

DRAFT

SOY PROTEIN/ISOFLAVONE RESEARCH Challenges in Designing and Evaluating Intervention Studies

Scientific Workshop

July 28-29, 2009

**Bethesda North Marriott Hotel and Conference Center
Bethesda, Maryland**

Goal:

1. To provide guidance for the next generation of soy protein/isoflavone human research.

Workshop Objectives:

1. To identify methodological issues relative to exposures and interventions that may confound study results and interpretation.
2. To identify scientifically sound and useful options and solutions for dealing with these issues in the design, conduct, reporting of results, and interpretation of ongoing and future studies.

DAY 1: Tuesday, July 28

8:00 Welcome

Paul Coates
Director
Office of Dietary Supplements, NIH

Josephine Briggs
Director
National Center for Complementary and Alternative Medicine, NIH

8:15 Introduction

Objective: (1) Address workshop purpose and organization; (2) Describe NIH's investment in soy research.

Marguerite Klein, Office of Dietary Supplements, NIH

8:25 Keynote Address: What are the issues? Why are we concerned?

Objective: (1) Provide a summary of the issues related to animal, epidemiological, and clinical research in soy protein and isoflavones, including lack of product characterization, confounders, measurement challenges, etc. (2) Discuss how epidemiologic studies may lead to clinical studies. (3) Hypothesize why clinical studies may not confirm epidemiologic studies and why there may be contradictory results among clinical studies.

Keynote Speaker: Stephen Barnes, University of Alabama at Birmingham

9:10 Q&A

9:20 **Session 1: Panel Discussion: What are methodologic considerations and experiences uniquely related to soy protein/isoflavone intervention studies?**

Objective: (1) Describe challenges and opportunities of designing, conducting, and interpreting soy clinical studies in specific health/disease-related areas. (2) Address the proposed mechanisms by which soy may affect these health outcomes. (3) Address considerations for product and dose selection. (4) Consider factors that would advance the state of soy science in specific health/disease-related areas. (5) Determine how challenges can be addressed.

Lead Discussant: Connie Weaver, Purdue University

Panel Discussants:

- Howard Hodis (cardiovascular disease), University of Southern California
- D. Lee Alekel (bone health), Iowa State University
- Leena Hilakivi-Clarke (cancer), Georgetown University
- Carey Gleason (cognition), William S. Middleton Memorial

10:40 **BREAK**

11:00 **Session 2: What is the population exposure to soy protein and isoflavones and other phytoestrogens? How does this exposure impact clinical studies?**

Objectives: (1) Describe the current soy exposure of the overall general U.S. population in and by subgroups. (2) Report population data on biomarkers of exposure to isoflavones/phytoestrogens.

Lead Discussant: Mark Messina, Loma Linda University

11:00 **U.S. exposure to soy from foods and supplements**

Pam Horn-Ross, Northern California Cancer Center

11:15 **Biomarkers of isoflavone/phytoestrogen exposure (NHANES)**

Michael Rybak, Centers for Disease Control and Prevention

11:30 **Population exposure outside the U.S.--Asia**

Chisato Nagata, Gifu University, Japan

11:45 **Panel Discussion:** How does population exposure influence the advancement of science of soy health outcomes and specific study designs (e.g., eligibility criteria, adherence monitoring)?

12:20 **LUNCH**

1:20 **Session 3: What do we know about variability of the human response to soy?**

Objectives: (1) Address factors (e.g., genetics, gender, age, delivery matrix, endogenous/exogenous hormones, gut microbiome, timing of exposure, etc.) that influence ADME and the impact these have on selecting soy test agents, dose, dosing schedule and duration, study population, etc. (2) Describe how equol is expressed and the factors affecting equol production. (3) Address which liver enzymes may be regulated by soy and the potential for drug-soy interaction. (4) Suggest how variability in the human response will influence study designs, methods and interpretation.

Lead Discussant: Thomas Badger, University of Arkansas for Medical Sciences

1:20 **Factors influencing bioavailability**

Aedin Cassidy, University of East Anglia, United Kingdom

1:35 **Overview soy absorption, digestion, metabolism, excretion (ADME) and Equol**

Kenneth Setchell, Children's Hospital Medical Center

2:05 **Genetic polymorphisms: Modulatory effects**

Xiao Ou Shu, Vanderbilt University Medical Center

2:20 **Panel Discussion:** How will what is currently known about ADME and mechanisms (e.g., antioxidant, estrogenic, anti-inflammatory, induction of apoptosis) influence clinical study designs and methods employed?

3:10 **BREAK**

Session 3: (continued)

3:30 **Soy protein: Mechanism of action**

Martin Ronis, University of Arkansas for Medical Sciences

3:45 **Soy isoflavones: Mechanism of action**

Thomas Clarkson, Wake Forest University School of Medicine

4:00 **Interactions/negative consequences**

(WH's proposed titled) Dietary isoflavones and breast cancer -A complex issue of dose, timing and target tissue

William Helferich, University of Illinois

4:15 **Panel Discussion (continued)**

5:00 **ADJOURN DAY 1**

DAY 2: Wednesday, July 29

8:00 Session 4: What do we need to know about product composition?

Objectives: (1) Describe sources for soy isoflavone, phytoestrogen and soy protein in the U.S. diet and environment and how they have changed over time. (2) Understand the types of soy-containing products available in the U.S. market and tested in clinical studies. (3) Describe changes in composition over time. (4) Describe manufacturing processes and how this influences product composition of soy bioactives (including bioactives other than isoflavone and protein, e.g., folates, phytates, oxalates, sterols).

Lead Discussant: Lilian Thompson, University of Toronto, Canada

8:00 Composition of soy foods

Elaine Krul, Solae, LLC

8:15 Composition of soy dietary supplements

Mark Empie, Archer Daniels Midland Company

8:30 Panel Discussion: How does product composition affect design of clinical studies or how does clinical study purpose affect choice of product composition?

9:00 Session 5: What methods, tools, and resources have been and are available to estimate exposure and adherence to intervention protocols?

Objectives: (1) Identify food composition databases' strengths and limitations in capturing soy, soy protein, soy isoflavone, and phytoestrogen intake. (2) Describe the design, reliability and validity of diet assessment methods to quantify soy, soy protein, and isoflavone intake. (3) Address considerations for the design of epidemiologic and clinical studies.

Lead Discussant: Jennifer Nettleton, University of Texas Health Science Center at Houston

9:00 Food composition databases

Joanne Holden, U.S. Department of Agriculture

9:15 Diet intake assessment methods

Gertraud Maskarinec, University of Hawaii at Manoa

9:30 Panel Discussion: How does the estimation of exposure impact the design of and methods used in human studies? How may the different assessment methods of exposure/adherence be used appropriately?

10:00 BREAK

10:20 **Session 6: What are the available analytic methods to assess soy protein and isoflavones in foods and supplements, as well as metabolites in biologic fluids?**

Objectives: (1) Describe current and previous analytic methodologies for accurate identification and quantitation of soy isoflavones and protein in food and dietary supplements. (2) Describe methodologies to detect and quantify metabolites in biologic fluids. (3) Address method limitations and applicability. (4) Describe NIST's forthcoming soy-matrix standard reference material. (5) Address how these methods, past and present, may influence rationales for test agent, dose, exposure assessment and designs of clinical studies.

Lead Discussant: Jeanne Rader, U.S. Food and Drug Administration

10:20 **Analytic methods for isoflavones in biologic fluids**

Adrian Franke, University of Hawaii

10:35 **Analytic methods for isoflavones in foods and dietary supplements**

Mark Collison, Archer Daniels Midland Company

10:50 **Analytic methods for soy protein in foods and dietary supplements**

Helen Kim, University of Alabama at Birmingham

11:05 **Reference materials**

Catherine Rimmer, National Institute of Standards and Technology

11:20 **Panel Discussion:** How does the state of analytic methods impact the quality of nutrient databases and influence interpretation of past soy epidemiologic and clinical studies? How may newer methods influence development and interpretation of future studies? Which methods should biomedical investigators use for quality control of their test agents?

12:10 **LUNCH**

1:00 **Session 7: DISCUSSANT PANEL**

Objectives: (1) Summarize session presentations and discussions; (2) Provide opportunity for participant's final questions and comments.

Panel will address:

- What do we know?
- What don't we know?
- How do epidemiological data inform clinical studies?
- How do we get consistency in studies measuring the same endpoints/health outcomes?

Lead Discussant: Richard Nahin, National Center for Complementary and Alternative Medicine, NIH

Panel Discussants:

- Connie Weaver
- Mark Messina
- Thomas Badger
- Lilian Thompson
- Jennifer Nettleton
- Jeanne Rader

2:30 **BREAK**

2:50 **Session 8: SUMMARY OF WORKSHOP RECOMMENDATIONS**

Recommendations for investigators designing clinical studies.
Recommendations for interpreting past study results.
Recommendations for reporting results.
Recommendations for future research and development.

Presenter/Discussant: Johanna Dwyer, Tufts University

3:30 **WORKSHOP ADJOURNED**