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|  | **Site name** |  | **Safety assessment and reporting guideline** |
| Trial number |  | Sponsor |  |
| **Process for elicitation and management of adverse event (AE) reports:**  1. AEs will be assessed from screening throughout the trial  2. AEs will be recorded whether spontaneously reported by participants, observed by the trial staff or elicited by general questioning  3. AEs will be elicited by indirect questioning (no leading questions) during study days, with such questions as “How are you?” or “Is anything bothering you?”  4. Abnormal findings will be carefully considered and any participant who, in the judgment of the investigator may not safely complete the study, will be withdrawn  5 AEs will be followed up until resolution or agreement between the PI and the Sponsor Medical Monitor  6. SAEs, non-serious unexpected reactions and changes in nature, severity or frequency of risk factors, and new information impacting the risk/benefit profile – see overleaf for **Process flow for management of SAE reports** | | | |

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| **Process flow for management of SAE reports**  **Site responsibilities**  Investigator submits SAE form to sponsor within 24 hours of knowledge:   * Sponsor Pharmacovigilance dept. contact details: * Sponsor Medical Monitor contact details:   NB a life-threatening or fatal event will also be communicated within 2 hours of knowledge by phone  A preliminary causality assessment is performed by the investigator  **Medical monitor receipt**  (Within 1 working day of initial receipt)  Assess if life-threatening/fatal SUSAR  Assess whether there is a reason to stop study  Communicates with Sponsor as such  **Pharmacovigilance dept. receipt**  (Within 1 working day of initial receipt)  Confirm receipt of SAE form to site  Check whether case is valid  **Pharmacovigilance dept. initial assessment**  (Within 1 working day of initial receipt)  Triage case, MedDRA coding, case and causality assessment  Send initial assessment form to Medical Monitor  **Pharmacovigilance dept/QC**  (7-day report by day 4, 15-day reports by day 6, otherwise by day 6)  Data entry/QC/generation of CIOMS 1 report sent to Medical Monitor for review and approval  **Medical assessment**  (7-day report - within 1 working day, otherwise 3)  Confirmation of case assessment and sponsor causality assessment  **Medical monitor final review**  (7-day report by day 4, otherwise by day 8)  Review and comment on CIOMS 1 - returned to sponsor pharmacovigilance dept  **Send request for case follow up to investigator**  **Case tracking and filing**  **Sponsor case finalised**  Sponsor sends report to regulatory authorities by day 6 for life-threatening/fatal SUSARs, by day 13 for all other expedited SUSARs (with copy to investigator)  Sponsor sends CIOMS form to investigator for submission to HREC by day 6 (7-day reports) or 13 (15-day reports)  **Site submission to HREC**  Site sends CIOMS form to REC by day 7 or 15 as relevant  **EVENTS OTHER THAN SUSARs**  **Sponsor sends to site 6 monthly for submission to regulatory authority/HREC:**  - List of all SAEs worldwide  - List of non-serious unexpected reactions worldwide  **Site submission to DSMB/other necessary notifications**  **Site sends CIOMS to DSMB according to Charter**:  - Ad-hoc meetings for specific safety concerns, otherwise, at routine meetings  **Site sends to regulatory authority and HREC:**  - Notification of change in nature, severity or frequency of risk factors (within 15 days and in 6 monthly reports)  - New information impacting risk/benefit profile (3 days and 6 monthly reports) |