

Duke Comprehensive Cancer Center Investigational Chemotherapy Service

Pharmacist Protocol Review Checklist

PROTOCOL INFORMATION	
Title:	
PI:	Date:
TITLE PAGE	
<input type="checkbox"/> Are the titles of the protocol and consent identical? <input type="checkbox"/> Investigational drug supply clearly indicated in title page?	
SCHEMA	
<input type="checkbox"/> Verify key elements	<input type="checkbox"/> Is a schema provided? <input type="checkbox"/> Is the research plan apparent from the schema? <input type="checkbox"/> Does the drug related treatment information provided coincide with information in other protocol sections? <input type="checkbox"/> Does the schema reflect the correct dosing, days and agent? <input type="checkbox"/> Are the agents listed in the order they are to be given?
PATIENT ELIGIBILITY	
<input type="checkbox"/> Are the appropriate eligibility and exclusion criteria related to drug therapy included?	<input type="checkbox"/> Renal or hepatic function, prior therapy, prior exposure to investigational agent <input type="checkbox"/> Are there appropriate maximum creatinine values or other lab values <input type="checkbox"/> Will the eligibility criteria allow for the initiation and completion of the drug therapy? (i.e. is the need for central venous access device clear) <input type="checkbox"/> Ability to swallow: If oral drug must be swallowed whole and no liquid form/extemporaneous formulation/stability in food or liquid exist, does the protocol exclude patients that are unable to swallow tablets or capsules? <input type="checkbox"/> Blood pressure (BP). If there is a BP requirement (e.g. an anti-VEGF agent or monitoring BP during an etoposide infusion) <input type="checkbox"/> Females of child-bearing potential: are pregnant/lactating females excluded? <input type="checkbox"/> Concomitant medications: Are they identified if that may exclude a patient from participating in the study?
DRUG FORMULATION, AVAILABILITY, AND PREPARATION	
<input type="checkbox"/> Investigational agent pharmaceutical information	<input type="checkbox"/> How Supplied: Include the agent's chemical name, other names, available dosage forms, ingredients and packaging as appropriate. Also state the agent's supplier, i.e., investigational product supplied by DCTD. <input type="checkbox"/> Preparation (how the dose is to be prepared): Include reconstitution directions and directions for further dilution if appropriate. <input type="checkbox"/> Storage: Include the storage requirements for the original dosage form, reconstituted solution and final diluted product, as applicable.

	<ul style="list-style-type: none"> <input type="checkbox"/> Stability: Include the stability of the original dosage form, reconstituted solution and final diluted product, as applicable. <input type="checkbox"/> Route of Administration: Include a description of the method to be used and the rate of administration if applicable. For example, continuous intravenous infusion over 24 hours, short intravenous infusion over 30 to 60 minutes, intravenous bolus, etc. Describe any precautions required for safe administration. <input type="checkbox"/> Other Information: Include any significant potential drug interactions, incompatibilities, special handling, or patient care implications. <input type="checkbox"/> Adverse Events: Adverse event information should be included in the ADVERSE EVENTS: LIST AND REPORTING REQUIREMENTS section of the protocol. For investigational agents the list of adverse events in the protocol must be comprehensive. Note: The Informed Consent document should contain a list of all known adverse events. All adverse events in the informed consent should be written in laymen's terms.
<input type="checkbox"/> Commercial agent pharmaceutical information	<ul style="list-style-type: none"> <input type="checkbox"/> Product description: Include any dosage form(s), ingredients, and packaging applicable to the protocol. Also state the agent's supplier or state that it is commercially available. <input type="checkbox"/> Preparation (how the dose is to be prepared): Investigators may refer the reader to the package insert for 'standard' preparation instructions. If the agent is to be prepared by 'non-standard' or protocol specific fashion, the reconstitution directions and instructions for further dilution must be included. Appropriate storage and stability information should be included to support the method of preparation. <input type="checkbox"/> Route of administration: Include a description of the method to be used in this protocol and the rate of administration, if applicable. For example, continuous intravenous infusion over 24 hours, short intravenous infusion over 30 to 60 minutes, intravenous bolus, etc. Describe any precautions required for safe administration. <input type="checkbox"/> Refer the reader to the package insert for complete information. <input type="checkbox"/> Adverse Events: Adverse event information should be included in the ADVERSE EVENTS: LIST AND REPORTING REQUIREMENTS section of the protocol. The investigator should list the events most likely to occur in this protocol and refer the reader to the agent's package insert for the comprehensive list of adverse events. Note: The Informed Consent document should contain a list of all known adverse events. All adverse events in the informed consent should be written in laymen's terms.
TREATMENT PLAN	
<input type="checkbox"/> Required information	<ul style="list-style-type: none"> <input type="checkbox"/> Generic drug name, dose, route, duration of infusion <input type="checkbox"/> Are there clear recommendations "for sequential vs. concomitant order of drug administration? For multi-agent protocols, the order of drug administration should be clearly delineated. <input type="checkbox"/> Does the stability data support the schedule and method of administration? <input type="checkbox"/> Are required supplemental medications (i.e. premeds) present in treatment plan, e.g. ranitidine and dexamethasone for paclitaxel? <input type="checkbox"/> For investigational agents, make sure that this is indicated in the body of the

	treatment plan so that prescribers are aware of the non-commercial source
<input type="checkbox"/> Consistency	<input type="checkbox"/> Is the treatment plan consistent with study objectives and background? Is it clear and concise (i.e. could you treat the patient using this plan)? <input type="checkbox"/> Treatment instructions should be explicit. No detail (no matter how small) should be omitted. Avoid assumptions <input type="checkbox"/> Is the dose expressed in the same and correct units throughout the protocol (e.g. <i>mg/m2/dose</i> or <i>mg/kg/dose</i>)? Doses should be delineated per dose and not per day. <input type="checkbox"/> For NCI IND agents, is the treatment section consistent with the NCI monograph? <input type="checkbox"/> Do all references to appendices actually refer to the appropriate appendix? Are inter-section references correct?
<input type="checkbox"/> Drug administration	<input type="checkbox"/> Suggested information: infusion solution, concentration, compatibility, stability and hydration recommendations. <input type="checkbox"/> Is standardized drug dilution & compatibility consistent with known stability data (e.g. etoposide)?
<input type="checkbox"/> Dose rounding guidelines	<input type="checkbox"/> Are they needed? Are they provided? <input type="checkbox"/> May be helpful for oral medications, but not necessary for parenterals. <input type="checkbox"/> Parenteral doses may need to be rounded to 5% <input type="checkbox"/> Are they appropriate, brief, and simple to use? <input type="checkbox"/> Do they round to the nearest tablet size (or half tablet size if appropriate)? <input type="checkbox"/> Consider recommending a dosing table which outlines dose by weight or BSA if rounding guidelines are complicated.
<input type="checkbox"/> Parenteral Administration	<input type="checkbox"/> Drug products should be prepared within documented stability and sterility guidelines in accordance with practitioners' local clinical and institutional policies and procedures. Drug containers should be changed at least daily unless extended stability and sterility data are available. <input type="checkbox"/> In protocol descriptions and orders for treatment, drug dosage should be expressed as the total amount of drug that will be administered from a single drug container, <i>i.e.</i> , the total amount of drug per syringe, bag, or other container that will be dispensed. An exception to this rule applies to drug products with extended stability, where a drug is administered from a single container for greater than 24 hours. In such cases, treatment plans and prescribers' orders should specify the amount of drug that is administered during each 24-hour interval. Product container labels should always identify the amount of drug within the container. <input type="checkbox"/> For drug admixtures that can be prepared in more than one way, practitioners should institute <i>a priori</i> , standard and consistent methods governing how each drug will be prepared and administered. <input type="checkbox"/> Include specific fluid volumes and types when possible. <i>Bolus infusion (administration duration ≤ 24 hours):</i> <input type="checkbox"/> Express the amount of drug per container. <input type="checkbox"/> Include the rate of administration, the infusion duration, and days

	<p>on which the drug is to be administered.</p> <p>Drug products stable for ≥ 24 hours - (Containers are prepared daily):</p> <ul style="list-style-type: none"> <input type="checkbox"/> Express the dose per container. <input type="checkbox"/> Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses. <input type="checkbox"/> State that the agent must be prepared daily. <p>Drug products stable for ≥ 24 hours - (Containers are prepared for multiple days):</p> <ul style="list-style-type: none"> <input type="checkbox"/> Express the dose as the amount of drug administered per day and indicate the number of days for which it is administered. <input type="checkbox"/> Include the total dose (as a function of BSA, weight, etc., when appropriate) in parentheses. <input type="checkbox"/> State that this is a multi-day preparation and for how long the preparation should be infused.
<input type="checkbox"/> Oral Administration	<ul style="list-style-type: none"> <input type="checkbox"/> Describe drug dosages and schedules as the amount of drug that will be given (or taken) each time the drug 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 5days <input type="checkbox"/> Include guidelines regarding 'rounding-off' doses to the nearest capsule or tablet size. Although breaking a tablet into halves at best approximates an accurately measured dose, treatment plan rounding-off rules should indicate whether tablet formulations should be broken to deliver a calculated dosage. <input type="checkbox"/> Whenever possible, include instructions about whether drugs should be administered (or taken) with food and any dietary restrictions. <input type="checkbox"/> Include information about whether drug can be crushed, dissolved, etc. for patients who can not swallow whole tablet/capsule.
ANCILLARY TREATMENTS	
<input type="checkbox"/> Cytokines	<ul style="list-style-type: none"> <input type="checkbox"/> Are criteria included, if applicable. Are these guidelines appropriate for the treatment regimen?
<input type="checkbox"/> Other treatments	<ul style="list-style-type: none"> <input type="checkbox"/> Are other treatments (radiotherapy, surgery, supportive therapy [antibiotics, antiemetics, chemoprotectants]) required by a treatment regimen clearly described? <input type="checkbox"/> Complete instructions including appropriate indication, dosage, administration route, schedule, restrictions to use, and any other relevant data should be explicitly stated. <input type="checkbox"/> Is there a statement regarding antiemetics as the choice of the local institution? <input type="checkbox"/> Can you discern the sequence of therapies given? <input type="checkbox"/> Are there occasions where combined modality treatment is not feasible or difficult to give? <input type="checkbox"/> Are the directions or recommendations for drug stabilities and administration feasible for the average institution and patient? (e.g. unreasonably short stabilities or too many IV lines required)

DOSE MODIFICATION AND MANAGEMENT OF TOXICITY

- Treatment Modification**
 - Treatment plans should explicitly identify when treatment (typically dosage) modifications are appropriate.
 - Treatment modifications and the factors predicating treatment modification should be explicit and clear.
 - All treatment modifications should be expressed as a specific dose rather than as a percent of the starting dose.
 - Are criteria provided to modify drug doses or delay therapy based on adverse events? e.g. neutropenia, neuropathy, mucositis, other toxicities)
 - Are there standardized dosage adjustments for clinical conditions? e.g. renal or hepatic dysfunction, limb loss, low counts.
 - If dose calculation involves a complicated equation, e.g. Calvert formula for carboplatin AUC, make sure sample calculations include appropriate units.
 - Should additional criteria be added or deleted?
 - Are criteria available for when to use ideal vs actual vs adjusted body weight?

CHEMOTHERAPY SAFETY CONSIDERATION / EXPRESSION AND NOMENCLATURE

- General Guidelines**
 - Do not abbreviate** drug names or treatment schedules. Abbreviations can be misinterpreted.
 - Use complete approved **generic drug names**. Brand names and abbreviations are not acceptable (e.g., specify 'carboplatin' instead of *CBDCA*, 'cisplatin' instead of *CDDP*).
 - Treatment instructions should be explicit**. 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 drugs products should not include information for a tablet formulation).
 - Use consistent notation** in expressing quantifiable units, (ex. either; 1mcg or 1mg; every 6 hours; kg or m²)
 - The word, "Units"** should be spelled 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") are not allowed. The decimal point may not be seen, resulting in a 10-fold overdose.
 - In expressing units that are less than the whole number one, the dosage should be written with a decimal point preceded by a zero (i.e., ".125 mg" not "0.125 mg"). Without the 'zero' prefix, the decimal point may be missed resulting in a dosing error.
 - Body weight** - Drug dosages may be expressed as a function of body surface area, body weight, or may be calculated to produce a pharmacokinetically-targeted endpoint (e.g., serum or plasma concentration or area under the curve AUC). Treatment plans should specify whether absolute (i.e., actual), ideal, or lean body weight is used in calculating drug dosage as a function of

body weight. In addition, an equation describing how that value is calculated should appear in the treatment plan if drug dosage is a function of a calculated ideal or lean body weight. If drug dosage is a function of a calculated pharmacokinetic endpoint, the equation(s) describing how that value is calculated should also appear in the treatment plan.

- Contiguous treatment days** - Treatment plans should specify the total number of days a drug is administered and the cycle day that treatment commences. Include parenthetically the cycle days on which treatment occurs.
- Non-contiguous days** - Treatment plans should specify the cycle days on which each dose should be given.
- Cycle (or Course) duration** - Treatment cycle duration (or length) should be specified. 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:**
 - Administration duration should be clearly indicated. If a drug is to be administered on more than one day per cycle, each cycle day should be explicitly identified.
 - "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 drug 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. Directions indicating events for the twelve o'clock hours should be explicitly expressed (spell out) "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.

ADDITIONAL COMMENTS

**Adapted from CALGB protocol checklist