

118th MEETING OF THE NATIONAL CANCER ADVISORY BOARD (NCAB)
MEETING OF THE SUBCOMMITTEE ON CLINICAL INVESTIGATIONS

May 22, 2001
1:00 p.m. - 2:00 p.m.

Welcome/Opening Comments – Dr. Larry Norton

Dr. Larry Norton chaired the meeting of the Subcommittee on Clinical Investigations with Dr. Ellen Feigal, Deputy Director, Division of Cancer Treatment and Diagnosis, serving as Executive Secretary. The two agenda items were: 1) preliminary results of a short study conducted on how widely the currently existing NCI policy related to access of data from the Data Safety Monitoring Committees (DSMC) is known; and 2) impact on institutions of the newly broadcast NCI document summarizing the essential elements of an adequate data and safety monitoring plan for clinical trials. Dr. Norton directed attendees' attention to three handouts as background material for the discussion: (1) the questionnaire given to Disease or Modality Committee Chairs of the Clinical Trials Cooperative Groups; (2) a copy of the Grant Policies Web page under the NCI Division of Extramural Activities Web site ([HYPERLINK](http://deainfo.nci.nih.gov/grantspolicies/index.htm) <http://deainfo.nci.nih.gov/grantspolicies/index.htm>)

<http://deainfo.nci.nih.gov/grantspolicies/index.htm> ; and (3) a document entitled "Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute."

Results of the Questionnaire for Determining Awareness of NCI's Policy on Data Safety Monitoring Committees (DSMC) by Various Members of the Clinical Trials Cooperative Groups – Dr. Larry Norton

Dr. Norton reviewed the results of a four-question study submitted to the chairs of Disease or Modality Committees of the Cooperative Groups. The purpose of the study was to determine their knowledge of NCI's policy on allowing access to information discussed at DSMC meetings. The study had a 64% response rate. Overall, approximately half of the Disease or Modality Committee Chairs recognized that they could request prepublished data, on a confidential basis, from the Cooperative Groups' DSMCs. Approximately one-quarter of the respondents said they may not make this request for planning of new clinical trials, and one-quarter did not know. For the second question, only one-third of the respondents knew that they could request data from an intergroup trial in which the respondent's group is participating from the DSMC of another NCI-supported Cooperative Group. A third of the respondents felt they were not able to request such data, and a third did not know. The third question addressed whether respondents felt that they could request data from DSMCs of trials in which the respondent's group was not involved. Only 17 percent of the respondents answered yes. For the fourth and final question of the study, 42 percent of the respondents felt that there was a difference in the review of requests for data depending on when during the patient randomization process such a request occurred. Overall, the answers to the questionnaires demonstrated a heterogeneity of knowledge of the rules and that a significant percentage of people responsible for or participating in the planning of clinical trials do not know

they can ask the DSMCs for these types of information. This study focused on the participants' knowledge of whether they could request the information; it did not address whether such requests would be approved.

Dr. Feigal commented that the results of the survey are preliminary, but they indicate that further educational efforts are needed and/or clarification of our NCI policy is needed. She felt that the first step is to discuss the study results with the Clinical Trial Cooperative Group Chairs at the upcoming June meeting. Dr. Norton concurred, and felt that a request for remediation should follow this discussion with the Group Chairs. Dr. Norton suggested that NCI or the Groups Chairs conduct a subsequent study to monitor effectiveness of the corrective intervention.

Issues Concerning Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute – Dr. Larry Norton

Dr. Norton introduced the second agenda item as a continuation of the discussion initiated after the NCAB presentation by Dr. Robert Wittes, Deputy Director for Extramural Science, and Director, Division of Cancer Treatment and Diagnosis, on: "Policy Update: Common Approaches to Early Phase Data Safety and Monitoring Practices." The requirements of the Data Safety Monitoring plan are detailed in the handout entitled Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute. Dr. Feigal mentioned that an update to the Behavioral section is available on the Web site, and she drew attention to the increasing oversight function that institutions must undertake in conducting clinical research. Dr. Norton initiated discussion by asserting that despite their importance, regulatory requirements could crush investigators' ability to conduct clinical trials, since these requirements already have an impact on the time investigators spend with patients. Moreover, institutions discourage doctors from performing clinical trials because of the hidden costs associated with these trials. Fewer younger doctors are encouraged by their institutions to initiate clinical trials. The multiple barriers to performing clinical trials have taken their toll, because the number of trials is decreasing every year.

A discussion ensued about the involvement of both doctors and patients in clinical trials. Dr. Susan Love felt that many clinical trials do not address significant questions and, therefore, do not generate patient or doctor enthusiasm. The suggestion was made to conduct some research on why patients who could be in clinical trials are not participating in such studies. The data generated could provide some insight as to the types of modifications needed to increase participation in clinical trials. Dr. Norton requested that Subcommittee members scrutinize the specifics of the Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute document, as well as the general issues concerning regulatory requirements, and provide some specific actions that can be brought to the Board.

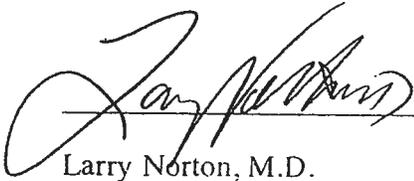
Dr. Wittes explained that NIH mandated the Institutes articulate and implement plans for data and safety monitoring of clinical trials. The NCI document is an attempt to provide guidance to the Institutes as they develop their plans. Although this document has now been formalized as "Version 1," it is undergoing a reiterative process within the

Institutes. NCI intends to provide funding to support this mandate; however, this will come out of the same pool of money used for research. Dr. Norton mentioned the importance of increasing awareness by the public and Congress of the hidden costs associated with clinical trials. Dr. Wittes noted that many of the requirements for grants reflect society's concerns over the processes and do not impact the actual science. Dr. Norton called for suggestions to address the critical issue of compliance with regulatory requirements and other hidden costs of clinical research.

Dr. Klausner felt that it would be helpful to have a feedback mechanism reflecting how NIH guidelines are being implemented by clinical investigators. Dr. Sharp suggested an audit of 20 sites to quantitate the number of manpower hours used to fulfill all the regulatory requirements.

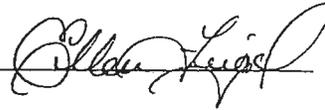
Conclusion

Dr. Norton ended the Subcommittee meeting stating that he hoped that specific actions would be derived from future deliberations and be brought back to the Board.



Larry Norton, M.D.

Chairman



Ellen Feigal, M.D.

Executive Secretary