CTRC Approach

• Risk assessment process is undertaken for each study adopted by the CTRC involving recruitment of human participants
  • All CTIMPs & non-CTIMPs
  • Any exceptions discussed by CTRC operational team (e.g. Feasibility study/Delphi consultation)

• Undertaken as early as possible during study set-up

• Obtain overall risk score (high, medium, low), however, the process is used to:
  • Identify potential vulnerabilities in trial design & methodology
  • Form a common understanding by all stakeholders on trial risks
  • Facilitate a risk-proportionate approach to trial activities
    • Development of the trial management and monitoring strategies
    • Regulatory requirements
Responsibilities

• Authorship
  • Relevant CTRC staff including supervising staff (e.g. trial management, data management, information systems and statistics)
  • Chief Investigator
  • Sponsor representative
  • Any additional expertise required

• Reviewed by CTRC Operational Team

• Approval
  • Sponsor
  • Chief Investigator
  • CTRC Director
Review

- Risk Assessment revisited when change in:
  - Protocol procedures
  - Monitoring plan
  - Data management plan
  - Case report forms
  - Benefit:risk considerations identified in developmental safety update report
  - Reference safety information
  - Or if circumstances indicate that re-assessment is required
3 main hazard areas considered

- Patient hazards
  - Safety - Intervention*, Experience of clinical team, Protocol procedures (additional tests)
  - Rights - Consent procedures, Confidentiality

- Study hazards – Completion of trial, Reliability of results

- Organisational hazards – Information systems, Intellectual property, Liability, Reputation, Service impact

Hazard: anything that could cause harm
Risk: probability that harm will be caused by the hazard

*3 level categorisation (type A, B or C) doesn't constitute as full risk assessment but has implications
### Format

Based on Clinical Trials Toolkit Assessment of Risk document

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Management Strategies</th>
<th>Impact if it happens</th>
<th>Likelihood of it happening</th>
<th>Risk IxL</th>
<th>Central Monitoring</th>
<th>Monitoring At Sites</th>
</tr>
</thead>
</table>

- Includes a description of why it is a hazard
- Management strategies proposed to minimise the hazards
- Score & justification (level of harm caused by specific hazard if was to occur)
- Score and justification (probability of each specific hazard occurring)

- Scoring takes into account management strategies
- Each specific hazard has own score

- Central monitoring proposed
- Typically for CTRC trials monitoring at sites undertaken if triggered by central monitoring findings

[www.ct-toolkit.ac.uk/_db/_documents/MPTrials2.pdf](http://www.ct-toolkit.ac.uk/_db/_documents/MPTrials2.pdf)
Challenges

- Time consuming
- Subjective
- Achieving consistency across projects

Many trials undertaken by the CTRC:
- Involve similar hazards & risks
- Require similar management and monitoring strategies

Solution

- Made assumptions about a ‘generic’ trial
- Developed a ‘generic’ risk assessment based on assumptions
- Assess & document how each trial deviates from the ‘generic’ assumptions & risk assessment
Development

- Reviewed 4 recently conducted CTRC risk assessments
- Developed with CTRC safety working group
- Piloted in 2 CTIMPs
  - 1 x phase II (type B intervention)
  - 1 x phase IV (type A intervention)
- Piloting in cohort study with many sub-studies

Findings

- Much quicker
- Easier to identify risks unique to each trial/study
New Process - Generic RA

- Example of assumptions made: multi centre phase III, type A intervention, low volume of safety reporting expected, web-based randomisation, MACRO database, primary outcome data collected as part of routine care, oversight committees in place...

- Each specific hazard in the generic RA is given a hazard number to enable cross-referencing

<table>
<thead>
<tr>
<th>Main Hazard Area Example</th>
<th>Generic Hazard Example</th>
<th>Specific Hazard Examples</th>
</tr>
</thead>
</table>
| 1. Patient Hazards (Rights and Safety) | 1.2. Inexperienced Clinical Team | 1.2.1 Incorrect advice given  
1.2.2 Inclusion of ineligible patients  
1.2.3 Deviation from study assessments  
1.2.4 Incomplete/incorrect data collection  
1.2.5 Delay in data return |
New Process – Trial Specific

• Trial specific RA documents for each hazard in the generic RA if the hazard:
  • Is not applicable
  • Is applicable & requires:
    • No changes to the text or scores;
    • Variation to score(s) – details provided
    • Change to or additional management/monitoring activities NOT affecting score – details provided

• Any additional risks are documented
• ‘Points to consider’ are provided under each grouping of hazards for guidance
Future steps

- Finalise Risk Assessment SOP
- Scores currently calculated separately in Excel

Suggestions to incorporate all into Excel or include a Macro in Word to calculate the scores

Possible solutions

Considerations:
- Changing generic risk assessment into MCR/DoH/MHRA ‘Risk adapted approaches’ template
- Development of a ‘generic’ monitoring plan