Appendix 5 FLOW CHART OF THE PROCESS OF CLASSIFYING AND REPORTING ADVERSE EVENTS

Adverse Events;

'Any untoward medical occurance in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment'

Is the Adverse Event Serious?

Serious Adverse Event;

Any untoward medical occurance that at any dose

- results in death
- Is life threatening
- requires in patient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant diability/incapacity OR
- is a congenital anomaly/ birth defect

YES

If identified in the protocol as critical to safety evaluations, report to the sponsor according to the reporting requirements and within the time periods specified in the protocol. Often on CRF.

Investigator Reports to SPONSOR

No notification required if the SAE is specified in the protocol as one which does not need to be reported

Sponsor has responsibility for ensuring that investigator is informed of their reporting responsibilitites;

- SAEs should be reported 'Immediately '(orally or in writing)- Within 24hrs is a good guideline
- Followed 'immediately' by a detailed written report
- For reported death of a subject, the investigator shall supply the sponsor and the Ethics Committee with any additional information requested.

Causality- Does the investigator / Sponsor suspect SAE was caused by the IMP?

NO

Sponsor keeps a record of all SAEs reported. Licencing authority may request in writing to see this record. Usually reported to Authority as Annual Safety Report

NO



Serious Adverse Reaction (SAR)

Is the SAR expected?

- Has it been reported before?
- If it has been reported before is the current reaction of an expected magnitute or frequency?

NO



All SARs, both expected and unexpected, are reported through an annual report to the licencing authority and relevant ethics committee.

Report includes:

- A list of SAEs relating to the IMP in that trial and any other trial of that product conducted by the same sponsor.
- The safety of the subjects of those trials

Report annually on anniversary of approval

Suspected Unexpected Serious Adverse drug Reaction (SUSAR)

'An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product)'

If fatal or life threatening;

Sponsor must

- Record
- Report to ;
 - •licencing authority,
 - competant authorities of any other EEA state where the trial is being conducted, and
 - •the relevent ethics committee

WITHIN 7 DAYS OF LEARNING OF THE SUSAR.

•Follow up information must be provided within a further 8 days

If not fatal or life threatening

Sponsor must report to the above bodies with 15 days

- Sponsor informs all investigators
- •Authority and ethics committee keeps a record of all SUSARs reported