For IRB use only, not to be included in patient information.

This model informed consent form has been reviewed by the DCP/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document which are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to the risks or alternatives sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language, justification and a copy of the IRB minutes must be forwarded to the Southwest Oncology Group Operations Office for approval before a patient may be registered to this study.

Readability Statistics:	Flesch Reading Ease	61.8 (targeted above 55)
	Flesch-Kincaid Grade Level	8.7 (targeted below 8.5)

S0000, Selenium and Vitamin E Cancer Prevention Trial (SELECT)

This is a clinical trial (a type of research study). Clinical trials include only people who choose to take part. Please take your time to make your decision. Discuss it with your family and friends.

You are being asked to take part in this study because you are a healthy man and have never been told that you have prostate cancer. African American men who are of age 50 or older are eligible. Men of other ethnic groups aged 55 or older are eligible. The reason for this age difference is that prostate cancer appears at younger ages in African American men than in men of other ethnic groups.

WHY IS THIS STUDY BEING DONE?

Prostate cancer is the cancer (aside from skin cancer) found most often in U.S. men. Most men with prostate cancer do not die of this disease. Five-year survival rates are high due to early detection. However, even non-fatal prostate cancer can hurt your quality of life. For example, prostate cancer can cause sexual problems, urinary problems, pain in the bones, and pain in the lower back during bowel movements or during ejaculation.

The purpose of this study is to compare the effects (good and bad) of the study supplements. The supplements are selenium (*L*-selenomethionine), vitamin E (alpha-tocopherol), selenium plus vitamin E, and placebo (a pill containing no active substances). We want to see whether the supplements, other than the placebo, can prevent or reduce the occurrence of prostate cancer.

[Note to Institution: Remove the next paragraph if your site is not participating in the Health Related Quality of Life (HRQL). Participants include all CCOPs and selected VACSP sites.] *(5/25/01) (2/14/02)*

We also want to find out what the quality of life is like for men in this study. You will fill out forms to explain how you feel. It is very important to have your view about how you have been feeling while you are in the study. This is especially important because you are healthy and this study is being used for

possible prevention of cancer rather than as a treatment for a disease. By completing a form regularly, you will help describe the effect of this study on your quality of life.

In past studies of selenium's effects on other cancers, possible effects on reducing prostate cancer were found. However, a large study looking at the effects of selenium on prostate cancer has never been done. In past studies of vitamin E, it has also been linked with reduced prostate cancer. Again, a large study looking at the effects of vitamin E on prostate cancer has never been done. Past studies focused on effects on other types of cancer.

No studies looking at the effect of using both selenium and vitamin E have been done. Based on past studies using other agents as well as the two supplements we are testing here, we believe that men may get an added benefit from using these two supplements together.

While a formal study testing the effects of these supplements on preventing prostate cancer has not been done, the benefits of taking these supplements is strongly suggested. Please be aware that you have a twenty-five percent chance (1 in 4) of being assigned to receive neither of these supplements (placebos only). *(Paragraph added 5/25/01)*

The main purpose of this trial is to learn more about prostate cancers in healthy men that are found as part of regular medical care. We want to know whether the study supplements can prevent or decrease these cancers.

Optional Projects

We would also like to store samples of your blood, toenail clippings and tissue for use in future research. These studies might include genetic studies and nutritional studies related to cancer and other diseases that are common in your age group. None of these would be of direct benefit to you, but could help us learn about other ways to prevent cancer.

Giving blood, toenail clippings or tissue for future research is up to you. You may show whether you want to have these samples collected and stored by checking the box(es) at the end of this form. *(5/25/01)*

(Paragraph deleted 5/25/01)

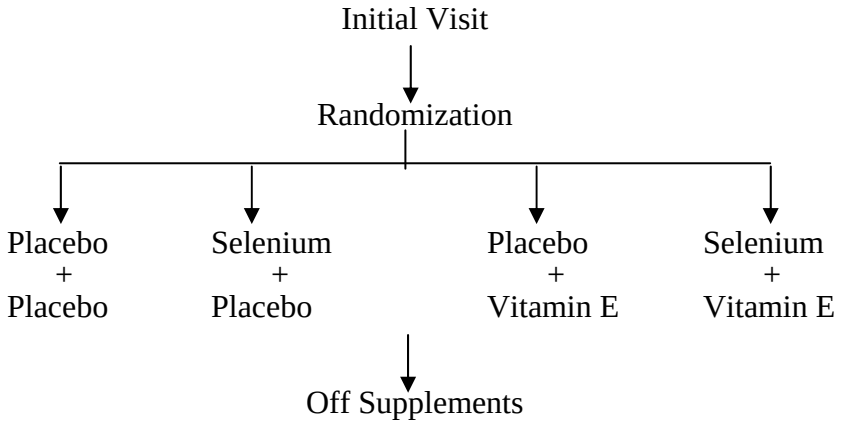
HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 32,400 men will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

This study has four study groups. One group will receive two placebos (no active medication), a second group will receive selenium and a placebo for vitamin E, another will receive vitamin E and a placebo for selenium, and the fourth group will receive selenium and vitamin E. One placebo pill will look and taste the same as the selenium pill, and the other placebo pill will look and taste the same as the vitamin E pill.

You will be "randomized" into one of these four study groups. This means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researcher will choose or know what group you will be in. A computer will assign the groups so you will have an equal chance of being placed in any group.



You will take two pills daily, one from each of two bottles. This will be continued for seven to twelve years (depending on when you entered the study). At the end of the study, all participants will be told which group they were in. (Participants may also be told which group they were in if there is a medical need to know.)

It is important to have all four of these study groups to study the effects of vitamin E and selenium. Thus we ask if you take part in this study, that you only take the supplements of vitamin E and selenium we supply. We also ask that you stop taking any other supplements (including multivitamins) containing vitamin E or selenium. We will provide you (and your significant other, if you wish) with multivitamins made for this study. These are very similar to multivitamins you can buy in stores, but were made without vitamin E and selenium. We ask that if you desire to take multivitamins, you use only these multivitamins provided during the study. You may want to ask your doctor about taking these multivitamins. The study does not require that you take them.

If you take part in this study, you will have the following tests:

- During the first year, you will have a randomization visit and then will be contacted at three and nine months by phone to see how you are doing. The phone calls should last about fifteen minutes. At the randomization visit you will be asked to fill out a form which asks about your diet and vitamin use. *(5/25/01)*

- You will have office visits every six months and have your remaining pills counted. You will receive a limited medical exam every year. If you wish you may also have a yearly exam of your prostate (digital rectal examination). If you wish you may also have a yearly blood test (prostate specific antigen-PSA) to look for evidence of prostate cancer. You will be given a separate brochure to provide you with background on these tests. These office visits should take less than an hour, but time frame will depend on the amount of testing you wish.

- During this study you may have to have surgery or a biopsy on your prostate. If the tissue from the surgery is either suspicious for cancer or has pre-cancerous changes (high grade prostatic intraepithelial neoplasia-PIN), tissue samples will be sent to a SELECT central laboratory to confirm this.

*[**Note to Institution**: Remove the next paragraph if your site is not participating in the serum level adherence assessment.]*

- You will also have blood drawn at some follow-up visits to test the level of vitamin E and selenium in your blood. This blood draw will be done at randomization and at six months, one year, two years, four years, six years, eight years and ten years after you begin the study. Participants who are known to have an infectious disease such as HIV or hepatitis will not be asked for their blood sample. *(2/14/02)*

***[Note to Institution**: Remove the next paragraph if your site is not participating in the Health Related Quality of Life (HRQL). Participants include all CCOPs and selected VACSP sites.] (5/25/01) (2/14/02)*

- You will be asked to answer quality of life questions before you are assigned to your study group. The Nurse/Clinical Research Associate at your institution will give you directions for filling out these forms. You will be asked to answer these questions several times to help us see what kinds of changes happen over time. You will be asked to answer these questions during your visits on years one, three, five and seven.

Optional Projects

Even if you choose to take part in this study, the following projects are *optional*, and require your extra consent. You may show whether you wish to take part in *any* of these by checking a box at the end of this form. *(5/25/01)*

1. *(contact database deleted 11/21/05)*

2. The activities listed below involve giving blood, toenail clippings, and tissue for future study. The blood and toenail clippings will be collected at the time of randomization.

   - *If you agree*, four teaspoons of blood will be drawn and sent to a central storage space for use in future research.

   - *If you agree*, toenail clippings will be sent to a central storage space to look at the amount of selenium in your body. (When you take selenium, higher levels of selenium collect in your toenails.)

   - *If you agree*, prostate tissue samples which are taken for medical reasons and sent to a central storage space (as explained on the previous page) may be kept for future research. At some research sites, prostate tissue samples without cancer may be sent *if you agree*. *(5/25/01)*

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for seven to twelve years. This will depend on what year of the study you started. If you started in the first year you will be in the study for about twelve years. If you started in the fifth year of the study you will be in the study for about seven years.

The researcher will take you off this study (i.e., you will stop receiving supplements) if you develop prostate cancer. If this happens, we ask you to keep making clinic visits every year and/or respond to phone calls. We would like to keep track of your health until the study is over.

You may also stop receiving supplements for any of the following reasons. The side effects of the supplements are too risky for you (see "What are the Risks of the Study, below.). You stop coming in for required visits. New information about the supplements comes out that suggests the supplements will not work or will be unsafe for you. It is unlikely, but the study may be stopped early due to problems with study supplement supply or lack of funding.

You may remove yourself from the study at any time for any reason.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for the side effects listed below. You should discuss these with the researcher and/or your regular doctor. There also may be other side effects that we cannot predict. Many side effects go away shortly after the pills are stopped. In some cases side effects can be serious or long lasting or permanent.

Most people believe that vitamins and food supplements have few and mild side effects. However, the doses used in this study are higher than the recommended daily requirements for selenium and vitamin E.

Placebo

These pills do not contain any active ingredients. These pills will look just like the pills containing vitamin E or the pills containing selenium; however, there should not be any side effects. The selenium-matched pills contain an inactive filler (dicalcium phosphate) and the vitamin E-matched pills contain soybean oil. *(2/14/02)*

If you have any difficulty taking soybean products, please discuss this with your doctor. *(2/14/02)*

Selenium

Selenium is found in many foods. The dose of selenium for this study is not expected to cause you any side effects. However, long term use of selenium at higher doses has been known to cause mild nausea, garlic breath (or "bad breath"), hair or nail changes, cough (symptoms of the common cold), bronchitis, dizziness, weakness, skin redness or rash, irritability and tiredness. One study did report an increased risk of non-melanoma skin cancer (particularly squamous cell skin cancer) with selenium use in patients who had previously had this disease. *(1/14/04)* **Removing selenium supplementation can reverse side effects. There may also be other side effects that we cannot predict.**

Vitamin E

No serious side effects have been linked to the use of vitamin E in the doses used for this study. One study did report an increased risk of stroke among male smokers taking this vitamin; however, this risk was seen only in male smokers who already had uncontrolled high blood pressure.

Combination

Based on prior studies, the combination of selenium and vitamin E is not expected to cause extra side effects. We do not expect either different side effects or more frequent or severe side effects than with each supplement given alone. As with the use of selenium and vitamin E alone, there also may be side effects from the combination that we cannot predict.

Samples of Tissue, Toenail Clippings and Blood Banking

There are very few risks to you.

The blood draw could cause minor pain and/or leave a bruise.

There is a remote risk that release of information from your research record would affect applications for insurance or jobs by you or other members of your family. The Southwest Oncology Group is in charge of making sure that this will not occur as a result of any research using your tissue, blood or toenail sample. Any research information about you is kept private.

If further projects are planned that require use of samples which can be directly linked to you, we will contact you and ask for this consent. (If you do not want to be contacted for future studies but would like to give your permission for these studies you can check a box at the end of this form.)

Genetic studies are very complex. They require many cells to explore how genes may affect the risk of prostate cancer. A small amount of your white blood cells may be "grown" in a laboratory to develop a "cell line" that can be used for this research.

You should face no extra risks beyond those mentioned above if your white blood cells are "grown" in the laboratory to develop a "cell line" for use in genetic research.

For more information about risks and side effects, ask the researcher or contact (NAME)_____.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

The main benefit this study hopes to provide is knowledge. We hope to find knowledge that will be useful to other men in the future. If the study shows that any of the study groups has had a good result, the people in the study who take that supplement(s) would receive this benefit. But the use of vitamin E and/or selenium supplements has not been shown to reduce or prevent prostate or other forms of cancer. So there is no guarantee that you will receive any benefit from being in the study. The researchers feel that being in this study will give you at least as good a chance of preventing prostate cancer as you might expect from other supplements or drugs.

The possible benefits of being in the study are the same as taking selenium and/or vitamin E without being in the study.

(Paragraphs deleted 1/20/03)

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

You may choose to be in other studies looking at other ways to prevent prostate cancer, if you are chosen to take part in such studies. One large study has shown that finasteride is effective in preventing prostate cancer in some men. However, men on the study who got prostate cancer while taking finasteride experienced a slightly higher rate of high g
rade tumors.
(1/14/04)

Some vitamin companies are selling selenium and vitamin E, as well as other nutrients, as supplements for prostate health. You may buy these supplements at your own expense without being on the study. *(sentence deleted 2/14/02)*

Please talk to your regular doctor about these and other options.

No one knows if any of these supplements prevents or helps prevent prostate cancer. *(1/14/04)*

WHAT ABOUT CONFIDENTIALITY?

The data about your participation in this study will be kept secret. It will be used only for research, as allowed by state and federal laws. As genetic research may find genetic knowledge about you, this knowledge will be kept secret to the full extent allowed by law. Your blood, toenail clippings, tissue and health information will not be labeled with your name. No one who works with these samples will have access to your name. Your name and any identity information will not be used in any reports.

Individual results about research done with your blood, toenail clippings or tissue will not be routinely given to you or your doctor. *(2/14/02)* These reports will not be put in your health record. The research will not have an effect on your care. You can be in the main study without having your blood, toenail clippings or tissue stored for future studies.

We cannot guarantee complete secrecy. We may disclose your personal data if required by law. Your records for this study will be sent by facsimile transmission (FAX machine) or over the Internet directly into a central computer. It is possible (although unlikely) that your records could be sent to the wrong FAX machine in error. Records sent by computer will be sent using current Internet security.

Groups that may inspect and/or copy your research records include: the National Cancer Institute; the Food and Drug Administration; the makers of the vitamin E, selenium and placebo pills for this study, and the Southwest Oncology Group.

If we publish the information we learn from this study, you will not be identified by name or in any other way.

WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance. *(5/25/01)* Added costs may be due to side effects, finding cancer or other diseases at your exam or from blood or tissue samples. *(5/25/01)* For example, your doctor may suggest a biopsy if you have an abnormal prostate exam (digital rectal examination-DRE) or blood test (prostate specific antigen-PSA). These costs are discussed further below. Please ask your nurse or doctor about any expected added costs. *(5/25/01)*

If you get hurt or sick from being in this study, emergency medical treatment is available. This treatment will be provided at the usual charge. No funds/funds have been set aside to pay you if you get hurt or sick. *(Local institutions must choose the option that best fits the hospital's situation)*

You or your insurance will be charged for medical care and/or hospital care if needed. While the PSA test (if you desire it) will be reimbursed at a set rate every year while you are on this study, other medical costs (including biopsy costs, if a biopsy is required) will be charged to you or your insurance. The PSA test that helps to find out whether you can be in this study will be (charged in the usual way/provided at a reduced rate). *(Local institutions must choose the option that best fits the hospital's situation). (5/25/01)*

You will receive no payment for taking part in this study. Getting to the study site is your own responsibility, and at your own cost. *(Local institutions may update this information as best fits their situation.)*

The cost of keeping research records will be paid by the study. The research requires that you receive certain standard tests, exams and office visits. These standard tests, exams and office visits will be (charged in the usual way/provided at a reduced rate). (*Local institutions must choose the option and outline in detail the participant financial responsibilities that best fit the hospital's situation) (5/25/01)*

The investigational supplements selenium, vitamin E and placebo will be provided free of charge for this study. A specially made multivitamin will also be provided for you and (if desired) your significant other free of charge for this study.

There will be no cost to you for any blood, toenail clippings or tissue stored by the Southwest Oncology Group.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is your choice. You may withdraw all or any part of your consent to be in the study at any time. You may choose not to receive further supplements. You may choose to withdraw from any extra project. *(11/21/05)* Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, before you decide to stop being in the study, we would like you to talk to your study doctor and your regular doctor. *(paragraph edited 1/14/04)*

If you choose to stop taking supplements, and later wish to return to the study (in the same study group), you can. However, if you stopped taking supplements because the supplement(s) caused health problems for you or others, you may not be allowed to take more supplements. If you stop taking your study supplements for any reason, you can still be a part of this study. This means you can continue clinic visits and provide information about your health by completing forms, being available to answer questions, or allowing us access to your medical records. *(1/14/04)* We would like to continue to watch your health whether or not you are taking supplements.

You may be in the Selenium and Vitamin E Cancer Prevention Trial and yet decline to have blood, toenail and tissue samples stored for future research. Further, if you first decide to have these samples stored for research, but later change your mind, you may do so by giving written notice of this to (**principal investigator**) at the (**participating institution**). The remains of your samples will then be destroyed. Your decision will not affect your care.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research. They will review this data throughout the study. Their review will not be given to you or your doctor. You will not know the results of their review unless it is clear that the supplements are working, or that they are causing serious harm.

If there is important new information from this or other studies that may affect your health, welfare, or willingness to stay in this study, you will be informed and may be asked to renew your consent to participate.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher *NAME(S)* at *TELEPHONE NUMBER*.

For questions about your rights as a research participant, contact the *NAME OF CENTER* Institutional Review Board (which is a group of people who review the research to protect your rights) at *TELEPHONE NUMBER*.

WHERE CAN I GET MORE INFORMATION?

[To IRB/Investigators: Attach information materials and checklist of attachments. Signature page should be at the end of package. You may also wish to include the following informational resources]

You may call the NCI's Cancer Information Service at
1–800–4–CANCER (1–800–422–6237) or TTY: 1–800–332–8615

Visit the NCI's Web sites…
cancerTrials: comprehensive clinical trials information
http://cancertrials.nci.nih.gov.
CancerNet™: accurate cancer information including PDQ
http://cancernet.nci.nih.gov.

You will get a copy of this form. You may also request a copy of the protocol (full study plan).

SIGNATURE

You are deciding whether or not to take part in this study. If you sign, it means that you have decided to volunteer to take part in this study, and that you have read and understood all the information on this form.

1. Participant _____ Date _____

2. Details regarding participation in the contact database project project were deleted 10/24/05 as this project is no longer being done in the SELECT study. *(added 11/21/05)*

Also, document your willingness to take part in additional studies by answering items 3 and 4 below. Your participation in any additional study is entirely voluntary and in no way effects your participation in SELECT. *(sentence updated and 3 - 4 added 5/25/01) (2/14/02)*

3. Sub-studies requiring active participation *(#3 updated 2/14/02)*

Some men will be asked to participate in special sub-studies requiring their <u>ACTIVE</u> participation.

I agree to be contacted with information about special sub-studies.

☐ **Yes** ☐ **No** **Initials: _____**

4. Sub-studies on stored specimens

We would also like to store your samples of blood, toenail clippings and tissue for further research. These studies might include genetic studies, and nutritional studies related to cancer and other diseases that are common in your age group. None of these would be of direct benefit to you, but could help us learn about other ways to prevent cancer or other health problems. Participants who are known to have an infectious disease such as HIV or hepatitis will not be asked for their blood sample. *(2/14/02)*

Please check box A or B or C and initial as indicated. *(2/14/02)*

A. ☐ **I refuse to allow my specimens to be collected.** *(5/25/01) (2/14/02)*

Initials: _____

OR

B. ☐ **I consent to collection of my blood, toenail clippings and prostate tissue specimens and to <u>ALL</u> future studies involving the use of my specimens. It is unnecessary to contact me further regarding studies on my stored blood, toenail clippings or prostate tissue specimens.** *(5/25/01) (2/14/02)*

Initials: _____

OR

C. ☐ **1.** **I specifically consent to the collections of the following specimens, the use of the blood and toenails in determining baseline nutrient levels, and the review and storage of prostate tissue:** *(2/14/02)*

Blood ☐ **Yes** ☐ **No** **Initials:** _____

Toenails ☐ **Yes** ☐ **No** **Initials:** _____

Prostate Tissue ☐ **Yes** ☐ **No** **Initials:** _____

2. **I specifically consent to the use of my stored specimens for the following types of research:** *(2/14/02)*

a. **My specimens may be kept for use in research to learn about, prevent, treat or cure cancer.** *(2/14/02)*

☐ **Yes** ☐ **No** **Initials:** _____

b. **My specimens may be kept for use in studies about other health problems (for example: diabetes, Alzheimer's disease and heart disease).** *(5/25/01) (2/14/02)*

☐ **Yes** ☐ **No** **Initials:** _____

c. **Someone from the Southwest Oncology Group may contact me in the future to ask me to take part in more research (outside of the research indicated in questions C2a and C2b above) involving the use of my stored specimens.** *(5/25/01) (2/14/02)*

☐ ☐

Yes **No** **Initials:** _____