Guidance for Completing the Nursing/Pharmacy Protocol Screening Form

Hyperlinks to Sections:

Section A: Complete Dosing Information: Dose, Route, Frequency and Rate of Infusion

Oral Medications:
Example: Participants will receive treatment with oral (this is the route) Drug "X" at a dose of ____ mg (this is the dose) once per day on Days 1-15 (this is the frequency) of each 28 day cycle.

Note:
- Oral medications must also include instructions on whether or not the study medication can be crushed, chewed or dissolved in water.
- If a participant drug diary is provided, see drug diary template in ONCPRO under "Clinical Investigator Toolkit." The drug diary must include complete dosing instructions. The dosing instructions must be consistent with the dosing instructions found in the protocol document, with NO discrepancies.

IV Medications:
Example: Study Drug "X" _____mg (this is the dose) administered via intravenous infusion (this is the route) over 60 minutes (this is the rate of infusion) on Day 1 of each cycle (this is the frequency).

Section B: Allowable Time Windows for Dosing: +/- "X" minutes.

Oral Medications:
Participants will receive treatment with oral Drug "X" at a dose of ____ mg once per day on Days 1-15 of each 28 day cycle. The participants should take their dose at approximately the same time every morning. If a participant forgets to take their dose, the dose should be taken no more than 4 hours after their regular dosing time.

Note:
- If an oral medication is given 2 or more times per day, the protocol should stipulate whether or not there is a minimum amount of time required between doses.
  Example: Study drug "X" 20mg will be administered orally three times per day on Days 1-21 of each cycle. Doses should be taken at least 6 hours apart.

IV Medications:
Study Drug "X" _____mg administered via intravenous infusion over 60 (+/- 10) minutes, on Day 1 of each cycle.

Note:
- If an IV study drug is given more than once per week, the minimum amount of time required between each infusion must be specified in the protocol.
  Example: Study Drug "X" ____mg administered IV over 90 minutes on Days 1, 4, 8, 11, 15 and 18 of each cycle. Infusions must be given at least 48 hours apart.

Section C: FDA Approved Drugs

Example #1:
Prednisone may be administered per institutional standard.
Dose modifications will be made according to local practice.

Example #2:
Prednisone may be administered per package insert.
For prednisone dose modifications, refer to the package insert.

Example #3:
Prednisone may be administered per MD discretion.
Dose modifications are at the discretion of the treating physician.

Section D: Order of Administration for Multiple Study Drugs

Example:
Drug A will be administered first, followed by Drug B.

Note:
- Also state here if there is a specific time frame that separates Drug A from the administration of Drug B, and so on: 'Administer Drug B 30 minutes following the end of the infusion of Drug A.'
- If there is NO specific time frame required between the administrations of each drug, the protocol should state that also.

Section E: Dose Calculations

It is DF/HCC's standard of practice to calculate the dose using the weight of the participant on each day of treatment.

If the protocol states something different than this, please ask the Sponsor if they will allow our standard of practice.

The Sponsor's response should be placed on the alert page as follows:

> "The Sponsor will allow DF/HCC to use their standard of practice for calculating the dose using the participant's weight on the day of treatment."

Section F: Criteria to Treat: Hematologic and Non-Hematologic and C1, D1 labs

Example:
In order to begin a new cycle of treatment, the following criteria must be met:

Hematologic:
- ANC ≥ 1,000/mcL
- Platelets ≥ 100,000/mcL
- Hemoglobin ≥ 9.0 g/dL

Non-hematologic:
- Total bilrubin ≤ 1.5 x ULN

All other non-hematologic toxicities must have resolved to CTCAE, version 4.0 grade ≤ 1 or baseline.

Note for Cycle 1, Day 1 Labs:
- The protocol must state whether or not the labs drawn on C1, D1 need to re-meet the eligibility criteria. If not, then the protocol must state what the criteria to treat is for C1, D1 (it may be the same as the criteria to treat to begin a new cycle or a different set of parameters – but it must be clearly defined either way).
- The protocol must state whether or not C1, D1 labs need to be resulted before treatment.

Section G: Parameters - When to Hold, Restart, and At What Dose

Example:

Drug X Dose Modifications (One Study Drug)

Grade 1	No dose modification or delay
Grade 2	▪ No dose modification or delay required. If toxicity is intolerable to participant, the treating physician has the discretion to hold study drug . ▪ If toxicity resolves within 14 days, the participant may resume study drug X at the same dose. ▪ If study drug must be held for > 14 days, the participant must be removed from study.
Grade 3	▪ Study Drug must be held until the toxicity resolves to ≤ Grade 1. ▪ If toxicity resolves within 14 days, the participant may resume study drug at the next lowest dose level. A maximum of 2 dose reductions are allowed. ▪ If study drug must be held for > 14 days, the participant must be removed from study
Grade 4	▪ Participant must be removed from study.

This section of the protocol must include:

- When to hold the drug (i.e., at what grade of toxicity is the study drug to be held?)
- When to restart drug (i.e., to what grade must the toxicity resolve before drug can be given?)
- What is the maximum amount of time that the drug can be held before the participant must be removed from study?
- At what dose should the drug be given when the drug can be resumed?
- How many dose reductions are allowed for a participant?
- When a study drug is held, particularly in the middle of a cycle, do the days of the cycle count change, i.e., does it impact the day of dosing and/or the day(s) study assessments are performed?

If there are MULTIPLE study drugs being utilized for a protocol, the following issues must also be addressed:

- If one drug is held for a toxicity state whether all of the other drugs must also be held.
- If one drug is discontinued for a toxicity state whether the participant may continue on study receiving the other drugs.

Section H: Criteria to Treat with a DLT Occurrence and Criteria to Treat Beyond Dose Limiting Toxicity (DLT) Cycle(s)

1. The protocol must state whether a participant experiencing a DLT during the DLT determining period must be removed from study or if he may continue on study at a reduced dose. The reduced dose must be defined in the protocol.

2. In Phase 1 trials, the Sponsor will often give guidance on how to manage toxicities for the DLT period only. Please note that the protocol must also stipulate how to handle toxicities for cycles that are outside of the DLT window (usually Cycle 2 and beyond). The following items must be addressed for cycles beyond the DLT period:
   - Criteria to treat (see Section F)
   - Toxicity management (see Section G)

Section I: Required Data Tables

The required data table usually has a corresponding section within the protocol that describes the required assessment. The required data table (s) must be consistent with the body of the protocol.

Example:

Required Data Table

Assessment	Day 1	Day 8	Day 15	Day 21
Vital Signs	*	*	*	*
Labs	*			
CT Scan				*

SECTION 6.7: Schedule of Assessments
Vital Signs: Vital Signs will be performed on Days 1 and 15 of each Cycle
Labs: Labs will be performed on Day 1 of each Cycle
CT scan: CT scan will be performed on Day 21 of each Cycle.

Note how there is a discrepancy between the required data table and Section 6.7 for the frequency of vital signs. This discrepancy must be reconciled with the Sponsor and the discrepancy must be either corrected in the protocol or clarified on the alert page (only for non-DF/HCC sponsored studies).

Windows for assessments:
When assessment times are specified, a window of time should be given to prevent violations. The assessments most in need of a window are: vital signs, PKs, EKGs and observation periods.

Example:
EKG 1 hour (+/-10 minutes) post end of infusion.

The use of the word "approximately" is also very helpful in relation to timed assessments.

Section J: Vomited Doses

The protocol must specify what is to be done if a participant vomits after dosing.

Examples:
- Vomited doses may not be retaken.
- If participant vomits within 30 minutes after taking the dose, the dose may be retaken.
- If participant vomits and the capsule can be seen, the dose may be retaken.
- If a participant vomits a dose, the participant should notify their physician who will instruct them whether or not to retake the dose.

Section K: Fasting and Food Requirements

Fasting Requirements:
If fasting is required for an oral drug, the protocol must state the required fasting time period BEFORE and AFTER the dose is to be taken.

Example:
- The participant must fast for 8 hours prior to taking the study drug and must continue to fast for 2 additional hours after dosing.

Food and/or Liquid Requirements:

Example:
- The participant should take their dose 1 hour after a light breakfast (i.e. toast, jelly and juice).
- The participant must take each dose with 8oz (240mL) of water.

Note:
Prohibited foods must be stated in the study drug administration section of the protocol as well as in the participant drug diary (oral meds) and/or participant dosing instruction sheet.

Example:
- Grapefruit, grapefruit juice and starfruit are not allowed while on study.

Section L: Protocol Schema

For DF/HCC initiated protocols, doses should not be provided in the schema. For externally initiated studies, if the sponsor is not willing to remove the doses from the schema, then the doses should be expressed in exactly the same way as they are expressed in the body of the protocol.

*Example of schema and treatment section **NOT expressed in exactly the same way**:*

- Schema expresses the total course dose to be given over the course of 4 days:
  "Cyclophosphamide 8gm/m2 IVB Days 1-4"

- Treatment Section of the protocol expresses the dose to be given on a daily basis on each of the 4 days:
  "Cyclophosphamide 2gm/m2 IVB Days 1-4"