AD_____

Award Number: DAMD17-99-1-9467

TITLE: Soy Supplementation and Prostate Cancer Prevention

PRINCIPAL INVESTIGATOR: Electra D. Paskett, Ph.D.

CONTRACTING ORGANIZATION: Ohio State University
Columbus, OH 43210

REPORT DATE: March 2005

TYPE OF REPORT: Final Addendum ($2^{ND}$)

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 074-0188*



| 1. AGENCY USE ONLY | 2. REPORT DATE | 3. REPORT TYPE AND DATES COVERED |
|---|---|---|
| | March 2005 | Final Addendum (2ND) (15 Feb 04 - 28 Feb 05) |

**4. TITLE AND SUBTITLE**
Soy Supplementation and Prostate Cancer Prevention

**5. FUNDING NUMBERS**
DAMD17-99-1-9467

**6. AUTHOR(S)**

Electra D. Paskett, Ph.D.

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

Ohio State University
Columbus, OH 43210

E-Mail: paskett-1@medctr.osu.edu

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSORING / MONITORING AGENCY REPORT NUMBER**

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for Public Release; Distribution Unlimited

**12b. DISTRIBUTION CODE**

**13. ABSTRACT (Maximum 200 Words)**

This project is conducting a randomized double-blind clinical trial to assess the ability of a soy protein dietary supplement to reduce prostate cancer risk in older men. A total of 120 men (60 white and 60 African-American) aged 50 years or older with high PSA levels but normal prostate biopsies will be randomized into one of two groups (soy protein supplementation with isoflavones or casein protein supplementation). The specific aims are: 1) to determine the impact of the interventions, including changes in clinical (PSA levels and prostate volume) and intermediate (Ki-67, apoptosis, sex-steroid receptors, angiogenesis, antioxidant enzyme expression) markers of prostate cancer risk; 2) to assess soy protein effects on hormone levels, plasma lipids/lipoproteins and blood pressure; and 3) to evaluate changes in health-related quality of life, including urinary symptoms and sexual functioning. This project involves a multidisciplinary team affiliated with the oncology, Epidemiology, health-related quality of life, biostatistics, and nutrition. NCI approved of the CALGB protocol delayed start-up of this study; recruitment has been continuous since March 2000. However, recruitment to this study was suspended during the course of the study per DOD Human Subjects Protection Office. Currently the study is open at13 Cancer and Leukemia Group B sites.

**14. SUBJECT TERMS**
Prostate Cancer

**15. NUMBER OF PAGES**
6

**16. PRICE CODE**

| 17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT | 20. LIMITATION OF ABSTRACT |
|---|---|---|---|
| Unclassified | Unclassified | Unclassified | Unlimited |

## Table of Contents

## INTRODUCTION

This study proposes to conduct a randomized double-blind clinical trial, which will assess the ability of a soy protein dietary supplement (a rich source of isoflavones) to reduce prostate cancer risk in older men. This project involves the collaborative efforts of a multidisciplinary team affiliated with the cooperative group, Cancer and Leukemia Group B (CALGB), which has substantial expertise in the areas of controlled clinical trials, oncology, epidemiology, health-related quality of life, biostatistics, and nutrition. If positive results are obtained in this trial, soy supplementation may provide an important tool for the prevention of prostate cancer.

Soybeans and other legumes contain large amounts of plant estrogens know as isoflavones. Specific isoflavones found in soy (genistein and diadzein) have been implicated in reducing breast, colon, and prostate cancer risk in both laboratory-based and observational studies [1]. Strong evidence for an effect on prostate cancer risk comes from cross-cultural studies, which have shown that prostate cancer rates are much lower in the Pacific Rim countries where soy products comprise a much higher proportion of the normal diet compared to the United States [2]. This project will randomize 120 men (60 white and 60 African-American) aged 55 years and older with high PSA levels but normal prostate biopsies into one of two groups (soy protein supplementation with isoflavones or casein protein supplementations). The specific aims are: 1) to determine the impact of the interventions, including changes in clinical (PSA levels and prostate volume) and intermediate (Ki-67, apoptosis, sex-steroid receptors, angiogenesis, antioxidant enzyme expression) markers of prostate cancer risk [3,4]; 2) to assess soy protein effects on hormone levels, plasma lipids/lipoproteins and blood pressure; and 3) to evaluate changes in health-related quality of life, including urinary symptoms and sexual functioning.

**BODY: Accomplishments associated with the approved statement of work.**

This grant was initially awarded to Dr. Paskett while she was on faculty at the Wake Forest University School of Medicine. In 2002, upon Dr. Paskett's move to The Ohio State University (OSU), the funds and the grant activities were transferred to the OSU. During the course of the entire funding period we developed and finalized the protocol and questionnaires, and put them through the approval process at the various agencies and institutions. We also developed and implemented our study coordination/administrative infrastructure which support the activities of the study at the other participating sites. OSU continues be the administrative/coordinating site for this study, in addition to being a clinical site which is involved in the recruitment of subjects for the study.

It should be noted that during the first years of the study it was only opened to limited sites within CALGB. However, during 2002 reporting period the study was opened to all CALGB sites, and the participating institutions have obtained their individual Institutional Review Board approvals and have begun recruitment. Wake Forest University School of Medicine continues to ship the soy products to all sites. Samples obtained from participants to this point are being batched at Ralston to be analyzed collectively. Specimen analyses are being paid for from matching funds that Dr. Paskett secured from OSU. Dr. Paskett has been working with the membership of the Urology Committee of the CALGB to promote the study and to enlist support. Through this effort one of the members of the Urology Committee, Dr. James Mohler, agreed to become CALGB study chair for this project.

There have been many factors that have impeded the recruitment process, however, we will continue to work within the CALGB infrastructure to complete this important study. Due to changes in prostate

biopsy procedures we still continue to experience slow recruitment. As noted in previous reports, more biopsy specimens are being gathered during the biopsy procedure, thus more likely than not, if a biopsy is performed, the diagnosis is 90% positive for cancer, reducing our pool of potential participants. We continue to wait approval of an amendment to add to the endpoint of change in PSA levels. This amendment should also help with our recruitment efforts. Recruitment also continues to be affected because of standing contracts (with pharmaceutical companies), many private urologists are pulling away from the low paying projects (such as ours) to use their patients for the higher revenue-generating projects. However, we have continued to employ various screening processes to help with recruitment activities. We have also had meeting with the urologists within CALGB and within our institutional communities to in order to elicit support for the study.

During the CALGB group meetings the clinical research associates are reeducated about the importance of this project. Research strategies are shared among the group and many institutions have begun to intensify screening efforts in their urology clinics. However, many of these patients have cancer or advanced disease which prohibits them from participating in the chemoprevention trials. As a result of this fact we feel that it may be necessary to approach community urologists about referring patients to participate in the study. We are hopeful that such partnership will enhance our accrual to this prostate cancer chemoprevention trial. In addition, we had some regulatory issues with the DOD Human Subject Protection Office which halted recruitment activities, however, this issue was resolved and the suspension that was placed on recruitment activities was lifted. Approval to move forward with the study was granted and recruitment activities were resumed.

## KEY RESEARCH ACCOMPLISHMENTS

- *Establishment of an administrative/coordinating unit to oversee the conduct of the project.*
- *Worked within the infrastructure of the CALGB to start the study and to recruit institutions to work on the study. As a result, the study has been opened up to all of the CALGB membership.*
- *Obtained approval from DOD and NCI to conduct the study.*
- *Continue to seek and obtain annual renewal of the project.*
- *Established Wake Forest University School of Medicine (WFUSM) as the centralized shipper of the ship the soy and casein supplements received to the participating sites. This allows us to maintain quality control of the nutritional based product being investigated in this study.*
- *Staff training sessions are held in conjunction with the annual meetings of the CALGB.*
- *Dr. Paskett presented the study to the members of the CALGB Urology Committee.*
- *Change in the CALGB study chair leadership.*

## REPORTABLE OUTCOMES

None to report during this reporting period.

## CONCLUSION

This is an addendum to the report we submitted March 2004. No major changes have occurred. As noted in previous reports, there have been many factors that have resulted in the delay of this project. However, we are hopeful that with the opening of the study to all CALGB sites and through Dr.

Paskett's work with members of the Urology Committee in CALGB to update the protocol, we should see a major increase in our accrual numbers. Please note that risks to subjects have not changed and all sites participating through CALGB has received approval from their local IRBs. Even though, we have depleted our funds awarded by DOD, we will continue to work on the study since the results of this study has the potential to advance the field of nutritional prevention of cancer. We would like to gratefully acknowledge that the support that we received from DOD has allowed us to build our administrative infrastructure for this important study, and will allow us to continue with our research efforts.

**REFERENCES**

1. Coward L., et al. The antitumor isoflavones, genistein and diadzein, in soybean foods of American and Asian diet. Journal of Agriculture and Food Chemistry, 1993;41:1961-1967.

2. Adlercreutz H, Mazur W. Phyto-estrogens and Western disease. Annals of Medicine, 1997;29: 95-120.

3. Crawford ED, DeAntoni EP, Ross CA. The role of prostate-specific antigen in the chemoprevention of prostate cancer. J Cell Biochem 1996; 25:149-155.

4. Kelloff GJ, Boone CW, Crowell JA, Nayfield SG, Hawk E, Malone. Risk biomarkers and current strategies for cancer chemoprevention. J Cell Biochem Suppl 1996; 25:1-14.