NCI Clinical Trials Policy

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The NCI Clinical Trials Policy

I. Background and Overview

The National Cancer Institute (NCI) supports clinical research involving human subjects and must ensure compliance with federal regulations including procedures to protect the safety of all participants and ensure the validity and integrity of the data and results. This document summarizes the information NCI needs to effectively monitor clinical trials. Relevant information can be found on cited web sites, including the PHS 398 Grant Application, SF424 (R&R) Grant Application, and PHS 2590 Non-Competing Grant Progress Report and in NCI requests for proposals, applications, program announcements, and funding opportunity announcements (http://grants.nih.gov/grants/forms.htm). Links to appropriate URLs are included throughout for convenience.

NCI supports an extensive portfolio of clinical trials including traditional contract and grant-funded research, standing clinical trials networks and studies of investigational and non-investigational interventions. This research is occurring during an era of great promise in terms of the scientific understanding of the biology of cancer and the availability of promising new molecularly-targeted agents. However, the scope, size and complexity of the resulting clinical trials enterprise has created significant new challenges that require better coordination of research efforts and smarter incorporation of correlative laboratory studies to optimize the nation's investment in clinical cancer research. Toward that end, the NCI has undertaken an extensive review of the clinical and translational research that it supports utilizing extensive external expertise via two committees, the Clinical Trials Working Group (CTWG) and the Translational Research Working Group (TRWG). The recommendations of these groups will result in important changes in NCI's policies that will help maximize the return on that investment. The first set of recommendations, from the CTWG, is reflected in NCI's Clinical Trials Policy as described below. This policy addresses the protection of human research participants in NCI-supported clinical trials, efforts to safeguard the integrity of the data that results from this research, and measures to enable effective monitoring of the research.

In the future, NCI's large clinical trials especially phase 3 trials, will be prioritized through disease specific steering committees. These steering committees are designed to facilitate the sharing of ideas among a broad range of clinical investigators, basic and translational scientists, NCI staff, community oncologists and patient advocates in the development of clinical trial concepts. Participation in disease specific steering committees, working groups, task forces, and/or focus groups, as recommended by the CTWG, will be a critical component of the development and prioritization of phase 3 clinical trials. As part of the CTWG Initiatives, the disease specific steering committees will organize periodic State-of-the-Science meetings to: 1) identify critical questions and unmet needs, 2) prioritize key strategies and future concepts to test, and 3) facilitate innovation. Based on input from the State-of-the-Science meetings, the disease specific steering committees will develop strategic priorities for future phase 3 trials and disseminate these priorities to the relevant oncology communities. Consequently, investigators who lead clinical research trials are expected to participate in the new prioritization and approval processes.

In the long term, the NCI Clinical Trials Policy will apply to all NCI-supported clinical trials including single site, multicenter, domestic, multinational, and international clinical trials. Initially, however, the policy is directed at clinical trials of pharmacologic, biological, surgical and radiation interventions, beginning with phase 3 trials and followed by phase 2 and phase 1 studies.

NCI's Clinical Trials Policy delineates the awardee's responsibilities for submitting required data and documentation to NCI (and other NIH offices, as applicable). The policy will be attached to the notice of award or addressed in the terms of contracts. Once notified of the award, the responsible NCI program or project officer will advise the awardee to begin the submission process. Initially, all submissions required by the NCI Clinical Trials Policy must be forwarded electronically or by mail to the responsible NCI staff, program or project officer, grants management officer, etc., according to the procedures of the awarding division. As the initiatives of the CTWG become fully implemented, data will be required to be reported electronically to NCI in a manner compliant with the standards specified by the NCI Center for Bioinformatics (NCICB).

All clinical research supported by NCI must comply with federal, state and local regulations. All clinical research supported by NCI that is conducted outside the United States must also comply with the regulations of the host country as well as US federal regulations. Whenever the regulations differ between authorities, the more restrictive regulation will apply.

Applicants for clinical trials research funding must comply with these regulations, policies, and guidelines in the preparation of their applications and proposals.

Note: These terms apply to each identifiable trial supported by the award.

II. NCI Clinical Trial Terms of Award

Awardees must comply with the Clinical Trial Terms of Award that will be incorporated in their Notices of Grant Award or Contract. Potential applicants are encouraged to contact appropriate NCI program staff concerning these policies.

NCI's Clinical Trial Terms of Award is detailed in the "NCI Clinical Terms of Award" document which is a companion to this document.

III. Requirements for Investigators

Applicants for clinical trials research must assure adherence to applicable regulations and guidelines by including the following in the proposal or application.

A. Research Plan

B. Data and Safety Monitoring Plan for Clinical Trials

Effective monitoring is essential for all clinical trials involving investigational drugs, devices, or biologics and other clinical research perceived to involve more than a minimal risk, including research on licensed products. Data and safety monitoring is intended to provide oversight and review of the conduct of the research, interim safety and efficacy data, and progress towards achieving the goals of the study. Plans for data and safety monitoring must be included in any application or proposal for research involving more than minimal risk. Final decisions regarding the type of monitoring to be used will be made jointly by NCI and the awardee prior to study initiation.

1. NIH policies

   NIH policies require that applications and proposals for studies with more than minimal risk to human participants include a plan for data and safety monitoring. NIH policies also require that protocols for clinical trials include detailed plans for monitoring and that phase 3 trials have an independent data and safety monitoring board (DSMB).

2. NCI policies

   Discussions with the responsible NCI program or project officer regarding appropriate data and safety monitoring and approval of the final monitoring plan by NCI will occur before patient enrollment begins and may include discussions related to the following examples from the NIH policy:

   - Phase 1: A typical phase 1 trial of a new drug or agent frequently involves relatively high risk to a small number of participants. The investigator and occasionally others may have the only relevant knowledge regarding the treatment because these are the first human uses. An institute may require the study investigator to perform continuous monitoring of participant safety with frequent reporting to institute staff with oversight responsibility.

   - Phase 2: A typical phase 2 trial follows phase 1 studies, and there is more information regarding risks, benefits and monitoring procedures. However, more participants are involved and the toxicity and outcomes are confounded by disease processes. An institute may require monitoring similar to that of a phase 1 trial or supplement that level of monitoring with individuals with expertise relevant to the study who might assist in interpreting the data to ensure patient safety.

   - Phase 3: A phase 3 trial frequently compares a new treatment to a standard treatment or to no treatment, and treatment allocation may be randomly assigned and the data masked. These studies usually involve a large number of participants followed for longer periods of treatment exposure. While short-term risk is usually slight, one must consider the long term effects of a study agent or achievement of significant safety or efficacy differences between the control and study groups for a masked study. An institute may require a DSMB to perform monitoring functions. This DSMB would be composed of experts relevant to the study and would regularly assess the trial and offer recommendations to the institution, awardee, sponsor or institute concerning its continuation.

3. NCI recommendations

   All NCI-funded and/or sponsored clinical research will be monitored commensurate with the degree of potential risk to study subjects and the size and complexity of the study. The NCI may recommend one of the following monitoring options:

   - The Principal Investigator (PI) – the study PI monitors the study with frequent reporting to the NCI.

- Independent Safety Monitor – a physician or other appropriate expert who is independent of the study and available in real time to review and recommend appropriate action regarding adverse events and other safety issues.

- Independent Monitoring Committee (IMC) or Safety Monitoring Committee (SMC) – a small group of independent investigators and biostatisticians who review data from a particular study for accuracy and completeness.

- Plans for assuring data accuracy and protocol compliance- Institutions should describe what quality-control procedures are in place for assuring data accuracy and completeness in studies funded by NCI.

  If an IND is in place, quality-control procedures are generally stipulated by the IND sponsor and may be simply referenced or summarized in the DSM plan. For studies not done under an IND, the institution should describe whatever procedures are in place to assure data integrity and protocol adherence.

- DSMB – an independent committee charged with reviewing safety and trial progress and providing advice with respect to study continuation, modification, and termination. The awardee may be required to use an established NCI DSMB or to organize an independent DSMB. All phase 3 clinical trials, including those studying licensed products, must be reviewed by a DSMB; other trials may require DSMB oversight as well.

  When a monitoring board is organized by the awardee, a description of the board including the roster and curriculum vitae for all participants must be approved by NCI before study initiation. The charter, operating procedures, or both, including proposed meeting frequency and plan for review of adverse events and management of potential conflicts of interest must be maintained by the awardee and provided to NCI upon request. Information on cumulative toxicities and recommendations regarding study continuance should be provided to the principal investigators to be shared with their IRBs.

4. Detailed policy and guidance for monitoring of clinical trials is available at the following URLs:

   - NIH Policy for Data and Safety Monitoring: http://grants.nih.gov/grants/guide/notice-files/not98-084.html
   - Further NIH Guidance on Data and Safety Monitoring for Phase 1 and Phase 2 trials: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html
   - Essential elements of data and safety monitoring plans for clinical trials funded by the NCI: http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines
     NCI Cooperative Group Data Monitoring Committee Policy (Phase 3 Trials): http://ctep.info.nih.gov/monitoring/index.html

C. Targeted Enrollment

A “Targeted/Planned Enrollment Table” must be submitted with the PHS 398 Grant Application and SF424 (R&R) grant application or contract proposal for most clinical trials

(excluding phase 1 toxicity trials). The table includes projected accrual and demographic information regarding the study population. Go to the Targeted/Planned Enrollment Table and links to other application forms on the PHS 398, SF424 (R&R), and PHS 2590 Web sites:

- http://grants.nih.gov/grants/forms.htm

IV. Submission Requirements

Before the actual conduct of the study, the awardee must submit the following as applicable:

A. Clinical Protocol, if Required by a Specific Funding Mechanism.

All versions of a protocol must be maintained by the awardee and must be submitted to NCI upon request.

B. Institutional Review Board or Independent Ethics Committee Approval

The awardee is responsible for maintaining all IRB or IEC notifications of protocol approval and submitting the material to the responsible NCI program or project officer as requested. This includes the name of the IRB or IEC and OHRP Federal-Wide assurance (FWA) number. Where other institutions are involved in the research, e.g., a multicenter study, each institution should obtain IRB or IEC approval of the protocol. Written documentation of approval from each institution must be maintained by the awardee and provided to NCI upon request and must include a copy of each IRB- or IEC-approved informed consent document identified by version number, date, or both.

Some countries have a national IRB or IEC for which protocol and informed consent approval may be required. This approval process may be in addition to or in lieu of local IRB or IEC approval. For countries with multiple levels of IRB review, written documentation of protocol approval from each IRB must be maintained and provided to NCI upon request, along with a copy of each IRB or IEC approved informed consent document, identified by version number, date, or both.

C. Data and Safety Monitoring

See section III.B. For information on Data and Safety Monitoring.

D. Investigational New Drug (IND) or Investigational Device Exemption (IDE) Requirements

All NCI-funded and/or sponsored research will be conducted in accordance and compliance with applicable federal regulations governing clinical research. Trials involving the use of investigational therapeutics, vaccines, or other regulated medical interventions will be conducted under a research protocol approved under a U.S. Food and Drug Administration (FDA) IND or IDE, and/or under the regulation of the appropriate regulatory authority in cases where the research is being conducted in a foreign country.

Note that, under certain circumstances, licensed products or devices used for a purpose other than that for which they were licensed may require an IND or IDE in accord with

applicable FDA regulations.

If the proposed clinical trial will be performed under an IND or IDE held by the NCI, then the NCI must approve the protocol and protocol related documents, such as the informed consent, and all protocol amendments before they are activated.

If the proposed clinical trial will be performed under an IND or IDE held by a sponsor other than the NCI, the awardee must provide NCI with the name and affiliation of the IND or IDE sponsor, the date the IND or IDE was filed with the FDA, the FDA IND or IDE number, any written comments from the FDA, and the written responses to those comments. The awardee must notify NCI if FDA, and/or other regulatory authorities, place the study on clinical hold and provide NCI any written comments from FDA, written responses to the comments, and documentation in writing that the hold has been lifted.

- In the case of a foreign regulatory filing, the awardee must provide NCI with written documentation from the regulatory body that the awardee is in compliance with local regulatory laws.
- Risk information regarding the intervention being studied (e.g., investigator's brochure, or information obtained through published literature review or other venue) must be maintained by the awardee and supplied to the NCI upon request.

For studies for which the NCI is not the IND or IDE holder, the investigator is required to follow all government regulations.

E. Recombinant DNA Advisory Committee

For clinical trials involving the deliberate transfer of recombinant DNA, and DNA or RNA derived from recombinant DNA into human research participants (human gene transfer), the awardee must provide NCI written documentation that the NIH Office of Biotechnology Activities (OBA) and Recombinant DNA Advisory Committee (RAC) review process has been completed and that institutional biosafety committee approval (from the clinical trial site) has been obtained. See the NIH Guidelines for Research Involving Recombinant DNA Molecules (http://www4.od.nih.gov/oba/Rdna.htm).

F. Requirements for Training in Human Subjects Protections

The awardee is responsible and must adhere to current government regulations for submitting written documentation to NCI that the awardee and all study staff responsible for the design or conduct of the research have received appropriate training in the protection of human subjects.

G. Other Requirements

The awardee must comply with all mechanism (e.g., N01, P01, P30, P50, R01, U01, U10, etc.) specific guidelines. Additional requirements may be determined on a case-by-case basis. NCI and the awardee must document the requests for and compliance with these additional requirements. The awardee must address in writing all safety, regulatory, ethical, and conflict of interest concerns raised by NCI staff to the satisfaction of NCI before participant enrollment can begin. Any resulting changes to an IRB/IEC approved protocol

must be reviewed and approved by the relevant IRB/IEC prior to participant enrollment.

The database of patient information accumulated in the course of treatment research, and the possibilities for large-scale collection of biologic samples with subsequent correlation of specific features with patient outcome, provide NCI-supported Clinical Investigators with unique opportunities to address scientific questions about molecular genetics, epidemiology, pathology, and other cancer-related topics. Such ancillary investigations can add considerable strength to the investigator's total scientific program and are encouraged.

Correlative studies are increasingly central to the interpretation of clinical trials data, particularly for studies of molecularly-targeted agents. Correlative science studies using laboratory or imaging markers or techniques for which NCI standards are established must adhere to those standards or present compelling justification for deviating from such standards. The Diagnostic Evaluations Branch of the Cancer Diagnosis Program (CDP) has provided guidelines for the design and development of correlative science studies. Correlative studies using novel laboratory markers or techniques for which standards do not yet exist must propose a set of validation standards to be used for the trial in question, and explain the rationale for the selected standards.

NCI Clinical Investigators are encouraged to collaborate with other NCI-funded programs. These collaborations may include advancing research ideas from pilot studies to phase 3 trials, providing correlative science services for NCI-funded studies, and participation in multi-site trials conducted throughout the NCI-supported clinical trials system.

V. Ongoing Reporting Requirements

Awardees must comply with all Clinical Trial Terms of Award throughout the course of the clinical trial. These requirements include the following.

A. Institutional Review Board or Independent Ethics Committee Actions

The awardee is responsible for maintaining all IRB/IEC notifications of protocol renewal, amendment, suspension, and termination for submission to NCI upon request. Where other institutions are involved in the research (e.g., a multicenter study), the protocol should be reviewed and approved by each institution's IRB/IEC. The IRB/IEC for each site will conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year, as described in 45 CFR 46.109. Documentation for all sites participating in multicenter studies will also be maintained by the awardee for submission to NCI upon request.

1. Continuing Review and Approval

The awardee is responsible for maintaining the following documentation for submission to NCI (program or project officer) upon request.

- Continuing IRB/IEC review and approval annually, at a minimum. A copy of the IRB/IEC letter of renewal.
- A copy of the current IRB/IEC approved protocol, identified by version number, date, or both (unless otherwise directed), as well as previously approved versions.

- A copy of the current IRB/IEC approved informed consent document, as well as previously approved versions.
- For countries with multiple levels of IRB/IEC review, written documentation of protocol review and approval from each IRB/IEC should be provided to the NCI, along with a copy of the IRB/IEC approved informed consent document, identified by version number, date, or both.

2. Amendment, Suspension, Termination

The awardee is responsible for maintaining documentation of any changes in IRB or IEC approval status for submission to NCI upon request, including the following:

- All amendments or changes to the protocol, identified by version number, date, or both. (Except in the case of imminent danger to participants, changes to the protocol must be approved by the IRB/IEC prior to clinical implementation.)
- All changes in informed consent documents, identified by version number, date, or both. (Except in the case of imminent danger to participants, changes to the informed consent form must be approved by the IRB/IEC prior to clinical implementation.)

The awardee is required to notify the NCI program director or project officer if any of the following occur:

- Unplanned termination or unplanned temporary suspension of patient accrual.
- Unplanned termination or temporary suspension of the protocol.
- Any change in IRB or IEC approval status.
- Any other problems or issues that could adversely affect the participants of the study.

Notification of any of the above changes must be made within three working days by email or fax, followed by a letter signed by the principal investigator and institution's business official detailing the change of status notification to the IRB or IEC. A copy of any IRB or IEC responses must also be provided.

3. Institutional Biosafety Committee (IBC) or the NIH Recombinant DNA Advisory Committee (RAC) Review

If a clinical protocol has been reviewed by an institutional biosafety committee (IBC) or the NIH Recombinant DNA Advisory Committee (RAC), the awardee must maintain information about the initial and ongoing review and approval if any and provide such documentation to NCI upon request.

B. Data and Safety Monitoring Reviews

The awardee will be responsible for maintaining documentation of ongoing data monitoring activities and will submit such to the NCI upon request.

NCI's Data and Safety Monitoring Guidelines for investigator initiated clinical trials may be found at: http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines, http://grants.nih.gov/grants/guide/notice-files/not98-084.html, and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

C. Safety Reporting Requirements

1. IND or IDE Reporting

The awardee must notify the responsible NCI program or project officer in writing if the FDA or other regulatory authorities place the study on clinical hold at any time during the conduct of the clinical trial.

If NCI holds the IND/IDE, then as the IND/IDE sponsor, it is NCI's responsibility to provide the FDA with safety reports of serious and unexpected adverse events that occur on trials that it sponsors. The awardee must report all adverse events to the appropriate NCI officials in compliance with the reporting instructions contained in the protocol for each clinical trial to ensure that NCI is able to meet its FDA reporting requirements.

Other adverse events documented during the course of the trial should be reported in accordance with the standard data reporting requirements established for the trial.

In case of specific problems or issues, the awardee will be required to respond in writing to specific concerns raised by NCI staff responsible for monitoring the trial in a timely manner as established by NCI staff on the basis of the seriousness of the issues or concerns.

2. Safety Reporting for Research not Performed under an IND /IDE, or Performed under an IND/IDE for Which NCI is NOT the Sponsor

Adverse events should be reported to the FDA in accordance with its procedures, with special attention to serious and unexpected adverse events.

D. Recombinant DNA Advisory Committee and Institutional Biosafety Committee

The awardee must submit copies of any adverse event and annual reports required by NIH Office of Biotechnology Activities and by the site IBC, if applicable. Safety reports must be clearly labeled as a "Safety Report" and must be submitted to the NIH Office of Biotechnology Activities (NIH OBA) and to the local Institutional Biosafety Committee within the timeframes set forth in Appendix M-I-C-4-b of the NIH Guidelines For Research Involving Recombinant DNA Molecules, http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html. Copies of all such reports will be maintained by the awardee and submitted to the NCI Program Officer if requested.

E. Requirements for Training in Human Subjects Protection

The awardee is required to submit documentation in the annual progress report that newly hired study staff, responsible for the design or conduct of the research, have received appropriate training in the protection of human subjects.

F. Inclusion Enrollment Reports

The "Inclusion Enrollment Report" includes cumulative accrual and demographic

information for all human subjects enrolled in the clinical research protocol. This report must be submitted annually. The annual submission of the enrollment report will coincide with each noncompeting renewal or annual progress report. Go to the Inclusion Enrollment Report and links to other application forms on the PHS 398 Web site.

G. Other requirements

The awardee must comply with all specific terms of award associated with their grant, cooperative agreement or contract. NCI and the awardee must document the requests for and compliance with these additional requirements.

VI. Additional Reporting Requirements

Summary clinical trials data from all NCI funded and sponsored trials will be submitted electronically at intervals based on the data reporting mechanism specified and in a format specified by NCICB reporting requirements. Data will include, but not be limited to, key demographics, treatment, toxicity and outcomes.

To help ensure patient safety and an optimal return on the nation's investment in cancer clinical trials, it is imperative not only that the completeness of data reporting be assured, but that sufficient capacity to monitor incoming data from all sponsored trials be present. Thus, as recommended by the CTWG and approved by the National Cancer Advisory Board (NCAB) in June 2005, the NCI is establishing a comprehensive database. This electronic database will contain complete, up-to-date information about the status of all NCI-funded and/or sponsored clinical research, regardless of drug development phase, type of intervention or treatment, study design, or program through which funding is provided.

For clinical trials supported by a grant or contract mechanism awarded by the NCI and for intramural clinical research, all data must be submitted in a manner compliant with the standards specified by the NCI Center for Bioinformatics (NCICB). These standards include but are not limited to the use of controlled vocabularies and common data elements as developed and defined through caCORE (http://ncicb.nci.nih.gov/NCICB/infrastructure). Specific content reporting requirements for the NCI trials data repository are being determined by NCICB in conjunction with the NCI Program staff, the CTWG and caBIG communities, and NCI leadership. Up-to-date information and details about these initiatives can be found at http://integratedtrials.nci.nih.gov and http://caBIG.nci.nih.gov. The NCI electronic database will be available to the scientific and clinical community with the appropriate level of clearance and coordinated with electronic submission requirements.

All trials entered into the database will be maintained in the database indefinitely, so that both active and completed studies will be included. Investigators will be required to submit data to NCI only once. The NCI will distribute data to all NCI staff that needs access. Reporting of required data will be a routine obligation for all NCI clinical trials, regardless of funding mechanism. Specific program guidelines will be updated to specify reporting requirements. Recruitment progress, indices of quality control, and related operational features must be reported at regular intervals to the NCI. Annual and final reports are required as with any grant or contract.

Registration of clinical trials (beginning with intervention phase 3 trials) on the caBIG database will be required within 21 days of activation. The database is required to be updated quarterly, or more often if the status of the trial changes.

To ensure the success of the implementation of this new reporting structure, the scientific community should contact their NCI Program Representative or staff from the NCI Coordinating Center for Clinical Trials (CCCT) for guidance and further clarification.

VII. Inquires

For additional information, please contact:

Clinical Trials Reporting Office
National Cancer Institute
2115 East Jefferson St., Mail Stop 8505
Rockville, MD 20852
Phone: 301-451-4384
Toll Free: 1-888-478-4423
Fax: 301-480-6641
Email: NCICTRP@mail.nih.gov

Live telephone support is available Monday to Friday, 8 a.m. to 8 p.m. Eastern Time, excluding federal holidays.

VIII. Additional Website References

Information on NCI Divisions/Branches: http://www.nci.nih.gov/aboutnci/organization/

Division of Cancer Treatment and Diagnosis: http://www.cancer.gov/dctd/

Division of Cancer Prevention: http://www.cancer.gov/prevention/

Cancer Control and Population Sciences: http://dccps.nci.nih.gov/

Division of Cancer Epidemiology and Genetics: http://dceg.cancer.gov/

Center for Cancer Research: http://ccr.nci.nih.gov/

Clinical Trials Cooperative Group Program: http://ctep.cancer.gov/resources/

Investigator's Handbook: http://ctep.cancer.gov/handbook/index.html

NCI-CTMB Guidelines for On-site Monitoring of Clinical Trials and CCOP Research Bases and the Cancer Trials Support Unit (CTSU):
http://ctep.info.nih.gov/monitoring/guidelines.html

Adverse Event Expedited Reporting System (AdEERS) Website:

http://ctep.info.nih.gov/reporting/adeers.html

Information on the NCI's Common Terminology Criteria for Adverse Events (CTCAE): http://ctep.cancer.gov/reporting/ctc.html

Information on Common Data Elements (CDE) approved for use in CTEP-sponsored clinical trials: http://ncicb.nci.nih.gov/NCICB/infrastructure/cacore_overview/cadsr

NIH data sharing policy and implementation guidance: http://grants2.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm

NCI Office of Acquisitions: http://rcb.cancer.gov/rcb-internet/

Information on the Clinical Trials Working Group (CTWG) initiative and its final report to the National Cancer Advisory Board in June 2005, entitled "Restructuring the National Cancer Clinical Trials Enterprise": http://integratedtrials.nci.nih.gov/ict/

Human Subjects in Clinical Research Links

- Association for the Accreditation of Human Research Protection Programs: http://www.aahrpp.org/www.aspx
- FDA
  - 21 CFR 50, Protection of Human Subjects: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&showFR=1
  - 21 CFR 56, Institutional Review Boards: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56&showFR=1
  - CDISC Study Data Tabulation Model: http://www.cdisc.org/models/sds/v3.1/index.html
- HHS Office for Human Research Protections: http://www.hhs.gov/ohrp/
  - 45 CFR 46, Protection of Human Subjects: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
  - Electronic Federalwide Assurances and IRB/IEC Registrations : http://ohrp.cit.nih.gov/efile/
  - International Compilation of Human Subject Research Protections: http://www.hhs.gov/ohrp/international/HSPCompilation.pdf
  - IRB Guidebook: http://www.hhs.gov/ohrp/irb/irb_guidebook.htm
  - Appendix: http://www.hhs.gov/ohrp/irb/irb_appendices.htm
- NIH Office of Human Subjects Research: http://ohsr.od.nih.gov/
  - Human Subjects Research Enhancement Awards: http://grants.nih.gov/grants/policy/hsrea/hsrea.htm
  - Inclusion of Women and Minorities: http://grants.nih.gov/grants/funding/women_min/women_min.htm
  - Amended NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research – Amended October 2001): http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html
  - NIH policy and guidelines on the inclusion of children as participants in research involving human subjects – policy implementation: http://grants.nih.gov/grants/funding/children/children.htm

  - NIH Certificates of Confidentiality Kiosk http://grants.nih.gov/grants/policy/coc/index.htm
- NIH Bioethics resources: http://bioethics.od.nih.gov/
  - Use of Human Tissue: http://bioethics.od.nih.gov/humantissue.html
  - Named Populations in Genetic Studies: http://bioethics.od.nih.gov/named_populations.html