

Guidance on Advanced Practice Providers Writing Study Agent Orders for NCI/CTEP-sponsored Clinical Trials

Background of CTEP Policies:

The Cancer Therapy Evaluation Program (CTEP) of the Division of Cancer Treatment and Diagnosis (DCTD)/National Cancer Institute (NCI) is responsible for implementing and monitoring the clinical development of investigational therapeutic anticancer agents. CTEP's policies are intended to ensure patient safety while providing the National Cancer Program with the most effective new agent development program as possible. Some policies reflect the regulatory requirements of the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS). Others have been developed based on policies at the NCI level, consensus among CTEP staff, the NCI Board of Scientific Advisors, and leaders in the community of clinical investigators. Specific policies and procedures continue to evolve; through these policies, CTEP, DCTD, and NCI aim to provide a flexible, responsive system within the constraints imposed by regulation and the program's size and scope. CTEP is aware of the expanding role of advanced practice providers (APPs) in caring for patients on NCI-sponsored clinical trials at sites and recently conducted a review of the CTEP policy.

The Evolving Role of APPs in Oncology Care and Clinical Trials

With the increasing complexities of delivering precision medicine in oncology, the role of APPs has grown in many oncology settings across the country, including at many NCI funded clinical trial sites. The Advanced Practitioner Society for Hematology and Oncology (APSHO) defines APPs to include nurse practitioners, physician assistants, clinical nurse specialists, advanced degree nurses and pharmacists. APPs are projected to become an essential part of the oncology team as the US population ages and the predicted shortage of oncologists unfolds.¹

In 2018, the American Society of Clinical Oncology (ASCO) in collaboration APSho, the American Academy of PAs, the Association of Physician Assistants in Oncology, and the Oncology Nursing Society (ONS) collaborated on a study of APPs in US-based cancer care delivery.² They identified over 5,300 APPs and concluded that the numbers may be well over 7,000 across the country. Multiple Principal Investigators (PIs) grantees from the NCI's Experimental Therapeutics Clinical Trials Network (ETCTN), the National Clinical Trials Network (NCTN) Lead Academic Participating Sites (LAPS) and the NCI's Community Oncology Research Program (NCORP) contacted NCI to share their experience as to how APPs are facilitating their site's ability to manage more complex NCI trials. Cancer centers with large numbers of APPs have created institution policies and credentialing processes to allow APPs to write orders for antineoplastic agents, in non-NCI clinical trials, without the need for a physician cosignature.

CTEP's Investigator Handbook (2014 version 1.2) only allows APPs to write study agent orders in NCI trials, if a qualified physician investigator cosigns their orders.³ Many sites asked the NCI to re-consider this need to require a cosignature, given many centers have created institutional policies to allow them to write study agent orders independently as many state practice and licensure laws offer this role expansion. PIs expressed that APPs should have the ability to practice to the full extent of their state licensure and institutional policies and that this would greatly enhance their ability to conduct NCI trials

¹ Advanced Practitioner Society for Hematology and Oncology, <https://www.apsho.org/page/AboutUs>

² Bruinooge, SS, et al, Journal of Oncology Practice, Vol. 14, issue 9, September 2018. PMID: 30629907

³ A Handbook for Clinical Investigators Conducting Therapeutic Clinical Trials Supported by CTEP, DCTD, NCI, 2014, (Version 1.2) https://ctep.cancer.gov/investigatorResources/investigators_handbook.htm

at their sites. Given these recent issues, NCI conducted a survey to better understand the evolving role of APPs across the three large NCI clinical trials networks.

CTEP APP Survey: Summary of Key Results

- There were 80 clinical trial site responses to an electronic survey that was conducted in March 2021 of grant PIs in the ETCTN, NCTN LAPS, and the NCORP. One hundred percent responded “yes” that their site has APPs involved in cancer care for their patients with many sites having over 30 APPs in their cancer center.
- Other key findings include:
 - Over 90% of sites have APPs involved in caring for patients on phase II and III clinical trials, with 68% involved in phase 1 trials.
 - Over 30% reported that their site allows APPs to write new antineoplastic orders with physician cosignature in clinical trials.
 - 42 (60%) of 71 respondents said APPs were involved in some way with ordering agents for trials (*either NCI or non-NCI trials, and either with or without a physician cosignature*)
 - Almost 60% of sites said that if NCI changed its policy to allow APPs to write antineoplastic orders for NCI trials without a cosignature, including investigational agents, they would be more involved in NCI treatment trials which they suggest may lead to improved study enrollment and retention of patients on study.
- During May-June 2021, the APP survey results were shared during virtual meetings with NCTN, NCORP, and ETCTN leadership and PIs. Discussions included the key role APPs play in serving as Non-Physician Investigators (NPiVR) on site clinical trial teams. The consensus among the leadership and investigators was overall support to allow APPs to write study agent orders without a physician cosignature at sites that have institution policies supporting this role expansion.

Revision of CTEP Guidelines for APPs and Ordering of Study Agents

Based on the survey results and review with NCI grantees, CTEP will revise the current policy. Patient orders for study agents including investigational (IND) agents, may be written by APPs that are registered in NCI’s Registration and Credentialing Repository (RCR) as NPiVRs without a physician cosignature, and are qualified per their institution’s policy, local and state laws and regulations, including requirements as mandated for international sites. (“Study agents” will be the inclusive term used throughout this document and related materials to mean any agents used in a clinical trial, including IND and standard of care agents).

Clinical trial site institutional policies must include information about their APP credentialing process for writing study agent orders. Sites must also include in their institution policies how the Guidelines for Good Clinical Practice (GCP) requirements for APPs are being met. This includes that a qualified physician investigator is responsible for all trial-related medical decisions, including providing oversight of APPs in their capacity of ordering study agents.⁴ The policy should be stored in the site’s regulatory files and be available for review.

⁴ International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2), November 9, 2016
<https://ichgcp.net/>

CTEP Implementation Plans

- CTEP Investigator’s Handbook has multiple sections under review and prior to having the new APP policy added, this document will serve as a separate policy document allowing qualified APPs to write study agent orders at qualified sites without the need for a physician cosignature; this document will be available on the CTEP website at:
 - https://ctep.cancer.gov/investigatorResources/investigators_handbook.htm
- CTEP CTMB audit guidelines have been updated to be consistent with this policy and shared with appropriate audit committees.
- The IND Prescribing task on the DTL template from the CTSU website has been updated to allow NPIVRs to hold this task.
- DTL templates for ongoing studies will be modified to allow NPIVRs to hold the IND Prescribing task.

Implementation for Lead Protocol Organizations:

1. Lead Protocol Organizations (LPOs) need to be aware that the Delegation of Tasks Log (DTL) template will allow APPs who are qualified and who are registered as NPIVRs to write study agent orders without physician cosignature.
2. LPOs will need to inform and educate site investigators and APPs about this policy change and will need to update LPO documentation to support this change.
3. LPOs and NCI will need to collaborate to enhance awareness of this policy change to sites.
4. LPOs collaborating with an industry partner that does not support APPs writing study agent orders when they are supplying the study agent, will need to have a study specific DTL with this limitation.

Implementation for Clinical Trial Sites:

1. Clinical trial sites will need to have institutional policies that include APP credentialing processes for writing study agent orders in clinical trials. Institution policies should include that a qualified physician investigator is responsible for all trial-related medical decisions according to GCP requirements, which includes oversight of qualified AAPs in their role of writing study agent orders. These institutional policies should be stored in the site’s regulatory files and be available for review.
2. Sites will need to ensure that APPs qualified to write study agent orders without a physician cosignature register and maintain an active registration status in RCR as an NPIVR and renew their registration and qualifications annually. RCR verifies professional licenses, including those for APPs, during the review process.
3. Site Clinical Investigators (CIs) will identify APPs qualified to write study agent orders on site DTLs, where required. For active or new studies with DTLs, the DTL Administrator or CI for each protocol must add the task of “IND prescribing” for each qualified NPIVR. In addition, the CI must sign the DTL for this new task assignment prior to the APP writing orders for study agents.

Questions:

- Questions regarding the APP policy should be sent to: NCICTEPComments@mail.nih.gov
- Questions related to adding APPs to the DTL may be sent to the CTSU Help Desk at CTSUcontact@westat.com