TARDIS – Working Practice Document – No: 032 RISK ASSESSMENT

Title	**Safety and efficacy of Clopidogrel when added to Aspirin and Dipyridamole in high risk patients with recent ischaemic stroke: a randomised controlled trial.** **Short Title: TARDIS (Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke)**		
EUDRACT No:	2007-006749-42	**MREC Reference Number:**	08/H1102/112
Sponsor:	The University of Nottingham	**Funding body:**	The British Heart Foundation

Hazard Category	**Hazard Description**	**Impact if it Happens** 1 – Low 2 – Moderate 3 – Significant 4 – Severe 5 – Catastrophic	**Likelihood of it Occurring** 1 – Remote 2 – Unlikely 3 – Possible 4 – Likely 5 - Certain	**Risk** (= Impact X Likelihood)	**Describe what control measures will be put in place to reduce the risk(s) to the lowest possible level.**
Trial Design	Insufficient non clinical or prior studies	2	1	2	Protocol summarises review of the available literature. We have performed previous laboratory and clinical trials.
	Unclear objectives/hypothesis/endpoints	3	1	3	Trial protocol clearly elucidates the trial objectives and endpoints.
	Lack of independent peer review	3	1	3	Peer reviewed during the funding process by the Stroke Association.
	Lack of expert input	3	1	3	Multiple experts in stroke care and antiplatelet therapy on the trial steering and data monitoring committee.
	Inadequate randomisation procedure	2	1	2	Computer randomisation using key prognostic variables for stratification and minimisation.
Participant Rights	Inadequate time for participant to reflect on taking part in the study	2	2	4	Participants and relatives will be given around 2 hours to decide, as is done in most acute stroke trials. Ethical approval obtained for consenting procedures.
	Coercion into participation or exclusion	3	1	3	Only GCP trained researchers will be allowed to recruit participants.
	Informed consent not taken	4	1	4	GCP training. Audit of consent procedures.
	Inability to withdraw from the study if participant desires	2	1	2	Patients will be informed that participation is voluntary and they are free to withdraw at any time without giving any reason.

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	Unauthorised disclosure of personal information as a result of taking part in the trial	4	1	4	Minimise staff having access to confidential information. To follow REC approved data protection procedures. Training and awareness. Secure database and server protection.
	Participant wishing to complain about any aspect of the study but unable to do so	3	1	3	Participants directed to hospital complaints systems. Contact details will be clearly listed in the information sheets.
	Failure to obtain accurate information on a participant's health status	2	1	2	Computerised data entry system flags to collect information on case report forms.
Participant Safety	Lack of management of SAEs	4	1	4	Patients instructed about notification of adverse events. System for expedited review will be in place-Trial protocol. Ethics approved system of reporting SAEs.
	Major bleeding events with triple antiplatelet therapy	4	2	8	Clear notification systems for event recording and reporting. Six monthly safety analysis by data monitoring committee. Interim analysis at the end of start up phase will assess safety.
	SUSAR	4	1	4	Expedited assessment by Chief Investigator. Urgent reporting to regulatory authorities. Protocol amendments if felt necessary by the regulatory authorities.
	Error in labelling of IMP	2	1	2	Double-check the labelling by pharmacy and research nurses.
	Error in dispensing of IMP	3	1	3	Hospital system checks will be used to prevent error.
	Failure to exclude pregnancy	3	1	3	Web based randomisation to flag all inclusion and exclusion criteria Patients less than 50 years will be excluded. If participant becomes pregnant after inclusion in the trial, adverse events will be closely monitored.
	Harm caused by collection of blood samples	1	1	1	Trained personnel to bleed patients.
	Needle stick injuries to clinical staff	3	1	3	Trained personnel. Hospital systems will be used for further management.

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Trial Completion	Failure to recruit to targets or complete the trial	3	3	9	Statistical input in design and power calculation. Trial divided into start-up and main phase. Start up phase interim analysis will analyse feasibility and safety.
	Loss of participants to follow up	2	3	6	Exclusion of participants where follow up is unlikely. Details of more than one next of kin to be collected. Final follow to be done by the trial-coordinating centre. Involvement of recruiting centre if patient cannot be contacted.
	Non robust systems for data collection	3	1	3	Web based system will be used for data collection. Database will be stored on secured University of Nottingham servers. Audit of source documents. GCP trained investigators.
	Trial committee failure to act on recommendations by the DMC	3	1	3	Stopping rules for the trial. Safety monitoring and Sponsor overview of the trial.
	Insufficient lack of monitoring	3	2	6	Sites visits by Trial Coordinating Centre personnel.
Trial Data Reliability	Lack of study power	3	1	3	Statistical input to design and power calculations.
	Violation of eligibility criteria	2	2	4	Trial management protocol. Web based system flags inclusion criteria. Treating patients as per intention to treat and ensuring patient safety. GCP trained investigators.
	Inadequate randomisation procedure	3	1	3	Computer based randomisation. To use manual randomisation only when systems/web servers are down.
	Samples incorrectly stored/transported	2	1	2	Coordinating centre will liaise with individual sites regarding transport. Audit of storage systems on site visit.
	Incorrect assessment of outcome measures	4	1	4	Simple outcome measures will be used. Adequate training provided at site visits and investigator meetings. Day 90 outcome will be performed by a limited number of trained researchers at the Coordinating Centre for all patients in UK.
	Incomplete or inaccurate recording of outcome data	3	1	3	Adequate training and resources to be provided. Validations checks in web based systems to avoid errors.

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	Lack of database backup and archiving	3	1	3	Use secure University of Nottingham servers for data storage and archiving. Servers are backed up off site daily.
	Other non adherence to study protocol	2	2	4	Trial protocol/ SOP/ Working practice documents will outline procedures to be followed.

Impact	Likelihood				
	1 Remote	2 Unlikely	3 Possible	4 Likely	5 Certain
1 Low	1	2	3	4	5
2 Moderate	2	4	6	8	10
3 Significant	3	6	9	12	15
4 Severe	4	8	12	16	20
5 Catastrophic	5	10	15	20	25

Risk Management Key

Action and time scales
Immediate action must be taken to manage the risk. Control measures should be put in place which will have the effect of reducing the impact of an event or the likelihood of an event occurring. A number of control measures may be required.
Significant resources may have to be allocated to reduce the risk. Where the risk involves work in progress urgent action should be taken.
Efforts should be made to reduce the risk, but the costs of prevention should be carefully measured and weighed against the impact of the event. Establish more precisely the likelihood of harm as a basis for determining the need for improved control measures.
On or below this level a risk is acceptable. Existing controls should be monitored and adjusted. No further action or additional costs are required. Consideration may be given to a more cost-effective solution or improvement that imposes no additional cost burden.
Acceptable risk. No further action or additional controls are required. Risks at this level should be monitored, and reassessed at appropriate intervals.

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date approved	Details of significant changes
1.0	1 June 2010	Assessed by Trial Steering Committee members, minor changes.
1.1	19 August 2010	Initial released version