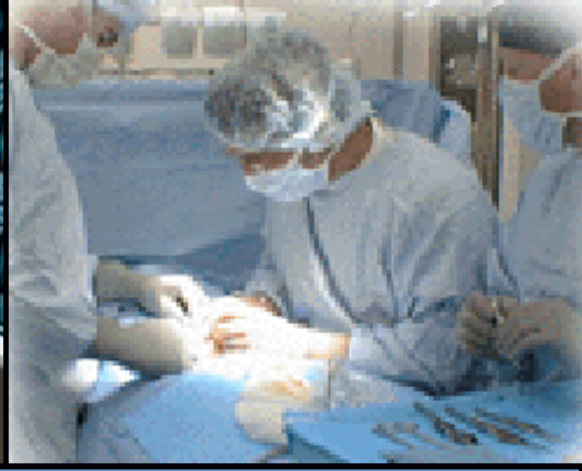
National Cancer Institute



Making Consent Forms More Concise: Revising the NCI's Consent Form Template

DHHS Meeting of the Secretary's Advisory Committee on Human Research Protections

March 13, 2013

Jeanne M. Adler, RN, MPH, CCRP
Cancer Therapy Evaluation Program
National Cancer Institute
adlerj@mail.nih.gov

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

NCI Informed Consent Template - Background

- 1997 – concerns voiced by research participants and investigators about informed consent documents for cancer treatment trials
  - *Too long, difficult to understand complicated concepts*
- NCI, OPRR, and FDA formed Informed Consent Working Group
  - *Investigators, nurses, advocates, IRB Chairs and members, ethicists, legal experts, communication experts, pharma representatives*
- Conferences and deliberations resulted in a Template that met several goals – still apply today:
  - *Ensures regulatory compliance*
  - *Standardizes ICD appearance for easier review by IRBs*
    - Builds IRB confidence in quality of ICDs
    - Discourages content changes at institutional level
  - *Establishes expectations of content of ICDs*
    - Cooperative Group, CTEP, and now CIRB reviewers agree on what is included and format
  - *Ensures NIH principles of plain language are included*
- Resulted in Website with recommendations for process as well as document

http://www.cancer.gov/clinicaltrials/education/simplification-of-informed-consent-docs/page2

Identification of a Problem

- **In the Literature**
  - *Albala (2010) "…Among the problems…are excessive length, complexity of wording."*
  - *Beardsley (2007) "The length of patient information and consent forms…is increasing with time. QuIC-A scores [which rates participants' objective knowledge of the clinical trial] were significantly higher for trials in which the …page count was seven or less."*
- **Elsewhere**
  - *Recent letters from IRB Chairs from Illinois, Maryland, and Ohio*
    - **"…consent forms are becoming longer and longer"**
  - *Comments from patient advocates, investigators, CRAs*
  - *AHRQ (2009) "[Informed consent] documents are long and written at a reading level beyond the capacity of most potential subjects." http://www.ahrq.gov/fund/informedconsent*
  - *AAMC, IOM*
  - *NCI staff members who review consents from studies nationwide share the same opinion*

National Cancer Institute

Immediate Actions Taken

- **'Snapshot' audit - length of phase 3 CTEP treatment trials**
  - ***97 studies***
  - ***Range: 5 to 35 pages***
  - ***Median: 16 pages***
- **Surveyed NIH Institutes for their consent form approaches**
  - ***Finding: many NIH Institutes using the NCI Template***
- **Conducted literature search for general and specific guidance on format and content**
  - ***Some information on risk presentation exists***
- **Surveyed cancer patient advocacy organizations and compiled concerns, for example:**
  - ***"Understanding technical terms"***
  - ***"Length of document"***
  - ***"Overwhelming number of potential side effects listed"***

Next Step: Draft Concise Template

- **Methodology**
  - ***'Blank slate' approach***
    - **Addressed 'basic' and 'additional' elements of informed consent per OHRP and FDA regulations**
    - **Goal was brevity yet including key concepts about trial that might affect one's decision to participate**
  - ***Retained plain language principles, including:***
    - **Writing for the reader**
    - **Using common, everyday words**
      - **Short words, sentences, and paragraphs**
    - **Displaying material correctly**
      - **Q&A format of Template titles and responses**
      - **Providing white space**
  - ***Eliminated repetition of information***

Three Test Cases

- **Applied draft concise informed consent template to three ICDs from existing CTEP-sponsored phase 3 trials**
- **Test cases were chosen based on length of ICD**
  - ***Chose those with 16 pages - median length from 'snapshot' audit***
  - ***Studies in lung, breast, and lymphoma***
- **Rewriting the ICDs, using the concise Template, reduced ICD length by more than half**
  - ***4,822 → 2,165 words, 7 pages (Test case 1)***
  - ***5,777 → 2,388 words, 7 pages (Test case 2)***
  - ***5,143 → 2,352 words, 7 pages (Test case 3)***

Concise Template – Developmental Strategy

- **Planning Committee was assembled, composed of representatives from NCI Divisions collaborating with CTEP on treatment trials and those conducting prevention trials:**
  - ***Office of the NCI Director***
    - **Coordinating Center for Clinical Trials**
    - **Office of Advocacy Relations**
    - **Office of Communications and Education**
  - ***Center for Cancer Research***
  - ***Cancer Diagnosis Program***
  - ***Cancer Imaging Program***
  - ***Cancer Therapy Evaluation Program***
  - ***Division of Cancer Control and Populations Sciences***
  - ***Division of Cancer Prevention***

Developmental Strategy (continued)

- **Planning Committee :**
  - *Discussed the problem*
  - *Reviewed relevant documents*
  - *Developed approach which would result in more concise ICDs for cancer trials*
- **Approach consisted of:**
  - *Constituting five working groups, each co-chaired by two individuals with specific expertise*
    - *Comprised of key stakeholders with expertise:*
      - **Patient Advocates, CIRB Chairs and members, CRAs, investigators, nurses, IRB Chairs, Cooperative Group regulatory and protocol development staff**
    - *Three WGs assigned sections of the template to revisit*
    - *One WG asked to consider language for companion studies*
    - *One WG asked to consider if informational attachments should be routinely used for informative purposes*

Working Group Co-chairs

- **Working Group 1 (Beginning of Template: background, required tests, intervention sections):**
  - ***Shlomo Koyfman, MD – clinical investigator***
  - ***Joan Westendorp, RN, MSN, OCN, CCRA – protocol coordinator***
- **Working Group 2 (Risks and benefits sections):**
  - ***Roy Smith, MD – former CIRB Chair***
  - ***Michael Paasche-Orlow, MD, MA, MPH – ICD expert***
- **Working Group 3 (Alternatives, privacy, injury, cost, rights, signature):**
  - ***Edward Goldman, JD – ICD expert***
  - ***Nancy Morton, MT, MPH – protocol coordinator***
- **Working Group 4 (Possible attachments):**
  - ***Barbara LeStage, MPH – patient advocate***
  - ***Mary McCabe, RN, MA – ICD expert***
- **Working Group 5 (Companion studies):**
  - ***Lisa Carey, MD – clinical investigator***
  - ***Laura Beskow, MPH, PhD – translational investigator***

Federal Regulatory Advisors Participating

- **OHRP**
  - ***Jerry Menikoff, JD, MPP, MD***
  - ***Julie Kaneshiro, MA***
  - ***Lisa Rooney, JD***
  - ***Lisa Buchanan, MA***
- **FDA**
  - ***Sandra Casak, MD***
  - ***Ruthann Giusti, MD***
  - ***Joanne Less, PhD***
  - ***Shan Pradhan, MD***

National Cancer Institute

Working Group Methodology

- **Working Group conference calls**
  - *Average of two WG conference calls to review assignment and draft text*
- **Face-to-face meeting held**
  - *Each Working Group's Co-chairs presented assigned drafts to assembled group including Planning Committee, Regulatory Advisors, and all Working Group members*
- **Working Group recommendations for consent form include:**
  - *Focus on how study is different from standard treatment rather than using limited space to describe standard treatment in detail*
  - *Concern about how to avoid drift in length over time*
    - Page counts; Word counts; Reading time estimates = section length limits
    - Stress role of CF – summarizing and documenting; not providing detailed descriptions that should be part of 'process'
  - *Attachments should be informative and optional*
  - *Correlative trials should be embedded into primary consent form and also be concisely worded*

Challenges and Controversies

- **Two titles**
  - *Understandable lay title*
  - *Official title for internet search and tracking by study staff*
- **Brief description of usual care**
  - *Places research into appropriate context*
- **Include procedures? Risks of procedures?**
  - *Only if part of research question, not if part of usual care*
- **How to refer to 'standard care', 'usual treatment', 'usual care', 'usual approach'**
  - *'Standard' varies across country, avoid 'treatment', 'care' is nebulous, use 'usual approach'*
- **How to refer to 'study doctor', 'your doctor', 'researcher'**
  - *Use 'study doctor' , 'researcher' refers to those leading trials*
- **Correlative trials should be embedded into ICD and also be concisely worded**
  - *Limit content to relevant descriptions of purpose, procedures, risks, benefits*
  - *Indicate willingness to participate by circling 'Yes' or 'No'*

New Template Features

- Text examples for different types and phases of studies, where appropriate
  - *Includes chemoprevention and imaging trials*
- Text provided for mandatory specimen collection, within primary consent, and optional specimen collection, located before signature line
- Contact information for study doctor in "Who can answer my questions about this research study?" section
  - *Easy to find for study participants*
    - One location to ask questions, discuss concerns, report side effects or injuries
- More text examples for optional studies, e.g., imaging correlatives
- Text for biobanking, optional research biopsy, and future studies developed by Cooperative Group Banking Committee in conjunction with experts in the field
- Complies with new FDA regulation, 21 CFR 50.25(c)
- Meets new CTEP electronic submission requirements, FDA mandate

Recommendations re Risk Presentation

- **Recommendations for risks section (WG2)**
  - ***Risks described from study participant perspective***
    - Easy to understand, meaningful
  - ***Similar frequency categories as previous Templates***
    - Clearer definition of frequency – "x out of one hundred" rather than percentage
  - ***Format risks into tables – "Tables of Possible Side Effects"***
    - Use different tables for experimental and standard arms; grouping by regimen
    - List risks by body system, keeping description at a general level using lay terms, such as, 'irregular heartbeat', or 'kidney damage' instead of 'ventricular tachycardia' or 'nephrotic syndrome'
  - ***Three tasks for CTEP***
    - Translate CTEP's risk profiles of IND agents into more general lay terms
      - *Eliminate the 1:1 inclusion of risks into risk profiles*
    - Develop repository of "Tables of Possible Side Effects" for CTEP IND agents
    - Develop repository of "Tables of Possible Side Effects" for commonly used commercial drugs and regimens

Translating CTEP's risk profiles of IND agents

- CTEP's IND agents have risk profiles based on Common Terminology Criteria for Adverse Events (CTCAE)
- CTCAE has already been translated into lay term dictionary
- Lay term dictionary has been updated to include "Informed Consent Term"
  - *Description of risk from the study participant's perspective*
- Risks are condensed using "roll-up" terms
  - *Specific exceptions allowed when necessary to fully inform prospective study participants*
- Posted on CTEP's website at: http://ctep.cancer.gov/

National Cancer Institute

NCI Scientific Term CTCAE-Informed Consent Term Spreadsheet (Excerpt)

CTCAE SOC (System, Organ, Class)	CTCAE Term	General Lay Term (Roll-up)	Informed Consent Term	Symptoms to be listed at the end of the Informed Consent Term	Directions
Gastrointestinal disorders	Gastric necrosis	Damage to organs	Damage to the stomach	which may cause belly pain	"belly pain" can be omitted if "belly pain“ is already listed
Gastrointestinal disorders	Diarrhea		*Diarrhea*		
Nervous system disorders	Headache		*Headache*		
Musculoskeletal and connective tissue disorders	Pain in extremity	Pain	Pain in arms, legs		
Respiratory, thoracic and mediastinal disorders	Dyspnea		*Shortness of breath*		
Respiratory, thoracic and mediastinal disorders	Pharyngeal mucositis		*Sore throat*		
General disorders and administration site conditions	Edema face	Swelling of the body	Swelling of the face		
General disorders and administration site conditions	Fatigue		*Tiredness*		

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

"Table of Possible Side Effects" Repositories

- Profiles for both CTEP-IND agents and commercial agents are in the process of being transformed into "Table of Possible Side Effects" format
- Regimens to be done next
- Posted on CTEP website http://ctep.cancer.gov/
- Building a "Table"?
  - *Spreadsheet and Instructions Document also posted*
    - Instructions to assist in the development of risk profiles for drugs for which there is no posted Table
    - Explain how to:
      - "Roll-up" certain terms
      - Order terms (by SOC)
      - Delete duplicates and determine exceptions
      - Combine similar terms on to one line

Excerpt - Template Risk Section

What risks can I expect from taking part in this research study?

If you choose to take part in this study, there is a risk that you may:

–Lose time at work or home and spend more time in the hospital or doctor's office than usual

–Be asked sensitive or private questions which you normally do not discuss

The (specify type of research intervention) used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects.

Here are important points about side effects:

–The researchers do not know who will or will not have side effects.

–Some side effects may go away soon, some may last a long time, or some may never go away.

–Some side effects may interfere with your ability to have children.

–Some side effects may be serious and may even result in death.

The tables below show the most common and the most serious side effects that we know about. There might be other side effects that we do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Table of Possible Side Effects of *Research Intervention*

COMMON, SOME MAY BE SERIOUS
OCCASIONAL, SOME MAY BE SERIOUS
RARE AND SERIOUS

Non-physical risks

Laboratory Tests will be monitored by Study Doctor

Important points about side effects

Risks are in 3 frequency categories

National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Sample "Table of Possible Side Effects of *Agent*"

National Cancer Institute

Table of Possible Side Effects of (*Insert Agent*)

COMMON, SOME MAY BE SERIOUS In 100 people receiving agent, more than 20 may have:
•Diarrhea, nausea, vomiting •Tiredness •Headache •High blood pressure which may cause blurred vision

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving agent, from 4 to 20 may have:
•Anemia which may require transfusion •Abnormal heartbeat which may cause fainting •Pain •Constipation, heartburn •Bleeding from multiple sites including nose bleed, or bleeding in the brain which may cause confusion •Internal bleeding which may cause black, tarry stool; blood in vomit or urine; or coughing up blood •Sores in mouth which may cause difficulty swallowing •Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

RARE AND SERIOUS In 100 people receiving agent, 3 or fewer may have:
•Heart attack or heart failure which may cause shortness of breath, swelling of ankles •Abnormal opening in internal organs •Stroke which may cause paralysis, weakness

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Additional Discussions during In-person Meeting

- **How should new Template be rolled out to maximize acceptance and utilization?**
  - ***Suggested a subcommittee to plan rollout***
  - ***Definitely wanted a memo to IRB chairs prepared that provides rationale for the shorter ICD***
  - ***Encouraged engaging OHRP and FDA to support new Template***
  - ***Proposed development of a white paper on this initiative***
  - ***Suggested presentations about how new Template was developed and expertise of those involved to the following:***
    - **Cooperative Group and CCOP Annual Conferences**
    - **PRIM&R Conference – engage IRB support**
      - **National IRB Chair conference call?**
    - **SoCRA Conference**
    - **AAHRPP Conference**

Current Status and Evaluation Methods

- **Current status**
  - *All changes received from Working Groups and others have been made and the revised Template is in review by OHRP and FDA*
  - *Distributed in February 2013*
    - Effective date of May 15, 2013 for CTEP trials
- **Evaluations conducted by NCI's Office of Market Research and Evaluation**
  - *Formative evaluation – qualitative, conducted with cancer survivors during Template development*
    - Recommendations included:
      - *Define frequency labels in Tables of Possible Side Effects*
      - *Clarify "extra tests" and correlative studies section*
  - *Outcome evaluation – being conducted on final version*
    - Cancer survivors will be randomized to consent form written following former Template vs. one for same trial written using revised Template

References for Slide 3 Citations

Albala, I., Doyle, M., & Appelbaum, P.S. The evolution of consent forms for research: A Quarter Century of Changes. IRB: Ethics & Human Research, 2010, 32(3), 7-11.

Beardsley, E., Jefford, M., & Mileshkin, L. Longer consent forms for clinical trials compromise patient understanding: so why are they lengthening? Journal of Clinical Oncology, 2007, 25, e13–e14.