MACE-ICH FAQ's

Site set up

Will we receive a hard copy site file? No, we won't be providing sites with a hardcopy version of the site file (for sustainability and version control reasons). Sites are however welcome to print and maintain a physical ISF if you prefer. All MACE-ICH ISF documents can be found on the website.

What constitutes a recruit? Recruitment (and therefore accrual) will be at the point of consent but theoretically, patients should be randomised immediately. If a patient was to be consented but not randomised for a genuine reason, the accrual would still count.

Is there funding available for archiving? No, there is no funding available for archiving.

Does radiology need to attend site training? No, we don't need radiology to attend. The research team will need to liaise with radiology to organise the research CT scan.

Screening & eligibility

Does the baseline scan need to be CT or is MRI acceptable? CT scan only

What patients do we need to include on the screening log? Please review any presenting patients with ICH stroke within 72 hours of onset for eligibility for the MACE-ICH trial. Patients who are eligible for the trial, should be recorded on RF1 Participant Screening and Enrolment Log (see below). This should include patients who are eligible for the trial, but are not recruited for another reason (i.e., lack of researcher capacity, out-of-hours, researcher not on delegation log). For patients who are ineligible for the trial (i.e, they do not meet the inclusion criteria, or they fulfil one or more of the exclusion criteria), the cumulative totals must be recorded and sent across to the coordinating centre monthly. Please refer to WPD 005 (Screening and Enrolment log) for further details.

Does the medic confirming eligibility need to be on the delegation log? A fully qualified medic needs to sign off eligibility, but they do not need to be on the delegation log.

Do we have to use the eligibility checklist? No, it isn't compulsory to use the eligibility checklist, but this may be helpful when checking that patients meet the criteria necessary to participate in MACE-ICH. Regardless of whether the eligibility checklist is used, eligibility must be signed off in the patient's medical notes.

In the inclusion criteria, can a patient be included if they meet only one of the following inclusion criteria:

- Cerebral oedema with or without evidence of mass effect
- At risk of developing oedema (limited GCS <9 (eye opening and motor only) and NIHSS>8)

Yes, patients only need to meet one of the above two criteria

Consent

Who can take consent? Consent can be taken by medics who are GCP trained and on the delegation log. Written informed consent will be sought but a documented, witnessed mark or oral consent due to physical inability to sign is permitted.

Can we use next of kin consent? If a patient does not have capacity, you can attempt the consent of a legal representative. Please use the correct paperwork for this. If the participant then regains capacity, you must attempt re-consent of the participant.

IMP

Does the medic prescribing the IMP need to be on the delegation log? Any medic on the delegation log can delegate the responsibility of prescribing the IMP to a medical doctor not on the delegation log. For example, many stroke teams are covered by several strata of junior doctors who may not be on the delegation log but could prescribe mannitol if a medic has confirmed eligibility and asked them to do the prescription.

Does the mannitol we procure need to be brand specific i.e. Baxter? Baxter is the main NHS supplier, but another brand can be used, as long as it is mannitol 10%.

How many mannitol infusion bags would you suggest we keep in stock on the ward? We would recommend having access to at least 4 bags, as a participant weighing over 50kg randomised to receive two doses of mannitol will need 4 bags in total.

Will the IMP label as per page 5 in the pharmacy manual be provided to site?
Sites will be asked to print their own labels. The format can vary from that shown in the pharmacy manual but needs to include the same details. Please ensure that the EudraCT reference on your labels is 2022-000283-22.

Do clinical staff administering the IMP need to be on the delegation log? No, the clinical staff administering the IMP do not need to be on the delegation log. The IMP should be administered in accordance with local policy.

Can a cannula already in situ for administration for other medications be used to administer the mannitol? It is preferable to use a different cannula to that used for administering other medications, but it is acceptable to use the same cannula if necessary.

Does treatment need to start within 72 hours of stroke onset? The participant must be randomised within 72 hours of stroke onset in order to be eligible for the trial. Treatment should also start within 72 hours of stroke onset - if there is a delay between randomising the patient and starting treatment, meaning treatment started after 72 hours, then a protocol deviation will need to be reported.

Can an estimated body weight be used to calculate the mannitol dose? Yes, it is acceptable to estimate a patient's weight.

Are there any rounding rules for body weight to be used to calculate the mannitol dose? Please round weight to the nearest 5kg and prescribe dose according to the dosing table. For example, for someone weighing 72.3kg, you would prescribe the dose shown for 70kg weight (70g).

What process should we follow to deliver partial amounts of the IMP infusion bags? When only part of an infusion bag is to be administered, please do so in accordance with local policy. Accordingly, the following two options are acceptable: (i) remove excess IMP from the infusion bag prior to setting up to administer to the participant, or (ii) set up the infusion pump such that it delivers the specified amount of IMP, with the excess IMP remaining in the bag for disposal afterwards.

How do we calculate serum osmolality?
Calculated serum osmolality:
2 × (Na+) + Glucose + Urea (all in mmol/L)
Alternatively, you can use the calculator on the following link: https://www.mdcalc.com/calc/91/serum-osmolality-osmolarity
Please note that this is a US based website that uses mg/dl instead of mmol/L - please change the units for sodium, glucose and BUN (this is the same as urea) to mmol/L before calculating and interpreting serum osmolality.

What dose of mannitol should be administered for participants weighing over 100kg? Anyone weighing more than a 100 kg should receive a dose of 100g infused as detailed in the table below:

Weight (kg)	**Dose (based on 1g/kg)**	**Volume and rate of Mannitol 10% solution (infuse at 10mL/min = 600mL/hour)**
40	40g	400mL over 40mins
45	45g	450mL over 45mins
50	50g	500mL over 50mins
55	55g	550ml over 55 mins
60	60g	600ml over 60 mins
65	65g	650mL over 65 mins
70	70g	700mL over 70 mins
75	75g	750mL over 75 mins
80	80g	800mL over 80 mins
85	85g	850mL over 85 mins
90	90g	900mL over 90mins
95	95g	950mL over 95 mins
100	100g	1000mL over 100 mins

Can the research delivery team (as opposed to pharmacy) be responsible for IMP labelling and accountability? Yes, as long as the activities requested in the pharmacy manual are being met, it is fine if the research team are to conduct the activity as long as the site clearly documents that this is the procedure and states where responsibilities lie (on a file note sent to the Coordinating Centre and filed in the ISF). If IMP is already stored on the ward, the following is acceptable:

- The research team can over label infusion bags with the MACE-ICH label either at the point when a participant is recruited and randomised to receive mannitol OR prior to recruitment such that it is 'ring-fenced' for use in the trial [sites to indicate their local process].
- The research team will complete the 'Stroke unit accountability log' (Appendix 3) to document IMP administered to participants. The research team will need to retain this in the ISF and email a copy to the coordinating centre upon request.
- It won't be necessary for the research team to complete the 'IMP transfer request form' (Appendix 1) as the IMP will already be on the ward. Nor will it be necessary for pharmacy to

complete the 'Pharmacy IMP inventory log' (Appendix 2) as they will maintain their own local records relating to the IMP being issued/returned to/from the ward.
- Unused/expired/damaged infusion bags will be destroyed as per local Trust procedures so there is no need for research teams/pharmacy to complete the 'Return of clinical supplies form' (Appendix 4) nor the 'Record of IMP destruction' (Appendix 5). Sites need to confirm their local process on the file note.

If pharmacy isn't taking accountability for the IMP (see point above), do they need to attend MACE-ICH training, maintain a pharmacy file, and be signed onto the delegation log? Pharmacy teams will be invited to attend pharmacy-specific training so that they are clear on the process, but it won't be necessary for them to maintain a pharmacy file (all documents to be retained in the ISF) nor to be signed onto the delegation log.

Will research teams still need to use their local over labelling worksheet from pharmacy if pharmacy isn't involved in IMP labelling/accountability? As pharmacy is not conducting the process then no, however sites may wish to.

Data collection

Is a catheter mandatory for monitoring urinary output? Monitoring of urine output will be according to local clinical practice and may include placement of a urinary catheter. A urinary catheter is not mandatory but if inserted, should be removed after treatment unless there is another reason according to the treating clinician.

Does a drug chart need to be uploaded for participants not randomised to mannitol? Yes**,** we would expect to see that 1 or 2 (as applicable) doses are recorded as having been administered.