DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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National Cancer Institute
Bethesda, Maryland 20892

MEMORANDUM

DATE: May 24, 2022

TO: Principal Investigators and Operations/Statistics Offices of NCI CTEP-Supported Clinical Trials Networks & Consortia and DCP-Supported NCI Community Oncology Research Program (NCORP) Research Bases

FROM: Meg Mooney, MD, Associate Director, CTEP, DCTD, NCI
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SUBJECT: Guidance for Imaging Adjustments for Patients on Clinical Trials at Sites Affected by the Current Shortage of Contrast Dye Media

The purpose of this memorandum is to provide background, management information, and guidance to the Cancer Therapy Evaluation Program (CTEP) and NCI Community Oncology Research Program (NCORP) clinical research community affected by the current X-ray contrast media shortage which is predominantly impacting contrast enhanced computed tomography (CT) procedures.

Recently, the FDA [1] reported "shortages of GE Healthcare's iohexol and iodixanol intravenous contrast media products for computed tomography imaging. In an April 19 letter to customers, GE Healthcare said it was rationing orders for its iohexol products after a COVID-19 lockdown temporarily shut down its production facility for iodinated contrast media in Shanghai, China."

This situation is affecting healthcare systems and imaging providers across the US and in other countries that utilize these agents. Due to the magnitude of the current supply shortage, other FDA approved iodinated contrast media may be used, but they may not be able to be rapidly acquired to compensate for the shortage even though their supply and production was not affected. As reported by Reuters [2], GE has been able to restart production and distribution from its facility in Shanghai and increase production at another one of its facilities in Ireland; however, the supply shortage is not expected to be resolved before the end of June 2022 at the earliest.

Most contrast enhanced CT imaging for patients enrolled in CTEP and NCORP studies is performed within usual clinical practice standards. Clinical trial protocols detail and reference anticipated timepoints for imaging, and while contrast enhanced CT may be the preferred or suggested imaging modality, the imaging decision is left up to the local clinical care team in the majority of protocols [3]. Clinical trial protocols may also already allow alternative imaging approaches.

General Guidance:

- Many healthcare systems and imaging providers affected by the current shortage have initiated a tiered system to manage both scheduling and use of contrast dye for medical imaging and procedures. Depending on the local situation, alternate imaging approaches may be chosen, imaging may be performed without contrast if medically appropriate, or imaging may be deferred.

Imaging for eligibility and measurement of disease for study endpoints appear to be the most critical aspects of trial conduct being affected by the current shortage. However, the local situations for sites appear to be vastly different. Following the local practice guidelines for imaging being instituted for clinical care of all cancer patients during this temporary shortage would be the appropriate approach/management plan for clinical trial patients as well.

- For clinical trials supported by the central NCI Imaging and Radiation Oncology Core (IROC), particularly under the NCI National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP), IROC stands ready to work with the Operations Offices and clinical trial leaders to review and/or issue trial specific guidance to help mitigate challenges and provide trial protocol-specific guidance upon request. **NCTN Groups and NCORP Research Bases, as well as other CTEP-supported trial networks that have trials covered by IROC, are encouraged to contact IROC for guidance on specific trials or for special circumstances when needed [4].** Other clinical trial network programs with trials not covered by IROC should contact their Lead Protocol Organizations (LPOs) for specific situations when needed as well.

- If a study protocol **does not** explicitly require imaging with IV contrast media, imaging performed without contrast or alternative imaging approaches (e.g., MRI) could be used if considered medically appropriate per the clinical practice guidelines instituted by the local site during the current shortage. In this situation, these imaging adjustments would **not** be considered protocol deviations.

- If a study protocol **does** explicitly require imaging with IV contrast media and/or explicitly excludes other imaging approaches, investigators should still follow the appropriate clinical practice guidelines instituted at their sites during the current temporary shortage, but these imaging adjustments would need to be reported as protocol deviations per usual reporting standards. The same would be required for imaging deferred outside protocol-specified timelines due to the shortage. It is hoped that most of these adjustments would be considered minor protocol deviations (i.e., alternative procedures that do not impact patient safety, compromise overall integrity of study data, or affect the willingness of patients to participate in the trial). However, it is possible that alterative procedures may be unavoidable and result in major deviations and should be reported as such if they occur.

- Investigators at local sites experiencing a shortage of IV contrast media should inform the appropriate Institutional Review Board (IRB) of record of this unexpected shortage for their trial patients. For sites using any of the NCI Central IRBs (CIRBs) as the IRB of record for their trials, this memorandum is being forwarded by CTEP and NCORP to the NCI CIRB Operations Office for notification on behalf of all sites.

References:

[1] **https://www.aha.org/news/headline/2022-05-10-fda-reports-shortage-ge-contrast-media-ct-imaging**

[2] **https://www.reuters.com/business/healthcare-pharmaceuticals/ge-unit-boosts-medical-dye-output-china-covid-lockdown-cuts-supplies-2022-05-10/**

[3] **https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Contrast-Media-Shortage**

[4] IROC has opened a central contact e-mail to help with communication: contrastquestion@IROCOhio.org