CHAPTER 5

INFORMED CONSENT GUIDELINES

Study Documents Referred to in this Chapter

- Verbal Consent
- Short Physical Performance Battery Consent
- Short Physical Performance Battery (SPPB)
- Informed Consent
- Study Eligibility Checklist

CHAPTER 5

INFORMED CONSENT GUIDELINES

5.1. INTRODUCTION

The success of every clinical trial depends on the cooperative participation of its subjects. For LIFE to succeed, the participants will be required to complete the screening visits and behavioral run-in, consent to enrollment in their assigned study arm, participate in the assigned group, return for all follow-up visits as indicated, and report health problems that may occur. To aid in meeting these objectives, we must obtain truly informed voluntary consent. If the consent process is simply a mechanical ritual, the trial could be jeopardized by a large number of early dropouts, poor adherence to interventions, and confusion about study protocol.

5.2. BASIC ELEMENTS OF INFORMED CONSENT

The Department of Health and Human Services (DHHS) guidelines set forth eight essential elements of informed consent:

Participants must be advised that the study involves research. An explanation must be given regarding the purposes of the research, the expected duration of the subject's participation and a description of the procedures to be followed, including identification of any experimental procedures.

It is essential that the participant understand that he or she will not necessarily be participating in a given intervention and that his or her treatment assignment may be determined by chance. The participant will be randomized to one of two programs: a successful aging program or a physical activity program. The participant will have an equal chance of being assigned to one of these groups.

It is critical that both groups be given equal importance. The hypothesis that the study that follows the LIFE pilot hopes to test is that physical activity can prevent disability. However, to be able to test this hypothesis there must a comparison group to which to compare the physical activity group. The ability to make a comparison will suffer if participants in the Successful Aging Program feel they are getting second best and thereby fail to fully participate in the study follow-up.

Participants should be told that they are expected to attend two formal screening/eligibility visits. During the first visit they will perform the Short Physical Performance Battery along with other physical performance tests. They will receive a physical exam, a Mini Mental Status Exam, and an ECG. Their blood pressure, height,weight, and waist circumference will be measured. They will be asked complete a variety of questionnaires about their health, medical history and the medications they are taking. They will be given a diary to record the fruits and vegetables they eat for one week and the minutes of exercise they do per day for one week

If they are still eligible for the LIFE study and agree to participate, they will be asked to return for Screening Visit 2. At this visit the diary will be reviewed and a blood sample collected for a variety of tests. This blood sample collection is optional and participants must choose to participate by indicating their choice in the boxes provided in the Informed Consent form. Participants at the Wake Forest and Sanford sites will also be asked to participate in cognitive testing. At the end of this visit, participants who remain eligible and willing will receive their assignment to one of the two study groups. It is important that participants have a clear idea of the time demands for both intervention groups including the time spent in the intervention and the time required for follow-up visits and phone calls.

5.2.1. Anticipated Benefits of the Trial Must Be Explained to Participants

Many participants appreciate the opportunity to be involved in relevant research and to contribute to medical knowledge. In the LIFE study, the knowledge we gain may or may not be specifically applicable to participants in the study. Results from the study will provide knowledge about interventions to prevent the development of walking disability in older adults. Because the LIFE Study is a pilot study, it is unlikely to yield a definitive answer on the main study hypothesis. The study will provide the necessary information to plan a much larger follow-up study. The pilot study is big enough to show how the interventions will affect health related measures such as depression scores, disability scales and physical performance measures.

All participants in the trial will be monitored closely. Tests associated with the study are provided at no cost to the participant.

There is no way of knowing in advance whether a particular participant will personally benefit from the treatment during the course of the trial. Care should be taken not to suggest that participants will benefit simply by entering the trial.

5.2.2. Attendant Discomforts and Risks Must Be Described

Participation in the LIFE study may involve some added risks and discomfort but every attempt will be made to closely monitor all participants. To reduce the risks, we have purposely excluded patients for whom the study might be unsafe.

However, in spite of our precautions, participants may experience risks and discomfort which include the following:

Risks of Blood Draw

While rare, the risks of drawing blood for the study include the possibilities of brief pain, becoming faint during the blood draw or developing a bruise or bump

following the blood draw, and there is a slight risk of infection at the site where blood was drawn.

Risks of Increasing Physical Activity

There may be some discomfort in the beginning of the study from the increase in physical activity. The possibilities include, but are not limited to, some muscle and joint stiffness. This stiffness generally subsides in 1 or 2 days, and is not considered to be serious. Some may experience an exercise-related injury such as a strain, sprain, or other injury to muscles or joints. There exists the possibility that certain physical changes may occur during participation in the physical activity. These include abnormal blood pressure, fainting, abnormal heart beats, and, in rare instances, heart attack, stroke, and death. There may be other risks that are currently not foreseeable.

5.2.3. Appropriate Alternative Procedures that Might Be Advantageous for the Subject Must be Disclosed

This mandate is often overlooked in written consent forms. It means that the participant should be told what options exist if he or she elects not to participate in the trial. The participant should be told that the alternate treatment available would be to obtain health screening evaluations or health related education, from the participant's health care provide. The participant could also choose to increase his or her activity level without enrolling in this study.

5.2.4. The Extent to Which Confidentiality of Records Identifying the Participant Will be Maintained Must Be Described

Confidentiality of all participant information is assured in all participating centers. No unauthorized personnel should have access to participant records or results of interviews or tests. Additionally, all record storage rooms should be

appropriately secured, and should contain necessary locked files or other storage equipment.

It may be useful to explain that in studies of this nature, numerical and alphabetic codes are assigned by which central study files may be linked to individual participants. Participants are not identified by name in any reports or publications.

5.2.5. Compensation

Prospective subjects must be advised of the availability or non-availability of medical treatment or compensation for physical injuries incurred as a result of participation in the study, and, if available, what they consist of, or where further information may be obtained.

It may be useful to distinguish between providing study treatment and follow-up free of charge and financial compensation for injuries incurred. The Federal Government is prohibited by law from committing funds that have not yet been appropriated by Congress, and no funds have been allocated for compensating injured subjects in trials such as the LIFE Study. The only recourse for such participants is to seek compensation through the courts or through negotiation with the clinical center involved.

Policies regarding compensation and reimbursement vary from institution to institution, so we cannot recommend a standard approach for all participating centers. Staff members should stress the fact that the chance of serious injury in LIFE is small but the government requires that compensation be discussed with participants if there is any risk at all. Legal terms and concepts should be translated into lay person's language, and the ideas should be made relevant to the LIFE study, not simply to research in general. Comments regarding compensation should be as brief as possible.

5.2.6. Contacts

Persons responsible for the study must offer an explanation of who to contact for answers to pertinent questions about the research and the participant's rights, and who to contact in the event of the development of side effects, a medical emergency or a research related injury to the participant.
One or more persons associated with the trial will be available to answer relevant questions while participants are contemplating participation.

Prospective subjects should be handed the names of these people on a card when they are first approached. If no names are provided, they may ask questions of persons not knowledgeable about the study and be given unclear answers or misinformation.

Once they are enrolled in the study, we recommend that participants receive written information regarding who to contact at any time about possible injuries occurred participation in the study or rights as a volunteer in the study.

5.2.7. Voluntary Participation

Participants must be told that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which he or she is otherwise entitled.

It is hoped that each participant will remain in the study until the trial is completed, but they have the right to withdraw at any time. This must be communicated to participants without luring them into the trial on a probationary "look and see" basis. Hesitant participants should be carefully evaluated to screen out those who are likely to withdraw early.

The right to withdraw from a trial is compromised if such behavior invokes penalties. This is the reason for the phrase, "without penalty or loss of benefits," and the idea should be explained to participants. If they drop out of the trial, the act of dropping out will not jeopardize their regular care.

The eight requirements of informed consent in the DHHS guidelines above refer primarily to categories of information that enable participants to make rational decisions regarding participation in clinical trials. Except for the stipulation that participant inquiries should be answered, these basic elements do not refer to the process of obtaining informed consent.

5.3. THE PROCESS OF OBTAINING CONSENT

Various studies indicate that the circumstances under which consent is obtained in clinical trials can have a profound influence on the participant's interpretation of information communicated during the consent discussion and on the freedom of participants to make their own decisions.

It is recommended that the following guidelines be followed to ensure that the consent we obtain will be as informed and voluntary as possible:

5.3.1. Study Information

Participants should be fully informed about the study and have adequate time to evaluate the pros and cons of participation. It is recommended that the Study Coordinator review the Informed Consent form with the participant and answers any questions. The Informed Consent form may be sent home with the participant so that he or she may carefully review it if necessary.

5.3.2. Study Discussion

Participants should be encouraged to discuss the study with anyone they wish, particularly family and friends who might be affected (for example, persons who might be needed to provide transportation).

Close associates of the participant may raise questions and considerations that the participant has overlooked, and questions that concern the family are better answered sooner than later. Furthermore, there is evidence to suggest that family support for studies of this kind increases the probability of participant cooperation during the course of the research.

5.3.3. No Proxy Consent

To be eligible for participation in the LIFE study, participants must have the capacity to give their own informed consent.

If a participant is incapable of understanding what is expected of him or her as a subject in the study, it is not permissible to obtain informed consent from a guardian. The study requires daily responsibilities that cannot be easily assumed by other persons. The participant is also free to discuss participation with his or her personal physician. Study investigators at each site can discuss the trial with prospective participants' physicians if they so desire after the participant gives consent to release medical records.

5.3.4. Environment for Informed Consent

The setting in which consent is obtained should be as private as possible so participants can freely ask questions without embarrassment.

If extraneous parties can hear the conversation, participants may be reluctant to ask appropriate questions.

To avoid pressuring the participant, only one person associated with the study

should be present when the participant reviews the consent forms.

If a second witness is required, he or she should be as unobtrusive and non-committal as the situation permits.

5.3.5. Obligations

The participant should be given a copy of the informed consent forms after they are signed, dated and witnessed.

Even though participants are free to withdraw from the study at anytime, the consent form spells out our obligations to the participant and the participant's obligations to the study while he or she is a subject.

5.3.6. Copies of Informed Consent

Participants should be encouraged to keep the consent forms.

The consent forms contain useful information about the study which participants may want to review from time to time. After the participant has signed the consent form, sites may forward the consent form to the Principal Investigator for his signature per their site specific operating procedures.

5.3.7. Witness Signature and Source Documentation

Anyone who signs a consent form should personally date it. If consent is obtained the same day that the participant's involvement in the study begins, the participant's records should document that consent was obtained prior to participation in the research. A general statement for source documentation should be included, such as, "All the required elements of informed consent were

presented to the patient. Voluntary consent was obtained and the participant's questions were answered prior to initiation of any research procedures."

5.3.8. Sample Informed Consent Forms

SAMPLE INFORMED CONSENTS CAN BE FOUND IN THE APPENDIX AND ARE POSTED ON THE "FORMS" WEBPAGE OF THE STUDY WEBSITE.

5.4. Reporting Requirements for Informed Consents and IRB Approval

The administrative coordinating center needs a copy of each clinic site's Approved Consent Form(s) and the copy of the IRB approval of the study protocol letter. The annual approval letter should be provided to the administrative coordinating center. Whenever changes are made to the consent form, a new, approved consent form and the letter of approval should be forwarded to the administrative center. Confirmation that this process is being followed will occur at the site visits at which time the site visit team will check that the approved and currently used informed consent forms are the same as those on file at the administrative coordinating center.

Original Informed Consent forms stay at the site. A copy is provided to the participant.

5.4.1. THREE CONSENTS TO BE OBTAINED

The LIFE study has three informed consent forms: one verbal and two written forms. The verbal consent is read prior to the beginning of the phone screening interview. If the participant fails to give consent, then a phone screen should not be done. If a participant provides verbal consent, then the assignment of a study

ID number will be taken as positive evidence that initial consent was obtained. The Phone Screening form may be administered as a face-to-face interview if the situation is warranted.

The second phase of the screening process is the conduct of the Short Physical Performance Battery. Only perspective participants who score lower than a 10 on this test will be eligible for the study. Based on preliminary studies done in preparation for the LIFE Study, we anticipate this requirement will lead to the highest number of exclusions. For this reason, this one component has been given its own consent form. This allows the clinics to avoid having to explain the entire study to ineligible subjects. This also allows this component to be performed off-site to prescreen prospective participants. If the participant continues to qualify after the SPPB, then the full informed consent form will be reviewed and signed before any further study procedures are performed.

In order to track the informed consent process, clinic staff should complete the Study Eligibility Checklist. If the participant fails to provide informed consent or withdraws consent at any stage, the box “informed consent not obtained” should be marked.

5.5. TRAINING IN THE PROTECTION OF HUMAN SUBJECTS

The NIH requires training in the protection of human research participants for all investigators who submit NIH applications for grants or contracts, as well as those investigators who receive new or non-competing awards for research involving human subjects. LIFE Study investigators and staff should be trained according to local institutional requirements. This requirement applies to the LIFE Study. For more information please see the following web site:

HYPERLINK http://grants.nih.gov/grants/policy/hs

http://grants.nih.gov/grants/policy/hs educ faq.htm

Be Informed about Informed Consent

Remember that Informed consent is not just a form. Rather, it is a process that involves the following steps:

- Giving a participant adequate information about the study
- Providing adequate opportunity for the participant to consider all options
- Responding to the participant's questions
- Ensuring the participant has comprehended the information
- Obtaining the participant's voluntary agreement to enter the study
- Continuing to provide information as the participant or situation requires

In order to be effective, the process should provide ample opportunity for the investigator, study staff and the participant to exchange information and ask questions.

Below are some frequently asked questions about the consent process.

Who can obtain consent from potential participants?

The NIH does not specify who can obtain consent from a potential participant. Some sponsors and IRBs require the clinical investigator to conduct the consent interview. Regardless, the person who conducts the consent interview should be knowledgeable about the study and able to answer questions. If someone other than the investigator obtains consent, the clinical investigator should formally delegate this responsibility and the person so delegated should have the

appropriate training to perform this activity.

21 Code of Federal Regulations (CFR) 50.27(a) requires that a copy of the consent document be given to the person signing the form.

No. The regulation does not require the copy of the form given to the participant to be a copy of the document with the participant's signature, although this is strongly encouraged. It must, however, be a copy of the IRB approved document that was given to the participant to obtain their consent.
However, as HIPAA language is included in the LIFE consent form, a copy must be given to the participant.
Do you have to have a witness to the consent process?

An impartial witness is only required if the participant cannot read, if the participant is incapable of understanding the consent document, or if the participant does not speak English. Otherwise, a witness is not required.

When a witness is required, must they observe the entire consent interview or only the signature of the participant?

When a witness is required, they must be present throughout the entire consent interview. The intended purpose is to have the witness attest to the accuracy of the presentation and the apparent understanding of the participant, not just the validity of the participant's signature.

How do you obtain informed consent from someone who speaks and understands English but cannot read?

Illiterate persons who understand English may have the consent read to them and "make their mark," if appropriate under applicable state law. Federal

regulations do permit the use of a short form for patients that cannot read. A short form is a document that states that the elements of informed consent as required by the Code of Federal Regulations have been presented orally to the participant. When this method is used, there must be an impartial witness to the oral presentation. Also, the IRB should approve a written summary of what is to be said to the participant. The participant must sign the short form. However, the witness must sign both the short form and a copy of the IRB approved summary. A copy of the summary and short form must be given to the participant. If you encounter an illiterate participant, consult with your IRB Chair to discuss your local guidelines.

A short form of the consent has not been approved and is not currently available from the Administrative Coordinating Center.