1) From the first inclusion until the last visit of the last subject.*

**E8-10. Recruitment start date**

Recruitment start date in MS

19/03/2020

In any country

19/03/2020

*(1) If not provided in the protocol.*

DRAFT

**F: Population of Trial Subjects****F1. What is the age span of the trial subjects?**

Less than 18 years	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 500
Please specify the estimated number of participants planned in each age range for the whole trial:		
In Utero	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 0
Preterm newborn infants (up to gestational age less than 37 weeks)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Newborn (0-27 days)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Infant and toddler (28 days - 23 months)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Children (2-11 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 240
Adolescent (12-17 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 240
Adult (18-64 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 20000
Elderly (greater than 65 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 20000

*The number of participants 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.*

**F2. What is the gender of the trial subjects?**

Female ☒ Yes ☐ No ☐ Not Answered

Male ☒ Yes ☐ No ☐ Not Answered

**F3. Please select the categories of the trial subjects:**

Healthy volunteers	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
Patients	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered
Specific vulnerable populations	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered

**F4. Planned number of subjects to be included:**

In the member state 50000

For a multinational trial:

In the European community: 48000

In the whole clinical trial: 50000

**F5. Plans for treatment or care after a subject has ended his/her participation in the trial. *If it is different from the expected normal treatment, please specify:***

It would not be appropriate for participants to continue to receive their study treatment after the end of the trial as it is an acute treatment for an acute condition.

**G1. and G2. Investigator Details****G1. National coordinating investigator** (for a multicentre trial) **or principal investigator** (for a single centre trial)

- ☒ National coordinating investigator  
☐ Principal investigator

Given name Peter  
 Family name Horby  
 Qualification (MD...) MBBS PhD FRCP  
 Institution name University of Oxford  
 Institution department name Nuffield Department of Medicine  
 Street address New Richards Building, Old Road Campus, Headington  
 Town/city Oxford  
 Post Code OX3 7LG  
 Country United Kingdom  
 Telephone 01865 612940  
 Fax  
 E-mail peter.horby@ndm.ox.ac.uk

**G2. Other principal Investigators** (for a multicentre trial)**IN1**

Given name Peter  
 Family name Horby  
 Qualification (MD...) MB BS 1992 University of London  
 Institution name OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST  
 Institution department name  
 Street address JOHN RADCLIFFE HOSPITAL  
 Town/city HEADLEY WAY  
 Post Code OX3 9DU  
 Country United Kingdom  
 Telephone  
 Fax  
 E-mail peter.horby@ndm.ox.ac.uk

*For multi-centre trials where the CI is also a local PI, please list the CI as a PI at G2 (single-centre).*

**G3. Central Technical Facility Details****G3. 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.***Organisation**

Central technical facility organisation name

Central technical facility organisation department  
 Contact person Given name  
 Contact person Family name  
 Street address  
 Town/city  
 Post code  
 Country  
 Work Telephone  
 Fax  
 E-mail

**Enter the details of any duties subcontracted to this central technical facility in this trial:**

Routine clinical pathology testing	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Clinical chemistry	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Clinical haematology	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Clinical microbiology	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Histopathology	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Serology / endocrinology	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Analytical chemistry	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
ECG analysis / review	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Primary/ surrogate endpoint test	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered
Other	<input type="radio"/> Yes	<input checked="" type="radio"/> No	<input type="radio"/> Not Answered

#### Network organisation details

#### G4. Network organisation details

Organisation  
 Contact person Given name  
 Contact person Middle name  
 Contact person Family name  
 Street address  
 Town/city  
 PostCode  
 Country  
 Telephone number  
 Fax number  
 E-mail

Activities carried out by the network

**G5. Organisations to whom the sponsor has transferred trial related duties and functions****G5. Subcontractor organisations.***Enter details of central CRO facilities supplying services for at least this Member State.*

Organisation

Department

Contact person Given name

Contact person Family name

Street address

Town/city

PostCode

Country

Telephone number

Fax

E-mail

**Enter the details of any duties/ functions subcontracted to this sponsor's subcontractor facility in this trial**

All tasks of the sponsor:

☐ Yes ☒ No ☐ Not Answered

Monitoring:

☐ Yes ☒ No ☐ Not Answered

Regulatory (e.g. preparation of applications to CA and Ethics Committee):

☐ Yes ☒ No ☐ Not Answered

Investigator recruitment:

☐ Yes ☒ No ☐ Not AnsweredIVRS<sup>(1)</sup> - treatment randomisation:☐ Yes ☒ No ☐ Not Answered

Data management:

☐ Yes ☒ No ☐ Not Answered

E-data capture:

☐ Yes ☒ No ☐ Not Answered

SUSAR reporting:

☐ Yes ☒ No ☐ Not Answered

Quality assurance auditing:

☐ Yes ☒ No ☐ Not Answered

Statistical analysis:

☐ Yes ☒ No ☐ Not Answered

Medical writing:

☐ Yes ☒ No ☐ Not Answered

Other duties subcontracted:

☐ Yes ☒ No ☐ Not Answered

**H: Ethics Committee**

**H1-1. Type of application**

*Please tick the Ethics Committee box and give information of the Ethics committee concerned.*

Ethics committee ☒

**H2-1. Limited Name and address of ethics committee:**

Organisation HRA REC Cambridge East

Work Address

PostCode

Country

Fax

**H2-2. Date of submission:**

12/03/2020

**H2-3. Current status of Ethics Committee Opinion at the time of submission to the National Competent Authority:**

☐ To be requested ☐ Pending ☒ Given

If "Given", please specify:

Date of opinion: 16/03/2020

State opinion: ☒ Accepted ☐ Not Accepted

**I: Signature Of The Applicant In The Member State**

**I1. I hereby confirm that /confirm on behalf of the sponsor (tick which is 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;
- ☒ The clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

**I2. Applicant of the request for the competent authority** (as stated in section C.1):

Date .....

Signature .....

Print name .....



J: Checklist

**J3. For details of the documents required for applications to the MHRA in the UK please see**  
**[http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/](http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Applyingforaclinicaltrialauthorisation/Whattosend/index.htm)**  
**[Applyingforaclinicaltrialauthorisation/Whattosend/index.htm](http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Applyingforaclinicaltrialauthorisation/Whattosend/index.htm)**

DRAFT