Assessment report Part II – DENMARK

1) ADMINISTRATIVE INFORMATION

CT number	2023-509703-33-00
Member State Concerned	Denmark
Title of the study	Empirical Meropenem versus Piperacillin/Tazobactam for Adult Patients with Sepsis (EMPRESS) trial
Name of sponsors	Rigshospitalet
IMPs (repeat for PR1, PR2…..)	Substance (name/ code): PIPERACILLIN SODIUM, TAZOBACTAM SODIUM, PIPERACILLIN, TAZOBACTAM, PIPERACILLIN MONOHYDRATE/SUB03840MIG, SUB04682MIG, SUB09867MIG, SUB10849MIG, SUB237761, , MEROPENEM TRIHYDRATE/SUB21617, Marketing authorisation status (MA number, MS where authorised etc): 40178/DK, 45320/DK Modified in relation to MA:

Has Part I been submitted prior to the submission of Part II?	Yes ☐ No ☒
If Yes	
Is there already a conclusion on part I?	Yes ☐ No ☐
Is the CT already approved in any member state?	Yes ☐ No ☐

2) GENERAL INFORMATION

Is the CT a low-interventional trial[1]?	Yes ☒ No ☐
First in man ☐, Phase I ☐, II ☐, III ☐, IV ☒, NA ☐	
Is the CT a cluster trial[2]?	Yes ☐ No ☒
Is the CT intended to be performed in more than one member state?	Yes ☐ No ☒
Does the CT involve more than one site in the concerned member states?	Yes ☒ No ☐
Does the CT include healthy volunteers?	Yes ☐ No ☒
Does the CT include female?	Yes ☒ No ☐
male?	Yes ☒ No ☐
Age group	
Adults (18-64 years)	Yes ☒ No ☐
Elderly (>= 65 years)	Yes ☒ No ☐
If < 18 years:	
In Utero	Yes ☐ No ☐
Preterm Newborn Infants (up to gestational age < 37 weeks)	Yes ☐ No ☐

[1] If yes – other demands for damage compensation, cfr. Art. 76
[2] If yes – other demands for informed consent, cfr. Art. 30

Newborns (0-27 days)	Yes ☐ No ☐
Infants and toddlers (28 days - 23 months)	Yes ☐ No ☐
Children (2-11 years)	Yes ☐ No ☐
Adolescents (12-17 years)	Yes ☐ No ☐
Does the CT include vulnerable persons?	Yes ☒ No ☐
If yes	
Minors	Yes ☐ No ☐
Incapacitated subjects	Yes ☒ No ☐
Pregnant women	Yes ☐ No ☐
Breastfeeding women	Yes ☐ No ☐
Subjects in emergency situations	Yes ☒ No ☐
Other groups	Yes ☐ No ☐
If yes specify:	
Are there study-specific procedures and/or interventions beyond the drug application?	Yes ☒ No ☐
If yes	
Specify: Questionnaires. No biological material is collected for the trial.	

3) INFORMED CONSENT FORMS
L1_ICF_Participant EMPRESS 2023-509703-33-00

Date/version of Informed Consent Form	V2, 01-03-2024 CTIS System version 2 Submission date 01-03-2024
Does the Informed Consent Form contain the correct title of the CT?	Yes ☒ No ☐
Does the Informed Consent Form contain placeholder for the dated signature of the person performing the interview?	Yes ☒ No ☐
Does this placeholder indicate the qualification of the person performing the interview?	Yes ☐ No ☐ NA ☒
Does the Informed Consent Form contain a placeholder for:	
The dated signature of the subject?	Yes ☒ No ☐ NA ☐
The dated signature of legally designated representative?	Yes ☐ No ☒ NA ☐
Does the subject or the legally designated representative confirm whether a copy of the Informed Consent Form (or the record) has been retained?	Yes ☒ No ☐ NA ☐
Does the subject or the legally designated representative declare that the information is understood?	Yes ☒ No ☐

Comment: The date on the informed consent form for participants must be corrected to 01-03-2024

before handing the form out to participants. This can be done as a non-substantial medication. The updated form must be submitted with the next substantial modification.

Conclusion

The Inform Consent Form fulfils the conditions in art. 29, 1.

L1_ICF_Relative EMPRESS 2023-509703-33-00

Date/version of Informed Consent Form	V1, 29-02-2024 CTIS System version 1 Submission date 01-03-2024
Does the Informed Consent Form contain the correct title of the CT?	Yes ☒ No ☐
Does the Informed Consent Form contain placeholder for the dated signature of the person performing the interview?	Yes ☒ No ☐
Does this placeholder indicate the qualification of the person performing the interview?	Yes ☐ No ☐ NA ☒
Does the Informed Consent Form contain a placeholder for: The dated signature of the subject? The dated signature of legally designated representative?	 Yes ☐ No ☒ NA ☐ Yes ☒ No ☐ NA ☐
Does the subject or the legally designated representative confirm whether a copy of the Informed Consent Form (or the record) has been retained?	Yes ☒ No ☐ NA ☐
Does the subject or the legally designated representative declare that the information is understood?	Yes ☒ No ☐

Conclusion

The Inform Consent Form fulfils the conditions in art. 29, 1.

L1_ICF_Relative EMPRESS 2023-509703-33-00

Date/version of Informed Consent Form	V1, 29-02-2024 CTIS System version 1 Submission date 01-03-2024
Does the Informed Consent Form contain the correct title of the CT?	Yes ☒ No ☐
Does the Informed Consent Form contain placeholder for the dated signature of the person performing the interview?	Yes ☒ No ☐
Does this placeholder indicate the qualification of the person performing the interview?	Yes ☐ No ☐ NA ☒
Does the Informed Consent Form contain a placeholder for: The dated signature of the subject? The dated signature of legally designated representative?	 Yes ☐ No ☒ NA ☐ Yes ☒ No ☐ NA ☐
Does the subject or the legally designated representative confirm whether a copy of the Informed Consent Form (or the record) has been retained?	Yes ☐ No ☐ NA ☒
Does the subject or the legally designated representative declare that the information is understood?	Yes ☒ No ☐

Conclusion

The Inform Consent Form fulfils the conditions in art. 29, 1.

4) WRITTEN INFORMATION

Is the Information sheet sufficiently comprehensive, concise, clear, relevant, and understandable to a layperson?	Yes ☒ No ☐
Does the information sheet describe adequately nature, objectives, benefits, implications, risks, and inconveniences, of the clinical trial?	Yes ☒ No ☐
Does the information sheet adequately describe the subject's rights and guarantees regarding his or her protection, in particular his or her right to refuse to participate and the right to withdraw from the clinical trial at any time without any resulting detriment and without having to provide any justification?	Yes ☒ No ☐
Does the information sheet adequately explain that withdrawal of the informed consent will not affect the results of activities already carried out and the use of data obtained, based on informed consent, before its withdrawal?	Yes ☒ No ☐
Does the information sheet adequately describe the conditions under which the clinical trial is to be conducted, including the expected duration of the subject's participation in the clinical trial?	Yes ☒ No ☐
Does the information sheet adequately describe:	
The possible treatment alternatives?	Yes ☒ No ☐
The follow-up measures if the participation of the subject in the clinical trial is discontinued?	Yes ☒ No ☐
Post trial treatment options?	Yes ☐ No ☐ NA ☒
Does the information sheet provide information about the damage compensation according to national law of concerned member state	Yes ☒ No ☐
Does the information sheet provide:	
The EU trial number?	Yes ☒ No ☐
Information about the availability of the clinical trial results (that the summary of the results of the clinical trial and a summary presented in terms understandable to a layperson will be made available in the EU database)?	Yes ☒ No ☐
Does the information sheet provide adequate information about planned personal data collection and processing?	Yes ☒ No ☐
Does the information sheet provide adequate information about planned collection, storage and future use of biological samples?	Yes ☒ No ☐

In the case of a trial with minors:	
Is there Informed Consent documents adequately paying attentions to the information needs of these subjects?	Yes ☐ No ☐
In the case of a trial with incapacitated subjects:	
Is there Informed Consent documents adequately paying attentions to the information needs of these subjects?	Yes ☐ No ☐

In the case of a trial in an emergency situation: Are there Informed Consent documents to obtain consent from the subject and/or legally designated representative to continue the participation of the subject in the CT after the intervention?	Yes ☒ No ☐

Conclusion

The written information fulfils the conditions in art. 28 and 29.

5) PROTECTION OF PERSONAL DATA

Has a statement been submitted by the sponsor or his or her representative that data will be collected and processed in compliance with Regulation (EC) No 45/2001 and **national data protection legislation** implementing Regulation (EU) 2016/679, respectively?	Yes ☒ No ☐
Will the subject (or his or her legally designated representative) be asked to consent to the use of his or her data and/or biological samples outside the protocol of the clinical trial for other scientific purposes? *If Yes* Will the subject be informed that this consent may be withdrawn at any time by the subject or his or her legally designated representative?	Yes ☐ No ☒ Yes ☐ No ☐

6) COMPENSATION

Is there no undue influence, including that of a financial nature, exerted on subjects to participate in the clinical trial? In trials with incapacitated subjects, minors, pregnant or breastfeeding subjects: Are no incentives or financial inducements given to the subjects or their legally designated representatives, except for compensation for expenses and loss of earnings directly related to the participation in the clinical trial?	Yes ☒ No ☐ Yes ☒ No ☐

7) RECRUITMENT

Is the procedure for inclusion of subjects described in detail in the protocol or a separate document?	Yes ☒ No ☐
Is it clearly described what the first act of recruitment is?	Yes ☒ No ☐
Does the person performing the interview have the required qualification according to the law of concerned member states?	Yes ☒ No ☐
Is the recruitment of subjects planned to be done through advertisement?	Yes ☐ No ☒
If yes:	
Have copies of the advertising material been submitted, including any printed materials, and audio or visual recordings. been submitted?	Yes ☐ No ☐
Has an outline of the procedures proposed for handling responses to the advertisement been submitted?	Yes ☐ No ☐
Have copies of communications used to invite subjects to participate in the clinical trial been submitted?	Yes ☐ No ☐

Have arrangements for information or advice to the respondents found not to be suitable for inclusion in the clinical trial been described?	Yes ☐ No ☐
Are the arrangements for recruitment of subjects adequate?	Yes ☒ No ☐

8) SUITABILITY OF THE INVESTIGATOR

Is there an informative CV?	Yes ☒ No ☐
Is previous experience obtained from work with clinical trials described?	Yes ☒ No ☐
Is previous experience obtained from work with patient care described?	Yes ☒ No ☐
Have certificates describing adequate ICH/GPV training been submitted?	Yes ☒ No ☐
Has a financial disclosure been submitted?	Yes ☒ No ☐
Have institutional affiliations, that might influence the impartiality of the investigators been presented?	Yes ☒ No ☐
Is the investigator qualified in accordance with national law? *(medical doctor as defined in national law, or a person following a profession which is recognised in the Member State concerned)*	Yes ☒ No ☐

9) SUITABILITY OF THE FACILITIES

Has a list of the planned clinical trial sites with name and position of the principal investigators?	Yes ☒ No ☐
And the planned number of subjects at the sites been submitted?	Yes ☒ No ☐
Has a written statement been submitted describing the suitability of the clinical trial sites adapted to the nature and use of the investigational medicinal product? (issued by the head of the clinic/institution at the clinical trial site or by some other responsible person, according to the system in the Member State concerned)	Yes ☒ No ☐
Does this statement adequately describe:	
The suitability of facilities?	Yes ☒ No ☐
The equipment?	Yes ☒ No ☐
The human resources?	Yes ☒ No ☐
The expertise of the site?	Yes ☒ No ☐

10) PROOF OF INSURANCE COVER OR INDEMNIFICATION

Is the arrangement for damage compensation in accordance to **national law**?	Yes ☒ No ☐

11) FINANCIAL AND OTHER ARRANGEMENTS

Is there a description confirming adequate financing of the clinical trial is ensured?	Yes ☒ No ☐
Are financial transactions and compensation paid to subjects adequate?	Yes ☒ No ☐

Are financial transactions and compensation paid to the investigator/site for participating in the clinical trial adequate?	Yes ☒ No ☐
Are there any other agreements between the sponsor and the site adequate?	Yes ☐ No ☐ NA ☒

12) LIST OF QUESTIONS TO THE SPONSOR

See CTIS for list of considerations sent during assessment process as RFI.

All queries been answered satisfactorily.

13) ASSESSMENT OF THE SPONSOR´S RESPONSE

Are all queries resolved?	Yes ☒ No ☐
Condition: The date on the informed consent form for participants must be corrected to 01-03-2024 before handing the form out to participants. This can be done as a non-substantial medication. The updated form must be submitted with the next substantial modification.	

14) FINAL DECISION

The Clinical trial is approvable	☐
The Clinical trial is not approvable	☐
The Clinical trial is approvable subjects to conditions	☒

Ethics committee that participated in the assessment of the application

Committee (1) on meeting date: 14-02-2024

A list of committee members in each of the MREC committees can be seen here:

Committee 1: https://nationaltcenterforetik.dk/raad-og-komiteer/de-videnskabsetiske-medicinske-komiteer/medlemmer-af-videnskabsetisk-medicinsk-komite-1

Committee 2: https://nationaltcenterforetik.dk/raad-og-komiteer/de-videnskabsetiske-medicinske-komiteer/medlemmer-af-videnskabsetisk-medicinsk-komite-2

Committee 3: https://nationaltcenterforetik.dk/raad-og-komiteer/de-videnskabsetiske-medicinske-komiteer/medlemmer-af-videnskabsetisk-medicinsk-komite-3

Please note that a committee member may have been absent from the meeting due to scheduling conflicts. Furthermore, if a committee member had a conflict of interest, they would thus not have participated in the discussion and assessment of the application.

If a sponsor requires a specific list of members who participated in the application, they may contact MREC for this information (kontakt@dvmk.dk).

The approval is valid for the following trial sites and investigators

- Holbaek Sygehus, Mette Krag
- Aarhus Universitet, Steffen Christensen
- Region Midtjylland (Randers), Helle Bundgaard
- Region Midtjylland (Viborg), Christoffer Sølling

- Region Midtjylland (Herning), Thomas Tværmose Troelsen
- Rigshospitalet (neuroanæstesi), Kirsten Møller
- Rigshospitalet (intensiv), Morten Hylander Møller
- Rigshospitalet (thoraxanæstesi), Peter Buhl Hjortrup
- Rigshospitalet (kardiologi B), Christian Hassager
- Roskilde University, Thomas Hildebrandt
- Aalborg University Hospital, Bodil Steen Rasmussen
- Regionshospital Nordjylland, Malgorzata B Pawlowicz-Dworzanska
- Kolding Sygehus, Anne Brøchner
- Odense University Hospital, Jens Michelsen
- Herlev Hospital, Anne Sofie Andreasen
- Hvidovre Hospital, Ronni Plovsing
- Hillerod Hospital, Morten Bestle
- Bispebjerg Hospital, Theis Itenov
- Slagelse Hospital, Klaus Marcussen
- Hvidovre Hospital, Thomas Benfield
- Esbjerg og Grindsted Sygehus, Henrik Nørlund
- Rigshospitalet (Infektionssygdomme), Marie Helleberg
- Region Sjælland (Køge), Lars Peter Kloster Andersen
- Odense University Hospital, Isik Johansen
- Nykøbing F Sygehus, Hans Fjeldsøe-Nielsen

List of documents on the basis of which the decision was made

List of submitted documents can be accessed via Full Trial Information in CTIS.

15) CONSIDERATIONS SUBSTANTIAL MODIFICATION #1 (SM-1)

See CTIS for list of considerations sent during assessment process as RFI.

All queries have been answered satisfactorily.

16) ASSESSMENT OF THE SPONSOR'S RESPONSE SUBSTANTIAL MODIFICATION #1 (SM-1)

Are all queries resolved?	Yes ☒ No ☐

17) FINAL DECISION SUBSTANTIAL MODIFICATION #1 (SM-1)

The Clinical trial is approvable	☒
The Clinical trial is not approvable	☐
The Clinical trial is approvable subjects to conditions	☐