Division of AIDS Risk Worksheet Guidelines

The worksheet is designed to assign risk levels to protocols for prioritizing clinical site monitoring resources. To ensure consistency of responses, please refer to the following guidelines while completing the worksheet.

Note: For the ease of the user, blue text on the worksheet will have a visible definition, explanation, or guidance associated with it when hovering over it with your cursor. However, if a section of the worksheet is greyed out/inactive, you will not be able to hover over blue text until that section is activated. Also, if prompted, please close out of all Adobe update notifications as only IT can update programs on NIAID DAIDS computers.

While the top section of the form will be pre-populated by Regulatory Support Contractor (RSC) personnel, please ensure that you complete the fields: MO Name and **MO Completion Date** and indicate whether this is an Initial Assessment or a Reassessment of a protocol before completing other sections of the Worksheet.

Logic checks have been programmed into the form. Based on the selection of an answer to a question, subsequent questions that are not applicable are greyed out and do not require completion. Remember to press the submit button at the bottom of the form once all information has been entered.

COMPLETITION INSTRUCTIONS FOR PROTOCOL RISK WORKSHEET

1. PROTOCOL INFORMATION

1.1. Will the clinical sites be monitored by a non-DAIDS entity (i.e., other than DAIDS Monitoring Contract)?

- o Yes
- o No
- o Decision is pending

1.2. Will this protocol be risk ranked?

- o Yes
- o No – This protocol will not be risk ranked because it is a protocol submitted for courtesy review or because DAIDS does not take responsibility as funder, sponsor, or clinical/safety monitor.

1.3. Is this a Clinical Trial?

Definition: A prospective study of human subjects designed to answer questions about biomedical or behavioral interventions, e.g., drugs, treatments, devices, or new ways of using known treatments to determine whether they are safe and effective. (DAIDS Glossary).

- o Yes
- o No

1.4. Select Study Risk Category?

- o Minimal Risk – Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons (45 CFR 46.303 (d)).
- o Greater than Minimal Risk – Greater than minimal with Minimal Risk being defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons (45 CFR 46.303 (d)).

1.5. In general, minimal risk studies are not monitored. Is an exception recommended to request monitoring of this minimal risk study?

- o Yes → Provide justification
- o No → **Stop – Submit form now.**

1.6. Highest Phase of the study:

For interventional studies for which there is no phase, check NA

- o NA
- o Phase I, Ib
- o Phase II, IIa, IIb (for therapeutic studies, including therapeutic vaccines) and II/III
- o Phase III, IIb (for vaccine and prevention studies) and III/IV
- o Phase IV (study product approved by FDA for indication and population)

Definitions:

- Phase I: Studies that are usually conducted with healthy volunteers and that emphasize safety. The goal is to find out what the drug's most frequent and serious adverse events are and, often, how the drug is metabolized and excreted.
- Phase II: Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition). For example, participants receiving the drug may be compared with similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.
- Phase III: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs.
- Phase IV: Studies occurring after FDA has approved a drug for marketing. These include postmarket requirement and commitment studies that are required of or agreed to by the sponsor. These studies gather additional information about a drug's safety, efficacy, or optimal use.

1.7. IND/IDE status:

If needed, refer to protocol title page, Protocol Management (quick summary), or refer to RAB. Are data intended to be used for a regulatory purpose (such as submission to an IND/IDE or NDA), or to alter standard of care recommendations?

- o Yes
- o No

1.8. Level of potential harm/toxicity related to intervention within the study population:

- o Low
- o Moderate
- o High – Specify

Definitions:

- Low potential for harm/toxicity – Safety profile well-described for the target population and mild/infrequent harm/toxicities expected overall, resulting in a highly favorable intervention risk/benefit ratio for the indication/population being studied. Life- threatening adverse events may be possible, but clearly occur only rarely.

Examples:

Treatment interventions*:* As expected with a well-established, first-line ARV

combination in the usual adult or pediatric clinic population.
Prevention interventions: Overall minimal harm/toxicities expected based on a very substantial amount of accumulated experience.

– Moderate potential for harm/toxicity – Safety profile for target population is not fully described (is under continued investigation) and/or moderate to severe grade harm/toxicities may be expected at moderately higher rate than for standard low risk interventions. Risk/benefit ratio is not as favorable, but still clearly acceptable for the indications/population being studied.

Examples:

Treatment interventions: Mild to severe adverse events may be expected to occur at a moderately higher frequency than for a well-established, first-line ARV combination, but life-threatening AEs expected to be rare.
Prevention/vaccine interventions: Early stage evaluation of new agents that could potentially have more than minimal harm based on (limited) existing data.

– High potential for harm/toxicity – Safety profile for the target population not yet described and/or moderate-to-severe or life-threatening harm/toxicity expected at a substantially higher rate than for low risk/standard interventions. Risk of harm is high but justified by expected benefit, or risk/benefit ratio is not yet established as clearly favorable for the population/indication being studied.

Examples:

Treatment interventions: Moderate to severe adverse events may be expected to occur substantially more frequently than with a well-established, first line ARV therapy and/or life-threatening events are expected to occur more frequently than rarely based on existing evidence. Also, first-in-human trials or only minimal safety data are available.

Treatment and Prevention interventions: Generally applicable only to first-in-human trials or very early stage evaluations with minimal available safety data.
(Continue to next)

2. HUMAN SUBJECTS PROTECTION

2.1. Will the protocol have any Vulnerable Populations?

Definition: Persons in a hierarchical structure or anyone who has compromised capacity for free consent because they are easy to manipulate as a result of their illness or socioeconomic condition. Examples include: children, prisoners, pregnant women, refugees, cognitively impaired, terminally ill, elderly, soldiers or students. (ICH E-6 and the OHRP IRB guidebook)

- o Yes
- o No

2.2. Are there additional privacy/confidentiality concerns?

- o Yes, Low – Concerns associated with standard clinical care or participation in any clinical trial.
- o Yes, Moderate to High – Research involving illegal behavior or questionnaires dealing with sensitive personal information.
- o No

3. STUDY COMPLEXITY

3.1. Level of study design complexity:

- Low – No placebo, may include no more than one randomization, may include two steps/phases/cohorts.
- Moderate to High - Use of placebo, more than one randomization (e.g. factorial design) and/or more than two steps/phases/cohorts; studies with multiple types of study populations (e.g. mothers and infants, HIV discordant couples); complex study agent administration/management.

3.2. Study visit intensity

What is the most intense study visit after the baseline/entry visit?

- Low – Only routine/non-intensive evaluations – For example: Un-timed blood draws; non-invasive sample collection/testing; simple, non-invasive imaging procedures; brief/simple questionnaires.
- Moderate – 1-2 non-routine evaluations – For example: Timed or invasive sample collections/testing; time-intensive imaging procedures; complex questionnaires; evaluations requiring coordination with multiple departments.
- High – More than 3 non-routine evaluations – For example: Time or invasive sample collection/testing; time-sensitive imaging procedures; complex questionnaires; coordination with multiple departments; OR any protocol mandated hospitalizations.

4. ADDITIONAL FACTORS

4.1. Specify factors to be considered for possible adjustment up or down of the priority level for the study:

- No additional factors
- Non-network study

Other issues – Specify and/or Notes to OCSO (in the available space below)

This section of the form is accessible at all times to allow highlighting specific issues and adding notes to OCSO.

INSTRUCTIONS FOR SUCCESSFULLY SUBMITTING COMPLETED WORKSHEET

- Click "**Submit**" located at the bottom of the worksheet
- When the **Select Email Client** pop-up window appears, select "**Desktop Email Application**"
- Click "**OK**"

After you click "OK", your completed worksheet will automatically go to the Outlook inbox of the Protocol Risk Coordinator who is Jennifer Plummer and an automatic notice will generate and be sent to your email address that your worksheet has been successfully submitted for processing. Within two (2) business days the Protocol Risk Coordinator will send you an email with your protocol risk level.

You also have the option to reset the Worksheet.