OTEST

Oxford Track-&-Trigger Electronic System for Trauma.

A randomised stepped wedge trial comparing the effects of an integrated electronic "Track-and-Trigger" system and a paper-based "track-and-trigger" system on the length of patients stay from admission date to 'fit for discharge'.

Protocol Version 5.2 18/11/2010

Ethics Ref: 11/HO308/11

Chief Investigator:	Dr Peter Watkinson
Investigators:	Professor Lionel Tarassenko Dr James Price Sarah Webb
Steering Committee	As above including; Dr David Clifton Dr Jacqueline Birks (Statistician) Simon Noel Julie Wright
Sponsor:	Oxford Radcliffe NHS Trust
Funder:	Biomedical Research Council
Signatures:	

Amendment History

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
	2.0	24/06/2010	Dr Peter Watkinson	
	3.0	11/08/2010	Dr Peter Watkinson	
	4.0	06/10/2010	Jessica Cottrell	Protocol adapted to ORH template and guidance.
	4.1	15/10/2010	Dr Peter Watkinson Jessica Cottrell	Protocol adapted to ORH template and guidance.
	5	28/10/2010	Dr Peter Watkinson Jessica Cottrell	Protocol adapted to ORH template and guidance.
	5.1	11/11/2010	Dr Peter Watkinson Jessica Cottrell	Adjusted in light of Trust R&D feedback
	5.2	18/11/2010	Dr Peter Watkinson	Adjusted in light of NIGB feedback

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Synopsis

Study Title	**O**xford **T**rack & Trigger **E**lectronic **S**ystem for **T**rauma
Internal ref. no.	
Type of study	Clinical trial of electronic versus paper based observation charting
Trial Design	Randomised stepped wedge trial
Trial Participants	Patients admitted to the John Radcliffe Trauma Unit
Planned Sample Size	2000
Planned Trial Period	8 months
Primary Objective	Will the implementation of an electronic based track and trigger system improves relevant patient outcomes in comparison to an optimised paper based version
Secondary Objectives	Will an electronic track and trigger improve compliance with track and trigger algorithms in comparison to a paper based system.
Primary Endpoint	Length of stay (from admission to Trauma Unit to "fit to discharge").
Secondary Endpoints	Patient outcome measures • Hospital length of stay • In hospital mortality • 30 day mortality following ward admission • Unplanned admissions to intensive care • Number of cardiac arrest calls Compliance measures • Appropriate escalation in observation frequency • Appropriate escalation in clinical intervention
Device Name	VitalPAC
Manufacturer Name	The Learning Clinic
Principle intended use	Electronic patient observation record with automated track and trigger scoring.
Length of time the device has been in use.	The product was first fully implemented in May 2005 in Portsmouth Hospitals NHS Trust

Background and rationale

Deterioration in physiological observations has been repeatedly shown to precede adverse outcomes (1,2). However these physiological alterations commonly go unrecognised, resulting in treatment delay (3). Delays in appropriate treatment are known to worsen outcomes in critically ill patients (4,5). The National Institute for Clinical Excellence therefore recommends that all acute hospitals should implement a "track and trigger" system, which identifies abnormal observations and triggers alerts to appropriate medical staff using weighted scoring (6). However, "Track-and-Trigger" systems have not been shown to affect hospital length of stay or mortality (7).

Previous work has suggested that “track-and-trigger” systems may fail because scores are not correctly assigned, summary scores are not correctly calculated or because the appropriate observation rate and clinical escalations for a given summary score are not enacted (8-10). An electronically-based "Track-and-Trigger" system can be designed to automatically (correctly) assign scores to any physiological observation, compute the summary score (9) and prompt the actions designated as appropriate for the summary score, so improving system performance. The facility to display recent observations and summary scores on a central station may improve the ability of senior nursing staff to recognise patient deteriorations early.

Recognising these possibilities, the National Institute for Clinical Excellence made a research recommendation to "assess the clinical effectiveness of automated (electronic) monitoring systems compared with manual recording systems in identifying people at risk of clinical deterioration" (6).

Objectives

Primary objective: to assess whether the implementation of an integrated electronic "track-and-trigger" system improves relevant patient outcomes in comparison to an optimised paper-based system.

Secondary objective: to assess whether the implementation of an integrated electronic "track-and-trigger" system improves compliance with "track-and-trigger" algorithms in comparison to a paper-based system.

Study design

A randomised stepped wedge trial comparing the effects of an integrated electronic "Track-and-Trigger" system and a paper-based "track-and-trigger" system on hospital length of stay in adult trauma patients.

The study consists of three parts:

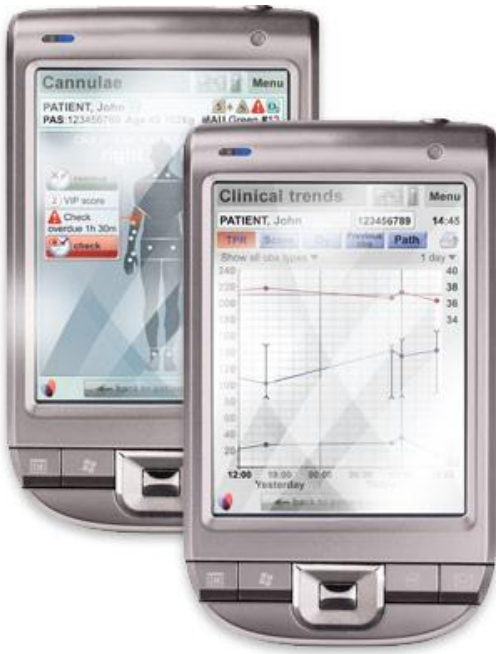
1. Installation of system and checking (4 weeks).

2. Training of ward staff in the use of both systems (4 weeks).

3. A randomised stepped wedge trial of the clinical and compliance effects of the implementation of an integrated electronic "track-and-trigger" system. There are 12 zones across 2 wards (5 four-bed bays each comprising a zone, and 6 side-rooms on each ward, each group of 6 comprising a zone). The integrated electronic "track-and-trigger" system will be introduced to incremental zones following random allocation (2000 patients, estimated time 8 months).

Control: a paper evidence-based “track-and-trigger” system on which physiological observations of blood pressure, pulse, oxygen saturation, temperature and conscious level are recorded. A score is manually assigned to each observed physiological value dependent on that value’s position within the range of values seen in hospitalised patients. The scores for each physiological value are manually summed to provide a single (summary) measure of the patient’s physiological status. The frequency of subsequent observations and the clinical response (see escalation algorithm, appendix 1) to a patient’s physiological status are then set by following an algorithm based on the summary measure. The control arm is essential to allow comparison with the current standard system, a comparison recommended by the National Institute for Clinical Excellence.

Intervention: physiological observations will be entered onto a tablet personal computer or personal digital assistant both integrated with a central display station. Scores will be automatically assigned and summed. The time of the next observation set and the appropriate clinical response will be automatically displayed according to the escalation algorithm. Visual warnings will be displayed if an observation set or clinical response is delayed. This study will use the VitalPAC v 1.2 system (The Learning Clinic, UK) to provide this functionality. The product and its software will be fully localised to both trust standards and those specific to the trauma unit (and has already been deployed in several NHS Trusts).



VitalPAC PDA

Care in either group will commence on admission to the ward and continue until hospital discharge.

Study population: 2000 adult trauma patients.

Primary endpoint: time from the first set of observations on the ward to “fit to discharge”. “Fit to discharge” is defined as either discharged from the ward to home or alternative care or accepted by social services as a “delayed discharge”.

Secondary endpoints:

Patient outcome measures: hospital length of stay following ward admission, in-hospital mortality, unplanned admissions to intensive care, cardiac arrest calls and 30 day mortality following ward admission.

Compliance measures: appropriate escalation in frequency of observations, appropriate clinical escalation.

Study participants:

Inclusion criteria: all patients > 16 years admitted to two trauma wards for an eight month period.

Exclusion criteria:

1. Patients whose treatment plan is palliative at admission to the trauma ward.
2. Patients with a learning disability.
3. Patients unable to speak English and without a suitable translator.
4. Patients in the custody of HM Prison Service.

Study procedures: The introduction of the integrated electronic "track-and-trigger" system will require all ward staff to be educated (by the trial nurses) in the data entry processes and the interpretation of the displays on personal digital assistants, tablet personal computers and the central display station. Ward staff will be trained to educate subsequently appointed and temporary staff in the usage of the devices.

In the event of a system failure, staff will revert to the paper-based system.

Informed consent: The National Information Governance Board has been successfully approached for support under section 251 of the NHS act 2006 to process patient identifiable information without consent. This is required to allow the trial to fully replicate the effects of an entire ward running an integrated electronic "track-and-trigger" system, and to allow complete zones to use the system. Retrospective consent to allow review of the notes will be asked for by post on two occasions. Refusal will result in the patient's notes not being used to gather

information for the study. As initial interviews with trauma patients suggests there to be very little concern about being involved in the study, a patient's consent will be presumed if they do not withdraw from the study . A patient will retain the right to withdraw their consent at any time either in writing or by telephone. In addition the investigator may discontinue a patient from the study at any time if the investigator considers it necessary for any reason.

Study assessments:

Study nurses will extract the following information from the patient's notes and enter it into a trial specific data entry form.

1. The date and time of the first set of observations on the ward
2. In-hospital mortality
3. Unplanned admissions to Intensive Care – defined as any admission to the Intensive Care unit not occurring as a result of further surgery which was not planned at the commencement of therapy.
4. Cardiac arrest calls
5. Appropriate escalation in the frequency of observations – defined as the next observation occurring within 1 hour of the time recommended in the escalation algorithm.
6. Appropriate clinical escalation – for those clinical escalations where clinical documentation should occur as a result of escalation – documentation of

clinical escalation, or a consequence of clinical escalation within 1 hour of the time recommended in the escalation algorithm.

Separate research personnel, unaware of the allocation of the patient will document:

7. The date and time of discharge as recorded on the hospital admissions system.

8. The “fit-to-discharge” point (to be taken as 12:00 on the day of acceptance by social services as a “delayed discharge”).

Interventions

The ward staff will be (re)trained in the use of the paper-based system and trained in the use of the electronic system at the start of the trial. Formal re-training in both systems will occur at two monthly intervals. During the initial stages of data collection physiological observations will be entered onto a tablet personal computer or personal digital assistant both integrated with a central display station, all inter-connected wirelessly. Scores will be automatically assigned and summed. The time of the next observation set and the appropriate clinical response will be automatically displayed according to the escalation algorithm. Visual warnings will be displayed if an observation set or clinical response is delayed. Prompts and warnings will be displayed on the portable devices whenever a patient’s chart is reviewed, and on a ward status view. Prompts and warnings will also be displayed on the central station. Warnings will be cleared for an observation set by completion of the required set of

observations. Warnings will be cleared for a clinical response by the ward nursing staff documenting that the required response has occurred, or is no longer needed.

Randomisation and power calculation

Given the entirely novel nature of this pilot study there are no data on which to perform a power calculation. From the admission rate to the trauma unit, we estimate that 2000 patients will be entered into the trial over an eight month period. We believe this to be sufficient to show a clinically relevant decrease in hospital length of stay. The trauma unit admits a small number of patients electively for a planned <48 hour admission. These patients will, for operational reasons have their physiological observations documented using the system in operation in the clinical zone to which they are allocated. However, they will be excluded from length of stay analyses.

A stepped wedge randomised controlled trial design has been chosen, in which sequential roll out of the electronic system to zones on the two wards in random order over a number of time periods will occur. A cluster randomised trial of multiple separate units powered to detect a mortality effect would be the optimal study design. However this would require a much higher level of funding, for which positive results from a trial such as this would be required. A randomised controlled trial of individual patients would not allow assessment of the effects of introducing the intervention into a clinical area. The stepped wedge randomised controlled trial design minimises some of the limitations of a before and after design, enabling the effect of time on the effectiveness of the electronic system to be analysed.
Our two trauma wards were chosen as they are laid out such that they can be simply divided into zones, and contain a population of complex trauma patients (within a

regional centre) who would be expected to have a relatively high rate of rectifiable clinical deteriorations. Early detection and clinical escalation might be expected to reduce their period of deterioration, and so reduce length of stay. The current preventable mortality rate is however low. There are 12 zones across 2 wards (5 four-bed bays each comprising a zone, and 6 side-rooms on each ward, each group of 6 comprising a zone). The integrated electronic “track-and-trigger” system will be introduced to incremental zones following random allocation such that over the study period an equal number of patients will have been allocated to treatment and control groups.

The randomisation schedule and codes will be supplied by the Centre for Statistics in Medicine, University of Oxford, under the guidance of Jacqueline Birks (Medical Statistician).

Data capture

The electronic transfer of the participants' vital sign physiological data and 'Track and Trigger' score to the secure ORH SQL 2008 server from the client devices will occur via the hospitals secure wifi networks. The transfer of physiological data from the paper based arm will be carried out manually by the trial nurses. Patients will be assigned a research participant number for the trial on their admission. All patient data will be connected to this number when stored electronically. No patient identifiers (such as name, NHS or hospital number) will be loaded onto the SQL 2008 Server. The patients’ demographic details and their allocated research participant number will be held on a separate database, on the NHS computer of Dr Peter Watkinson (Principal Investigator). This computer will be password protected,

and kept in a research facility behind two locked doors which require key card access. This data will be backed up onto a separate drive within the research facility.

Research nurses will need to have access to the patient's medical record to enable linkage with the research data, and to assess patient outcome measures. It would not be practical to train and monitor all of the nurses in the direct care team in collecting this data, and it would prove a burdensome addition to their workload. The anonymised data will then be analysed by Prof. L Tarassenko (coPI) and his Research Assistants, as well as by Dr James Price (coPI), Dr Lauren Bailey (coPI) and Dr Peter Watkinson (PI). The data analysis machines will be Windows PC computers used within the secure Oxford Radcliffe Hospitals domain.

The end of the trial

The trial will end following recruitment of 2000 patients. The trial will only be stopped prematurely by the Data Monitoring Committee following recommendation by the Data Monitor, or if mandated by the ethics committee or competent authority.

Safety reporting

There are no anticipated risks to patients. Further details can be found in the ethics section.

Reporting of AE: All AE's occurring during the study observed by the investigator or reported by the participant, whether or not attributed to the device under investigation will be recorded on the CRF as specified in the protocol.

A completed ORH SADE reporting form (http://www.oxfordradcliffe.nhs.uk/research/documents/Template-SeriousAdverseEventsReportingForm-ORHv1.doc) should be faxed to the Principal Investigator (fax: 01865 857611). The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to device, other suspect drug or device and action taken. Follow-up information should be provided as necessary.

The Principal Investigator will report all serious adverse event (SAE)/serious adverse device event (SADE)/unanticipated adverse device effects (UADE)s (for definitions see appendix 4) will be reported to the sponsor/legal representative and manufacturer and the Oxford Radcliffe Hospitals Research and Development department within one working day of the investigator team becoming aware of them using the ORH SADE reporting form (by fax: 01865 222648) giving as much information about the incident as possible, and will be signed by the PI or Co-investigator. The Research and Development Department will acknowledge receipt of the event documentation within two working days. The principal investigator will include an assessment as to whether the study can proceed; any changes necessary to the protocol should be included in this assessment. The ORH R&D Department will undertake an initial review of the information and ensure it is reviewed by the ORH/University of Oxford Trial Safety Group Medical Monitor.

Events will be followed up until resolution, any appropriate further information will be sent by the research team in a timely manner. The relationship of AEs to the device will be assessed by a medically qualified investigator or the sponsor/manufacturer and will be followed up until resolution or the event is considered stable.

Reports of related and unexpected SAEs will be submitted to ethics within 15 days of the Chief Investigator becoming aware of the event, using the SAE report form for non-CTIMPs published on the National Research Ethics Service serious adverse event form (appendix 2): http://www.nres.npsa.nhs.uk/applications/after-ethical-review/safetyreports/safety-reports-for-all-other-research/

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Reporting to the MHRA will be done in liaison with the Chief Investigator and the Manufacturer.

The manufacturer has a legal obligation to report all events that need to be reported to the Nominated Competent Authority immediately (without any unjustifiable delay) after a link is established between the event and the device, but no more than:

- 2 days following the awareness of the event for Serious Public Health Threat.
- 10 days following awareness of the event for Death or unanticipated serious deterioration in health.
- 30 days following the awareness of the event for all other event meeting the SAE criteria.

All ADE that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.

Study specific AE: In the event of any of the following occurring to any patient within the study, a Serious Adverse Events form will be completed by a member of the trial team:

1. Failure to document clinical observations leading to delay in diagnosis of a patient deterioration as a result of failure of the integrated electronic "track-and-trigger" system. The delay must be judged by the patient's consultant to have resulted in life-threatening consequences to the patient, or the patient's death. (Delays in recognition of deterioration as a consequence of system failure which do not meet these criteria will be separately reported).

2. Failure of the integrated electronic "track-and-trigger" system to correctly calculate the summary score leading to delayed escalation. The delay must be judged by the patient's consultant to have resulted in life-threatening consequences to the patient, or the patient's death. (Delays in recognition of deterioration as a consequence of system failure which do not meet these criteria will be separately reported).

3. Failure of the integrated electronic "track-and-trigger" system to correctly display the appropriate observation or clinical escalation, leading to delayed escalation. The delay must be judged by the patient's consultant to have resulted in life-threatening consequences to the patient, or the patient's death.

(Delays in recognition of deterioration as a consequence of system failure which do not meet these criteria will be separately reported).

Any other events associated with the integrated electronic “track-and-trigger” system which are felt to have been deleterious to the patient will be separately reported, but will not be classified as a Serious Adverse Event unless deemed to meet published criteria by the Principal Investigator.

Annual Reports: In addition to the above reporting the Chief Investigator will submit once a year, throughout the trial, or on request a progress/safety report to the REC and R&D.

Statistics

Number of participants: 2000 patients will be enrolled into the study over an 8 month period to achieve equal number of patients in the treatment and control groups.

Analysis of endpoints: The primary endpoint will be assessed using survival analysis. A significance level of p=0.05 will be taken as indicating a difference between groups. Analyses of proportion will be undertaken using χ^2 test or Fisher’s exact test, as appropriate.

Procedure for Accounting for Missing, Unused, and Spurious Data: All data will be double entered into an SQL database by two trial nurses. Missing/discordant data fields will be automatically flagged to allow resolution.

Procedures for Reporting any Deviation(s) from the Original Statistical Plan: The trial will be registered (EUDRACT). Any change in the statistical plan will be reported both to EUDRACT and in the final report.

Inclusion in Analysis: The outcomes of all patients allocated to a study arm will be analysed on an intention-to-treat basis (primary outcome). The outcomes of those who actually received the intervention (electronic monitoring) will also be analysed.

Ethics

The National Information Governance Board has been successfully approached for support under section 251 of the NHS act 2006 to process patient identifiable information without consent. The reasoning was as follows:

1. No additional procedure or observation will occur to the patients involved in the study.
2. The physiological data required is already collected and recorded on paper as part of the patient record.
3. Electronic “track-and-trigger” data entry is already part of standard practice in some United Kingdom hospitals.

4. To optimally test the intervention, patients need to be monitored immediately from their admission to the ward and not wait until a trial nurse becomes available.

5. The effect of the intervention across complete trial zones, and complete wards cannot be assessed without the inclusion of all patients within the zone/ward.

Declaration of Helsinki: the Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

ICH Guidelines for Good Clinical Practice: the Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

Approvals: the protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), regulatory authorities (MHRA in the UK), and host institution(s) for written approval. The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

Participant confidentiality: All members of the research team will have confidentiality clauses in their contracts and will be well informed of the NHS code of confidentiality and the Caldicott principles. The trial staff will ensure that the participants' anonymity is maintained. Patients will be assigned a trial number through a case report file (CRF). All patient data will be connected to this number when stored electronically. Patient names or other identifiers will not be recorded electronically. All trial paperwork will be held in a locked file behind two locked doors. The trial computer, on which analysis of the anonymised data will take place will be

password-protected and kept in a research-specific area behind two locked doors. The electronic “Track-and-Trigger” system will be protected by the Oxford Radcliffe NHS Trust electronic security system (see network security policy v2). The study will comply with the Data Protection Act 1998 which requires data to be anonymised as soon as it is practical to do so.

Steering Committee

The trial is guided by a steering committee. The steering committee, in the development of this protocol and throughout the trial will take responsibility for:

1. The need to change the protocol for any reason
2. Monitoring and supervising the progress of the trial

Data monitoring

A data monitoring committee will be convened, consisting of experts in the field and the trial statistician. The safety of the trial will be reviewed by an external data monitoring committee after 200 patients have received the intervention, and after each subsequent 200 patients. Dr Jacqueline Birks will provide data and statistical guidance to the committee.

The data monitoring committee will be responsible for stopping the trial in the event of a substantial mortality effect being found.

The study may be monitored or audited by representatives of the ORH Research and development department for compliance with the Department of Health Research Governance Framework for Health and Social Care 2005.

Direct access to data/source documents

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

Trial funding

The trial will be funded by the Biomedical Research Council. At the time of print this totalled £83,417

Insurance for the VitalPAC products will be provided by The Learning Clinic. VitalPAC is CE marked and registered as a Class I medical device. They will provide employers liability cover up to £10m and public/product liability and professional indemnity cover up to £5m.

NHS bodies are legally liable for the negligent acts and omissions of their employees. If a patient is harmed whilst taking part in a clinical trial as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. The Oxford Radcliffe NHS Trust, therefore, cannot agree in advance to pay compensation in

these circumstances. In exceptional circumstances an ex-gratia payment may be offered.

Publication Policy

The lead author for all papers will be Dr Peter Watkinson**.** The authors have no vested interest in the results, which will be published regardless of outcome, in peer-reviewed journals. The final version will be agreed by the steering committee before submission.

Study Personnel

Principal Investigator: Dr Peter Watkinson

Co-investigators: Dr James Price, Professor Lionel Tarassenko, Dr Lauren Bailey, Sarah Webb.

Research Nurses: Jessica Cottrell

Trial Steering Committee: Dr Peter Watkinson, Dr David Clifton, Professor Lionel Tarassenko, Simon Noel, Sarah Webb, Dr Jacqueline Birks

Statistician: Dr Jacqueline Birks

References

1. Cretikos M, Chen J, et al. The objective medical emergency team activation criteria: A case-control study. Resuscitation 2007;73:62-72

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7. The MERIT study investigators. Introduction of the medical emergency team (MET) system: a cluster-randomised controlled trial. The Lancet 2005; 365 (9447):2091-2097

8. Smith AF, Oakley RJ. Incidence and significance of errors in a patient 'track and trigger' system during an epidemic of Legionnaires' disease: retrospective case note analysis. Anaesthesia 2006; 61: 222–8

9. Prytherch D, Smith GB, et al. Calculating early warning scores - a classroom comparison of pen and paper and hand-held computer methods. Resuscitation 2006; 70: 173–8

10. Subbe CP, Gao H, Harrison DA. Reproducibility of physiological track-and-trigger warning systems for identifying at-risk patients on the ward. Intensive Care Med 2007; 33: 619–24

Appendix 1: Oxford Radcliffe SADE form

SAE No (for office use only): ☐☐☐

Oxford Radcliffe Hospitals NHS
NHS Trust

Serious Adverse Events Reporting Form

No of Pages including attachments ☐☐☐

R&D Department, Room 13, Manor House, The John Radcliffe Hospital
Oxford, OX3 9DZ
Tel: 01865 222143 Fax: 01865 222648

- *Please complete by filling in the grey boxes electronically, printing out and signing and then fax within **one working day** of awareness to **01865 222648**. Please note that there are drop down boxes with options you can select.*
- *Refer to the SAE Reporting Form Completion Guidelines for guidance. If you would like to fill it out by hand, please refer to the completion guidelines for options listed in the drop down boxes.*
- *The original should be filed in the Trial Master file. Please ensure that the event is recorded in patient hospital notes and case report form where applicable.*
- *For confidentiality reasons please **DO NOT** save the electronic version of the completed form.*

1. Summary

Report type
Criteria for definition of SAE
Chief Investigator's name
Study number
Date of SAE awareness
Start date of SAE
Stop date of SAE or state if ongoing
Keywords *(SAE Diagnosis or main symptoms)*
Subject initials
Subject ID

2. Narrative

Please provide an account of the event, similar in format to that of a discharge summary. Mention any relevant lab data or diagnostic tests.

3. Evaluation of Event

Outcome
Severity
Action taken with study drug
Other action:
Withdrawn due to SAE? ***Yes/No***

4. Subject Details

Subject DOB
Age
Sex
Height
Weight

SAE No (for office use only): ☐☐☐

5. Suspect Drug(s)

Suspect Drug 1

Drug
Route
Dose details
Indication
Batch number
Expiry date
Start date of drug
Stop date or state if ongoing
If stopped/ lowered dose, did the event resolve after this? ***Yes/No/NA***
If reintroduced did event reappear? ***Yes/No/NA***

Suspect Drug 2 ***(if applicable)***

Drug
Route
Dose details
Indication
Batch number
Expiry date
Start date of drug
Stop date or state if ongoing
If stopped/ lowered dose, did the event resolve after this? ***Yes/No/NA***
If reintroduced did event reappear? ***Yes/No/NA***

Attach supplemental pages if there are more than 2 suspect drugs

6. Death Details ***(if patient died)***

Date of death
Cause of death
Cause of death obtained from

7. Relevant Medical/Surgical History

No. of medical/surgical history CRF pages attached:
If no CRF pages attached, describe relevant medical history

8. Concomitant Medication

No of concomitant medication CRF pages attached
If no CRF pages attached, describe details of conc meds

9. Study Details

Study title
Protocol version or date
Eudract number
Study Design
If blinded, blind broken? ***Yes/No/NA***
(Consider unblinding if SUSAR)
Is there a trial specific Safety Monitoring Committee for this study? ***Yes/No***

SAE No (for office use only): ☐☐☐

10. Principal Investigator Details ***(site specific, and if different from Chief Investigator)***

Name of PI
Address
Telephone
Fax
Email address

Signature of reporter

Date of signing
Full name
Designation
Contact telephone
Email address

This section is to be completed by a medically qualified investigator

11. Causality and Expectedness

Evaluation of causal relationship with suspect drug 1

Evaluation of causal relationship with suspect drug 2 (if applicable)

If the causal relationship is not clear, please indicate how you came to your decision.

If causal relationship is *"related"*, was this event "*expected"* based on the investigators brochure, summary of product characteristics and/or protocol i.e. is it a Suspected Unexpected Serious Adverse Event (SUSAR) and requires expedited reporting to the Medicine and Healthcare Products Regulatory Agency and Ethics Committee?
Yes/No

Signature of Medically Qualified Investigator

Date of signing
Full name
Designation
Contact telephone
Email address

----------END OF DOCUMENT----------

Appendix 2: NPSA Serious Adverse Event Form

National Patient Safety Agency

National Research Ethics Service

REPORT OF SERIOUS ADVERSE EVENT (SAE)

(For all studies except clinical trials of investigational medicinal products)

The Chief Investigator should report any SAE that is both related to the research procedures and is unexpected. Send the report to the Research Ethics Committee that gave a favourable opinion of the research within 15 days of the CI becoming aware of the event. For further guidance see: *http://www.nres.npsa.nhs.uk/applicants/review/after/safety.htm*.

1. Details of Chief Investigator

Name:	
Address:	
Telephone:	
Email:	
Fax:	

2. Details of study

Full title of study:	
Name of main REC:	

Main REC reference number:	
Research sponsor:	
Sponsor's reference for this report: (if applicable)	

3. Type of event

Please categorise this event, ticking all appropriate options:

Death ☐	Life threatening ☐	Hospitalisation or prolongation of existing hospitalization ☐
Persistent or significant disability or incapacity ☐	Congenital anomaly or birth defect ☐	Other ☐

4. Circumstances of event

Date of SAE:	
Location:	
Describe the circumstances of the event: *(Attach copy of detailed report if necessary)*	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Declaration

Signature of Chief Investigator:	
Print name:	
Date of submission:	

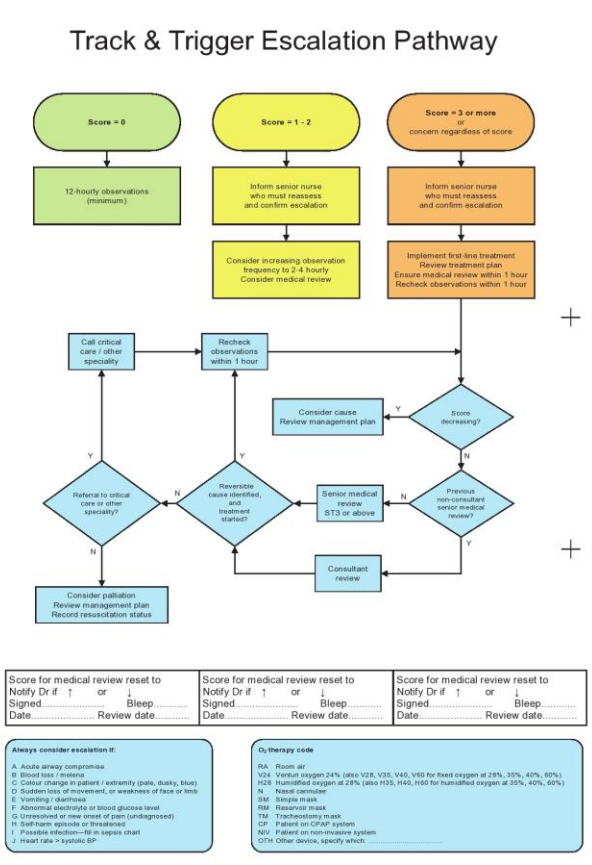
6. Acknowledgement of receipt by main REC (please insert name):

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back to Chief Investigator (or other person submitting report)
Copy to be kept for information by main REC.

Appendix 3: Track and Trigger algorithm



Appendix 4: Serious event definitions

Adverse Event (AE):

An AE or adverse event is:

Any untoward medical occurrence in a patient or clinical investigation participants caused by the device under investigation, which does not necessarily have to have a causal relationship with Device.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of the device, whether or not considered related to the device.

Adverse Device Effect (ADE)

All untoward and unintended responses to the medical device.

The phrase "responses to a medical device" means that a causal relationship between the device under investigation and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the device qualifies as a device effect.

This also includes any event resulting from insufficiencies or inadequacies in the instruction for use or deployment of the device and includes any event that is a result of a user error.

Serious Adverse Event (SAE):

SAE is an adverse event that

- ♣ Led to death
- ♣ Led to foetal distress, foetal death or congenital abnormality or birth defect.
- ♣ Led to serious deterioration in the health of the subject that
    - Resulted in a life-threatening illness or injury
      NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
    - Resulted in a permanent impairment of a body structure or a body function

- Required in-patient hospitalisation or prolongation of existing hospitalisation
- Resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
- Other important medical events*
  *Other events that may not result in death, are not life threatening, or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

Serious Adverse Device Effects (SADE):

A serious adverse device effect (SADE) is any untoward medical occurrence seen in a patient that can be attributed wholly or partly to the device which resulted in any of the characteristics or led to a characteristics of a Serious adverse event.

SADE is also any event that may have led to these consequences if suitable action had not been taken or intervention had not been made or if circumstances has been less opportune.

All cases judged by either the reporting medically qualified professional or the sponsor.

Unanticipated Adverse Device Effect (UADE):

Any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of the subject.