Supplementary material

Table S1. List of 114 potential failure modes by core and its sub-process

Process	Sub-process	Potential Failure Mode
obtaining informed consent	Initial Informed Consent	Subject information sheet and the informed consent form have not been received from sponsor on time.
obtaining informed consent	Initial Informed Consent	Clinical research coordinators do not check whether the institutional review board approval date on the informed consent form is most up-to-date. Instead, they use an outdated version of subject information sheet and the informed consent form.
obtaining informed consent	Initial Informed Consent	Screening of two or more studies are in progress at the same time.
obtaining informed consent	Initial Informed Consent	Subject information sheet and the informed consent is not prepared.
obtaining informed consent	Initial Informed Consent	The screening clinical research coordinator does not provide subjects with detailed information about the visit schedule.
obtaining informed consent	Initial Informed Consent	The investigator provides subjects with partial information of study.
obtaining informed consent	Initial Informed Consent	Explanation of the clinical trial to subjects using medical jargons.
obtaining informed consent	Initial Informed Consent	Investigators do not ask if a clinical trial participant had any additional questions about the study before they sign the informed consent form at the first time. The investigator do not document issues discussed during the informed-consent obtaining session. Subjects cannot or do not ask a question.
obtaining informed consent	Initial Informed Consent	Clinical trial participants do not take sufficient time to decide whether to participate in the study before they sign the informed consent form.
obtaining informed consent	Initial Informed Consent	Omission of subjects' own handwritten signature or misspelling of date.
obtaining informed consent	Initial Informed Consent	Omission of investigator's own handwritten signature or misspelling of date. Signature between each enrollment log and informed consent form are different.
obtaining informed consent	Initial Informed Consent	The screening clinical research coordinator did no check omission of signature and misspelling of date on informed consent form written from investigators or subjects.

obtaining informed consent	Initial Informed Consent	The screening clinical research coordinator did not hand out the copy of the subject information sheet and the informed consent form to subjects.
obtaining informed consent	Initial Informed Consent	The screening clinical research coordinator did not file original subject information sheet and signed informed consent form in the study binder.
obtaining informed consent	Initial Informed Consent	The screening clinical research coordinator did not double-check on overall the informed consent form.
obtaining informed consent	Initial Informed Consent	No documentation of completed informed consent process in source document/electronic medical record.
obtaining informed consent	Re-consenting	Subject information sheet and the informed consent form have not been received from sponsor at re-consenting.
obtaining informed consent	Re-consenting	Because clinical research coordinators use an outdated version of the informed consent form, clinical trial participants do not get the most up-to-date information about the study and study drug in a timely manner.
obtaining informed consent	Re-consenting	Failure to attend study team education session for re-consenting
obtaining informed consent	Re-consenting	Outdated version of subject information sheet and informed consent form is not discarded.
obtaining informed consent	Re-consenting	Not checking subject's schedule for visit.
obtaining informed consent	Re-consenting	Subject information sheet and informed consent form is not prepared
obtaining informed consent	Re-consenting	The investigator didn't explain amended part of the protocol to study subjects.
obtaining informed consent	Re-consenting	Investigators do not ask if a clinical trial participant had any additional questions about the study before they sign the ICF at re-consenting. The investigator do not document issues discussed during the informed-consent obtaining session. Subjects cannot or do not ask a question.
obtaining informed consent	Re-consenting	Omission of subjects' own handwritten signature or misspelling of date at re-consenting.
obtaining informed consent	Re-consenting	Omission of investigator's own handwritten signature or misspelling of date at re-consenting. Signature between each enrollment log and informed consent form are different.
obtaining informed consent	Re-consenting	No records of source documentation regards to subject's withdraw of the study.
obtaining informed consent	Re-consenting	The screening clinical research coordinator did not hand out the copy of the subject information sheet and the informed consent form to subjects at re-consenting.
obtaining informed consent	Re-consenting	The screening clinical research coordinator did not hand out the copy of the subject information sheet and the informed consent form to subjects after re-consenting.
obtaining informed consent	Re-consenting	The screening clinical research coordinator did not file original subject information sheet and signed informed consent form in the study binder after re-consenting.

obtaining informed consent	Re-consenting	The screening clinical research coordinator did not double-check overall process after re-consenting.
obtaining informed consent	Re-consenting	No documentation of completed re-consenting process in source document/electronic medical record.
site personnel training	Maintenance	Lists of required qualification/training/experience of site personnel are missing.
site personnel training	Training - initial	New staff do not complete the assigned training and education within the pre-specified timeline. Training for new staff are inconsistent or inadequate.
site personnel training	Training - study specific	Incomplete or inadequate study-specific training.
site personnel training	Training - study specific	Absence of training which is related to the study.
site personnel training	Training - ongoing	Compulsory trainings are not maintained.
site personnel training	Training - on the job training	Fail to maintain continuous training.
site personnel training	Documentation Requirements [Training Folder]	The training folder in the site master file is not updated in a timely manner. Incomplete or inadequate training records are found in the site master file.
site personnel training	Maintenance	The annual training plan is not evaluated regularly for its appropriateness. Additional training plans do not incorporate the results of the evaluation.
screening and patient identification/enrollment	Screening Preparation	Identifying some of site staffs who were not complete training.
screening and patient identification/enrollment	Screening Preparation	Failure to prepare screening setting completely.
screening and patient identification/enrollment	Screening Preparation	Failure to prepare the expected list of subjects for screening visit.
screening and patient identification/enrollment	Screening Preparation	Delay or omission to notify screening schedule.
screening and patient identification/enrollment	Screening Preparation	Failure to prepare screening kit.
screening and patient identification/enrollment	Screening Preparation	The study subject does not arrive on time.
screening and patient identification/enrollment	Screening Preparation	Failure to identify subjects without ID.
screening and patient identification/enrollment	Screening	The screening clinical research coordinator did not check whether the informed consent form was obtained.
screening and patient identification/enrollment	Screening	Some part of the screening sheet is not completed.

screening and patient identification/enrollment	Screening	Some physical examination is missed/not completed.
screening and patient identification/enrollment	Screening	Omission of physical examination records and the detailed medical history records for the study subject.
screening and patient identification/enrollment	Screening	A copy of informed consent form and other information about study did not provided to subjects. Absence of records about providing copy of informed consent form and other information about study.
screening and patient identification/enrollment	Screening	The investigator did not review screening result.
screening and patient identification/enrollment	Screening	Because the screening clinical research coordinator is not able to recognize needs for re-examination, re-examination is not done.
screening and patient identification/enrollment	Screening	Because the screening clinical research coordinator does not check subject's eligibility, screening results were not informed to the study subject.
screening and patient identification/enrollment	Screening	The screening log is uncompleted.
document management including source documents and essential documents	Source Documentation	The source document is not specified.
document management including source documents and essential documents	Source Documentation	The worksheet/book is not developed based on the protocol.
document management including source documents and essential documents	Source Documentation	Use of the worksheet/book without internal/external review.
document management including source documents and essential documents	Source Documentation	Accesses for the source documents are restricted for the clinical research associate.
document management including source documents and essential documents	Source Documentation	Delay of the worksheet/book modification. The worksheets/books are not separately filed by their version.
document management including source documents and essential documents	Source Documentation	Missing items recorded in worksheet/book for study procedure Omission in sign.

document management including source documents and essential documents	Source Documentation	Source documents are not reviewed or signed in a timely manner.
document management including source documents and essential documents	Source Documentation	The clinical research form has written without review of the source documents.
document management including source documents and essential documents	Source Documentation	Missing filing of parts of the source documents.
document management including source documents and essential documents	Site Master File	No delegation of the staff managing the site master file.
document management including source documents and essential documents	Site Master File	Inappropriate site master file is developed.
document management including source documents and essential documents	Site Master File	Missing review for documents before filing.
document management including source documents and essential documents	Site Master File	Required essential documents are not filed appropriately. Filing is done without standards or a proper archiving system.
document management including source documents and essential documents	Site Master File	Missing, incomplete, or outdated essential documents in the site master file. Essential documents are not separately filed by their version.
document management including source documents and essential documents	Site Master File	Essential documents are not checked for completeness.
document management including source	Archiving	The document archiving room is unavailable. The procedures of document archiving are absent

documents and essential documents		
document management including source documents and essential documents	Archiving	No delegation of the staff managing the document archiving. The records of document archiving are absent
document management including source documents and essential documents	Archiving	Failure to transfer the documents to staff managing the document archiving.
document management including source documents and essential documents	Archiving	Absence of records for the transferred the study document.
document management including source documents and essential documents	Archiving	The document archiving request form is not reviewed.
document management including source documents and essential documents	Archiving	The archived period of the study documents are violated the contract, protocol and/or KGCP.
document management including source documents and essential documents	Archiving	Failure to aware the end of document retention period. Improper management of the archiving expired documents.
document management including source documents and essential documents	Archiving	Absence of records for action after the document retention period ends. Missing notice the records to a principal investigator.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Training for safety management such as reporting serious adverse event and suspected unexpected serious adverse reaction is not completed. Absence of training records for safety management such as reporting serious adverse event and suspected unexpected serious adverse reaction.
safety management such as reporting serious adverse	SAE Process	Training of voluntary adverse event reporting is omitted.

event (SAE) and suspected unexpected serious adverse reaction (SUSARs)		
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Failure to recognize and record adverse events.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Omission or delay to identify whether adverse events is serious adverse event
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Omission or Delay to check the causality of adverse events. Staff who is not delegated as investigator judged causality of adverse events. Improper action on the serious adverse event.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Failure to check serious adverse event information from source documents.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Serious adverse event is not reported within 24 hours after recognition.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious	SAE Process	Omission to discuss about serious adverse event and solve queries with a sponsor.

adverse reaction (SUSARs)		
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Serious adverse event not reported to the Institutional Review Board.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Improper records for serious adverse event in a case report form.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Reporting additional supporting documentations for serious adverse event to the sponsor is omitted and delayed.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Failure to document reasons why the subjects do not offer additional information for serious adverse event
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	No medical follow-up observation and/or follow-up actions.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Failure to document additional information for serious adverse event from the subject.

safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Reporting for additional information for serious adverse event is delayed and case report form for additional information is not finalized.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	Omission to discuss about additional information for serious adverse event and solve queries with a sponsor.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	A delay in or no reporting of follow up report to Institutional Review Board.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	SAE Process	The serious adverse event form is not archived in site master file.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	Suspected unexpected serious adverse reaction report is not delivered. Suspected unexpected serious adverse reaction report is not reviewed.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	Lack of communication of suspected unexpected serious adverse reaction report with appropriate site staffs.
safety management such as reporting serious adverse	Safety Updates	Additional information for suspected unexpected serious adverse reaction are not reported to institutional review board.

event (SAE) and suspected unexpected serious adverse reaction (SUSARs)		
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	The study subject will not receive additional safety information.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	Absence of a documentation of provided safety information.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	Failure to record documents for withdrawal of consent/study.
safety management such as reporting serious adverse event (SAE) and suspected unexpected serious adverse reaction (SUSARs)	Safety Updates	Reports for suspected unexpected serious adverse reaction and/or institutional review board’s approval for that are not archived in site master file.
inspection readiness	Before	Absence of standard operating procedure for inspection. Absence of review and education of SOP for inspection.
inspection readiness	Before	Failure to prepare the place for inspection
inspection readiness	Before	Schedule for inspection is not informed to site staffs.
inspection readiness	Before	Failure to prepare of requested documents.
inspection readiness	Before	Failure to check documents missing
inspection readiness	During	Absence of the investigators in intro-meeting unexpectedly.
inspection readiness	During	Inappropriate response for inspector's request.
inspection readiness	During	Absence of the investigators in the closing meeting.
inspection readiness	Post	Improper return of documents about the study after inspection

inspection readiness	Post	Improper documentation process of inspection results.