Witness Statement Ref. No. 179/1

NAME OF CHILD: Adam Strain

Name: Sarah Branch

Title: Dr

Present position and institution:

Manager – Special Populations Group, Vigilance and Risk Management of Medicines Division, Medicines and Healthcare products Regulatory Agency (MHRA)

Previous position and institution:

At the time of the child's death on 28th November 1995, I was a Pharmaceutical Assessor in the Parallel Import Unit, Licensing Division, MHRA. Since that time I have held a number of assessment and management posts within the MHRA.

Membership of Advisory Panels and Committees:

I was a member of the British Pharmacopoeia (BP) Committee P (Pharmacy), which became the Pharmacy Expert Advisory Group, from 2003 until 31st December 2010. Before that I was a member of BP Committee C (General Chemicals).

Previous Statements, Depositions and Reports:

N/A

OFFICIAL USE:
List of reports attached:

Ref:	**Date:**	

Particular areas of interest:

(1) The likelihood, if any, of a connection between the manufacturers of Solution 18 and hospitals/trusts/medical personnel that could improperly affect decisions on procurement or appropriate fluid administration?

The MHRA has no information on potentially improper links between manufacturers of Solution 18 and hospitals/trusts/medical personnel. Enforcement of the legislation on promotion of medicines in Northern Ireland is a matter for the DHSSPSNI. I am not aware of any complaints about promotion of solution 18 products in any part of the UK in the last 7 years (the period for which we retain records of cases).

(2) Whether you agree with the statement of the Working Group that: "There is a risk of hyponatraemia and electrolyte imbalance with the use of all intravenous fluids."

The minutes of the Committee on Safety of Medicines Working Group on Paediatric Medicines of 21 November 2001 reflect the discussion held and the views of the experts present at that time. The literature review carried out for the purposes of the consideration by the Working Group found a clear association between hypotonic intravenous fluids and hyponatraemia. I am in agreement with that statement.

(3)

(a) What more can be done to raise the possible safety concerns regarding Solution 18 as a 'regulatory issue'?

(b) What more can be done to raise the possible safety concerns regarding Solution 18 as a 'clinical practice issue'?

(c) Do you agree with the actions taken in NPSA No. 22 to 'Remove sodium chloride 0.18% with glucose 4% intravenous infusions from stock and general use in areas that treat children?' Do you consider that this is sufficient protection, or do you consider that more can be done eg extending this prohibition to adult wards?

We are currently conducting a further review of all the available data on the risk of hyponatramia associated with the use of 0.18% saline/4% glucose solutions to determine whether regulatory action is required. This review will take into account the actions already taken by NPSA in England and Wales and relevant professional bodies. It will consider the need for further action such as revisions to product information and communication to healthcare professionals.

(4)

(a) Do you believe, almost 10 years after the safety review (the Safety Review paper prepared by Doctor Katharine Cheng in October 2001 on Hyponatraemia and 4% Dextrose/0.18% Saline in Children for the Committee on Safety of Medicines Working Group on Paediatric Medicines), that 'suitable warnings about the development of hyponatraemia in children should be included in product information' to safeguard against poor clinical practice or training?

(b) With particular reference to the products included at paragraph 14 above, is the current product information of Solution 18 products adequate?

See answer to (3).

(5) The procedure and effectiveness of reporting of adverse effects from medication or solutions to the MHRA through ADROIT (Adverse Drug Reactions Online Information Tracking) where such adverse effects arise out of 'clinical practice'.

The MHRA and the Commission on Human Medicines (CHM) run the UK's spontaneous adverse drug reaction (ADR) reporting scheme - called the Yellow Card Scheme. This receives reports of suspected adverse drug reactions (ADRs) or side effects from healthcare professionals and patients for medicines and vaccines. The Scheme has been in operation since 1964 and has a proven record in quickly identifying new safety signals. Yellow Cards received are included on a database (previously the Adverse Drug Reactions Online Information Tracking database, now the Sentinel database) which enables analysis of the data for new safety signals.

Health professionals and patients report suspected ADRs on a voluntary basis. For pharmaceutical companies there is a legal requirement to report serious ADRs for their drugs to the MHRA. The Yellow Card Scheme receives approximately 25,000 reports per year although the number of reports received does not provide the number of people who suffer adverse reactions to drugs as it is associated with an unknown and variable level of under-reporting; the total number of people who experience ADRs is not known. Reporting rates may be influenced by the seriousness of reactions, how easily reactions are recognised, how often a particular drug is used, and publicity about a drug.

A report of a suspected ADR may be due to the intrinsic qualities of the medicine itself, by the way the medicine is used by the patient or healthcare professional or a combination of both. Healthcare professionals and patients are asked to report regardless of any doubts they may have about a causal relationship between the ADR and the medicine. Spontaneous reporting schemes such as the Yellow Card Scheme have a proven track record in identifying suspected ADRs to medicines associated with inappropriate use or medication error.

When a signal of a suspected ADR arises an assessment is undertaken to determine whether there is a causal association with a particular medicine. If a causal association is likely, possible risk minimisation measures will be considered. These can include restriction of the product to particular patient populations and/or provision of warnings prescribers and patients about a new adverse reaction. If the risk cannot be minimised and is considered to outweigh the benefits of the medicine, consideration will be given to the removal of the product from the market.

(6) Whether there has been any further review of Solution 18 and if so its conclusions

See answer to (3).

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

Signed: Sarah Branch **Dated:** 1 Dec 2011

NOT FOR PUBLICATION
WORKING GROUP ON PAEDIATRIC MEDICINES

MINUTES OF THE MEETING HELD ON WEDNESDAY 21st NOVEMBER 2001 AT 2 P.M. IN THE 19th FLOOR CONFERENCE ROOM, MARKET TOWERS

Members Present **MCA**
Professor J Collier
Dr T L Chambers
Dr R MacFaul (item 7)
Mr T Nunn (item 6)
Dr G Rylance
Professor R L Smyth
Professor T Stephenson (item 6)
Dr S Watkins

Others

Apologies
Professor Aynsley-Green
Professor M Kendall
Professor K Park

Secretary

+ not present for items 9 to 17

Announcements/apologies

1.

2.

3. Apologies have been received from Professors Ansely-Green, Kendall and Park.

4. **Minutes of the meeting of 10 July 2001**

5. **Terms of Reference**

ORAL UPDATES

6.

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PAPERS

11.

12. **New safety signal : 4% dextrose/0.18% saline and fatal hyponatraemia**

12.1 The WG noted **Tabled Paper III.**

12.2 A review of hyponatraemia and the use of 4% dextrose/0.18% saline in children was presented to the WG. The MCA/CSM has recently received a report of fatal hyponatraemia in a child following the use of 4% dextrose/0.18% saline after surgery. The WG was asked to advise on whether they considered hyponatraemia and 4% dextrose/0.18% saline in children to be a safety concern, whether there was any concern for children in situations other than after surgery, whether there were specific indications for this particular solution in paediatric practice and whether there should be any changes to SPCs. The WG advised that there is a risk of hyponatraemia and electrolyte imbalance with the use of all intravenous fluids. There was a risk of hyponatraemia with the use of 4% dextrose/0.18% saline in situations other than after surgery, for example, diarrhoea and vomiting and diabetic ketoacidosis. The solution is used as a standard maintenance fluid in paediatric practice and was designed specifically to provide maintenance requirements of dextrose and saline. The WG considered that the crucial issue was careful monitoring of fluid balance in the post-operative period, with particular attention in avoiding fluid if the patient was oliguric, a physiological response to surgery. The WG considered that the issue of hyponatraemia related more to clinical practice rather than to medicines regulation and advised that there should be no changes to product information.

13.

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18. **Any Other Business**

19. Date and time of next meeting