INQUIRY SCHEDULE OF MEDICATIONS: CLAIRE ROBERTS
22nd October 1996

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
RECTAL DIAZEPAM					
Prescription				WS-138/1, Dr Webb at pg 18, Q11, *"I believe Dr Sands requested rectal diazepam but I am not certain that he actually prescribed it."* *"I have recorded in my note that Claire improved following rectal diazepam and this would be common in a child with non convulsive status. In a child who is not having seizure activity diazepam may cause sedation and rarely can cause respiratory depression."* WS-137/2, Dr Sands at pg 13, Q15, *"I think it likely that I suggested a trial dose of rectal diazepam."* WS-141/1, Dr Stewart at p.9 Q20(d), *"I asked Dr Sands how much he wanted me to prescribe and he told me 5mg."*	Ref: 237-002-008 Dr J.K. Aronson states that the onset of action of diazepam would be expected to occur within 10-30 minutes. As diazepam is a sedative, it would tend to reduce the Glasgow Coma Scale (GCS) score and impair other neurological functions for the duration of its action. He states that this drug has a long duration of action and is metabolised in the body to a compound that has an even longer duration of action. The effect of a single dose could last as long as 1-2 days, therefore the dose administered to Claire could have reduced her GCS score during the last hours of her life, and this drug would have made it more difficult to have accessed the extent to which Claire's neurological impairment was due to the primary illness, but would not have contributed to her death.
Not clear	5mg once-only	Dr Sands Dr Stewart	090-022-053 (Clinical History, Examination & Progress) 090-026-075 (Prescription Sheet)		
Administration					
12.15[1]	5mg	EN Linsky	090-026-075 (Prescription Sheet) 090-040-141 (Nursing records)		
PHENYTOIN					
Prescription				WS-138/1, Dr Webb at pg 23, Q16, *"Intravenous phenytoin was the first choice drug for all prolonged seizures in childhood who had failed to respond to diazepam."*	Ref: 237-002-009 Dr. J.K. Aronson, has stated that a dose of 635mg of Phenytoin (18mg/kg in Claire's case) one would use 12.7ml of such a solution (obtained from 3 vials) and give it intravenously at a rate no greater than 72mg/kg/minute) or over no less than 9 minutes.
14.30	635mg[2] loading dose and 60mg	Dr Webb	090-022-054 (Clinical History,		

[1] Dr Webb noted that Claire appeared to improve after rectal diazepam 5mg given at 12.30 (Ref: 090-022-053). Nursing Records (Ref: 090-040-141) at 2.00pm refers to 5mgs of rectal diazepam 'given'.

[2] Phenytoin bolus (or loading) dose was wrongly calculated by Dr Stevenson in the clinical notes as 632mgs when it should have been 432mgs (18x24).

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
	every 12hrs either IV or orally.[3]	Dr Stevenson	Examination & Progress) 090-026-075 (Prescription Sheet)	WS-138-1, Dr Webb at pg 24, Q16, *"a loading dose of 432mg of IV phenytoin should have no effect on Claire's respiratory drive. ... I would not expect an additional dose of 8mg/kg to have any ill effects on Claire. Her subsequent phenytoin level was just above the recommended treatment range. ... This would normally be given in normal saline as a solution."* *Q17 " ... phenytoin has no effect on respiratory function."* WS-139/1, Dr Stevenson at pg 17, Q28, *"I am unable to recall whether I was aware of the error in this prescription and if I was what action I took. I now know that it was an incorrect calculation, as it should have been 432mg."*	Ref: 237-002-009 Dr. Aronson has stated that if this drug was clinically indicated, then a loading dose of 18mg/kg i.e. 432mg would have been appropriate. Ref: 237-002-009, 10 Dr. Aronson states that the onset of action of IV phenytoin is 30-60 minutes, and the effect lasts for up to 24 hours. He would have expected some adverse reactions to the overdose of 635mg phenytoin since the dose was about 50% more than was indicated. The most common adverse reactions of this drug affect the central nervous system including decreased coordination, slurred speech, mental confusion, somnolence, drowsiness but since Claire was unconscious when she was given the phenytoin most of these effects, if they occurred, would not have been detectable. The drug would also have reduced Claire's GCS score and would have made it more difficult to assess Claire's progress and the extent to which Claire's neurological impairment was due to the primary illness. However this would not be a reason to withhold effective treatment, and the clinician who administered such treatment would make allowance for its effects on neurological markers of progress. Ref: 237-002-010, 11 Dr. Aronson states that the usual range of serum concentrations associated with a beneficial effect is 10-20mg/L, and toxic reactions are more likely at concentrations above 20mg/L. Administration of 635mg would be expected to result in a post-distribution serum concentration of 26.5 mg/L. Claire's serum concentration result was 23.4mg/L at about 7 hours after the loading dose – Dr. Aronson says at that time he would have
Administration					
14.45	635mg[4]	Dr Stevenson	090-026-075 (Prescription Sheet) 090-040-141 (Nursing Records)		
Administration					
21.30	60(mg?)[5]	Unknown[6]	090-026-073 (Prescription Sheet) 090-026-077 (Regular Prescriptions – Drug Recording Sheet)		
Administration					
24.00	110(ml?)	SN Murphy	090-038-135 (Fluid Balance & IV		

[3] The exact nature of the fluids in which the Phenytoin and Acyclovir were dissolved in is unknown.
[4] The loading dose is not recorded on the Fluid Balance & IV Prescription Sheet (090-038-135).
[5] Note: Ref: 090-038-135 Fluid Balance & IV Prescription Sheet records Phenytoin at 24.00hrs at 110 (mls?) – it is unclear when it started (possibly 11pm?) . The nursing notes at 11pm (Ref: 090-040-138) refer to IV Phenytoin erected by doctor and run over one hour – cardiac monitor in situ throughout infusion. This dosage is not recorded on the Drug Recording Sheet (090-026-077)
[6] Dr J Hughes – Ref WS-140/1, p.4, Q7(a) says she re-wrote the Prescription Sheet at 9.30pm and recorded the administration of Acyclovir at 9.30pm. Neither Barbara Maxwell nor Lorraine McCann admits to recording "A" [Phenytoin] on the Drug Recording Sheet at this time.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
			Prescription Sheet)		expected a concentration of 22mg/L, although it is difficult to make predictions in an individual at any dose. However he states it would have taken about 9.5 hours for the serum concentration to fall to the upper limit of the target range, and this is consistent with Claire's concentration of 23.4 mg/L. Toxic concentrations of phenytoin can be associated with seizures but it is impossible to say whether Claire's seizure at 15:10/25 was due to phenytoin toxicity, an underlying infection, hyponatraemia, some other cause or a combination of any of these. Ref: 237-002-011 Dr Aronson also states that after a loading dose, the serum phenytoin concentration should be checked before the administration of a maintenance dose. As the maintenance dose was due at 23:00, measurement at 21:00 would have been expected to have allowed enough time for the result to be reported before the next dose was due. Dr. Aronson states that one would not start to give the maintenance dose until the result of the serum measurement was known. Ref: 232-002-009 Prof Neville - Does not think that giving IV phenytoin was appropriate at that stage without proof that non-convulsive status epilepticus was present. He does not think that a significant overdose is likely to have materially affected the outcome. The overdose might have reduced conscious level but he does not think that this is likely to have had a major effect on diagnosis or management. Ref: 234-002-006 Dr Scott-Jupp – thinks the error is irrelevant and the starting dose mentioned in the literature is somewhat arbitrary. He says the important thing is to check blood levels at intervals after starting medication to ensure they are within an acceptable range. In this case this was done as appropriate and the level was acceptable.
Administration					
01.00	60(ml?)[7]	SN McCann	090-038-135 (Fluid Balance & IV Prescription Sheet)		

[7] Note: The Fluid Balance & IV Prescription Sheet (090-038-135) seems to indicate that Claire had received a further 60ml by 01.00hrs and 170ml in total.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
MIDAZOLAM					
Prescription				WS-138/1 Dr Webb at pg 32, Q22, *"I considered Claire was still having epileptic seizure activity and felt that Midazolam was an appropriate short acting benzodiazepine to try and stop her seizures. She had previously shown a response to another benzodiazepine (diazepam). The administration of intravenous treatment for status epilepticus routinely involves the administration of an intravenous loading dose followed by a slow infusion. The loading dose should have been given at 0.15mg/kg stat and I do not know how a dose of 0.5mg/kg was charted."* WS-139/1, Dr Stevenson at pg 20, Q30, *"...could indicate a typographical error on my part and the actual entry should be 12mg and not '120mg' as it may read."* At pg 21, *"it is possible that I forgot to sign that I had given it."* WS-139-/2, Dr Stevenson at pg 9, Q15, *"I accept that I cannot be certain the exact dose I gave, other than give the opinion that if 120mg of Midazolam had been given as a single dose that would have had a profound effect on a child, which would have been obvious at the time of administration."*	Ref: 237-002-014 Dr. Aronson states that 120mg of midazolam, even if given over 24 hours, is a very large dose and would have caused major anaesthesia, coma, severe respiratory depression and possibly death. Dr. Aronson also states that midazolam should be given slowly by intravenous infusion, titrating the dose against the clinical response. He explains that midazolam has its onset of action at about 2 minutes after an injection. He also states that midazolam is a sedative which would tend to reduce the GCS score and impair other neurological functions for the duration of its action – this would have made it more difficult to assess the extent to which Claire's neurological impairment was due to her primary illness. Ref: 237-002-016 Dr. Aronson states that the effect of each drug (diazepam, phenytoin and midazolam) would have tended to worsen the GCS score by sedative effects on the brain. The effect of 120mg of midazolam would have been much greater on its own than the effects of each of the other drugs, possibly even in combination. He observes that Claire's score fell from 9 to between 6 and 8, which suggests that the sedative effects were not as great as might have been expected from such a dose. Ref: 232-002-009 Prof Neville, *"the giving of midazolam was inappropriate because there was no confirmation by EEG of the diagnosis. ...a drop in sodium level and cerebral oedema may themselves provoke seizures and I would expect this possibility would be taken into consideration."* Ref: 232-002-016 Prof Neville – *"My reading of this is that*
15.10 (?)	12mg[8] IV stat followed by 2.88 mg/h infusion	Dr Webb Dr Stevenson	090-022-055 (Clinical History, Examination & Progress) 090-026-075 (Prescription Sheet)		
Administration					
15.25	120mg[9]	Dr Stevenson	090-026-075 (Prescription Sheet) 090-040-141 (Nursing Notes)		
Prescription					
15.10	69mg at 2mls/hr over 24 hrs	Dr Webb	090-022-055 (Clinical History, Examination & Progress) 090-038-136 (Intravenous Fluid Prescription Sheet)		

[8] The calculation of (1) 0.5 x 24 = 12mg IV Stat, (2) 2 x 24 = 2.88mg/hr infusion = 69mg/24 hrs is recorded on the clinical records at Ref: 090-022-055. This does not correspond with the drugs 'once only' prescription sheet at 090-026-075 which records a dosage of 120mg.

[9] The dosage is noted as 120mg by Dr R Stevenson but not initialled as 'Given' Ref: 090-026-075 (Prescription Sheet) although the nursing records (Ref: 090-040-141) notes stat IV hypnovel at 3.25pm.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
		Dr Stevenson	090-026-075 (Prescription Sheet)		*12mg IV stat dose of Midazolam was calculated as 0.5mg/kg and it was given. . ... so this is an overdose. ...could have caused or contributed to this fall in Claire's GCS. There was no evidence that Claire needed this dose of medicine. It was a big dose. It likely reduced her conscious level and therefore reduced her breathing...Therefore it was likely to have exacerbated her condition. ... The midazolam did not treat her underlying condition or the cerebral odema."* Ref: 231-002-031 Mrs. Sally Ramsay states that it would have been preferable to administer midazolam and phenytoin intravenously in an appropriately equipped high dependency unit or Intensive Care setting. She says a GCS of 8 and the need for complex IV therapy should have prompted discussion between nursing and medical staff about admission to PICU
Administration					
17.00	0.8mls	SN Ellison	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
18.00	1.9mls	SN Ellison	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
19.00	2.8mls	SN Ellison	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
20.00	1.2mls	SN Ellison	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
21.00	2mls	SN McCann	090-038-135 (Fluid Balance & IV Prescription Sheet)		

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
Prescription				WS-140/1, Dr Hughes at pg 21, Q30, *"I do not recall rewriting the prescription but on reviewing the notes the original midazolam dose needed to be changed. The original prescription was full and therefore the whole thing was rewritten."* [at 21.30hrs]. At pg 22, Q31, "*the nursing notes refer to the increase in prescription rate. I do not recollect who directed this."*	
21.30	Increased by 0.1ml every 5 mins until running at 3mls/h[10]	Dr Hughes	090-026-073 (Prescription Sheet) 090-040-141 (Nursing Records)		
22.00	2.2mls	SN McCann	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
23.00	3.0mls	SN McCann	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
24.00	2.9mls	SN Murphy	090-038-135 (Fluid Balance & IV Prescription Sheet)		
Administration					
01.00	2.5mls	SN McCann	090-038-135 (Fluid Balance & IV Prescription Sheet)		

[10] Note: Dr Hughes did not record this increase in Midazolam in Claire's clinical notes.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
Administration					
02.00	2.2mls	Unknown	090-038-135 (Fluid Balance & IV Prescription Sheet)		
CEFOTAXIME					
Prescription				WS-140/1, Dr Hughes at pg 24, Q33, *"I have no recollection of the events but according to the prescription sheet I administered the drug* [Cefotaxime] *at 5.30pm ... this was to address meningitis."* WS-138/1, Dr Webb at pg 40, Q24, *"Cefotaxime is a broad spectrum antibiotic widely used in cases of potential intracranial infection to cover the common causes of bacterial meningitis. I believe it was administered at 5.30pm and 11.20pm on 22nd October 1996 (090-026-077."*	
17.00	600mg[11] IV	Dr Webb Dr Stevenson	090-022-055 (Clinical History, Examination & Progress) 090-026-075 (Prescription Sheet) 090-040-141 (Nursing Records)		
Administration					
17.30	600mg	Dr Hughes	090-026-077 (Regular Prescriptions – Drug Recording Sheet)		

[11] Note: The Nursing Records (P Ellison) (Ref: 090-040-141) say the first dose of Clarofan (Cefotaxime) is done at 9.30pm but this is actually the second dose of Claforan (Cefotaxime) as the first dose was administered at 17.30. The second dose is not noted on the Regular Prescriptions – Drug Recording Sheet at Ref: 090-026-077 but is noted on the Prescription Sheet at Ref: 090-026-075. Cefotaxime was administered by IV but it is not recorded on the Fluid Balance & IV Prescription Sheet (090-038-135) and the volume/nature of the diluents is unknown.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
Administration					
21.30[12]	600mg	Unknown	090-040-141 (Nursing Records) 090-026-075 (Prescription Sheet)		
Administration					
23.20	600mg	SN McCann	090-026-077 (Regular Prescriptions – Drug Recording Sheet)		
PARACETAMOL					
Prescription					
Unknown	240mg	Unknown[13]			
Administration					
20.25	240mg	SN Ellison	090-026-077 (Regular Prescriptions – Drug Recording Sheet)		

[12] Note: This dosage is not noted on the Regular Prescriptions – Drug Recording Sheet (Ref: 090-026-077).
[13] Note: At 20.25 Dr J Hughes was the Doctor on call although this may have been prescribed earlier.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
ACYCLOVIR					
Prescription				WS-140/1, Dr Hughes at pg 25, Q33, *"I have no recollection of events but according to the prescription sheet I administered Acyclovir at 9.30pm. .... This was to address encephalitis. ... The medicines were given at the time they were prescribed for."* WS-138/1 Dr Webb at pg 41, Q24, *I recommended that Claire receive Cefotaxime and Acyclovir at 5pm. I would have expected this to have been started within an hour or two. ... There was no delay in the administration of Cefotaxime to Claire and I do not know why there was a delay in administering the Acyclovir.*	
17.00	240mg	Dr Webb	090-022-055 (Clinical History, Examination & Progress) 090-026-075 (Prescription Sheet)		
		Dr Stevenson	090-040-141 (Nursing Records)		
Administration					
21.30[14]	60 (mls?)	Dr J Hughes	090-038-135 (Fluid Balance & IV Prescription Sheet) 090-040-138 (Nursing Records) 090-026-077 (Regular Prescriptions – Drug Recording Sheet)		
Administration					
22.00	60 (mls?)[15]	SN McCann	090-038-135		

[14] Note: Ref: 090-038-135 Fluid Balance & IV Prescription Sheet – it is not clear if a 60mls dose was administered at 21.00 hrs and again at 22hrs or if a total of 60mls was administered between 21.00 and 22.00hrs. The Nursing Records (090-040-138) at 9.30pm refer to a first dose of IVAcyclovir erected by a doctor and run over one hour.

TIME	DOSAGE	CLINICIAN / NURSE	REF	WITNESS COMMENTS	EXPERT COMMENTS
			(Fluid Balance & IV Prescription Sheet)		
SODIUM VALPROATE (EPILIM)					
Prescription				WS-137/1, Dr Sands at pgs24-25, *"I do not recall being present at this time* [during Dr Webb's attendance with Claire at 17.00] *however I may well have been there as I gave Sodium Valporate as instructed by Dr Webb at 17.15pm."* WS-137/1, Q12(h): Dr Sands does not recall why he did not administer the acyclovir and cefotaxime ordered by Dr Webb at 17.00 when he (Dr Sands) attended Claire at 17.15 to administer the sodium valporate. He says other staff may have given these intravenous medications.	Ref: 237-002-015 Dr. Aronson thinks it unlikely that this drug contributed to Claire's hyponatraemia. He expects that the onset of action of IV sodium valproate, which is not a sedative, would have been 30-60 minutes and that it would not have affected Claire's neurological assessment. Ref: 232-002-009 Prof Neville , *"..the IV valporate was inappropriate because there was no confirmation by EEG of the diagnosis. . ...a drop in sodium level and cerebral oedema may themselves provoke seizures and I would expect this possibility would be taken into consideration."* Ref: 234-002-006 Dr Scott-Jupp, *"At the time ... I think this was an appropriate intervention."*
17.00	20mg/kg IV bolus as an initial dose followed by infusion 10mg/kg IV over 12hrs	Dr Webb Dr Sands	090-022-055 (Clinical History, Examination & Progress) 090-026-075 (Prescription Sheet) 090-040-141 (Nursing Records)		
Administration					
17.15	400mg	Dr Sands	090-026-075 (Prescription Sheet) 090-040-141 (Nursing Records)		
HEPSAL					
Prescription					
	5mg IV	Dr Stevenson	090-026-075 (Prescription Sheet)		

[15] Note: It is not clear from the Fluid Balance & IV Prescription Sheet (090-038-135) if Claire had received 60mls Acyclovir in total at 22.00 hrs.