Ensuring Institutional Compliance with ClinicalTrials.gov Registration and Reporting Requirements

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Problem/Issue Statement
Research is the conduct of systematic investigations, review of study materials and sources, and establishment of previously learned facts, in order to reach new conclusions. Especially when human subjects are involved, these efforts must be transparent and accessible in order to aid with recruitment, provide feedback to those who generously participate in research, ensure the validity of the results, and make the data available for other research so that the world may continue to benefit from previously learned facts.

FDAAA 2007 enacted legislation to ensure that certain research – applicable clinical trials – be registered and results reported on a publicly available database – ClinicalTrials.gov, for the very purpose of formalizing human subject research and results tracking in the United States. The ICMJE has applied a broader definition of applicable trials, and recommends that more than 1,000 subscribing journals apply this definition when reviewing submissions for publication. More recently, CMS rules require submission of an NCT number with all research-related billable services. However, compliance with the regulations and rules varies widely by and within institutions where research is conducted. Ultimately, sponsors of applicable clinical trials will be held accountable for compliance, and enforcement of the regulations is anticipated.

The intent of this poster is to describe for other organizations the process we have undergone to ensure institutional compliance with FDAAA 2007 regulations pertaining to registration and reporting of applicable clinical trials, as well as with the new CMS rule related to billing for services conducted in a qualifying clinical trial.

CSMC Research Program Audit
In 2013, our Compliance Team conducted a comprehensive institutional audit for compliance with FDAAA 2007 requirements, as well as ICMJE expectations, regarding registration, updating and results reporting on ClinicalTrials.gov. Most applicable clinical trials conducted at our site are sponsored by industry or cooperative groups, and CT.gov registration, updating and results reporting is the responsibility of the sponsor. However, an average of 25 studies approved each year are investigator-initiated and are deemed “applicable” by either the FDAAA regulations or the ICMJE standards. Our baseline audit looked at 50 active clinical trials approved since FDAAA was enacted and that were investigator-initiated (for which the CT.gov requirements are the investigator’s responsibility). These are the trials for which the institution, as the employer of the investigator-sponsor, may be at risk for non-compliance.

In addition, the new CMS rule (effective January 1, 2014) made it mandatory to report a clinical trial number (generated through CT.gov registration) on claims for items/services provided in clinical trials that are qualified for coverage. Thus, our audit also included a review of all active studies that were deemed qualifying clinical trials through our Medicare Coverage Analysis (MCA) process. A total of 333 studies were included in this review, some of which overlapped with the applicable clinical trials audit.

*The applicable trial determination can be nuanced and subjective in certain cases.*

Findings
The general findings of the baseline applicable clinical trials audit indicated we were in full compliance with registering 54% of our investigator-initiated applicable trials on CT.gov. For studies requiring registration under FDAAA, 82% were registered. For studies requiring registration under ICMJE standards, however, only 32% were registered. Our institutional policy adheres us to the broadest definition of an applicable clinical trial – the ICMJE definition – for registration purposes, so that CSMC investigators will not be precluded from later publishing results of their research. FDAAA also requires updates and results reporting in CT.gov. However, 22% of studies registered in compliance with FDAAA did not have any updates posted, though they should have posted updates based on current study status. None of the FDAAA applicable trials were due to report results at the time of the audit. Our institutional policy requires posting updates and results on CT.gov only for studies meeting the FDAAA definition of an applicable clinical trial.

The review of CMS qualifying clinical trials yielded a 90% compliance rate for CT.gov registration.

Overall, we found that there was a need for enhanced educational efforts, infrastructure and monitoring to ensure institutional compliance on an ongoing basis. In addition, the new CMS rule required us to put a system in place to ensure the NCT number issued upon completion of CT.gov registration would be captured for billing purposes.

Graphical Summaries of Findings

Implementation of Changes
To address the findings of our internal audit, we implemented the following changes:

- Follow-up with individual investigators/study teams that were found to be not compliant.
- Discussion of CT.gov registration and results reporting during post-approval monitoring and compliance activities (i.e., routine audits, site initiation visits, informational meetings, etc.), as well as at special educational workshops.
- Automated reminders added to our online application system to provide notifications to investigators/study teams of applicable clinical trials/qualifying clinical trials requiring CT.gov registration (and updating/results reporting, as necessary);
- Ongoing monitoring of applicable/qualifying trials’ compliance with CT.gov registration on a regular basis, through enhancements to our online application system that allow us to capture the NCT number for each trial;
- Providing NCT numbers to our Finance Department for billing of research procedures in qualifying clinical trials; and
- Conducting annual internal audits to ensure compliance improvement on a wide scale.

Since the audit, we are currently at 100% compliance for registration of applicable trials approved at our site in 2014.

Future Program Enhancement Plans
Findings from each annual internal audit may involve further programmatic changes. These might include more hands-on HSPP office involvement in assisting investigators/study teams with registration and results reporting, or mandatory training for certain investigators/research teams.

Suggestions for Other Sites
All sponsors conducting applicable clinical trials are subject to the FDAAA 2007 regulatory requirements for registration and results reporting on CT.gov. Substantial penalties from expected enforcement may include revocation of federal funding and/or refusal to publish data resulting from non-compliant trials. Effective January 2015, billable services for CMS qualifying clinical trials will be returned without processing if not accompanied by an NCT number. Getting a handle on and rectifying non-compliance for which institutions are at risk before enforcement becomes the norm is a wise investment of resources.

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