

## Chapter 2

### Recruitment

#### RECRUITMENT PROCEDURES

**Sampling Frame:** As a starting point, the NIA LLFS investigators will use Center for Medicare and Medicaid Services (CMS) data as a first step in identifying families with high numbers of long-lived individuals by using the CMS denominator file and name and address lists to recruit study subjects (the proposed recruitment plan is described below).

CMS will provide the LLFS with the Medicare 2004 denominator file (Parts A and B) (without name and address). Analyses of the denominator file will focus on people who:

- Are at least 79 years old on January 1, 2005
- Have no recorded date of death
- Are not in the end-stage renal disease (ESRD) or hospice programs
- Live in zip codes "near" (within 2 hours driving distance) to one of the 3 US study centers responsible for enrolling families and collecting data (Boston University, Columbia University, and the University of Pittsburgh).

The denominator file will enable accurate estimates of numbers of eligible individuals, and help the NIA LLFS investigators to finalize the sampling strategy and to select the CMS ID's for the pilot and subsequent mailings. The Minimum Data Set (MDS) or nursing home-based data (when available) for these enrollees will also be used to assist with the determination of sampling and recruitment strategies.

For the Denmark Field Center, this same information is easily accessible and has been obtained from a thorough analysis of Church Records which was completed for a previous study. As a result, families which meet the inclusion/exclusion criteria for LLFS have already been identified for the Danish component, resulting in a minimal recruitment phase.

**Construction of the Recruitment List:** The NIA LLFS investigators will analyze the data from the denominator file and will return to CMS a finder file of health insurance claim numbers (HICs) identifying a group of beneficiaries whom we would like to approach for recruitment. The finder file will be a stratified random sample of all people potentially eligible for the LLFS that is also over-sampled for the oldest old.

In addition to the names and addresses, CMS will be requested to provide additional information for these subjects from the CMS utilization files (for example, regarding hospice use, institutional status, the presence of dementia codes). The additional information may be used to further narrow the list of individuals to be contacted in order to more efficiently meet the study's eligibility criteria.

**Recruitment:** There will be no cold calling of potential participants nor will recruitment take place at physician practices. Potential study participants will be recruited from a random sample of Center for Medicare Services enrollees as described above. The mailing will be done in collaboration with CMS and the NIA, which have prepared an Inter-agency Agreement for which approval for this mailing has been granted. Study participants will also be recruited from the community using mailed brochures, posters, web-based media and newspaper advertisements as well as community presentations at churches and senior centers. Additional mailing lists will be obtained through government agencies and purchased public domain lists from various commercial vendors.

**Pilot Study Phase:** The initial pilot recruitment phase (Phase 1) is designed to collect information on the sibship size of potential study participants, to gauge response rates and the proportion of people who may require additional follow-up, such as additional mailings or a follow-up telephone call. The pilot phase will consist of a mailing of a brochure with a reply card to approximately 5,000 people per each of the 3 sites over a 4 month period (500 people per site every 2 weeks with an intervening week to analyze the recruitment effort). For those who send a positive response card, a telephone interview for eligibility will be conducted. If an eligible individual (and at least 2 family members) express an interest in participating in the LLFS, we schedule an examiner to enroll this person in the study. The pilot phase will be performed in April, 2006 through August, 2006.

If the respondent selects the option on the reply card to request no further contact, no further contact will be made. If there is no response within 2 weeks of the initial mailing, follow-up calls will be made to non-responders when a phone number can be found. In addition, we will resend the recruitment materials if a new forwarding address is obtained.

During the pilot phase, we will estimate the proportion of non-responders (a) who are successfully contacted via follow-up telephone calls, and (b) non-responders whom we are unable to locate. In addition, we will estimate refusal and enrollment rates and the proportion of the mailings that are returned with 'address unknown'. Based on the experience from the pilot phase the study will adapt recruitment methods to improve recruitment success of the sampled community.

**Formal Recruitment Phase:** If the results of the pilot mailings indicate the feasibility of using the CMS address list for the recruitment of additional study participants, the study will proceed to a second recruitment phase, in which each of the three sites will contact a currently estimated 75,000 Medicare beneficiaries (or until recruitment goals have been met) to generate a total enrollment of 750 families, or 250 families per site. Subjects subsequently enrolled in the LLFS, will be requested to provide permission to the LLFS to access their Medicare and MDS (if the subject has been or is in a nursing home) files in order to obtain medical history data.

The University of Southern Denmark, will also recruit and enroll a corresponding 250 families, resulting in an overall Study target of 1,000 families for LLFS.

**Mailing:** The study brochure is mailed with a letter from the Principal Investigator to age-eligible older adults. Each selected potential subject will be mailed an invitation to the study, with an opportunity to say yes or no. If the response is "yes," they will be called. If the response is "no," they will not be called. If there is no response, we will call to determine whether they are willing to participate. A total of 4 calls will be performed for unanswered calls in an attempt to reach the potential enrollee. The telephone interviewers will confirm eligibility as described in the Eligibility section above. Potential participants will be informed in detail about the study and all questions regarding study participation will be answered in accordance with each individual field centers' IRB Recruitment Procedures.

**Telephone Screen of Proband:** Verbal consent will be obtained over the phone to conduct the screening process, also over the phone. The need for a signed consent at this screening stage of the study has been waived because this study meets the following criteria: The research procedures present no more than minimal risk of harm to the involved subjects and involve no procedures for which written consent is normally required outside of the research context. We believe the information being obtained during the screening phone call is the same type of information that would be collected on patients setting up an appointment for issues related to aging. The telephone screening interview includes questions on family history of longevity. This screening information includes basic demographic information (age, race), parents' age at death, total number, vital and health status of all biological children and siblings. This information is needed to calculate a score utilizing the Family Longevity Scoring System (FLoSS) to rank

eligible families according to their degree of clustering for longevity. With this FLoSS, the LLFS can then prioritize which families it will recruit for enrollment.

Another purpose of the telephone screening questionnaire is to collect important information related to the distribution of FLoSS to determine if our initial definition of familial longevity is appropriate because our current FLoSS criterion is based on family study data from a Danish cohort. If the subject does not meet inclusion criteria, all the information collected during the screening process will be retained without identifiers.

### **Method to assess familial exceptional longevity (EL):**

**Family Longevity Score (FLoSS) Pilot Phase (1/06 through 12/8/2006):** There are several ways to characterize those families in which a particular trait (like EL), seems to be clustering. The degree of excess familial sharing of a trait (such as EL), called the Family Longevity Score (FLoSS) can be defined by first calculating an Individual Risk Score (IRS) for each person. The IRS is an approximate z-score which contrasts  $O$ , the age-at-death (or current age if still alive) with  $E$ , the life expectancy for the sex/birth year cohort for that individual.

$$IRS = \frac{(O^* - E)}{\sqrt{E}}$$

The more positive the IRS the longer an individual lives past their life expectancy whereas the more negative the IRS the more premature the death of the individual. Note that the formula actually uses  $O^*$  instead of  $O$  (age-at-death).  $O^* = O$ , except for those subjects who are still alive but who have not yet reached  $E$  (their sex/birth cohort life expectancy), in which case  $O^* = E$ , and the  $IRS = 0$ . Thus subjects get "credit" and a positive IRS for living past their life expectancy, but do not get "penalized" if they are still alive and not yet reached their life expectancy. The Family Longevity Score is then the average of all IRS scores for members of that family. Thus, the more positive the FLoSS, the more excess longevity there is in the family, whereas the more negative the FLoSS, the greater is the prematurity of death in that family in the aggregate. We may use the FLoSS to rank families by their degree of familial EL, and thus, the FLoSS is a powerful way to select families for recruitment into our Long Life Family Study.

### **Family Longevity Score (FLoSS) Prime Score (eff. December 9, 2006 to present):**

In recruiting families for the LLFS, we need to assign priority for enrollment to those with the greatest potential utility for phenotypic and genetic studies of exceptional survival in families. However, a family can be very impressive because many of its members achieved extreme old age, but of little use to our study (that requires DNA for future genetic studies) if most of the old siblings have died.

We have devised a new scoring system for ranking families that incorporates the following principles: all family members who survived to a specified minimal age, whether or not living currently, contribute to the score; an individual's contribution to the overall family score increases with the rarity of the age achieved (current or at death) as a function of the survival percentile for the relevant birth-year/sex cohort; a deceased person adds less than a living member of the same age and birth cohort; persons "dying young" decrease the family score.

The Family Longevity Selection Score (FLoSS prime) measures the exceptionality of a sibship's survival, while providing a bonus for exceptionally old *living* sibs, because they are potential study participants and DNA donors.

We compute the FLoSS prime as the sum of scores calculated for each sibling, based on sex and birth year cohort ( $C$ ), survival status, and age ( $A$ ). Let  $A^*$  be the expected age at death, given survival to age  $A$  for a

person in cohort C, and let  $p(x|C)$  be the probability of survival to at least age "x" for a person in cohort C, conditional on survival to age 40. The sibling's score is

$-1 - \ln(p(A|C))$ , if he or she died at age A, and

$[-1 - \ln(p(A^*|C))] + \max\{0, [-1 - \ln(p(A|C))]\}$ , if he or she is alive at age A.

We use survival probabilities conditional on achieving age 40 because, in LLFS, we chose to consider only siblings aged 40 or older. (Clearly, the formula can apply with any age minimum, including none.) The probabilities are computed using sex-and-birth-year cohort-specific tables provided by the Social Security Administration (<http://www.ssa.gov/OACT/NOTES/as116/as116LOT.html>). Specifically,  $p(x|C)$  is computed (only when x is at least 40), as the ratio of the number of subjects in cohort C that are alive at age X to the number of subjects in cohort C alive at age 40. The life expectancy  $A^*$  (given A and C) is obtained from the same tables. The FLoSS prime score is then the average of all scores for each individual members of that family. Thus, the more positive the FLoSS prime the more excess longevity there is in the family, whereas the more negative the FLoSS prime, the greater is the prematurity of death in that family in the aggregate. We may use the FLoSS prime to rank families by their degree of familial EL, and thus, the FLoSS prime is a powerful way to select families for recruitment into our Long Life Family Study. From 12/9/2006 forward, the FLoSS prime score for eligibility for LLFS will be 7.0

## ELIGIBILITY: INCLUSION/EXCLUSION CRITERIA

Prior to delving into the specific details of Recruitment for the LLFS, it may be useful to provide a summary of the various enrollment criteria that need to be tracked throughout the recruitment process. It is important to keep in mind that there are two levels of 'recruitment': (a) individuals (Proband and family members); and (b) Family Unit. In order to successfully recruit (b), you must first adequately evaluate and recruit (a).

<b>Inclusion Criteria (If applicable, pursue recruitment)</b>	<b>Exclusion Criteria (If applicable, do NOT pursue recruitment)</b>
Proband is $\geq 80$ years of age and Family is FLoSS-Eligible	Not in ESRD or Hospice Program
Have no recorded date of death	Does not meet the minimum FLoSS based on FLSI
Live w/in appropriate catchment area of a U.S. Field Center	Suffers from a medical condition that would impede participation (severe hearing impairment, dementia, etc.)
At least 1 living sibling residing in appropriate catchment area of a US Field Center	At the time of screening, will <u>not</u> consent to provide the requested blood sample (as part of the in-home visit)
At least 1 living offspring (of either Proband or Sibling) residing in appropriate catchment area of a US Field Center	At the time of screeners, will not contact other family members to participate.

**Figure 1. Inclusion/Exclusion Criteria**

**Recruitment of the Family:** If a Proband is part of an eligible family (FLoSS  $\geq 8.0$  based on preliminary data from our Danish collaborators or FLoSS prime  $\geq 7$  based on LLFS pilot data as of 12/06 see below), they will then be asked to contact potentially interested family members to introduce the study. Full names and contact information will be obtained only for those indicating a willingness to be contacted. These individuals will be contacted, and verbal consent will be obtained before the family members are screened as to their ability to participate.

A Family Unit will be deemed qualified for individual enrollment visits if at least 3-4 family members (proband, sibling, 1 child of proband or sibling, and, preferably, a spouse of an offspring) provide their verbal consent to participate via completion of the Family Member Telephone Screening (TS1a), thereby satisfying the Minimum Family Size (MFS) criteria. Although 3 family members (not including a spouse of an offspring) is the minimum requirement, we plan to recruit the largest families possible; therefore, based on results of the initial telephone interview, larger families will be targeted first. All attempts should be made to recruit all available and willing family members beyond the minimum requirement (i.e. additional children of the proband and/or his/her sibling(s)). As part of the enrollment visit, written informed consent will be obtained. For family members electing not to participate, study investigators will make no attempt to identify or contact them. Key individuals will be identified as facilitators within families. When possible, enrollment visits can be organized around normal family gatherings (family reunions, picnics, etc.) to reach a number of individuals at one time. When distance precludes or when it is impossible to gather a large group, the family will be characterized through individual visits.

Once a family unit has met the necessary criteria, written informed consent will be obtained in-person prior to any research activities.

### **Call-Back Script:**

Since it is likely that several family members will become tired from the screeners and, therefore, need to be re-called to complete the phone surveys, a suggested script has been developed for this purpose. Please use this script upon initiating the follow-up phone call to collect the rest of the information:

***Script:** Hello [his/her name], this is [Identify yourself] from [Identify Institution] from the LLFS which is a family study on longevity. We nearly completed our phone interview with you on [date of initial phone call] and I'm calling to complete the remainder of the interview with you. Do you have some time to finish the interview at this time? It will only take few minutes.*

*[If "No"]:* Right now is not a good time. Ok, do you know when a better time would be for me to give you a callback?

*Date:* \_\_\_\_\_ *Time:* \_\_\_\_\_

*[If "Yes"]:* When we last spoke we ended talking about [summarize end of previous discussion]. Do you remember? We will continue with the next question which is [proceed with next question].

## **LLFS FAMILY LONGEVITY SCORE INSTRUMENT (FLSI) – PROBAND (FLSI a/k/a TS1):**

### **Instructions for Administration:**

**Background:** This questionnaire is administered to prospective participants generally by telephone. It is used as the first screen to measure both eligibility and willingness for enrollment. The questions included are designed to (1) obtain basic demographic information about prospective participants and their family members to establish a Family Longevity Score (FLoSS), and (2) rule out prospective participants who do not meet the necessary inclusion criteria. There are several ways in which prospective participants can be classified as ineligible; (1) they are too young, and don't meet the age criterion for entry into the study; (2) they do not have a living sibling who is old enough to meet the age criterion for entry into the study; (3) neither the prospective participant nor their sibling has a living child; (4) the prospective participant is demented or has severe hearing impairment or health problems which will make cooperation with study procedures difficult. (See also, *Figure 1*).

There are two initial scripts "(a)" or "(b)" at the beginning of the FLSI (a/k/a TS1) along with verbal consent script on p. 2. The first script "(a)" is designed to be used with potential participants who have already expressed an interest in the study by mailing back a reply card or by calling the field center. The second script "(b)" is designed to be used with potential participants who did NOT respond to the initial mailing of the brochure. These latter interviews, which will occur following a successful telephone contact, are likely to be more difficult and to involve more explanation of the study and the importance of including all very long-lived people and their families. You will be prompted at the outset of the interview as to which script to follow based on the type of contact.

The FLSI can be completed by the interviewer either online through the Data Entry System or via hard copy form. If completing online, the Family Longevity Selection Score will be calculated automatically (after Questions 1-27 have been answered) and the interviewer can proceed with the remaining questions. If completing the FLSI on a paper form, a return phone call may be necessary once the FLoSS is calculated. One exception would be if the Screenee is obviously not eligible; to facilitate this, a hard copy table will be provided to the Recruiters so that those who would not meet our eligibility can be easily identified.

### **Detailed Instructions:**

The interviewer will be communicating with potential participants that have been identified from Medicare (CMS) enrollment lists or from purchased mailing lists, media responses or other IRB approved recruitment avenues. However, the potential participant may not be the person who picks up the telephone. So the first task in the interview is to identify to whom you are talking. (For example, often an adult child of the potential participant will be the person who wants to learn more about the study before making a decision about whether or not the family will participate). The interview form and this MOP provide guidelines for administering the questionnaire either to the potential participant or to a Family Reporter of the participant. In addition, as mentioned above, one of the aims of the interview is to determine whether the potential participant has severe hearing impairment, is too cognitively impaired or too medically frail to be able to either complete the telephone screening interview or to participate in the study. If you believe that the potential participant is having difficulty in responding to your questions, there is a section of the questionnaire that prompts you to record this information and terminate the interview. Ultimately, it is the interviewer's responsibility to make this determination as the interview unfolds. These interviews should not be administered until the verbal consent script has been read and the prospective Screenee has agreed.

The interviewer first marks the method by which the form is completed – either direct data entry into the computer or completed on the paper form.

**Interviewer Note:** The next step is to determine the level of telephone contact. Mark box #1 if the FLSI is being initiated as a result of a returned reply card or from a telephone call from someone who received a mailing – administer **Script A**. Mark Box #2 if the FLSI is being initiated as a result of someone responding to an announcement, PR or other media but did not receive a mailing – administer **Script A**. Mark box #3 if you are calling someone as follow-up to our mailing and they did NOT return a card – administer **Script B**. This script provides additional information on the purpose of the study. From this point forward, the FLSI is identical for all types of responders.

**Script A:** *"I am calling from [insert you institution here] about the Long Life Family Study, a family study of longevity. We hope to discover how some people and their families live long lives. I am calling because you expressed interest in this study. May I ask who I am speaking with? Are you [insert Screenee's name]? If not Screenee, ask "May I please speak with [insert Screenee's name]?"*

**Script B:** *"I am calling from [insert your institution here] about the Long Life Family Study, a family study of longevity. We hope to discover how some people and their families live long lives. I am calling because we sent you some information about our study and we would like to provide you with some additional background to help you decide if you wish to participate in this study. May I ask who I am speaking with? Are you [insert Screenee's name]? **If not Screenee, ask "May I please speak with [insert Screenee's name]."***

After administering either script, mark the choice 'yes' or 'no' as to whether you are speaking with the Screenee or a Family Reporter.

If you are not speaking with the Screenee, then ask: *"What is your relationship to [name of Screenee]?"* Choose the appropriate response. If none of the listed choices apply, mark 'other' and specify the relationship.

**Verbal Informed Consent: This script has been developed to obtain verbal consent from the Screenee in lieu of the typical informed consent obtained in person.**

**Script:** *Is it okay to speak with you now and tell you more about this project? This will take approximately 15 minutes.*

**Verbal Consent Script:** *We're asking [you/Screenee] to participate in an important international study of long life, particularly within families. [Your/Screenee's] name was chosen at random from a list of older Medicare users. The Centers for Medicare and Medicaid Services is cooperating with the National Institutes of Health on this study. Two other American universities [insert names here] and the University of Southern Denmark are also part of this study. Our goal is to find out what common traits are present in families with long-lived individuals. By sharing information with us, you can help improve the health of future generations, including your own children and grandchildren.*

*Before inviting people to participate in our study, we would like to ask some questions to see if [your/Screenee's] family is eligible. [You/Screenee] do not have to answer any questions that [you/Screenee] do not feel comfortable with. All of the information that I receive from [you/Screenee], including [your/Screenee's] name and any other identifying information, will be kept strictly confidential and secured under lock and key. Please note, none of the study investigators involved, nor their staff members, will attempt to identify or contact specific family members based on the relationship information obtained during this phase of the interview. [Your/Screenee's] participation is voluntary; [you/Screenee] do not have to answer these questions.*

**Question 1: Script:** *"Do I have your permission to ask you some questions about yourself/Screenee and your (his/her) family?"* Select either "yes" or "no" to document whether or not the Screenee has provided verbal consent. This interview should not be administered until the prospective participant/Family Reporter has agreed to answer the questions. If they do not agree, then terminate the interview by thanking them for speaking with you.

### **Contact Information:**

**Questions 2a-2d:** Verify contact information of the Screenee. If you are completing this information directly into the Data Entry System, this information will be filled in for you. If you are completing it on hard copy, you will need to write in the information from the reply card or from the database. This information is crucial because instructions for the preparation for the enrollment and assessment visit are sent to this address, and the phone number is used to remind participants of appointments. Check the accuracy of the address and phone number carefully.

Questions 3a-3d: We are also asking you to obtain the name and telephone number of the Family Reporter, for the case where the Family Reporter is not the potential participant. It is important to obtain this information in addition to that of the potential participant, since this is likely to be the person who will be making the arrangements for further telephone interviews of other family members and/or for the in person assessment.

Question 4: If contact has been established with the Screenee by some means other than a returned postcard, proceed with asking Q4. This question asks about where the participant or Family Reporter heard about the study. This information is useful for tailoring recruitment strategies. **Please be sure to mark all that apply.**

Question 5a: This question was added in 8/07 in order to classify probands that may reside outside of any of the 3 US field centers catchment area. This will now allow for the proper calculation of eligibility (at least 2 individuals reside in any of the 3 US field centers) in Question 31 on Page 28 of the questionnaire. Please mark "yes" or "no" and then proceed to Question 5b.

Questions 5b-5d: These questions were added on 3/29/07 with the purpose of front loading two key eligibility questions. Regardless of the family FLoSS score, if there are no living siblings or offspring, the family would not be eligible for LLFS. So, first ask Question 5b, if the answer is "NO", the Screenee has no living siblings, then proceed to Script (a) on Page 4. If the answer to Question 5b is "Yes", proceed to Question 5c. If the answer to Question 5c is "No", then the interview is terminated by reading Script (a). If the answer is "Yes", then proceed to Script (b), which will introduce the fact that we would like to ask the Screenee more questions (i.e., the complete TS1).

Question 6a-6b: Ask the participant or Family Reporter for his/her (Screenee's) age. Record the given age on the form in Question 6a. These questions are self-explanatory. Be sure to provide the date of birth in the format of the example provided.

Question 7: Gender. These questions are self-explanatory. Be sure to provide the date of birth in the format of the example provided.

Questions 8 and 9: The NIH requires that all studies involving humans report the gender and ethnic make-up annually. In addition, we plan to use this information in our calculations of how exceptionally long lived the individual is (individual risk score), so it is useful for us to have the information. The NIH distinguishes between "ethnicity" and "race." Question 8 asks about Latino/Hispanic ethnicity. Question 9 asks about race. Some individuals may refuse to provide this information. If the Screenee or Family Reporter appears to be reluctant to answer this question, explain that we are required by the NIH to ask the question but that s/he may refuse to provide this information and still be eligible for the study.

### **Assessment of Health Status, Ability to Communicate and Competency:**

Question 10: Interviewer does not ask this question but assesses the potential participant's ability to communicate. If the participant is hard of hearing or cannot talk clearly or does not seem to understand the questions the interviewer should mark "YES," and terminate the interview using the script at the end of this question. This question will be skipped if the Screenee is not the proband.

Question 11: Read the question and the first 5 responses. Do not read the "Don't know" and "Refused" responses.

Please Note: At this point, continue to Question 12 if speaking with the Proband. If not, skip to Q14a.

Question 12: The interviewer may not recognize certain medical problems. If you are unsure write the participant's verbatim response in the margin and do not mark an answer for this question and continue with the interview. Check with the administrative center and your site PI to see if the condition warrants exclusion. Complete the questionnaire and follow-up with the participant appropriately.

Question 13a-b: For Question 13a, read the script and then write in the participant's response verbatim. Any references to family or living long is fine. Interviewer then marks the appropriate box in Q13b as to their judgment whether the potential participant comprehends the study. If the potential participant clearly does not comprehend the study, end the interview using the script at the end of Q14b.

Questions 14a and b: If speaking with a Family Reporter – Read Question 14a regarding hearing or serious health problems of the Screenee only if the person is a Family Reporter. For Q14b, ask "Do you think he/she would understand the purpose of this study in order to provide informed consent?" If no, then terminate the interview using the script below the question. If yes, continue to Q15a.

### **Assessment of Family History of Longevity:**

**Interviewer Script:** *Now I would like to ask you some questions about long life in [your/Screenee's] family. Please feel free to tell me if you don't know the answer to a question, but please try to give your best guess. I am going to ask about [your/Screenee's] biological children, [your/Screenee's] biological brothers and sisters. We are using the word "biological" to describe individuals that are related to [you/Screenee] by birth, meaning that they share a blood relationship with [you/Screenee]. Please note that none of the study investigators will attempt to identify, or contact specific family members based on the relationship information you provide unless you give us consent to do so at a later point in time.*

Questions 18a – 27a: Self-explanatory. Mark the appropriate response and continue to B.

Questions 18b – 27b: Self-explanatory. Mark the appropriate response and continue to C.

Questions 18c – 27c: If sibling still living, ask questions D through I for each sibling. If sibling is deceased, ask questions J through N for each sibling. If vital status of sibling is not known, proceed to Q18o-r – Q27o-r.

Questions 18d – 27d: **Current age in years.** A best guess for an age is better than unknown. Probe for the participant's best guess. If the participant absolutely will not give a guess then enter D for the age.

Questions 18d1: If the answer to Q18d-27d is an estimate, then check the box in Q18d1-Q27d1 to record it as such.

Questions 18e – 27e: This question is self-explanatory. Ascertain where the siblings live. Include city, state, and/or country.

Questions 18f – 27f: Interviewer – **Do Not Ask:** Does this person live within 2-3 hours of the 3 field centers.

Questions 18g – 27g: Read the question and the first 5 responses. Do not read the "Don't Know" and "Refused" responses.

Questions 18h – 27h: This question is self-explanatory. Ascertain how many living biological children for this living sibling.

Questions 18i – 27i: Ask the screenee how many of these nieces and nephews live within 2-3 hours of the three US Field Centers of New York City, NY, Boston, MA, or Pittsburgh, PA.

Questions 18j – 27j: ***Age at time of death.*** Best guess for an age is better than unknown. Probe for the participant's best guess. You may offer a choice of decades such as "would you say that your (Screenee's) (brother/sister's) age of death was in their 40's, 50's, 60's, 70's, 80's, or 90's. If you probe with a choice of decades, you must cover a full range otherwise the limited range will produce bias. If the participant absolutely will not give a guess then enter N for the age.

Questions 18j(1): If the answer to Q18j-27j is an estimate, then check the box in Q18j(1)-Q27j(1) to record it as such.

Questions 18k – 27k: ***Year of Birth.*** As detailed above, this is a difficult question for many people. Often people will try to figure out year of birth by calculating backwards from the calendar year of the age at death. They often identify the calendar year of death of their sibling by relating age at death to important family events, like weddings or graduations. So for example, the Screenee or Family Reporter may say that "sibling" died a year before their child's wedding, when "sibling" was XX years old and the wedding took place in year XXXX. There are many variations on this example. Record all this verbatim, exactly as given, and then do the calculations as quickly as possible to make sure that the result of the calculations makes sense.

Questions 18l – 27l: ***Cause of Death.*** To appropriately calculate the Family Longevity Score, we need to know whether the person died prematurely due to an accident, injury or war. Read the questions and the "yes" and "no" responses. Do not read the "Don't know" and "Refused" responses.

Questions 18m – 27m: This question is self-explanatory. Ascertain how many living biological children for this living sibling.

Questions 18n – 27n: Ask the screenee how many of these nieces and nephews live within 2-3 hours of the three US Field Centers of New York City, NY, Boston, MA, or Pittsburgh, PA.

When vital status is marked as unknown in Q18c-27c, then:

Question 18o-27o: This question is self-explanatory. Ask for their best guess if unknown. If they don't know, enter D.

Question 18o(1)-27o(1): If the answer to Q18o-27o is an estimate, then check the box in Q18o1-Q27o1 to record it as such.

Question 18p-27p: ***Year of Birth.*** As detailed above, this is a difficult question for many people. Often people will try to figure out year of birth by calculating backwards from the calendar year of the age at death. They often identify the calendar year of death of their sibling by relating age at death to important family events, like weddings or graduations. So for example, the Screenee or Family Reporter may say that "sibling" died a year before their child's wedding, when "sibling" was XX years old and the wedding took place in year XXXX. There are many variations on this example. Record all this verbatim, exactly as given, and then do the calculations as quickly as possible to make sure that the result of the calculations makes sense.

Question 18p(1)-27p(1): If the answer to Q18p-27p is an estimate, then check the box in Q18p(1)-Q27p(1) to record it as such.

Question 18q-27q: This question is self-explanatory. Ascertain how many living biological children for this living sibling.

Question 18r-27r: Ask the screenee if they know how many of their brothers/sisters children live within 2-3 hours of the three US Field Centers of New York City, NY, Boston, MA, or Pittsburgh, PA. If unknown, mark as D.

If Screenee has more than 10 biological siblings, please use additional forms to record this information for those brothers and sisters.

**Calculation of Family Longevity Score:** Do not ask this; the computer program will calculate it for you. Please write in the FLoSS score (prior to December 2006 and FLoSS prime score thereafter. Remember, if you are completing this form on paper, then you will have to call the potential participant or Family Reporter back to indicate their eligibility. However, a lookup table will be provided to the Recruiters so they can clearly identify families that will not meet our eligibility criteria. This will eliminate a return phone call to these individuals.

### **Screenee Eligibility and Family Eligibility:**

Questions 28-30: **Screenee Eligibility** - Do not ask these questions. The interviewer now reviews eligibility criteria and answers each question and marks the boxes. The DES automatically fills these answers if completed directly in the DES.

Questions 31-32: **Family Eligibility** - Do not ask these questions. The interviewer now reviews eligibility of family and answers each question and marks the boxes. Based on the results of this section, follow the instructions and administer **Script 1, 2, or 3 on the preceding page**. The DES automatically fills these answers if completed directly in the DES.

### Important Addendums:

- Chapter 24 – Long Distance Visit Protocol was added January 2007 to address issues specific to recruiting families that completely or partially reside outside of the field center catchment areas. Please refer to this Chapter for specific protocol issues. A summary of the relevant issues related to recruitment are provided below:
  - In December 2006 it was decided that exceptional families that reside in a cluster completely outside of the three US Field center catchment areas can be enrolled and seen if their FLoSS score is  $\geq 15$ . These families will be recruited in accordance with the Long Distance Visit Protocol. See Chapter 24 for the protocol.
    - However, locating and enrolling local families within a field center's respective catchment area will remain the top priority.
    - Families who's key triad was split between a local field center and long distance can be recruited provided they have a FLoSS score of  $\geq 15$ . See Chapter 24 for details.
  - In December 2006 it was also decided that recruiting family members that reside outside of the three catchment areas will be permitted in order to complete the recruitment of families that were originally identified within the field center's catchment area (i.e., "Extending a Local Family Long Distance Visit"). These visits will be coordinated by the Travel Review Committee and formal approval by the Executive-PI Committee. Refer to protocol in Chapter 24.

- As of December 2007, Q31-32 were revised to accommodate the decision to recruit **Split Local and Long Distance families** with FLoSS  $\geq 7$ . This refers to those families in which the key triad (proband, sibling, offspring) reside split between the local catchment area and outside the three catchment areas (i.e., requiring a Long Distance visit to complete the triad.
  - The proband or living sibling is required to reside within one of the US field centers in order to recruit these split families.
  - Q31-32 now refer to the ability to recruit at least 2 siblings in the family and also to verify that one member of the key triad lives within the three US catchment areas.

**If "YES" for Questions 28 to 32, then:**

**Script 1:** *[Your/Screenee's] family is unusually long-lived compared to others we have screened. We are interested in finding out more about [you/Screenee] and [your/his or her] family so that we can discover how some people and their families live to a very old age. In this next part of the study, we would like to ask [you/him or her] and several members of [your/his or her] family to participate so that we can get a more complete picture of [your/his or her] family's structure, health and functioning. The study will collect information about [your/his or her] family's medical history and about [your/his or her] family members' physical activity and mental functions, such as memory. We will also ask [you and your / Screenee and his/her] family members for a blood sample so that we can look for factors in the blood that may increase chances for a long life and successful aging.*

- (a) *Do you think that [you/Screenee] and other members of [your/Screenee's] family would be interested in participating in this next phase of the study, including providing a blood sample?*

If "YES", proceed to **Item B**. The option "No" should only be used if the Screenee clearly expresses that there is no way that they would be involved in this study. If so, then proceed to **Item J** and check the answer that best fits their reason for not participating. If the recruiter feels that the Screenee's concerns can be addressed, they should try to do so. If the Recruiter deems that the Screenee is unsure, check "Don't know" and probe for the reason that the person is unsure. It is up to the Recruiter to do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website. If "Don't know" is marked, the Recruiter should call back the potential participant at a later time after materials have been sent and/or the Screenee had the chance to think about the study.

- (b) *Do [you/Screenee] have a living spouse?*

If "YES", go to **Item C**; if "NO" proceed to **Item H**.

- (c) *Is [he/she] the biological [father/mother] of any of [your/Screenee's] children?*

If "YES", go to **Item D**; if "NO" proceed to **Item H**.

- (d) *What is [his/her] age?*

Self-explanatory and then proceed to **Item E**.

- (e) *Does [he/she] live with [you/Screenee]?*

Self-explanatory. Ascertain whether the spouse lives with the proband being screened and then proceed to **Item F**.

(f) *Does [your/Screenee's] spouse have any living siblings age 85 and older.*

This question is to identify whether it is worthwhile to screen the spouse as a potential proband. Answer the question and then proceed to **Item G**.

(g) *Would you be willing to ask [him/her] if we can contact them to discuss participation in this study?*

If "YES", go to TS2; Record contact information; and then proceed to **Item H**. If "NO", proceed to **Item H**.

(h) *Before we move forward, would [you/he or she] be willing to contact at least two family members (one sibling and one child) and ask them if we can contact them to discuss the study and answer any questions that they may have?*

If "YES", go to **Item I**; if "NO" proceed to Item J.

(i) *May I ask you who you plan to contact; first names only? [Interviewer: Please write down the first names of these individuals, in order of age, on the Family Contact Information Worksheet (TS2).] Thank you. We will call you back in one week to confirm with you that [your family members/they] are interested in speaking with us.*

*When is the best time to call you back? \_\_\_\_\_ AM/PM \_\_\_\_\_ Day.*

*If you or your family member would like to contact us, we can be reached toll-free at XXX-XXX-XXXX.*

(j) *If "No", could you please indicate your reason(s)?* Interviewer – check all that apply.

Once the reason for declining participation are revealed, the Recruiter should do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website. If there is some indication after further discussion that the potential participant may be interested at a later date, go back to (a) and mark "Don't know" and call back the potential participant at a later time after materials have been sent and/or the Screenee had the chance to think about the study. If the answer is an obvious "No", mark the reason and then end the interview using the End Interview script provided.

**IF "NO" to Family Longevity Score of  $\geq 8$  prior to December 2006,  $\geq 7$  thereafter (Question 28), but answers to Questions 29-32 are YES:**

**Script 2:** *Thank you for your time. The information you provided is very important to us. It will help us discover how some people and their families live to a very old age. At this point in our study, we have all the information that we need for now. However, it is possible that as the study continues, we may need to speak with you again. Therefore, we would like to keep [your/Screenee's] contact information on file so that we may contact [you/Screenee], if necessary. Interviewer – please mark the box as to whether the individual is will to be contacted in the future or not. We greatly appreciate the time and interest you have shown in our study.*

**Regardless of Family Longevity Score, if answer was "NO" to any of Screenee Eligibility Questions 29-31 or "NO" to Question (a) or (h) under Script 1:**

**Script 3:** *Thank you for your time. The information you provided is very important to us. It will help us discover how some people and their families live to a very old age. We greatly appreciate the time and interest you have shown in our study.*

**INSTRUCTIONS FOR RELATIVE CONTACT INFORMATION FORM (TS2):**

**Instructions For Administration:**

**Recommended Resources:** *Proband's completed FLSI Interview (or summary report).*

**\*Note:** *For the purpose of this section, Proband refers to the "Potential Proband" of any family which appears to be eligible for the Study based on the initial results of the FLSI.*

In Section 1 of this form, the Proband of a family which appears to be eligible based on the FLSI (FLoSS is above the designated cut-point, no exclusion criteria), is re-contacted. At this time, the Proband (or his/her FR) will be asked to identify his/her siblings to document the family's Pedigree.

In Section 2 of this form, the primary goal is to obtain information on any additional relatives who the Proband or FR has contacted and who have agreed to be contacted by LLFS personnel regarding participation in the Study. Section 2 of this form is an ongoing, continuous process and should be updated whenever additional family members are identified and have agreed to be contacted. **Please Note: The Interviewer will make three attempts to obtain complete information on all siblings and family members; however, if the Proband or family representative is unable to provide additional information after the third attempt, no additional attempts will be made.**

In Section 3 of this form, the purpose is to close the interview with the proband and let him/her know that we will need to speak with them again to get information on their family structure once some other family members have agreed to participate. This section also is used to identify a Designated Family Reporter for deceased siblings' branch of the family.

1. Section 1- Proband's Siblings: The first objective of this form is to identify the Proband's **complete sibship (including full- or half-siblings) and obtain the relevant information requested.** This is the first step in identifying a family pedigree. It is important that this section be completed during this telephone contact and that this information be obtained from the Proband, if at all possible. If not, it should be obtained from the Family Reporter (FR), as identified by Proband.

**Interviewer Script 1:** *Hello, may I speak with \_\_\_\_\_. This is \_\_\_ with the [Institute Name]'s Long Life Family Study. Today, we would like to speak with you to attempt to identify additional members of your family who would be willing to speak with us about the Study. First we would like to ask you about your brother(s)/sister(s). Is this okay?*

[If No]: Ask the Proband whether you can call him/her back once [he/she] has obtained the necessary information. Alternatively, he/she may want to designate an alternative FR. If the Proband will provide the information, proceed to Section 1.

[If Yes]: *Very good; thank you very much.* Proceed with Section 1.

**Name of Proband:** Begin by writing the Last, First, and Middle Names (in that order) of the Family's Proband on the line provided above Section 1. If Proband is female, provide her Maiden Name.

**Sibling # :** Fill in the #1 for the first sibling, on the line provided; be sure to ask the Proband to start with the eldest sibling first. ***Interviewer Tip:*** *Prior to making this call, it is recommended that you review FLSI, Q18(a)-28(j); with this information, you can pre-fill information into (b), (c) and a portion of (g), as well as how many siblings the Proband reported having.*

**(a) Sibling Name:** Ask the Proband to provide that sibling's name, recorded as Last, First, Middle and Maiden Name on each line provided in (a).

**(b) Relationship:** Check the appropriate box in (b), which will indicate the 'gender' of this sibling.

**(c)-(h) Sibling Vital Status/Willingness to be Contacted/Medical Condition:** Indicate the vital status of this sibling by checking one appropriate box in (c). If this sibling is deceased, skip to (h) and ask whether this sibling ever had any of the medical conditions listed in this section and check all that apply. If the sibling is alive, continue with (d) and (f) to determine whether [he/she] is willing to be contacted, or whether contact has not yet been made. If contact has not been made, proceed with the next sibling.

If the Proband is unable to determine whether the sibling is willing to be contacted, ask [him/her] if it would be feasible to contact/re-contact the sibling to make a determination. [If No]: Proceed to the next sibling. [If Yes]: Inform the Proband that you will proceed with this interview, but you will be back in touch at a later date regarding this sibling's willingness to participate. You may also provide the Proband the option of having the sibling contact you directly (provide with necessary contact information).

If the individual providing the information is unwilling to tell the siblings about this study, probe for the reason and select the closest response in (e). If the individual is contacted about the study, but the person is unwilling to be contacted, probe for the reason and mark the closest answer in (g).

**(i) Contact Information:** If the sibling is willing to be contacted, proceed to (f) and complete all contact information of this sibling.

**Important Note:** Prior to initiating contact with any individual identified at this stage, LLFS staff must query the existing database for each name obtained to determine if a Study ID has been previously assigned (i.e. via CMS list); this should also be done even if the individual has not provided consent to be contacted. If an LLFS ID# has been assigned, that number is to be recorded in the space provided at the bottom. For those who do not appear in the DES system, an LLFS ID# will be assigned according to the protocol outlined in the Data Entry System Appendix of the LLFS MOP. This number should also be documented in the space provided on this form, as well as on FLSIa (a/k/a TS1a). Upon obtaining consent to contact, this ID# will be transferred to the TS1a; the TS1a will be entered using the family member's personal ID#, not that of the Proband.

Repeat steps (a)-(i) for every one of Proband's siblings, including full- or half-siblings. The interviewer should place the appropriate "Sibling #" on the line provided at the top of each block in Section 1. The number of siblings reported here should match the total number reported in FLSI. **Please Xerox additional sheets, as needed, and append to this form.**

When the above steps have been completed for all siblings, proceed with Section 2, as outlined below.

2. **Section 2 – Proband's Additional Relatives:** The purpose of this section is identify the Proband's additional **family members** and obtain the relevant information requested. Again, this is an ongoing process and information for this section can also be obtained from family members other than the Proband, as they are contacted; however, it is important that information on the same individual is not entered more than once. **Please Note:** *Information on relatives beyond the Third Generation (i.e. Proband's Parents, Proband/Siblings, and Offspring) does NOT need to be documented for the purpose of this Study.*

**Important Note:** Prior to initiating contact with any individual identified at this stage, LLFS staff must query the existing database for each name obtained to determine if a Study ID has been previously assigned (i.e. via CMS list); this should also be done even if the individual has not provided consent to be contacted. If an LLFS ID# has been assigned, that number is to be recorded in the space provided at the bottom. For those who do not appear in the DES system, an LLFS ID# will be assigned according to the protocol outlined in the Data Entry System Appendix of the LLFS MOP. This number should also be documented in the space provided on this form, as well as on TS1a. Upon obtaining consent to contact, this ID# will be transferred to the TS1a; the TS1a will be entered using the family member's personal ID#, not that of the Proband.

**Interviewer Script 1:** *Thank you so much. Do you feel up to continuing this interview?*

[If No]: Ask the Proband whether you can call him/her back once [he/she] has obtained the necessary information. Alternatively, he/she may want to designate an alternative FR.

[If Yes]: If the Proband would like to proceed, continue with Section 2, Interviewer Script 2.

**Interviewer Script 2:** *Thank you so much for providing me with information regarding your siblings. We will now proceed your other family members. Have you talked to any other relatives regarding this study?*

[If No]: *Would it be helpful for me to send you additional information regarding the study?* [If Yes]: *I will send out additional information to you today. Would it be OK to call you next week to see if you have been able to contact your relatives?* [If Yes]: *What day and time would be best to contact you? (Fill in date and times on the Relative Contact Information Form). Thank you and I will call you on XXXX at XXXX time.* **[If No]: Attempt to determine whether or not this person is willing to participate. If not, determine whether it would be possible to obtain an alternative Designated Family Reporter (FR) and record that person's contact information on the last page of this Screener.**

[If Yes]: *Wonderful; who have you spoken with?* [Obtain name and relationship to Proband.]

**Name of Proband:** Begin by recording the Last, First, and Middle Names (in that order) of the Family's Proband on the line provided above Section 2. If Proband is female, provide her Maiden Name.

**Relative #:** Begin by filling in #1 for the first Relative on the line provided.

**(a) Relative's Name:** Ask the Proband (or FR) to provide the Relative's Last, First, Middle and, if appropriate, Maiden Name on each line provided in **(a)**.

**(b) Relationship of Relative:** Refer to the choices outlined in the corresponding "Response Form" in Appendix B of the LLFS MOP; write in the correct relationship in the blank provided.

**Related by Which Sibling?** Refer to the Sibling #s assigned in Section 1 to determine to which sibling this relative is related; write that sibling's name and corresponding Sibling # in the space provided.

- (c) **Willingness to be Contacted:** Ask the Proband/other LLFS family member whether or not this family member has been told about this research study. Indicate the response in the appropriate box.

[If No]: Ask whether or not [he/she] plans to contact [him/her]. Inform the Proband that you will proceed with this interview, but you will be back in touch at a later date regarding this relative's willingness to participate. You may also provide the Proband the option of having the family member contact you directly (provide with necessary contact information). If the individual is unwilling to contact this family member, please mark the closest answer in (d).

[If Yes]: If the Proband has told the relative about the study, proceed to (d).

- (d) **Determine whether you may contact this relative.** If this relative *is unwilling to be contacted*, probe for a reason and mark the closest answer in (f). If the relative is *undecided*, check the appropriate box and determine whether it would be helpful to check back with the Proband at a later date to ask whether the relative has decided. If the relative *has agreed to be contacted*, proceed to (e).

- (e) **Contact Information:** If the relative is willing to be contacted, proceed to (e) and complete all contact information for this relative. Repeat Q(a)-(e) for each relative contacted.

The subsequent section (right-hand column in Q(g)) is for office use and tracking purposes only. This section is to be completed following the administration of the Family Member Screener (TS1a) to each family member. As the TS1a is completed for each appropriate family member, check the box to indicate that this has been done and proceed to the next line to indicate whether this relative has met the enrollment criteria. Finally, note the date on which the Family Member Screener was scheduled and completed. (*Note to Interviewer: This information will not be entered into the DES System; it is for your tracking purposes only.*)

**Please Note:** Repeat these steps for each of Proband's relatives that are identified throughout the course of the screening process. This is a rolling process and new relatives can be and may be identified at any time throughout the course of screening the Proband and his/her family. Continue to update the TS2 form, Section 2 as needed, as well as data entry for each new relative identified. **Please Xerox appropriate, additional sheets, as needed, and append to this form.**

3. **Section 3 – Conclusion of Interview:** The interviewer is to inform the Proband that additional questions regarding [his/her] relatives will need to be asked a later time (once the family is enrolled). Efforts should be made to obtain the information from the Proband, however, if the Proband indicates [he/she] would prefer another family member be contacted to do this, the contact information should be documented. This section also is used to identify a Designated Family Reporter for deceased siblings' branch of the family.

- (a) **Interviewer Script:** *"Thank you for answering our questions. The information you provided is very helpful. We still need to gather just a bit more information from the family members you identified to determine whether we can schedule you and your family for the next phase of this study. If enough people in your family agree to participate, you and your family members will be invited to take part in an in-person visit. This interview can be scheduled at your convenience either in your*

*home or at our clinic. During the visit, a trained clinical staff member will obtain medical and personal information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, blood pressure and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed in approximately 3 hours. We will use all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.*

*Our next step will be to contact your siblings and determine their interest in participating. If your family is enrolled into the study, we will need to obtain additional information about your family structure, including your parents, spouse(s), and children. Therefore, we would like to call you back. Is this agreeable to you?*

Check the appropriate box to indicate whether the Proband agreed to be called back.

- (b) [If Yes]: Go to **Script in (b)** and then end the interview: *Is there a preferred day/time to call you back?* Indicate date/time on lines provided.
- (c) [If No]: Go to **Script in (c)**: *Is there someone else in your family who we can contact to provide this information?* If no, end interview.

[If Yes]: Proceed with the completion box by confirming that this new designated Family Reporter (DFR) has been notified by the Proband about this study, its requirements, and is willing to be contacted? [If No]: Attempt to ask the proband whether *[he/she]* can call this person to accomplish that and arrange a time to call back.

[If Yes]: Document the name, contact information and best time to call this FR in the space provided.

- (d) If any of the Proband's siblings are deceased, the Study would like to obtain Pedigree information for this Index Person's family (i.e., children and spouse(s)). Therefore, it is important to identify a Family Reporter for this Index Person's branch. Go to **Script in (d)**: *Is there someone we can contact to obtain information about your [brother/sister]'s family?* [If Yes] Proceed with the completion box by confirming that this new designated Family Reporter (DFR) has been notified by the Proband about this study, its requirements, and is willing to be contacted? [If No]: Attempt to ask the proband whether *[he/she]* can call this person to accomplish that and arrange a time to call back.

## **TELEPHONE SCREENING INTERVIEW - FAMILY MEMBER (TS1a):**

**Background and Purpose:** At this time, you will be contacting those individuals who have provided verbal consent via the Proband or another relative. The purpose of this form is to document verbal consent from each relative to participate in the Study. When a minimum of Proband, one sibling and one child consent,

the Minimum Family Size (MFS) requirement is met and the family is enrolled. The Family Member Telephone Screening Interview (TS1a) is the point at which LLFS personnel confirm each family member's willingness to participate, recruit each family member into the study and, finally, schedule an enrollment visit with these family members.

A family will be enrolled if at least 3 family members (proband, sibling and 1 offspring of either proband or sibling) have indicated their willingness to participate. Also at this point, the recruiter may begin scheduling the in-home visit (a/k/a enrollment visit). Examinations will be scheduled beginning with families who are potentially the largest. For family members electing not to participate, study investigators will make no attempt to identify or contact them. Key individuals will be identified as facilitators within families. When possible, enrollment visits can be organized around normal family gatherings (family reunions, picnics, etc.) to reach a number of individuals at one time. When distance precludes or when it is impossible to gather a large group, the family will be characterized through individual visits.

There are two situations under which a family member may be interviewed utilizing the Family Member Screening Interview (TS1a): (1) the family has not yet met the Minimum Family Size (MFS) to be enrolled; or (2) the family has already met the (MFS).

1. **Minimum Family Size (MFS) Has Not Been Met.** If by obtaining the consent of this relative, the MFS is not yet met, then an enrollment visit should not be scheduled. *Script C*, found at the end of the interview, demonstrates our interest in this family and this family member, as well as providing information about the components of the LLFS assessments, and determining the willingness of Screenee to participate if the MFS is met at a future time.
2. **Minimum Family Size (MFS) Met.** If this Screenee consents and by doing so, the MFS for the family is met, then the entire family is enrolled and in-home visits can be scheduled. In this case, *Script D* at the end of the interview should be read. This script includes an invitation to the Screenee to participate in the study, provides information about the components of the LLFS assessments, and starts the process of scheduling an in-person enrollment and assessment visit.

### Detailed Instructions:

**Confidentiality:** Information obtained through these screening interviews is to be kept separate from all other study data, in a subject's a written consent form has not yet been signed.

**Interviewer Note:** This interview entails calling a family member that has verbally consented to be contacted, via the Proband or another previously screened family member. Before you begin, please determine whether the MFS has been met for enrollment of the family by reviewing the TS2; record this piece of information on the face sheet of the TS1a. This information is necessary to deliver the correct eligibility script at the end of this interview. Refer to the notes at the End of Interview which will help guide you.

**Interviewer Script:** *Hi, my name is [insert your name here] and I am calling from [insert your institution here] about the Long Life Family Study. We are attempting to learn why some families have more relatives living to a very old age than some other families. [Insert family member's name] told us that they spoke with you and that you are interested in learning more about participating in this family study. [Insert Proband's name] has had the good fortune to live a long life. That is why we are asking you to participate with [him/her] in an important international study of longevity. In addition to our university, this study is being conducted at two other American universities [insert names here], as well as at the University of Southern Denmark. Our goal is to find out what families with histories of long-*

*lived individuals have in common. By participating in this study with your family members, you may have an opportunity to help improve the health of future generations.*

*We have already spoken with [insert Proband's name] about your family, but if it is okay with you, we have some questions we would like to ask you. Based on the telephone interview, some family members will be invited to participate in a more detailed part of this study. This would involve seeing you in person. You do not have to answer any questions that you do not want to. All information that I receive from you, including your name and any other identifying information, will be strictly confidential and kept under lock and key. Your participation is voluntary; you do not have to answer these questions. This will take approximately 5 minutes. Is it okay to speak with you now?*

Mark the "Yes" or "No" box. If no, determine a day and time when the family member can be called again to complete the screening interview

**Question 1: Script:** *"Do I have permission to ask you some questions about yourself?"* This interview should not be administered until the prospective participant has agreed to answer the questions. If they do not agree, inquire as to an alternative time to contact them; if they still do not agree, then terminate the interview by thanking them for speaking with you.

### **Contact Information:**

**Questions 2a-2d:** *Verify the contact information of the Screenee.* Note that we would like to have two phone numbers, one for daytime and one for evening. This information is crucial because instructions for the preparation for the enrollment and assessment visit are sent to this address, and the phone number is used to remind participants of appointments. Check the accuracy of the address and phone number carefully. If the person lives outside of the US, put the country in the city field.

### **Demographic Information:**

**Question 3-4: Age and Date of Birth.** Ask the participant for his/her age and date of birth. Record the given age and date of birth on the form. Be sure to use the format provided in the example. Check to make sure that the two pieces of information are consistent (e.g., if birth date is 1920, then the person should be 85 years old ).

**Question 5: Gender.** This question is self-explanatory.

**Question 6: Relationship to Proband.** Determine the relation of the family member to the Proband, referring to the Proband by name. Be sure to determine the precise biological relationship, for example, full-sibling versus half-sibling or full-niece versus half-niece. Use the "other" category as necessary. If participant is a niece or nephew of Proband, be sure to note to which of Proband's siblings they are related.

**Assessment of Health Status.** These are the main questions that determine personal eligibility of the family member that is being screened. There are two ways in which a family member can be deemed ineligible (1) if their health status is so poor that they would not be able to participate in or to complete the study assessments, or (2) if they do not have a clear understanding of the purpose of this study and thus appear to be too cognitively impaired to be able to participate in or to complete the study assessments.

**Protocol Note:** As of December 2006, siblings that have cognitive impairment can be enrolled into LLFS (but not as part of the key triad) via the proxy consent protocol. See Chapter 5, Interviewing Guidelines for Proxy Administration.

**Question 7:** Read the question and the first 5 responses. Do not read the "Don't know" and "Refused" responses. Select only one response.

**Question 8:** The interviewer may not recognize certain medical problems. If you are unsure write the participant's verbatim response in the margin and do not mark an answer for this question and continue with the interview. Check with the administrative center and your site PI to see if the condition warrants exclusion. Complete the questionnaire and follow-up with the participant appropriately.

If the Screenee is definitely physically unable to participate in the study because of the presence of advanced cancer or a serious medical condition, then read **Script A – End Interview:**

*"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age." END OF INTERVIEW*

If the Screenee is definitely *physically* able to participate in the study, then continue with the interview by skipping to Q9a.

If the Screenee is unsure of whether or not s/he has a condition which makes him/her physically unable to participate in the study, then say s/he should take some time to think it over, and ask for a date and time when the interview can be continued.

**Assessment of Understanding of LLFS:** This section asks the participant to provide a brief statement of their understanding of the purpose of the LLFS, in order to determine their ability to provide informed consent.

**Interviewer Script for Those Continuing:** *Before we continue, I want to ask you what is your understanding of the purpose of the LONG LIFE Family Study?*

**Question 9a-9b:** Write in the participant's response. Any references to family, living long or research is fine. Interviewer then marks the appropriate box in Question 9b as to their judgment whether the potential participant comprehends the study. If the potential participant clearly does not comprehend the study, end the interview using the **Script B**. If the family shows willingness and interest in a cognitively impaired family member to be enrolled in LLFS, please refer to Chapter 5, Interviewing Guidelines for Proxy Administration for protocol details.

**Question 9c:** Interviewer does not ask the next question but assesses the potential participant's ability to communicate. If the participant is hard of hearing or cannot talk clearly or does not seem to understand the questions the interviewer should mark "YES" and terminate the interview using **Script B**.

**Script B – End Interview:** *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age." END OF INTERVIEW*

**Eligibility and Enrollment:** At this point in the Family Member Telephone Screener, the scripts and questions diverge, depending on whether the family has already met the Minimum Family Size (MFS) requirement.

A. **Minimum Family Size Not Been Met.** If the Screenee is eligible and willing at the end of the interview, the family may still not be eligible because not enough eligible family members have agreed to participate. In this case, do not schedule an enrollment visit. Read Script C which demonstrates our

interest in this family member and in this family and provides information about the components of the LLFS study assessments and determines the Screenee's willingness to participate if the family is eligible. Then ask **Questions 10a-10e**, as appropriate once the family has been deemed eligible.

**Script C – Minimum Family Size Not Been Met:** *"Thank you for answering our questions. We still need to gather just a bit more information from your family members to determine whether we can schedule you and your family for the next phase of this study. In that phase, we are interested in studying families over two generations – with at least 2 family members in the oldest generation and one from the offspring generation). If enough people in your family agree to participate, you and your family members will be invited to take part in an in-person visit. This interview can be scheduled at your convenience either in your home or at our clinic. During the visit, a trained clinical staff member will obtain medical and personal information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, blood pressure and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed in approximately 3 hours. We will use all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.*

*"While we are in the process of contacting your family members already identified by other relatives, would you be willing to ask your [brothers/sisters, aunts/uncles, nieces/nephews or cousins] if we can contact them to discuss the study and answer any questions they may have? May I ask who you plan to contact? First names only please and their relationship to [Insert Proband's Name Here]. **Note to Interviewer: Record this information on TS2.** When I call you back in a week or so regarding your families' eligibility, I will be confirming that you spoke with these family members and they are interested in speaking with us."*

- B. **Minimum Family Size Met.** If the Screenee is eligible and willing at the end of the screening interview, and the family now meets the MFS requirement for enrollment, then proceed with scheduling an in-person visit for this family member. **Proceed to Script D, Questions 10a-10e.** **Script D** includes an invitation to the Screenee to participate in the study, provides information about the components of the LLFS study assessments, and attempts to schedule an in person enrollment and assessment visit. **Questions 10a-10e** are related to the scheduling of an in-person or a telephone visit. Preference should always be given to an in-person visit, as there are a number of panels that involve direct assessment of physical function, anthropomorphic characteristics and physiologic function that cannot be conducted via a telephone interview. In addition, the blood draw is critical to the ability of the study to conduct genetic research on longevity. For all these reasons, participants should be encouraged to have an in person visit, either at their home, or at a university based clinic. However, participants are not *required* to have an in-person visit, and telephone visits should be scheduled if that is the only option.

**Script D – Minimum Family Size Met:** *Thank you for answering our questions. The information you provided is very helpful. At this point, we would like to invite you to participate in an in-person visit so that we can gather more information about your health and find out what common traits are present in families with long-lived individuals. This interview can be scheduled at your convenience either in your home or at our clinic. During the visit, a trained clinical staff member will obtain medical and personal*

*information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, blood pressure and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed in less than 3 hours. We will use all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.*

**Question 10a: *In-Person Visit.*** If the Screenee answers "YES" to Question **10a**, then proceed to Question 10c. The option "No" should only be used if the Screenee clearly expresses that there is no way that they would be involved in this study. If so, then proceed to Question 10b. If "Don't know" is marked, the Recruiter should call back the potential participant at a later time after materials have been sent and/or the Screenee had the chance to think about the study.

**Question 10b: *Refuses.*** Check the answer that best fits their reason for refusing participation and then end the Interview using the End Interview Script provided. If the Recruiter feels that the Screenee's concerns can be addressed, they should try to do so. If the individual is refusing due to not willing to provide a blood draw, if they are not a member of the key triad, they can be recruited providing they will give a saliva sample. If the Recruiter deems that the Screenee is unsure after further discussion they can check "Don't know" and probe for the reason that the person is unsure. It is up to the Recruiter to do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website.

**Question 10c: *Location of In-Person Examination.*** Mark whether the Screenee prefers a home or clinic in-person examination. If Screenee chooses 'home' or 'clinic', proceed with scheduling the visit. If they provide a response to the 'other' option, ask Q10c to provide the option of a Telephone Visit.

***Suggested Script for Scheduling/Confirming Appointment:*** "We are currently scheduling in-person visits for the week of \_\_\_\_\_. Are you available on \_\_\_\_\_? (Work with subject to schedule a convenient time.) The visit will take about 3 hours to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the visit. Do you have any questions at this time? We will call you the day before your visit to confirm the date and time. The visit will take under three hours to complete. Do you have any questions at this time?"

*We are very excited about meeting you in-person on \_\_\_\_\_ [day/date] at \_\_\_\_\_ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

If the family member that you are screening lives out of town, and requests a distant visit or will be visiting the area in the future, mark "Other" and specify the location of the distant visit (City/State) or a projected date to follow-up with the individual as to when they will be in the area. As of December 2006, complete a Long Distance Travel Request Form and submit to the current Travel Chair and also to Amy Sleeter for consideration. Please see Chapter 24 for more specific details. Please end the interview for those desiring a distant visit with the following script, "We will follow up with as soon as possible to update you when we will be in your area."

**Question 10d: Telephone Visit.** This is asked to provide the Screenee the option of a combination Telephone Interview(s), Mailed Questionnaires and a visit to their Primary Care Physician (for blood collection), avoiding a clinic or in-home examination. If they answer "Yes", then proceed with the **Telephone Visit Script:**

**Telephone Visit Script:** " We are currently scheduling telephone visits for the week of \_\_\_\_\_. Are you available on \_\_\_\_\_? (Work with subject to schedule a convenient time.) The call will take about \_\_\_\_\_ [minutes/hours] to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the call. Do you have any questions at this time?"

We are very excited to talk to you on \_\_\_\_\_ [day/date] at \_\_\_\_\_ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye. **END OF INTERVIEW**

**Question 10e:** If the Screenee answers "NO" to Q10d, then ask Q10e and proceed with the **End Interview Script:**

**End Interview Script:** "Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age. If you decide at a later date that you would like to participate in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW**

**Questions 11a – 11g are only asked for those in Proband Generation Only:**

**Question 11a: Living Spouse.** If "Yes", go to Q11b; if no end interview by confirming appointment and administering the End Interview Script at the end of Q11g on page 7.

**Question 11b: "Is [he/she] the biological [father/mother] of any of your children?"** For the Proband Generation, we are only interested in seeing the biological parent of the offspring that we are recruiting. If "YES", go to Q11c; if "NO", then go to the End Interview Script at the end of Q11g on page 7.

**Question 11c: Age of Spouse.** Enter in years and then go to Q11d.

**Question 11d:** Self-explanatory. Ascertain whether the spouse lives with the family member being screened. This is for informational purposes only, it is not an exclusion if the spouse does not live with the Proband generation individual (i.e., Proband lives in a nursing home, but spouse lives with his/her daughter). Proceed to Q11e.

**Interviewer answers Q11e, do not ask participant:**

**Question 11e: "Does spouse live within 2-3 hours of the New York City, Boston, MA or Pittsburgh, PA field centers?"** Self-explanatory. Proceed to Question 11f.

**Question 11f: "Does your spouse have any living siblings age 85 and older."** This question is to identify whether it is worthwhile to screen the spouse as a potential proband. Answer the question and then proceed to Question 11g.

**Question 11g Verbal Consent.** Please ask the family member if they are willing to invite their spouse to participant in LLFS. If "Yes", go to TS2, Section 2 and record the contact information and follow procedures outlined in Chapter 23 of the Manual of Procedures for screening and enrolling control spouses. If "No", end interview and remind the family member of his/her appointment details.

**End Interview Script:** *"Would you be willing to ask your [brothers/sisters, aunts/uncles, nieces/nephews or cousins] if we can contact them to discuss the study and answer any questions they may have? May I ask who you plan to contact? First names only, please, and their relationship to [Insert Proband's name here]."*  
**Record this information on TS2.** *"I will call you back in a week or so to confirm that you spoke with these family members and they are interested in speaking with us."*

**Questions 12a – 12e are only asked for those in Offspring Generation Only:**

Question 12a: **Living Spouse.** If "Yes", go to Q12b; if no end interview by confirming appointment and administering the End Interview Script at the end of Q12e on page 8.

Question 12b: **Age of Spouse.** Enter in years and then go to Q11c.

Question 12c: Self-explanatory. Ascertain whether the spouse lives with the family member being screened. This is for informational purposes only, it is not an exclusion if the spouse does not live with the family member. Proceed to Q12d.

**Interviewer answers Q12d, do not ask participant:**

Question 12d: **"Does spouse live within 2-3 hours of the New York City, Boston, MA or Pittsburgh, PA field centers?"** Self-explanatory. Proceed to Question 12e.

Question 12e **Verbal Consent.** Please ask the family member if they are willing to invite their spouse to participant in LLFS. If "Yes", go to TS2, Section 2 and record the contact information and follow procedures outlined in Chapter 23 of the Manual of Procedures for screening and enrolling control spouses. If "No", end interview and remind the family member of his/her appointment details.

**End Interview Script:** *"Would you be willing to ask your [brothers/sisters, aunts/uncles, nieces/nephews or cousins] if we can contact them to discuss the study and answer any questions they may have? May I ask who you plan to contact? First names only, please, and their relationship to [Insert Proband's name here]."*  
**Record this information on TS2.** *"I will call you back in a week or so to confirm that you spoke with these family members and they are interested in speaking with us."*

**For Index Person(s) Only:**

Questions 13a-13c are to be asked only of the Index Person(s) (i.e. Proband's participating siblings). These questions are designed to determine if s/he would like to continue on with the interview and complete the Pedigree Information Form (PIF) at this time.

Question 13a: **Can Proceed to PIF?** [If "Yes"]: Proceed with the PIF questionnaire which is discussed, in detail, in Chapter 14 of the LLFS MOP. [If "No"]: Proceed to Question 13b to determine if there is a better day/time to re-contact the individual to complete the PIF.

Question 13b: **Schedule a time for PIF.** [If "Yes"]: Proceed with scheduling a day/time to call them back and thank them for their assistance. [If "No"]: Only proceed to Question 13c if it appears that the Index person is unwilling to do it at a later date. Administer the following script:

*"In order to conduct in-person visits on your family, we will need to have you or someone your designate provide some additional information about your family structure."*

**Question 13c: *Identifying a Designated Family Reporter.*** If the Index is unwilling to provide the information for the PIF, ask if there is another family member from that branch willing to provide this information. [If "Yes"]: Obtain the information requested in the box labeled "Family Reporter", including all necessary contact information for this individual. [If "No"]: End interview using the following script:

*"Thank you so much for the information you have provided. We greatly appreciate the time and interest you have shown in our study. If you decide at a later date that you would like to participate in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye"*

***Interviewer Note: It is important that as the interviewer you make all attempts to either obtain the information directly from the Index or obtain a designated reporter. Without the PIF information, the value of the family to the study will be compromised.***

### **TELEPHONE SCREENING INTERVIEW – CONTROL SUBJECTS (TS1a-c)**

Please refer to Chapter 3 of the LLFS Manual of Procedures.

Study Documents Referred to in this Chapter:

- Family Longevity Selection Score Instrument - Proband (FLoSS-I a/k/a TS1)
- Telephone Screening Interview - Family Member (TS1a)
- Proband Relative Contact Information Form (TS2)
- Pedigree Information Form (PIF)
- LLFS Telephone Screening Interview - Control Subject (TS1a-c)