Witness Statement Ref. No. WS-342/2

NAME OF CHILD: Lucy Crawford (Rachel Ferguson Governance)

Name: Ian S.Young

Title: Professor

Present position and institution:

Professor of Medicine, Queen's University Belfast

Consultant in Clinical Biochemistry, Belfast Health and Social Care Trust

Previous position and institution:
[As at the time of the child's death]

Membership of Advisory Panels and Committees:
[Identify by date and title all of those between January 1995-December 2004]

Previous Statements, Depositions and Reports:
[Identify by date and title all those made in relation to the child's death]

096-007-039 Statement to the PSNI

091-010-060 4/5/2006 Deposition to the Coroner

WS-178-1 - Inquiry Witness Statement (PDF 1.8MB)

WS-178-2 - Supplemental Inquiry Witness Statement (PDF 9MB)

WS-178-3 - Supplemental Inquiry Witness Statement (PDF 1.7MB)

WS-178-5 - Supplemental Inquiry Witness Statement (PDF 10MB)

OFFICIAL USE; List of previous statement, depositions and reports attached:		
Ref:	**Date:**	

Other points you wish to make including additions to any previous Statements, Depositions and or Reports
[Please attach additional sheets if more space is required]

THIS STATEMENT IS TRUE TO THE BEST OF MY KNOWLEDGE AND BELIEF

Signed: Ian Young

Ian Young

Dated: Submitted in draft form on 2/9/13 and in this format on 24/2/14

1) My report of 18/6/13 suggests that Lucy's sodium would have been 124 mmol/l prior to the infusion of 500 mls 0.9% NaCl, and 126 mmol/l if 250 mls 0.9% NaCl had been infused. In calculating these figures, I made a minor algebraic error. However, correcting this has no significant effect on the result of my calculations, and the figures in my report of 18/6/13 are essentially the same as those produced by the calculations on page 7 of Dr. Haynes' new report (253-004; 9/8/13), with which I agree.

2) On page 8 of his new report Dr.Haynes goes on to perform calculations based on the assumption that 0.9% NaCl might distribute initially in extracellular water (ECW) rather than total body water (TBW). He explains the basis of this assumption in his report. While I understand his argument, and agree that the subsequent details of his calculation are correct, I do not believe that this assumption is likely to be valid and cannot find any support for it in the published literature.

3) In contrast to Dr. Haynes, I believe that the redistribution of infused osmoles into total body water would have been sufficiently rapid for this approach to the calculation (using extracellular water rather than total body water) to be invalid. However, I cannot support this opinion from published literature either. In the absence of experimental evidence either way, this, therefore, remains an area of disagreement between us, though, as discussed below, I think the disagreement is of limited relevance.

4) Dr.Haynes and I agree that if Lucy's sodium had fallen over six hours to a nadir of 124-126 (or even 127) mmol/l, this would have been sufficient to explain her cerebral oedema. It is not necessary to assume a sodium nadir lower than this.

5) On page 9 of his new report, Dr.Haynes refers to Arieff's belief that rate of fall of serum sodium was not linked to cerebral oedema. Dr.Haynes suggests that this has been over-interpreted. In contrast, I believe that Arieff's statement was very clear and that his position reflected a strand of opinion which was present in the 1990s. However, both Dr.Haynes and myself disagree with Arieff's position on this point; we believe that rate of fall in serum sodium is linked to risk of hyponatraemia, as was argued in the 1990s by others and is the dominant view today.

6) Finally, I wish to comment on recent research of relevance to the question of idiosyncratic response to hyponatraemia, and the possibility that individuals may differ significantly in terms of their tendency to develop cerebral oedema. There is currently interest in the role of a group of proteins known as aquaporins which exist within cell membranes and are involved in water transport across them (Verkman, 2012). Aquaporin-4 is a key water transporter within brain tissue, and it has been suggested that genetic variation in the aquaporin-4 gene might influence the tendency to develop cerebral oedema. For instance, a single nucleotide polymorphism (rs9951307) at the 3' end of the aquaporin-4 gene has been

associated with severe cerebral oedema in patients with a middle cerebral artery stroke, whereas patients without this polymorphism are resistant to cerebral oedema (Kleffner, 2008). A number of genetic variants have been identified in the aquaporin-4 gene which might influence risk of cerebral oedema in the presence of hyponatraemia (Sorani 2008). If this is the case, then children with unusual mutations or variations in the aquaporin-4 gene might be at particular risk of cerebral oedema in the presence of hyponatraemia. While there is currently no proof that this is the case, this provides an example of the type of biological mechanism which might explain why some individuals are prone to cerebral oedema in a particular clinical situation (such as hyponatraemia) while others might not be affected.