National Program 107
Human Nutrition

Accomplishment Report 2007-2011








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Human Nutrition

ACCOMPLISHMENT REPORT 2007–2011

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ACTION PLAN 2009-2013

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BACKGROUND AND GENERAL INFORMATION

Human nutrition research is important for improving life at all stages. While deficiency diseases are no longer the public health problem they used to be, much work remains to track changes in the food supply and dietary habits; define optimal levels of nutrient intake; and discover novel health-promoting compounds in foods and nutrient interactions with special interest on the prevention of obesity and related conditions.

The vision for the USDA/Agricultural Research Service (ARS) National Program 107 (NP 107), *Human Nutrition*, is that well-nourished Americans will make health-promoting diet choices on the basis of scientific evidence. Consequently, our mission is to define the role of food and its components in optimizing health throughout the life cycle for all Americans by conducting research of high national priority.

The program aims to improve the nutrition and health of the American people by enhancing the quality of the American diet and improving related health behaviors through research. Distinctive aspects of NP 107 research include: an emphasis on a food-based approach to improving health; the core capability to sustain long-term research in areas deemed of high priority for the Nation's health; the availability of state-of-the-science equipment and facilities for human research across the lifecycle; and the conduct of multidisciplinary research to improve the American food supply.

Unique national resources that are part of NP 107 include the Nutrient Data Laboratory; the Food Surveys Research Group, which produces the "What We Eat in America" (WWEIA) portion of the National Health and Nutrition Examination Survey (NHANES) in collaboration with the National Center for Health Statistics (a division of the Centers for Disease Control and Prevention, CDC); and the Food Composition and Methods Development Laboratory, which develops and improves methods for food analysis. In addition, each of the six Human Nutrition Research Centers (HNRCs) has a metabolic kitchen that can accommodate inpatient or outpatient studies. The kitchens have larger capacity than any at universities. Other unique capabilities include room calorimeters at five of the six centers, which allow live-in studies for extensive monitoring of energy expenditure.

The U.S. food supply provides high quality foods that allow people to meet their nutritional requirements at lower relative cost than in any setting in history. Because of the wide variety of inexpensive, convenient, and tasty foods available, it is easy for people to consume too many calories and insufficient essential nutrients unless they have access to relevant knowledge and choose to use that knowledge. Improper nutrition, in combination with a sedentary lifestyle, contributes to obesity, type 2 diabetes, hypertension, cardiovascular disease, some types of cancer, gallbladder disease, and osteoarthritis. At least 7 in 10 Americans will be affected by one or more of these conditions.

NP 107 identifies nutritive and health-promoting components in foods, evaluates the nutritional value of diets eaten by people in America, determines how consumption of specific foods or food components in combination with appropriate physical activity can enhance the health of the population, and develops strategies to improve food choices and modify related lifestyle factors

(e.g., increased physical activity) to promote health among Americans. This knowledge provides valuable information to policymakers, farmers, food processors and manufacturers, and consumers.

NP 107 is not aimed at treating or curing disease but instead is focused on maintaining health and preventing disease through food-based recommendations. In the past, nutrition research addressed nutrient requirements to avoid deficiencies, which are now of less concern in the United States. Rather, overconsumption and caloric imbalance have become more significant issues for the average American. Further, individuals respond differently to dietary interventions, prompting the need for "personalized" nutrient requirements. To meet this need, ARS nutrition research has begun to incorporate genomic, epigenomic, and metabolomic technologies. Researchers are also actively investigating non-nutrient components (i.e., those with no known human requirement) of foods, such as a variety of plant chemicals that have health-promoting activities. Partnerships with other Federal, non-profit, and industry agencies and groups allow ARS to leverage funds and build upon common research goals.

NP 107 addresses four over-arching components that were identified by the National Program Leaders (NPLs) in collaboration with the Center Directors of the HNRCs following a stakeholder meeting in February 2007, which was attended by about 120 individuals representing Federal agencies, commodity groups, non-profit groups, the food industry, and academia. Following that meeting, the NPLs met with ARS lead scientists in NP 107 to determine which of the priorities identified by our stakeholders could be adequately addressed with the resources available to the program. This effort resulted in an Action Plan. Concepts were solicited from NP 107 scientists on the topics that had been chosen and, through a back-and-forth process with the NPLs, objectives were developed for new projects. Projects plans were written by the scientists, which were verified by the NPLs as addressing the objectives that had been assigned to them. Each project plan was reviewed by a panel of extramural scientists—this activity was conducted by the Office of Scientific Quality Review (OSQR). Finally, following revision and approval by OSQR, new research projects were initiated. While the majority of projects were initiated at the same time, a sizeable minority were started later as a result of budget issues, Congressional redirections, or as the result of changes in scientist availability due to retirements, deaths, new hires, etc. The NPLs maintain contact with numerous stakeholders through both formal and informal meetings so priorities are modified over time. However, the problem statements describe broad enough concepts that they have not required modification since the Action Plan was written.

The research projects at the three cooperating HNRCs went through the same process of internal development and review. Readers should be aware that ARS support for individual projects at the HNRCs generally amounts to no more than half of each center's budget, so other funds must be obtained through grants, usually from the National Institutes of Health (NIH) or other funding agencies. It should also be clear that scientists must write grant applications that are competitive, and these often are only partially related to ARS-approved objectives. Funding is never duplicated for these projects; additional funding must be complementary to ARS-funded objectives. While ARS does not maintain central records for grants awarded to the three cooperating HNRCs, we know that each one obtains approximately half of its research funds through grants to individual scientists. Scientists at the Federal centers also write grants and

receive outside funding from a variety of sources. Those funds are used solely for research (i.e., they do not pay investigator salaries) and thus may allow for substantial increases in research scope and depth.

HOW THIS REPORT WAS CONSTRUCTED AND WHAT IT REFLECTS

This report is a distillation of some of the most significant research accomplishments of the past 5 years achieved by scientists working in NP 107. The rationale for NP 107 is based on the recognition that the main use of agricultural production is to serve as food for humans and as feed for animals that are, in turn, part of the human food chain. There is a tension between providing the greatest productivity of commodities and improving the nutrition of those foods. While this is not a simple either/or proposition, many view it that way. The goal of NP 107 scientists is to identify components of foods or whole foods themselves that influence health and to test them *in vitro*, in animal models, and in humans.

In this report, NP 107 accomplishments and their impact are organized and presented according to research components and their constituent problem statements, as described in the 2009–2013 Action Plan. Under the problem statements, accomplishments are reported with specific reference to anticipated products identified as targets in the Action Plan. Although some of the accomplishments highlighted from the first 2 years really reflect the prior Action Plan, most of the projects conducted under the earlier plan have relevance to the current Action Plan.

For the most part, the content of this accomplishment report is derived from the 2007–2011 NP 107 annual reports and the reports of the constituent research projects. This report stresses the actual impacts of those accomplishments and, where relevant, cites key publications or Web addresses to document those accomplishments.

STRUCTURE OF NP 107

The components comprising the current action plan are as follows:

- Nutrition Monitoring and the Food Supply
- Scientific Basis for Dietary Guidance for Health Promotion and Disease Prevention
- Prevention of Obesity and Related Diseases
- Life Stage Nutrition and Metabolism

There are currently 45 Congressionally-appropriated projects in NP 107; many projects, particularly at the cooperating HNRCs, have subordinate projects that also have undergone external peer review prior to implementation, which brings the total to 68 projects. Eighteen projects respond to a single problem statement and the remainder addresses two or three. Because each project may address more than one problem statement, the list below shows how many projects in the program address the problem statements in this report. This amounts to 104 assignments to problem statements. In addition, some accomplishments in the table below may be repeated under more than one problem statement.

Problem Statement	No. of Projects
1A	3
1B	1
1C	4
1D	2
2A	29
2B	10
3A	19
3B	14
3C	2
4A	14
4B	6

Funding for NP 107 represents about 7 percent of the ARS appropriation. About 95 percent of the funding for NP 107 is distributed to six HNRCs, located in Beltsville, Maryland; Grand Forks, North Dakota; Davis, California; Boston, Massachusetts; Little Rock, Arkansas; and Houston, Texas. The first three HNRCs are fully Federal centers, meaning they are owned and operated exclusively by the U.S. government and all the scientists are Federal employees; some support staff are not. The other three centers are cooperatively operated with academic institutions: the Boston center with Tufts University, the Little Rock center with the University of Arkansas for Medical Sciences, and the Houston center with Baylor College of Medicine. At those three centers, the overwhelming majority of scientists are employed by the academic institutions and they obtain at least half of their funding from sources other than ARS, usually from NIH and other granting agencies. In addition to research conducted at the six HNRCs, the program has research projects in Ithaca, New York; Baton Rouge, Louisiana; and the Lower Mississippi Delta (Figure 1).

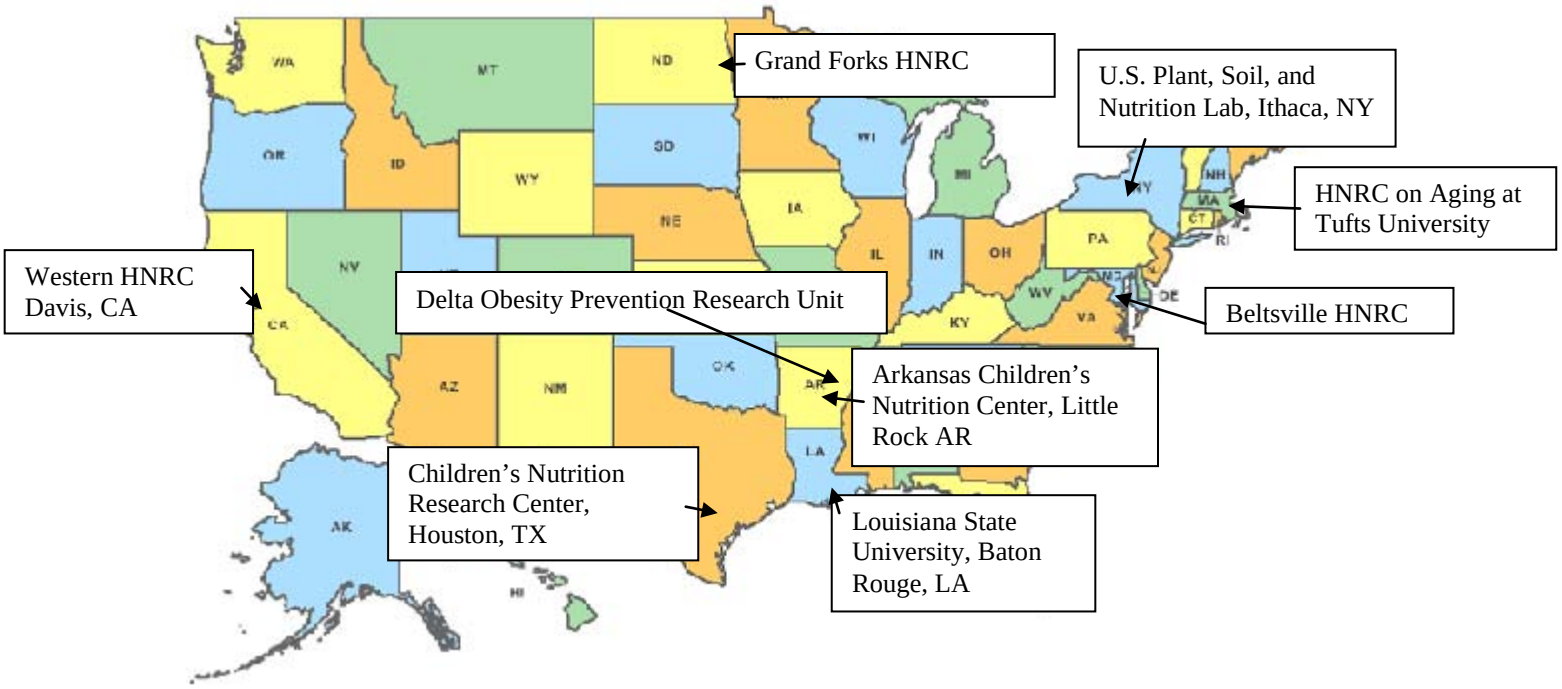


Figure 1. The scientists assigned to NP 107 currently conduct research at nine locations across the United States, including six HNRCs. Locations vacated by NP 107 in the past 3 years include the ARS Southern Regional Research Center, in New Orleans, Louisiana; and the Pennington Biomedical Research Center, in Baton Rouge, Louisiana.

The Delta Obesity Prevention Research Unit (DOPRU) is headquartered in Little Rock, Arkansas, but research is implemented in rural areas of Arkansas, Mississippi, and Louisiana through work carried out by ARS scientists and in collaboration with six partner institutions: Arkansas Children's Hospital Research Institute, University of Arkansas at Pine Bluff, the University of Southern Mississippi, Alcorn State University, Southern University, and the Pennington Biomedical Research Center (terminated in 2010). Each of the projects in the unit was redirected following an ARS proposal in 2007 to move this funding elsewhere and subsequent restoration following Congressional interest. New projects, with increased emphasis on obesity prevention research on an adequate scale without the community-based participatory paradigm were designed in collaboration with the ARS Office of National Programs and approved by OSQR in 2010. In 2012, the ARS scientist positions at DOPRU are all vacant and the project is again slated for termination in the President's 2013 budget submitted to Congress.

Output/Outcomes

The main output from NP 107 is peer-reviewed scientific publications, in contrast to many of the other national programs in ARS in which, for example, germplasm releases of new crop varieties, new breeds of food animals, patents, licenses, and other indicators of technologies developed are important measures. Because the total number of research publications over the period 2007–2011 was 2,704 it is not possible to provide a complete bibliography as part of this report. Almost all citations can be retrieved via online search by author or topic. We have, however, extracted sample accomplishments that have had an impact in the field of nutrition or

are expected to for recent publications. The gauge for impact is a high citation rate or use in authoritative reports from the Institute of Medicine (IOM). We have arbitrarily chosen 20 citations as the minimum number demonstrating high impact. For perspective, the highest cited nutrition journal is the *American Journal of Clinical Nutrition*, and its impact factor is just over 6. The mean number of citations in biomedical research is 2, according to the Institute for Scientific Information, so we feel well justified in choosing 20 as our cutoff. But we have listed a small number of papers highlighted fewer times where appropriate. Historically, NP 107 research has provided the majority of evidence for development of the Dietary Reference Intakes (DRI) by IOM committees. However, over the last 8 years, only a single DRI report has been updated and, given the current state of the science and the budget, it is unlikely these reports will be commissioned by the Federal government at a pace that consumers used to experience. Therefore, most of the publications listed in this report that have been in press for more than a year are accompanied by rates of citation to show impact on the nutrition research community.

In addition to peer-reviewed publications, another indicator of productivity of NP 107 is the release of databases on food composition and data on dietary intake and nutrition from NHANES. This information is extensively used by other Federal agencies, private companies in the food industry and related areas, and by academic researchers. We have discovered that ARS is routinely not credited as the source of these data, so it is essentially impossible to judge the true impact of these data. For example, there have been about 1,046 citations in peer-reviewed research papers to the "What We Eat in America" food intake survey, yet 5,480 papers were published during 2007–2011 that are listed in PubMed using the search terms NHANES and nutrition. Clearly, some of those 5,480 papers may not be relevant but enough are to appreciate the difference between actual citations of our data and publications that use it. The same is true for the National Nutrient Database for Standard Reference (SR) and special interest databases that are all freely available via the World Wide Web.

While projects are cited as the source of accomplishments, individual results contribute to addressing the problem statements that form the research questions identified with stakeholder input as being the most important issues for NP 107 during this time period. The responsibility of the NPLs is to maintain coordination among projects and locations and to minimize duplication. This is accomplished in collaboration with the Deputy Administrator for Nutrition, Food Safety, and Quality in the Office of National Programs and the Center Directors of the six HNRCs. In addition to coordination among projects, the NPLs facilitate interactions among scientists at different HNRCs and with other national programs. For example, many plant breeders in ARS are eager to enhance the nutritional profile of their crops, so we have had scientists conduct research either in animal models or in humans for the health effects of, for example, increased avenanthramides in oats, increased β-carotene in cauliflower, or metabolomic identification of polyphenols and their metabolites from grapes after consumption by volunteers. In addition to working with plant breeders in NP 301 (Plant Genetic Resources, Genomics and Genetic Improvement), nutrition scientists in ARS have ongoing collaborations with scientists in NP 306 (Quality and Utilization of Agricultural Products) and NP 106 (Aquaculture).

COMPONENT 1: NUTRITION MONITORING AND THE FOOD SUPPLY

Developing advice to the general public and the medical community regarding the best diets to achieve optimal health requires an in-depth understanding of the U.S. food supply. The USDA-ARS is the primary agency that monitors the U.S. food supply, and ARS nutrition monitoring data are the foundation for USDA dietary guidance as well as many regulatory programs. ARS data also are foundational for programs/policy developed by foreign governments and private institutions. Data developed by the programs in nutrition monitoring are perhaps the most visible and utilized in all of ARS.

Problem Statement 1A: ***Determine Food Consumption and Dietary Patterns of Americans.***

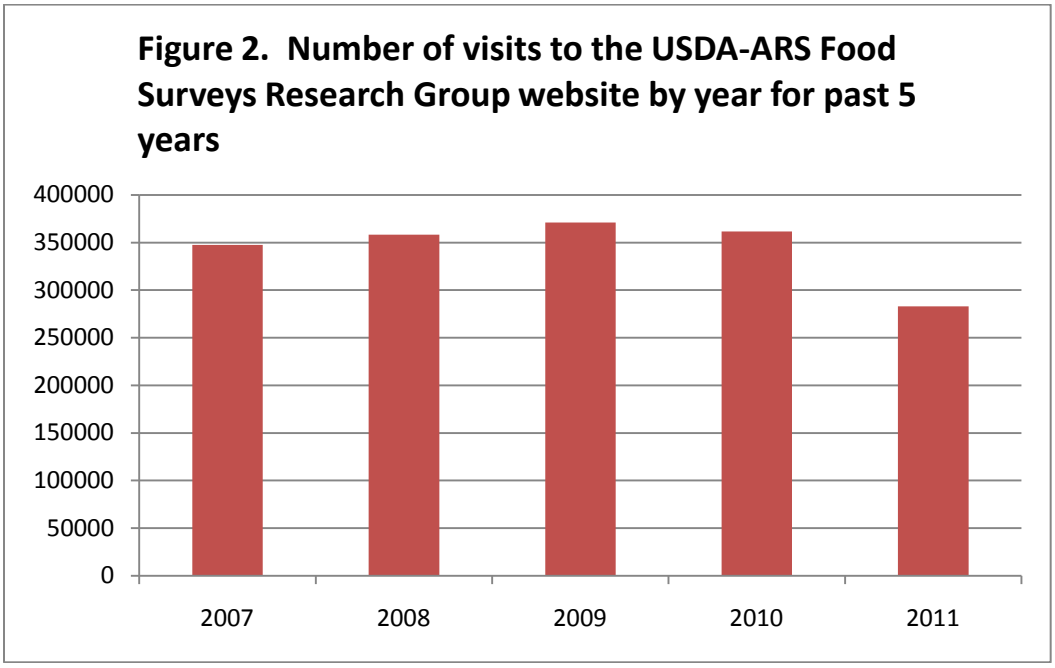
Anticipated Product 1: Biennial release of nationally representative data on the food and nutrient intake of Americans.

ARS monitors food consumption/intake patterns of Americans in joint partnership with the National Center for Health Statistics (NCHS), a division of the Centers for Disease Control and Prevention (CDC) in the U.S. Department of Health and Human Services (DHHS). This is done through the National Health and Nutrition Examination Survey (NHANES) What We Eat in America (WWEIA) survey, which is the dietary intake interview component of NHANES. WWEIA-NHANES is the only nationally representative dietary survey conducted in the United States. ARS collects, disseminates, and evaluates the food and nutrient intake data and develops methods and systems for dietary data collection, processing, and quality control to support the survey. The ARS Food Surveys Research Group (FSRG) has the leadership role for dietary data collection and processing of WWEIA. WWEIA data are released every 2 years as one dataset. The first WWEIA data release was for 2001–2002 and the most recent data release is 2007–2008. WWEIA data are posted on the NHANES Web pages for the respective survey year. The DHHS is responsible for the sample design and data collection, and ARS is responsible for the survey's dietary data collection methodology, maintenance of the databases used to code and process the data, and data review and processing. USDA also funds the collection and processing of a second day of dietary intake data (DHHS funds the first day), which are used to develop variance estimates and calculate usual nutrient intakes.

The ARS dietary surveillance program also maintains the Food and Nutrient Database for Dietary Studies (FNDDS) that is used by other agencies and researchers to analyze data from the diet survey by providing weights of typical food portions along with nutrient content. This function has been a part of USDA since 1935 (Family Food Consumption and Dietary Levels; Miscellaneous Publication # 405, U.S. Department of Agriculture). This dietary survey information has broad research and policy applications (e.g., monitoring the nutritional adequacy of American diets, measuring the impact of food fortification on health, developing dietary policy such as the Dietary Guidelines for Americans, estimating exposure of population groups to food contaminants, evaluating the nutritional impact of USDA food assistance programs, and assessing demand for agricultural products).

The importance of this work also extends to attempts to mitigate risk of chronic diseases such as diabetes and heart disease that are the primary public health concerns in the United States today.

There is much to indicate that many of these health conditions are linked to a poor diet, but the data are equivocal and more research is needed. Intakes of foods and nutrients are reliable indicators that allow associations to be made between diet and health or disease risks; consequently, these data are essential for devising public health recommendations about diet. Reliable and valid estimates of intakes of particular foods, food ingredients, dietary supplements, and other bioactive substances are also important for evaluating the progress in meeting key objectives in such national public health initiatives as Healthy People 2010 and the Dietary Guidelines for Americans 2010. Dietary intake data also are used for regulatory purposes. The FSRG Web site was visited 1,721,497 times in the past 5 years (Figure 2) and WWEIA-NHANES and associated datasets and methodologies developed by FSRG were cited in at least 1,046 peer-reviewed publications in the period of 2007–2011.



Release of WWEIA 2007–2008. WWEIA 2007–2008, released in 2010 includes food energy and 64 nutrients/food components, including Vitamin D (D2 + D3). New nationwide dietary intake data were collected in WWEIA for the years 2007–2008 and were released on the Internet for public use. The data include information on dietary intakes of 9,255 individuals from two nonconsecutive-day, 24-hour dietary recalls along with sample weights that can be used to estimate dietary intakes of the U.S. population. This release also contains data that have been analyzed and released on the Web in summarized data tables and dietary data briefs. Twenty-eight tables were added to the eight available for WWEIA-NHANES 2005–2006, and these report nutrient intakes from food and the contribution of protein, carbohydrates, fat, and alcohol in the American diet as well as percentage of nutrients contributed by foods eaten away from home, at breakfast, at lunch, at dinner and as snacks; distribution of snack occasion; and distribution of meal patterns. The tables also provide dietary information for individuals aged 2 and older based on income level and ethnicity. Dietary data briefs on milk consumption and adolescent snacking were also developed and released on the Web.

These data are used by Federal- and state-level decision makers and researchers in such tasks as monitoring the nutritional adequacy of U.S. diets, modeling the impact of food fortification on nutrient intakes, estimating exposure of population groups to contaminants, developing dietary guidance, and assessing the demand for agricultural products. Linked with health indicators from other components of the NHANES, these data provide opportunities to study relationships between eating patterns and health conditions. The data are accessible from www.ars.usda.gov/ba/bhnrc/fsrg.

U.S. Department of Agriculture, Agricultural Research Service. 2010. *What We Eat In America, NHANES 2007–2008:* Documentation and data files. Available at: http://www.ars.usda.gov/Services/docs.htm?docid=18354
http://www.ars.usda.gov/Services/docs.htm?docid=13793

U.S. Department of Agriculture, Agricultural Research Service. 2011. *Snacking patterns of U.S. adults: What We Eat In America, 2007–2008.* Available at: www.ars.usda.gov/Services/docs.htm?docid=19476.

U.S. Department of Agriculture, Agricultural Research Service. 2011. *MyPyramid intakes and snacking patterns of U.S. adults: What We Eat In America, 2007–2008.* Available at: www.ars.usda.gov/Services/docs.htm?docid=19476.

U.S. Department of Agriculture, Agricultural Research Service. 2011. 2007–2008 What We Eat In America, NHANES Tables 37–40. Available at: www.ars.usda.gov/Services/docs.htm?docid=18349.

Update and Release of the Food and Nutrient Database for Dietary Studies. Scientists in Beltsville, Maryland compiled and released the FNDDS 4.1 in 2010. The FNDDS is an extensive database of foods consumed in the United States that is used to code foods and portion sizes and to calculate nutrients for the WWEIA-NHANES. It contains information for more than 7,000 foods including data for food energy, 64 other nutrients, and weights for common portions. Most data are derived from the USDA National Nutrient Database for Standard Reference (see below). New versions of FNDDS are released every 2 years to accompany the release of the WWEIA-NHANES data.

Ahuja, J.K., Lemar, L.E., Omolewa Tomobi, G., Goldman, J.D., Moshfegh, A.J. 2009. The impact of revising fats and oils data in the US Food and Nutrient Database for Dietary Studies. *J Food Comp Anal.* 2009; 225:s63-s67. [0 Citations.]

Anticipated Product 2: New information on enhanced dietary assessment methods to improve the study of diet and health relationships.

Extending the USDA Automated Multiple Pass Method (AMPM). ARS researchers in Beltsville, Maryland developed a dietary instrument termed the Automated Multiple Pass Method (AMPM) that assists with 24-hour dietary recalls. This instrument has been used in the

WWEIA-NHANES survey, but not elsewhere. In 2007 the use of this instrument and its companion materials and components were used to establish research collaboration with the University of Puerto Rico and its Study of Social Environment and Family Factors Associated to Childhood Obesity among Elementary School Students from Public and Private School in Puerto Rico. As part of this collaboration, the Food Surveys Research Group provided the USDA Dietary Intake System, including the AMPM and SurveyNet, the computer-based food coding and analysis system, whereas nutritionists at the University of Puerto Rico have evaluated the recipes and made recommendations for updates, for Puerto Rican foods reported in WWEIA-NHANES. These activities represent transfer of ARS-based technology to parties outside of ARS, and the data collected provides unique information on Hispanic nutritional issues.

Collaboration in the Healthy Aging in Neighborhoods of Diversity Across the Life Span Study (HANDLS): The primary objective of HANDLS is to create a representative, 20-year longitudinal study across the lifespan focused on investigating the differential influences of race and socioeconomic status on health. The study sample includes white and black Americans 30–64 years of age from both low and high socio-economic strata residing in Baltimore City, Maryland. ARS scientists in Beltsville, Maryland collaborated on the dietary component of HANDLS by providing scientific and technical support for dietary data collection that began in autumn 2005. ARS personnel conducted numerous training sessions for HANDLS staff on the use of the AMPM and SurveyNet for coding and analysis of dietary intake data. During dietary data collection was underway; FSRG scientists provided technical oversight of the data processing steps and systems, thereby assuring data quality and integrity.

http://www.ars.usda.gov/research/projects/projects.htm?ACCN_NO=408032&showpars=true&fy=2009

Anticipated Product 3: Knowledge of the food intake, dietary patterns, and nutritional adequacy of Americans, including population subgroups of varying ages, ethnicities, and income levels; and interpretation of the data relative to food and nutrition policy and programs.

Scientists in Beltsville, Maryland have prepared numerous special interest reports using data gathered from WWEIA-NHANES regarding the U.S. food supply. For example, *What We Eat in America, NHANES 2005–2006: Usual Nutrient Intakes From Food and Water Compared to 1997 Dietary Reference Intakes for Vitamin D, Calcium, Phosphorus, and Magnesium* was developed and released online. The report was requested by and developed for deliberations of the IOM Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. A special database on the vitamin D values in the foods reported in national dietary surveys was developed and released online. The database is entitled “Vitamin D Addendum to the USDA Food and Nutrient Database for Dietary Studies 3.0.” The vitamin D values were derived from the USDA National Nutrient Database for Standard Reference, Release 22.

http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/0506/usual_nutrient_intake_vitD_ca_phos_mg_2005-06.pdf

Bailey RL, Dodd KW, Goldman JA, Gahche JJ, Dwyer JT, Moshfegh AJ, Sempos CT, Picciano MF. Estimation of total usual calcium and vitamin D intakes in the United States. *J Nutr.* 2010;140:817–22. [33 Citations.]

National estimates of daily intakes of retail food commodities. Through collaboration with the Economic Research Service, foods reported in national dietary surveys were disaggregated into 65 unique retail food commodities in order to report on amounts of those commodities consumed daily. Three sets of tables were released on the Web that summarized food intakes across the 65 commodities for 23 age-gender groups for national dietary surveys conducted between 1994–96 and 1998; 1999–2000; and 2001–2002. These estimates provide unique data to assess food intakes of Americans closer to the farm gate. The Food Intakes Converted to Retail Commodities Database (FICRCD) that converts foods reported in the surveys from 1994 to 2002 as well as the Methodology and User Guide for FICRCD were also released on the Web; all are accessible along with the data tables from the FSRG Web site (http://www.ars.usda.gov/main/site_main.htm?modecode=12-35-50-00)

Problem Statement 1B: ***Determine Food Consumption and Dietary Patterns of "At-Risk" Populations in the United States.***

The prevalence of many nutrition related health problems is greater for minority, rural, low socio-economic, and some ethnic groups, which has led to the designation of "at-risk" populations. Some pockets of at-risk populations are not sampled in national surveys. Rather, populations with similar demographic characteristics are used to represent these at-risk groups with the role of culture, ethnicity, attitudes, beliefs toward food, and food availability concerns not taken into account. Small regional surveys as well as longitudinal and epidemiological studies are needed to better understand the role of food, physical activity, and related behaviors contributing to the health disparities of these populations.

This problem statement is addressed by two programs; one in Boston, Massachusetts and the DOPRU headquartered in Little Rock, Arkansas. The DOPRU is the only research program in the United States dedicated to studying rural at-risk populations and their nutritional problems. The goal of the program is to evaluate the role of Dietary Guidelines for Americans in preventing obesity and reducing chronic disease related factors associated with obesity in the Delta region of Arkansas, Louisiana, and Mississippi. DOPRU brings together the expertise of seven institutions in the three state region: Arkansas Children's Hospital Research Institute, University of Arkansas at Pine Bluff, University of Southern Mississippi, Alcorn State University, Pennington Biomedical Research Center and Southern University and A&M College. The goal of DOPRU is to conduct research addressing nutrition-related health problems in the delta region, especially in relation to obesity.

The research consists of three major objectives: identify barriers and facilitators to adherence to the Dietary Guidelines for Americans (DGA) and examine how differential profiles of adherence relate to obesity in children and adults of the Delta region; extend the behavioral knowledge gained from the Healthy Eating and Lifestyle for Total Health Study, as well as from Foods of Our Delta (FOODS 2000) and other food availability and food cost surveys in the Delta; to adapt existing DGA eating patterns, such as the USDA MyPyramid and the DASH Eating Plan, for the

Lower Mississippi Delta population; and evaluate the effectiveness of the adapted DGA eating patterns, with and without physical activity, in reducing weight gain and risk factors for obesity-related chronic disease in the Lower Mississippi Delta population through the use of interventional studies.

To date, the DOPRU has produced a relatively small amount of research (as judged by peer-reviewed scientific articles) despite the large coordination of centers and researchers (135 salaried employees). A PubMed search under the name of the research leader who is a co-author on all Delta OPRU studies found 25 publications since 2007, and outside of a few reports on diet quality, and reports generated from other ARS scientists, most publications have been cited less than 6 times.

Anticipated Product 1: Knowledge of food choices, food and nutrient intake, dietary patterns, and physical activity of at-risk population sub-groups not sampled in the national survey.

Health challenges within the Hispanic community. Subpopulations within the United States often present specific and serious health challenges not observed in the overall population. The Boston Puerto Rican Health Study is an ongoing longitudinal cohort study designed to examine the role of psychosocial stress on presence and development of allostatic load and health outcomes in Puerto Ricans, and potential modification by nutritional status, genetic variation, and social support. This study follows an initial cohort of 1,500 self-identified Puerto Ricans aged 45–75 years residing in the Boston metropolitan area. Participants completed a comprehensive set of questionnaires and blood, urine, and salivary samples were extracted for biomarker and genetic analysis. Measurements are repeated at a 2-year follow-up. The majority of the cohort is female (70 percent), and many have less than an 8th grade education (48 percent), and fall below the poverty level (59 percent). Baseline prevalence of health conditions is high for this age range: considerable physical (26 percent) and cognitive (7 percent) impairment, obesity (57 percent), type 2 diabetes (40 percent), hypertension (69 percent), arthritis (50 percent), and depressive symptomatology (60 percent).

The contemporary Puerto Rican population is genetically heterogeneous and originated from three ancestral populations: European settlers, native Taíno Indians, and West Africans. This rich-mixed ancestry of Puerto Ricans provides the intrinsic variability needed to untangle complex gene-environment interactions in disease susceptibility and severity. The genetic ancestry of 1,129 subjects from the Boston Puerto Rican Health Study was estimated based on genotypes of 100 ancestry informative markers (AIMs) and the ancestral composition of this population was 57.2 percent European, 27.4 percent African, and 15.4 percent Native American. African ancestry was negatively associated with type 2 diabetes and cardiovascular disease, and positively correlated with hypertension. It is likely that the high prevalence rate of diabetes in African Americans, Hispanics, and Native Americans is not due to genetic variation alone, but to the combined effects of genetic variation interacting with environmental and social factors.

Tucker KL, Mattei J, Noel SE, Collado BM, Mendez J, Nelson J, Griffith J, Ordovas JM, Falcon LM. The Boston Puerto Rican Health Study, a longitudinal cohort study on health disparities in Puerto Rican adults: challenges and opportunities. *BMC Public Health.* 2010;10:107. [17 Citations.]

Lai CQ, Tucker KL, Choudhry S, Parnell LD, Mattei J, García-Bailo B, Beckman K, Burchard EG, Ordovás JM. Population admixture associated with disease prevalence in the Boston Puerto Rican health study. *Hum Genet.* 2009;125:199–209. [27 Citations.]

Gao X, Nelson ME, Tucker KL. Television viewing is associated with prevalence of metabolic syndrome in Hispanic elders. *Diabetes Care.* 2007;30:694–700. [19 Citations.]

Anticipated Product 2: New culturally appropriate and validated methods for measuring dietary intake, physical activity, and related behaviors for these population sub-groups.

Development of a regional food-frequency (FFQ) questionnaire used for assessing carotenoid intake in the Lower Mississippi Delta. To facilitate gathering knowledge of nutritional patterns in the Lower Mississippi Delta two regional FFQs were developed, validated, and utilized to examine the association between carotenoid intakes as measured by both FFQ and their corresponding measures in serum, and to report on dietary food sources of carotenoids in Jackson Heart Study participants. This study was a cross-sectional analysis of data for 402 African American men and women participating in the Diet and Physical Activity Sub-Study of the JHS.

On average, carotenoid intakes and serum concentrations were not lower in this southern African American population than the general U.S. population. Major dietary sources of alpha-carotene are orange vegetables; sources of beta-carotene and lutein plus zeaxanthin include mustard, turnip and collard greens; the primary source of beta-cryptoxanthin is orange juice; and the primary source of lycopene is tomato juice. The two regional FFQs developed for a southern U.S. population and used as dietary assessment tools in the Jackson Heart Study appear to provide reasonably valid information for most of these carotenoids.

Talegawkar SA, Johnson EJ, Carithers TC, Taylor HA, Bogle ML, Tucker KL. Carotenoid intakes, assessed by food-frequency questionnaires (FFQs), are associated with serum carotenoid concentrations in the Jackson Heart Study: validation of the Jackson Heart Study Delta NIRI Adult FFQs. *Public Health Nutr.* 2008;11:989–97. [16 Citations.]

Measures of fruit and vegetable intake in Mississippi and Arkansas children. The WillTry instrument is a psychometric tool designed to measure children's willingness to try fruits and vegetables and oriented toward use in the DOPRU study. WillTry surveys were interviewer-administered to 284 children in an elementary school and summer day camps located in rural Mississippi and Arkansas communities. Evaluation was for internal consistency, test-retest reliability, and predictive validity. The WillTry food scale had substantial reliability and internal consistency. Results of the regression analysis for percent consumption of foods offered on WillTry response confirmed the predictive validity of the instrument and provides evidence that

it can be used as a measure of willingness to try fruits and vegetables in rural, southern US children aged 5–14 years of age.

Thomson JL, McCabe-Sellers BJ, Strickland E, Lovera D, Nuss HJ, Yadrick K, Duke S, Bogle ML. Development and evaluation of WillTry. An instrument for measuring children's willingness to try fruits and vegetables. *Appetite.* 2010;54:465–72. [0 Citations.]

Anticipated Product 3: New information on food availability and accessibility of these at-risk populations to inform policy decisions at the state and national level.

Characterization of nutritional adequacy in the Lower Mississippi Delta. The diet quality of 1,699 adults in the Lower Mississippi Delta (LMD) was determined by telephone survey and by using the Healthy Eating Index (HEI) to 1) identify potential and needed interventions, 2) determine population subgroups needing special attention, and 3) compare regional intakes with national intakes. Age, race, and income of adults in the LMD affected overall diet quality. Black Americans had lower grain, vegetable, milk, and variety scores than did whites. The consumption of grains and vegetables was associated with lower odds ratios for being overweight. The LMD adults had a lower HEI score than did the adults in NHANES 1999–2000 and more adults in the LMD ate a poor diet.

Food supply adequacy within three food store types also was assessed in the LMD. A regional food store survey was conducted in 225 food stores in 18 counties to determine availability and quality of 102 food items in 62 supermarkets, 77 small/medium stores, and 86 convenience stores. On average, supermarkets carried 96 percent of the items that compose the Thrifty Food Plan. Mean percentage of Thrifty Food Plan items carried in small/medium stores was 50 percent. Convenience stores carried 28 percent of the Thrifty Food Plan items. Supermarkets had higher overall quality ratings and quality ratings for fresh and frozen foods compared with small/medium and convenience stores, but the number of supermarkets in this region is limited. Consequently, community residents with limited transportation to reach supermarkets may experience limited food supply adequacy.

These studies highlight the nutritional challenges facing adults in the LMD. Low-income and young-adult households in the LMD are in need of nutrition interventions with an emphasis on increasing grain, fruit, and vegetable intakes. Because socioeconomic factors affect diet quality, a multimodal, longitudinal approach appears needed to improve nutritional health.

Johnson GS, McGee BB, Gossett JM, Thornton A, Simpson PM, Johnson C, Richardson V, Bogle M, James-Holly D, McCabe-Sellers B. Documenting the need for nutrition and health intervention for middle-aged and older adults in the Lower Mississippi Delta region. *J Nutr Elder.* 2008;27:83–99. [1 Citation.]

McCabe-Sellers BJ, Bowman S, Stuff JE, Champagne CM, Simpson PM, Bogle ML. Assessment of the diet quality of US adults in the Lower Mississippi Delta. *Am J Clin Nutr.* 2007;86:697–706. [17 Citations.]

Zoellner J, Connell CL, Santell R, Fungwe T, Strickland E, Avis-Williams A, Yadrick K, Lofton K, Rowser M, Powers A, Lucas G, Bogle ML. Fit for life steps: results of a community walking intervention in the rural Mississippi delta. *Prog Community Health Partnersh*. 2007; 1:49-60. [5 Citations.]

Problem Statement 1C: *Provide U.S. Food Composition Data*

ARS provides nationally representative food and dietary supplement composition data that are critical to the support of nutrition monitoring, nutrition research, food regulation, labeling, and trade, and to the development of dietary guidance and education. This also supports dietary surveillance by providing food composition data. ARS does this by compiling and maintaining analytical data for commonly eaten U.S. foods; the first USDA food composition tables were published in 1891 by W.O. Atwater and C.D. Woods, who assayed the refuse, water, fat, protein, ash, and carbohydrate content of approximately 200 different foods.

Continuing this task today is challenging because of a rapidly changing U.S. food supply, evolving consumer food choices, and growing demand for data on newly discovered, potentially health-promoting food components. The U.S. food supply comes from institutions (e.g., school lunches), restaurants and quick-food establishments, purchased fully prepared items from retail outlets that are taken home to eat, semi-prepared items from retail establishments that are taken home to finish preparing and eat, unprepared foods (e.g., fruits and vegetables) from retail establishments or directly from producers (e.g., farmer's markets) that are taken home to be prepared and eaten and dietary supplements consumed as a pill, tablet or beverage.

There are hundreds of thousands of different items in the U.S. food supply, many of which are retail items that are reformulated at regular intervals, and some of which (e.g., bread and milk) are fortified with key nutrients. Additionally, the chemical composition of a retail food item is affected by harvesting and processing techniques and the composition of the raw commodity (e.g., meats, fruits and vegetables) may be affected by factors such as plant/animal species or variety, portion of the plant or animal eaten, agricultural production methodology and season and location of production. These factors make the U.S. food supply a dynamic and fluid entity that must be constantly monitored.

There is a need for food composition data for essential nutrients as well as new, potentially health-promoting compounds. Accurate and current food and dietary supplement composition databases must be compiled and maintained utilizing appropriate and standardized approaches for data acquisition, evaluation, compilation, and dissemination. This challenge is met by multiple programs within USDA-ARS which develop and/or maintain numerous databases including the National Nutrient Database for Standard Reference, the Dietary Supplements Ingredients Database, the caloric content of restaurant foods and specific chemical/nutrient databases for constituents such as flavonoids and choline.

To support the effort of obtaining food compositional data, research also is needed on methods of statistical sampling, composition analyses, and quality control, and must include the development of state-of-the-art analytical methods for food and dietary supplement composition analyses.

Partnerships are critical to accomplishing this work. ARS and the Department of Health and Human Services are partnering with the National Food and Nutrient Analysis Program (NFNAP) that enables nutrient analyses of foods that are major contributors of nutrients and other health promoting food constituents in the U.S. food supply. The Dietary Supplement Ingredient Database also was created through this program partnership. The National Institutes of Health's National Cancer Institute and Office of Dietary Supplements are lead DHHS agencies for NFNAP.

Anticipated Products 1 & 2: 1. Current and accurate food and dietary supplement databases for essential nutrients and health-promoting components.
2. New and improved analytical methods for food constituents and libraries of essential nutrient and health-promoting compound profiles.

The need for up-to-date and reliable data characterization of the nutrient content of the U.S. national food supply is essential to researchers, policy makers, food regulatory agencies and nutrition professionals as well as the general public. Today these data are primarily collected and maintained by the USDA-ARS National Nutrient Data Bank (NDB), a repository of information for up to 146 nutrients for over 7,900 foods (many data are from analyses conducted by ARS). These data are made publicly available through multiple databases, the primary one being the USDA National Nutrient Database for Standard Reference (SR). These data have been called the "Gold Standard" of food composition databases, and a "National Treasure" that must be maintained.

In addition to the SR database, the ARS also maintains other databases with information on dietary supplements, choline, flavonoids, isoflavones, and fluoride, oxalic acid in vegetables and proanthocyanidins and caloric content of restaurant food. No other government, governmental agency, state or private institution or facility does this; additionally these are base data used by many other public and private databases within the U.S. and other countries (other such databases rearrange the data, display it in different ways and add functionality, but careful inspection of most commercial or proprietary databases reveals that base analytical data are from ARS). The Nutrient Data Laboratory (NDL) which develops and administers SR also collects data from published (including the scientific literature) and unpublished source such as the food industry, other government agencies, and research conducted under contracts initiated by USDA's Agricultural Research Service. A rigid quality assurance program ensures that data obtained from outside sources is reliable and valid. A controlled and sophisticated system for analyzing the nutrient content of commonly eaten foods ensures that samples are collected from diverse and representative areas followed standard and acceptable methods of analysis.

Food composition data supplied by the ARS are essential for multiple public and private sector goods and services. For example other agencies within USDA use ARS data to help develop dietary guidelines; FDA uses food composition data to determine food label compliance; the ARS and CDC use ARS data in conjunction with measures of food intake to determine the nutrient intake of the American public; the food industry often uses the data to impute label values; the Canadian government uses SR data as base data for its own food composition tables; the University of Minnesota uses ARS data as base data for a proprietary database it has

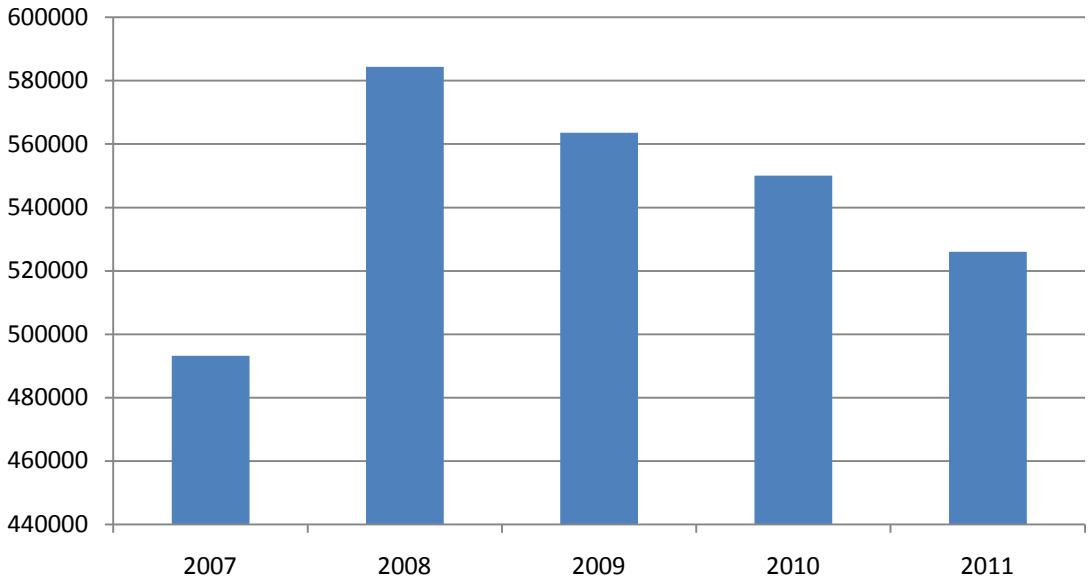
developed; and several private nutritional databases use ARS data as the basis for determining nutritional composition of meals.

To support the measures of components in the database, research also is needed to develop analytical methods for food and dietary supplements. To this end ARS has developed state-of-the-art methods for determining the chemical composition of various foods, nutrients and non-nutritive components of foods.

Nutrient Databases assembled and maintained by ARS. Continuous monitoring of the nutritional content of common U.S. foods has been a USDA priority since 1891. ARS researchers from Beltsville, Maryland have the primary responsibility for collecting and maintaining this data and the data is made publicly available through multiple databases, the primary one being the USDA National Nutrient Database for Standard Reference (SR). There are other smaller specialty databases including ones for flavonoids and choline. The SR database is a repository of information for up to 146 nutrients for over 7,900 foods (most data are from analyses conducted by contract with ARS).

Updated versions of SR have been yearly for the past 5 years; the 24th version of SR was released in 2011. Over the period of 2007–2011 there were 2,717,346 visits to the SR website (see Figure 3) and at least 1,046 peer-reviewed publications (Figure 4) have referenced it (although it is difficult to obtain accurate numbers because many studies that utilize the data do not reference it).

Figure 3. Visits to the USDA-ARS food composition database website (by year for past five years)



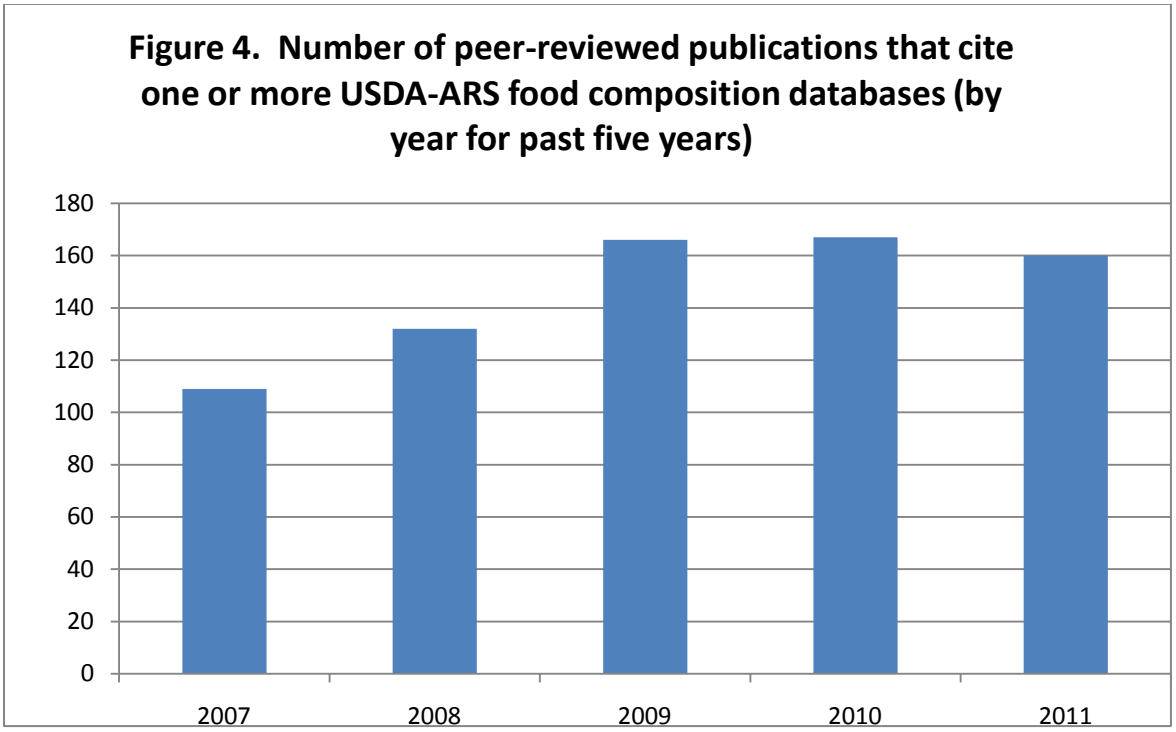
Updates to SR have been more substantial than simply revising existing information as updates include expanded and new information. In 2011 the update included, for the first time, information on vitamin D in 4100 foods (this was made possible because another ARS laboratory

developed and validated a simplified vitamin D assay; see below), total nutrient content data on 200 subsistence foods used by several Native American tribes and expanded data on Hispanic foods.

U.S. Department of Agriculture, Agricultural Research Service. 2011. USDA National Nutrient Database for Standard Reference, Release 24. Nutrient Data Laboratory Home Page, http://www.ars.usda.gov/nutrientdata

Beecher, G, Stewart, K, Holden, JM, Harnly, JM, Wolf, WR. Legacy of Wilbur O. Atwater: human nutrition research expansion at the USDA-interagency development of food composition research. *J Nutr.* 2009;139:178-184. [8 Citations.]

Haytowitz, DB, Pehrsson, PR, Holden, JM. The National Food and Analysis Program: A decade of progress. *J Food Compost Anal.* 2007;21:S94–S102. [27 Citations.]



Plant food composition – non-nutritive components. Plants contain numerous constituents that are not recognized as essential nutrients, but nevertheless may play key roles in mitigating the risk of chronic disease. The benefits of many of these chemicals are being studied in many models, but often the basic information concerning concentrations in specific plant foods is not known. Moreover, the concentration in a specific plant type varies depending on attributes such as genetic strain, location and production method. ARS researchers at multiple locations have reported the concentrations of many phytochemicals in many foods produced under a variety of conditions, and much of this information has been compiled into specialty databases maintained by ARS. Databases that have been developed or updated during the period of 2007-2011 include flavonoids (updated 2009) and isoflavonoids (updated 2008). ARS researchers at multiple

locations also have been involved in the analyses of many phytochemicals and plant components that have not been cataloged into databases. These analyses and databases are seminal datasets for the preliminary investigation of relationships between intake and human biological response. Such data help the entire community of natural product nutritionists understand the bounds and variability of these compounds in foods. They benefit many human nutrition researchers who are studying the health benefits of such compounds but need such basic data to devise experimental plans, and they are essential for plant breeders who consider the nutritional implications of selective plant breeding.

Perry, A, Rasmussen, H, Johnson, EJ. Xanthophyll (lutein, zeaxanthin) content in fruits, vegetables and corn and egg products. *J. Food Compost Anal.* 2009;22:9–15. [28 Citations.]

Pehrsson, PR, Patterson, KY, Perry, CR. The fluoride content of select brewed and microwave-brewed black teas in the United States. *J. Food Compost Anal.* 2011;24:971–975.

Mi, JC, Howard, LR, Prior, RL, Morelock, T. Flavonoid content and antioxidant capacity of spinach genotypes determined by high-performance liquid chromatography/mass spectrometry. *J Sci Food Agric.* 2008;88:1099–1106. [7 Citations.]

Huynh, B-L, Palmer, L, Mather, DE, Wallwork, H, Graham, RD, Welch, RM, Stangoulis, JCR. Genotypic variation in wheat grain fructan content revealed by a simplified HPLC method. *J Cereal Sci.* 2008:48:369–378. [9 Citations.]

Bolling, BW, Blumberg, JB, Oliver Chen, C-Y. The influence of roasting, pasteurisation, and storage on the polyphenol content and antioxidant capacity of California almond skins. *Food Chem.* 2010;123:1040–1047. [5 Citations.]

Dietary Supplements Ingredients Database. More than 50 percent of Americans take some form of dietary supplement; consequently this in addition to diet is a major source of nutrients and other compounds. Other than stated label values, almost no information is available concerning the content and content variability of dietary supplements, especially multi-vitamin and mineral supplements. ARS scientists in Beltsville, Maryland collaborated with the Office of Dietary Supplements, National Institutes of Health to develop the Dietary Supplements Ingredients Database that was released in 2009. This publicly available database includes composition data for adult MultiVitamin and Mineral supplements, data application tables, a research summary, an on-line adult multi-vitamin and mineral supplement calculator, and instructions for the use of the files. This database gives researchers and healthcare professionals access to information on analytically validated levels of ingredients in a variety of dietary supplements including children's multi-vitamin and mineral supplements, fish oil and flaxseed oil products containing omega-3-fatty acids, and botanically -based supplements. When combined with information from the USDA-ARS Dietary Database for Standard Reference, it allows for the calculation of total nutrient intake from all sources.

Roseland, JM, Holden, JM, Andrews, KW, Zhao, C, Schweitzer, A, Harnly, J, Wolf, WR, Perry, CR, Dwyer, JT, Picciano, MF, Betz, JM, Saldanha, LG, Yetley, EA, Fisher, KD, Sharpless, KE Dietary supplement ingredient database (DSID): Preliminary USDA studies on the composition of adult multivitamin/mineral supplements. *J. Food Comp Anal.* 2008;21:S69–S77. [14 Citations.]

Dwyer, JT, Picciano, MF, Leila, SM, Betz, JM, Fisher, KD, Saldanha, LG, Yetley, EA, Coates, PM, Radimer, K, Bindewald, B, Sharpless, KE, Holden, J, Andrews, K, Zhao, C, Harnly, J, Wolf, WR, Perry, CR. Progress in development of an integrated dietary supplement ingredient database at the NIH Office of Dietary Supplements. J *Food Compost Anal.* 2006;19:S108–S114. [12 Citations.]

Caloric content of restaurant food. Reversing the rising incidence of obesity requires that consumers reduce their caloric intake, and this requires knowledge of the caloric content of particular foods. The proportion of food eaten away from home, particularly at restaurants, is steadily increasing. Some restaurants provide caloric information for their foods, but the accuracy of this data is not known. ARS-supported scientists from Boston, Massachusetts, compared laboratory measurements of calories for 269 fast food and sit-down chain restaurant food items collected at multiple locations across multiple states to the calories listed on menus and websites. On average, the analyzed calories were only 10 calories higher than stated, however 19 percent of the items tested were under-reported by more than 100 calories; this problem was especially prevalent for items listed at less than 300 calories. This information will induce restaurants to more accurately state the caloric content of their food, which will in turn be of help to the consumer attempting to decrease caloric intake.

Urban LE, McCrory MA, Dallal GE, Das SK, Saltzman E, Weber JL, Roberts SB. Accuracy of stated energy contents of restaurant foods. *JAMA.* 2011;306:287–93.

Urban LE, Dallal GE, Robinson LM, Ausman LM, Saltzman E, Roberts SB. The accuracy of stated energy contents of reduced-energy, commercially prepared foods. *J Am Diet Assoc.* 2010;110:116–23. [9 Citations.]

Developing analytical methods to confirm food identity. The American diet originates from all corners of the world, and this often leads to serious problems of contamination and/or loss of identity. One example is the melanin contamination of numerous foods originating from China. It is impossible to analyze for all known contaminants and adulterants in all imported food, so a reliable means of confirming the identity of foods is needed. ARS Scientists at Beltsville, Maryland developed methods to generate unique “fingerprints” of plant chemical constituents and metabolites that identify plants with 100 percent accuracy. Examples of analyses that used this method include green tea and ginseng; different species and growing locations were determined with a relatively easy to perform assay. Such techniques have great potential importance for manufacturers and regulatory agencies who must verify the identity and origin of plants used in processed foods. The method also has application for verifying ingredients in dietary supplements as well as discovering adulteration or misbranding of products.

Chen P, Luthria D, Harrington PB, Harnly JM. Discrimination among Panax species using spectral fingerprinting. *J AOAC Int.* 2011;94:1411–21.

Sun J, Chen P, Lin LZ, Harnly JM. A non-targeted approach to chemical discrimination between green tea dietary supplements and green tea leaves by HPLC/MS. *J AOAC Int.* 2011;94:487–97.

Development of analytical techniques to support efforts in food composition. Data regarding the chemical composition of food is only as strong as the analytical methodology that it based on. ARS scientists have been in the forefront of developing these methods. Because of the lack of good analytical methods, vitamin D had not been included in foods in previous releases of the SR nutrient database, and this was the impetus for scientists at Beltsville, Maryland to develop a robust and accurate method. The developed method was used to analyze multiple foods, including mushrooms and fluid milk and results were incorporated into the SR database. The immediate impact of the work was the finding that the vitamin D content of some fluid milk was well below the label value (or even completely absent), and publication of the values was an incentive for manufacturers to be more careful regarding vitamin D fortification, and ensure that actual values were within the error bounds stated on the label. ARS scientists at Beltsville also developed a method to determine B vitamins in dietary supplements, and that work allowed development and publication of the Dietary Supplements Ingredients Database (see above). Analytical methods depend on accurate standards, and ARS scientists at Beltsville have worked with the National Institute of Standards and Technology to help validate standards for use in food composition research.

Byrdwell W C. Comparison of Analysis of Vitamin D-3 in Foods Using Ultraviolet and Mass Spectrometric Detection. *J Ag Food Chem.* 2009;57:2135–2146. [13 Citations.]

Patterson, KY, Phillips, KM, Horst, RL, Byrdwell, WC, Exler, J, Lemar, LE, Holden, JM. Vitamin D content and variability in fluid milks from a U.S. Department of Agriculture nationwide sampling to update values in the National Nutrient Database for Standard Reference. *J Dairy Sci.* 2010;93:5082–5090. [7 Citations.]

Phillips, KM, Wolf, WR, Patterson, KK, Sharpless, KE, Amanna, KR, Holden, JM. Quality and performance evaluation of reference materials for the determination of nutrients in foods. *Accred Qual Assur.* 2007;12:126–133. [Citations not available.]

Problem Statement 1D: *Enhance the Health-Promoting Quality of the Food Supply*

Plant and animal food products provide a broad range of nutrients and health-promoting non-nutritive components that help reduce the risk of diet-related chronic diseases and promote healthier lives for all. Knowledge of how these components of the food production continuum influence the quality of the final food product is critical to assuring the availability of a nutritious food supply. However, the density of these components varies from food to food, as a result of both genetic attributes and environmental factors. These influences include crop production practices, traditional breeding or genetic modification of food crops, environmental variables such as water, temperature, or atmospheric carbon dioxide, and post-harvest processing methods,

all of which can lead to changes in the nutritional quality and health-promoting composition of foods. This knowledge is essential to devising and executing new strategies that will further enhance the health-promoting qualities of foods.

Anticipated Product 1: Knowledge of individual genes that control the accumulation of essential nutrients or the synthesis of health-promoting components in foods.

ARS scientists have been at the forefront of identifying nutritional deficiencies that can be solved by food-based approaches, and then developing crops that are ideally suited for such an approach. Such ARS research is cross cutting in nature; it is conducted at several locations, involves partners form other ARS nutrition centers (especially for testing foods in clinical trials) and often involves partners from other ARS programs. Some of this work has received international attention. Specific examples follow.

Golden Rice as a Source of Vitamin A. Vitamin A deficiency (VAD) is a debilitating condition that can cause irreversible blindness, xerophthalmia and death. In 2005 it was estimated that over 200 million women and children in 122 countries suffered VAD. Rice is a staple food for many of the children in VAD countries and rice is a very poor source of Vitamin A. An international project was begun to make rice enriched in beta-carotene, a precursor to vitamin A, and test the efficacy of such rice as a component of a strategy for ameliorating VAD. To this end, ARS researchers in Houston, Texas grew isotopically-labeled golden rice by hydroponics and then fed servings of the rice to healthy adults (the human feeding experiment was conducted by ARS scientists at Boston, Massachusetts). Results showed that, following consumption, labeled beta-carotene was absorbed intact and the subsequent conversion to vitamin A occurred at a ratio of 3.8 to 1 (as compared to ratios of up to 27:1 estimated previously for colored vegetables). Such results show that Golden Rice could be very effective as a component of a strategy to ameliorate VAD in rice-consuming areas of the world.

Tang G, Qin J, Dolnikowski GG, Russell RM**,** Grusak MA. Golden Rice is an effective source of vitamin A. *Am J Clin Nutr.* 2009;89:1776–83. [35 Citations.]

Maize as a vehicle for improving vitamin A status. Vitamin A deficiency is prevalent in many developing countries, especially in Africa. Biofortification of common crops has been used to increase the intake of limiting nutrients, and high beta-carotene maize was developed for this purpose. However, improved intake only results in improved vitamin A status if the beta-carotene can be converted to vitamin A. ARS-supported scientists from Boston, Massachusetts, fed high beta-carotene maize labeled with stable isotopes (the labeling was conducted an ARS scientist in Houston, Texas) to Zimbabweans who have low vitamin A status and showed that the beta-carotene was efficiently converted to vitamin A. This study shows that in vitamin A-deficient populations that consume maize as a major portion of their diet, beta-carotene biofortified maize is an effective means of improving nutritional status.

Muzhingi T, Gadaga T, Siwela A., Grusak M , Russell R, and Tang G. Yellow maize with high beta-carotene is an effective source of vitamin A in healthy Zimbabwean men. *Am J Clin Nutr.* 2011;94:510–519.

Maize with improved iron (Fe) bioavailability. Iron bioavailability in maize is relatively low; hence populations that consume maize as a staple in their diet are at risk for Fe deficiency. In previous years ARS scientists in Ithaca, New York identified regions in the maize genome that influence Fe bioavailability, and produced relatively small amounts of a high and low bioavailable Fe maize. This maize was then produced in relatively large quantities (approximately 3 tons). A poultry feeding trial using maize from this large harvest has confirmed the nutritional benefits of the "high" Fe maize. This is the first in a series of studies to identify specific genomics regions harboring genes that control the bioavailability of iron in a staple food crop, and to produce this crop consistently in a large quantity. This research has the potential to significantly improve Fe bioavailability to both humans and animals consuming maize as a major part of their diet, and thus help alleviate iron deficiency.

Lung'aho MG, Mwaniki AM, Szalma SJ, Hart JJ, Rutzke MA, Kochian LV, Glahn RP, Hoekenga OA. Genetic and physiological analysis of iron biofortification in maize kernels. *PLoS One.* 2011;6:e20429.

Improving calcium bioavailability from plant foods. Calcium, a mineral element essential for many functions in humans, is found in a variety of plant foods. However, the bioavailability of plant-derived calcium depends to a large extent on whether calcium oxalate crystals form in the plant, as these crystals render the calcium unavailable to the human. ARS scientists from Houston, Texas have discovered a plant gene that governs the formation of calcium oxalate. When this gene is "turned off" very little oxalate is formed and calcium bioavailability is greatly enhanced. Manipulation of this gene in plants of agricultural importance will result in plant foods with greatly increased calcium bioavailability.

Morris J, Nakata PA, McConn M, Brock A, Hirschi KD. Increased calcium bioavailability in mice fed genetically engineered plants lacking calcium oxalate. *Plant Mol Biol.* 2007;64:613–8. [11 Citations.]

Soybean constituents with anti-cancer effects. Soybeans are increasingly popular as both a nutritious and health-promoting food. In cooperation with colleagues from Tulane University, ARS scientists at New Orleans, Louisiana, and Beltsville, Maryland, showed that a newly discovered class of soy compounds called glyceollins has activity against human prostate cancer cells in cell culture and inhibit more than one growth pathway when compared to genistein, the more commonly found active ingredient in soy. If this work is confirmed in humans, these compounds could be useful for dietary prevention of prostate cancer. The scientists are also learning how to increase the concentration of glyceollins in soybeans to provide added health benefits.

Boué SM, Tilghman SL, Elliott S, Zimmerman MC, Williams KY, Payton-Stewart F, Miraflor AP, Howell MH, Shih BY, Carter-Wientjes CH, Segar C, Beckman BS, Wiese TE, Cleveland TE, McLachlan JA, Burow ME. Identification of the potent phytoestrogen glycinol in elicited soybean (Glycine max). *Endocrinology.* 2009;150:2446–53. [18 Citations.]

Anticipated Products 2: New information about the effects of production practices and environmental conditions on the nutritional quality of the U.S. food supply in terms of nutrient content and bioavailability.

Poultry Model to Assess Fe Bioavailability. Combating iron deficiency in humans is partially accomplished by improving iron bioavailability. Iron bioavailability is affected by many factors and rapid, reliable measures of iron bioavailability are essential nutritional tools. ARS researchers at Ithaca, New York have been leaders in developing and using *in vitro* measures of iron bioavailability that are good as initial screening tools, but more complex in vivo models are needed. Recently they developed surgical and feeding protocols that enable the use of the modern broiler chicken to assess Fe bioavailability from foods. This surgical model incorporates the unique anatomy of the chicken intestine allowing test substances (containing Fe) to be infused into the intestinal lumen and the measurement of absorption of that Fe via blood sampling from the duodenal vein. Essentially, these techniques enable measurement of Fe absorption from an "isolated" segment of live intestine under controlled conditions on an animal whose size and blood volume make it practical for repeated measurement of Fe uptake over a prolonged period of time (i.e., 2 hours). This model is useful for development of staple food crops such as maize, wheat, lentils and beans for improved Fe bioavailability.

Tako E, Rutzke MA, Glahn RP. Using the domestic chicken (Gallus gallus) as an in vivo model for iron bioavailability. *Poultry Sci.* 2010;89:514–21. [6 Citations.]

Beiseigel JM, Hunt JR, Glahn RP, Welch RM, Menkir A, Maziya-Dixon BB. Iron bioavailability from maize and beans: a comparison of human measurements with Caco-2 cell and algorithm predictions. *Am J Clin Nutr.* 2007;86:388–96. [20 Citations.]

COMPONENT 2: SCIENTIFIC BASIS FOR DIETARY GUIDANCE FOR HEALTH PROMOTION AND DISEASE PREVENTION

The dietary guidelines are advice to the population of the U.S. on how to eat in a manner that promotes optimal health and minimizes the risk of chronic disease. The dietary guidelines are developed from the best available science, and much of the ARS program in human nutrition is oriented toward supplying the best available science.

Problem Statement 2A: *Identify Roles of Food, Nutrients, Food Components, and Physical Activity in Promoting Health and Preventing Disease*

Population-based research has linked dietary patterns and the intakes of specific nutrients/non-nutritive food components with health and decreased risk of chronic disease. At the same time, advances in laboratory sciences have created new tools and opportunities that have increased our understanding of how foods, nutrients, and other food components, along with physical activity, can promote health and prevent disease. ARS researchers elucidate the roles of food components in minimizing the risk of diseases such as cardiovascular disease and cancer and in maintaining physiological functions necessary for optimal health and well-being, including sensory systems (such as vision), immune competence, brain function, reproductive systems, gastrointestinal health, bone health, and muscular function. More accurate data on the relationship between nutrition, physical activity, and health will lead to better estimates of requirements, metabolic consequences, and recommendations for optimal intake levels. ARS research in this area is conducted at multiple locations, with multiple scientists working on multiple projects. Work at multiple sites allows for different expertise to be applied to different facets of the same problem.

Anticipated Product 1: Improved knowledge of mechanisms whereby foods and biologically active food components, as well as physical activity and lifestyle factors alter physiological functions.

Reduction of inflammation by dietary ingredients. Chronic inflammation is increasingly implicated as a risk factor for cardiovascular disease. Dietary methods of reducing chronic inflammation could result in significant savings in the cost of healthcare in the U.S., and significant improvement in lifestyle to citizens. ARS scientists in Davis, California have conducted studies in humans searching for dietary factors that mitigate such risks.

Dietary (n-3) PUFA is one factor that may reduce chronic inflammation and the anti-inflammatory effects of docosahexaenoic acid (DHA) in hypertriglyceridemic were studied in subjects who received no supplements for the first 8 d and then received either DHA or olive oil for 90 d. DHA supplementation decreased the number of circulating neutrophils; reduced concentrations of C-reactive protein, interleukin-6 and granulocyte monocyte-colony stimulating factor; increased the concentration of anti-inflammatory matrix metalloproteinase-2; and the number of circulating neutrophils was negatively associated with the weight percent of n-3 lipids in RBCs. These results provide support for the hypothesis that DHA may lessen the inflammatory response by altering blood lipids and their fatty acid composition.

In a recently published study, the same group fed freeze-dried strawberry powder to obese subjects to determine and measured lipid profiles and blood markers of inflammation. Compared with a control intervention strawberry powder reduced plasma concentrations of cholesterol and small HDL-cholesterol particles, and increased LDL particle size and reduced risk factors for CVD, stroke and diabetes in obese volunteers, suggesting a potential role for strawberries as a dietary means to decrease obesity-related disease.

Collectively these results suggest that incorporation of higher amounts of many ingredients/foods currently consumed at lower levels into the diet could result in reduced risk of some chronic diseases, and thus reduce the burden of healthcare in the U.S.

Kelley DS, Siegel D, Fedor DM, Adkins Y, Mackey BE. DHA supplementation decreases serum C-reactive protein and other markers of inflammation in hypertriglyceridemic men. *J Nutr.* 2009;139:495–501. [28 Citations.]

Zunino SJ, Parelman MA, Freytag TL, Stephensen CB, Kelley DS, Mackey BE, Woodhouse LR, Bonnel EL. Effects of dietary strawberry powder on blood lipids and inflammatory markers in obese human subjects. *Br J Nutr.* 2011;Nov 9:1–10.

Plasma acylcarnitine, fatty acid metabolism and diabetes. The increasing rate of obesity is tied to increasing incidence of diabetes; both conditions are major public health concern. Inefficient long-chain fatty acid (LCFA) combustion is associated with insulin resistance, but molecular links between mitochondrial fat catabolism and insulin action are controversial. ARS scientists in Davis, California have studied plasma acylcarnitine profiles in the hope that they would identify distinct metabolite patterns reflective of muscle fat catabolism. Contrary to an initial hypothesis, genotype had a negligible impact on plasma metabolite patterns, but comparison of nondiabetics vs. type 2 diabetics revealed a striking increase in the concentrations of fatty acylcarnitines reflective of incomplete LCFA beta-oxidation in the latter. These results are consistent with the hypothesis that inefficient tissue LCFA beta-oxidation increases tissue accumulation of acetyl-CoA and generates chain-shortened acylcarnitine molecules that activate proinflammatory pathways implicated in insulin resistance.

Adams SH, Hoppel CL, Lok KH, Zhao L, Wong SW, Minkler PE, Hwang DH, Newman JW, Garvey WT. Plasma acylcarnitine profiles suggest incomplete long-chain fatty acid beta-oxidation and altered tricarboxylic acid cycle activity in type 2 diabetic African-American women. *J Nutr.* 2009;139:1073–81. [37 Citations; one of J Nutr. Top 10 Most Cited Articles 2009-2010.]

Nutrition, Physical Activity and Sarcopenia in the elderly. Sarcopenia, the age-associated loss in skeletal muscle mass, is a contributing factor to the observed declines in physiological capacity and functional performance with advancing age. The economic impact of sarcopenia has been estimated at $18.5 billion, annually. ARS scientists in Boston, Massachusetts are world leaders in the study of nutrient modulation and how it may mitigate sarcopenia.

Some studies have focused on characterizing sarcopenia and developing tools to predict functional performance. For example, a study examined the influence of lower extremity body

composition and muscle strength on the severity of mobility-disability in 57 community-dwelling older adults. Subjects underwent an objective assessment of lower extremity functional performance and body composition was also determined. Total Leg Lean Mass was a strong independent predictor of the level of functional impairment suggesting that lower extremity muscle mass is an important determinant of physical performance among functionally-limited elders. A longitudinal study that assessed whole muscle and single muscle fiber alterations in older adults evaluated 8.9 years apart showed that muscle strength and whole muscle force of the knee extensors were significantly lower at follow-up, but unloaded shortening velocity did not change. This suggests that muscle function may be preserved in the elderly by surviving fibers that compensate for changes in muscle strength.

Whether moderate physical exercise can improve sarcopenia-related functional is the rationale for The Lifestyle Interventions and Independence for Elders, a Phase 3 multicenter randomized controlled trial designed to compare a supervised moderate-intensity physical activity program with a successful aging health education program in 1,600 sedentary older persons followed for an average of 2.7 years. This study is in progress and results are expected to have important public health implications for the large and growing population of older sedentary men and women.

Frontera WR, Reid KF, Phillips EM, Krivickas LS, Hughes VA, Roubenoff R, Fielding RA. Muscle fiber size and function in elderly humans: a longitudinal study. *J Appl Physiol.* 2008;105:637–42. [35 Citations.]

Reid KF, Naumova EN, Carabello RJ, Phillips EM, Fielding RA. Lower extremity muscle mass predicts functional performance in mobility-limited elders. *J Nutr Health Aging.* 2008;12:493–8. [32 Citations.]

Fielding RA, Rejeski WJ, Blair S, Church T, Espeland MA, Gill TM, Guralnik JM, Hsu FC, Katula J, King AC, Kritchevsky SB, McDermott MM, Miller ME, Nayfield S, Newman AB, Williamson JD, Bonds D, Romashkan S, Hadley E, Pahor M; LIFE Research Group. The Lifestyle Interventions and Independence for Elders Study: design and methods. *J Gerontol A Biol Sci Med Sci.* 2011;66:1226–37. [61 Citations.]

Anticipated Product 2. Measurement of bioavailability of nutrients and food components and factors that modulate their levels in the body.

Factors affecting bioavailability of trace elements in foods. Trace elements are of nutritional interest, many as essential nutrients and some as toxins; thus preserving trace element homeostasis is essential. Homeostasis is maintained by balancing absorption with losses; absorption is partially dependent on other dietary factors, some of which promote and others of which inhibit absorption. ARS scientists at Grand Forks, North Dakota have been leaders in characterizing trace element bioavailability from foods and factors that may affect that bioavailability.

Calcium status is critical for multiple functions, and moderately low calcium can impair long-term bone health. It has been suggested that meat consumption impairs calcium retention and to

assess this postmenopausal women were fed low or high amounts of Ca in combination with low or high protein diets. High, compared with low dietary protein increased calcium retention from the low-calcium, but not the high-calcium diet. High dietary protein decreased urinary deoxypyridinoline and increased serum insulin-like growth factor I without affecting parathyroid hormone, osteocalcin, bone-specific alkaline phosphatase, or tartrate-resistant acid phosphatase. These results demonstrate that under practical dietary conditions, increased dietary protein from animal sources is not detrimental to calcium balance or short-term indicators of bone health.

Cadmium is a trace element recognized primarily for potential deficiency, and cadmium accumulation has been cited as a reason for limiting sales of some U.S. agricultural products to the E.U. and other nations. Understanding factors affecting cadmium absorption and retention is essential for designing trade policies that are fair but protect the consumer. ARS scientists with a history of cadmium research reviewed and summarized the effects of marginal deficiencies of zinc, iron and calcium on the enhancement of absorption and organ accumulation and retention of dietary Cd in animals. These marginal deficiencies enhanced Cd absorption as much as ten-fold from diets containing low Cd concentrations similar to that consumed by some human populations. This suggests that people who are nutritionally marginal with respect to Zn, Fe, and Ca are at higher risk of Cd toxicity diseases than those who are nutritionally adequate. Results from these studies also suggest that the bioavailability of Cd is different for different food sources. This has implications for the design of food safety rules for Cd. The review stressed that a more comprehensive understanding of the biochemistry involved in the bioavailability of Cd from foods would help resolve food safety questions and provide the support for a badly needed advance in international policies regarding Cd in crops and foods.

Selenium is an essential nutrient for humans, and maintaining adequate selenium status may mitigate the risk of several chronic diseases including some cancers. Wheat may contain high concentrations of selenium, but the bioavailability from different mill fractions is unknown. Selenium bioavailability from multiple milled wheat fractions was determined in rats based on the ability of Se from the fractions to restore Se-dependent enzyme activities and tissue Se concentrations in Se-deficient rats. Results showed that Se from wheat flour fractions was nearly 100 percent available by a number of measures including tissue selenium concentrations and enzyme activities. However bioavailability from wheat shorts was only about 85 percent, and from bran about 60 percent. These results have implications for the development of products with higher concentrations of bran and whole grains.

Hunt JR, Johnson LK, Roughead ZK. Dietary protein and calcium interact to influence calcium retention: a controlled feeding study. *Am J Clin Nutr.* 2009;89:1357–65. [41 Citations.]

Reeves PG, Chaney R.L. Bioavailability as an issue in risk assessment and management of food cadmium: a review. *Sci Total Environ.* 2008;398:13–9. [30 citations.]

Reeves PG, Gregoire BR, Garvin DF, Hareland GA, Lindlauf JE, Johnson LK, Finley JW. Determination of selenium bioavailability from wheat mill fractions in rats by using the slope-ratio assay and a modified torula yeast-based diet. *J Agric Food Chem.* 2007; 55:516–22. [10 Citations.]

Bioavailability of polyphenolic substances. Numerous reports suggest that relatively uncharacterized phytochemicals in plant foods may play a role in ameliorating chronic disease. However, health benefits of polyphenols first depend on absorption and metabolic mechanisms that deliver the compounds and their bioactive metabolites to responsive tissues. Most of these mechanisms have not been studied; as a consequence much of the information disseminated to the public regarding the benefits of polyphenols is based on studies that have not considered the bioavailability/metabolic issues that may impact efficacy.

Anthocyanins are phytochemicals found in dark colored vegetables and recent studies indicate that anthocyanin intake conveys a variety of health benefits. ARS researchers at Beltsville, Maryland have conducted a series of studies of anthocyanin bioavailability. Healthy human subjects were fed different amounts of steamed red cabbage or pureed strawberries, and anthocyanin content was measured in the urine. Results showed that red cabbage anthocyanin metabolites, both as intact and metabolized forms (glucuronidated and methylated anthocyanins) were present in urine and that increasing doses resulted in increasing concentrations in the urine. In healthy adults fed pureed strawberries pelargonidin 3-glucoside was the major anthocyanin in the puree, and pelargonidin 3-glucoside and 3 monoglucuronides were excreted in urine after ingestion, demonstrating absorption. Kinetic analysis demonstrated that anthocyanin absorption continued to increase linearly through the highest dose (400 g), showing that bioavailability is not inhibited at high dietary levels. These studies are critical to understanding the function of anthocyanins as they show that absorption increases with dose and that multiple metabolites are generated, some of which may be bioactive. Based on these results, mechanistic studies can focus on the actions of anthocyanins demonstrated to bioavailable.

Found only in oats, the polyphenol avenanthramides may contribute to the heart health benefits associated with this whole grain. However, no information had been available regarding the absorption of avenanthramides in humans. ARS scientists in Boston, Massachusetts characterized in healthy older adults the bioavailability and excretion of two doses avenanthramides extracted from oats in a controlled clinical trial. They found these compounds were quickly absorbed, reached their maximum concentration in plasma after 2 hours, and were eliminated from the circulation by 10 hours. These results demonstrate that oat avenanthramides are absorbed and ongoing studies are determining the physiological significance of this.

Charron CS, Clevidence BA, Britz SJ, Novotny JA. Effect of dose size on bioavailability of acylated and nonacylated anthocyanins from red cabbage (Brassica oleracea L. Var. capitata). *J Agric Food Chem.* 200727;55:5354–62. [21 Citations.]

Carkeet C, Clevidence BA, Novotny JA. Anthocyanin excretion by humans increases linearly with increasing strawberry dose. *J Nutr.* 2008;138:897–902. [16 Citations.]

Chen CY, Milbury PE, Collins FW, Blumberg JB. Avenanthramides are bioavailable and have antioxidant activity in humans after acute consumption of an enriched mixture from oats. *J Nutr.* 2007;137:1375–82. [26 Citations.]

Anticipated Product 3. Demonstration in cell and animal model systems that these factors reduce the risk of disease/dysfunction.

Curcumin inhibits adipogenesis. The current epidemic of obesity places great emphasis on understanding biological controls of fat production and accumulation, and especially on understanding dietary factors that may inhibit these processes. Scientists at the ARS center in Boston, Massachusetts have studied the relationship between angiogenesis and the growth of adipose tissue. Dietary polyphenols may suppress growth of adipose tissue through their antiangiogenic activity and by modulating adipocyte metabolism. The ARS scientists demonstrated in cultured cells and mice that curcumin, the major polyphenol in turmeric spice, suppressed 3T3-L1 differentiation, caused apoptosis, and inhibited adipokine-induced angiogenesis of human umbilical vein endothelial cells. Supplementing the high-fat diet of mice with curcumin did not affect food intake but reduced body weight gain, adiposity, and microvessel density in adipose tissue. In addition curcumin altered the expression of multiple enzymes and cell signals and led to increased oxidation and decreased fatty acid esterification. The curcumin suppression of angiogenesis in adipose tissue together with its effect on lipid metabolism in adipocytes may contribute to lower body fat and body weight gain, and thus increased dietary curcumin may have a potential benefit in preventing obesity.

Ejaz A, Wu D, Kwan P, Meydani M. Curcumin inhibits adipogenesis in 3T3-L1 adipocytes and angiogenesis and obesity in C57/BL mice. *J Nutr.* 2009;139:919–25. [50 Citations; one of J. Nutr. Top 10 Most Cited Articles 2009-2010.]

Effects of carotenoids unrelated to vision. Carotenoids have been extensively studied for their conversion to vitamin A, and for the health effects mediated by this conversion. However, carotenoids may have other benefits unrelated to the known functions of vitamin A, and these benefits may have implications for lowering the risk/severity on many chronic diseases. ARS scientists at several locations have been leaders in the search for undiscovered benefits of carotenoids and vitamin A unrelated to vision.

Type 1 juvenile diabetes mellitus (T1D), while not receiving as much attention as the Type 2 condition, affects a quarter of a million individuals in the U.S. under the age of 20 and dietary means of controlling the disease or mitigating risk could be an important weapon in the battle with the disease. T1D is characterized by an immune response resulting in inflammation and progressive destruction of the insulin-producing beta cells. ARS researchers at Davis, California demonstrated in non-obese diabetic mice that diets rich in polyphenols or vitamin A have protective effects against autoimmune inflammatory attack of the islet beta cells and have the potential to reduce the onset and pathogenesis of autoimmune diabetes.

Obesity and associated co-morbidities is the greatest health threat facing the U.S. and diet is central to the problem. Although calorie-dense foods are certainly the primary dietary factor, other dietary factors also may contribute to the disease. Of interest are metabolic perturbances resulting from calorie-rich diets. A team of researchers from Boston, Massachusetts including an ARS scientist, showed in mice that vitamin A-derived retinaldehyde is present in rodent fat, binds retinol-binding proteins (CRBP1, RBP4), inhibits adipogenesis and suppresses peroxisome

proliferator-activated receptor-gamma and RXR responses. These results suggest a role for retinaldehyde as a distinct transcriptional regulator of the metabolic responses to a high-fat diet.

The intake of the carotenoid lycopene has been associated with a lower risk of many cancers. ARS scientists at Boston, Massachusetts have used cells in culture as well as mouse models to study whether lycopene inhibits processes associated with tumorigenesis. Lycopene converts to apo-10'-lycopenoids, and this inhibited the growth of several human lung epithelial cell lines. Additionally it decreased chemically-induced lung tumorigenesis in the A/J mouse model. These observations demonstrate that apo-10'-lycopenoic acid is a biological active metabolite of lycopene and may be a potential chemopreventive agent against lung tumorigenesis.

Zunino SJ, Storms DH, Stephensen CB. Diets rich in polyphenols and vitamin A inhibit the development of type I autoimmune diabetes in non-obese diabetic mice. *J Nutr.* 2007;137:1216–21. [23 Citations.]

Ziouzenkova O, Orasanu G, Sharlach M, Akiyama TE, Berger JP, Viereck J, Hamilton JA, Tang G, Dolnikowski GG, Vogel S, Duester G, Plutzky J. Retinaldehyde represses adipogenesis and diet-induced obesity. *Nat Med.* 2007;13:695–702. [88 Citations.]

Lian F, Smith DE, Ernst H, Russell RM, Wang XD. Apo-10'-lycopenoic acid inhibits lung cancer cell growth in vitro, and suppresses lung tumorigenesis in the A/J mouse model in vivo. *Carcinogenesis.* 2007;28:1567–74. [30 Citations.]

Blueberries and whole-body insulin resistance in high fat-fed mice. Dietary approaches to mitigating the risk of diabetes are crucial to reducing the health care burden of this disease. Adipose tissue (AT) inflammation promotes insulin resistance (IR) and other obesity complications and AT inflammation and IR are associated with oxidative stress, adipocyte death, and the scavenging of dead adipocytes by macrophages. ARS scientists at Boston, Massachusetts compared mice fed obesitogenic (high-fat) diets supplemented with whole blueberry powder for 8 wk to unsupplemented controls. They reported a pattern of gene expression in adipose tissue of high-fat fed mice suggesting a global upregulation of inflammation and increased oxidative stress. This shift was attenuated or nonexistent in mice fed the high-fat diets supplemented with blueberries. Furthermore, mice fed the high-fat, blueberry supplemented diets were protected from insulin resistance and hyperglycemia coincident with reductions in adipocyte death. These results suggest that inclusion of blueberries in the diet can provide metabolic benefits to combat obesity-associated pathology.

DeFuria J, Bennett G, Strissel KJ, Perfield JW 2nd, Milbury PE, Greenberg AS, Obin MS. Dietary blueberry attenuates whole-body insulin resistance in high fat-fed mice by reducing adipocyte death and its inflammatory sequelae. *J Nutr.* 2009;139:1510–6. [30 Citations; one of J. Nutr. Top 10 Most Cited Articles 2009-2010.]

Health benefits of tea. Tea has received much attention in recent years for many purported health benefits, most of which are suggested to be mediated through polyphenols. Initial studies are needed to establish potential mechanisms and biochemical effects, and many of these studies are focusing on modulation of chronic inflammation. ARS scientists in Beltsville, Maryland have

studied the ability of dietary green tea to modulate gene expression in rats. They have demonstrated that dietary green tea increased anti-inflammatory tristetraprolin protein mRNA levels by 50–140 percent but decreased pro-inflammatory cytokine mRNA such as Tnf and Cox2 by 30-40 percent, suggesting that modulation of TTP mRNA levels accounts for tea's anti-inflammatory properties. Other studies have shown green tea extract regulates gene expression in the glucose uptake and insulin signaling pathway in rats fed a fructose-rich diet. These studies establish that modulation of chronic inflammation by green tea is an area that could yield potentially important results related to human health.

Cao H, Kelly MA, Kari F, Dawson HD, Urban Jr JF, Coves S, Roussel AM, Anderson RA. Green tea increases the anti-inflammatory tristetraprolin and decreases the pro-inflammatory tumor necrosis factor mRNA levels in rats. *J Inflammation.* 2007;4:1–12. [41 Citations.]

Cao H, Hininger-Favier I, Kelly MA, Benaraba R, Dawson HD, Coves S, Roussel AM, Anderson R.A. Green tea polyphenol extract regulates the expression of genes involved in glucose uptake and insulin signaling in rats fed a high fructose diet. *J Agric Food Chem.* 2007 25;55:6372–8. [55 Citations.]

Anticipated Product 4. Evidence that specific foods, nutrients, food components, and physical activity improve health in human studies.

Approaches to eliminate malnutrition in children from very poor regions. Malnutrition in the young and very young can lead to life-long debilitating problems; malnutrition during childhood is an especial problem in developing nations. ARS scientists have conducted numerous studies with undernourished children in Malawi to better understand when and how to supplement them. One study used home-based therapy with ready-to-use therapeutic food (RUTF); children in southern Malawi diagnosed with moderate or severe malnutrition were treated with RUTF and followed for up to 8 weeks. Of 2,131 severely malnourished children and 806 moderately malnourished, 89 percent and 85 percent recovered, respectively. These results demonstrate that home-based therapy with RUTF yields acceptable results without requiring formally medically trained personnel and suggest further implementation in comparable settings should be considered.

Another approach utilized micronutrient-fortified lipid-based nutrient supplements that have proven useful in the rehabilitation of severely malnourished children. One hundred eighty-two 6-mo-old healthy rural Malawian infants were randomly assigned to several groups including a lipid-based supplement groups for 12 months. Infants receiving the supplement had much less stunting at 36 months, positive weight-for-age changes and length-for-weight changes; half dose supplements did not have the same impact. These results show that such supplements fed for 12 months are likely to have a positive and sustained impact on the incidence of severe stunting. Collectively the results provide several different or perhaps complementary approaches for improving the health status of young children in areas of severe malnutrition. Supplementation trials are ongoing.

Linneman Z, Matilsky D, Ndekha M, Manary MJ, Maleta K, Manary MJ. A large-scale operational study of home-based therapy with ready-to-use therapeutic food in childhood malnutrition in Malawi. *Matern Child Nutr.* 2007;3:206–15. [17 Citations.]

Phuka, J.C., Maleta, K., Thakwalakwa, C., Cheung, Y.B., Briend, A., Manary, M.J., Ashorn, P. Postintervention growth of Malawian children who received 12-mo dietary complementation with a lipid-based nutrient supplement or maize-soy flour. *Am J Clin Nutr.* 2009;89:382–90. [13 Citations.]

Phuka J, Ashorn U, Ashorn P, Zeilani M, Cheung YB, Dewey KG, Manary M, Maleta K. Acceptability of three novel lipid-based nutrient supplements among Malawian infants and their caregivers. *Matern Child Nutr.* 2011;7:368–77. [5 Citations.]

Green tea catechins, exercise and abdominal fat loss in obese adults. ARS scientists have done much work with green tea and components of green tea in cell culture and animal models; ARS scientists at Boston, Massachusetts have extended this work to humans. The influence of a green tea catechin beverage consumption on body composition and fat distribution in overweight and obese adults was evaluated during exercise-induced weight loss. One hundred seven adults were randomly assigned to receive a beverage containing catechins or a control beverage with no catechins for 12 wk. Participants were asked to maintain constant energy intake and engage in > 180 min/wk moderate intensity exercise. There was a trend toward greater loss of body weight in the catechin group compared with the control group. Percentage changes in fat mass did not differ between the catechin and control groups but percentage changes in total abdominal fat area, subcutaneous abdominal fat area and fasting serum triglycerides were greater in the catechin group. These findings suggest that green tea catechin consumption enhances exercise-induced changes in abdominal fat and serum triglycerides.

Maki KC, Reeves MS, Farmer M, Yasunaga K, Matsuo N, Katsuragi Y, Komikado M, Tokimitsu I, Wilder D, Jones F, Blumberg JB, Cartwright Y. Green tea catechin consumption enhances exercise-induced abdominal fat loss in overweight and obese adults. *J Nutr.* 2009;139:264–70. [28 Citations; one of J. Nutr. Top 10 Most Cited Articles 2009-2010].

Bean consumption and heart health. Dry beans, pulses, and legumes are under-consumed foods in the Western Diet, and increasing consumption of these foods may have significant benefits for the mitigation of chronic disease. ARS scientists in North Dakota fed adults at risk of metabolic syndrome an entrée of either beans or chicken soup daily for 12 weeks. Bean consumption altered in vitro assessments of bacterial fermentation, changed bacterial populations and reduced total, HDL and LDL cholesterol. These results provide add to the increasing evidence that dry beans, pulses and legumes need to be incorporated into the American diet in much higher amounts, and that such dietary changes may have significant health benefits including improvement of lipid profiles associated with cardiovascular disease.

Finley JW, Burrell JB, Reeves PG. Pinto bean consumption changes SCFA profiles in fecal fermentations, bacterial populations of the lower bowel, and lipid profiles in blood of humans. *J Nutr.* 2007;137:2391–8. [20 Citations.]

Vitamin K and Human Health. Vitamin K has been extensively studied for its role in blood coagulation, but increasing evidence suggests that the vitamin K may impart health benefits independent from that function. Scientists at Boston, Massachusetts are world leaders in studying vitamin K metabolism in relation to functions other than blood coagulation; during the period of 2007-2011 they have contributed more than 35 peer-reviewed publications to the scientific literature and have been cited more than 450 times.

Chronic inflammation is implicated in many chronic diseases and dietary patterns that reduce chronic inflammation could have major public health benefits. Although vitamin K has been implicated in regulation of inflammation little is known about regulation of inflammation in humans. Associations between measures of vitamin K status and a panel of blood-circulating pro-inflammatory substances in 1,381 men and women found that individuals with high vitamin K status had substantially lower overall inflammation, suggesting a possible protective role for vitamin K in inflammation.

Other work has examined the role of vitamin K in bone and vascular health. Limited evidence has suggested that vitamin K supplementation may mitigate bone loss in the elderly. However, a 3-year study in 452 healthy, elderly men and women supplemented with vitamin D and calcium, with or without vitamin K, found that supplemental vitamin K did not further reduce bone loss for men and women already eating a healthy diet.

Devising diets and nutritional supplement plans for optimal health in the aged requires knowledge of the nutritional status of such individuals, but little is known about the determinants and heritability of vitamin K status in humans. A study of older men and women found that dietary vitamin K intake is just one of many factors influencing vitamin K status in older men and women; biomarkers of vitamin K were influenced by many environmental factors but circulating vitamin K was primarily under heritable control.

Shea MK, Booth SL, Massaro JM, Jacques PF, D'Agostino RB Sr, Dawson-Hughes B, Ordovas JM, O'Donnell CJ, Kathiresan S, Keaney JF Jr, Vasan RS, Benjamin EJ. Vitamin K and vitamin D status: associations with inflammatory markers in the Framingham Offspring Study. *Am J Epidemiol.* 2008;167:313–20. [42 Citations.]

Booth SL, Dallal G, Shea MK, Gundberg C, Peterson JW, Dawson-Hughes B. Effect of vitamin K supplementation on bone loss in elderly men and women. *J Clin Endocrinol Metab.* 2008;93:1217–23. [44 Citations.]

Shea MK, Benjamin EJ, Dupuis J, Massaro JM, Jacques PF, D'Agostino RB Sr, Ordovas JM, O'Donnell CJ, Dawson-Hughes B, Vasan RS, Booth SL. Genetic and non-genetic correlates of vitamins K and D. *Eur J Clin Nutr.* 2009;63:458–64. [27 Citations.]

Health benefits and bioavailability of phytochemicals from berries. Plants produce many phytochemicals that do not have a specific function but are believed to be protective against chronic disease. Indeed much of the reason why the dietary guidelines urge much higher fruit and vegetable consumption is because of epidemiologic evidence linking such consumption to

lower risk of chronic disease. However we lack understanding of the basic metabolism of these substances.

For a specific phytochemical to be efficacious *in vivo* it must be absorbed and be present within the body, i.e. it must be bioavailable. Consequently determining bioavailability is a crucial first step in determining the bioefficacy of a particular phytochemical. ARS scientists at Boston, Massachusetts reported that anthocyanins are identifiable in various tissues of pigs fed blueberry diets, demonstrating bioavailability. Pigs were fed up to 4 percent blueberries for 4 weeks and anthocyanins were quickly removed from blood but were detected in all tissues; 11 intact anthocyanins were quantified in the brain cerebellum and cortex, eye, and liver. Thus, anthocyanins are bioavailable and can accumulate in tissues, including those beyond the blood brain barrier.

Aging brings a multitude of health challenges including loss of function in the eyes and brain (age-related cognitive senescence; advanced degeneration may be associated with development of Alzheimer's). Dietary strategies that help maintain function throughout the aging process could be a critical component of our health care system and result in significant end-of-life health care cost savings. ARS scientists at Boston, Massachusetts have demonstrated that dietary supplementation with berries can forestall and reverse the deleterious effects of aging on neuronal functioning and behavior, and these beneficial effects may be the result of plant polyphenols. While fruits and vegetables may have direct effects on oxidative stress and inflammation in aging, polyphenolic compounds may also enhance protective signaling and neuronal growth. Other analyses indicated that berry fruit diets increase both proliferation and survival of new neurons compared to control. They also suggest that one of the major mechanisms involved in the effects of blueberries is the specific reductions in the numerous signals that are generated by oxidative stress which results in the generation of products such as specific cytokines that are deleterious to brain and neuronal function. ARS scientists at Boston, Massachusetts also have demonstrated that anthocyanins and related phytonutrients can influence gene expression in the retina in a manner that could promote eye health. These results suggest that numerous dietary phytochemicals may be important in preserving health during aging.

Shukitt-Hale B, Lau FC, Joseph JA. Berry fruit supplementation and the aging brain. *J Agric Food Chem.* 2008;56:636–41. [57 Citations.]

Kalt W, Blumberg JB, McDonald JE, Vinqvist-Tymchuk MR, Fillmore SA, Graf BA, O'Leary JM, Milbury PE.J Identification of anthocyanins in the liver, eye, and brain of blueberry-fed pigs. *Agric Food Chem.* 2008;56:705–12. [45 Citations.]

Milbury PE, Graf B, Curran-Celentano JM, Blumberg JB. Bilberry (Vaccinium myrtillus) anthocyanins modulate heme oxygenase-1 and glutathione S-transferase-pi expression in ARPE-19 cells. *Ophthalmol Vis Sci.* 2007;48:2343–9. [48 Citations.]

Problem Statement 2B: ***Improve the Scientific Basis for Updating National Dietary Standards and Guidelines***

There is an ongoing need to improve the scientific basis for the types and amounts of nutrients and other health-promoting food factors required to maintain health and prevent disease, and this need evolves with the development of new information and application of new methods to examine specific physiologic functions. At present, few nutrient standards and dietary guidelines can be individualized and little is known about the variability in nutrient needs among different life stage groups, particularly in children and older adults. ARS research will focus on increasing the certainty and specificity of information about the health impacts of foods, nutrients, and other food components, as well as physical activity. This will allow the development of national nutrient recommendations and dietary guidelines based on a firmer scientific foundation and enhance the usefulness of such guidance in programs that rely upon them. Research will focus on nutrients and other health-promoting food components of high public health interest.

Research Needs:
Researchers will evaluate the quantitative needs for nutrients, as well as the inter-individual variability in those needs, effects of excess intakes, and interactions of nutrients and other health-promoting food components in specific at-risk populations. ARS research will develop methods to assess adequacy and excess of nutrients and other food factors, and efforts will include validation of biomarkers of exposure and impact. Researchers will also examine the individual variation of requirements due to effects of genetics, epigenetics, lifestyle, and physical environment, and they will seek to develop effective methods to communicate dietary guidance to consumers, policymakers, and researchers.

Anticipated Product 1. Enhanced scientific basis for improved estimates for requirements and safe intake ranges of nutrients and other food components.

Vitamin D levels and health. Vitamin D and calcium represent nutrients where there is expertise at several of the HNRC's and coordination by the NPSs has led to international leadership in this area. The Bone Health lab at the ARS HNRCA at Tufts University is one of the top groups in study of vitamin D. In a study among elderly Americans given vitamin D supplements for one year, scientists at the ARS nutrition center in Boston, Massachusetts found that increased body weight decreases absorption of vitamin D and results in lower blood levels of this essential vitamin. Since Americans are heavier on average than in the past, vitamin D requirements may have increased, in part, as a result of increased body fat. These data are important for making recommendations about how much vitamin D is needed to raise blood levels to desirable levels. Also in 2009, members of this group conducted a meta-analysis of randomized controlled trial of vitamins D2 or D3 and concluded that supplemental vitamin D in a dose of 700-1000 IU reduced risk of falling in older individuals by 19 percent. This paper has been cited 230 times since its publication. To gauge the impact on the field, 20 articles published since 2007 by this group have been cited more than 38 times, with the highest garnering 494 citations.

The 2011 DRI report on calcium and vitamin D used information generated by NP 107 scientists to modify the recommended requirements for these nutrients. Additionally, Steven Abrams, MD,

from our Children's Nutrition Research Center, was a member of the expert committee that authored the report. Work from our Grand Forks HNRC on calcium balance studies allowed the establishment of an Estimated Average Requirement for calcium, which replaced the less informative value of an Adequate Intake level. Multiple studies on vitamin D from NP 107 scientists were cited by the IOM committee in building the evidence base for the new recommendations. Although not used by the DRI committee, our scientists also observed a positive correlation between serum vitamin D levels and cognition in the elderly, particularly in association with executive function. This last paper has been cited 41 times in the last 2 years.

Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, Wong JB, Egli A, Kiel DP, Henschkowski J. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ.* 2009;339:b3692. [235 Citations.]

Hunt CD, Johnson LK. Calcium requirements: new estimations for men and women by cross-sectional statistical analyses of calcium balance data from metabolic studies. *Am J Clin Nutr.* 2007;86:1054–63. [16 Citations.]

Lynch MF, Griffin IJ, Hawthorne KM, Chen Z, Hamzo M, Abrams SA. Calcium balance in 1-4-y-old children. *Am J Clin Nutr.* 2007;85:750–4. [8 Citations.]

Abrams SA, Hicks PD, Hawthorne KM. Higher serum 25-hydroxyvitamin D levels in school-age children are inconsistently associated with increased calcium absorption. *J Clin Endocrinol Metab.* 2009;94:2421–7. [18 Citations.]

Buell JS, Scott TM, Dawson-Hughes B, Dallal GE, Rosenberg IH, Folstein MF, Tucker KL. Vitamin D is associated with cognitive function in elders receiving home health services. *J Gerontol A Biol Sci Med Sci.* 2009;64:888–95. [41 Citations.]

Liu E, Meigs JB, Pittas AG, McKeown NM, Economos CD, Booth SL, Jacques PF. Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in nondiabetic adults. *J Nutr.* 2009;139:329–34. [57 Citations; one of J. Nutr. Top 10 Most Cited Articles 2009–2010.]

The Dietary Reference Intakes for Vitamin A underestimate the contribution of provitamin A carotenoids. Another example of expertise on a class of nutrients distributed across several of the HNRC's is carotenoids and retinoids. Work in this area includes analysis of content in foods, bioavailability, metabolism, effects of health, and cellular and molecular mechanisms of action. Bioconversion of carotenoids to vitamin A was estimated by the IOM in 2001 to be 12:1 for dietary β-carotene and 24:1 for β-cryptoxanthin or α-carotene. Research from three of the HNRCs indicates these estimates substantially underestimate actual bioconversion to vitamin A. These data are applicable to the American population but have more public health impact on those that consume lesser amounts of preformed vitamin A, whether in developing countries or Americans who follow a vegetarian diet.

Grune T, Lietz G, Palou A, Ross AC, Stahl W, Tang G, Thurnham D, Yin SA, Biesalski HK. Beta-carotene is an important vitamin A source for humans. *J Nutr.* 2010;140:2268S–2285S. [6 Citations.]

Wang J, Wang Y, Wang Z, Li L, Qin J, Lai W, Fu Y, Suter PM, Russell RM, Grusak MA, Tang G, Yin S. Vitamin A equivalence of spirulina beta-carotene in Chinese adults as assessed by using a stable-isotope reference method. *Am J Clin Nutr.* 2008;87:1730–7. [15 Citations.]

Ho CC, de Moura FF, Kim SH, Burri BJ, Clifford AJ. A minute dose of 14C-β-carotene is absorbed and converted to retinoids in humans. *J Nutr.* 2009;139:1480–6. [12 Citations.]

Burri BJ, Chang JS, Neidlinger TR. β-Cryptoxanthin- and α-carotene-rich foods have greater apparent bioavailability than β-carotene-rich foods in Western diets. *Br J Nutr.* 2011;105:212–9.

Folate helps preserve ends of chromosomes. The ends of chromosomes, called telomeres, regulate the integrity of DNA, and when shortened, contribute to aging and cancer. Telomeres were the subject of the 2009 Nobel Prize in Physiology or Medicine, highlighting their importance in health research. Scientists at the ARS nutrition center in Boston, Massachusetts reported that folate levels in the blood influence telomere length, affecting both DNA integrity and DNA methylation in white blood cells of healthy men. Higher folate levels combined with longer telomeres are associated with slower aging and less cancer.

Paul L, Cattaneo M, D'Angelo A, Sampietro F, Fermo I, Razzari C, Fontana G, Eugene N, Jacques PF, Selhub J. Telomere length in peripheral blood mononuclear cells is associated with folate status in men. *J Nutr.* 2009;139:1273–8. [9 Citations.]

Meal frequency has variable effects on body composition and health. Although consumption of 3 meals per day is the most common pattern of eating in industrialized countries, a scientific rationale for this meal frequency with respect to optimal health is lacking. A diet with less meal frequency can improve the health and extend the lifespan of laboratory animals, but its effect on humans has never been tested. Healthy subjects consumed all of the calories needed for weight maintenance in either 3 meals/d or 1 meal/d for 6 months. When consuming 1 meal/d, subjects had a significant increase in hunger; a significant modification of body composition, including reductions in fat mass; significant increases in blood pressure and in total, LDL-, and HDL-cholesterol concentrations; and a significant decrease in concentrations of cortisol. Lower levels of TNF-α, IL-17, MCP-1 and MIP-1β were produced by peripheral blood monocytes from subjects consuming 1 meal/d. Subjects consuming 1 meal/d exhibited higher morning fasting plasma glucose levels, greater and more sustained elevations of plasma glucose concentrations, and a delayed insulin response in the oral glucose tolerance test compared with subjects consuming 3 meals per day. Levels of ghrelin were elevated in response to the 1-meal-per-day regimen. Fasting levels of insulin, leptin, ghrelin, adiponectin, resistin, and BDNF were not significantly affected by meal frequency.

Stote KS, Baer DJ, Spears K, Paul DR, Harris GK, Rumpler WV, Strycula P, Najjar SS, Ferrucci L, Ingram DK, Longo DL, Mattson MP. A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults. *Am J Clin Nutr.* 2007:981–8. [20 Citations.]

Carlson O, Martin B, Stote KS, Golden E, Maudsley S, Najjar SS, Ferrucci L, Ingram DK, Longo DL, Rumpler WV, Baer DJ, Egan J, Mattson MP. Impact of reduced meal frequency without caloric restriction on glucose regulation in healthy, normal-weight middle-aged men and women. *Metabolism.* 2007;56:1729–34. [11 Citations.]

Dixit VD, Yang H, Sayeed KS, Stote KS, Rumpler WV, Baer DJ, Longo DL, Mattson MP, Taub DD. Controlled meal frequency without caloric restriction alters peripheral blood mononuclear cell cytokine production. *J Inflamm (Lond).* 2011;7:6–19.

Anticipated Product 2. Better estimates of inter-individual variation in nutrient requirements, including genetic bases for such variation.

Creation of a database of gene by environment interactions affecting the risk of cardiovascular disease. Genetics have long been known to have a major role in the risk of cardiovascular disease, and there is increasing evidence for many environmental factors such as diet, exercise, alcohol and tobacco use. However, little attention has been paid to how genetics and environment interact to affect risk. ARS-supported scientists from Boston, Massachusetts have developed from the literature a database of such interactions relevant to nutrition, blood lipids, cardiovascular disease and diabetes. More than 2,000 studies of interactions gleaned from the literature presently are in the database. The database has been built in a manner that will in the future allow it to be incorporated into a larger database that will include information on traits and substances that can be measured in the individual. This database will greatly increase the capacity to develop new information related to diet/genetics interactions and will accelerate new discoveries in this area.

Lee YC, Lai CQ, Ordovas, JM, Parnell LD. A database of gene-environment interactions pertaining to blood lipid traits, cardiovascular disease and type 2 diabetes. *J Data Mining Genomics Proteomics.* 2011. 2:1000106**.**

Dietary carbohydrates linked to health. Several studies on dietary carbohydrates and health were conducted by scientists in Boston, Massachusetts. One found that the variability of the glycemic index (blood sugar response to a fixed amount of carbohydrate from different foods) within and between individuals was on the order of 40 percent, a degree of variability too great to be of use in making dietary recommendations. Another study at this location found that age-related macular degeneration, the leading cause of blindness among the elderly, is increased by about 10 percent by consumption of high amounts of refined carbohydrates. Follow-up studies in other populations have confirmed the earlier observation.

Vega-López S, Ausman LM, Griffith JL, Lichtenstein AH. Interindividual variability and intra-individual reproducibility of glycemic index values for commercial white bread. *Diabetes Care.* 2007;30:1412–7. [23 Citations.]

Chiu CJ, Milton RC, Klein R, Gensler G, Taylor A. Dietary carbohydrate and the progression of age-related macular degeneration: a prospective study from the Age-Related Eye Disease Study. *Am J Clin Nutr.* 2007;86:1210–8. [19 Citations.]

Chiu CJ, Robman L, McCarty CA, Mukesh BN, Hodge A, Taylor HR, Taylor A. Dietary carbohydrate in relation to cortical and nuclear lens opacities in the Melbourne Visual Impairment Project. *Invest Ophthalmol Vis Sci.* 2010 51:2897-905. [4 Citations.]

Sleep deprivation linked to obesity and diabetes. Researchers at the ARS Center in Houston, Texas discovered that animals with a disrupted circadian clock, or daily sleep cycle, at the fat cell level became heavier and gained more body fat on a normal diet than animals without this mutation. When challenged with a high fat diet, the mutant animals not only gained more weight than animals with normal sleep patterns but also became insulin resistant, a physiological change that is a precursor to diabetes. This information contributes to an understanding of why alterations in the internal biological clock of people, such as those caused by working the night shift or experiencing other sleep disruptions, may result in greater risk for developing obesity and diabetes.

Bray MS, Young ME. Regulation of fatty acid metabolism by cell autonomous circadian clocks: time to fatten up on information? *J Biol Chem.* 2011;286:11883–9. [5 citations.]

Anticipated Product 3. More complete data on nutrient adequacy in specific vulnerable population groups.

New MyPyramid developed for older adults. Scientists from the ARS center in Boston, Massachusetts updated the Food Guide Pyramid for Older Adults to reflect the new USDA food pyramid and the 2005 Dietary Guidelines for Americans. Emphases for older Americans include physical activity, adequate water intake, and possible use of dietary supplements for a few less consumed nutrients such as vitamins B12 and D. The new pyramid was released on the Web and in print in an academic nutrition journal.

Lichtenstein AH, Rasmussen H, Yu WW, Epstein SR, Russell RM. Modified MyPyramid for Older Adults. *J Nutr.* 2008;138:5–11. [20 Citations.]

Access to healthy diets limited by cost. A diet containing recommended amounts of fruits, vegetables, and whole grains is believed to be associated with better weight maintenance and health outcomes. ARS scientists in Davis, California conducted a study of 112 low-income households that purchased and prepared their own food. The researchers found that diet cost was inversely related to diet quality and that the diets these households could afford had more calories per unit weight, more total fat and saturated fat, and less vitamin C and A than recommended. Based on these findings, diet cost appears to be a barrier to eating a healthy diet in the United States, particularly for consumers in the low income brackets.

Townsend MS, Aaron GJ, Monsivais P, Keim NL, Drewnowski A. Less-energy-dense diets of low-income women in California are associated with higher energy-adjusted diet costs. *Am J Clin Nutr.* 2009;89:1220–6. [25 citations.]

Breakfast and meal patterns are important to health and performance. Scientists at the ARS Center in Little Rock, Arkansas found that children who skipped breakfast were less attentive and had slower visual cue response times than children who ate breakfast. These findings suggest that breakfast facilitates brain and motor processes that are important for learning in school. Using data from the USDA "What We Eat in America/NHANES" national dietary survey, ARS scientists in Beltsville, Maryland found that 80 percent of Americans consume breakfast on any given day. On average breakfast was found to be proportionately lower in calories and higher in vitamins and minerals than other meals, demonstrating the importance of breakfast to the overall quality of American diets. Further, other ARS scientists at Beltsville, Maryland demonstrated that consuming a single meal per day, in contrast to several meals per day, adversely influences risk for diabetes and cardiovascular disease. Such meal pattern information has broad implications for federal and state nutrition policy and programs.

Pivik RT, Dykman RA. Event-related variations in alpha band activity during an attentional task in preadolescents: Effects of morning nutrition. *Clin Neurophysiol.* 2007;118:615–32. [Citations not available.]

Carlson O, Martin B, Stote KS, Golden E, Maudsley S, Najjar SS, Ferrucci L, Ingram DK, Longo DL, Rumpler WV, Baer DJ, Egan J, Mattson MP. Impact of reduced meal frequency without caloric restriction on glucose regulation in healthy, normal-weight middle-aged men and women. *Metabolism.* 2007;56:1729–34. [21 Citations.]

Anticipated Product 4. Validated biomarkers for dietary exposure and health.

The human serum metabolome is revealed. Metabolomics is the study of small molecules that have biological activity in an organism. The first systematic catalog of all identifiable metabolites in human blood serum was published by an international consortium including ARS scientists from Davis, California; the latter measured the lipid metabolites in serum which make up about three-fourths of all identifiable molecules. This information was published in a scientific journal and made freely available on the Web at http://www.serummetabolome.ca. It enables researchers to link dietary and environmental changes with alterations in serum metabolites and prevention of chronic diseases, including heart disease, obesity and diabetes.

Psychogios N, Hau DD, Peng J, Guo AC, Mandal R, Bouatra S, Sinelnikov I, Krishnamurthy R, Eisner R, Gautam B, Young N, Xia J, Knox C, Dong E, Huang P, Hollander Z, Pedersen TL, Smith SR, Bamforth F, Greiner R, McManus B, Newman JW, Goodfriend T, Wishart DS. The human serum metabolome. *PLoS One.* 2011;6(2):e16957. [39 Citations.]

Anticipated Product 5. Strategies and interventions capable of motivating consumers to use dietary guidance.

Whey protein supplements result in decreased weight and body fat. Research by ARS scientists at Beltsville, Maryland found that about two ounces of whey protein but not soy protein or carbohydrate in the diets of overweight or obese volunteers for 5 months resulted in significant loss of weight, fat mass, and waist circumference. These research findings signify differences in the ability of different types of protein to affect metabolism and the potential to reduce the prevalence of obesity.

Baer DJ, Stote KS, Paul DR, Harris GK, Rumpler WV, Clevidence BA. Whey protein but not soy protein supplementation alters body weight and composition in free-living overweight and obese adults. *J Nutr.* 2011;141:1489–94. [6 citations.]

Texas school lunch nutrition policy changes and designed nutrition interventions improve the nutrition of school children. Scientists at the ARS Center in Houston, Texas tracked the dietary intakes of middle-school children before and after enactment of the Texas Public School Nutrition Policy in 2004 that was designed to improve the nutrition of school children. Children consuming mostly foods from the National School Lunch Program (NSLP) had higher intakes of most nutrients, milk, fruit and vegetables, and lower intakes of sweetened beverages, snack chips, candy than students eating non-NSLP foods. However, findings also indicated the need to reduce saturated fat and sodium in the NSLP. That report has been cited 28 times. The ARS scientists went on to design a program that offered baskets of free fresh fruits or vegetables daily in a Houston high school and found that 39 percent of students at the intervention school ate fruit at least two times per day compared with only 27 percent at the control school ($p<0.05$) while 22 percent met the vegetable guidelines at the intervention school and only 18 percent at the control school ($p<0.05$).

Cullen KW, Watson K, Zakeri I. Improvements in middle school student dietary intake after implementation of the Texas Public School Nutrition Policy. Am J Public Health. *Am J Public Health.* 2008;98:111–7. [23 Citations.]

Davis EM, Cullen KW, Watson KB, Konarik M, Radcliffe J. A Fresh Fruit and Vegetable Program improves high school students' consumption of fresh produce. *J Am Diet Assoc.* 2009;109:1227–31. [6 Citations.]

COMPONENT 3. PREVENTION OF OBESITY AND RELATED DISEASES

The prevalence of obesity and overweight continues to increase; currently, an estimated 66 percent of adult Americans fit within these categories (body mass index > 25kg/m^2). Among children and adolescents aged 2-19 years, the prevalence of overweight increased from 14 to 17 percent between 1999 and 2004 alone. These trends are unprecedented in U.S. history and are an important underlying cause of many related disorders, including cardiovascular disease, Type 2 diabetes and several cancers, as well as escalating health care costs. Reduction of excess weight is difficult to achieve and even harder to sustain, and experts are becoming increasingly aware of the critical need for effective, proven methods for the primary prevention of weight gain.

Problem Statement 3A: *Understand the Causes and Consequences of Obesity and Related Disorders*

Obesity is a complex condition with multiple etiologies. To understand this problem, it is important to explore dietary, biological, behavioral, and environmental factors influencing the development and consequences of obesity and related disorders across the lifespan.

Research Needs:
New information on genetic, epigenetic, neuroendocrine, and other biological mechanisms as well as behavioral and environmental factors underlying the development of obesity and related disorders is needed to understanding susceptibility and for devising strategies to promote and/or maintain healthy weight and body composition. Research will utilize molecular, cell, animal, and human models to unravel the complex problem of obesity, using innovations in biomarkers, statistical tools, complex modeling, bioinformatics, and instrumentation.

Anticipated Product 1. A more comprehensive knowledge of the biology underlying the development and consequences of obesity and related disorders, including the role of food and food components, gene-diet interactions, neuroendocrine and metabolic pathways, inflammation, and gut environment.

Maternal obesity affects energy metabolism in offspring. It is known that children of obese mothers are more likely to be obese. While shared behaviors contribute to this observation, there are inherited biological differences that also affect energy balance. Using a rat model of obesity, ARS-supported scientists at Little Rock, Arkansas found that obesity in mothers led to epigenetic changes in some genes, dysfunction of the mitochondria, organelles that control energy metabolism in the cell, and to impairment of burning fatty acids for fuel. These data help explain how and why maternal obesity can be passed on to offspring who are more likely to develop obesity, insulin resistance, and nonalcoholic fatty liver disease.

Borengasser SJ, Lau F, Kang P, Blackburn ML, Ronis MJ, Badger TM, Shankar K. Maternal obesity during gestation impairs fatty acid oxidation and mitochondrial SIRT3 expression in rat offspring at weaning. *PLoS One.* 2011 6:e24068.

Maternal obesity programs energy balance in offspring. Researchers in Little Rock, Arkansas found that male offspring of obese rats gain more weight and fat mass, along with developing insulin resistance, when fed high-fat diets. The scientists identified multiple genes and proteins in the liver and blood that change before development of obesity, suggesting that in utero exposure to maternal obesity programs multiple aspects of energy balance and offers potential ways to control weight gain if the same metabolic changes occur in humans. The 2008 paper has been cited 81 times, indicating the substantial interest in this phenomenon.

Shankar K, Harrell A, Liu X, Gilchrist JM, Ronis MJ, Badger TM. Maternal obesity at conception programs obesity in the offspring. *Am J Physiol Regul Integr Comp Physiol.* 2008 294:R528-38. [81 Citations.]

Shankar K, Kang P, Harrell A, et al. Maternal overweight programs insulin and adiponectin signaling in the offspring. *Endocrinology.* 2010;151:2577–89. [13 Citations.]

Diet shown to influence non-gene-based inheritance of obesity. In a phenomenon known as epigenetics, traits such as obesity can be inherited based not on changes in genes themselves but on the shape of DNA strands. In research at the ARS nutrition center in Houston, Texas epigenetics was shown to influence the inheritance of obesity over three generations in agouti mice. Expression of the agouti gene caused increasing hyperphagic obesity over the three generations. This trait was modifiable by high consumption of methyl donors, which included folic acid, vitamin B_{12}, betaine and choline. If these studies in laboratory animals are confirmed in humans, simple dietary changes could prevent an inherited tendency toward obesity. This research report has been cited 76 times since its publication.

Waterland RA, Travisano M, Tahiliani KG, Rached MT, Mirza S. Methyl donor supplementation prevents transgenerational amplification of obesity. *Int J Obes.* 2008;32:1373–137. [76 Citations.]

A variation in a common gene is associated with food intake and obesity. The epidemic of obesity and overweight has resulted in a critical need for methods of predicting risk to an individual as well as predicting the possible benefit of therapeutic interventions. ARS-funded researchers in Boston, Massachusetts conducted a large study to investigate the role of variation in a specific gene (APOA2 -265T) for regulation of food intake and body weight. People carrying this genetic variation only developed obesity when they consumed a diet high in saturated fat diet. This finding will contribute to efforts to identify individuals susceptible to diet-induced obesity, and will ultimately allow for specifically tailored dietary recommendations to reduce their risk of obesity and cardiovascular diseases.

Corella D, Peloso G, Arnett DK, Demissie S, Cupples LA, Tucker K, Lai CQ, Parnell LD, Coltell O, Lee YC, Ordovas JM. APOA2, dietary fat, and body mass index: replication of a gene-diet interaction in 3 independent populations. *Arch Intern Med.* 2009;169:1897–906. [16 Citations.]

Estimating the changes in energy flux that characterize the rise in obesity prevalence. The daily energy imbalance gap associated with the current population weight gain in the obesity epidemic is relatively small. However, the substantially higher body weights of populations that have accumulated over several years are associated with a substantially different total energy expenditure and total energy intake, or energy flux. An ARS scientist at Houston, Texas was a member of a team that developed an equation relating energy flux to body weight in adults for the purpose of estimating the rise in energy flux associated with the obesity epidemic. Cross-sectional data from doubly labeled water studies in 1,399 adults from multiple centers was analyzed in linear regression models; weight was the dependent variable and energy flux was the independent variable. Equations were compared with those for children and applied to population trends in weight gain. Results suggested that substantial increases in energy intake haave driven the increases in body weight over the past 3 decades. Adults had a higher proportional weight gain than children for the same proportional increase in energy intake, mostly because of a higher fat content of the weight being gained. The obesity epidemic will not be reversed without large reductions in energy intake, increases in physical activity, or both.

Swinburn BA, Sacks G, Lo SK, Westerterp KR, Rush EC, Rosenbaum M, Luke A, Schoeller DA, DeLany JP, Butte NF, Ravussin E. Estimating the changes in energy flux that characterize the rise in obesity prevalence. *Am J Clin Nutr.* 2009;89(6):1723–8. [66 Citations; one of Am J Clin Nutr Top 10 Most Cited 2009-2010.]

Inclusion of whole grains and/or fiber-rich cereals in the diet correlate with less abdominal fat deposition. Foods high in dietary fiber may play an important role in regulating body weight but few studies have examined the relationship between dietary fiber from different sources and body fat. ARS funded researchers at Boston, Massachusetts examined the relationship between grain intake and measures of body fat. Higher whole-grain and cereal fiber intakes were associated with improved body mass index, less total body fat and less fat in the abdominal region (the fat mass that is most strongly associated with obesity-linked disorders). This research suggests that increasing intakes of cereal fiber, particularly from whole-grain sources, may be one means of limiting body fat and decreasing the risk of obesity-related health disorders.

McKeown NM, Troy LM, Jacques PF, Hoffmann U, O'Donnell CJ, Fox CS. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. *Am J Clin Nutr.* 2010;92:1165–71. [12 Citations.]

Anticipated Product 2. Improved understanding of the interplay between biology and behavior and the contribution of behavioral and environmental factors to the development of obesity and related disorders in the diverse American population.

Controlling stress may result in selection of a better diet. The roles of stress or stress hormones and their relationship to food choices and body weight/body composition of middle-aged women are unknown. ARS researchers at Davis, California found that greater perceived stress was associated with lower fruit, vegetable, and protein intake, greater consumption of salty snacks, lower participation in physical activity, and a higher intake of sweets, particularly in those with Type 2 diabetes. Many of these effects were related to concentrations of the hormone

cortisol. These findings demonstrate that self-perceived stress and reactivity to it influence food choice and food intake, and that controlling stress may have a large impact on factors associated with obesity.

Laugero KD, Falcon LM, Tucker KL. Relationship between perceived stress and dietary and activity patterns in older adults participating in the Boston Puerto Rican Health Study. *Appetite.* 2011;56:194-204.

Stress and decision-making functions are a factor in weight loss. The variability in weight loss and maintenance of those losses among individuals are unexplained and are often attributed to non-compliance with diet or exercise. ARS scientists at Davis, California discovered that person-to-person differences in weight loss were associated with levels of the stress hormone cortisol in saliva and executive function on a mental acuity test. Taken together, these results indicate stress responses may be a significant determinant of weight status and, since many people react differentially to stress, indicates the need for focused weight loss strategies rather than a one-size-fits-all approach.

Witbracht MG, Laugero KD, Van Loan MD, Adams SH, Keim NL. Performance on the Iowa Gambling Task is related to magnitude of weight loss and salivary cortisol in a diet-induced weight loss intervention in overweight women. *Physiol Behav.* 2012;106:291–7.

Parental feeding style affects obesity in young children. A large study of parents of children in Head Start programs across two states revealed parents whose feeding styles were characterized as authoritative, authoritarian, indulgent, or uninvolved. The indulgent feeding style was significantly associated with higher BMI of the children after controlling for a number of factors including parental BMI, child temperament, and parental affect. These results can be used to help parents develop feeding styles that do not contribute to excess consumption and weight in their children. This paper has been cited 23 times since its appearance.

Hughes SO, Shewchuk RM, Baskin ML, Nicklas TA, Qu H. Indulgent feeding style and children's weight status in preschool. *J Dev Behav Pediatr.* 2008;29:403–10. [23 Citations.]

Anticipated Product 3. Tools such as biomarkers (including gene expression and "omics" tools), statistical tools, complex modeling, bioinformatics, and instrumentation for the measurement of diet, physical activity, and health status.

A variation in a common gene is associated with food intake and obesity. The epidemic of obesity and overweight has resulted in a critical need for methods of predicting risk to an individual as well as predicting the possible benefit of therapeutic interventions. ARS-funded researchers in Boston, Massachusetts conducted a large study to investigate the role of variation in a specific gene (APOA2 -265T) for regulation of food intake and body weight. People carrying this genetic variation only developed obesity when they consumed a diet high in saturated fat diet. This finding will contribute to efforts to identify individuals susceptible to diet-induced obesity, and will ultimately allow for specifically tailored dietary recommendations to reduce their risk of obesity and cardiovascular diseases.

Corella D, Tai ES, Sorlí JV, Chew SK, Coltell O, Sotos-Prieto M, García-Rios A, Estruch R, Ordovas JM. Association between the APOA2 promoter polymorphism and body weight in Mediterranean and Asian populations: replication of a gene-saturated fat interaction. *Int J Obes (Lond).* 2011;35:666-75.

Corella D, Peloso G, Arnett DK, Demissie S, Cupples LA, Tucker K, Lai CQ, Parnell LD, Coltell O, Lee YC, Ordovas JM. APOA2, dietary fat, and body mass index: replication of a gene-diet interaction in 3 independent populations. *Arch Intern Med.* 2009;169:1897–906. [16 Citations.]

Problem Statement 3B: ***Develop and Evaluate Strategies to Prevent Obesity and Related Diseases***

It is critically important to help people maintain a healthy weight and prevent obesity with its consequences. To date, interventions have generally not been effective. Researchers must develop a better understanding of how to help people adopt and sustain healthful food choices and physical activity patterns (lifestyles). Research is needed on food choices and physical activity behaviors, what influences them, as well as development and evaluation of innovative measurement and intervention strategies that will promote healthy weights at the individual, family, and community levels.

Research Needs:
To identify methods of promoting change in diverse populations, researchers must develop knowledge of how socio-demographic, environmental (cultural, community, neighborhood, institutional, social), economic, psychological, and biological factors influence food choices and physical activity practices of children, adolescents, and adults. Better measures of food choices, dietary intake, physical activity, and related variables can improve the quality of the research. There is a need for research on single or multi-component interventions in order to identify effective change methods for healthier lifestyles, as well as for new technologies to obtain better measures and behavior change in groups using them.

Anticipated Product 1. Knowledge of the relationships among demographic, social, environmental, economic, psychological, biological, and behavioral variables leading to unhealthy weight gain and obesity.

Maternal overweight programs obesity in offspring. Observational studies of people indicate a link between obesity in mothers and development of overweight in children. Due to interaction of genetics and environment, it is almost impossible to establish causal relationships in human studies. ARS researchers in Little Rock, Arkansas used an animal model to find that obese females gave birth to normal weight offspring but the progeny were much more susceptible to becoming overweight in later life than offspring from normal weight mothers. These results may partially explain the rapid increase in obesity seen in the U.S. over the last 30 years and afford the ability to test biological mechanisms and dietary interventions relatively quickly. Subsequent studies using this model revealed that offspring of obese mothers developed abnormal insulin and adiponectin levels and subsequent increased deposition of adipose tissue.

Shankar K, Harrell A, Liu X, Gilchrist JM, Ronis MJ, Badger TM. Maternal obesity at conception programs obesity in the offspring. *Am J Physiol Regul Integr Comp Physiol.* 2008;294:R528–38. [101 Citations.]

Marecki JC, Ronis MJ, Shankar K, Badger TM. Hyperinsulinemia and ectopic fat deposition can develop in the face of hyperadiponectinemia in young obese rats. *J Nutr Biochem.* 2011;22:142–52.

Shankar K, Kang P, Harrell A, Zhong Y, Marecki JC, Ronis MJ, Badger TM. Maternal overweight programs insulin and adiponectin signaling in the offspring. *Endocrinology.* 2010;151:2577–89. [18 Citations.]

Moderate exercise alone by teens does not increase energy expenditure. In the debate over the relative roles of diet and exercise in controlling weight, it is unclear what effect each has on maintaining health body weight. Researchers at the ARS lab in Houston, Texas found that 12 weeks of moderate intensity exercise for 30 minutes four times per week in lean and obese sedentary adolescents did not change overall energy expenditure. Fat oxidation increased in the lean, but not obese, subjects. However, fat accumulation in the liver and abdomen decreased in obese adolescents. These data suggest that even more exercise and/or calorie restriction is an essential component of a successful weight control strategy and that obese teens require more exercise than their lean counterparts to increase fat burning.

van der Heijden GJ, Sauer PJ, Sunehag AL. Twelve weeks of moderate aerobic exercise without dietary intervention or weight loss does not affect 24-h energy expenditure in lean and obese adolescents. *Am J Clin Nutr.* 2010;91:589–96. [2 Citations.]

van der Heijden GJ, Wang ZJ, Chu ZD, Sauer PJ, Haymond MW, Rodriguez LM, Sunehag AL.A 12-week aerobic exercise program reduces hepatic fat accumulation and insulin resistance in obese, Hispanic adolescents. *Obesity (Silver Spring).* 2010;18(2):384–90. [36 Citations.]

Risk of nonalcoholic fatty liver disease in obese children. The increase in obesity among children and adults has focused research and clinical interest in the development of nonalcoholic fatty liver disease (NAFLD). Almost 1,000 Hispanic children 4-19 years were measured for weight, body, composition, diet, physical activity, fitness, maturation, and blood biochemistry. Fasting serum alanine transferase (ALT) was used as an indicator of NAFLD. Fasting serum ALT was elevated in 24 percent of overweight children and in only 4 percent of non-overweight children. The proportion of "at risk" children was not influenced by gender, age, or maturation. The risk for elevated ALT was predicted by the severity of obesity, central adiposity, hyperinsulinemia, hypertriglyceridemia, elevated thyroid-stimulating hormone, and systemic inflammation.

Quirós-Tejeira RE, Rivera CA, Ziba TT, Mehta N, Smith CW, Butte NF. Risk for nonalcoholic fatty liver disease in Hispanic youth with BMI > or =95th percentile. *J Pediatr Gastroenterol Nutr.* 2007;44:228–36. [43 Citations.]

Anticipated Product 2. Innovative, valid, reliable, and feasible methods for better measures of food choices and intake, physical activity, and related variables.

ARS develops the new "gold standard" in 24-hour dietary recalls. Scientists from ARS developed a computer-aided, interviewer-administered 24-hour dietary recall entitled the Automated Multiple-Pass Method (AMPM) that was validated for assessment of energy intake using doubly-labeled water in 524 healthy volunteers. Normal weight subjects under-reported energy intake by less than 3 percent and 78 percent of men and 74 percent of women were classified as acceptable energy reporters (within 95 percent of the ratio of energy intake to total energy expenditure). As weight of the subjects increased, underestimation also increased to around 18 percent. The major types of errors were mass (incorrect portion size) and deletion (forgetting food eaten) errors when actual measurement of intake was assessed alongside use of the AMPM recall.

Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, Paul DR, Sebastian RS, Kuczynski KJ, Ingwersen LA, Staples RC, Cleveland LE. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *Am J Clin Nutr.* 2008;88:324–32. [62 Citations.]

Rumpler WV, Kramer M, Rhodes DG, Moshfegh AJ, Paul DR. Identifying sources of reporting error using measured food intake. *Eur J Clin Nutr.* 2008;62:544–52. [12 Citations.]

Improved monitoring of physical activity. In preparation for deployment of activity monitors in the NHANES survey, ARS scientists at Beltsville, Maryland compared two types of accelerometers for estimation of physical activity and found that the instruments gave significantly different results. Although the activity monitors predicted physical activity on the same scale (counts/min), the results between the two brands were not directly comparable. However, the data were comparable if a conversion equation was applied, with better results for log-transformed data. In a larger study, the same research group found the estimated average adherence of 524 subjects was 15.8 +/- 3.4 hrs/day for approximately 11.7 +/- 2.0 days when the target was to obtain 24-hr usage data. Simulated data loss due to removal of the activity monitors during sleeping hours in the 24-hr database resulted in biased estimates of physical activity, but not for total energy expenditure. Losing as little as one hour of data from the 24-hr dataset during waking hours resulted in significant biases and variability in the estimate of physical activity. Inserting a constant value for sleep and imputing estimates for missing data during waking hours significantly improved the estimates of physical activity.

Paul DR, Kramer M, Moshfegh AJ, Baer DJ, Rumpler WV. Comparison of two different physical activity monitors. *BMC Med Res Methodol.* 2007;7:26. [9 Citations.]

Paul DR, Kramer M, Stote KS, Spears KE, Moshfegh AJ, Baer DJ, Rumpler WV. Estimates of adherence and error analysis of physical activity data collected via accelerometry in a large study of free-living adults. *BMC Med Res Methodol.* 2008;8:38. [9 Citations.]

Modeling energy expenditure in children yields highly accurate estimates. Scientists at the ARS Houston center used multivariate adaptive regression splines models based on observable participant characteristics, heart rate, and accelerometer counts for prediction of minute-by-minute EE, and hence 24-h total EE (TEE), against a 7-d doubly labeled water (DLW) method in children and adolescents. Prediction of TEE was within 11 kcal/day relative to DLW. This is the most accurate assessment yet reported.

Butte NF, Wong WW, Adolph AL, Puyau MR, Vohra FA, Zakeri IF. Validation of cross-sectional time series and multivariate adaptive regression splines models for the prediction of energy expenditure in children and adolescents using doubly labeled water. *J Nutr.* 2010;140:1516–23. [3 Citations.]

Assessment of body composition in infants. ARS scientists evaluated the performance of air-displacement plethysmography using the PEA POD apparatus for measuring body composition in healthy infants weighing 2.7 – 7.1 kg and compared that with a 4-compartment body-composition model, which was based on measurements of total body water, bone mineral content, and total body potassium. The PEA POD system provided rapid, reliable, and accurate measures of percent body fat. Because of the ease of use and minimum safety concerns, this method is expected to be widely adopted in research and clinical settings. This report has been cited 35 times since its publication.

Ellis KJ, Yao M, Shypailo RJ, Urlando A, Wong WW, Heird WC. Body-composition assessment in infancy: air-displacement plethysmography compared with a reference 4-compartment model. *Am J Clin Nutr.* 2007;85:90–5. [38 Citations.]

Anticipated Product 3. Proven effective procedures (including intervention mapping, protocols, and curricula) for promoting change in social, community, psychological, biological, and behavioral variables at all points in the pathways to the development of obesity in different types of individuals, families, and communities.

Intensive lifestyle changes needed to help children prevent obesity. Although many factors contribute to development of obesity, many interventions target a single factor such as one food group or exercise and follow subjects for relatively short periods of time. ARS-supported scientists at Houston, Texas found that focusing on improved eating and exercise habits using behavioral modification strategies to individualize plans led to decreases in body mass index, subcutaneous fat, serum cholesterol and triglycerides in a group of overweight Mexican-American adolescents and these changes were maintained over 2 years. These findings indicate the benefit of intensive, daily intervention and point to future development of more cost-effective programs that can achieve the same benefits.

Johnston CA, Tyler C, Fullerton G, McFarlin BK, Poston WS, Haddock CK, Reeves RS, Foreyt JP. Effects of a school-based weight maintenance program for Mexican-American children: results at 2 years. *Obesity (Silver Spring).* 2010;18:542–7. [2 Citations.]

“Rolling store” can improve diet and weight of minority women. Improved access to healthy foods, along with recipes on how to prepare them, led to significant increases in vegetable and fruit consumption and significant weight loss over a 6-month period in rural, overweight, African-American women. In cooperation with Baton Rouge researchers, ARS scientists in Little Rock, Arkansas provided the women with fresh fruits and vegetables weekly from a truck parked at a community center, or “rolling store,” and provided monthly lessons with a nutrition educator on preparing healthier meals. This successful intervention could serve as a model for improving the diet and health of people with limited access to supermarkets.

Kennedy BM, Champagne CM, Ryan DH, Newton R Jr, Conish BK, Harsha DW, Levy EJ, Bogle ML; Lower Mississippi Delta Nutrition Intervention Research Initiative. The "Rolling Store:" an economical and environmental approach to the prevention of weight gain in African American women. *Ethn Dis.* 2009;19:7–12. [Citations not available.]

Tailored physical activities for minority girls results in sustained exercise. There is limited research on the types of activities that are most effective for promoting moderate and vigorous physical activity (MVPA) in children, particularly girls from minorities who are at increased risk of developing obesity. Traditional fitness, sport skills, games, dancing, and flexibility sessions were assigned while participants wore activity monitors. Traditional fitness sessions elicited the highest percent of MVPA (mean time spent in MVPA = 32 percent), followed by dancing and games (mean time spent in MVPA = 21 percent), sports skills (mean time spent in MVPA = 18 percent), and flexibility (mean time spent in MVPA = 7 percent). Step aerobics and rumba fitness elicited the highest proportions of MVPA. Activities with the broadest appeal to specific groups should be emphasized as a means of controlling weight gain.

Olvera N, Graham M, McLeod J, Kellam SF, Butte NF. Promoting moderate-vigorous physical activity in overweight minority girls. *Int J Pediatr.* 2010;pii:415123. [2 Citations.]

Use of personal technologies to motivate change in nutrition and activity behaviors. A group of scientists at the ARS center in Houston has pioneered the use of video games developed for use on computers or smart phones by both children and their parents. Partnering with software companies has enabled them to develop attractive games that have been documented to improve eating and physical activity by using mediating variable models. This is in contrast to providing free Wii Active video games to 700 9-12 year olds who showed no change in overall physical activity as a result of receiving them. A fully Internet-based intervention designed for African-American 8-10-year old girls over 8 weeks resulted in significant improvements in fruit, juice, and vegetable consumption as well as physical activity; this pilot study serves as proof-of-principle that this approach will be successful. Programs tailored to different age and ethnic groups as well as children with diabetes or those who are cancer survivors are under study now.

Cerin E, Barnett A, Baranowski T. Testing theories of dietary behavior change in youth using the mediating variable model with intervention programs. *J Nutr Educ Behav.* 2009;41:309–18. [22 Citations.]

Baranowski T, Buday R, Thompson DI, Baranowski J. Playing for real: video games and stories for health-related behavior change. *Am J Prev Med.* 2008;34:74–82. [51Citations.]

Thompson D, Baranowski T, Cullen K, Watson K, Liu Y, Canada A, Bhatt R, Zakeri I. Food, fun, and fitness internet program for girls: pilot evaluation of an e-Health youth obesity prevention program examining predictors of obesity. *Prev Med.* 2008;47:494–7. [12 Cit.]

Problem Statement 3C: *Evaluate the Role of the Dietary Guidelines for Americans in Preventing Obesity*

The *Dietary Guidelines for Americans* (DGA) are a central component of U.S. food and nutrition policy and provide authoritative recommendations on dietary intake and physical activity for long-term health. The DGA provide advice on food choices and appropriate levels of physical activity for maintenance of healthy weight, and thus are anticipated to be an effective tool for prevention of weight gain in the United States. However, because few Americans currently follow the DGA and because the DGA have never been tested as a complete package for their acceptability and efficacy for preventing weight gain, research studies are needed to address the general question of adherence to the DGA and whether high levels of adherence to both the food and physical activity recommendations prevent the development of obesity in children and adults.

Research Needs:
The 2005 DGA Advisory Committee identified a number of key overarching research topics that should be addressed and the results made available for future DGA deliberations. Two specific topics were to "determine the barriers for complying with the DGA among children, low-income populations, and various ethnic groups," and "to identify various mechanisms to motivate individuals to change their eating behaviors and habits." There is also a need to study the impact of the DGA dietary and physical activity recommendations, when optimally implemented, on body weight, body composition, and expected health outcomes

Anticipated Product 1. Enhanced knowledge of barriers and facilitators to DGA adherence that will promote greater acceptance and adoption of healthy dietary and activity patterns in the general U.S. population.

This study is ongoing and manuscripts are currently in preparation. This project was initiated in 2007 to address the 2005 *Dietary Guidelines for Americans* with funds from the Lower Mississippi Delta Nutrition Intervention Research Initiative at a time when this was proposed for termination. Subsequently, funding for Delta NIRI was restored and this project had inadequate funding for completion. An application for research support was submitted to Dairy Management Inc. and with that funding, most data needed were collected.

The project was conducted at six sites – five Human Nutrition Research Centers (except the Arkansas Children's Nutrition Center) and The Delta Obesity Prevention Research Unit. Ethnic groups sampled were Caucasians, African-Americans, Hispanics, and American Indians. Both children (5^{th} graders) and adults were surveyed to determine barriers and facilitators to following the individual *Dietary Guidelines for Americans* as published in the 2005 edition. This was the first multi-site project conducted by NP 107 and has gone much more slowly than anticipated, but it is expected that multiple manuscripts from this study will appear in the next couple of

years. Statistical analyses are being done by collaborators at the HNRC's in Houston and Boston for the main study and ancillary studies at other HNRC's. Since there are not major differences in the dietary recommendations between the 2005 and 2010 editions of the *DGA*, there is no concern that the data will be outdated.

Need for improving food accessibility in the rural Mississippi Delta region. ARS-supported scientists assessed food availability for products that are included in the USDA Thrifty Food Plan (TFP) in three types of stores: supermarkets, small/medium stores, and convenience stores. On average, supermarkets carried 96 percent of the items that compose the TFP. Mean percentage of TFP carried in small/medium stores was 50 percent. Convenience stores carried 28 percent of the TFP items. Because the number of supermarkets in this area is limited, community-based nutrition interventions should include partnerships with small/medium food retailers while trying to impact residents' food choices within those stores. This study has been cited 24 times. Inadequate access to food contributes to food insecurity and less healthy eating patterns. In a survey of 1,000 residents of this area, food secure adults scored higher on the Healthy Eating Index than food insecure adults (P=0.0001), but the regression model showed no differences when multiple factors were included. The latter finding points to the fact that the overriding variable is poverty and not rural location. Food secure individuals consistently achieved higher percentages of the Dietary Reference Intakes (specifically Estimated Average Requirements and Adequate Intakes) than food insecure individuals, with the greatest differences seen for vitamin A (P<0.0001), copper (P=0.0009), and zinc (P=0.0022) and very little difference for vitamins C (P=0.68) and E (P=0.32). Both populations consumed diets extremely low in fiber. This paper has been cited 22 times.

Connell, CL, Yadrick, K, Simpson, PB, Gossett, JB, McGee, BB, Bogle, ML. Food Supply Adequacy in the Lower Mississippi Delta. *J Nutr Educ Behav.* 2007;39:77–83. [22 Citations.]

Champagne CM, Casey PH, Connell CL, Stuff JE, Gossett JM, Harsha DW, McCabe-Sellers B, Robbins JM, Simpson PM, Weber JL, Bogle ML; Lower Mississippi Delta Nutrition Intervention Research Initiative. Poverty and food intake in rural America: diet quality is lower in food insecure adults in the Mississippi Delta. *J Am Diet Assoc.* 2007;107:1886–94. [43 Citations.]

Anticipated Product 2. Improved understanding of the efficacy of the DGA's recommended dietary and physical activity patterns in the primary prevention of unhealthy weight gain.

Inclusion of whole grains and/or fiber-rich cereals in the diet correlate with less abdominal fat deposition. Foods high in dietary fiber may play an important role in regulating body weight but few studies have examined the relationship between dietary fiber from different sources and body fat. ARS funded researchers at Boston, Massachusetts examined the relationship between grain intake and measures of body fat. Higher whole-grain and cereal fiber intakes were associated with improved body mass index, less total body fat and less fat in the abdominal region (the fat mass that is most strongly associated with obesity-linked disorders). This research suggests that increasing intakes of cereal fiber, particularly from whole-grain sources, may be one means of limiting body fat and decreasing the risk of obesity-related health disorders.

McKeown NM, Troy LM, Jacques PF, et al. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. *Am J Clin Nutr.* 2010;92:1165–71. [12 Citations.]

Importance of choosing nutrient-dense foods for weight control. The *Dietary Guidelines for Americans* recommend choosing energy-dense versions of most foods which are, therefore, more nutrient-dense. A pair of studies from ARS-supported scientists in Houston, Texas examined the relationship between energy density of the diet with risk of developing obesity in both children and adults using NHANES data. Both studies found that dietary energy density is an independent predictor of increased weight and higher waist circumference. In adults, there was also significantly elevated fasting insulin and signs of the metabolic syndrome. These studies show that selection of nutrient-dense foods is associated with reduced risk of obesity and some of its metabolic consequences.

Mendoza JA, Drewnowski A, Christakis DA. Dietary energy density is associated with obesity and the metabolic syndrome in U.S. adults. *Diabetes Care.* 2007;30:974–9. [46 Citations.]

Mendoza JA, Drewnowski A, Cheadle A, Christakis DA. Dietary energy density is associated with selected predictors of obesity in U.S. Children. *J Nutr.* 2006;136:1318–22. [31 Citations.]

Anticipated Product 3. Necessary data to revise the DGA, if needed, and justification for no revisions if the data support this.

As part of the planning process for NP 107, it was determined that the *Dietary Guidelines for Americans* had never been tested in their entirety as a package to reduce the risk of obesity or any other chronic conditions. A controlled feeding trial was designed in 2006-2007 with the expectation that increased funding would be made available; the funding from termination of the Delta NIRI was expected to be available for this activity, as well. This effort was put on hold since there was no additional funding forthcoming and the cost of doing a well-controlled feeding trial was excessive.

COMPONENT 4. LIFE STAGE NUTRITION AND METABOLISM

The metabolism, nutrient requirements, and health effects of food components in humans vary across stages of the life span. Dietary intake early in life, including intake of the mother before and during pregnancy, has major effects on development, child health, and disease prevention later in life. At later stages of the life span, diet affects the processes of maturation, aging, and cognitive and physical functioning. For example, the increased prevalence of chronic disease and disability among the elderly population may be modified by improved nutrition. Mammalian development is intimately reliant upon nutrients and other food components, which serve as building blocks, signaling molecules, and enzyme cofactors. Furthermore, "nutritional programming" occurs during certain critical periods when nutrition affects developmental processes, resulting in permanent or long term changes in structure, function, gene expression, and consequently, disease susceptibility. Overall, these processes remain poorly understood.

Problem Statement 4A: *Understand Mechanisms by which Nutrition Promotes Healthy Development and Function from Conception to Old Age*

There is a need for increased knowledge of relevant basic and fundamental processes of development and aging, how these processes are influenced by diet, nutrition, and other factors (e.g., physical activity, gut microflora, co-morbid conditions) in order to identify nutrient requirements and appropriate dietary composition and patterns; research is also needed to identify other lifestyle strategies to improve metabolic, physiologic, and cognitive function and health at each stage of the life span.

Research Needs:
Knowledge will be generated on the fundamental mechanisms by which food components and physical activity influence growth, development, and aging as well as the means by which these biological stages themselves affect nutrient requirements. Effective strategies will be developed to improve physiologic and cognitive functioning through diet, nutrition, and physical activity interventions.

Anticipated Product 1. Increased knowledge of basic physiological processes related to age-specific alterations in cell, tissue, and organ metabolism throughout the lifespan and the impact of these developmental changes on nutrition and health.

Beneficial bacteria improve intestinal function. Probiotics are helpful bacteria that live in the intestine. ARS scientists Beltsville, Maryland found that ingestion of these bacteria improved both intestinal immune function and the barrier function that keeps harmful bacteria from entering the body while scientists in Little Rock, Arkansas reported that diet regulates development of immune tissue in the gastrointestinal tract of neonatal pigs. These studies have potential to provide better advice for infant feeding and healthier dairy products that naturally contain probiotic bacteria.

Solano-Aguilar G, Dawson H, Restrepo M, Andrews K, Vinyard B, Urban JF Jr. Detection of Bifidobacterium animalis subsp. lactis (Bb12) in the intestine after feeding of sows and their piglets. *Appl Environ Microbiol.* 2008;74:6338–47. [3 Citations.]

Helm RM, Golden C, McMahon M, Thampi P, Badger TM, Nagarajan S. Diet regulates the development of gut-associated lymphoid tissue in neonatal piglets. *Neonatology.* 2007;91:248–55. [6 Citations.]

The intestinal microbiome differs in children with irritable bowel syndrome (IBS). Fecal samples from 22 children with IBS and 22 healthy children were analyzed for bacterial species using two methods – 454 pyrosequencing and hybridization to a 16S rRNA microarray capable of detecting >8700 bacterial taxa. Amounts of several bacterial species were altered in children with IBS. For example, a more than 10-fold greater percentage of γ-proteobacteria characterized IBS samples even though a minor component of all samples; one prominent component of this group was *Haemophilus parainfluenzae*. Using supervised learning techniques, the researchers were able to classify IBS samples with a success rate of 98.5 percent based on the bacterial species present. In addition, a novel *Ruminococcus*-like organism was associated with IBS. Finally, greater frequency of painful symptoms correlated with increased abundance of several bacterial taxa from the genus *Alistipes*. This pioneering work has the potential for dietary prevention and possible antibiotic therapy for an intractable chronic condition. Although in print only since last November, this paper has already been cited 14 times.

Saulnier DM, Riehle K, Mistretta TA, Diaz MA, Mandal D, Raza S, Weidler EM, Qin X, Coarfa C, Milosavljevic A, Petrosino JF, Highlander S, Gibbs R, Lynch SV, Shulman RJ, Versalovic J. Gastrointestinal microbiome signatures of pediatric patients with irritable bowel syndrome. *Gastroenterology.* 2011;141:1782–91. [14 Citations.]

Anticipated Product 2. Increased data on how the biologically relevant effects of diet, nutrition, and physical activity on cellular function influence physiology, behavior, and health of individuals at different life stages.

Characterization of sarcopenia is being led by ARS lab. The Sarcopenia Lab at the HNRC on Aging is one of the leaders in this area, having coined the term and being in the forefront of studies on the loss of muscle mass that accompanies aging. This condition leads to impaired mobility and falls, costing the healthcare system hundreds of millions of dollars annually. Studies that have been particularly well cited include a longitudinal survey of changes in whole muscle and individual muscle fibers in men who were 70 years old at the start and followed for about 9 years. Single muscle fiber contractile function was preserved in older humans in the presence of significant alterations at the whole muscle level. This suggests that surviving fibers compensate to partially correct muscle size deficits in an attempt to maintain optimal force-generating capacity. This paper was cited 37 times. The other paper reported that chronic over-consumption of calories coupled with deleterious intakes of saturated or trans-unsaturated fatty acids inconsistent with the recommendations outlined in the *Dietary Guidelines for Americans* have been shown to increase the risk of insulin resistance. Furthermore, lack of exercise, which can have a profound effect on skeletal muscle lipid turnover, is implicated in this lipid-induced insulin resistance.

Frontera WR, Reid KF, Phillips EM, Krivickas LS, Hughes VA, Roubenoff R, Fielding RA. Muscle fiber size and function in elderly humans: a longitudinal study. *J Appl Physiol*. 2008;105:637–42. [37 Citations.]

Corcoran MP, Lamon-Fava S, Fielding RA. Skeletal muscle lipid deposition and insulin resistance: effect of dietary fatty acids and exercise. *Am J Clin Nutr*. 2007;85:662–77. [69 Citations.]

Omega-3 fatty acids influence cardiovascular development in infants. Infants fed formula supplemented with the omega-3 fatty acid DHA ,or breast milk that naturally contains this fatty acid, had lower heart rates than those not getting this lipid. Scientists at the ARS Nutrition Center in Little Rock, Arkansas, also identified a positive effect on heart rate variability, suggesting that DHA—regardless of its source—exerts a developmental effect on the nervous system that controls heart function. These results indicated that current infant formulas, no matter what their protein source, promote normal infant development.

Pivik RT, Dykman RA, Jing H, Gilchrist JM, Badger TM. Early infant diet and the omega 3 fatty acid DHA: effects on resting cardiovascular activity and behavioral development during the first half-year of life. *Dev Neuropsychol*. 2009;34:139–58. [9 Citations.]

Soy-based infant formula not found to impair brain development. Soy infant formula contains phytoestrogens – chemicals with structures similar to estrogen – and has been banned in several countries based on concerns that these compounds pose a developmental risk to infants. In the first well-controlled, longitudinal study to examine this issue, scientists at the ARS Center in Little Rock, Arkansas found that resting brain electrical activity, a measure of brain development, did not differ between infants fed milk-based or soy-based formula during their first 6 months of life, the period during which phytoestrogen exposure from soy formula would be highest. These findings will help reduce parental and food industry concerns regarding the use of soy infant formula. This publication is an interim report from a large, longitudinal study of infant either breastfed, of given cow's milk-based formula or soy formula followed from birth through six years of age. An interim report published in 2009 has been cited 43 times to date.

Jing H, Pivik RT, Gilchrist JM, Badger TM. No difference indicated in electroencephalographic power spectral analysis in 3- and 6-month-old infants fed soy- or milk-based formula. *Matern Child Nutr*. 2008;4:136–45. [8 Citations.]

Badger TM, Gilchrist JM, Pivik RT, Andres A, Shankar K, Chen JR, Ronis MJ. The health implications of soy infant formula. *Am J Clin Nutr*. 2009;89:1668S–1672S. [43 Citations.]

Breakfast and meal patterns are important to health and performance. Scientists at the ARS Center in Little Rock, Arkansas found that children who skipped breakfast were less attentive and had slower visual cue response times than children who ate breakfast. These findings suggest that breakfast facilitates brain and motor processes that are important for learning in school. Using data from the USDA "What We Eat in America/NHANES" national dietary survey, ARS scientists in Beltsville, Maryland, found that 80 percent of Americans consume breakfast on any

given day. On average breakfast was found to be proportionately lower in calories and higher in vitamins and minerals than other meals, demonstrating the importance of breakfast to the overall quality of American diets. Further, other ARS scientists at Beltsville, Maryland demonstrated that consuming a single meal per day, in contrast to several meals per day, adversely influences risk for diabetes and cardiovascular disease. Such meal pattern information has broad implications for federal and state nutrition policy and programs. (2007)

Pivik RT, Dykman RA. Event-related variations in alpha band activity during an attentional task in preadolescents: Effects of morning nutrition. *Clin Neurophysiol.* 2007;118:615–32. [5 Citations.]

Pivik RT, Tennal KB, Chapman SD, Gu Y. Eating breakfast enhances the efficiency of neural networks engaged during mental arithmetic in school-aged children. *Physiol Behav.* 2012;106:548–55.

Helping underweight women have healthier pregnancies. Successful pregnancy requires expansion of blood volume and blood vessels. This is achieved through production of the signal molecule, nitric oxide, which is derived from the amino acid arginine. ARS researchers in Houston, Texas discovered that underweight women produced more arginine and more nitric oxide early in pregnancy compared with normal weight women but did not respond with the expected expansion of blood volume. These findings suggest that underweight women need more arginine and nitric oxide than normal weight women to maintain increased blood volume during pregnancy and this may be achieved by alterations in dietary precursors.

Kurpad AV, Kao C, Dwarkanath P, Muthayya S, Mhaskar A, Thomas A, Vaz M, Jahoor F. In vivo arginine production and nitric oxide synthesis in pregnant Indian women with normal and low body mass indices. *Eur J Clin Nutr.* 2009;63:1091–7. [5 Citations.]

Anticipated Product 3. Further development of appropriate tools and models to investigate changes in metabolic status at all stages of the lifespan, including growth, development, and aging, and how these affect nutrient requirements.

Neonatal piglets are a preferred model for human intestinal development and metabolism. A series of studies from the ARS center in Houston points to the value of using young piglets as a model in answering multiple questions about development, growth and nutrition. A 2007 paper from this group reported that gastrointestinal tissue consumed 20 percent of dietary methionine and that site was a major source of whole-body trans-methylation and trans-sulfuration. (This paper has been cited 28 times.) This same group studied five infants and found that splanchnic extraction was the major fat of glutamate and this amino acid is not a significant gluconeogenic substrate in infants. Using the young, cannulated pig as a model, the researchers found that one-third to one-half of enteral glutamate was oxidized by the intestine so even large doses of this amino acid is limited by that metabolic fate. Additional research from this group revealed that the stimulation of protein synthesis by feeding in most tissues of the neonate is regulated by the post-prandial rise in amino acids. However, the feeding-induced stimulation of protein synthesis in skeletal muscles is independently mediated by insulin as well as amino acids. (This paper has been cited 26 times.)

Riedijk MA, Stoll B, Chacko S, Schierbeek H, Sunehag AL, van Goudoever JB, Burrin DG. Methionine transmethylation and transsulfuration in the piglet gastrointestinal tract. *Proc Natl Acad Sci U S A.* 2007;104:3408–13. [30 Citations.]

Janeczko MJ, Stoll B, Chang X, Guan X, Burrin DG. Extensive gut metabolism limits the intestinal absorption of excessive supplemental dietary glutamate loads in infant pigs. *J Nutr.* 2007;137:2384–90. [10 Citations.]

Haÿs SP, Ordonez JM, Burrin DG, Sunehag AL. Dietary glutamate is almost entirely removed inits first pass through the splanchnic bed in premature infants. *Pediatr Res.* 2007;62:353–6. [5 Citations.]

Suryawan A, O'Connor PM, Bush JA, Nguyen HV, Davis TA. Differential regulation of protein synthesis by amino acids and insulin in peripheral and visceral tissues of neonatal pigs. *Amino Acids.* 2009;37:97–104. [26 Citations.]

Problem Statement 4B: ***Define the Nutritional Bases for, and Consequences of, Nutritional Programming***

Mammalian development proceeds via a specific series of irreversible steps that progressively increase the complexity of body structures, functions, and gene expression patterns. The irreversible nature of biological development involves diverse “critical windows,” developmental periods during which specific milestones must be achieved to lay the groundwork for subsequent steps. Research in nutritional programming will lead to nutritional recommendations during critical periods of development in order to optimize long-term as well as short-term health. This will be achieved through in vitro, animal, and human studies.

Research Needs:

Improved knowledge of mammalian development and the specific mechanisms by which nutrients affect these processes is necessary to develop nutritional interventions and strategies to enhance health over the life course. Potential mechanisms to be investigated include alterations in cell number, tissue remodeling, and epigenetic changes. Researchers also need to identify the critical windows during which nutritional status can induce long term or permanent changes in mammalian structure, function, and gene expression, as well as the specific nutrients and food components that affect developmental outcomes. There is also a need to elucidate the complex relationship between maternal nutrition and nutrition of the embryo, fetus, and infant. Human studies of nutritional programming will also benefit from the identification of biomarkers to serve as indicators of nutritional exposures during critical developmental periods.

Anticipated Product 1. More accurate information about the fundamental mechanisms responsible for long-term development and molecular regulation of organ structure, function, and metabolism, and an improved understanding of how specific nutrients and other food components induce permanent changes in these processes.

Epigenetic changes demonstrated in humans for the first time. At metastable epialleles, epigenotype is established stochastically in the early embryo then maintained in differentiated lineages, resulting in dramatic and systemic interindividual variation in epigenetic regulation. Epigenetic changes result in heritable characteristics that are due not to altered DNA, but to methylation or other changes that affect the three-dimensional conformation, of genes. For years, this phenomenon has been observed in a variety of animal models for human health and disease. Now, ARS-supported scientists at Houston, Texas have proof that this occurs in humans. In rural Gambia, food availability is highly season-dependent. DNA methylation of specific genes was elevated in children conceived during the rainy season when food availability was considerably reduced and this remained altered at least through 9 years of age. These results prove that epigenetic changes need to be considered in evaluating risk of many diseases and document the effects of early environment on establishment of heritable changes that are likely permanent. Furthermore, study of metastable epialleles should lead to improved understanding of the role of interindividual epigenetic variation in human disease.

Waterland RA, Kellermayer R, Laritsky E, Rayco-Solon P, Harris RA, Travisano M, Zhang W, Torskaya MS, Zhang J, Shen L, Manary MJ, Prentice AM. Season of conception in rural gambia affects DNA methylation at putative human metastable epialleles. *PLoS Genet.* 2010 6:e1001252. [14 Citations.]

Improved knowledge of cellular development processes. Fetal mammals are capable of regeneration in a variety of tissues, whereas the typical default response to injury in adult mammals consists of inflammation and scar tissue formation. One component of regeneration is the recruitment of resident progenitor and stem cells to a site of injury. Adult mice were subjected to midsecond phalanx amputation of the third digit of the right hind foot and either treated with chemotactic extracellular cellular matrix (ECM) degradation products or left untreated. Mice treated with ECM degradation products showed an accumulation of heterogeneous cells that expressed markers of multipotency. Cells isolated from the site of amputation were capable of differentiation along neuroectodermal and mesodermal lineages, whereas cells isolated from control mice were capable of differentiation along only mesodermal lineages. The present findings demonstrate the recruitment of endogenous stem cells to a site of injury, and/or their generation/proliferation therein, in response to ECM degradation products. Knowledge of stimuli for replacement of damaged cells could eventually lead to prevention and/or treatment of many chronic conditions.

Agrawal V, Johnson SA, Reing J, Zhang L, Tottey S, Wang G, Hirschi KK, Braunhut S, Gudas LJ, Badylak SF. Epimorphic regeneration approach to tissue replacement in adult mammals. *Proc Natl Acad Sci U S A.* 2010;107:3351–5. [25 Citations.]

Epigenetic changes to DNA during normal development and carcinogenesis. Methylation of genes is prominent in differentiated cells compared to undifferentiated stem cells and there are analogous changes as cells are malignantly transformed. The latter also serve as a useful model of accelerated alterations that occur during normal development. Of particular note is that only about 100 of 30,000 promoter genes are methylated so these provide a useful focus for targeted research. ARS-supported scientists in Houston have produced a series of papers on these changes that have quickly become highly cited. Twenty-eight of their papers since 2007 have been cited 20 or more times with three papers cited between 124 and 207 times, documenting the importance of this work to the fields of normal and malignant development.

Kellermayer R, Balasa A, Zhang W, Lee S, Mirza S, Chakravarty A, Szigeti R, Laritsky E, Tatevian N, Smith CW, Shen L, Waterland RA. Epigenetic maturation in colonic mucosa continues beyond infancy in mice. *Hum Mol Genet.* 2010;19:2168–76. [5 Citations.]

Waterland RA, Kellermayer R, Rached MT, Tatevian N, Gomes MV, Zhang J, Zhang L, Chakravarty A, Zhu W, Laritsky E, Zhang W, Wang X, Shen L. Epigenomic profiling indicates a role for DNA methylation in early postnatal liver development. *Hum Mol Genet.* 2009;18:3026–38. [12 Citations.]

Kondo Y, Shen L, Cheng AS, Ahmed S, Boumber Y, Charo C, Yamochi T, Urano T, Furukawa K, Kwabi-Addo B, Gold DL, Sekido Y, Huang TH, Issa JP. Gene silencing in cancer by histone H3 lysine 27 trimethylation independent of promoter DNA methylation. *Nat Genet.* 2008;40:741–50. [196 Citations.]

Anticipated 2. More thorough knowledge of the critical periods of development during which targeted nutritional and physical activity interventions are most likely to have long-term health benefits.

Maternal obesity programs energy balance in offspring. Researchers in Little Rock, Arkansas found that male offspring of obese rats gain more weight and fat mass, along with developing insulin resistance, when fed high-fat diets. The scientists identified multiple genes and proteins in the liver and blood that change before development of obesity. Mitochondrial function is known to be associated with fatty acid oxidation in the liver. Several markers of hepatic mitochondrial function were reduced in offspring of obese dams. These included SIRT3 mRNA, mitochondrial protein content, electron transport chain complexes (II, III, and ATPase), and fasting PGC-1α mRNA expression suggesting that *in utero* exposure to maternal obesity programs multiple aspects of energy balance and offers potential ways to control weight gain if the same metabolic changes occur in humans.

Borengasser SJ, Lau F, Kang P, Blackburn ML, Ronis MJ, Badger TM, Shankar K. Maternal obesity during gestation impairs fatty acid oxidation and mitochondrial SIRT3 expression in rat offspring at weaning. *PLoS One.* 2011 6:e24068. [2 Citations.]

Folate and its relationship to carcinogenesis. Although adequate folate nutrition appears to have some anti-cancer properties, there is also concern that excess folate levels, particularly unmetabolized folate in the circulation, may increase the risk for colorectal cancer. This was

suggested by work from ARS-supported scientists at the HNRC on Aging in Boston and has been cited 167 times. Analysis of folate in normal, adenomas, and cancer tissue is being done for a large number of samples as follow-up to this observation but results from this are not yet available. In another study to examine differential needs for folate among the population, this group found the MTHFR 677TT genotype was associated with increased plasma homocysteine and decreased plasma folate. The MTHFR 677TT genotype was also associated with a≈34% lower DNA uracil content (P = 0.045), whereas the G allele of the GGH - 124T>G SNP was associated with a stepwise increase in DNA uracil content (P = 0.02). Because the accumulation of uracil in DNA induces chromosome breaks, the GGH -124 T>G SNP may modulate the risk of carcinogenesis. This paper has been cited 22 times. In related work on cell cultures from human colon, this group found changes consistent with DNA damage-induced activation of cell-cycle checkpoints and cellular adaptation to folate depletion. Folate-depletion-induced changes in the Wnt/APC pathway as well as in genes involved in cell adhesion, migration and invasion may underlie observed relationships between folate status and cancer risk. This paper has been cited 29 times.

Mason JB, Dickstein A, Jacques PF, Haggarty P, Selhub J, Dallal G, Rosenberg IH. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. *Cancer Epidemiol Biomarkers Prev.* 2007;16:1325–9. [176 Citations.]

DeVos L, Chanson A, Liu Z, Ciappio ED, Parnell LD, Mason JB, Tucker KL, Crott JW. Associations between single nucleotide polymorphisms in folate uptake and metabolizing genes with blood folate, homocysteine, and DNA uracil concentrations. *Am J Clin Nutr.* 2008;88:1149–58. [22 Citations.]

Crott JW, Liu Z, Keyes MK, Choi SW, Jang H, Moyer MP, Mason JB. Moderate folate depletion modulates the expression of selected genes involved in cell cycle, intracellular signaling and folate uptake in human colonic epithelial cell lines. *J Nutr Biochem.* 2008;19:328–35. [29 Citations.]

Anticipated Product 3. Improved ability to relate the results of studies in animal models of nutritional programming to the human situation.

Epigenetic regulation of the same gene in mice and humans. In order to extrapolate from animals studies to humans, it is important to show the same basic genetic, epigenetic, and metabolic changes occur in response to nutritional modulation. Scientists at the ARS HNRC in Little Rock found that maternal obesity induced by high-fat diet impaired skeletal development through down-regulation of the HoxA10 gene, which may lead to lower bone mass later in life. This gene has been shown to play a regulatory role in a variety of human cells, including osteoblasts.

Chen JR, Zhang J, Lazarenko OP, Kang P, Blackburn ML, Ronis MJ, Badger TM, Shankar K. Inhibition of fetal bone development through epigenetic down-regulation of HoxA10 in obese rats fed high-fat diet. *FASEB J.* 2012;26:1131-41.

Porcine Immunology and Nutrition Database developed. ARS scientists at Beltsville, Maryland started a database for porcine genes relevant to immunology. It is generally acknowledged that the pig is a better model for humans that are most rodents. These, and other, researchers have found that about 80 percent of the genes expressed in swine gastrointestinal immune tissue, which is about two-thirds of the total immune system, have identity with those from humans while in mice the percentage is just 20 percent In particular, appearance on other chromosomes and proximity to other genes and promoters makes it difficult to extrapolate from the mouse to human even though that has become the most commonly used animal model. The PIN database has almost 5,000 registered users and has become the *de facto* source for gene comparisons between swine and humans among immunologists and nutritionists using that model.

Porcine Immunology and Nutrition Database:
http://www.ars.usda.gov/services/docs.htm?docid=6065

CONCLUSIONS

Overall, NP 107 achieved much of what was outlined in the current Action Plan. It is recognized that the current Action Plan is dated 2009-2013 and this assessment report covers progress through the end of 2011; as a result, included here are a number of accomplishments that were initiated under the Action Plan for 2005-2009 since they apply to goals of the current plan. The quality of the research can be judged primarily by the high citation rate of research papers, only a small fraction of which are highlighted above. This is particularly true for assessing creation of new knowledge and advancing the science in the areas of interest. We have purposely excluded citations to review papers which average much higher rates than do original research papers. For example, a 2006 review article on estimation of optimal serum concentrations of 25-hydroxyvitamin d for multiple health outcomes by members of the bone lab at the HNRCA at Tufts is the fourth most cited article from the *Am J Clin Nutr* with 775 citations to date.

The needs of other Federal agencies have been priorities for NP 107 as described above. Prioritization occasionally led to some outcomes being deferred. The creation and release of the Food Portions Equivalents Database (FPED), a successor to the MyPyramid Equivalents Database (MPED) designed for the 2010 *Dietary Guidelines for Americans*, was delayed by inadequate funding – but inter-agency transfers from several departments will allow this new database to be released in the near future that will correspond with the particular years of release of NHANES data, allowing translation of food intake to recommended servings of whole grains, added sugars, solid fats, etc. as recommended by the *DGA*. MPED was originally created at the request of the USDA Center for Nutrition Policy and Promotion so they could provide data on the MyPramid Tracker website but has also been used by many epidemiologists at other Federal agencies and at universities. The food composition database is also being updated for nutrients of concern to regulatory agencies, with emphasis on *trans* fats and sodium as foods are reformulated to decrease those components.

While it should be clear that almost all the researchable issues expressed in the problem statements have been addressed by the combined output of NP 107, it should also be apparent that these are big questions which will require considerable additional work from a number of approaches. The nutrition monitoring capacity of the program is a unique, ongoing fully-Federal responsibility that no other entity would do if we had to scale back or drop them. Improvement of the nutritional value of the food supply is also an ongoing process that will likely be continuous both from the standpoint of breeding new varieties of plant and animal foods and from the perspective of the food processing industry. Defining how nutrients affect health is an enormous set of questions that will likely not be resolved in the long-term, particularly as more compounds are identified that have health effects. Since the majority of Americans are now overweight or obese, it should be apparent to even the casual observer that there are no simple answers and that research on nutrition, behavior, and weight is the only means by which solutions will be developed. The final component of NP 107 is to conduct research on life stage nutrition and metabolism. It should be noted that three of the six HNRC's (the three operated cooperatively with academic institutions) have Congressionally-mandated missions to conduct research on nutritional needs of children, pregnant women, or the aging population. The proportion of elderly in this country is growing faster than any other demographic group and that

group uses the highest proportion of health-care dollars so the potential for return on investment is this area is great.

An additional measure of impact not quantified in this report is the success of achieving extramural funding. At the three cooperating HNRC's, non-ARS scientists are expected to generate at least half their salaries and research support from grants, usually from the National Institutes of Health. In fact, about half the total operating budgets of the three centers is derived from grants. ARS does not maintain records of those grants since they are to the respective academic organizations. For ARS scientists, the norm for many years was to depend on project funding to complete all work. In the last two years, ARS administration has actively encouraged procurement of soft funds to supplement base funding. In the period 2007-2011, NP 107 scientists received 117 awards worth a cumulative total of $38.4 million. For 2010 (the last year for which we have these data), 43 percent of all proposals from NP 107 scientists were funded and of proposals to major competitive programs, 32 percent received funding which is about double the success rate at NIH.

List of Acronyms

AIM	Ancestry Informative Marker
AMPM	Automated Multiple Pass Method
ARS	Agricultural Research Service
CDC	Centers for Disease Control and Prevention
DASH	Dietary Approaches to Stop Hypertension
DGA	Dietary Guidelines for Americans
DHA	DocosaHexaenoic Acid
DHHS	U.S. Department of Health and Human Services
DOPRU	Delta Obesity Prevention Research Unit
DRI	Dietary Reference Intake
FCL	Food Composition Laboratory
FDA	Food and Drug Laboratory
FFQ	Food Frequency Questionnaire
FICRCD	Food Intakes Converted to Retail Commodities
FNDDS	Food and Nutrient Database for Dietary Studies
FSRG	Food Surveys Research Group
FY	Fiscal Year
HANDLS	Healthy Aging in Neighborhoods of Diversity Across the Life Span Study
HEI	Healthy Eating Index
HNRC(s)	Human Nutrition Research Center(s)
IOM	Institute of Medicine
LMD	Lower Mississippi Delta
NCHS	National Center for Health Statistics
NDB	National Nutrient Databank
NDL	Nutrient Data Laboratory
NFNAP	National Food and Nutrient Analysis Program
NHANES	National Health and Nutrition Examination Survey
NP	National Program
NPL	National Program Leader
RUTF	Ready-to-Use Therapeutic Food
SR	National Nutrient Database for Standard Reference
T1D	Type I Juvenile Diabetes Mellitus
USDA	United States Department of Agriculture
VAD	Vitamin A Deficiency
WWEIA	What We Eat In America

Appendix 1

National Program 107 – Human Nutrition

ACCOMPLISHMENT REPORT 2007 – 2011

Relationship of This National Program to the ARS Strategic Plan
Outputs of NP 107 research support the "Actionable Strategies" associated with the performance measures shown below from the ARS Strategic Plan for 2006–2011, Objective 5.2: *Promote Healthier Eating Habits and Lifestyles.*

Performance Measure 5.2.1: Monitor food consumption/intake patterns of Americans, including those of different ages, ethnicity, regions, and income levels, and measure nutrients and other beneficial components in the food supply. Provide the information in databases to enable ARS customers to evaluate the healthfulness of the American food supply and the nutrient content of the American diet. **Target:** Databases on food composition and nutrient intake will be used by ARS customers to conduct human nutrition research; to establish Federal dietary policy guidelines, food assistance and feeding programs, and food labeling; and to develop nutrition education tools to improve the health of the American people.

Performance Measure 5.2.2: Define the role of nutrients, foods, and dietary patterns in growth, maintenance of health, and prevention of obesity and other chronic diseases. Assess bioavailability and health benefits of food components. Conduct research that forms the basis for and evaluates nutrition standards and Federal dietary recommendations. **Target:** ARS research results will be used in authoritative reports on national human nutrition standards and dietary guidance as well as to establish Federal nutrition policy and regulations to safeguard the health of the American people.

Performance Measure 5.2.3: Publish research findings not encompassed under the other performance measures for this objective likely to significantly advance the knowledge of human nutrition, extensively influence other researchers in the same or related field, or yield important new directions for research. **Target:** Research studies will be published in peer reviewed literature that will strongly influence the field of human nutrition and/or demonstrate impact through high citation rates.

APPENDIX 2

National Program 107 – Human Nutrition

ACCOMPLISHMENT REPORT 2007 – 2011

Research Projects in National Program 107*

[By Action Plan Component]

COMPONENT 1: NUTRITION MONITORING AND THE FOOD SUPPLY

1235-52000-059-00D
MEASUREMENT SYSTEMS FOR DETERMINATION OF VITAMINS IN FOODS AND DIETARY SUPPLEMENTS – W. Wolf (P), W. Byrdwell, J. Harnly, P. Chen, and D. Luthria; Beltsville, Maryland.

1235-52000-060-00D
FINGERPRINTING AND PROFILING METHODS FOR CHARACTERIZATION OF FOODS AND DIETARY SUPPLEMENTS – J. Harnly (P), W. Byrdwell, P. Chen, and D. Luthria; Beltsville, Maryland.

1235-52000-061-00D
USDA NATIONAL NUTRIENT DATABANK FOR FOOD COMPOSITION – J. Holden, M. Exler, D. Haytowitz, L. Lemar, P. Pehrsson, and 2 vacancies; Beltsville, Maryland.

1235-52000-062-00D
DIETARY SUPPLEMENTS INGREDIENT DATABASE – J. Holden (P); Beltsville, Maryland.

1235-53000-016-00D
WHAT WE EAT IN AMERICA - DIETARY SURVEY: DATA COLLECTION, INTERPRETATION, DISSEMINATION, AND METHODOLOGY – A. Moshfegh (P), J. Anand, J. Ahuja, R. Lacomb, R. Sebastian, S. Bowman, D. Rhodes, J. Montville, L. Steinfeldt, and 2 vacancies; Beltsville, Maryland.

1907-42520-004-00D
KNOWLEDGE OF SOIL-PLANT-HUMAN FOOD SYSTEMS TO ENHANCE IRON AND ZINC BIOAVAILABILITY IN PLANT FOODS – R. P. Glahn (P), L. Kochian, and M. Pineros; Ithaca, New York.

1950-51000-071-01S
ENERGY REGULATION DURING THE ADULT LIFESPAN – *S. Roberts* and *E. Saltzman*; Boston, Massachusetts.

6401-51000-002-00D
Dietary Intake Patterns Associated with Excess Adiposity in U.S. Children – J. Thomsom and L. Tussing-Humphreys; Stoneville, MS.

6435-53000-002-00D
PHYTOESTROGENIC EFFECTS OF ELICITOR INDUCED ISOFLAVONOIDS IN LEGUMES – S. Boue (P); *New Orleans*, Louisiana.

*For the sake of consistency, projects are listed and organized in Appendix 1 according to the ARS project number used to track projects in the Agency's internal database. A (P) after a scientist's name indicates the project's principal investigator. Names in *italics* are non-ARS researchers

COMPONENT 2: SCIENTIFIC BASIS FOR DIETARY GUIDANCE FOR HEALTH PROMOTION AND DISEASE PREVENTION

1235-51000-052-00D
BIOAVAILABILITY AND HEALTH BENEFITS OF PHYTONUTRIENTS – J. Novotny Dura (P), S. Britz, and B. Clevidence; Beltsville, Maryland.

1235-51000-055-00D
DIET AND IMMUNE FUNCTION RELATED TO INFECTIOUS AND ALLERGIC DISEASE – H. Dawson (P), N. Schoene, A. Smith, J. Urban, and G. Solano-Aguilar; Beltsville, Maryland.

1235-51530-009-00D
MACRO- AND MICRONUTRIENT MODULATION OF BIOMARKERS OF CHRONIC DISEASE AND INDICATORS OF NUTRITIONAL ADEQUACY – D. Baer (P), B. Clevidence, J. Novotny Dura, S. Britz, and W. Rumpler; Beltsville, Maryland.

1235-51530-053-00D
MOLECULAR AND CELLULAR BASES OF HEALTH-PROMOTING FOOD COMPONENTS IN PREVENTION OF CHRONIC DISEASES – T. Ty Wang (P), H. Dawson, N. Schoene, J. Urban, and G. Solano-Aguilar; Beltsville, Maryland.

1235-51530-054-00D
DIETARY AND LIFESTYLE FACTORS AFFECTING FOOD INTAKE AND ENERGY METABOLISM IN LEAN AND OVERWEIGHT INDIVIDUALS – W. Rumpler (P) and 3 vacancies; Beltsville, Maryland.

1907-42520-004-00D
KNOWLEDGE OF SOIL-PLANT-HUMAN FOOD SYSTEMS TO ENHANCE IRON AND ZINC BIOAVAILABILITY IN PLANT FOODS – R. Glahn (P), L. Kochian, and M. Pineros; Ithaca, New York.

1950-51000-067-01S
NUTRITION, AGING, IMMUNE AND INFLAMMATORY RESPONSES IN HEALTH AND DISEASES – S. Meydani (P), J. Barnett, and D. Wu; Boston, Massachusetts.

1950-51000-067-02S
BIOACTIVE FOOD COMPONENTS AND MODULATION OF ATHEROSCLEROSIS AND ANGIOGENESIS – M. Meydani (P) and M. Zang; Boston, Massachusetts.

1950-51000-068-01S
NUTRITION, PHYSICAL ACTIVITY, AND SARCOPENIA IN THE ELDERLY – R. Fielding; Boston, Massachusetts.

1950-51000-069-01S
MUSCULOSKELETAL HEALTH IN THE ELDERLY – B. Dawson-Hughes (P) and S. Harris; Boston, Massachusetts.

1950-51000-069-02S
VITAMIN K: FOOD COMPOSITION, BIOAVAILABILITY AND ITS ROLE IN HUMAN HEALTH – S. Booth (P); Boston, Massachusetts.

1950-51000-070-12S
NUTRITIONAL DETERMINANTS OF BRAIN AGING AND COGNITIVE DECLINE – I. Rosenberg (P) and N. Crivello; Boston, Massachusetts.

1950-51000-072-01S
Lipoproteins and Nutrition – B. Asztalos, S. Lamon-Fava, and E. Shaefer (P); Boston, Massachusetts.

1950-51000-072-02S
DIET AND BIOMARKERS OF CARDIOVASCULAR HEALTH – A. Lichtenstein (P) and N. Matthan; Boston, Massachusetts.

1950-51000-073-01S
PHYTOCHEMICALS AND AGING: BIOAVAILABILITY, METABOLOMICS, AND BIOACTIVITY – J. Blumberg (P) and C.Y. Chen; Boston, Massachusetts.

1950-51000-073-02S
DIETARY CAROTENOIDS, RETINOIDS, AND BIOACTIVATES ON HEALTHY AGING – G. Tang (P) and K. Yeum; Boston, Massachusetts.

1950-51000-074-01S
ONE-CARBON NUTRIENTS IN THE PREVENTION OF CANCER – J. Mason (P) and J. Crott; Boston, Massachusetts.

1950-51000-074-02S
NUTRITIONAL DETERMINANTS OF NON-ALCOHOLIC STEATOHEPATITIS IN HEPATIC CARCINOGENESIS – X.D. Wang (P) and C. Liu; Boston, Massachusetts.

1950-51520-011-01S
THE ROLE OF B VITAMINS AND ONE CARBON METABOLISM IN AGING – J. Selhub (P); Boston, Massachusetts.

1950-51520-012-01S
NUTRITION, OBESITY, CARDIOVASCULAR HEALTH AND GENOMICS – C.Q. Lai, L. Parnell, and *J. Ordovas* (P); Boston, Massachusetts.

1950-51530-009-01S
EPIDEMIOLOGY APPLIED TO PROBLEMS OF AGING AND NUTRITION –P. Jacques (P), M. Morris, and N. McKeown; Boston, Massachusetts.

1950-51530-009-02S
DIETARY ASSESSMENT AND EPIDEMIOLOGY – K. Tucker (P); Boston, Massachusetts.

5306-51520-007-00D
MINERAL AND VITAMIN INTERVENTIONS FOR AT-RISK POPULATIONS – M. Van Loan (P), L. Allen, and L. Huang; Davis, California.

5306-51530-017-00D
DIET, INFLAMMATION AND PREVENTION OF CHRONIC DISEASE – D. Hwang (P) and D. Kelley; Davis, California.

5306-51530-018-00D
DIETARY MODULATION OF IMMUNE FUNCTION AND OXIDATIVE STRESS – C. Stephensen, S. Zunino, B. Burri, and W. Hawkes; Davis, California.

5450-51000-045-00D
DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM – H. Zeng (P), L. Yan, and G. Combs; Grand Forks, North Dakota.

5450-51000-046-00D
BONE METABOLISM IN OBESITY – J. Cao (P) and 2 vacancies; Grand Forks, North Dakota.

5450-51000-047-00D
BIOLOGY OF OBESITY PREVENTION – E. Uthus (P), Vacant, and G. Combs; Grand Forks, North Dakota.

5450-51000-048-00D
FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH – M. Picklo, G. Combs, and Vacant; Grand Forks, North Dakota.

6250-51000-051-10S
MINERAL ABSORPTION AND METABOLISM IN CHILDREN – M. Grusak, *S. Abrams (P), P. Etcheverry, and K. Gabbay*; Houston, Texas.

6250-51000-051-20S
MODIFYING PLANT TRANSPORT PROCESSES FOR ENHANCED NUTRITIONAL QUALITY OF PLANT FOODS – P. Nakata, M. Grusak (P)*, K. Hirschi, and S. Abrams*; Houston, Texas.

6250-51000-052-20S
CLINICAL INVESTIGATIONS ON NUTRITION AND CHILD DEVELOPMENT – *W. HEIRD (P), F. JAHOOR, M. MANARY, J. BELMONT, R. SHULMAN, AND G. YONGTAO*; Houston, Texas.

6250-51000-054-20S
FUNCTIONAL GENOMICS OF LACTATION: EFFECTS OF GENETICS, HORMONES AND SUBSTRATES – M. Haymond (P), D. Hadsell, and M. Rijnkels; Houston, Texas.

6251-51000-006-02S
EFFECTS OF DIET/NUTRITIONAL STATUS ON PSYCHOLOGICAL/PSYCHONEUROPHYSIOLOGICAL DEVELOPMENT AND OTHER BRAIN-RELATED FUNCTIONS OF CHILDREN – R.T. Pivik, P. Casey, T. Badger (P), M. Ronis, and 2 vacancies; Little Rock, Arkansas.

6251-51000-006-03S
DIETARY INFLUENCES ON PSYCHOLOGICAL AND PHYSIOLOGICAL FUNCTION IN CHILDREN – R.T. Pivik (P), J. Szabo, J. Snow, and 2 vacancies; Little Rock, Arkansas.

COMPONENT 3: PREVENTION OF OBESITY AND RELATED DISEASES

1235-51000-054-00D
ANTIOXIDANT POLYPHENOLS IN IMPAIRED BRAIN AND HEART FUNCTIONS ASSOCIATED WITH OBESITY AND METABOLIC DISEASES – R. Anderson (P), N. Schoene, and J. Park; Beltsville, Maryland.

1235-51530-053-00D
MOLECULAR AND CELLULAR BASES OF HEALTH-PROMOTING FOOD COMPONENTS IN PREVENTION OF CHRONIC DISEASES – T. Ty Wang (P), H. Dawson, N. Schoene, J. Urban, and G. Solano-Aguilar; Beltsville, Maryland.

1950-51000-071-02S
REGULATION OF ADIPOCYTE AND ADIPOSE TISSUE METABOLISM IN OBESITY RELATED INFLAMMATION AND METABOLIC DISORDERS – A. Greenberg (P) and M. Obin; Boston, Massachusetts.

1950-51000-072-02S
DIET AND BIOMARKERS OF CARDIOVASCULAR HEALTH – A. Lichtenstein (P) and N. Matthan; Boston, Massachusetts.

1950-51000-074-02S
NUTRITIONAL DETERMINANTS OF NON-ALCOHOLIC STEATOHEPATITIS IN HEPATIC CARCINOGENESIS – X.D. Wang (P) and C. Liu; Boston, Massachusetts.

1950-51520-012-01S
NUTRITION, OBESITY, CARDIOVASCULAR HEALTH AND GENOMICS – C.Q. Lai, L. Parnell, and *J. Ordovas* (P); Boston, Massachusetts.

1950-51530-009-01S
EPIDEMIOLOGY APPLIED TO PROBLEMS OF AGING AND NUTRITION – P. Jacques (P), M. Morris, and N. McKeown; Boston, Massachusetts.

5306-51530-019-00D
LINKING FOODS, BEHAVIOR AND METABOLISM TO PROMOTE A HEALTHY BODY WEIGHT – N. Keim (P), L. Huang, J. Newman, S. Adams, and K. Laugero; Davis, California.

5450-51000-045-00D
DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM – H. Zeng (P), L. Yan, and G. Combs; Grand Forks, North Dakota.

5450-51000-046-00D
BONE METABOLISM IN OBESITY – J. Cao (P) and 2 vacancies; Grand Forks, North Dakota.

5450-51000-048-00D
FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH – M. Picklo (P), G. Combs, and vacant; Grand Forks, North Dakota.

5450-51000-049-00D
DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE – L. Whigham (P), L. Jahns, S. Raatz, Vacant, and J. Roemmich; Grand Forks, North Dakota.

6250-51000-053-10S
PREVENTION OF CHILDHOOD OBESITY THROUGH LIFESTYLE CHANGES – T. Baranowski (P) and J. Baranowski, Houston, Texas.

6250-51000-053-20S
PREVENTION OF CHILDHOOD OBESITY THROUGH LIFESTYLE CHANGES – N. Butte (P) and T. O'Connor; Houston, Texas.

6250-51000-053-30S
WEB-BASED AND MULTI-MEDIA INTERVENTIONS TO PROMOTE HEALTHY EATING AND PHYSICAL ACTIVITY IN FAMILIES AND YOUTH – D. Thompson *(P) and K. Cullen*; Houston, Texas.

6250-51000-053-40S
DEVELOPMENT OF OBESITY-RELATED EATING BEHAVIORS IN CHILDHOOD – S. Hughes (P); Houston, Texas.

6250-51000-053-50S
UNDERSTANDING ENVIRONMENTAL FACTORS AND BEHAVIORAL CHANGES FOR CHILDHOOD OBESITY PREVENTION – T. Nicklas (P) Houston; Texas.

6250-51000-053-60S
Physical Activity Interventions to Prevent Childhood Obesity – A. Sunehag and J. Foreyt (P); Houston, Texas.

6250-51000-053-70S
Childhood Obesity Risk Factor Characterization – J. Mendoza (P); Houston, Texas.

6250-51000-055-10S
THE CIRCADIAN CLOCK IN NUTRITIONAL METABOLISM AND OBESITY – L. Fu (P); Houston, Texas.

6250-51000-055-30S
CHARACTERIZATION OF DIET-INDUCED CHANGES IN ADIPOSE TISSUE LEUKOCYTES – C.W. Smith (P); Houston, Texas.

6250-51000-055-40S
METABOLIC REGULATION IN OBESITY DEVELOPMENT – D. UPCHURCH (P); Houston, Texas.

6251-51000-006-02S
EFFECTS OF DIET/NUTRITIONAL STATUS ON PSYCHOLOGICAL/PSYCHONEUROPHYSIOLOGICAL DEVELOPMENT AND OTHER BRAIN-RELATED FUNCTIONS OF CHILDREN – R.T. Pivik (P), P. Casey, T. Badger, M. Ronis, and 2 vacancies; Little Rock, Arkansas.

6251-51000-007-03S
IDENTIFY DIETARY FACTORS HAVING BENEFICIAL OR ADVERSE HEALTH EFFECTS, AND DETERMINE THEIR IMPACT ON GROWTH, DEVELOPMENT AND HEALTH – R. Simmen (P), M. Ronis, N. Fang, S. Nagarajan, T. Badger, S. Korourian, and 3 vacancies; Little Rock, Arkansas.

6251-51000-007-04S
THE ROLE OF DIETARY FACTORS ON GROWTH, DEVELOPMENT AND HEALTH – *R. SIMMEN, M. RONIS, T. BADGER (P), P. CASEY, A. ANDRES, J.R. CHEN, K. SHANKAR, J. MARECKI, X. WU*, AND 3 VACANCIES; Little Rock, Arkansas.

6251-51000-008-00D
DELTA OBESITY PREVENTION RESEARCH PROGRAM – M. Grusak (P) and 3 vacancies; Little Rock, Arkansas.

6251-51000-008-49S
DELTA OBESITY PREVENTION RESEARCH UNIT - BAYLOR COLLEGE OF MEDICINE (ARS HEALTH PROJECT) – M. Bogle (P) and *T. Nicklas*; Little Rock, Arkansas.

6251-51000-008-50S
DELTA OBESITY PREVENTION RESEARCH UNIT - TUFTS UNIVERSITY (ARS HEALTH PROJECT) – M. Bogle (P) and *K. Tucker*; Little Rock, Arkansas.

6251-51000-008-51S
DELTA OBESITY PREVENTION RESEARCH UNIT - ARKANSAS CHILDREN'S HOSPITAL RESEARCH INSTITUTE – M. Bogle (P), *B. Brady, J. Weber, J. Robbins, N. Hays, P. Moore, W. Ward, and J. Whiteside*; Little Rock, Arkansas.

6251-51000-008-52S
DELTA OBESITY PREVENTION RESEARCH UNIT - ALCORN STATE UNIVERSITY – M. Bogle (P), *W. Newell, M. Rowser, D. Idleburg, and A. Morris;* Little Rock, Arkansas.

6251-51000-008-53S
DELTA OBESITY PREVENTION RESEARCH UNIT - PENNINGTON BIOMEDICAL RESEARCH UNIT – M. Bogle (P)*, P. Katzmarzyk, B. Kennedy, and C. Champagne*; Little Rock, Arkansas.

6251-51000-008-54S
DELTA OBESITY PREVENTION RESEARCH UNIT - SOUTHERN UNIVERSITY AND A&M COLLEGE – M. Bogle (P)*, B. McGee, G. Johnson, L. Fuller, S. Hutchinson, R. Kelly, D. Collins, A. Thornton, C. Duncan, and D. Butler;* Little Rock, Arkansas.

6251-51000-008-55S
DELTA OBESITY PREVENTION RESEARCH UNIT - UNIVERSITY OF ARKANSAS, PINE BLUFF – M. Bogle (P), *J. Garner, Y. Gao, and F. Taylor*; Little Rock, Arkansas.

6251-51000-008-56S
DELTA OBESITY PREVENTION RESEARCH UNIT - UNIVERSITY OF SOUTHERN MISSISSIPPI – M. Bogle (P), *V. Kamali, C. Connell, and K. Yadrick;* Little Rock, Arkansas.

6251-51000-008-58S
DELTA OBESITY PREVENTION RESEARCH UNIT SUMMER RESEARCH FOOD ANALYSIS – M. Bogle (P) *and C. Champange;* Little Rock, Arkansas.

6251-51000-008-61S
DELTA OBESITY PREVENTION RESEARCH - DELTA HEALTH ALLIANCE – M. Bogle (P), J. Thomson, L. Tussing-Humphreys, and *K. Fox;* Little Rock, Arkansas.

6401-51000-001-00D
OBESITY PREVENTION IN THE MISSISSIPPI DELTA REGION OF MISSISSIPPI – L. Tussing-Humphreys (P) and J. Thomson; Stoneville, Mississippi.

COMPONENT 4: LIFE STAGE NUTRITION AND METABOLISM

1950-51000-067-01S
NUTRITION, AGING, IMMUNE AND INFLAMMATORY RESPONSES IN HEALTH AND DISEASES – S. Meydani (P), J. Barnett, and D. Wu; Boston, Massachusetts.

1950-51000-070-10S
NUTRITIONAL MODULATION OF GAIT AND COGNITION IN AGING – B. Shukitt Hale (P) and *R. Kanarak;* Boston, Massachusetts.

1950-51000-070-12S
NUTRITIONAL DETERMINANTS OF BRAIN AGING AND COGNITIVE DECLINE – I. Rosenberg (P) and N. Crivello; Boston, Massachusetts.

1950-51000-071-03S
METHODOLOGY DEVELOPMENT: ENERGY INTAKE AND BODY COMPOSITION ASSESSMENT IN THE ELDERLY – J. Kehayias (P); Boston, Massachusetts.

1950-51000-074-01S
ONE-CARBON NUTRIENTS IN THE PREVENTION OF CANCER – J. Mason (P) and J. Crott; Boston, Massachusetts.

1950-51000-075-02S
USING NUTRITION AND PROTEOLYSIS TO DELAY AGE RELATED MACULAR DEGENERATION AND CATARACTS – *A. Taylor (P) and F. Shang;* Boston, Massachusetts.

1950-51530-009-02S
DIETARY ASSESSMENT AND EPIDEMIOLOGY – K. Tucker (P); Boston, Massachusetts.

5306-51520-007-00D
MINERAL AND VITAMIN INTERVENTIONS FOR AT-RISK POPULATIONS – M. Van Loan (P), L. Allen, and L. Huang; Davis, California.

6250-51000-052-20S
CLINICAL INVESTIGATIONS ON NUTRITION AND CHILD DEVELOPMENT – *W. HEIRD (P), F. JAHOOR, M. MANARY, J. BELMONT, R. SHULMAN, AND G. YONGTAO*; Houston, Texas.

6250-51000-054-10S
ORGAN-SPECIFIC METABOLISM AND GROWTH UNDER VARYING NUTRITIONAL CONDITIONS DURING DEVELOPMENT – M. FIOROTTO (P) AND J. MARINI; Houston, Texas.

6250-51000-054-20S
FUNCTIONAL GENOMICS OF LACTATION: EFFECTS OF GENETICS, HORMONES AND SUBSTRATES – M. Haymond (P), D. Hadsell, and M. Rijnkels; Houston, Texas.

6250-51000-054-30S
NUTRIENT REGULATION OF BLOOD AND BLOOD VESSEL FORMATION – K. HIRSCHI (P) AND M.H. CHEN; Houston, Texas.

6250-51000-055-20S
NUTRITION AND INTESTINAL DEVELOPMENT AS REGULATORS OF HEALTH PROTEIN ANABOLISM AND DISEASE PREVENTIONS – D. BURRIN (P) *AND T. DAVIS*; Houston, Texas.

6250-51000-055-50S
NUTRITION AND EPIGENETIC PROGRAMMING OF OBESITY DURING DEVELOPMENT – R. Waterland (P), V. Van Den Veyver, and L. Shen, Houston, Texas.

6251-51000-006-02S
EFFECTS OF DIET/NUTRITIONAL STATUS ON PSYCHOLOGICAL/PSYCHONEUROPHYSIOLOGICAL DEVELOPMENT AND OTHER BRAIN-RELATED FUNCTIONS OF CHILDREN – R.T. Pivik (P), P. Casey, T. Badger, M. Ronis, and 2 vacancies; Little Rock, Arkansas.

6251-51000-006-03S
DIETARY INFLUENCES ON PSYCHOLOGICAL AND PHYSIOLOGICAL FUNCTION IN CHILDREN – R.T. Pivik (P), J. Szabo, J. Snow, and 2 vacancies; Little Rock, Arkansas.

6251-51000-007-03S
IDENTIFY DIETARY FACTORS HAVING BENEFICIAL OR ADVERSE HEALTH EFFECTS, AND DETERMINE THEIR IMPACT ON GROWTH, DEVELOPMENT AND HEALTH – R. Simmen (P), M. Ronis, N. Fang, S. Nagarajan, T. Badger, S. Korourian, and 3 vacancies; Little Rock, Arkansas.

6251-51000-007-04S
THE ROLE OF DIETARY FACTORS ON GROWTH, DEVELOPMENT AND HEALTH – R. *SIMMEN, M. RONIS, T. BADGER (P), P. CASEY, A. ANDRES, J.R. CHEN, K. SHANKAR, J. MARECKI, X. WU, AND 3 VACANCIES*; Little Rock, Arkansas.

APPENDIX 3 – SELECTED SUPPORTING INFORMATION ON IMPACT OF NP107 SCIENTISTS

Major Awards from National and International Organizations:

Sara Booth, HNRCA – American Society of Nutrition ELR Stokstad Award 2007

Sang Woon Choi, HNRCA – The Mead Johnson Award from the American Society for Nutrition 2008

Jimmy Crott, HNRCA – American Society for Nutrition Bio-Serv Award in Experimental Animal Nutrition 2009

Joel Mason, HNRCA – Mary Swartz Rose Senior Investigator Award, American Society for Nutrition 2010

Diane McKay, HNRCA – "Göttinger Innovations-Preis für praktische Hypertensiologie" (Goettingen Innovation Award for Practicable Hypertension Research), Blutdruckinstitut Goettingen, Germany 2011

Simin Meydani, HNRCA – Robert H. Herman Award in Clinical Nutrition, American Society of Nutrition, 2008

Susan Roberts, HNRCA – E.V. McCollum Award, American Society for Nutrition 2009

Jose Ordovas, HNRCA –Recipient of the Pan-American Nutrition and Food Research Award, 2011; Recipient of the Gregorio Maranhon Nutrition Award, 2011; Recipient of the Jose Mataix Nutrition Award, 2011; Recipient of the Gregorio Varela Award for excellence in Nutrition Research, 2010; Recipient of the 2007 Centrum Award from the American Society of Nutrition "for recent investigative contributions of contemporary significance to the understanding of human nutrition"; Winner of the Grand Prix de la Science de l'Alimentation de L'Académie Internationale de la Gastronomia for 2011, given to an Institution or individual contributing exceptionally to the progress of Food and Nutrition Research at the international level.

Lindsay Allen, WRRC – Conrad Elvehjem Award for Public Service in Nutrition, American Society for Nutrition 2009

Darshan Kelley, WRRC – Robert H. Herman Award for Clinical Nutrition, American Society for Nutrition 2010

Dennis Bier, CNRC – Nutrition Award, The American Academy of Pediatrics 2007

Robert Waterland, CNRC – Nick Hales Award, International Society for Developmental Origins of Health and Disease 2009

Elected Officers of National/International Organizations:

Angelo Azzi, HNRCA – President International Union of Biochemistry and Molecular Biology 2006-Present; Past President Society for Free Radical Research International 2010

Andrew Greenberg, HNRCA –Elected to Council of The Obesity Society 2007-Present

Jose Ordovas, HNRCA – President of the Board of Trustees of the Instituto Madrileno de Estudios Avanzados en Alimentacion (IMDEA). (2007-Present); President of the Scientific Advisory Board and Board of Trustees of IMDEA (SPAIN) (2007-Present) President Scientific Committee Centro de Investigación de Tecnología Agroalimentaria del Gobierno de Aragón (SPAIN) (2007-Present)

Ernst Shaefer, HNRCA – President, Kinetics and Metabolism Society, affiliated with the Council on Arteriosclerosis, Thrombosis, and Vascular Biology, American heart Association
Lindsay Allen, WRRC – Vice-President, International Union of Nutritional Sciences, 2005-Present
James Harnly, BHNRC – Board of Directors, AOAC International 2008-Present

Service on Major Committees:

Elizabeth Johnson, HNRCA –International Carotenoid Society (*treasurer*) 2011-2014; CARIG (*treasurer*) 2009-2012; International Carotenoid Society (*steering committee member*) 2008-2012
Alice Lichtenstein, HNRCA – Vice-chair, Examination of Front-of-Package Nutrition Rating Systems and Symbols, Institute of Medicine, National Academy of Sciences 2010-2011; Co-chair, NHLBI, Adult Treatment Panel [ATP] IV (Cholesterol Guidelines) 2008-Present
Lindsay Allen, WRRC – National Associate, National Research Council/National Academy of Sciences 2011-Present; Chair, WHO Technical Consultation on Iron and Vitamin Status Indicators 2011; Chair, WHO Technical Consultation on Nutrient Profiling 2010-Present; Institute of Medicine, Front-of-Pack Labeling Committee 2009-2011; Chair, WHO Technical Consultation on Moderate Malnutrition 2008
Steven Abrams, CNRC – Institute of Medicine's (Food and Nutrition Board) "Panel on Calcium and Vitamin D" Appointment: March 2009-Nov. 2010; American Academy of Pediatrics, Committee on Nutrition. July 2009-present
Karen Cullen, CNRC – Member: Institute of Medicine Committee on Nutrition Standards for the Child and Adult Food Care Program Meal Requirements 2009-2010; Member: Institute of Medicine Committee on Nutrition Standards for the National School Lunch and Breakfast programs 2008-2009
Thomas Badger, ACNC – American Society for Nutrition, Public Policy Committee 2005-Present;Scientific Advisory Board, Soy Nutrition Institute 2005-Present; FASEB Science Policy Committee; FASEB Board of Directors 2008-Present

Editorial Boards:

David Baer, BHNRC – Nutrition Research 2004-Present
Craig Byrdwell, BHNRC –*Lipids*
James Harnly, BHNRC – AOAC International 2007-Present
David Haytowitz, BHNRC – Journal of Food Composition and Analysis 2010-2013
Joseph Urban, BHNRC – Parasite Immunology 1996-2008
Sara Booth, HNRCA – Advances in Nutrition, Associate Editor 2010-Present
Bess Dawson Hughes, HNRCA – Bone; Osteoporosis International
Andrew Greenberg, HNRCA – Endocrinology 2008-Present; Obesity 2008-Present
Alice Lichtenstein, HNRCA – Associate Editor Journal of Lipid Research 2003-Present
Nicola McKeown, HNRCA – British Journal of Nutrition, 2009 – 2011; Nutrition Today 2009 - Present
Mohsen Meydani, HNRCA –Journal of Nutrition and Metabolism 2009-Present; *Biogerontology* 2005-2010*; Current Nutrition & Food Science* 2005-Present

Laurence Parnell, HNRCA –Frontiers in Nutrigenomics, since 2011; Case Reports in Genetics, since 2011

Guangwen Tang, HNRCA – Journal of Pharmacy and Nutrition Sciences (JPANS), an Official Journal of the Educational Forum, University of Karachi-Pakistan; WORLD JOURNAL OF METHODOLOGY, 2011-2015.

Kyung-Jin Yeum, HNRCA - Nutrition Research and Practice 2007-Present; Journal of Nutritional Disorders & Therapy 2011

Jean-Marc Zingg, HNRCA – Guest Editor of the journal "Molecular Aspects of Medicine" 2007; "Biofactors" 2008

Jay Cao, GFHNRC – J Nutrition & Diet Therapy 2011; J Cytology & Histology 2010

Gerald Combs, GFHNRC –Biological Trace Element Research, 1983-Present

Sean Adams, WRRC – Journal of Nutrition, 2007-2013; Advances in Nutrition, 2010-2013; Nutrients, 2009-2011

Lindsay Allen, WRRC – Editor, Encyclopedia of Human Nutrition 2003-2005 and 2008-Present

Darshan Kelley, WRRC – Nutrition Research, 1993-Present; Lipids, Associate Editor 2001-September 2011; Journal of Nutrition, 2007-Present; British Journal of Nutrition, 2008-Present.

Steven Abrams, CNRC – Contributing Editor, Nutrition Reviews, 2003-Present; Co-Editor, Neonatology section, Up-To-Date (Pediatrics): 2005-Present; Associate editor, American Journal of Clinical Nutrition – 2007-2012 (5 yr term)

Dennis Bier, CNRC – Editor-in-Chief, American Journal of Clinical Nutrition 2007-Present

Xinfu Guan, CNRC –Frontiers in Bioscience and Co-Editor of Encyclopedia of Bioscience 2007-2010; Journal of Endocrinology & Metabolic Syndrome 2011-Present

Morey Hammond, CNRC – Journal of Clinical Endocrinology & Metabolism 2005–2009

Paul Nakata, CNRC – Plant Science 2007-Present

Clifton Smith, CNRC – Journal of Leukocyte Biology 1995-Present

Martin Ronis, ACNC –Editorial Board – Experimental Biology and Medicine 2002–2008; Editorial Board – World Journal of Hepatology 2009-2013

*Center Abbreviations:
BHNRC: Beltsville Human Nutrition Research Center
HNRCA: Human Nutrition Research Center on Aging at Tufts University
GFHNRC: Grand Forks Human Nutrition Research Center
ACNC: Arkansas Children's Nutrition Center
CNRC: Children's Nutrition Research Center at Baylor College of Medicine
WHNRC: Western Human Nutrition Research Center

Appendix 4 - NP 107
PEER-REVIEWED RESEARCH PUBLICATIONS
BY
LOCATION AND YEAR

	2007	2008	2009	2010	2011	TOTAL
Beltsville HNRC	79	80	68	54	38	**319**
HNRC on Aging at Tufts	217	195	215	205	200	**1,032**
Plant, Soil, and Nutrition Lab	11	13	18	4	7	**53**
Grand Forks HNRC	39	35	36	22	39	**171**
Delta Obesity Prevention Research Unit	5	4	4	4	5	**22**
Children's Nutrition Research Center at Baylor	147	127	150	162	129	**715**
Arkansas Children's Nutrition Center	28	34	28	43	26	**159**
Western HNRC	35	44	50	30	34	**193**
New Orleans and Baton Rouge, LA	1	4	14	12	9	**40**
GRAND TOTAL	**562**	**536**	**583**	**538**	**488**	**2,704**