EXAMPLE TREATMENT AND SCHEMAS

Study Treatment:

GENERAL GUIDELINES

• Do not abbreviate agent names or treatment schedules. Abbreviations can be misinterpreted.
• Use complete approved generic agent names. Brand names and abbreviations are not acceptable (e.g., specify 'CARBOplatin' instead of CBDCA, 'CISplatin' instead of CDDP).
• Write treatment instructions clearly and explicitly. No detail (no matter how minor) should be omitted; however, avoid unnecessary redundancy.
• Delete extraneous information that may confuse readers (e.g., protocols that use only injectable agents products should not include information for a tablet formulation).
• Use consistent notation in expressing quantifiable units, (e.g., either; 1 mcg or 1 mg; qid or Q6h; kg or m2)
• Do not use abbreviations that appear on The Joint Commission/Institute of Medicine "do not use" list. In particular, do not use trailing zeroes or the Greek letter μ.
• Spell out the word, "units" out to avoid confusion; a letter "U" can be easily mistaken for a zero and may result in a 10-fold overdose.
• Decimal Points - Never trail a whole number with a decimal point followed by a zero (i.e., "5 mg" not "5.0 mg"). The decimal point may not be seen, resulting in a 10-fold overdose.
• In expressing units that are less than the whole number 1, the dosage should be written with a decimal point preceded by a zero (i.e., "0.125 mg" not ".125 mg"). Without the 'zero' prefix, the decimal point may be missed resulting in a dosing error.
• Contiguous treatment days - Specify the total number of days the agent is administered and the cycle day that treatment commences in the treatment plan. Include parenthetically the cycle days on which treatment occurs.
• Non-contiguous days - Specify the cycle days on which each dose should be given in the treatment plan.
• Cycle (or Course) duration – Specify the treatment cycle duration. When a treatment regimen is 21 days in duration, the regimen will be repeated on the twenty-second, forty-third, sixty-fourth…, etc. days following treatment initiation.

Duration of administration:

• Indicate administration duration clearly. If an agent is to be administered on more than one day per cycle, explicitly identify each cycle day.
• "Day One" typically describes the day on which treatment commences when treatment day enumeration is arbitrary. Avoid using 'day 0 (zero)' when describing treatment schedules unless it is necessary (e.g., when describing the day on which hematopoietic progenitor cells are administered after a cytotoxic conditioning regimen in transplantation protocols).

• Clarify total dose planned per treatment course - In all treatment plans (protocols) and agent orders, identify and append parenthetically the total dose (as a function of body weight or surface area) that patients are to receive during a treatment course (or cycle).

Administration Dates and Times - When appropriate include specific starting days and times. Be very clear (spell out) in directions for the twelve o'clock hour "12:00 noon" and "12:00 midnight." Expressing time by 24-hour clock notation ('military time') likewise precludes errors due to ambiguous 'a.m.' and 'p.m.' time notations.

Example:
Bolus infusion (administration duration < 24 hours):
• Express the amount of agent per container.
• Include the rate of administration, the infusion duration, and days on which the agent is to be administered.

Example:
"XYZ" 15 mg/m2 diluted in 50 mL 0.9% sodium chloride injection, infuse intravenously over 15 minutes for one dose on day 1 (total dose/cycle = 15 mg/m2)
Agent products stable for > 24 hours - (Containers are prepared daily):
• Express the dose per container.
• Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses.
• State that the agent must be prepared daily.

Example:
"XYZ" 8 mg/m2 per day diluted in 50 mL 0.9% sodium chloride injection, administer by continuous intravenous infusion over 24 hours, daily for three days starting on day 1 (days 1, 2, and 3; total dose/cycle = 24 mg/m2 over 72 hours). A new IV bag should be prepared daily for 3 days.
Agent products stable for > 24 hours - (Containers are prepared for multiple days):
• Express the dose as the amount of agent administered per day and indicate the number of days for which it is administered.
• Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses.
• State that this is a multi-day preparation and for how long the preparation should be infused.

Example:
"XYZ" 8 mg/m2 per day diluted in 50 mL 0.9% sodium chloride injection, by continuous intravenous infusion for three days starting on day 1 (total dose = 24 mg/m2 over 72 hours). This is a multi-day infusion to be infused over 72 hours.
Continuous infusions that require multiple agent product containers:
• Express the dose per container.
• Include the total dose (as a function of BSA, weight…, etc., when appropriate) in parentheses.
• Include the total number of containers used per day.

Example:
"XYZ" 1 mg/m2 diluted in 50 mL 0.9% sodium chloride injection, administer by continuous intravenous infusion over three hours, every three hours for three days, starting on day 1 (8 bags/day, total dose = 24 mg/m2 over 3 days)

ORAL ADMINISTRATION
• Describe agent dosages and schedules as the amount of agent that will be given (or taken) each time the agent is administered, not as a total daily dose that will be given (or taken) in divided doses, (e.g., 20 mg orally every 6 hours for 5 days vs. 80 mg per day, given in four divided doses for 5 days
• Include guidelines regarding 'rounding-off' doses to the nearest capsule or tablet size.
• Whenever possible, indicate whether agents should be administered (or taken) with food and explain dietary restrictions.

CONCOMITANT (ANCILLARY) MEDICATIONS
• Clearly identifiy supportive care and essential ancillary medications required by a treatment regimen.
• State complete instructions including appropriate indication, dosage, administration route, schedule, restrictions to use, and any other relevant data explicitly.

TREATMENT MODIFICATIONS
• Define the maximum number of allowable dose reductions before treatment must stop
• include consistent descriptions of modifications among a study's treatment arms for the same agent
• Use consistent terminology for the same meaning
• Describe exactly how a toxicity must resolve before treatment can be resumed or doses re-escalated
• Explain exactly how modifications are to be handled during a cycle or at the start of the next cycle
• Specify how modifying or stopping therapy of one agent impacts the rest of the treatment regimen
• Use values for CTCAE grades consistent with the actual definition

For dose escalation studies (particularly for patients treated at the initial dose levels), the maximum number of allowable dose level reductions in the dose modification section must be less than or equal to the number of available dose levels defined in the treatment section.

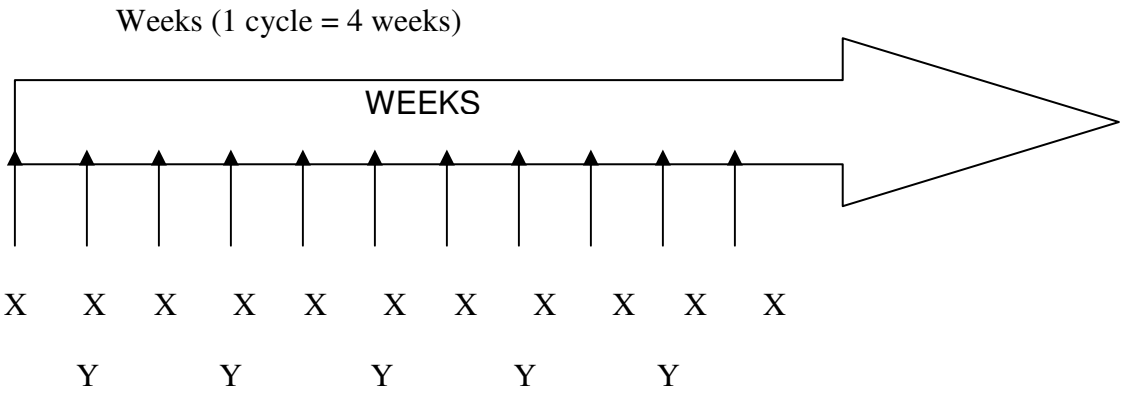
Example: Phase I/II Safety Study

Dose level	Drug X	Drug Y
-1	15 mg IV weekly	5 mg/kg IV every 2 weeks
0	15 mg IV weekly	10 mg/kg IV every 2 weeks
1*	20 mg IV weekly	10 mg/kg IV every 2 weeks
2**	25 mg IV weekly	10 mg/kg IV every 2 weeks

*** Starting dose**

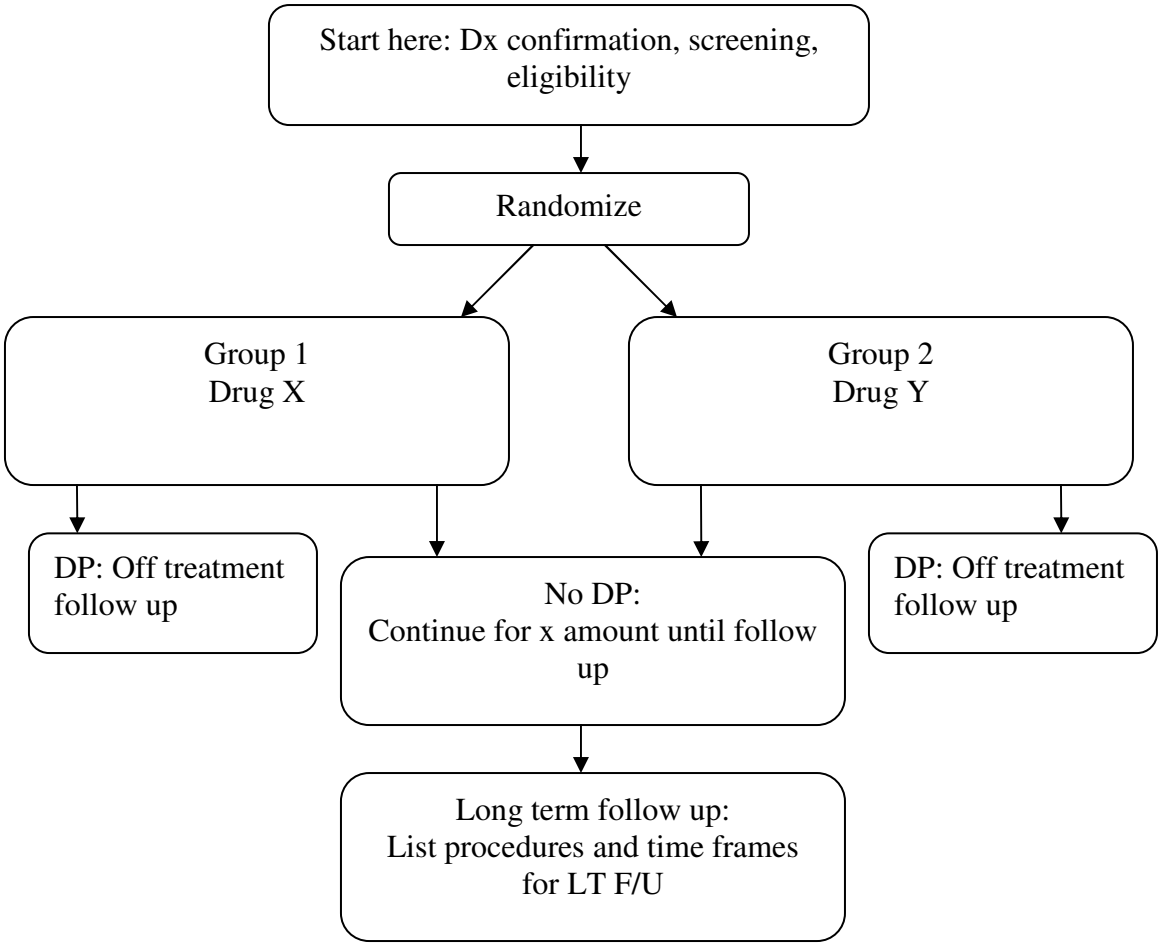
**** If no DLT is found at dose level 2, the phase II portion of the study will continue at that dose level.**

Example: Phase II Clinical Activity / Safety Study



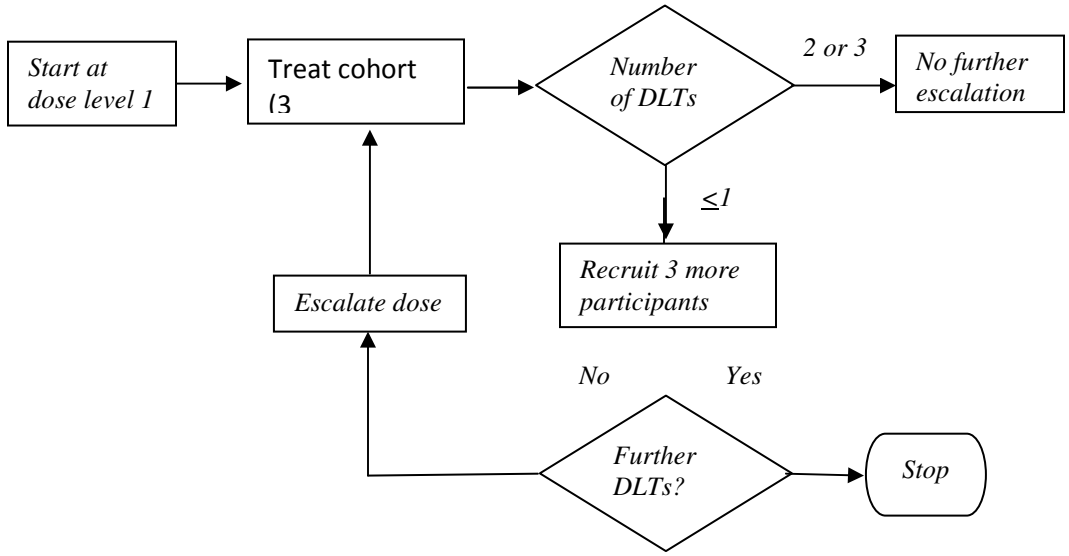
Example: Schema Flowchart (generic)

Another way to find out what will happen during the research study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



EXAMPLE OF TREATMENT SCHEMA

Example: Phase I Dose Escalation trial



Example: Randomized trial