Template Writing – Background

Before you begin writing the protocol, consider the *phase* and *IND status* of your study. These two factors will significantly impact the content of the protocol.

Phases:

Each phase of a cancer study has a general purpose which gives insight into the general aims of a protocol:

Phase	Description
Pilot	The initial study examining a new method or treatment (National Cancer Institute 2014). Not the first trial in humans (see phase I).
Feasibility	These studies are used to determine whether an intervention is appropriate for further testing; in other words, they enable researchers to assess whether or not the ideas and findings can be shaped to be relevant and sustainable. (Bowen et al. 2009)
Phase I	The first step in testing a new treatment in humans. These studies test the best way to give a new treatment (for example, by mouth, intravenous infusion, or injection) and the best dose. The dose is usually increased a little at a time in order to find the highest dose that does not cause harmful side effects. Because little is known about the possible risks and benefits of the treatments being tested, phase I trials usually include only a small number of patients who have not been helped by other treatments (National Cancer Institute 2014). Phase I studies often involve dose escalation schemas. This is to provide the maximum tolerated dose of the drug, or treatment regimen, being studied.
Phase Ib	These studies are usually conducted in patients diagnosed with the condition, who demonstrate some biomarker, surrogate, or possibly clinical outcome that could be considered for "proof of concept." Proof of concept in a Phase 1b study typically confirms the hypothesis that the current prediction of biomarker, or outcome benefit is compatible with the mechanism of action. (Lilly 2013)
Phase I/II	A trial to study the safety, dosage levels, and response to a new treatment (National Cancer Institute 2014). *Phase IIa and IIb studies, though less strictly defined, are also common designs for research studies. Phase IIa studies traditionally focus on dose-responses, targeted patient populations, and dose frequency. Phase IIB studies traditionally focus on more rigorous clinical trials to provide extensive information on dosing and safety.
Phase II	A study to test whether a new treatment has an anticancer effect (for example, whether it shrinks a tumor or improves blood test results) and whether it works against a certain type of cancer (National Cancer Institute 2014).
Phase II/III	A trial to study response to a new treatment and the effectiveness of the treatment compared with the standard treatment regimen (National Cancer Institute 2014). *Phase IIIa and Phase IIIb are less common designs for research studies and have somewhat variable definitions but are still useful when understanding research protocols. Phase IIIa are efficacy and safety trials that support the initial claims made by the sponsor. Phase IIIb are additional studies conducted to increase patient exposure.
Phase III	A study to compare the results of people taking a new treatment with the results of people taking the standard treatment (for example, which group has better survival rates or fewer side effects). In most cases, studies move into phase III only after a treatment seems to work in phases I and II. Phase III trials may include hundreds of people (National Cancer Institute 2014).
Phase IV	A type of clinical trial that studies the side effects of a treatment after it has been approved and is being marketed. These trials include thousands of people and look for side effects that were not seen in earlier trials. Also called post-marketing surveillance trial (National Cancer Institute 2014).

IND – Investigational New Drug:

Before beginning to write a protocol, please consider whether an IND application is needed. If an IND is required additional language must be added to the protocol (i.e. FDA reporting requirements, safety monitoring, etc…) – please see the protocol template for the specific details.

- When is an IND (Investigational New Drug) required?
  - For a study with an investigational drug
  - For a study with an approved drug that is being used for a different indication, in a different dosing form (IV vs. oral), or for a dose range not covered by current labeling.
    - NOTE: an IND is only required for these studies if the change in dosing, route of administration, or patient population **significantly increases the risk of the product**
- When is an IND not required:
  - Generally not required when all criteria are met:
    - No intent to support new use or labeling change
    - No intent to support change in advertising
    - No factor such as route of administration, dosage, or population increases risk
    - Compliance with FDA informed consent and IRB review requirements
    - Conducted by a qualified investigator
    - No promotion of product as safe or effective treatment for condition under study

Bibliography

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