Title:	**Protocol Audit Risk Assessment to Determine the Level of Targeted Source Data Verification During a CP-CTNet Audit**
Version:	1.0
Version Date:	October 16, 2025

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
1.0	OCT-16-2025	Original version of document.

1. INTRODUCTION AND PURPOSE

This document describes the criteria and process used to assign CP-CTNet protocols a risk level for Targeted Source Data Verification (TSDV) during an audit.

In August of 2013, the FDA released its *Guidance for Industry* 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.

Protocol audit risk assessment is used to determine which Case Report Forms (CRFs) in Rave are selected for source data verification during an audit.

The protocol audit 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 DMASC's Targeted Source Data Verification (TSDV) Worksheet.

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

2. DEFINITIONS

Term	Definition
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
FDA	Food and Drug Administration
OTC	Over-the-Counter
PSRC	Protocol and Safety Review Committee
SOC	Standard of Care
TSDV	Targeted Source Data Verification

3. PROCEDURES

CP-CTNet protocols are assigned to one of 3 possible audit TSDV risk levels: Low, Intermediate, or High by the PSRC during the Consensus/Concurrence review of the first submission of a protocol after concept approval. The audit risk level assigned to the protocol is reported in the Consensus/Concurrence review document.

The PSRC uses the *CP-CTNet FORM003 Protocol Audit Risk Level Assessment Form* to consider each of the following categories (for additional information (see *Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products MRC/DH/MHRA Joint Project Version 10th October 2011*) when assigning the risk level:
- Agent categories:
    - Approval Status
    - Toxicity
    - Administration

If there is no study agent, all 3 categories related to study agent are skipped.
- Clinical procedures associated with the protocol (i.e., procedure risk, SOC v. non-SOC)

The reviewer must first consider the type of study population (healthy volunteer vs a targeted population), and then selects the risk level that best describes the protocol's clinical procedures.

The reviewer also takes into account whether a Standard Of Care (SOC) procedure required for the protocol would be performed regardless of whether an individual was participating in the study or not. If the procedure would be performed regardless of study participation, it is not included in the risk assessment UNLESS the protocol calls for a modification of the standard procedure. For example, in a pre-surgical window of opportunity trial, participants are recruited from a pool of patients that are going to be having surgery whether or not they are in the study. The fact that they are having surgery provides an opportunity to obtain tissue samples for the study but does not put the participant at increased risk. However, if the protocol asks that the surgical procedure be modified, for example, to remove a piece of normal tissue during the surgery, the risk associated with obtaining that extra tissue is taken into account in the risk assessment. 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 a larger biopsy than is standard is requested to provide tissue samples for research purposes only, the risk of obtaining the extra or larger sample(s) is included in the assessment.

- Health status of the study population
- Participants' ability to provide informed consent

Using the table on the Protocol Audit Risk Level Assessment Form, the PSCR reviewer selects the appropriate risk level (L =l ow; I = intermediate; H = high) for each of the above listed categories.

In many cases, the risk level will vary among categories. The audit risk level will be based on the highest level of risk assigned to any one individual category. For example, if Agent Approval Status, Toxicity, Administration and Storage, Clinical Procedures and Participant Health Status are all low risk, but the Ability to Provide Informed Consent meets the high-risk criteria because the study population is under the age of 10, the audit risk level assigned to the protocol is High. This will ensure that the audit is performed with an adequate level of source data verification.

4. ADDITIONAL INFORMATION

Please send questions and comments to the DMASC Audit Team at Audit_CP-CTNet@frontierscience.org.

5. REFERENCES

Resource	ID	Location
CP-CTNet Protocol Audit Risk Level Assessment Form	CP-CTNet FORM003	Program Resources
Oversight of Clinical Investigations —A Risk-Based Approach to Monitoring U.S.	Website	https://www.fda.gov/media/116754/download

Resource	ID	Location
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		
Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products MRC/DH/MHRA Joint Project Version 10th October 2011	Website	https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf

6. APPENDICES

None