Title: Protocol Risk Assessment to Determine the Level of Targeted Source Data Verification During a CP-CTNet Audit

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
1.0	Sep-02-2021	Original version of document

1. INTRODUCTION AND PURPOSE

In August of 2013, the FDA released its Guidance for Industry[1] regarding the oversight of clinical investigations using a risk-based approach. This approach focuses on the study parameters that are the most critical to the protection of the rights, welfare and safety of study participants and the quality of study data. The purpose of protocol risk assessment is to help determine the level and focus of source data verification required during an audit. This document describes the criteria[2] and process used to assign a risk level to a CP-CTNet protocol. The protocol risk level is a key part of the algorithm that determines the level of source data verification that will occur for each participant chart selected for review during an audit. The algorithm itself is described in the DMACC's Targeted Source Data Verification (TSDV) Worksheet.

Note: This document is intended for DCP and DMACC use.

2. DEFINITIONS

Term	Definition
DCP	Division of Cancer Prevention
FDA	Food and Drug Administration
OTC	Over-the-Counter
SOC	Standard of Care
TSDV	Targeted Source Data Verification

3. PROCEDURES

The protocol risk level is assigned by the DCP study team during the protocol review process and documented on the Consensus Review of the first submission of a protocol (after concept approval). Risk (low, intermediate or high) is assessed for each of 7 categories: agent approval status, toxicity, administration and storage; clinical procedures; health status of the study population; and participant's ability to provide informed consent (see the *CP-CTNet DMACC Protocol Risk Level Assessment Form*).

The specific risk level criteria for each category appear with a check box (□). When there is more than one check box for a risk level, the protocol only needs to meet ONE of the criteria to merit assignment of that risk level to that category. For each of the 7 categories, place a check mark in the box that most accurately describes the protocol being assessed. For the agent approval status and clinical procedures categories, the risk level criteria differ by type of agent (OTC vs FDA regulated) or type of participant (healthy volunteer vs targeted). The criteria that pertain only to one type of agent or one type of participant are listed beneath a bolded header indicating that they apply only to that case.

It is expected that the assessed risk level will vary from one category to the next. When this occurs, the highest of the assessed risk levels is assigned to the protocol to help ensure that the audit is performed with an adequate level of source data verification.

Note: When assessing the risk of clinical procedures, the risk associated with a standard of care (SOC) procedure that would be performed whether or not the individual was participating in the study is not included in the protocol risk assessment UNLESS the protocol calls for modification of the SOC procedure. For example, in a pre-surgical window of opportunity trial, participants are

recruited from a pool of patients that are already scheduled for surgery. The scheduled surgery provides an opportunity to collect tissue for endpoint analysis but is not part of the study intervention as long as there is no modification of the surgical procedure itself in order to obtain the tissue samples. So, if the protocol calls for a piece of tissue to be removed from a tumor after it is excised there is no increased risk to the participant above that associated with the SOC, but if the protocol calls for a sample of normal tissue to be removed from an organ during the surgery to excise a tumor from that organ, the degree of risk associated with obtaining that extra sample alone is taken into account. The same would hold true for a study that "piggy-backs" the collection of tissue samples for research purposes only onto a SOC biopsy. If no extra tissue is taken for research purposes only, there is no additional risk, but if a sample of normal appearing tissue is requested or two biopsies per location rather than one, or a larger biopsy than is standard is requested to provide tissue samples for research purposes only, the risk of obtaining those extra samples or a larger sample is included in the assessment.

[1]*Oversight of Clinical Investigations —A Risk-Based Approach to Monitoring* U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER)Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Office of Good Clinical Practice (OGCP), Office of Regulatory Affairs (ORA) August 2013

[2]Adapted from Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products MRC/DH/MHRA Joint Project Version 10th October 2011

4. REFERENCES

- CP-CTNet DMACC Protocol Risk Level Assessment Form

5. APPENDICES

None