

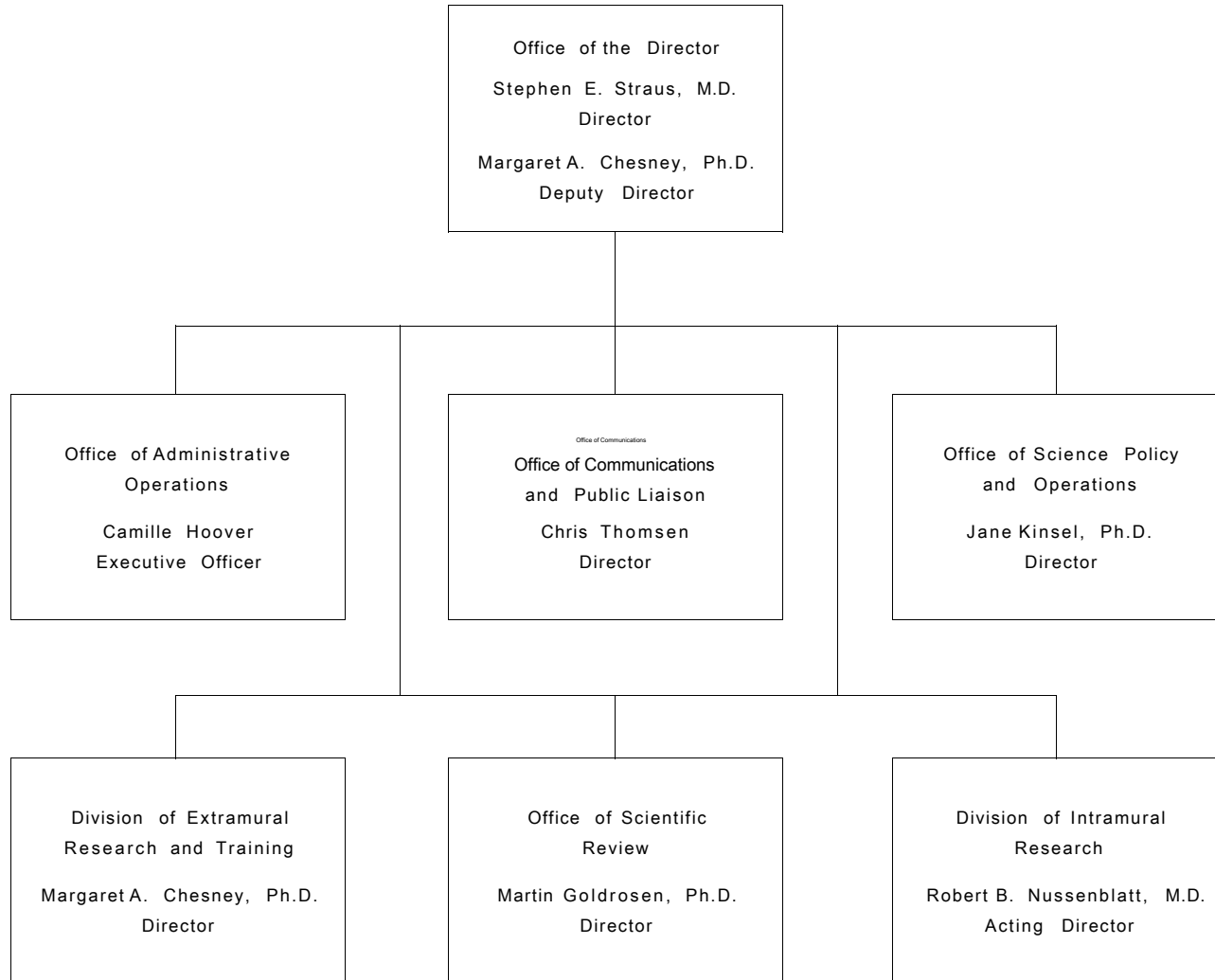
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

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NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine



NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

For carrying out section 301 and title IV of the Public Health Service Act with respect to complementary and alternative medicine, [\$123,116,000] ***\$122,692,000.***

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005].

**National Institutes of Health
National Center for Complementary and Alternative Medicine**

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	117,752,000	123,116,000	122,692,000
Enacted Rescissions	-774,000	-1,011,000	0
Subtotal, Adjusted Appropriation	116,978,000	122,105,000	122,692,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	-385,000	0	0
Comparative transfer to NIBIB for Radiology Program	0	0	0
Comparative transfer to Buildings and Facilities	-35,000	0	0
Comparative transfer to/from other NIH ICs for NIH Roadmap	385,000	0	0
Subtotal, adjusted budget authority	116,943,000	122,105,000	122,692,000
Unobligated Balance, start of year	0	0	0
Revenue from Breast Cancer Stamp 2/	0		
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	116,943,000	122,105,000	122,692,000
Unobligated balance lapsing	-2,000	0	0
Total obligations	116,941,000	122,105,000	122,692,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:

FY 2004 - \$485,000 FY 2005 - \$5,000,000 FY 2006 - \$5,000,000

Excludes \$0 in FY 2005 and \$0 in FY 2006 for royalties.

Justification

National Center for Complementary and Alternative Medicine

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.
 Reauthorizing legislation will be submitted.

Budget Authority:

FY 2004		FY 2005		FY 2006		Increase or	
Actual		Appropriation		Estimate		Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
69	\$ 116,943,000	78	\$122,105,000	79	\$122,692,000	1	\$587,000

This document provides justification for the Fiscal Year 2006 activities of the National Center for Complementary and Alternative Medicine (NCCAM), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2006 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

Increasing CAM Knowledge, Seeking New Horizons: NCCAM in 2004

Introduction

In celebrating its first 5 years as an NIH Center, the National Center for Complementary and Alternative Medicine (NCCAM) reflects on its contributions to the science of complementary and alternative medicine (CAM). To date, the Center has funded more than 1,200 projects at approximately 260 institutions to better comprehend diverse CAM practices and to determine which approaches may prove beneficial. The NCCAM 2005-2009 Strategic Plan¹ outlines a compelling agenda for the next 5 years in exploring CAM healing practices, training CAM researchers, and disseminating authoritative information to the public and professional communities.

The Plan prioritizes among the many opportunities for research investment informed by survey data on CAM use collected in 2002 from more than 31,000 Americans. Funded by NCCAM and included in the CDC's National Health Interview Survey (NHIS), the survey affords the most comprehensive overview to date of Americans' attitudes toward and uses of CAM.² The data results are revealing, showing that 75 percent of respondents turned to CAM at some point in

¹ To read the Plan, visit the NCCAM Web site at <http://nccam.nih.gov/about/plans/2005/index.htm>.

² Barnes P, Powell-Griner E, McFann K, Nahin R. *CDC Advance Data Report #343*. Complementary and Alternative Medicine Use Among Adults: United States, 2002. May 27, 2004.

their lifetime and that 62 percent used C A M in the year before being surveyed. The top two reasons stated for using C A M were back pain and head and chest colds. Prayer was cited as the most frequently used C A M practices, followed by use of natural products, particularly echinacea. Because earlier national surveys had not consistently included prayer and mega-vitamin therapy as C A M practices, NCCAM analyzed the 2002 NHIS data by including *and* excluding both practices.

Other data analyses are also under way, with NCCAM awarding four grants in FY 2004 to examine NHIS data on CAM use in minority populations. These and subsequent analyses will do more than merely improve understanding of who is using which C A M therapies, when, and why. Rather, they will continue to inform NCCAM's research goals, benefiting its initiatives and the partnerships NCCAM seeks. So useful could such data be that the Center is supporting a C A M supplement to the CDC's 2007 NHIS; the 5 years between the NHIS C A M surveys will help illuminate trends in CAM use. Below are key themes in NCCAM's research portfolio, informed by an increased understanding of Americans' CAM use and their beliefs about CAM therapies. In addition to the textboxed story of discovery on acupuncture and the science advance on echinacea, additional science advances are boldfaced for ease of identification.

Mind-Body Medicine: Exploring the Connection

Recognizing the role of social and behavioral factors in illness and health, NCCAM is supporting studies to gauge the effectiveness of behavioral interventions for a range of diseases. To help people with early stage HIV, NCCAM-funded researchers are planning a clinical trial of a meditation-based approach to reduce stress and manage emotions. Results will determine whether and how this approach can slow the progression of HIV. Other investigators are testing a yoga treatment for people with general anxiety disorder, while still others are evaluating the behavioral and physical effects of aromatherapy on those experiencing stress. Another award enables scientists to expand research on how stress and gender-based differences alter mind-body interactions in health and disease.

The mind-body portfolio also includes studies on the placebo response, especially in treating Parkinson's disease (PD) and major depressive disorder (MDD). Because PD has well-delineated clinical signs, it is well suited for analysis of clinical improvements that may arise from a patient's expectation of recovery—a positive placebo response. The outcome should enhance the design of future PD clinical trials and help scientists and practitioners harness the power of positive expectations to facilitate healing. MDD project researchers hope to clarify how interpersonal factors and patient characteristics contribute to the improvement often seen in MDD patients given a placebo as treatment.

NCCAM-funded researchers also are testing the effects of tai chi mind-body therapy and Iyengar yoga—which concentrates on correcting structural imbalances in the physical body, with close attention to the placement of the feet, hands, and pelvis and alignment of the spine, arms, and legs—in chronic heart failure and hypertension. Scientists hope to define the role of tai chi in managing heart failure in order to better understand this treatment's mechanism of action and provide a preliminary analysis of its costs and benefits. The Iyengar yoga investigation is

studying the safety and efficacy of a structured exercise program in people with high-normal blood pressure to stage I hypertension.

C A M and the Brain

NCCAM also is exploring the use of CAM in addressing disorders and diseases of the brain. For example, in parallel with conventional scientists working to identify ways to prevent and treat neurodegenerative diseases, CAM researchers are studying the potential neuroprotective properties of botanicals and dietary supplements. **NCCAM grantees demonstrated in 2004 that extracts of schisandra fruit (*Schisandra chinensis*) and the tabu-no-ki tree (*Machilus thunbergii*) protected cultured neural cells from oxidative damage and might eventually yield new choices in treating neurodegenerative disorders caused by oxidative stress.** Highlighted below is research on CAM therapies that may address brain-related health challenges ranging from stroke to insomnia.

Cerebral Ischemia. Cerebral ischemia—the interruption of sufficient blood flow to the brain—can increase the risk of stroke. Although estrogen appears effective in reducing cerebral ischemic damage in stroke victims, the hormone's potential neuroprotective effects have been overshadowed by reports of health risks associated with hormone therapy (HT). To identify HT alternatives, NCCAM funds research on the potential protective effects of soy-based phytoestrogens in the brain and on the neuroprotective effects of combined herbal therapy in limiting brain injury after a severe stroke.

Alzheimer's Disease (AD). Scientists estimate that 4 million Americans have AD,³ numbers that may increase markedly as baby boomers age. NCCAM supports research on ways to prevent or slow the progression of AD through studies on the potential protective effects of botanical agents such as *Ginkgo biloba* extract and aged garlic extract (AGE). Projects range from advancing understanding of the underlying cellular mechanisms of *Ginkgo biloba* to validating AGE as a potentially safe, well-tolerated, cost-effective herbal therapy for AD. NCCAM also supports the largest randomized Phase III clinical trial to date of *Ginkgo biloba* to prevent dementia in the elderly. Regardless of its outcome, this trial has set the standard for such studies and will afford new insights into the natural history and prognostic factors underlying dementia. Other research targets mind-body therapies for AD patients' caregivers, who suffer significant stress, depression, and elevated mortality.

Multiple Sclerosis (MS). In addition to being diminished neurologically, about half of all MS patients struggle with depression.⁴ Two recently published, double-blind, placebo-controlled pilot studies reported that supplementation with ethyl eicosapentanoic acid (EPA), an omega-3 fatty acid that is a key ingredient of fish oil, significantly reduced depression. Given the high prevalence of depression in MS patients and fish oil's low side effects, NCCAM is funding a 6-month study of the safety and effectiveness of fish oil supplements for mild-to-moderate depression in those with MS. This study also will evaluate the impact of fish oil on

³ Alzheimer's Disease Education and Referral Center, Service of the National Institute on Aging, National Institutes of Health. Accessed at <http://www.alzheimers.org/generalinfo.htm#howmany> on December 15, 2004.

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Sanford, M E, Petajan, JH. *Multiple Sclerosis and Your Emotions*. New York: National Multiple Sclerosis Society. 2003. Accessed at <http://www.nationalmssociety.org/Brochures-MSandEmotions1.asp> on December 16, 2004.

inflammatory mediators associated with both depression and M S , with possible implications for the relationship between depression and other inflammatory diseases.

Pain. Chronic pain sufferers often seek relief through C A M therapies, such as chiropractic, massage, acupuncture, and herbal and botanical remedies. As a contributor to the N I H Pain Consortium, NCCAM supports research on pain's core causes and possible solutions. In F Y 2004, N C C A M ' s investment in pain research yielded two key findings on neuropathic pain and pain reduction. Often seeming to have no cause, neuropathic pain responds poorly to standard pain treatment, may worsen over time, and can lead to serious disability. Phantom limb syndrome, the most dramatic example of neuropathic pain, occurs when an arm or leg has been removed, but the brain still receives pain messages from the nerves that once carried impulses from the missing limb. **In 2004, NCCAM grantees demonstrated that millimeter wavelength electromagnetic waves could reduce the symptoms of' neuropathic pain.**

Also this past year, NCCAM researchers demonstrated that some foods possess pain-relieving properties. **In one study, extracts of tart cherry (*Prunus cerasus*) were shown to suppress inflammation-induced pain behavior in rats.** Pain reduction may have been related to the anti-inflammatory and antioxidant properties of a class of pigmented compounds known as anthocyanins. In a study of pain induced by bone cancer, soy-fed mice were shown to experience less pain than those in a control group. A better understanding of how dietary constituents and phytonutrients moderate pain may yield further treatments to help patients with chronic pain. N C C A M ' s grantees also examined the use of taurine, a ubiquitous dietary amino acid, for the neuropathic pain common in diabetics. Pilot studies are examining the optimal amount of chiropractic care for treatment of chronic headaches and the value of a relaxation intervention to aid in pain management during minimally invasive surgery.

Pinpointing Acupuncture's Impact. Despite the longevity of acupuncture as a therapeutic practice, scientific research into its basic mechanisms is relatively recent, and little is known about how it elicits responses from the brain and body. NCCAM is supporting research that integrates whole brain functional magnetic resonance imaging (fMRI) with psychophysiological monitoring to analyze acupuncture's effect on brain activity. Other N C C A M - f u n d e d studies are examining acupuncture as a therapeutic intervention. For instance, researchers are using acupuncture to determine whether a complementary therapeutic approach, Jin Shin Tara (acupressure-like touch), can diminish stroke-associated functional disabilities, such as aphasia, a language disorder, during the stable period after an individual has suffered a stroke. NCCAM also is supporting technical advancements in the field of acupuncture to promote greater understanding of how acupuncture affects the brain and body. Thus, a recent Small Business Innovation Research (SBIR) grant will encourage development and commercialization of a small, hand-held sensor system to objectively measure acupuncture needle torque in a clinical setting. Such a device will have immediate applications in acupuncture research by providing a means to record and control the needling stimulus and correlating needling response with treatment outcome.

Story of Discovery: Ancient Acupuncture Provides Modern Pain Relief for Arthritis

His remains lay frozen for some 5,000 years until being discovered in 1991 in the Tyrolean Alps along the Italian/Austrian border. Nicknamed Oetzi by his discoverers, this well-preserved Neolithic hunter provides a link to Europe's prehistory. Analysis of Oetzi's remains has taught us much about how he lived and died, as even his clothes, tools, and weapons were remarkably intact. X-rays of Oetzi's body indicate that this middle-aged man had suffered arthritis of the hip joints, knees, ankles, and spine. Nearly 60 tattoos traversed his body; initially considered ornamental, they revealed a striking coincidence to key acupuncture points, including those now used in treating arthritis. *Did Oetzi receive an early form of acupuncture?* While the significance of these markings is still to be learned, their presence offers a tantalizing link to one of humanity's oldest medical practices.

Acupuncture—the practice of inserting thin needles into specific body points to improve health and well-being—was articulated by Chinese practitioners more than 2,000 years ago, eventually spreading throughout the world. Only in recent years, however, has careful scientific inquiry begun to shed light on acupuncture's possible mechanisms and potential benefits, especially in treating the pain of conditions such as arthritis. N C C A M has been building a portfolio of basic and clinical research that is now revealing the power and promise of applying stringent research methods to ancient practices like acupuncture. For example, NCCAM-funded investigators recently reported findings from the longest, largest randomized, controlled Phase III clinical trial of acupuncture ever conducted. Their results demonstrate that acupuncture, when used for treating osteoarthritis of the knee, reduces pain and improves function better than either of a pair of control interventions. Osteoarthritis, the most common form of arthritis, is a major cause of pain, limitation of activity, and health care utilization, especially in the elderly.

The trial culminated studies by an interdisciplinary team that included rheumatologists, licensed acupuncturists, and biostatisticians, collaborating to ensure that the research methodology was conducted as acupuncture has been traditionally practiced. Initially, the team developed and tested its approach through pilot Phase I studies and a small randomized, single-blind Phase II study. These studies were groundbreaking in their use of a "sham" acupuncture control (a placebo) to demonstrate that patients did not just get better because they were receiving care (a placebo response), but because the experimental therapy actually provided relief. Knowledge gained from the pilot studies guided the study team in designing new features for the multicenter Phase III trial involving 570 arthritis patients assigned randomly to receive one of three treatments: acupuncture, sham treatment, or participation in an educational control group that followed a self-help course based on the Arthritis Foundation model. Patients were assessed for 26 weeks to allow enough time for them to realize the benefits and durability of whichever treatment they received.

For the first time, a clinical trial with sufficient complexity, size, and duration has shown that acupuncture reduces the pain and functional impairment of osteoarthritis of the knee. However, because the study permitted participants to continue taking their standard anti-inflammatory medications, this trial established that acupuncture is an effective adjunct, not alternative, to conventional arthritis treatment, further reducing disability and improving patients' quality of life. These results provide a logical framework for understanding how acupuncture could be successfully employed in an integrated care environment.

Berman B M , Lao L, Langenberg P, Lee W L , and Hochberg M C . Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Arm Intern Med* in press, Dec 21, 2004.

Sleep Disturbances. A 2003 poll found that 67 percent of older adults have sleep problems.⁵ If untreated, sleep disturbances are associated with increased risks of depression and early mortality. Although Americans are increasingly turning to herbal supplements such as valerian⁶

⁵ National Sleep Foundation 2003 poll. Accessed at www.sleepfoundation.org/2003poll.cfm on November 2, 2004.

⁶ Although valerian is used as a sedative for a range of disorders, scientific evidence is insufficient to support its use for conditions other than as a mild sedative for nervous tension and a sleep aid for insomnia.

for relief, the efficacy of these substances must be determined. NCCAM-funded research is assessing how valerian affects sleep quality in older adults, including sleep disturbances in PD patients, while collecting data for a possible large clinical trial. Research seeks to determine the effective dosage and pharmacokinetic properties of valerian, including assessment of adverse side effects. Results released in 2004 of an NCCAM-funded Agency for Healthcare Research and Quality review of melatonin suggest that melatonin supplements may be effective when used in the short term to help people with insomnia fall asleep faster and earlier in the evening.⁷ In addition to also supporting an in-depth mechanistic study of hops (*Humulus lupulus*) to alleviate sleep disturbances, NCCAM funds research to evaluate how mind-body CAM interventions, such as yoga, may alleviate physiological causes of chronic insomnia.

Dietary Supplements: Botanicals and Our Health

Herbal products are among the Nation's most popular CAM therapies. Although many believe these products to be safe because they are "natural" or have been used in some parts of the world for centuries, few have undergone sufficient study for safety and efficacy. Thus, NCCAM supports studies, including a number of multicenter Phase III clinical trials, to gather data on the safety and efficacy of popular herbal remedies.

Cranberries and UTIs. After funding the preparation of well-characterized products and matching placebo controls, NCCAM now supports interrelated basic and clinical studies of cranberry's health benefits and mechanisms of action. The berry's most widely touted health benefit is in preventing urinary tract infections (UTIs), of potential help to the 25 percent of women who experience a bacterial UTI at least once in their lifetime.⁸ NCCAM funds several Phase II clinical trials to determine cranberry's dose ranges and optimal treatment duration in studies on UTI prevention. Other research is examining the pharmacokinetics and renal clearance of cranberry's major components and to identify potential interactions between cranberry and pharmaceuticals, especially the antibiotics frequently prescribed for UTIs. To determine which, if any, factors are responsible for clearing or preventing infection, NCCAM also funds research on cranberry's ability to acidify urine and its anti-inflammation, antioxidant, and anti-adhesive qualities, which prevent bacteria from sticking to the cells of the urinary tract.

The Power of Probiotics. Probiotics are live microorganisms that are consumed to confer a health benefit. However, little research has been done on the complex interactions between probiotic organisms and host factors, such as immune function and the microorganisms that inhabit the gut and mouth, often called normal flora. NCCAM funds studies to examine whether probiotic microorganisms can help colitis sufferers by protecting the intestines from diarrhea-producing organisms. Other research studies the potential for probiotics to eradicate *Staphylococcus aureus* from the nasal passages of patients with end-stage renal disease. This bacterium is frequently resistant to multiple antibiotics and causes considerable morbidity in dialysis patients.

⁷ *AHRQ Issues New Report on the Safety and Effectiveness of Melatonin Supplements*. Press Release, December 8, 2004. Agency for Healthcare Research and Quality, Rockville, MD. Accessed at <http://www.ahrq.gov/news/press/pr2004/melatnpr.htm> on December 20, 2004.

⁸ Doctor Joseph F. Smith Medical Library. Wausau, Wisconsin: The Thompson Corporation. Accessed at <http://www.chclibrary.org/micromed/00044700.html> on November 2, 2004.

Calming Asthma and Allergies. Up to 50 percent of asthma patients⁹ use some form of CAM.¹⁰ However, CAM's role in asthma therapy is uncertain, with few well-controlled scientific studies demonstrating efficacy. To address this research void and expand treatment options for asthma and allergy sufferers, NCCAM supports research to identify promising CAM therapies and their underlying mechanisms. One study is assessing a mixture of traditional Chinese herbs, called "Food Allergy Herbal Formula 1" (FAHF-1), for its ability to block the potentially fatal anaphalactic response triggered by peanut allergy and to determine the formula's mechanism of action in basic and clinical studies. NCCAM recently established the Translational Research Center for CAM Therapy of Asthma to employ biochemical and cellular methods to provide a rationale for using gamma tocopherol, a potent form of Vitamin E, to treat the inflammatory processes in the airways that trigger asthma. In nearly completed research, *Ginkgo biloba* and borage oil (*Borago officinalis*) are being tested in a randomized controlled trial to determine whether the products can inhibit release of inflammatory mediators of asthma. **Another recent study in mice demonstrated the benefit of the Chinese herbal formula MSSM-002 in taming allergic asthma; the compound helped improve airway function by acting on the cellular and biochemical mediators of airway inflammation.**

Supplements and Heart Health? With heart disease still the Nation's leading cause of death,¹¹ NCCAM has made research on cardiovascular diseases (CVD) a priority. One study is investigating how hawthorn (*Cretageus oxyacantha*) affects contractions and confers cardioprotection. Research in animals is exploring the ability of grape seed extract (*Vitis vinefera*) and American ginseng (*Panax quinquefolium*) to protect the heart from ischemia/reperfusion damage, which occurs when the heart is denied then re-supplied with oxygen in a subtle, yet chronic fashion that often ends in congestive heart failure. NCCAM also supports investigations of green and black tea extracts (*Camellia sinensis*) to determine their ability to reduce cholesterol absorption and biosynthesis in postmenopausal women and patients at high risk for CVD.

Botanical Therapies for Cancer. NCCAM investigates many CAM therapies—especially botanicals—that hold promise for treating and preventing cancer. One study examines the Chinese herbal formula ZYD88 for its ability to kill prostate cancer cells in an animal model. In another project, investigators are evaluating an extract of African frankincense (*Boswellia carterri*), boswellin, for its ability to inhibit cell growth and induce apoptosis—cell death—in mice and rat models. With lung cancer still a major public health concern, NCCAM also supports research on a "Selected Vegetables and Herbs Mix," known as Dr. Sun's SV Soup, for its ability to delay the progression of non-small cell lung cancer (NSCLC). The rationale for this study came from the NCI Best Case Series program, which provides an independent review of medical records and medical imaging from patients treated with unconventional cancer therapies. A rigorously designed, placebo-controlled study is testing these findings in patients who are receiving conventional treatment. Another NCCAM grantee is pursuing parallel studies in mice

⁹ In 2002, CDC's National Center for Health Statistics reported that more than 20 million American adults and children were diagnosed with and still had asthma. Accessed at <http://www.cdc.gov/nchs/fastats/asthma.htm> on November 2, 2004.

¹⁰ Steurer-Stey C, Russi E W, and Steurer J. Complementary and alternative medicine in asthma: do they work? *Swiss Med Wkly* 132:338-344, 2002.

¹¹ Arias E, Anderson R N, Hsiang-Ching K, Murphy S L, Kochanek K D. Deaths: Final data for 2001. National vital statistics reports; V o l 52 No 3. Hyattsville, Maryland: National Center for Health Statistics. 2003.

to assess Sun's Soup anti-tumor efficacy and to elucidate how it works at cellular and molecular levels.

Science Advance: Popular Echinacea Product Not Effective in Treating Pediatric URIs

Upper respiratory infections (URIs) are a significant health challenge to children, who average six to eight colds a year typically lasting 7 to 9 days. Symptoms frequently require medical attention, with winter colds accounting for nearly 40 percent of doctor visits by 1- to 5-year-olds. To alleviate URI symptoms, parents often give their children decongestants, antihistamines, and cough suppressants, despite little evidence that these medications are effective in children under age 12. Perhaps because conventional medications for pediatric URIs haven't been proven effective, many parents seek alternative treatments to relieve their children's URI symptoms. About 11 to 21 percent of children in North America receiving care from conventional clinicians also use alternative therapies, particularly for respiratory, ear, nose, and throat symptoms. Echinacea is one of the most commonly used alternative therapies for treating these symptoms, but limited data exist on its safety and efficacy in children.

NCCAM investigators conducted a randomized, double-blind, placebo-controlled trial of 407 healthy 2- to 11-year-olds. Participants were given an echinacea product or a placebo for up to three URIs over 4 months. Parents recorded the duration and severity of symptoms and adverse events. No differences were observed between the groups in the duration, severity, days with fever, and rate of adverse events *except* for an increased incidence of rashes in children given echinacea. In addition to being associated with an increased risk of rash, the echinacea product was not effective in treating URI symptoms. While this study is one of many using different, unstandardized echinacea products, it is among the largest, most carefully performed and the result of joint efforts among trained CAM practitioners and mainstream investigators. Additional research will examine the safety and efficacy of other, better standardized echinacea products in treating URIs and in perhaps preventing colds.

Taylor JA, Weber W, Standish L, Quinn H, Goesling J, McGann M, and Calabrese C. Efficacy and safety of echinacea in treating upper respiratory tract infections in children: a randomized controlled trial. *JAMA* 290(21):2824-2830, 2003.

Future Plans: Milk Thistle for Chronic Liver Disease. Chronic liver disease claimed the lives of more than 20,000 Americans in 2002, disproportionately affecting minorities.¹² Hepatitis C and alcoholic liver disease are leading causes of end-stage liver disease. Antiviral therapy for hepatitis C is effective in only about half of the patients with the common form of the disease, while the only therapy for end-stage liver disease is transplantation. To help alleviate liver disease, NCCAM and NIDDK organized a 1999 symposium on CAM therapies for liver diseases, with a goal of identifying the best opportunities for study. The botanical milk thistle (*Silybum marianum*) emerged as most promising. Through the SBIR program, NCCAM initiated development in 2000 of a standardized milk thistle product suitable for use in basic and clinical trials. As development of this clinical trial grade material neared completion in FY 2004, NCCAM and NIDDK held a workshop to outline options for Phase I/II studies on the safety and tolerability of milk thistle in patients with alcoholic hepatitis, hepatitis C, and non-alcoholic steatohepatitis. A formal solicitation for these studies is in preparation; research will help determine if a Phase III trial is likely to be successful, and if so, the conditions under which it will be performed.

¹² Centers for Disease Control and Prevention. "Deaths: Final Data for 2002." National Vital Statistics Reports, Vol. 53, No. 5. October 12, 2004.

Obesity and Diabetes: Can C A M Help Battle the Bulge?

The C D C estimates that 64 percent of adult Americans are overweight, 30 percent of whom are considered obese.¹³ About 15 percent of children ages 6 to 19 are overweight, almost double the rate of two decades ago¹⁴ In 2004, in response to the Nation's growing obesity epidemic, the U . S . Department of Health and Human Services unveiled a comprehensive strategy that included an N I H obesity research initiative.

N C C A M ' s interest in obesity research complements the N I H obesity research agenda, with projects to examine the safety and efficacy of several popular diets. The Center funded research in 2004 on the metabolic consequences of low- and high-carbohydrate diets. It also supports studies on C A M interventions, such as meditation, qi gong (Chinese-based breathing exercises), and acupuncture, to treat obesity and binge eating and to help maintain weight. These studies should clarify the role that dietary approaches and interventions can play in weight loss. To stimulate further obesity research, N C C A M is cosponsoring trans-NIH initiatives on such issues as childhood obesity and obesity prevention and treatment.

Diabetes, a disease linked to obesity, is also an important target of N C C A M ' s obesity research portfolio. According to the C D C , more than 6 percent of the U . S . adult, noninstitutionalized population has Type 2 diabetes,¹⁵ the most common form of the disease. Diabetics and those at risk for the disease use various C A M therapies that purport to treat, manage, and even prevent diabetes. The dietary supplement chromium is the subject of several N C C A M - f u n d e d studies. Investigators are examining the role chromium could play in ameliorating insulin resistance, as well as the molecular basis of chromium action and its impact on insulin-resistant conditions at the cellular level. With ginseng root a popular natural remedy used in treating and preventing diabetes, N C C A M is supporting research on the metabolic effects of ginseng and ginsenoside Re (a major ginseng component) in people with impaired glucose tolerance. Scientists hope to determine how well patients tolerate ginseng and ginsenosides, with outcomes possibly

catalyzing development of a new approach to treat and prevent Type 2 diabetes.

Special Populations: Minorities, Women, and C A M

A Tapestry of C A M Practices. A 2003 N C C A M - f u n d e d study of Black and White seniors from rural Mississippi found that although respondents of both races commonly used prayer, vitamins, exercise, meditation, and herbs, they differed in age and education level. In addressing the research literature gap on C A M use among elderly Americans of different racial backgrounds, particularly in rural America, the study found that Black C A M users were older and less educated than their White peers. FY 2004 initiatives are examining the interplay of race and ethnicity in C A M use. One study, for instance, will analyze four data sets, including the

¹³ Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. *Nutrition and Physicals Activity: FAQs*. Accessed at <http://www.cdc.gov/nccdphp/dnpa/obesity/faq.htm#adults> on December 15, 2004.

¹⁴ Centers for Disease Control and Prevention, National Center for Health Statistics. *Health & Stats*. Accessed at <http://www.cdc.gov/nchs/products/pubs/pubd/hestats/overwght99.htm> on December 15, 2004.

¹⁵ Centers for Disease Control and Prevention, National Center for Health Statistics. *Summary Health Statistics of U.S. Adults, 2002 National Health Interview Survey, Series 10, Number 222*. Accessed at <http://www.cdc.gov/nchs/fastats/diabetes.htm> on November 3, 2004.

NCCAM-facilitated 2002 NHIS data on C A M use, to determine how age, gender, and locale affect various minorities' use of C A M in managing highly prevalent chronic conditions, such as diabetes. Researchers hope to identify patterns of C A M use—frequency, duration, method of payment—to construct a clearer picture of how Black, Hispanic, and Native Americans use CAM therapies. Understanding these patterns will help direct future research to answer *why* specific populations use certain C A M therapies—such as for cultural reasons, easy access, economic factors, or efficacy—and ultimately help health care providers better meet their health care needs.

Other N C C A M research analyzes demographic and medical factors at work in how low-income Black and White adults use C A M therapies to manage asthma; how middle age and older White, Black, Hispanic, and Chinese Americans employ C A M to manage atherosclerosis, hypertension, coronary heart disease, diabetes, and arthritis; and how Asian American and Pacific Islanders compare between subgroups and with White Americans in C A M use. Researchers are evaluating the relationship of acculturation, perceived discrimination, access to conventional medical care, and health status to better understand health disparities. Another NCCAM study examines CAM use in midlife women from five racial/ethnic groups, comparing the 2002 NHIS data and the annual FY 2006 followup visit of 3,300 midlife women in the longitudinal Study of Women's Health Across the Nation (SWAN) cosponsored by N C C A M . Researchers will examine demographic, lifestyle, and medical factors responsible for women's initial and continued C A M use in an effort to determine whether women differ by race/ethnicity in the therapies they choose and whether therapies selected change with menopausal status.

A research initiative planned for FY 2006 will support planning grants to foster collaborative interactions between investigators at minority/minority-serving institutions (M/MSIs) and C A M research centers, botanical research centers, and N C C A M - f u n d e d investigators at established research institutions. The goal: to help researchers at M / M S I s partner with CAM-experienced researchers so that they can successfully compete for peer-reviewed C A M research support. Beyond improving access to NCCAM resources, this program will encourage research on health disparities among minority populations. Through another F Y 2006 initiative, NCCAM seeks to stimulate C A M projects at institutions that have already secured N I H funding for centers to conduct health disparities research.

C A M and Women's Health. Findings from the Women's Health Initiative on the risks and benefits of HT for menopausal symptoms show that more women are seeking C A M therapies. By 2025, the number of post-menopausal women in the United States is expected to soar. With many more American women perhaps considering C A M therapies for menopausal symptoms, NCCAM has developed a diverse research portfolio to explore use of CAM in treating these symptoms, including hot flashes and osteoporosis. Some studies are examining the safety and efficacy of a range of C A M modalities women now use to treat these symptoms; others address more basic science questions, such as a therapy's mechanism of action. An N C C A M - f u n d e d study will use state-of-the-art molecular biology techniques to determine how botanicals used to treat menopausal symptoms target specific estrogen receptors. Also supported is a study to collect and test botanicals used by Guatemalan and Costa Rican women in managing menopausal symptoms; these botanicals are not now used in this country.

Preparing for clinical studies of CAM therapies for hot flashes, NCCAM convened scientists in January 2004 to assess the quality of outcome measures. The group determined the need for improved sternal skin conductance systems, a sensor system that provides objective measures of hot flashes; a September 2004 RFA for Phase I SBIR applications followed. RFA cosponsors included the National Institute on Biomedical Imaging and Bioengineering, the National Institute on Aging (NIA), and the Office of Research on Women's Health; the goal is to begin funding projects in FY 2005. In March 2005, an NCCAM-NIA state of the science meeting will review management of the transition to menopause. In FY 2006, NCCAM will look to expand its menopause portfolio to strengthen understanding of the physiologic processes underlying hot flashes, improve objective and subjective measures of menopausal changes and symptoms, and develop animal models for *in vivo* screening of potential hot flash therapies.

NCCAM's research portfolio also addresses other important health challenges exclusive to women—endometriosis and premenstrual syndrome (PMS)—as well as those that affect more women than men, such as UTIs, osteoporosis, fibromyalgia, osteoarthritis, breast and other cancers, and cardiovascular disease. For example, NCCAM funded a developmental center to study acupuncture's effect on chemotherapy-induced neutropenia, a blood disorder that increases the risk of infection, in ovarian cancer patients and on chronic pelvic pain in young endometriosis patients. Another study funded in FY 2004 is examining the molecular mechanism of VAC (*Vitex Agnus-castus*L.), a botanical used to treat mood swings associated with PMS.

New Horizons: NCCAM Charts Its Course

In addition to the activities and initiatives described above, NCCAM pursued two efforts in 2004 that reflect its evolution as an NIH Center. As noted in the introduction, one is the development of its second Strategic Plan, marking the Center's graduation from the first critical 5 years as an NIH component. Building on the foundation laid in its first 5-year plan, NCCAM reviewed its accomplishments, summarized lessons learned, and noted the challenges ahead in developing the new Plan. The Center also sought extensive public input, the advice of NCCAM staff, and the recommendations of experts in CAM and relevant sciences.

NIH Roadmap:

A second effort signifies NCCAM's organizational maturity: its leadership of a critical NIH Roadmap for Medical Research activity to advance translational research. Through a working group chaired by NCCAM's Director, NCCAM hopes to lead the way toward a new, effective, and cost-efficient model of translational research. The goals that NCCAM is pursuing on behalf of the NIH community and as leader of this effort will benefit smaller organizations such as itself and others that seek to move basic research into safe, well-designed clinical trials.

The NIH Neuroscience Blueprint:

Overview -- The Blueprint is a framework to enhance cooperation among fourteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces

through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration a day-to-day part of how the N I H does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

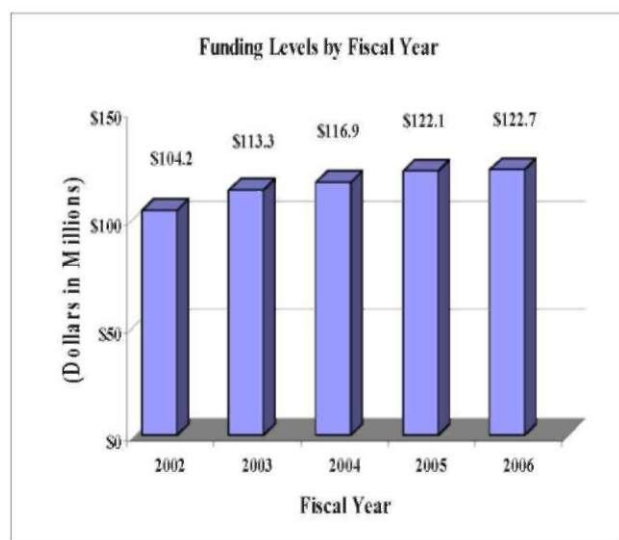
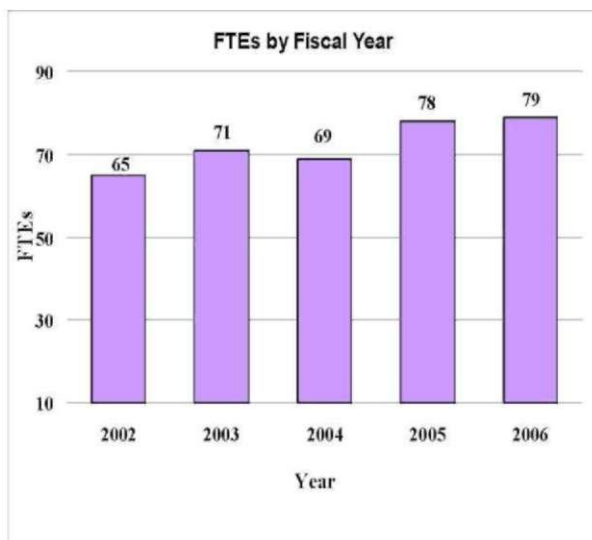
FY2005 -- For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the N I H and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts.

FY2006 -- Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology.

Budget Policy

The Fiscal Year 2006 budget request for N C C A M is \$122,692,000 which represents an increase of \$587,000 and 0.5 percent over the FY 2005 Appropriation. Also included in the FY 2006 request, is N C C A M ' s support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the N I H Overview.

A five year history of FTEs and Funding Levels for N C C A M are shown in the graphs below.

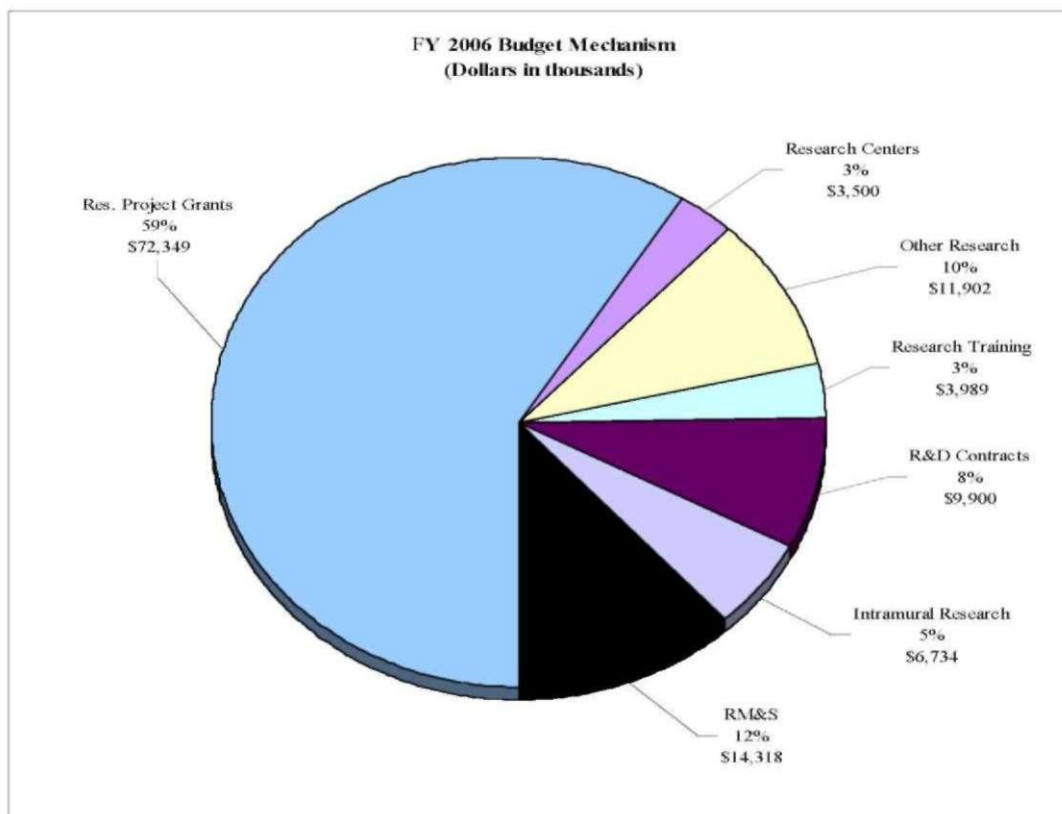


NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. The average cost of competing RPGs will be held at the FY2005 level. There will be no inflationary increases for direct, recurring costs in noncompeting continuation RPGs.

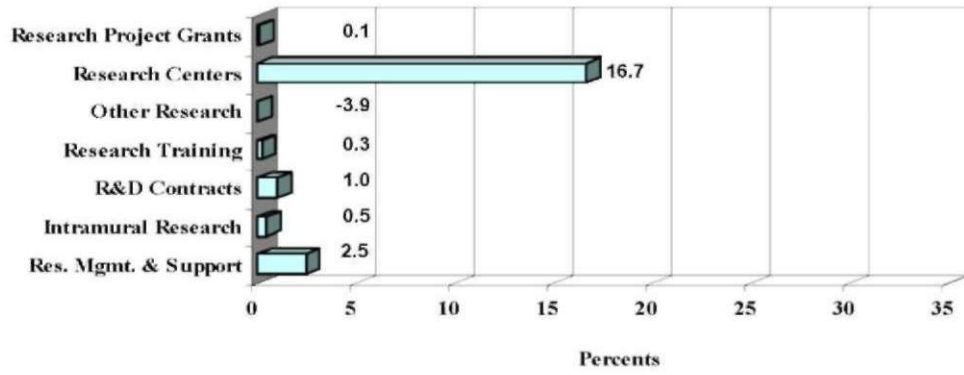
Advancement in medical research is dependent on attracting the best and the brightest to pursue careers in biomedical research. In the Fiscal Year 2006 request, stipend levels for post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will increase by 4.0% for those with 1-2 years of experience, with all other stipends remaining at the FY2005 levels. NIH will also provide an increase of \$500 per post-doctoral fellow, for increased health insurance costs. This increase in stipends and health benefits is financed within the FY2006 request by reducing the number of Full-Time Training Positions by 0. NCCAM will support 74 pre- and postdoctoral trainees in full-time training positions.

The Fiscal Year 2006 request includes funding for 4 research centers, 63 other research grants, including 17 clinical career awards, and 13 R & D contracts. Intramural Research and Research Management and Support receive increases of 0.5 percent, the same as the NIH total increase. NCCAM is participating in the NIH Neuroscience Blueprint. The FY2006 request includes \$100,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiatives, and the Neuromouse project.

The mechanism distribution by dollars and percent change are displayed below:



**FY 2006 Estimate
Percent Change from FY 2005 Mechanism**



Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Research Projects:						
Noncompeting	99	\$37,372,000	128	\$43,524,000	161	\$54,201,000
Administrative supplements	(7)	419,000	(10)	750,000	(10)	750,000
Competing:						
Renewal	1	261,000	1	266,000	1	262,000
New	98	24,888,000	94	24,453,000	53	13,878,000
Supplements	2	514,000	2	532,000	2	524,000
Subtotal, competing	101	25,663,000	97	25,251,000	56	14,664,000
Subtotal, RPGs	200	63,454,000	225	69,525,000	217	69,615,000
SBIR/STTR	8	2,683,000	8	2,743,000	8	2,734,000
Subtotal, RPGs	208	66,137,000	233	72,268,000	225	72,349,000
Research Centers:						
Specialized/comprehensive	7	7,720,000	4	2,940,000	4	3,393,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	49,000	0	60,000	0	107,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	7	7,769,000	4	3,000,000	4	3,500,000
Other Research:						
Research careers	39	5,734,000	39	5,887,000	39	5,900,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	500,000	0	0
Biomedical research support	0	2,000	0	3,000	0	2,000
Minority biomedical research support	0	0	0	0	0	0
Other	24	5,834,000	24	5,996,000	24	6,000,000
Subtotal, Other Research	63	11,570,000	63	12,386,000	63	11,902,000
Total Research Grants	278	85,476,000	300	87,654,000	292	87,751,000
Research Training:	FTEs		FTEs		FTEs	
Individual awards	11	406,000	11	413,000	11	413,000
Institutional awards	63	3,545,000	63	3,566,000	63	3,576,000
Total, Training	74	3,951,000	74	3,979,000	74	3,989,000
Research & development contracts (SBIR/STTR)	13 (0)	9,752,000 (5,000)	13 (0)	9,800,000 (5,000)	13 (0)	9,900,000 (5,000)
Intramural research	FTEs		FTEs		FTEs	
Intramural research	15	4,310,000	18	6,700,000	18	6,734,000
Research management and support	54	13,454,000	60	13,972,000	61	14,318,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Buildings and Facilities		0		0		0
Total, N	69	116,943,000	78	122,105,000	79	122,692,000
(RoadMap Support)		(385,000)		(772,000)		(1,094,000)
(Clinical Trials)		(30,499,076)		(31,700,000)		(31,900,000)

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004		FY 2005		FY 2006		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:		99,179		\$101,433		\$101,640		\$207
Subtotal, Extramural research		99,179		101,433		101,640		207
Intramural research	15	4,310	18	6,700	18	6,734	0	34
Res. management & support	54	13,454	60	13,972	61	14,318	1	346
Cancer Control & Prevention	0	0	0	0	0	0	0	0
Total	69	116,943	78	122,105	79	122,692	1	587

Summary of Changes

FY 2005 Estimate		\$122,105,000	
FY 2006 Estimated Budget Authority		122,692,000	
Net change		587,000	
CHANGES	FY 2005		Change from Base
	FTEs	Budget Authority	FTEs Budget Authority
A. Built-in:			
1. Intramural research:			
a. Within grade increase		\$1,573,000	\$24,000
b. Annualization of January 2005 pay increase		1,573,000	15,000
c. January 2006 pay increase		1,573,000	28,000
d. One less day of pay		1,573,000	(6,000)
e. Payment for centrally furnished services		845,000	4,000
f. Increased cost of laboratory supplies, materials, and other expenses		4,282,000	29,000
Subtotal			94,000
2. Research Management and Support:			
a. Within grade increase		7,275,000	118,000
b. Annualization of January 2005 pay increase		7,275,000	67,000
c. January 2006 pay increase		7,275,000	129,000
d. One less day of pay		7,275,000	(28,000)
e. Payment for centrally furnished services		1,746,000	9,000
f. Increased cost of laboratory supplies, materials, and other expenses		4,951,000	46,000
Subtotal			341,000
Subtotal, Built-in			435,000

Summary of Changes—continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	128	\$44,274,000	33	\$10,677,000
b. Competing	97	25,251,000	(41)	(10,587,000)
c. SBIR/STTR	8	2,743,000	0	(9,000)
Total	233	72,268,000	(8)	81,000
2. Research centers	4	3,000,000	0	500,000
3. Other research	63	12,386,000	0	(484,000)
4. Research training	74	3,979,000	0	10,000
5. Research and development contracts	13	9,800,000	13	100,000
Subtotal, extramural				207,000
6. Intramural research	FTEs 18	6,700,000	FTEs 0	0
7. Research management and support	60	13,972,000	1	(55,000)
8. Cancer control and prevention	0	0	0	0
9. Construction		0		0
10. Building and Facilities		0		0
Subtotal, program		122,105,000		152,000
Total changes	78		1	587,000

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	78	79	1
Full-time equivalent of overtime & holiday hours	0	0	(0)
Average ES salary	\$0	\$0	\$0
Average GM / G S grade	11.8	12.1	0.3
Average GM / G S salary	\$75,854	\$81,164	\$5,310
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$80,220	\$81,824	\$1,604
Average salary of ungraded positions	121,854	124,291	2,437
OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	\$4,424,000	\$4,555,000	\$131,000
11.3 Other than Full-Time Permanent	2,112,000	2,172,000	60,000
11.5 Other Personnel Compensation	158,000	162,000	4,000
11.7 Military Personnel	171,000	175,000	4,000
11.8 Special Personnel Services Payments	148,000	150,000	2,000
Total, Personnel Compensation	7,013,000	7,214,000	201,000
12.0 Personnel Benefits	1,727,000	1,777,000	50,000
12.1 Military Personnel Benefits	108,000	112,000	4,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	8848,000	9,103,000	255,000
21.0 Travel & Transportation of Persons	280,000	285,000	5,000
22.0 Transportation of Things	40,000	42,000	2,000
23.1 Rental Payments to G S A	0	0	0
23.2 Rental Payments to Others	0	0	0
23.3 Communications, Utilities & Miscellaneous Charges	120,000	125,000	5,000
24.0 Printing & Reproduction	130,000	135,000	5,000
25.1 Consulting Services	140,000	145,000	5,000
25.2 Other Services	4,617,000	4,783,000	166,000
25.3 Purchase of Goods & Services from Government Accounts	11,362,000	11,162,000	(200,000)
25.4 Operation & Maintenance of Facilities	175,000	180,000	5,000
25.5 Research & Development Contracts	3,700,000	3,800,000	100,000
25.6 Medical Care	30,000	32,000	2,000
25.7 Operation & Maintenance of Equipment	130,000	135,000	5,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	20,154,000	20,237,000	83,000
26.0 Supplies & Materials	700,000	800,000	100,000
31.0 Equipment	200,000	225,000	25,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	91,633,000	91,740,000	107,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	0	0	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	113,257,000	113,589,000	332,000
Total Budget Authority by Object	122,105,000	122,692,000	587,000

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	\$4,424,000	\$4,555,000	\$131,000
Other Than Full-Time Permanent (11.3)	2,112,000	2,172,000	60,000
Other Personnel Compensation (11.5)	158,000	162,000	4,000
Military Personnel (11.7)	171,000	175,000	4,000
Special Personnel Services Payments (11.8)	148,000	150,000	2,000
Total Personnel Compensation (11.9)	7,013,000	7,214,000	201,000
Civilian Personnel Benefits (12.1)	1,727,000	1,777,000	50,000
Military Personnel Benefits (12.2)	108,000	112,000	4,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	8,848,000	9,103,000	255,000
Travel (21.0)	280,000	285,000	5,000
Transportation of Things (22.0)	40,000	42,000	2,000
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities and Miscellaneous Charges (23.3)	120,000	125,000	5,000
Printing and Reproduction (24.0)	130,000	135,000	5,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	140,000	145,000	5,000
Other Services (25.2)	4,617,000	4,783,000	166,000
Purchases from Govt. Accounts (25.3)	5,262,000	5,062,000	(200,000)
Operation & Maintenance of Facilities (25.4)	175,000	180,000	5,000
Operation & Maintenance of Equipment (25.7)	130,000	135,000	5,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	10,324,000	10,305,000	(19,000)
Supplies and Materials (26.0)	700,000	800,000	100,000
Subtotal, Non-Pay Costs	11,594,000	11,692,000	98,000
Total, Administrative Costs	20,442,000	20,795,000	353,000

NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

SIGNIFICANT ITEMS IN HOUSE, SENATE, AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108-188)

Item

Ameliorating Liver Disease - The Committee notes that NIDDK has completed efforts to synthesize and calibrate the production of milk thistle, which will now make possible clinical trials to demonstrate its value in slowing the progression of non-alcoholic steatohepatitis and to reduce the side effects of hepatitis C interferon treatments. The Committee urges NCCAM to pursue research to demonstrate the value of milk thistle to ameliorate liver disease **(Page 101)**.

Action taken or to be taken

The National Center for Complementary and Alternative Medicine (NCCAM) continues to support a vigorous research portfolio on milk thistle (*Silybum marianum*), a botanical used widely by CAM practitioners to treat liver and gallbladder diseases.¹ In late 2001, NCCAM, in collaboration with NIDDK, funded a Small Business Innovative Research award for the development of research-grade milk thistle product. With an anticipated completion date of June 2005, this standardized product will be used by scientists to conduct basic and clinical research to determine potential of the botanical to prevent and treat liver disease.

Before large-scale (Phase III) studies are possible, NCCAM will fund Phase I and II studies to examine the pharmacokinetics, bioavailability, dosing effects, and safety and efficacy of milk thistle as a potential treatment for liver disease. Research areas of interest include determining milk thistle's ability to slow the progression of non-alcoholic steatohepatitis and to reduce the side effects of interferon treatments for hepatitis C. One such study underway is a Phase I/II open label, randomized dose-finding study on the use of oral Siliphos™ in patients with chronic hepatitis C with stages II, III, and IV liver fibrosis. Participants are individuals who have not responded to, or are poor candidates for, interferon-based treatment and who have persistently high levels of the enzyme ALT, an indicator of liver disease. In FY 2005, NCCAM will partner with a supplier of clinical-grade milk thistle and plans to issue an RFA to solicit Phase I and Phase II studies.

In other research efforts to promote liver health, NCCAM is supporting several studies to clarify the role of S-Adenosyl-L-Methionine (SAME) in liver function and injury. SAME plays a central role in regulating the growth and death of liver cells. Improving understanding of SAME's role supports NCCAM research on the synergistic effects of SAME and

¹ Agency for Healthcare Research and Quality, Department of Health and Human Services. "Milk Thistle: Effects on Liver Disease and Cirrhosis and Clinical Adverse Effects." *Evidence Report/Technology Assessment*. Number 21. Accessed at www.ahrq.gov/clinic/epcsums/milktsu.htm.

dilinoleoylphosphatidylcholine (DLCP), both of which help protect liver cells and, when combined, may hold promise in treating and preventing liver cirrhosis.

Item

Osteoporosis - The Committee encourages NCCAM to conduct research on women in their thirties and forties with respect to bone health and nutrition, including the use of supplements and nutraceuticals, in an effort to determine whether such strategies can prevent osteoporosis and fractures in later life. In addition, the Committee encourages support for research on the effects of complementary and alternative medicine on bones and pain management in people with metabolic bone diseases (**Page 101**).

Action taken or to be taken

NCCAM is bringing scientific rigor to the study of plant-based estrogen-like compounds called phytoestrogens -- which purportedly confer the bone-health benefits of hormone therapy, but without its reported side effects. For example, a 2003 NCCAM-funded literature review examined the safety of isoflavones, a class of phytoestrogens found in soy products and red clover in people of all ages and both sexes. This topic was deemed important as the food industry has created many products that contain or have been enhanced with isoflavones. Although the review concluded that isoflavones taken orally at daily doses less than 2 mg/kg body weight can be considered safe, it was not designed to address efficacy in preventing osteoporosis.²

In FY 2004, NCCAM built on this review on several fronts. For example, the Center funded research to compare HT, black cohosh, a multibotanical preparation, with and without soy diet counseling, and placebo for their relative ability to slow bone loss. NCCAM also supports research to examine herbs that appear to inhibit proliferation of breast cancer cells and breast tumor formation and could lead to the discovery of new products that enhance bone health while protecting other tissue. Additional FY 2004 research targets the metabolic consequences of low- and high-carbohydrate diets. Yet another approach is examining the impact of therapeutic touch on bone metabolism in postmenopausal women who have fractured a wrist and on *in vitro* bone formation.

Three additional FY 2004 efforts seek to further enhance understanding of osteoporosis. Collaborating with the National Institute on Aging, NCCAM approved funding for the Study of Women's Health Across the Nation (SWAN), a multicenter, multiethnic, community-based longitudinal study now in its third wave of data collection. Among changes in women's health during late perimenopause and early postmenopause, SWAN III will continue to monitor bone loss and incidence of fractures, possible results of osteoporosis. NCCAM also supports a collaborative Purdue University-University of Alabama Botanicals Center that will target, among other research studies, isoflavones and osteoporosis. And, finally, the Center funded an AHRQ review in FY 2004 on the safety and efficacy of soy in addressing osteoporosis and other menopause-related conditions.

² Barnes S. Phyto-estrogens and osteoporosis: what is a safe dose? *British Journal of Nutrition* 89 (Suppl 1):S101-S108, 2003.

Item

Chromium and Diabetes - Recent research has demonstrated that chromium picolinate can restore normal glucose metabolism by enhancing insulin sensitivity. Impaired insulin sensitivity is a major factor leading to the development of type 2 diabetes and cardiovascular disease. In clinical studies in people with type 2 diabetes, chromium supplementation has been shown to significantly reduce elevated blood sugar levels and improve long-term blood sugar control. The beneficial effects were predominantly seen in populations who were overweight and insulin resistant. Since it has been shown that many Native Americans have severely impaired insulin sensitivity and are overweight, a strong case can be made to support the hypothesis that chromium supplementation can significantly help Native American populations. In addition to potential treatment benefits, chromium supplementation in overweight pediatric populations may restore normal glucose metabolism, and thereby reduce or delay the onset of diabetes. Therefore, NCCAM is encouraged to expand upon these early findings to support research on chromium supplementation as a safe, effective, low cost nutritional therapy for type 2 diabetes **(Page 101)**.

Action taken or to be taken

NCCAM supports a range of studies on the safety and effectiveness of CAM modalities in preventing and treating diabetes and insulin resistance syndrome. For example, ginseng root a commonly used CAM product, has been purported to improve glucose tolerance and prevent type 2 diabetes. In FY 2004, NCCAM supported a pilot trial at the University of Washington to study the metabolic effects of ginseng in patients with impaired glucose tolerance. The Center also funded a project to determine how the Chinese herbal medicine cordyceps senensis (CS) affects glucose metabolism. In addition, NCCAM supported a study in FY 2004 to examine whether taurine, an amino acid that functions as an antioxidant, may reduce the effects of diabetic neuropathy, a painful and often serious complication of diabetes. Further, NCCAM's Intramural Research Program continues to focus on better understanding of the role insulin plays in diabetes, hypertension, and obesity and whether certain CAM therapies may be effective in combating these debilitating and costly diseases.

While use of chromium supplements among diabetics is common, and small, non-controlled clinical trials have shown initial but promising results, limited scientific evidence exists to determine whether these supplements can alleviate diabetes symptoms and reduce the need for insulin supplements in patients with type 2 diabetes. To enhance scientific knowledge on the use of chromium as a potential adjuvant therapy for type 2 diabetes and impaired glucose tolerance, NCCAM teamed in FY 2002 with the NIH Office of Dietary Supplements (ODS) and NIDDK on a Program Announcement (PA). The PA was designed to encourage research on the mechanism of action of chromium on insulin secretory and signaling pathways and to conduct clinical studies to assess the safety and efficacy of chromium as an adjuvant treatment for type 2 diabetes and/or impaired glucose tolerance. The PA resulted in NCCAM's support of three awards on chromium and insulin resistance.

One NCCAM project is examining the long-term effects of chromium supplementation to prevent or forestall the progression of insulin resistance and dyslipidemia in non-human primate models. Another NCCAM award seeks to determine how chromium may enhance insulin action, while yet another supports a randomized, double-blind, placebo-controlled pilot clinical trial in

adults to investigate the potential effects of chromium on glucose tolerance and certain vascular functioning. In FY 2005, the Center, with the N I H O D S and N I D D K , plans to evaluate the results of these studies and other research results on chromium supplementation and to consider future research directions in the treatment and prevention of type 2 diabetes.

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108-345)

Item

Alternative therapies - The Committee expects that funding for existing and new centers supported by NCCAM will be maintained. The Committee further expects NCCAM to undertake field investigations and a program for the collection and evaluation of outcome data on promising alternative therapies. The Committee expects NCCAM to expand its support of CDC's field investigations program and of A H R Q 's literature reviews and data-analysis efforts, and to develop and disseminate a comprehensive set of fact sheets on C A M therapies to inform the public and health professionals of the state of scientific knowledge about these therapies. The Committee once again calls upon NCCAM to increase the number of research grants and centers awarded to C A M institutions. The Committee believes that in order to assure an adequate C A M research infrastructure and to encourage quality research at these institutions, greater support and resources from NCCAM to these institutions are needed **(Page 157)**.

Action taken or to be taken

As part of its efforts to provide the public and health care practitioners with scientific answers about the safety and efficacy of complementary and alternative medicine (CAM), NCCAM remains committed to a strong and multifaceted centers program. Scientific evaluation of CAM practices, however, presents special challenges, including needed increases in research capacity at C A M institutions and difficulties in studying C A M products that vary widely in composition and are already in use. To address such challenges, NCCAM funds a number of Centers Programs, including the Centers of Excellence for Research on C A M and Developmental Centers for Research on C A M . Centers of Excellence support experienced researchers at some of the Nation's leading universities for 5 years, enabling them to apply cutting-edge technologies to identify the potential benefits and underlying mechanisms of C A M practices. Developmental Centers, in turn, provide some of the Nation's major C A M institutions with 3 years of funding to build research programs through partnerships with established research institutions.

In October 2004, NCCAM funded several major awards to expand the scope and impact of its research centers portfolio, including three new Centers of Excellence that will strengthen its research portfolio in Mindfulness-Based Stress Reduction, Traditional Chinese Medicines and acupuncture, and translational research. NCCAM also funded three new Developmental Centers for Research on CAM that will focus on immune system response, placebo effects, and osteopathic manipulation therapy. Together, these new centers will address a range of health conditions that include H I V / A I D S , alcoholism, drug addiction, asthma, chronic pain, and cancer. In FY 2005, NCCAM will partner with the NIH Office of Dietary Supplements (ODS), the National Institute for Environmental and Health Sciences, and other N I H Institutes and Centers to issue new awards under the Centers for Dietary Supplements: Botanicals Program to support research as well as training and career development opportunities.

Formation of the Cancer Working Group (CWG) of the National Advisory Council for Complementary and Alternative Medicine (NACCAM) reflects NCCAM's commitment to soliciting innovative CAM approaches to the treatment and prevention of disease from practitioners in the field. Comprising NACCAM members, basic and clinical investigators, practitioners, clinicians, and patient advocates, the CWG assesses evidence collected through NCI's Best Case Series Program, including medical records, medical imaging, and pathology reports, to evaluate a CAM treatment's therapeutic effect on a relevant group of cancer patients.

Through the NCCAM-chaired NIH Trans-Agency CAM Research Coordinating Committee, NCCAM fosters research collaborations among several Federal agencies, including the CDC, Federal Trade Commission, Food and Drug Administration, Department of Defense, and the Agency for Healthcare Research and Quality (AHRQ). NCCAM looks forward to working with the CDC on relevant field investigations and to exploring potential research partnerships with its Division of Nutrition and Physical Activity. Also, following on the success of the CAM supplement developed for the 2002 National Health Interview Survey, NCCAM and the CDC are collaborating on an expanded CAM supplement for the 2007 survey.

In FY 2004, NCCAM funded AHRQ reviews on the safety and efficacy of melatonin and soy. In FY 2005, NCCAM, in collaboration with the NIH ODS, will fund AHRQ to review clinical data on the safety and efficacy of berries and their mechanisms of action in animal and *in vitro* studies. These reviews help inform possible future directions for NCCAM research.

Disseminating authoritative information on CAM to public and professional communities remains a key part of NCCAM's mission. In FY 2004, NCCAM released a variety of publications in both print and electronic format, including Spanish language translations, to inform readers of the latest developments in CAM research. New in NCCAM's *Research Report* series are *Questions and Answers About Using Magnets for Pain* and *About Chiropractic and Its Use in Treating Low-Back Pain*. Consumer advisories include important information on colloidal silver products and the use of echinacea in treating children's colds. In FY 2005, NCCAM plans to publish fact sheets that address CAM use in diabetes and rheumatoid arthritis, a new series called *Herbs-at-a-Glance*, and additional education pieces. Partnering with the

National Cancer Institute, NCCAM also will develop a brochure on CAM and cancer.

Item

Ameliorating Liver Disease - The Committee notes that NIDDK has completed efforts to synthesize and calibrate the production of milk thistle, which will now make possible clinical trials to demonstrate its value in slowing the progression of non-alcoholic steatohepatitis and to reduce the side effects of hepatitis C interferon treatments. The Committee urges NCCAM to pursue research to demonstrate the value of milk thistle to ameliorate liver disease (**Page 158**).

Action taken or to be taken

Please refer to pages NCCAM - 25 and NCCAM - 26 of this document for NCCAM's response to this significant item regarding ameliorating liver disease.

Item

Bone Health and Nutrition - The Committee urges NCCAM to conduct research on women in their 30s and 40s with respect to bone health and nutrition, including the use of supplements and nutraceuticals, in an effort to determine whether such strategies can prevent osteoporosis and fractures later in life. In addition the Committee urges support for research on the effect of complementary and alternative medicine on bones and pain management in people with metabolic bone diseases (**Page 158**).

Action taken or to be taken

Please refer to page NCCAM - 26 of this document for NCCAM's response to this significant item regarding bone health and nutrition.

Item

Native Hawaiian Healing - The Committee encourages the preservation and documentation of Native Hawaiian traditional cultural healing practices (**Page 158**).

Action taken or to be taken

Although growing CAM use by Americans as a whole is well documented, much needs to be learned about traditional medicine and CAM use in Indigenous/Native populations, including those of Native Hawaiians. Research can illuminate how traditional beliefs and practices may affect health status and behaviors and how they may be integrated into conventional disease prevention and health care efforts. Indigenous/Native peoples have practiced traditional systems of medicine for thousands of years. However, with much of the information on these practices being transmitted through oral traditions and interventions varying across practitioners and Tribal cultures, attempts to conduct scientific research on these systems have been challenging.

NCCAM regards America's diverse racial and ethnic groups as valuable resources for learning about systems of healing and health practices outside conventional medicine. Believing that research on Indigenous/Native traditional medicine systems may benefit more people if these systems are better understood and characterized, NCCAM plans in FY 2005 to convene a working group to establish communication and facilitate research collaborations among traditional and conventional Indigenous/Native healers.

Anticipated outcomes of this effort are enhanced communications with Indigenous/Native peoples, including Native Hawaiians, and facilitating meaningful and culturally relevant CAM research. The goals of this effort are to identify (1) areas ripe for research, (2) best practices and priorities for research in collaboration with Indigenous/Native communities, (3) methods for conducting culturally sensitive and scientifically valid results, and (4) appropriate ways to integrate the holistic approaches of traditional medicine into allopathic care. In FY 2005, NCCAM will continue its efforts to expand the participation in biomedical research of underrepresented investigators and clinicians, including Indigenous/Native peoples.

Item

Parkinson's Disease - The Committee encourages NCCAM to continue exploration of the neuroprotective qualities of B vitamins and antioxidant phytochemicals in berries via animal models. Research with animals has shown that diets containing berry fruits, such as blueberries,

in addition to B vitamins may forestall and could reverse many of the neurological changes associated with age-related neurodegenerative conditions, such as Parkinson's and Alzheimer's disease (Page 158).

Action taken or to be taken

Through support for basic and clinical research, NCCAM seeks to shed light on the safety and efficacy of botanical products, such as *Ginkgo biloba* and other dietary supplements and antioxidants, to prevent and treat the devastating effects of neurological disorders, including Parkinson's, Alzheimer's, and Huntington's diseases and multiple sclerosis. NCCAM supports several projects on the use of vitamins and antioxidants, including research on the potential of berries and other fruit extracts to prevent and treat disease, including neurodegenerative conditions. With evidence mounting that mitochondrial decay plays an important role in aging and age-related neurodegenerative diseases, the Center supported research in animal models in FY 2004 to test whether high doses of B vitamins would prevent or treat such decay in the elderly, perhaps improving their motor, cognitive, and neuromuscular functioning.

Preliminary studies suggest that resveratrol, an antioxidant compound found in grape skin and red wine, may play various roles in moderating oxidative stress and inflammation. In FY 2004, NCCAM supported research to better understand how this antioxidant might protect the brain from chronic neurodegenerative conditions, such as Alzheimer's disease and other age/vascular-related dementias. The Center also funded FY 2004 research to determine how bioflavonoid-rich extracts, including green tea leaf extract and citrus bioflavin, may lower lipid levels in animal models. Because vascular changes due to lipid deposits may be linked to age-related dementia, such studies could provide better insight into preventing and treating brain disease.

In FY 2004, NCCAM partnered with the National Institute on Aging to continue support for the largest-ever clinical trial to prevent the onset of dementia using *Ginkgo biloba*. Enrolling more than 3,000 patients, this clinical trial will provide the richest data to date on the possible neuroprotective effects of this dietary supplement and new knowledge on the health status of this elderly cohort. The Center also funded in FY 2004 the Emory University Center for Complementary and Alternative Medicine in Neurodegenerative Diseases to conduct studies of promising C A M approaches to preserving or enhancing the function and quality of life in Parkinson's, Huntington's, and Alzheimer's patients. Studies will examine pharmacologic and nutritional therapies and herbal and natural medicines, such as the effects of valerian root extract and melatonin on patients with Parkinson's disease sleep disturbance. Further FY 2004 funding was provided to the Oregon Center for Complementary and Alternative Medicine in Neurological Disorders to investigate the use of antioxidants and mind-body approaches in treating neurodegenerative and demyelinating diseases.

In FY 2005, NCCAM, in conjunction with the NIH ODS, will support an AHRQ evidence-based review of the *in vitro*, animal, and clinical data on the safety and efficacy of berries in preventing and treating Alzheimer's and Parkinson's diseases. The results of this analysis should be complete in 2006. Using the knowledge gained from this and other studies, NCCAM will vigorously pursue promising research directions on the use of berries or other C A M modalities in preventing and treating neurological disease.

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
Complementary and Alternative	Section 41B	42§285b	Indefinite	\$118,126,000	Indefinite ^a	\$118,703,000
National Research Service Awards	Section 487(d)	42§288	a/	3,979,000	b/	3,989,000
Total, Budget Authority				122,105,000		122,692,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

b/ Reauthorizing legislation will be submitted.

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation ^{1/}
2000	50,168,000	68,000,000	56,214,000	68,753,000
Rescission				(363,000)
2001	71,362,000	78,880,000	100,089,000	89,211,000
Rescission				(54,000)
2002	100,063,000	99,288,000	110,000,000	104,644,000
Rescission				(52,000)
2003	112,547,000	112,547,000	111,149,000	114,149,000
Rescission				(742,000)
2004	116,202,000	116,202,000	117,902,000	117,752,000
Rescission	0	0	0	(774,000)
2005	121,116,000	121,116,000	121,900,000	123,116,000
Rescission	0			(1,011,000)
2006	122,692,000			

J/ Reflects enacted supplemental, rescissions, and reappropriations.

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Office of the Director	7	7	7
Office of Administrative Operations	15	16	16
Office of Communication and Public Liasion	7	7	7
Office of Science Policy and Operations	9	9	9
Division of Extramural Research and Training	12	14	15
Office of Scientific Review	4	7	7
Division of Intramural Research	15	18	18
Total	69	78	79
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)
FISCAL YEAR	Average GM/GS Grade		
2002	11.2		
2003	11.2		
2004	11.6		
2005	11.8		
2006	12.1		

NATIONAL INSTITUTES OF HEALTH
National Institute of

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	0	0	0
Total - ES Salary	\$0	\$0	\$0
GM/GS-15	10	10	10
GM/GS-14	12	14	15
GM/GS-13	9	9	9
GS-12	12	12	12
GS-11	4	4	4
GS-10	0	0	0
GS-9	4	4	4
GS-8	3	4	4
GS-7	4	6	6
GS-6	0	0	0
GS-5	0	1	1
GS-4	1	1	1
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	59	65	66
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	2	5	5
Senior Grade	0	0	0
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	2	5	5
Ungraded	27	27	27
Total permanent positions	61	70	71
Total positions, end of year	88	97	98
Total full-time equivalent (FTE) employment, end of year	69	78	79
Average ES salary	\$0	\$0	\$0
Average GM/GS grade	11.6	11.8	12.1
Average GM/GS salary	\$73,581	\$75,854	\$81,164