SERIOUS ADVERSE EVENT REPORTING:

Serious adverse events are defined as follows:

- **Requires in-patient hospitalisation or prolongation of hospitalisation**
- **Is immediately life threatening**
- **Results in persistent or significant disability or incapacity**
- **Results in death**

All Serious Adverse Events (SAEs) need to be reported to the study team whether they are suspected to be related to study medication and/or trial process or not.

THE PROCESS:

PITCH Research Nurse (RN) becomes aware that a randomised child has become a SAE.

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- RN reports SAE to Trial Coordinator (TC) (Ceire Costelloe Tel: 07810264771) as soon as possible.
- Research Nurse gives child's CRF to TC as soon as possible.
- If TC unavailable, then report to Principal Investigator (PI) (Alastair Hay Tel: 07817495050) as soon as possible.
- All SAE's should be reported to both TC and PI within 24 hours of onset.
- SAE reported to child's GP if not already aware.

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- RN to establish and note down in as much detail as possible, the course of events leading to SAE from (a) their own point of view and (b) that of parent. The following information is specifically needed:
  - Names, doses, times of administration of study medicines and any other medication
  - Information on clinicians or NHS contacts made since randomisation up until the point TC informed of SAE
  - The opinion of parent as to whether being in the trial helped or hindered their ability and willingness to contact the NHS.
- TC to establish NHS contacts[†] since randomisation.
- Call them to inform of SAE and request current notes of their consultation with child ASAP. Follow up with a fax to the contact, **with a copy of the completed trial consent form**. Templates for faxes and cover sheet are located here:

L:\Studies\PITCH\Trial management\SAEs and AEs\SAEs\SAE reporting templates

- RN to keep in regular contact with parent to establish how SAE is progressing. TC to keep in regular contact with RN.

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- Once the following information has been obtained the 'SAE initial report form' can be completed:
  - All consultation notes from sites where SAE child has had contact with NHS since randomisation
  - Notes of events from randomisation to SAE event from (a) RN's point of view and (b) parents point of view. Template can be found here:

L:\Studies\PITCH\Trial management\SAEs and AEs\SAEs\SAE reporting templates

NB: AH is happy to interpret any medical notes and summarise for the initial report.

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- Completed Initial report and clinical notes to be sent to at least two of the following clinicians (A Hay, A Emond, K Schroeder, or M Fletcher – contact details in Whereabout's file) to be independently assessed* for the following:
  - SAE caused by study medication or any concomitant medication
  - SAE caused, hindered or helped by child being in the trial process
- Clinicians to send back brief written report as soon as possible to TC
- 'SAE Follow-up report' to be completed, based on any further information obtained from parent, clinical contacts with child and clinicians assessments.

Caused by study medication?

SAEs that are life threatening or cause death - report to DMSC within 7 days.
All other SAEs report to DMSC within 15 days.
(DMSC Chair is Dr Reg Bragonier, email: Reg.Bragonier@nbt.nhs.uk
Dr Bragonier's secretary, Ms Elaine Cordey, Tel: 0117 9595327)

Yes
(therefore a Serious Adverse Reaction i.e. SAR). **Report to child's GP**.

No
(Therefore not a reaction)

Expected SAR

Suspected Unexpected SAR (SUSAR)

Caused by study involvement = **Yes**

Caused by study involvement = **No**

Report to DMSC. Report **annually** to MHRA & Ethics

SUSAR is death/life threatening: Report to DMSC & MHRA no later than **7 days**

For all other SUSARs: Report to DMSC & MHRA no later than **15 days**

Caused by any concomitant medication? = **Yes**

Caused by any concomitant medication? = **No**

* From TMG meeting 14 December 2004: Causality assessment will usually been done while blind to the medicine. We may decide to make a more informed (unblinded) decision about causality of all AEs at the end of the trial.

Sent initial and follow up report to DMSC within 15 days and await response and advice.

Implement any recommendations/changes to prevent re-occurrence.

† - For GP surgeries, this will be the Practice Manager in the first instance

DEFINITIONS:

Adverse event: any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

Adverse reaction: any untoward and unintended response in a subject to an investigational medicinal product, which is related to any dose administered to that subject.

Serious adverse event,
Serious adverse reaction,
Or Unexpected serious adverse reaction:
These are any adverse event, adverse reaction or unexpected adverse reaction respectively that results in any of the following:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect (not applicable for Pitch trial)

PHARMACOVIGILANCE

(and our legal obligations – see 'the medicines for human use in clinical trials regulations 2004')

SUSARs - Suspected Unexpected Serious Adverse Reactions
A sponsor must ensure that all relevant information about a Suspected Unexpected Serious Adverse Reaction, which occurs during the course of a clinical trial in the UK that is fatal or life-threatening is:

a) recorded
b) reported asap to the licensing authority and the ethics committee but no later than 7 days after the sponsor was first aware of the reaction

For all other SUSARs (i.e those that are not fatal or life-threatening, so for the PITCH trial this would be those requiring hospitalisation or prolongation of hospitalisation or resulting in persistent or significant disability or incapacity) a report to the licensing authority and ethics committee shall be made asap but no later than 15 days.

The licensing authority shall keep a record of all the SUSARs relating to an investigational product that is brought to it's attention. They will also ensure that the details of those reactions are entered into the European database (Eudract).

SSARs – annual list of Suspected Serious Adverse Reactions and safety report.

A list of all SSARs must be reported annually to the licensing authority and to the ethics committee. The report on the safety of the subjects in the trial must also be given.