



Subject ID:

# Cooling in Mild Encephalopathy Trial (COMET)

## Case Report Form

Version 1.3 (06/08/2018)

*Please use black ink to complete this form.*

*Do not leave any blank fields or unanswered questions*

Study Centre

Subject ID

 -



Subject ID:

### INCLUSION CRITERIA AND RECRUITMENT

- A. Was the baby born > 35 weeks? Yes  (included) No  (excluded)
- B. Is the birth weight of the baby ≥ 1800g? Yes  (included) No  (excluded)
- C. Was there any of the following: Yes  (included) No  (excluded)

- a) Age less than six hours
- b) Metabolic acidosis (pH<7.0 and/or BE<-16 in cord gas or blood gas within one hour of birth?  
OR pH or BE is borderline (pH<7.15 to 7.0) and/or BE>-10 to -16 with evidence of perinatal asphyxia:  
either an acute obstetric event (e.g. cord prolapse, abruption, shoulder dystocia)
- OR
- Need for continued resuscitation or ventilation at 10 minutes and/or 10 min Apgar <6
- c) Evidence of mild HIE at least 2 abnormalities on a NICHD neurological examination performed between 1 and 6 hour of birth:

D. Stage of Neonatal Encephalopathy (NE) on neurological examination (on recruitment).

No NE  (exclude)      Mild NE  (include)      Moderate NE  (exclude)      Severe NE  (exclude)

CATEGORIES (TOTAL 6, 9 SIGNS)	SIGNS OF NEONATAL ENCEPHALOPATHY (NE) IN EACH CATEGORY (Circle the most appropriate level)			
	NORMAL	MILD	MODERATE	SEVERE
<b>1. Level of consciousness</b>				
	Alert, Responsive to external stimuli (state dependent, eg. post feeds)	Hyper-alert, has a stare, jitteriness, high-pitched cry, exaggerated responds to minimal stimuli, inconsolable	Lethargic	Stupor/coma
<b>2. Spontaneous activity</b>				
	Changes position when awake	Normal or Decreased	Decreased activity	No activity
<b>3. Posture</b>				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers, wrist usually)	Moderate flexion of distal joint, Complete extension	Decerebrate
<b>4. Tone</b>				
	Strong flexor tone in all extremities + strong flexor hip tone	Normal or Slightly increased peripheral tone	Hypotonia (focal or general) or Hypertonia	Flaccid Rigid
<b>5. Primitive reflexes</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Suck	Strong, easily illicit	Weak, poor	Weak but has a bite	Absent
Moro	Complete	Partial response, Low threshold to illicit	Incomplete	Absent
<b>6. Autonomic system</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Pupils	In dark: 2.5-4.5 mm. In light: 1.5-2.5 mm.	Mydriasis	Constricted	Deviation/ dilated/ non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160)	Bradycardia (HR < 100)	Variable HR
Respirations	Regular respirations	Hyperventilation (RR > 60/min)	Periodic breathing	Apnea or requires ventilator
<b>TOTAL SCORE</b>				

*For eligibility for COMET infant should have at least 2 neurological abnormalities (in either mild, moderate or severe), but not ≥ 3 categories that are moderate or severe.*



Subject ID:

E. Was infant sedated at the time of above neurological exam?  
(sedation does not affect eligibility)

Yes                      No

F. Will baby be more than 6 hours old when cooling is started?

Yes (excluded)                       included)

G. Have parents given consent for recruiting baby into COMET trial?

Yes (included)                       No (excluded)

H. Name of the person obtaining parental consent:

I. Role of the person obtaining parental consent:

**If the patient is eligible AND the parents have consented for study participation AND equipment is available, please proceed to next section for randomisation.**

### RANDOMISATION

**Once you randomise the participant, you will need to start taking observations immediately.**

**Please ensure you have a Tecotherm/Criticool machine readily available as well as a rectal temperature monitor.**

**Please check the COMET Quick Reference Guide for Randomisation Instructions before proceeding**

Which group was the baby randomised to?

1. Normothermia  $36.5\text{ }^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  for 24 hours then usual care for a further 48h
2. Whole body cooling ( $33.5^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ ) for 24 hour followed by rewarming at  $0.5^{\circ}\text{C}$  per hour
3. Whole body cooling ( $33.5^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ ) for 48 hour followed by rewarming at  $0.5^{\circ}\text{C}$  per hour
4. Whole body cooling ( $33.5 \pm 0.5^{\circ}\text{C}$ ) for 72 hour followed by rewarming at  $0.5^{\circ}\text{C}$  per hour

J. When was cooling started?  
(cooling group only)

   

(Date DD/MM/YY)

 

(Time: 24h)

K. Age of baby at start of cooling?  
(cooling group only)

 

(Hours:mins)

L. Was blood collected at randomisation  
(i.e before start of cooling)

Yes

No

M. Was blood collected at  $80 \pm 4$  hours after randomisation.  
(i.e after re-warming)

Yes

No

N. Was 'Faros' attached before 6 hours of age (upto 24 hours).

Yes

No

Subject ID:    **DELIVERY INFORMATION**

1. Date and time of birth:

(Date DD/MM/YY)

(Time: 24h)

2. Gestational age at birth (Weeks/Days):

3. Baby's birth weight (g):

4. Head circumference (cm) on day 1:

5. Baby's sex:

F

M

6. What was the baby's Apgar score at 1, 5, 10 minutes of age? *(Please write NA if not available)*

Score	2	1	0	1min	5min	10min
<b>Activity</b>	Active	Arms and legs flexed	Absent			
<b>Pulse</b>	>100ppm	<100ppm	Absent			
<b>Grimace</b>	Sneezes, coughs, pulls away	Grimaces	No response			
<b>Appearance (colour)</b>	Normal over entire body	Normal except extremities	Cyanotic or pale all over			
<b>Respirations</b>	Good, crying	Slow, irregular	Absent			
<b>Total Score</b>						

7. When was the heart rate higher than 100ppm? *(Please write NA if not born in hospital)*At birth 1 min 5 min 10 min





Subject ID:

Reduced fetal movements Yes  No  NK

(If yes, what was duration?)  (hours)

Assisted breech delivery Yes  No  NK

19. What was the cord pH? Arterial  NK   
Venous  NK

20. How was this baby delivered? (tick one box only)  
Pre-labour caesarean section  In labour caesarean section (Emergency)   
Spontaneous vaginal delivery  Instrumental vaginal delivery

21. Was there prolonged rupture of membranes (>24 hours)? Yes  No  NK

22. Were there any complications at the delivery? Yes  No  NK   
*E.g: preeclampsia, placental abruption, cord prolapse, shoulder dystocia, etc.*

If yes, please describe:

23. Was there Premature Rupture of Membranes (PROM) or Preterm Premature Rupture of Membranes (PPROM)?  
Yes, PPROM  Yes, PROM  No, none  NK

24. Place of delivery:  
In-born (same as the cooling centre)   
Out-born – at another hospital (give name)    
Out-born – at home

25. Age at admission to the neonatal unit :     
(Time: 24h)

**Instructions for completing the form**

Subject ID:    

Group	Rectal temperature	Axilla temperature
Normothermia	Nil	4 hourly until 80 hours
24 hours cooling	2 hourly until 32 hours	4 hourly from 32 hours until 80 h
48 hours cooling	2 hourly until 56 hours	4 hourly from 56 hours until 80 h
72 hours cooling	2 hourly until 80 hours	Nil

*NB: In addition all cooling groups require temperatures at 0,1, and 2 hours, and usual care babies require axillary temperature at 0,1 and 2 hours*

- Please note the time of randomisation as given from the randomisation system. That is the Hour 0 you will need to document in the monitoring data (below).
- **Collect blood at randomisation (<6 h of age) and 80 ± 4 hours after randomisation (i.e after re-warming, if applicable) in PAXGENE bottle**
- **Attached faros within 6 hours of age (upto 24 hours from randomisation)**



Subject ID:

### MONITORING DATA

#### Day 1

#### First Hour from Randomisation:

This 24hr period commenced on:  
*(randomisation time)*

(Date DD/MM/YY)

(Time: 24h)

Time since randomisation	Exact time (24h)	Rectal T (°C)	Axilla T (°C)	HR (bpm)	Shivering (Y/N)	NPAS score*	Morphine dose (mcg/kg/h)	Breathing support (V=Invasive ventilation; C=CPAP; O=Oxygen; N=None)
0 hour	Time of randomisation							
1 hour	<input type="text"/>							
2 hours	<input type="text"/>							
4 hours	<input type="text"/>							
6 hours	<input type="text"/>							
8 hours	<input type="text"/>							
10 hours	<input type="text"/>							
12 hours	<input type="text"/>							
14 hours	<input type="text"/>							
16 hours	<input type="text"/>							
18 hours	<input type="text"/>							
20 hours	<input type="text"/>							
22 hours	<input type="text"/>							
<b>24 hours</b>	<input type="text"/>							<i>*If in 24h cooling group, stop cooling and rewarm at 0.5°C per hour.</i>

\*Neonatal Pain, Agitation and Sedation Scale



Subject ID:

**Day 1: CLINICAL DETAILS**

*(Please enter the worst results from the first 24h or write ND if not done)*

Hb (g/dL)  WBC (mm<sup>3</sup>)  Platelets  CRP (mg/L)

Blood gas  A / V / C  pH  PCO<sub>2</sub>  BE  + / -   
(please circle) (please circle)

PT  APTT  INR

Fluids IV only  IV & Oral  Oral only

Where there definite seizures in last 24 hours? Yes  No

Seizure type: Clinical only  aEEG only  Clinical and aEEG

Age at seizures (please round up to the nearest hour)

Anti-convulant therapy None  Phenobarbitone only  Additional drugs

aEEG. Normal  Moderate voltage abnormality  Severe voltage abnormality

*Please download the first 24 hour aEEG data and send to Imperial*

**NICHD examination at 24 (+6) hours**

CATEGORIES (TOTAL 6, 9 SIGNS)	SIGNS OF NEONATAL ENCEPHALOPATHY (NE) IN EACH CATEGORY (Circle the most appropriate level)			
	NORMAL	MILD	MODERATE	SEVERE
<b>1. Level of consciousness</b>				
	Alert, Responsive to external stimuli (state dependent, eg. post feeds)	Hyper-alert, has a stare, jitteriness, high-pitched cry, exaggerated responds to minimal stimuli, inconsolable	Lethargic	Stupor/coma
<b>2. Spontaneous activity</b>				
	Changes position when awake	Normal or Decreased	Decreased activity	No activity
<b>3. Posture</b>				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers, wrist usually)	Moderate flexion of distal joint, Complete extension	Decerebrate
<b>4. Tone</b>				
	Strong flexor tone in all extremities + strong flexor hip tone	Normal or Slightly increased peripheral tone	Hypotonia (focal or general) or Hypertonia	Flaccid Rigid
<b>5. Primitive reflexes</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Suck	Strong, easily illicit	Weak, poor	Weak but has a bite	Absent
Moro	Complete	Partial response, Low threshold to illicit	Incomplete	Absent
<b>6. Autonomic system</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Pupils	In dark: 2.5-4.5 mm. In light: 1.5-2.5 mm.	Mydriasis	Constricted	Deviation/ dilated/ non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160)	Bradycardia (HR < 100)	Variable HR
Respirations	Regular respirations	Hyperventilation (RR > 60/min)	Periodic breathing	Apnea or requires ventilator
<b>TOTAL SCORE</b>				
<i>For eligibility for COMET infant should have at least 2 neurological abnormalities (in either mild, moderate or severe), but not ≥ 3 categories that are moderate or severe.</i>				



Subject ID:

**Day 2: MONITORING DATA**

This 24h period commenced on

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(Date DD/MM/YY)

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(Time: 24h)

Time since randomisation	Exact time (24h)	Rectal T (°C)	Axilla T (°C)	HR (bpm)	Shivering (Y/N)	NPAS score*	Morphine dose (mcg/kg/h)	Breathing support (V=Invasive ventilation; C=CPAP; O=Oxygen; N=None)
26 hour	<input type="text"/>							
28 hours	<input type="text"/>							
30 hours	<input type="text"/>							
32 hours	<input type="text"/>							*If in 24h cooling group, remove rectal probe and change to 4h axillary Temp monitoring now
34 hours	<input type="text"/>							
36 hours	<input type="text"/>							
38 hours	<input type="text"/>							
40 hours	<input type="text"/>							
42 hours	<input type="text"/>							
44 hours	<input type="text"/>							
46 hours	<input type="text"/>							
<b>48 hours</b>	<input type="text"/>							*If in 48h cooling group, stop cooling and rewarm at 0.5°C per hour.

\*Neonatal Pain, Agitation and Sedation Scale



Subject ID:

**Day 2: CLINICAL DETAILS**

*(Please enter the worst results between 24 to 48h or write ND if not done)*

Hb (g/dL)  WBC (mm<sup>3</sup>)  Platelets  CRP (mg/L)

Blood gas  A / V / C  pH  PCO<sub>2</sub>  BE  + / -   
(please circle) (please circle)

PT  APTT  INR

Fluids IV only  IV & Oral  Oral only

**Were there definite seizures between 24 to 48h?** Yes  No

Seizure type: Clinical only  aEEG only  Clinical and aEEG

Age at seizures (please round up to the nearest hour)

Anti-convulant therapy None  Phenobarbitone only  Additional drugs

aEEG Normal  Moderate voltage abnormality  Severe voltage abnormality

(between 24 to 48 h, if available)

**NICHD examination at 48 (+6) hours**

CATEGORIES (TOTAL 6, 9 SIGNS)	SIGNS OF NEONATAL ENCEPHALOPATHY (NE) IN EACH CATEGORY (Circle the most appropriate level)			
	NORMAL	MILD	MODERATE	SEVERE
<b>1. Level of consciousness</b>				
	Alert, Responsive to external stimuli (state dependent, eg. post feeds)	Hyper-alert, has a stare, jitteriness, high-pitched cry, exaggerated responds to minimal stimuli, inconsolable	Lethargic	Stupor/coma
<b>2. Spontaneous activity</b>				
	Changes position when awake	Normal or Decreased	Decreased activity	No activity
<b>3. Posture</b>				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers, wrist usually)	Moderate flexion of distal joint, Complete extension	Decerebrate
<b>4. Tone</b>				
	Strong flexor tone in all extremities + strong flexor hip tone	Normal or Slightly increased peripheral tone	Hypotonia (focal or general) or Hypertonia	Flaccid Rigid
<b>5. Primitive reflexes</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Suck	Strong, easily illicit	Weak, poor	Weak but has a bite	Absent
Moro	Complete	Partial response, Low threshold to illicit	Incomplete	Absent
<b>6. Autonomic system</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Pupils	In dark: 2.5-4.5 mm. In light: 1.5-2.5 mm.	Mydriasis	Constricted	Deviation/ dilated/ non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160)	Bradycardia (HR < 100)	Variable HR
Respirations	Regular respirations	Hyperventilation (RR > 60/min)	Periodic breathing	Apnea or requires ventilator
<b>TOTAL SCORE</b>				
<i>For eligibility for COMET infant should have at least 2 neurological abnormalities (in either mild, moderate or severe), but not ≥ 3 categories that are moderate or severe.</i>				



Subject ID:

**Day 3: MONITORING DATA**

This 24h period commenced on

(Date DD/MM/YY)

(Time: 24h)

Time since randomisation	Exact time (24h)	Rectal T (°C)	Axilla T (°C)	HR (bpm)	Shivering (Y/N)	NPAS score*	Morphine dose (mcg/kg/h)	Breathing support (V=Invasive ventilation; C=CPAP; O=Oxygen; N=None)
50 hour	<input type="text"/>							
52 hours	<input type="text"/>							
54 hours	<input type="text"/>							
56 hours	<input type="text"/>							<i>*If in 48h cooling group, remove rectal probe and change to 4h axillary Temp monitoring now</i>
58 hours	<input type="text"/>							
60 hours	<input type="text"/>							
62 hours	<input type="text"/>							
64 hours	<input type="text"/>							
66 hours	<input type="text"/>							
68 hours	<input type="text"/>							
70 hours	<input type="text"/>							
<b>72 hours</b>	<input type="text"/>							<i>*If in 72h cooling group, stop cooling and rewarm at 0.5°C per hour.</i>
74 hours	<input type="text"/>							
76 hours	<input type="text"/>							
78 hours	<input type="text"/>							
80 hours	<input type="text"/>							

\*Neonatal Pain, Agitation and Sedation Scale



Subject ID:

**Day 3: CLINICAL DETAILS**

*(Please enter the worst results between 48 to 72 h or write ND if not done)*

Hb (g/dL)  WBC (mm<sup>3</sup>)  Platelets  CRP (mg/L)

Blood gas  A / V / C  pH  PCO<sub>2</sub>  BE  + / -   
(please circle) (please circle)

PT  APTT  INR

Fluids IV only  IV & Oral  Oral only

Were there definite seizures between 48 to 72 h? Yes  No

Seizure type: Clinical only  aEEG only  Clinical and aEEG

Age at seizures (please round up to the nearest hour)

Anti-convulant therapy None  Phenobarbitone only  Additional drugs

aEEG Normal  Moderate voltage abnormality  Severe voltage abnormality

(between 48 to 72 h, if available)

**NICHD examination at 72 (+6) hours**

CATEGORIES (TOTAL 6, 9 SIGNS)	SIGNS OF NEONATAL ENCEPHALOPATHY (NE) IN EACH CATEGORY (Circle the most appropriate level)			
	NORMAL	MILD	MODERATE	SEVERE
<b>1. Level of consciousness</b>				
	Alert, Responsive to external stimuli (state dependent, eg. post feeds)	Hyper-alert, has a stare, jitteriness, high-pitched cry, exaggerated responds to minimal stimuli, inconsolable	Lethargic	Stupor/coma
<b>2. Spontaneous activity</b>				
	Changes position when awake	Normal or Decreased	Decreased activity	No activity
<b>3. Posture</b>				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers, wrist usually)	Moderate flexion of distal joint, Complete extension	Decerebrate
<b>4. Tone</b>				
	Strong flexor tone in all extremities + strong flexor hip tone	Normal or Slightly increased peripheral tone	Hypotonia (focal or general) or Hypertonia	Flaccid Rigid
<b>5. Primitive reflexes</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Suck	Strong, easily illicit	Weak, poor	Weak but has a bite	Absent
Moro	Complete	Partial response, Low threshold to illicit	Incomplete	Absent
<b>6. Autonomic system</b> (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Pupils	In dark: 2.5-4.5 mm. In light: 1.5-2.5 mm.	Mydriasis	Constricted	Deviation/ dilated/ non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160)	Bradycardia (HR < 100)	Variable HR
Respirations	Regular respirations	Hyperventilation (RR > 60/min)	Periodic breathing	Apnea or requires ventilator
<b>TOTAL SCORE</b>				
<i>For eligibility for COMET infant should have at least 2 neurological abnormalities (in either mild, moderate or severe), but not ≥ 3 categories that are moderate or severe.</i>				



Subject ID:

**Day 4 till discharge**

Date and time rewarming was started  
*(write NA is not cooled)*

*(Date DD/MM/YY)*

*(Time: 24h)*

Age of the baby at the start of re-warming

hours

Date and time when rectal temperature  $\geq 36.5^{\circ}\text{C}$

*(Date DD/MM/YY)*

*(Time: 24h)*

Total duration of cooling therapy

hours

Age at which full breast/bottle feed was established  
*(If baby was discharged on NG feeds, please write NA)*

days

Was MRI done before hospital discharge Yes  No  Please explain why.....

Age at MRI scan  days

Discharge destination Home  Other hospital  Name.....

Age at discharge home  days

**Summary of the events during hospital stay**

- Age at the onset of seizures: \_\_\_\_\_ hours *(write NA if no seizures)*
- Duration of seizures: \_\_\_\_\_ hours *(time between 1<sup>st</sup> and last seizure. Write SINGLE if only 1 seizure)*
- Duration of anti-convulsive therapy: \_\_\_\_\_ days.

	Y/N	Date(s)	Please give details
Hypotension requiring inotropes			
Persistent Pulmonary Hypertension			
Coagulopathy requiring blood products			
Culture positive sepsis			
Thrombocytopenia requiring platelets			
Persistent metabolic acidosis			
Subcutaneous fat necrosis			
Rectal temp $\geq 38^{\circ}\text{C}$			

Were there any protocol deviations No  Yes

If yes, please explain.....

CRF completed by (name/designation)..... Date.....

**Please send this CRF to [j.mendoza@imperial.ac.uk](mailto:j.mendoza@imperial.ac.uk) within 24 hours of discharge**