

APPENDIX A - DEFINITIONS

Note: Definitions adapted from Vermont Oxford Network and The International Neonatal Consortium, Neonatal Adverse Event Severity Scale (INC NAESS)

(Available at: <https://vtoxford.zendesk.com/hc/en-us/articles/4405064008467-2022-Manual-of-Operations-Part-2-Release-26-2-PDF-> and <https://pubmed.ncbi.nlm.nih.gov/31537552/>)

The following are documented as adverse events in the **first 72 hours of age ONLY**:

BRADYCARDIA

- Heart rate < 80 beats per minute sustained for at least 30 minutes.

TACHYCARDIA

- Heart rate > 200 beats per minute sustained for at least 30 minutes.
- Tachycardia NOT related to atropine use, hyperthermia or another confirmed adverse event such as infection.

The following are documented as adverse events at **ANY time during admission** (i.e., from randomisation until discharge/death)

BACTERIAL SEPSIS AND/OR MENINGITIS

- One or more of the following bacterial pathogens was recovered from a blood and/or cerebrospinal fluid culture obtained.
- Up to three bacterial pathogens may be recorded.
- See list of pathogens in Appendix B

BRONCHOPULMONARY DYSPLASIA (BPD)

A preterm infant < 33 weeks gestation will be deemed to have BPD if they require respiratory support at 36 weeks PMA (adapted from VON criteria and Bronchopulmonary Dysplasia: Executive Summary of a Workshop (Higgins et al (16))). BPD will be graded as follows:

Grades	Invasive MV	nCPAP or HFNC > 2L/min	NC ≤ 2L/min
I		21 %	22 – 29 %
II	21 %	22 – 29 %	≥ 30 %
III	> 21 %	≥ 30 %	

Abbreviations: MV = mechanical ventilation; nCPAP = nasal continuous positive airway pressure; HFNC = high flow nasal cannula; NC = nasal cannula; min = minutes

COAGULATION DISORDER

- Abnormal blood clotting or bleeding that requires intervention with blood products.

PERIVENTRICULAR – INTRAVENTRICULAR HAEMORRHAGE (PIH), WORST GRADE

- If a cranial ultrasound was performed on or before Day 28, the worst grade of PIH will be documented using the criteria below.
 - Grade 1: Subependymal germinal matrix haemorrhage only
 - Grade 2: Intraventricular blood, no ventricular dilation
 - Grade 3: Intraventricular blood, ventricular dilation
 - Grade 4: Intraparenchymal haemorrhage

FOCAL INTESTINAL PERFORATION

- Surgically confirmed based on visual inspection of the bowel at the time of surgery or post-mortem examination that demonstrates a single focal perforation with the remainder of the bowel appearing normal, or clinically confirmed if they do not satisfy the definition for NEC.

FUNGAL INFECTION

- Document if a fungus was recovered from a blood culture obtained from either a central line or peripheral blood sample.

RETINOPATHY OF PREMATURITY (ROP)

If a retinal examination was performed, document the worst stage on any exam in the eye with the most advanced stage.

- Stage 1: Presence of demarcation line (+/- abnormal vascularization)
- Stage 2: Presence of intraretinal ridge
- Stage 3: Presence of a ridge with extraretinal fibrovascular proliferation
- Stage 4: Partial retinal detachment
- Stage 5: Total retinal detachment

NECROTIZING ENTEROCOLITIS (NEC)

Must be diagnosed at surgery, at post-mortem examination, or with clinical and diagnostic imaging using the following criteria.

- At least one of the following clinical signs present:
 - Bilious gastric aspirate or emesis
 - Abdominal distension or discoloration
 - Occult or gross blood in stool (no fissure),

AND

- At least one of the following diagnostic imaging findings present:
 - Pneumatosis intestinalis
 - Hepato-biliary gas
 - Pneumoperitoneum

PATENT DUCTUS ARTERIOSUS (PDA)

- At least one of the following findings is present
 - Left to Right or bidirectional ductal shunt on Doppler echo
 - Systolic or continuous murmur

AND

- At least two of the following findings are present:
 - Hyperdynamic precordium
 - Bounding pulses
 - Wide pulse pressure
 - Pulmonary vascular congestion, cardiomegaly, or both

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PNEUMOTHORAX

- The presence of extra-pleural air diagnosed by chest radiograph or needle aspiration (thoracentesis)

PULMONARY HAEMORRHAGE

- Frank blood with respiratory compromise requiring escalation of respiratory support.

SEIZURES

- Record seizures as adverse events only if:
 - o Status epilepticus: > 30 minutes duration within any hour, OR
 - o Recurrent seizures: each > 30 seconds per hour requiring > 1 anti-seizure drug within a 3-day period.
- Seizures should preferably be EEG confirmed.
- Can be electro-clinical or electrographic only.

SEVERE APNOEA

- Two or more apnoeas per hour requiring bag-mask ventilation.

SEVERE HYPOTENSION

- Requiring inotropes to maintain blood pressure.

APPENDIX B

BACTERIAL PATHOGENS

- *Achromobacter* species [including *A. xylosoxidans* (also known as *Alcaligenes xylosoxidans*) and others]
- *Acinetobacter* species including multidrug-resistant *Acinetobacter*
- *Aeromonas* species
- *Alcaligenes* species [*A. xylosoxidans* and others]
- *Bacteroides* species
- *Burkholderia* species [*B. capeciae* and others]
- *Campylobacter* species [*C. fetus*, *C. jejuni* and others] including drug-resistant *Campylobacter*
- *Chryseobacterium* species
- *Citrobacter* species [*C. diversus*, *C. freundii*, *C. koseri* and others]
- *Clostridium* species
- *Enterobacter* species [*E. aerogenes*, *E. cloacae*, and others] including Carbapenem-resistant *Enterobacter*
- *Enterococcus* species [*E. faecalis* (also known as *Streptococcus faecalis*), *E. faecium*, and others] including Vancomycin-resistant *Enterococcus*
- *Escherichia coli* including Carbapenem-resistant *Escherichia coli*
- *Flavobacterium* species
- *Haemophilus* species [*H. influenzae* and others]
- *Klebsiella* species [*K. oxytoca*, *K. pneumoniae* and others] including Carbapenem-resistant *Klebsiella* and Cephalosporin-resistant *Klebsiella*
- *Listeria monocytogenes*
- *Moraxella* species [*M. catarrhalis* (also known as *Branhamella catarrhalis*) and others]
- *Morganella morganii*
- *Neisseria* species [*N. meningitidis*, *N. gonorrhoeae* and others] including drug-resistant *N. gonorrhoeae*
- *Pantoea*
- *Pasteurella* species
- *Prevotella* species

- Proteus species [P. mirabilis, P. vulgaris and others]
- Providencia species [P. rettgeri and others]
- Pseudomonas species [P. aeruginosa and others] including multidrug-resistant Pseudomonas aeruginosa
- Ralstonia species
- Salmonella species including drug-resistant Salmonella serotype Typhi
- Serratia species [S. liquefaciens, S. marcescens and others]
- Staphylococcus coagulase positive [aureus] including Methicillin-resistant Staphylococcus aureus and Vancomycin-resistant Staphylococcus aureus
- Stenotrophomonas maltophilia
- Group B Streptococcus or GBS [also known as Streptococcus agalactiae]
- Streptococcus anginosus [formerly Streptococcus milleri]
- Streptococcus pneumoniae
- Streptococcus pyogenes [Group A Streptococcus]