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August 6, 2007

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Re: Proposed Decision Memo for Clinical Trial Policy (CAG-00071R2)

Dear Dr. Phurrough:

On behalf of the Association of Academic Health Centers (AAHC), I am pleased to provide comments on the Proposed Decision Memorandum for Second Reconsideration of the Clinical Trial Policy, renamed the Clinical Research Policy (CAG-00071R2), issued by the Centers for Medicare & Medicaid Services (CMS) on July 19, 2007. I wish to applaud the agency for seeking to improve and clarify issues and for addressing many of the concerns raised by the academic health center community during the first reconsideration of this policy last year.

The AAHC, a national, non-profit association representing more than 100 of the 133 academic health centers nationwide, is dedicated to improving the nation's health care system by mobilizing and enhancing the strengths and resources of the academic health center enterprise in health professions education, patient care, and research.

A second reconsideration of the clinical trial policy (CTP) is essential given the enormous impact of clinical trials not only on Medicare beneficiaries but also on all people suffering from illness and disease. Our hope is to ensure that clinical research and the advances that emerge from this vital endeavor both continue and thrive in the U.S. with the help and support of CMS.

With regard to the proposed changes:

- The AAHC is pleased to note that clinical research has been defined to align with the definition in human subjects regulations and the NCD renamed to clinical research policy (CRP) to include all clinical research.
- The AAHC is also pleased with the clarification of the definition of routine clinical services and the examples provided.

- Finally, the AAHC applauds the agency for clarifying usual patient care as including routine clinical services *and* investigational clinical services in clinical research when the investigational clinical services would be covered outside of the clinical research.

The AAHC appreciates the benefits that the new CRP will provide the academic health center enterprise in enrolling increasing numbers of Medicare beneficiaries. However, the AAHC would caution that overall the proposed policy and standards does place increased, if not excessive, administrative burdens on institutions, sponsors, and principal investigators (PIs) that when taken together could slow the pace and growth of clinical research in the U.S.

To ease the transition from the current Clinical Trial Policy to the new Clinical Research Policy (CRP) and to enhance the final policy:

- The AAHC recommends that all federally-sponsored studies that have undergone review at the federal level (e.g., under IND or FDA approvals) be viewed as satisfying the standards represented by bullets 1-5.
- The AAHC recommends that CMS provide illustrative examples of how each standard should be addressed.

To facilitate analysis, discussion, and implementation, the AAHC strongly recommends that the policy be reformatted to ensure a user-friendly document, which includes standards clearly numbered and placed in a rational order that takes account of the billing process and the implementation needs of institutions.

The AAHC asks that the following specific issues be carefully addressed by CMS:

New Proposed Standards for Clinical Research to Support Medicare Coverage of Items and Services

The AAHC would appreciate some clarification and change in some of the specific new standards for clinical research to support Medicare coverage of items and services. With regard to:

Standards bullet #3: The research study does not unjustifiably duplicate existing studies.

- The AAHC recommends that CMS clarify what is meant by “the research study does not unjustifiably duplicate existing studies.”
- The AAHC recommends that existing studies be defined as “published studies” so as not to create confusion in the research community given there are concerns about what CMS is seeking in the extent and breadth of documentation for this standard.

Standards bullet #6: The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is FDA-regulated, it also must be in compliance with 21 CFR Parts 50 and 56.

- The AAHC recommends that CMS accept the submission or representation of an approval by a registered IRB of an institution holding a Federal-wide assurance as adequately addressing this standard.

Standards bullet # 8: The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards.

- The AAHC does not know what is meant or intended by this standard. It appears that CMS should list this standard which addresses the written protocol and notes that "the research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards," either "first" or "last" in this list. As currently drafted, this standard is misplaced and thus repetitive in asking again for the protocol to speak to all the Medicare standards which have already been addressed. What is CMS envisioning with this standard? Clarification is needed given the many differing views in the academic health center community on how to operationalize this standard.

Standards bullet #9: The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Studies of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR 312.81(a) and the patient has no other viable treatment options.

- The AAHC recommends that CMS change this standard to read: "The clinical research study is not designed to exclusively test toxicity or disease pathophysiology. Research studies, including some Phase I trials with protocols that commit to measuring therapeutic outcomes as one of the objectives, may meet this standard if studies are for acute conditions that pose substantial public health risks or diseases that are chronic, life threatening, or debilitating." Such wording would ensure that Phase I cancer trials that are so significant for Medicare beneficiaries are covered.

Standards bullet #11: The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than three (3) years after the end of data collection.

- The AAHC strongly urges that CMS include a statement that clearly specifies that this policy should not require any standards to be met that cannot be met before services are rendered.
- The AAHC recommends that CMS should delete the portion of this standard requiring fulfillment of the method and timing of public release of all pre-specified outcomes.

Dr. Steve Phurrough

Page 4

August 6, 2007

- Academic health centers and their PIs are motivated to publish research results independent of any requirement or condition for publication which cannot be met until years after the parties have performed and met their contract obligations for services.
- This condition is not a manageable standard; from an administrative standpoint, this standard opens academic health centers to substantial risks of liability.
- This standard makes it impossible to say all the standards are met and raises substantial concerns throughout the academic health center community. The standard asks institutions to attest to having satisfied a future condition over which they have little or no control.

Coverage of Usual Patient Care and Coverage with Evidence Development

The AAHC would like to note that it is not uncommon for an institutional consent form to indicate there are no charges to the study participant. In practice, services are often billed to insurance with an understanding that the sponsor will pay if insurance does not.

The proposed policy notes that "Medicare does not cover usual patient care when it is provided free to the Medicare beneficiary or when the study sponsor agreement with an investigator site or the informed consent documents provided to the patient specify that the clinical service will be provided free to all enrollees." The AAHC would like clarification on whether institutions would have to revise consent forms and delete mention of "free" or that Medicare cannot be billed if a sponsor is willing to pay for denials.

The AAHC is concerned that such language overlaps with the Medicare secondary payer (MSP) rules. While we realize that it cannot be addressed under this policy for administrative reasons, we would like to urge that CMS open a dialogue on this issue as soon as possible given that MSP rules continue to be problematic and hamper the ability of institutions nationwide to meet the spirit and letter of compliance.

Approval Process

The AAHC recommends that CMS set an extended period for implementation of the new policy. The AAHC suggests CMS provide a minimum of six months from the date of release of the policy until its implementation as institutions will need to create policies and procedures, educate staff, and most likely change current IT management and billing systems to allow for the capture of data pertinent to this policy. The proposal adds confusion and administrative burden without clearly identifying the intended value or benefit to the academic community or the public.

The AAHC believes that the proposed new plan related to posting certified studies on the CMS website and in the Federal Register is unnecessary and redundant. Adding the new proposed addition to the ClinicalTrials.gov number will require alterations to billing processes for all claims providers throughout the nation. The ramifications of this proposed posting plan could be significant with untold difficulties in determining which submitted claims are denials and which are not.

It has been the experience of the academic health center community that anything to do with changes to claim forms has been fraught with problems over the years. Thus,

- The AAHC recommends that CMS and the Part A and Part B Medicare contractors develop a process for denial of claims which would not place additional burdens on institutions to monitor the timing of the certification process.

The requirement by CMS for discussion on how the study meets each of the standards in this policy has been described as a "time consuming nightmare" by administrators and PIs nationwide because it is a redundant exercise. As written, this standard would mean that PIs would have to rewrite portions of the protocol in a discussion format to CMS.

The AAHC is also concerned about implementation for CMS and how the agency can ensure that bottlenecks do not occur in the system to possibly grind clinical trials to a halt. Therefore, the AAHC recommends a template checklist option.

Posting on the CMS website and annotating the certification on the ClinicalTrials.gov website would suffice to meet the needs of the academic health center community. If the final CRP requires both ClinicalTrials.gov and CMS registration, then the AAHC recommends that CMS commit to ten business days from the receipt of applications for the application to be viewed as complete and posted on the CMS website.

Exceptions

The proposed policy says Medicare will pay for "covered services in a clinical research study."

- The AAHC recommends that for the sake of consistency with the rest of the document, and to avoid confusion, the term "usual patient care" be used in this section rather than "covered services."
- The CMS chief medical officer is given authority to deny payment for "covered services" in a clinical research study that does not meet the criteria outlined in the policy or that jeopardized the health/safety of beneficiaries.
 - The AAHC suggests that a timeframe for such a determination be specified given that such a determination could occur years after the study has concluded, Medicare had been billed for services, and all parties had proceeded in good faith because all requirements for registering a study had been met.

Local Coverage Determinations

In terms of local coverage determinations, the AAHC recommends that CMS address issues of coordination between the agency and local Medicare contractors to ensure efficiencies in the system related to information submissions. CMS approval should be deemed to satisfy any duplicate information needed by the local contractors. In addition, the AAHC recommends that local contractors should not perform prospective review and approval if providers have the benefit of a process to ensure proper billing to third-party payers in clinical research trials.

Dr. Steve Phurrough
Page 6
August 6, 2007

Transition Plans

The transition plan is essential and the proposed plan is still confusing with the potential for unintended consequences that could hamper research efforts. Using the date of the first enrolled patient in a trial as the basis for applying the new policy will create significant and undue administrative burdens for academic health centers nationwide. The date of the first enrollment is not the milestone event in clinical trial administrative and billing processes. Using this marker may mean that studies that already have IRB approval will need to be re-reviewed and approved again by the IRB. All institutions track IRB approvals; few track enrollment dates. Thus, significant and unnecessary institutional transformations would be needed to meet the proposed standard.

The AAHC is not sure of CMS's intent on this standard and recommends that the policy implementation date be decided upon based on the date of initial IRB approval rather than the date of patient enrollment as currently proposed. The AAHC recommends that all studies with an initial IRB approval on or before the effective implementation date should be covered under the old Clinical Trial Policy and any studies without initial IRB approval be subject to the new Clinical Research Policy.

Please note that the AAHC recommendations go beyond questions of efficiency and productivity to speak to the larger research policy issues. Ultimately, the AAHC and CMS must ensure that the nation's clinical research is vibrant and effective. Otherwise, we run the risk of slowing advances in treatment for Medicare beneficiaries as well as all patients, diminishing the number of clinical researchers, and, as a result, dampening the vitality of the overall U.S. research enterprise and its preeminence in science. The AAHC stands ready to assist the CMS to ensure that appropriate, high quality regulatory requirements are developed and met.

Thank you for considering these recommendations which were developed by members of the AAHC's Forum on Regulation and the workgroup on education/external relations chaired by Samuel Tilden, MD, JD, LLM, deputy provost for human subjects research, research compliance officer, and professor of pediatrics at the University of Alabama at Birmingham. We have broad consensus on these issues and look forward to continuing to work with CMS to ensure successful implementation of the new policy.

Sincerely,



Steven A. Wartman, MD, PhD, MACP
President/CEO