DOCUMENT CONTROL PAGE

Title	**Title**: Guidelines for the Management of the Infant or Neonate with Hyperammonaemia **Version**: 1 **Reference Number**: PCCN7
Supersedes	**Supersedes**: Nil **Description of Amendment(s)**: New guideline – not applicable
Minor Amendment	**Date**: **Notified To**: **Date**: **Summary of amendments**:
Author	**Originated By**: Rachael Barber **Designation**: NWTS Consultant and Consultant Paediatric Intensivist , CMFT **Co-Authors**: (1) Adam Nicholls; (2) Suzie Emsden; (3) Sharryn Gardner; (4) Adam Sutherland; (5) Beth Jameson ; (6) Simon Jones **Designation**: (1) Paediatric SpR, RMCH (2) PICU Grid Trainee, Alder Hey (3) Emergency Medicine Consultant, Southport & Ormskirk Hospitals NHS Trust (4) PICU Senior Pharmacist, RMCH (5) Consultant in Metabolic Medicine, RMCH(6) Consultant in Metabolic Medicine, RMCH
Ratification	**Ratified by:** 1. CMFT (Host Trust): - Paediatric Medicines Management Committee (MMC) on: **4th September 2013** - Divisional Children's Clinical Effectiveness Committee on: **7th November 2013** 2. AHFT: - CDEG (Clinical Development & Evaluation Group) on: **21st March 2014**
Application	Children only
Circulation	**Issue Date**: **31st March 2014** **Circulated by**: Clinical Lead, North West & North Wales Paediatric Critical Care Network **Dissemination and Implementation**: NWTS & PCCN Network circulation lists
Review	**Review Date**: **21st March 2016** **Responsibility of**: Clinical Lead, North West & North Wales Paediatric Transport Service (NWTS)

Date placed on the Intranet: **31st March 2014**	**Please enter your EqIA Registration Number here**: **92/13**

1. Detail of Procedural Document

Guidelines for the Management of the Infant or Neonate with Hyperammonaemia.

2. Equality Impact Assessment

EqIA Registration Number: **92/13**

3. Consultation, Approval and Ratification Process

This guideline was developed with input from:
· North West and North Wales Paediatric Transport Service (NWTS).
· Representatives from the North West and North Wales Paediatric Critical Care Network (PCCN).
· Representatives from both Paediatric Intensive Care Units (Royal Manchester Children's Hospital and Alder Hey Children's Hospital).
· Representatives from the District General Hospitals within the PCCN.

These guidelines were circulated amongst the Consultants from both Paediatric Intensive Care Units (Central Manchester University Hospitals NHS Foundation Trust and Alder Hey NHS Foundation Trust), the Consultants from the North West and North Wales Paediatric Transport Service (NWTS), and Metabolic Consultants for comments on the **21st March 2013**.

These guidelines were circulated amongst the North West and North Wales Paediatric Critical Care Network for comments on the **24th April 2013**.

All comments received have been reviewed and appropriate amendments incorporated.

These guidelines were signed off by the Network/NWTS Clinical Lead on **19th July 2013**.

For ratification process see appendix 1.

4. References and Bibliography

See guidelines.

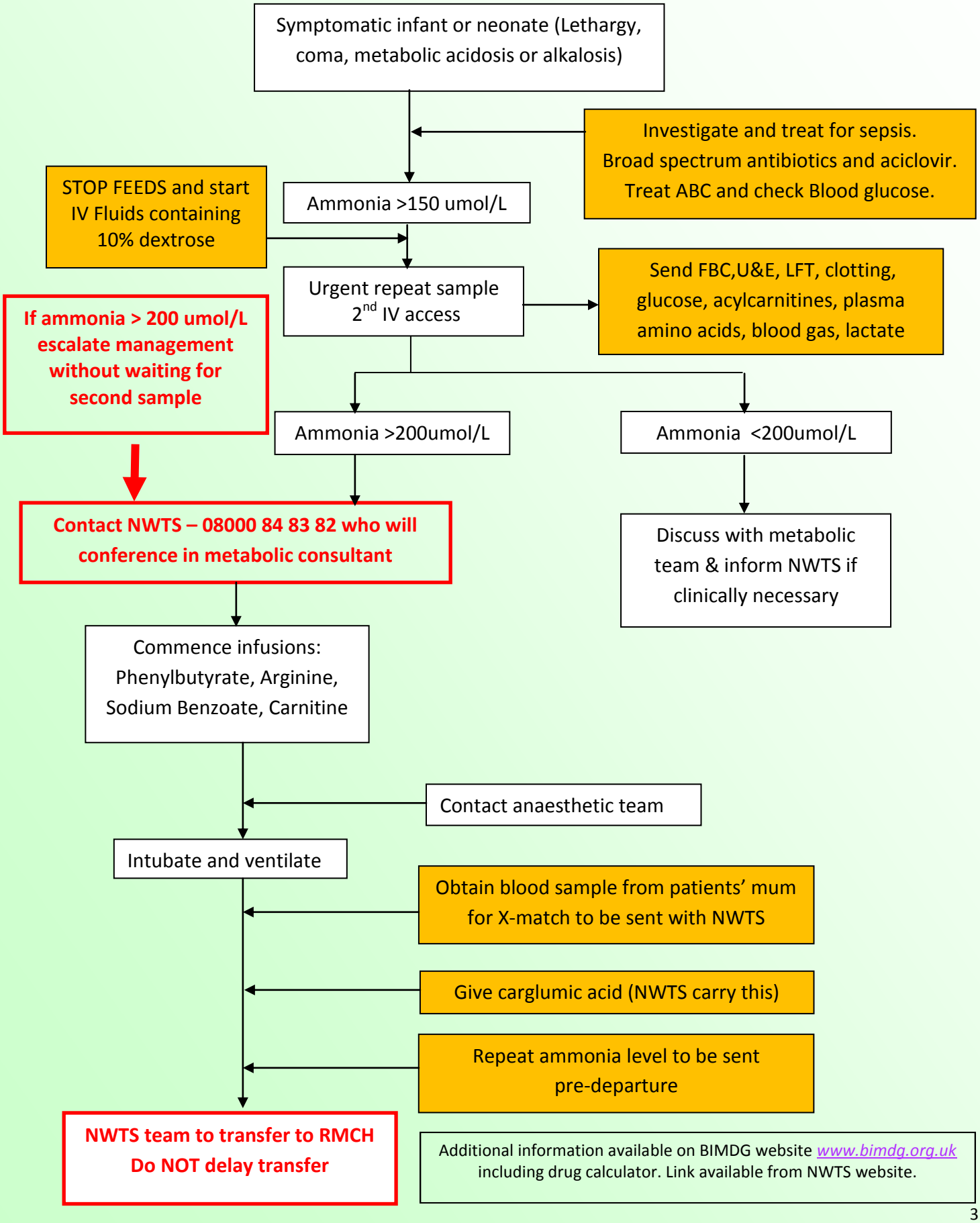
5. Disclaimer

These clinical guidelines represent the views of the North West and North Wales Paediatric Critical Care Network and North West and North Wales Paediatric Transport Service, which were produced after careful consideration of available evidence in conjunction with clinical expertise and experience.

The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Clinical advice is always available from NWTS on a case by case basis. Please feel free to contact NWTS (01925 853 550) regarding these documents if there are any queries.

Guidelines for the Management of the Infant or Neonate with Hyperammonaemia



Hyperammonaemia is a **medical emergency**. Prompt recognition, commencement of treatment and transfer of the child is vital for a good neurological outcome. Hyperammonaemia leads to direct neurological damage and outcome seems to be related to duration of hyperammonaemia and peak ammonia levels.

The goal of treatment should be to get the infant or neonate with raised ammonia >400umol/L that is resistant to pharmacological treatment onto haemofiltration within **6 hours** of identification.

Symptoms and Signs of hyperammonaemia

These can be subtle and varied. Suspect and check ammonia levels in the following:

Neonate	Child and adolescent
Vomiting Lethargy Poor feeding Encephalopathy Irritability Pulmonary haemorrhage Seizures Abnormal movements Temperature instability Low blood sugar Previous sudden death in family Unexplained metabolic acidosis Unexplained metabolic alkalosis	Vomiting Lethargy Encephalopathy Altered behaviour Signs of intoxication Previous sudden death in family Unexplained metabolic acidosis

Investigations

- **Send urgent ammonia on ice.** Ensure lab are aware that sample is being sent.
- Samples for ammonia should be **free flowing venous samples** – capillary samples can give spuriously high results.
- **If ammonia >150umol/L, repeat sample**
- **If ammonia >200umol/L, repeat sample BUT DO NOT DELAY STARTING TREATMENT**
- **Second IV access.** Send bloods for FBC, U&E, LFT, acylcarnitines, plasma amino acids (Lithium Heparin sample), blood gas, lactate.
- Collect urine sample for organic acids if possible (to be transferred with NWTS team to RMCH). Insertion of a urinary catheter will allow rapid collection of a sample in a critically ill patient.

Acute Management

- **Stop feeds and commence fluids containing 10% dextrose. Ideally this should be 0.9% saline with 10% dextrose or 0.45% saline with 10% dextrose if this is unavailable.** This reduces the patient's nitrogen load and also prevents hypoglycaemia.
- **Start broad spectrum antibiotics and acyclovir.** Sepsis and disseminated HSV can cause raised ammonia levels as can low cardiac output states.
- **Contact the NWTS team on 08000 848382. NWTS will conference in the metabolic consultant at RMCH.**
- **Commence infusions as directed by metabolic team (Doses and infusions in appendix).** Metabolic infusions should be commenced within 30 minutes once agreed by the metabolic consultant on call. Ammonia can rise precipitously in a decompensated metabolic disorder and delays of more than 30 minutes are not acceptable. Transferring drugs from RMCH or Alder Hey has been found to add a considerable delay to commencement of these drugs. All hospitals must have small supplies of *intravenous* sodium phenylbutyrate, sodium benzoate, L-arginine (arginine hydrochloride) and L-carnitine.
- **Contact anaesthetic team/neonatal team.** Patient will require intubation and ventilation for transfer. This is to reduce the metabolic demands on the baby and hence reduce ammonia production. Ensure endotracheal tube is well secured. Target normal saturations and CO2.

Pre Transfer Management

- NWTS team to administer **carglumic acid (Carbaglu)** on arrival at referring hospital. This is not stocked by many DGHs so will be carried by the NWTS team. It is given as a single enteral dose.
- **Obtain blood transfusion sample from neonate's Mother.** The sample must be labelled and sent with the NWTS team to facilitate cross-matching the baby (for haemofiltration).
- **Send a repeat ammonia sample pre-departure from DGH.** This result will determine the need for haemofiltration.
- Patient to be transferred to PICU at RMCH if at all possible for easier access to the metabolic team.

References:

- British Inherited Metabolic Disease Group: Undiagnosed hyperammonaemia. Diagnosis and immediate management, 2008. www.bimdg.org.uk
- British Inherited Metabolic Disease Group: Medicines used for the treatment of hyperammonaemia, 2008
- Leonard JV, Morris AAM, Diagnosis and early management of inborn errors of metabolism presenting around the time of birth, Acta Paediatrica, 2006; 95: 6-14
- Saudubray J-M, Sedel F, Walter JH. Clinical Approach to treatable inborn metabolic diseases: An introduction. J Inherit Metab Dis, 2006; 29: 261-274
- Schutze GE, Edwards MS, Adham BL, Belmont JW. Hyperammonaemia and neonatal herpes simplex infection. Paediatr Infect Dis J, 1990; 9; 749-5

MEDICATIONS FOR METABOLIC DECOMPENSATION

Sodium Benzoate	Loading Dose:	**250mg/kg over 90minutes**
	Maintenance Dose:	**250mg/kg/day by continuous infusion**
PREPARATION:	**Use the 1g in 5ml preparation.**	**Dilute 2.5g (12.5ml) to 50ml with 10% glucose**
ADMINISTRATION:	Loading Dose:	**5ml/kg over 90minutes**
	Maintenance Dose:	**0.2ml/kg/hr**
Sodium Phenylbutyrate	Loading Dose:	**250mg/kg over 90minutes**
	Maintenance Dose:	**250mg/kg/day by continuous infusion**
PREPARATION:	**Use the 1g in 5ml preparation.**	**Dilute 2.5g (12.5ml) to 50ml with 10% glucose**
ADMINISTRATION:	Loading Dose:	**5ml/kg over 90minutes**
	Maintenance Dose:	**0.2ml/kg/hr**
L-Arginine	Loading Dose:	**None**
(Arginine Hydrochloride)	Maintenance Dose:	**150-300mg/kg/day by continuous infusion**
PREPARATION:	**Maximum concentration should not exceed 100mg/ml**	
ADMINISTRATION using 10% premixed solution (Other solutions are available. Check calculations carefully)	Maintenance Dose:	**0.06-0.13ml/kg/hr**
Carglumic Acid	Loading Dose:	**250mg/kg as a single ENTERAL dose**
(Carbaglu®)	**NWTS WILL BRING CARBAGLU® WITH THEM**	
L-Carnitine	Usual dose:	**25mg/kg FOUR times a day**
PREPARATION:	**Dilute dose as required with 0.9% sodium chloride or glucose 10%**	
ADMINISTRATION:	**Give as a bolus over 2-3 minutes. Occasionally the metabolic team will request for this to be run as an infusion. The dose for this is on *www.bimdg.org.uk* website**	

Exact dose will vary with different metabolic disorders —and a final decision on doses will be made by the Metabolic consultant on call

Infusions can be administered PERIPHERALLY

Infusions are COMPATIBLE WITH EACH OTHER

Infusions are COMPATIBLE WITH GLUCOSE CONTAINING MAINTENANCE FLUIDS

Advice to Pharmacy Departments:

- These medications are time critical.

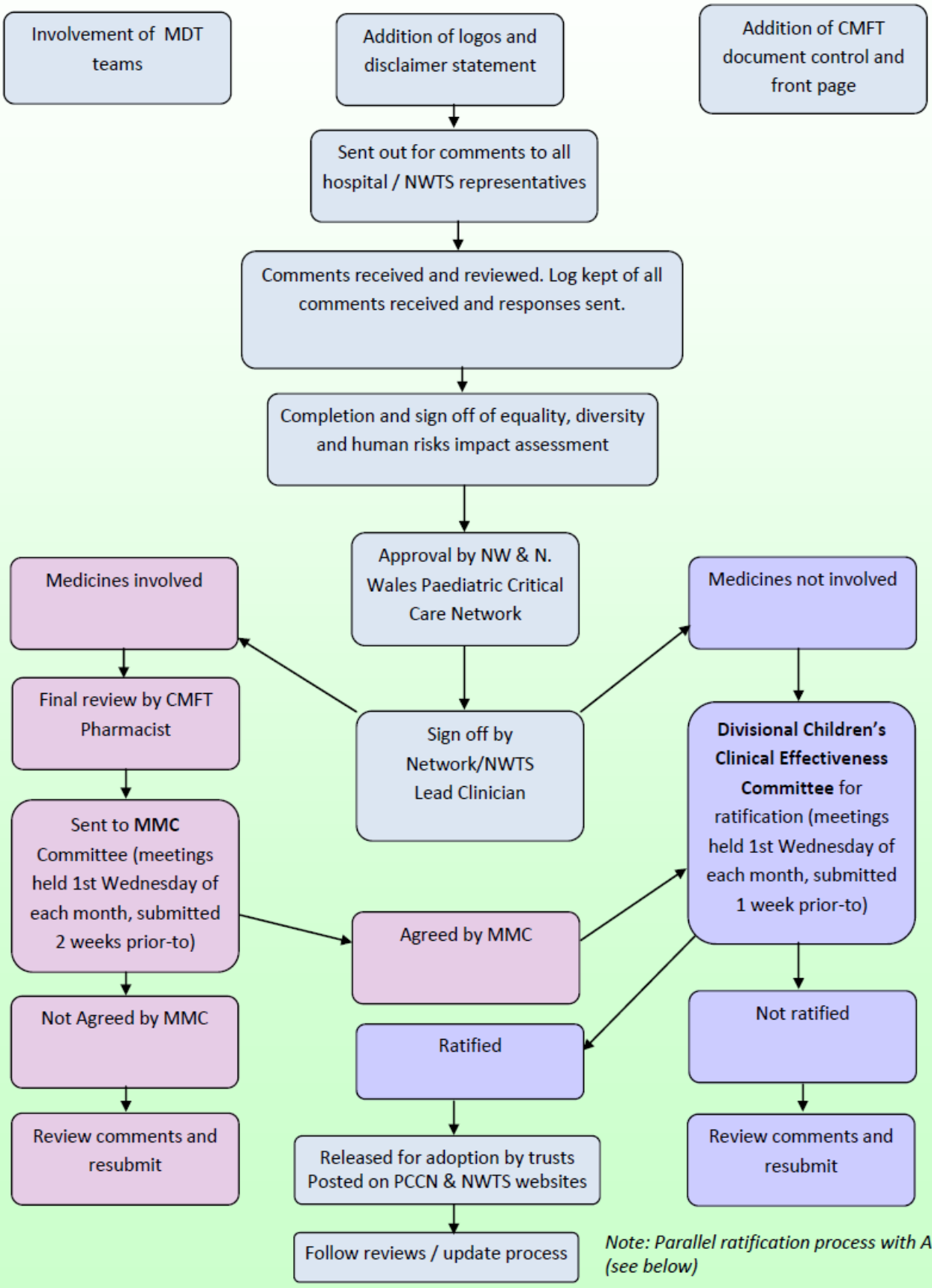
NWTS recommends that ALL sites have access to the following products WITHIN **30 minutes** OF REQUEST:

Sodium benzoate 1g in 5ml ampoules (10 ampoules)
Sodium phenylbutyrate 1g in 5ml ampoules (10 ampoules)
L-Arginine 10% 200ml vials (2 vials). Other strengths are acceptable.
L-Carnitine 1g in 5ml ampoules (5 ampoules)

Appendix 1

Alder Hey Children's NHS Foundation Trust | NHS North West & North Wales Paediatric Critical Care Network | Central Manchester University Hospitals NHS Foundation Trust

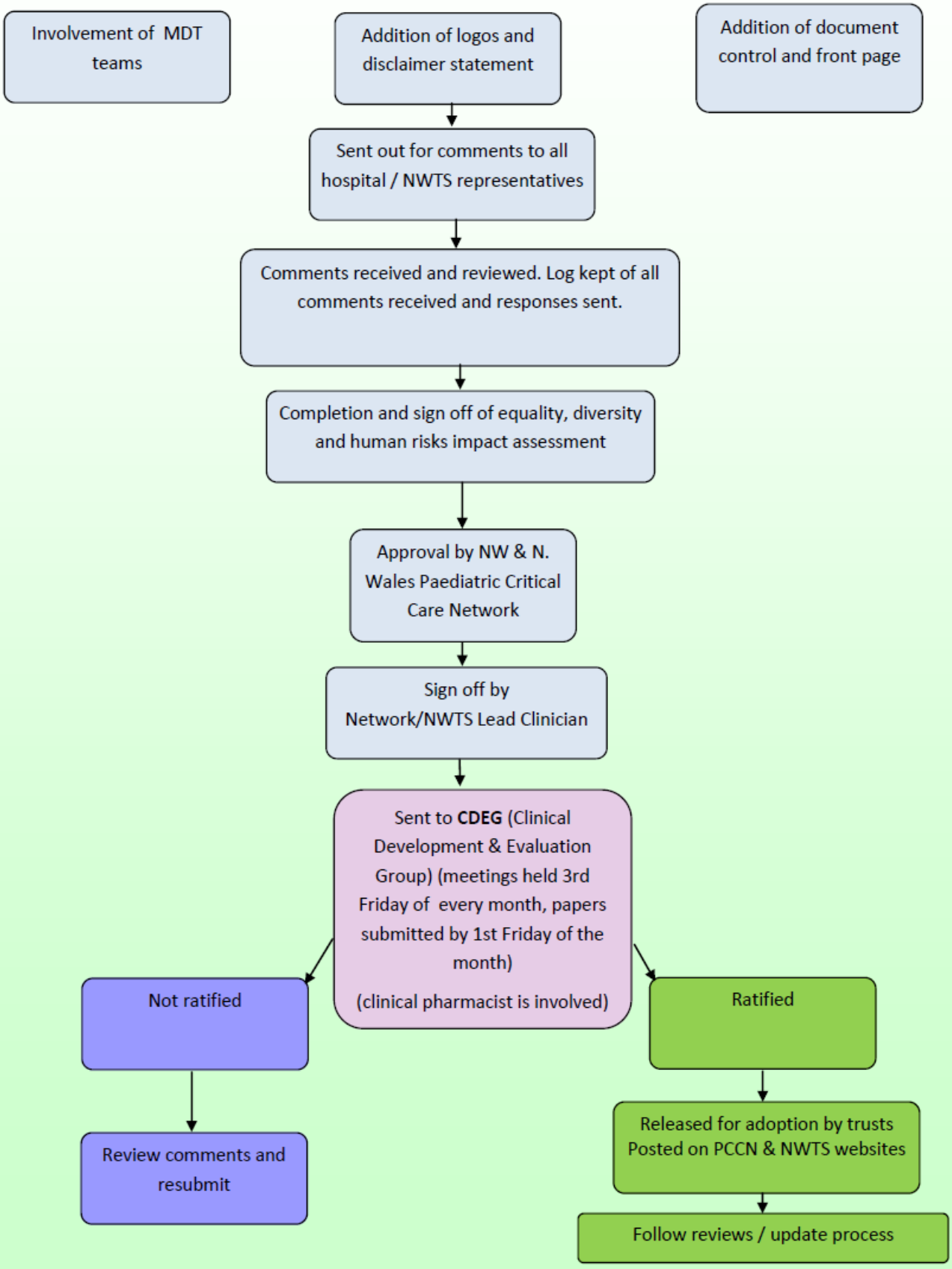
Ratification of Guidelines with Host Organisation (CMFT)



Appendix 1 continued

Alder Hey Children's NHS Foundation Trust | North West & North Wales Paediatric Critical Care Network | Central Manchester University Hospitals NHS Foundation Trust

Ratification of Guidelines with Alder Hey



Resources

www.crashcall.net - for intubation drugs / sedation regime

Contact numbers:
Regional Paediatric Intensive Care Unit Alder Hey Childrens Hospital 0151 252 5241
Regional Paediatric Intensive Care Unit Royal Manchester Childrens Hospital 0161 701 8000
NWTS (North West & North Wales Paediatric Transport Service) 01925 853 550

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Date of Review: 21st March 2016

Guideline contact point: Rachael.Barber@cmft.nhs.uk

Please visit our website for the most up to date version of this guideline:
www.nwts.nhs.uk
or
www.networks.nhs.uk/nhs-networks/north-west-north-wales-paediatric-critical-care

NWTS North West & North Wales Paediatric Transport Service

NHS North West & North Wales Paediatric Critical Care Network