**Monitoring Risk Level Tool**

Investigators conducting investigator–initiated interventional trials (regulated or non-regulated) can use this tool to assist them in determining the extent of site monitoring (i.e. GCP Monitoring) required for their trial. This tool is organized so that higher risk trials (i.e., phase 1 trials involving a novel investigational product) require the most monitoring. The descriptions for each monitoring level for the research categories can be seen in the legend below. This tool may be used assist with budget justification for funds dedicated towards study monitoring. Investigators should strive to meet or exceed the levels of monitoring outlined below.

The responsibility of determining the risk level of the trial lies with the Sponsor of the trial. For Investigator Initiated trials this may be an Investigator or Institution. Quality Assurance personnel may be involved. The risk level should be re-evaluated at pre-defined intervals, or more frequently if warranted by circumstances.

**PLEASE NOTE: The extent and frequency of monitoring should be determined primarily on risk, either to the participants or to the data. Studies that, by definition, fall under a lower monitoring level (i.e., Level 2/3) may need to be upgraded to a higher level based on risk exposure in the study. For example, a trial investigating a new surgical procedure that is not routinely done at your hospital may expose participants to a higher risk.**

In order for this tool to be effective, it must be used in conjunction with the trial protocol.

Particular emphasis should be placed on high risk/critical data points such as consent process, participant eligibility criteria, participant SAE’s and primary endpoints. Determining the maximum source data verification (SDV) error rate that, when exceeded, would result in additional (i.e. add-on) monitoring is an example of using the protocol in conjunction with this tool. Protocols that are more complex will require additional/more intensive monitoring. Examples of study design that would necessitate changes to the degree/intensity of monitoring include:

* Single vs. Multicentre studies
* Blinded vs. Unblinded studies
* Multiple study arms vs. Single arm studies

Monitoring frequency and methods (i.e., on site or remote) should be fluid in order to allow additional monitoring or type of monitoring if required. Recruitment rates are unpredictable – frequency and number of participant visits may change due to unforeseen circumstances and thus the monitoring frequency/method must adapt in order to accommodate these fluctuations. A review of the monitoring plan should be performed whenever a change to the protocol is made in order to ensure that the plan remains applicable to the conduct of the study.

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|  | **Level of Monitoring** |
| **Research Category** | **Monitoring Required** |
| **Phase 1**  Initial safety studies on a new drug, including the first administration of the drug into humans. Phase I trials are designed mainly to determine the pharmacological actions of the drug and the side effects associated with increasing doses. Pharmacokinetic as well as drug-drug interaction studies are usually considered Phase I trials. | **Level 1** |
| **Phase 2**  Clinical trials to evaluate the efficacy of the drug in patients with medical conditions to be treated, diagnosed or prevented and to determine the side effects and risks associated with drug. If a new indication for a marketed drug is to be investigated, then those clinical trials may generally be considered Phase II trials. | **Level 2** |
| **Phase 3**  Controlled or uncontrolled trials conducted after preliminary evidence suggesting efficacy of the drug has been demonstrated. These are intended to gather the additional information about efficacy and safety that is needed for further risk/benefit assessment of the drug |
| **Phase 4**  All studies performed after the drug has been approved by the regulator for the market, and used according to its marketing approval. These studies are often important for optimizing the drug's use. They may be of any type but must have valid scientific objectives. Commonly conducted studies include safety studies and studies designed to support use under the approved indication such as mortality and morbidity studies, or epidemiological studies. | **Level 3** |
| **Non-regulated Interventional**  Examples of non-regulated interventional studies include social/behavioural studies (studies involving interventions to modify behavior), studies using a Health Canada approved medical device in a randomized study, and studies comparing two standard of care treatments or procedures against one another. |

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| **Level 1** |
| **On-site or remote monitoring**  Source Data Verification (SDV) of the following critical data points for all participants:   * Informed consent process * Eligibility criteria * SAEs * Primary endpoints * Secondary endpoints (as appropriate) * Investigational Product (IP) accountability * Delegation log and protocol adherence   A percentage of case report form (CRF) SDV should be performed for a percentage (e.g. 10%) of enrolled participants. A justification of the percentage of CRFs and percentage of patients monitored should be documented prior to the finalization of the monitoring plan.  Review of training documentation, study regulatory file and essential documents.  **Frequency of visits**  Timing of visits must be customized based on study design and recruitment strategy and should be justified in writing in the monitoring plan. |
| **Level 2** |
| **On-site and remote monitoring**  SDV of the following critical data points for a subset of participants:   * Informed Consent process * Eligibility criteria * SAEs * Primary endpoints * Secondary endpoints (as appropriate) * CRF SDV\*. If errors are found greater than the predefined error-rate (protocol-specific and determined in advance - e.g., significant errors > 1 in 10 participant charts) then additional SDV (add-on monitoring) should be performed as required. Resources should be dedicated to areas that may be more relevant to patient safety and data integrity based on the requirements of the protocol. * Delegation log, IP accountability and protocol adherence must also be verified.   Review of training documentation, study regulatory file and essential documents can be performed remotely.  *\*Extent of CRF SDV is protocol-specific and is based on the type of data to be collected and its potential impact on endpoint analysis. Patient data review can be performed remotely or on-site. – De-identified source can be sent securely (e.g., fax or encrypted email) and compared against an electronic CRF (eCRF). Remote verification that a particular (critical) study-specific criterion was performed may also be done (e.g., de-identified x-ray inclusion criterion can be verified remotely to ensure that the procedure was performed prior to randomization). Consent forms are best verified on-site, the de-identified signature page of the consent form may serve as verification.*  **Frequency of visits**  Timing of visits must be customized based on study design and recruitment strategy and should be justified in writing in the monitoring plan.May consider setting up a peer review process at the site to have a coordinator not involved in the trial perform SDV/monitoring for the trial. Monitoring visits are recommended a minimum of once per year. |
| **Level 3** |
| **On-site monitoring or remote monitoring**  SDV of the following critical data points for a subset (e.g. 10%) of participants:   * Informed Consent process * Eligibility criteria * SAEs * Primary endpoints * Secondary endpoints (as appropriate). If errors are found greater than the predefined error-rate (protocol- specific and determined in advance e.g. significant errors > 1 in 10 participant charts) then additional SDV (add-on monitoring) should be performed as required. Resources should be dedicated to areas that may be more relevant to patient safety and data integrity based on the requirements of the protocol.   **On-site or remote monitoring**  CRFs/data generated should be reviewed for a proportion of enrolled participants.  Additional monitoring may be required based on findings. Verification of training documents,  study regulatory file and essential documents should be performed at least once as it is the Qualified Investigators/Investigator responsibility to ensure that staff is trained and that study documentation is stored/archived appropriately.  **Frequency of visits**  Timing of visits must be customized based on study design and recruitment strategy and should be justified in writing in the monitoring plan. |