MEETING MINUTES
OF THE
CENTERS FOR MEDICARE AND MEDICAID SERVICES
MEDICARE EVIDENCE DEVELOPMENT & COVERAGE
ADVISORY COMMITTEE

December 13, 2006

Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland

Medicare Evidence Development & Coverage Advisory Committee

December 13, 2006

Attendees

Chairperson
Alan M. Garber, M.D., Ph.D.

Vice-Chair
Alexander H. Krist, M.D.

Voting Member/Patient Advocate
Nancy Davenport-Ennis, B.A.

Voting Members
Wade M. Aubry, M.D.
Marc L. Berger, M.D.
Mark D. Grant, M.D., M.P.H.
Mark A. Hlatky, M.D.
Nora A. Janjan, M.D., M.P.S.A.
Bernard Lo, M.D.
Sanford J. Schwartz, M.D.
Jeremy Sugarman, M.D., M.P.H., M.A.

CMS Liaison
Steve E. Phurrough, M.D., M.P.A.

Consumer Representative
Linda A. Bergthold, Ph.D.

Industry Representative
Michael L. Ryan, Pharm.D.

Guest Expert Panelists
Barbara Alving, M.D.
Steven N. Goodman, M.D., M.H.S., Ph.D.
Cary Gross, M.D.
Steven A. Wartman, M.D., Ph.D.
Deborah Zarin, M.D.

Executive Secretaries
Janet Brock
Kimberly Long

Wednesday, December 13, 2006, 8:00 a.m.

The Medicare Evidence Development & Coverage Advisory Committee met on December 13, 2006, to discuss issues of concern from the public, questions posed by CMS, hear presentations, and make recommendations to refine the CMS policy regarding coverage in clinical trials.

The meeting began with a reading of conflict of interest issues, introductory remarks by Dr. Straube, Dr. Phurrough and Dr. Garber, and an introduction of the Committee.

CMS Presentation. Dr. Phurrough presented the panel with the current CMS clinical trial policy and areas of concern about the policy raised by staff or the public. He then presented changes that CMS has proposed for consideration by the panel, as reflected in the printed material that had been distributed.

Scheduled Presentations. The panel heard presentations from 13 speakers representing academic research centers, professional organizations, manufacturers and industry associations. The speakers commented and made recommendations concerning proposed changes to the CMS clinical trial national coverage determination (NCD).

Open Public Comments. Three members of the public who were not previously scheduled addressed the panel; they represented two manufacturers and a consumer interest group.

Questions to Presenters. The panel engaged in an extensive period of clarifying questions to various presenters.

Open Panel Deliberations and Voting. Following a charge to the committee by the chair, the panel conducted discussion among themselves and voted on each of the

questions 1 through 8. The results were recorded on individual tally sheets and compiled by staff. Further discussion was held among the panelists during the voting process.

Summary of the Recommendations.

Question 1. The panel was asked to consider options for the general standards which could include a broad definition of a good clinical study, use of the existing "highly desirable characteristics," and/or standards of good clinical research as defined in existing guidance documents and texts. The majority of the panel recommended the following general definition of clinical research: "Clinical research is the observation of events in groups of individuals who share a particular characteristic, such as a symptom, sign or illness; or a treatment or diagnostic test provided for the symptom sign or illness. Inferences are made based on comparisons of rates of predefined outcomes among groups. Procedures are in place to assure that the rights, safety, and wellbeing of study participants are protected." The majority of the panel recommended that this definition include types of studies and acceptable study designs. The majority of the panel recommended retaining the existing "highly desirable characteristics" to define a good clinical study with the addition of language that requires all studies to include written protocols.

Question 2a. There are currently three Medicare-specific criteria. The first is a statutory requirement and not a clinical study standard and will be removed. The majority of the panel recommended deletion of the standard about enrolling only patients with the diagnosed disease in interventional studies, and revision of the final to read, "The study must not be designed primarily to test toxicity or disease pathophysiology.

Phase I trials that have therapeutic intent as one of the objectives may meet the standard only if the disease is chronic, life threatening, or debilitating."

Question 2b. Five new Medicare-specific standards were posed. The majority of the panel recommended:

- the study must be registered on the ClinicalTrials.gov website; the study protocol must specify method and timing of public release of results regardless of outcome or completion of trial;
- the study must have explicitly discussed consideration of relevant subpopulations (as defined by age, gender, race/ethnicity, or other factors) in the study protocol; and
- a national coverage determination using coverage with evidence development (CED) may be used to define specific standards to qualify studies.

Question 3. The panel was asked to consider the criteria that studies must meet in order to be "deemed" to have met the definition of a good clinical study. The majority of the panel recommended that a study be "deemed" if:

- the study is reviewed and approved as scientifically sound and funded by a Federal agency;
- the study has been reviewed and approved as scientifically sound by centers or cooperative groups that are funded by a Federal agency;
- the study is conducted under an investigational new drug application (IND)reviewed by the FDA and authorized to proceed with the study if no deficiencies are identified by the FDA; and,
- the study has been required and reviewed by the FDA as a post-approval study.

Question 4. The majority of the panel recommended that IND Exempt studies be required to follow the same processes allowed under the revised Medicare Clinical Trial policy.

Question 5. The majority of the panel recommended that deemed status should not be conferred to studies that were approved but not funded by a Federal agency.

Question 6. The panel was presented with several examples of additional methods CMS might apply to approve studies for Medicare coverage. The majority of the panel recommended that any study required through a national coverage determination using coverage with evidence development (CED) to be approved for Medicare coverage. A majority of the panel also agreed that CMS should develop a mechanism to certify other entities to deem research studies. Examples of deeming entities include professional societies, private foundations, academic health centers, and university scientific review panels. The members urged that any process for approval of studies include representatives of the patient and provider community.

Question 7. The panel was presented with the following proposed language to clarify the definition of routine clinical services. "Routine clinical services include items and services that are: 1) available to Medicare beneficiaries outside of the clinical study, other than items or services that meet the definition of investigational clinical services; 2) used for patient management within the study only; 3) required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent); 4) used for the clinically appropriate monitoring of the effects of the item or service (e.g., blood tests to measure tumor markers); and 5) required for the

prevention, diagnosis or treatment of complications (e.g., blood levels of various parameters to measure kidney function).

The majority of the panel agreed that the proposed language does clarify the term "routine clinical services" when used in reference to the Medicare Clinical Trial policy.

Question 8. The majority of the panel recommended adopting the following definition of administrative services: "Administrative services are all non-clinical services such as investigator salaries; protocol development; recruiting participants; data quality assurance activities, statistical analyses; dissemination of findings; and study management. Administrative services are not covered."

Question 9. The majority of the panel recommended the CMS also adopt the following definition for investigational services: "Investigational clinical services are those items and services that are being investigated as an objective within the study for its effect on health outcomes including items and services involved in the control arm of the study. Investigational clinical services meeting one of the following conditions are covered.

- The item or service is currently available (covered) to the Medicare beneficiary outside the study
- The item or service is required through the NCD process for CED and is being evaluated for its effect on health outcomes
- (For non-coverage NCD)The item has been designated by the FDA as an HUD, has received HDE status and is the investigational item or service in a study that meets the requirements of the policy

- (No existing NCD) The item has been designated by the FDA as an HUD, has received HDE status and is the investigational item or service in a study that meets the requirements of the policy"

Adjournment. The meeting adjourned at 3:33 p.m.

I certify that I attended the meeting of the Medicare Evidence Development & Coverage Advisory Committee on December 13, 2006, and that these minutes accurately reflect what transpired.

Janet Brock

Janet Brock
Executive Secretary, MedCAC, CMS

I approve the minutes of this meeting as recorded in this summary.

Alan M. Garber, M.D., Ph.D.
Chairperson