DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

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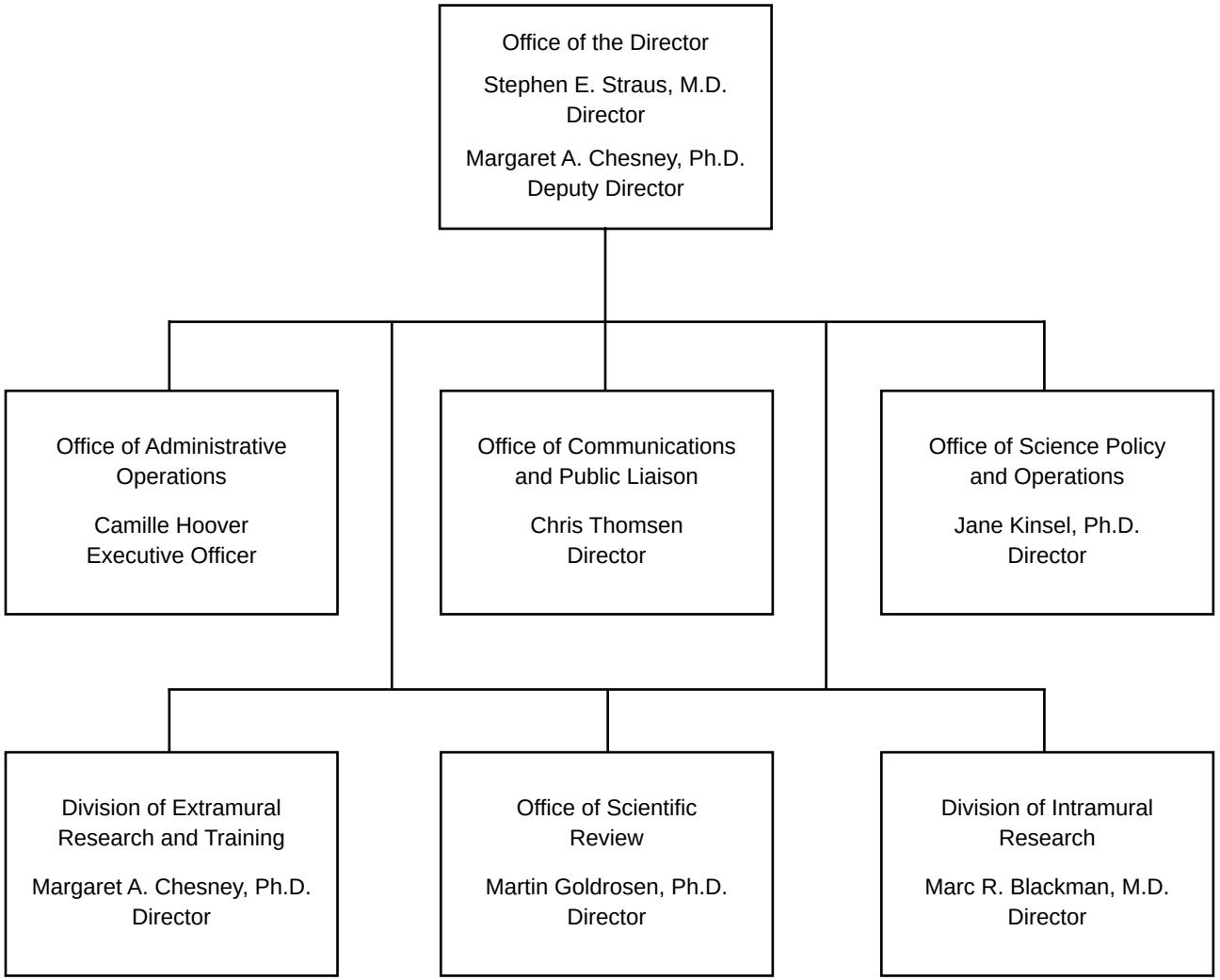


NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

For carrying out section 301 and title IV of the Public Health Service Act with respect to complementary and alternative medicine, [$117,752,000] *$121,116,000.*

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Omnibus Consolidated Appropriations Act for Fiscal Year 2004].

National Institutes of Health
National Center for Complementary and Alternative Medicine

Amounts Available for Obligation 1/

Source of Funding	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Appropriation	$114,149,000	$117,752,000	$121,116,000
Enacted Rescissions	(742,000)	(774,000)	---
Subtotal, Adjusted Appropriation	113,407,000	116,978,000	121,116,000
Comparative transfer to NIBIB for Radiology Program	(2,000)	(3,000)	(0)
Comparative transfer to Buildings and Facilities	(33,000)	(32,000)	(0)
Comparative transfer to Office of the Director for program changes	(105,000)	(0)	(0)
Subtotal, adjusted budget authority	113,267,000	116,943,000	121,116,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	113,267,000	116,943,000	121,116,000
Unobligated balance lapsing	(2,000)	---	---
Total obligations	113,265,000	116,943,000	121,116,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2003 - $509,000; FY 2004 - $550,000; FY 2005 - $600,000

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 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
71	$113,267,000	76	$116,943,000	82	$121,116,000	6	$4,173,000

This document provides justification for the Fiscal Year 2005 activities of the National Center for Complementary and Alternative Medicine (NCCAM), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2005 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

Introduction

Nearly 80 million Americans use some form of complementary and alternative medicine (CAM), such as herbal medicine, chiropractic manipulation, acupuncture, massage therapy, homeopathy, and yoga. That was the conclusion of the National Health Interview Survey conducted by the Centers for Disease Control and Prevention in 1999. However, unlike prescription drugs and devices approved by the U.S. Food and Drug Administration (FDA) after a lengthy process of basic, preclinical, and clinical research, little rigorous research supports the widespread use of CAM and the assumption that CAM approaches are safe and effective. The challenges to public health that this situation represents led to the creation of the National Center for Complementary and Alternative Medicine (NCCAM) in 1999.

NCCAM's goals are to determine the health benefits of CAM therapies and preventive strategies, to investigate their mechanisms of action, train and support investigators capable of undertaking open-minded but rigorous studies, and to allow the objective evidence to support the integration of safe and effective CAM therapies into conventional medical practice. Today, nearing its fifth anniversary, NCCAM has developed a forward-looking, broadly based research and training portfolio that capitalizes on the most significant opportunities in CAM. In FY 2003, building on its evolving platform of research activities, NCCAM identified six priority research areas: obesity, botanicals, acupuncture, brain-body interactions, neurodegenerative conditions, and HIV/AIDS. This justification narrative provides an overview of these high priority research efforts by summarizing recent findings, current projects, and future research.

Exploring CAM Interventions for Obesity

Far too many Americans—an estimated 66 percent of adults, 14 percent of adolescents, and 13 percent of children—are obese or overweight. A dominant factor in making obesity a high-priority public health problem in the United States is that it greatly increases one's risk for a daunting range of serious medical conditions, including high blood pressure, type 2 (non-insulin dependent) diabetes, coronary heart disease, congestive heart failure, stroke, and certain cancers.

Understanding, treating, and preventing obesity requires a multidisciplinary approach. Obesity results from complex interactions among human biology, behavior, and the environment. A host of biological factors have been identified that contribute to obesity, including chemical signals from the digestive tract and olfactory system; hormonal signals such as insulin, leptin, and glucocorticoids; and neural signals from and within the brain. NCCAM is committed to exploring popular approaches used to address obesity to see whether they can modify beneficially some of the biological and behavioral factors that engender and sustain obesity. NCCAM is supporting studies to answer persistent questions about the safety and efficacy of widely used and unvalidated CAM approaches to obesity and its many complications.

Scientific Advances in Obesity Research

At any given time, an estimated 45 percent of American women and 30 percent of men are trying, and often failing, to lose weight. Despite medical recommendations that a diet low in calories and fat is the best way to lose weight, more Americans are turning to alternative diets such as the seemingly counterintuitive Atkins diet plan which promotes a low carbohydrate, high-fat, high-protein regimen.

In FY 2003, NCCAM-sponsored researchers concluded and reported on a ground-breaking one year, multicenter clinical trial of obese persons to evaluate the effects of the Atkins diet on weight loss and risk factors for cardiovascular disease. As published in the *New England Journal of Medicine*, the study compared weight loss and cardiovascular risks of 33 severely obese people (12 men, 21 women) on the Atkins diet, with 30 others (8 men, 22 women) who consumed a conventional high-carbohydrate, low-fat, energy-deficit diet. After six months, those on the Atkins diet had lost significantly more weight (approximately 4 % more) than those on the conventional diet. Those on this low-carbohydrate diet also experienced improvements in certain risk factors for coronary heart disease such as levels of blood lipids. After one year, there was no longer evidence of a significant difference in weight loss between the two groups of dieters, leading investigators to call for additional research, involving longer-term studies and more participants, to accurately assess the longer-term risks and benefits of low-carbohydrate, high-fat diets. NCCAM is proud to lead the NIH support of this larger and more definitive study.

FY 2003 Awards: Expanding the Knowledge Base in Obesity Research

NCCAM funded in FY 2003 a number of additional studies of CAM approaches to obesity. One new project is designed to test the efficacy of qi gong, an ancient Chinese method of

self-healing, and a form of acupressure on long-term maintenance of weight loss. Other NCCAM projects focus on cellular and molecular aspects of obesity. One study will test whether the oral administration of glucosamine, a dietary supplement used by over 4% of Americans aged 65 and older to treat degenerative arthritis, causes significant resistance to insulin, a condition that predisposes one to diabetes. Another study will evaluate whether carnitine, a nutrient essential for the normal metabolism of fats, can reduce abdominal fat content, stimulate weight loss, and improve glucose utilization. In addition, NCCAM will continue support of other ongoing obesity-related projects, including a study of the benefits and risks of other popular weight-loss diets, studies of *Ginkgo biloba* on human insulin resistance syndrome, and research that may determine whether the production of nitric oxide by endothelial cells that line blood vessels helps regulate the relationship between high blood pressure and insulin resistance.

FY 2005: Future Directions in Obesity Research
As part of the overall trans-NIH assault on obesity, NCCAM will cosponsor two major initiatives in obesity research, *Neurobehavioral Basis of Obesity and Prevention and Treatment of Pediatric Obesity in Primary Care Settings*. The first seeks to bridge the gap between understanding the molecular and genetic regulation of food intake, and behavioral influences on obesity. The pediatric initiative will evaluate preventive and therapeutic strategies for obesity that could be recommended for children and adolescents in primary care settings, such as a physician's office, primary care clinic, or HMO.

Herbal medicine: Does it work? Is it safe?

An estimated 14% of Americans use herbal supplements, hoping that these botanical products can sustain or restore health. NCCAM is committed to investigating the safety of these products and determining whether they are effective.

Scientific Advances in Research on Herbal Products
In FY 2003, NCCAM-sponsored researchers made significant progress in research on botanicals. The results of one study indicate for the first time that an extract from the root of *Scutellaria baicalensis*, a Chinese herbal medicine also known as Chinese skullcap or Huang Qin, strongly inhibits cancer cell growth in the laboratory setting, both *in vitro* and *in vivo*, especially cells found in head and neck cancers. Each year in the United States, an estimated 70,000 people are diagnosed with head and neck cancers, which are typically resistant to multi-drug chemotherapy. The new study shows that not only does an extract of *S. baicalensis* inhibit the growth of human head and neck squamous cell carcinoma (HNSCC) cells *in vitro*, it also inhibits the activity of the cyclooxygenase-2 (COX-2) enzyme in mice with experimentally induced tumors composed of human cells. HNSCC cells produce large amounts of COX-2, which is necessary for the synthesis of prostaglandin E2 (PGE2), a component of normal cell membranes that accumulates to high levels in the tumors. The anticancer activity of *S. baicalensis* extract may be due to its ability to inhibit the synthesis of PGE2. Future studies will determine the herb's effects on regulating the cell replication cycle, and whether it can be used safely and effectively to treat patients suffering head and neck cancers.

In addition to confirming that some botanicals have promising effects on health related outcomes, NCCAM researchers found others that fail to show the benefits claimed. One example is guggulipid, a botanical extracted from the resin of the mukul myrrh tree (*Commiphora mukuk*), and marketed in the United States as a dietary supplement to help control blood cholesterol levels and maintain a "healthy heart." NCCAM-funded scientists found that neither the standard, or even higher doses of guggulipid significantly lowers the levels of the key low-density lipoprotein (LDL) form of cholesterol in people with high blood cholesterol. In the study, 103 adults with high blood cholesterol were randomly divided into three groups to test the effects of two doses of a standardized guggulipid extract against placebo. After eight weeks, there was no significant change in the levels of blood cholesterol, high-density lipoprotein cholesterol, or very low-density lipoprotein cholesterol in people receiving either dose of guggulipid extract.

Another study investigated whether supplementing a normal diet with cocoa products, including chocolate, reduces two known risk factors for cardiovascular disease—the oxidation of LDLs and certain inflammatory responses. Cocoa products contain flavonoids, chemicals with antioxidant and anti-inflammatory properties that occur in certain plant-derived foods including chocolate, cocoa, tea, grapes, and red wine. NCCAM-sponsored scientists studied 25 healthy volunteers whose diet was supplemented with cocoa products (36.9 g of dark chocolate bar and 30.95 g of cocoa powder drink) for 6 weeks. The investigators found that the consumption of cocoa products may help prevent LDL oxidation and possibly reduce the risk of cardiovascular disease, but they do not have anti-inflammatory effects, as measured by a series of biomarkers that are measures of lipid oxidation. The study does not point to a clear strategy for advising people to increase their consumption of cocoa products. NCCAM is actively pursuing research on other botanicals, like curcumin, with greater evidence of anti-inflammatory effects.

FY 2005: Future Directions in Research on Botanicals

In FY 2005, NCCAM will sponsor three important research initiatives on the use of botanicals as dietary supplements. One initiative, the Botanical Research Centers Program (BRCP), will support multidisciplinary studies of botanicals with the goal of generating information that could provide clear evidence regarding their public health benefits. The BRCP is a refinement of the botanical centers program set in place by NCCAM in partnership with the NIH Office of Dietary Supplements (ODS) and the National Institute of Environmental Health Sciences. These new centers will emphasize preclinical research, *in vitro* and in animal models, to define the chemical and biological effects of botanicals that may help predict their safety and effects in humans. The information could be used to develop strategies for Phase I and II clinical trials.

Importance of Herb-Drug interaction Research

Each week many Americans are at risk for interactions between drugs and herbal products or other natural supplements; a recent survey showed that 16 percent of U.S. adults taking prescription drugs were also using herbal products or other natural supplements at the same time. Herbal products are complex mixtures of naturally occurring chemical compounds, some of which are the basis for current prescription drugs. Therefore, they could have a broad array of interactions with conventional drugs. Herbals can enhance drug activity and evoke greater drug toxicity, or they can speed the metabolism of drugs and diminish their therapeutic benefits. Research has already shown that some herbal products interact with drugs by inhibiting or inducing the activity of specific enzymes in the liver that are critical for drug metabolism and elimination. Two specific enzymes, CYP3A4 and CYP2D6, are involved in the metabolism of approximately 80 percent of all drugs.

In 2003, NIH grantees published results showing the effect of selected herbal extracts on these two enzymes. For example, when extracts of garlic, *Ginkgo biloba*, or Siberian ginseng were given at doses comparable to those in dietary supplements, no effects on either CYP3A4 or CYP2D6 enzymes was seen. This suggests they are unlikely to alter blood levels and activities of most drugs. However, St. John's wort and the botanical mixture PC SPES, used by thousands of men with advanced prostate cancer, induced the activity of the CYP3A4 enzyme, potentially accelerating the metabolism of certain drugs including ones used to treat solid tumors, which would then reduce the drug's effectiveness. In addition, North American ginseng inhibited the activity of three additional liver enzymes that help metabolize certain drugs. This could lead to the accumulation of otherwise beneficial drugs at toxic levels. These studies illustrate the importance of examining the impact of commonly used herbals on drug metabolism in order to prevent potentially serious herb-drug interactions and NCCAM is leading the national effort to do so.

NCCAM, also in partnership with the ODS, has developed a comprehensive strategy for analyzing botanicals and developing more standardized products for use in rigorous basic and clinical studies. In FY 2004, NCCAM will initiate a program to ensure the character, quality, and purity of biologically active agents used in NCCAM-supported studies. In FY 2005, NCCAM and ODS plan to establish a Pharmacokinetic Assay Resource Center (PARC) to conduct *in vivo* testing of dietary supplements, including botanical products, and functional foods, such as studies of dose ranging, pharmacokinetics, and CAM-drug interactions. The PARC would allow quick and reliable screening for product manufacturers and information on dosing and formulations for researchers' use of products in Phase II and III clinical trials.

Another research initiative, *Basic and Clinical Research on Silybum marianum (milk thistle) in the Treatment of Hepatic Diseases*, will continue *in vitro* and animal studies to identify the biological effects of milk thistle, which is the most thoroughly studied botanical product used to treat liver disease. The research will include preliminary clinical studies to assess the effects of different doses of silymarin, derived from the milk thistle plant, to treat liver disease.

Discovering How Acupuncture Works and When To Use It

Acupuncture is one of the oldest, most common medical procedures in the world. Originating in China more than 2,000 years ago, the use of acupuncture to relieve or prevent pain has grown in popularity in the United States. A 1997 report from a Consensus Development Conference on acupuncture held at the National Institutes of Health (NIH) indicated that acupuncture is being "widely" practiced. NCCAM is evaluating the safety and efficacy of acupuncture, its possible mechanisms of action, and its ability to supplement or be an alternative to standard medication.

Science Advances in Acupuncture Research

NCCAM-funded researchers reported results of two significant studies of acupuncture and related techniques in FY 2003. In one study, scientists showed that electroacupuncture, a modern form of acupuncture in which electrical current is applied to the needles, may be an effective, non-invasive way to treat vomiting and symptoms of nausea. Abnormalities in gastric electrical rhythms (gastric dysrhythmia) can occur following a viral illness, in association with diabetes mellitus, or as a complication of certain types of gastric surgery. Not all patients have symptoms, but many experience severe nausea and protracted vomiting.

To determine whether electroacupuncture can reduce vomiting and other symptoms of nausea, NCCAM researchers evaluated the short-term effects of three different methods of electrical stimulation (short-pulse stimulation, long-pulse stimulation, and electroacupuncture) in dogs with motion sickness-like symptoms, including vomiting, induced by intravenous administration of vasopressin. Short-pulse stimulation and electroacupuncture, but not long-pulse stimulation, prevented vasopressin-induced vomiting and related symptoms. However, these two therapies had no effect on symptoms following a type of gastric surgery known as vagotomy. In contrast, long-pulse stimulation, but not short-pulse stimulation or electroacupuncture, could prevent vasopressin-induced gastric dysrhythmias but had no effect on vasopressin-induced nausea.

A second NCCAM-sponsored study indicates that electroacupuncture in combination with antiemetic drugs may be an effective treatment for the nausea and vomiting induced by chemo-therapy. The study was conducted in ferrets that received cyclophosphamide, a common chemotherapy agent. Like humans, ferrets often experience emesis following cyclophosphamide administration. The results indicate that electroacupuncture is most effective in preventing cyclophosphamide-induced emesis when used with a particular class of antiemetic drugs that act on serotonin receptors in the digestive tract. These laboratory studies confirm and extend preliminary observations from small clinical trials in which electroacupuncture appeared to relieve chemotherapy-induced vomiting.

FY 2003 Awards: Learning More About Acupuncture Therapy

NCCAM has awarded a grant to establish one of its first Centers of Excellence in CAM Research. This center will focus on determining the precise nerve and brain pathways that mediate the physiological effects of acupuncture. In addition, NCCAM funded a range of studies on acupuncture. Three involve the use of acupuncture to reduce pain, two are designed to reveal how acupuncture affects human brain activity, two will evaluate whether acupuncture helps alleviate irritable bowel syndrome, and three projects will test the effects of acupuncture on aspects of relaxation, mental health, and addiction.

One major clinical trial will assess whether acupuncture needling is more effective than placebo acupuncture; whether acupuncture needling tailored to the individual is more effective than standardized acupuncture; whether the placement of needles determines the effectiveness of acupuncture therapy; and whether acupuncture is a more effective therapy for chronic lower back pain than standard care. In another study, NCCAM researchers will use whole brain functional magnetic resonance imaging in combination with psychophysical, physiological, and genotyping measures to assess the effects of acupuncture. An important clinical pilot project will explore

whether acupuncture can be used to help treat major depression, a serious mental illness that affects nearly 10 million Americans each year.

Investigating New Therapies for Neurological and Neurodegenerative Disorders
Millions of Americans suffer from chronic neurodegenerative disorders, including multiple sclerosis (250,000-350,000), Alzheimer's (4.5 million), Parkinson's (500,000), and Huntington's diseases (30,000). Many others have experienced traumatic injury to the brain or spinal cord, which can result in severe disability. NCCAM research focuses on understanding and treating neurological and neurodegenerative disorders using *in vitro* studies, animal models, and small, targeted studies in affected populations.

Scientific Advances in Research on Neurological and Neurodegenerative Diseases
The prevalence of Alzheimer's disease (AD) may triple by the year 2050 as baby boomers age. There is no cure for AD; current forms of drug treatment aim to slow the decline in cognitive function. Recent data suggest that *Ginkgo biloba* extract can enhance cognitive function in AD patients, although these claims are not based on robust clinical trials. In FY 2003, NCCAM-funded researchers tested the effects of *Ginkgo biloba* treatment in transgenic mice that were genetically engineered to develop beta-amyloid plaques and a form of memory loss, molecular and neuropsychological findings like those seen in human AD. The researchers found that treating the mice for six months with oral *Ginkgo biloba* extract before any Alzheimer's-like symptoms appeared prevented much of the age-dependent impairment of spatial learning and memory observed in aged transgenic mice that did not receive *Ginkgo biloba*. However, *Ginkgo biloba* treatment had no effect on soluble beta amyloid levels or amyloid plaque deposition in the AD mouse model, leaving it unclear how this herbal product was able to alleviate age-dependent cognitive decline in the transgenic mice.

Two other NCCAM-sponsored studies explored different aspects of the complex series of events that follow traumatic spinal cord injury, and suggested possible strategies for treatment. The first study indicated that the death of nerve cells and their neighboring oligodendrocytes following spinal cord injury in rats is triggered in part by the overproduction of tumor necrosis factor alpha (TNF-α). Oligodendrocytes are non-neuronal cells of the central nervous system that make myelin, a fatty, insulating sheath necessary for normal nerve cell signaling. The recent study showed that levels of TNF-α peak within 1 hour after spinal cord injury is induced in rats, followed at four hours by an increase in nitric oxide (NO) levels. NO and the enzyme that makes it, iNOS, mediate cell death, a process called apoptosis. The NCCAM researchers blocked the ability of TNF-α to activate iNOS and raise NO levels by giving the rats antibodies against TNF-α. The new data suggest that, after spinal cord injury, TNF-α activates iNOS, which raises the tissue levels of NO, which then induces cell death. Because a number of herbal supplements have been shown to inhibit production of TNF-α, it may be possible to develop new therapeutic strategies for spinal cord injury.

NCCAM researchers have explored whether the age-related declines in cognitive function and neuropsychological performance in men are related to a decrease in circulating testosterone levels. Researchers conducted a long-term study of 407 male volunteers from the Baltimore Longitudinal Study of Aging. The average age of subjects at the start of the study was 64 years (range: 51 to 90

years), and the average duration of followup was 9.7 years. The results indicated that men who had a higher free testosterone concentration (FTI) tended to score better on tests of visual and verbal memory, visuospatial functioning, and visuomotor scanning. There were no associations between total testosterone or FTI and measures of verbal knowledge, mental status, or depressive symptoms. These results indicate a possible beneficial effect of circulating FTI on certain forms of cognitive performance in older men. Some dietary supplements boost androgenic (male) hormones, suggesting that they may slow some signs of aging. As in the Women's Health Initiative study of the female hormones estrogen and progestin, it is not known whether this anti-aging strategy would prove safe.

FY 2003 Awards: Neurological and Neurodegenerative Disorders
In FY 2003, NCCAM awarded funds to assess several CAM strategies for alleviating pain and the symptoms of chronic neurological conditions, including multiple sclerosis and fibromyalgia. One study is designed to assess whether plant-derived estrogens can suppress the symptoms of multiple sclerosis (MS) in mice induced to develop a similar condition. Another study will explore possible therapies, such as the Flexyx Neurotherapy System (FNS), which is a new form of biofeedback using electroencephalograph (EEG) or brainwave information.

Investigating Brain-Body Interactions

NCCAM's research program on brain-body (or mind-body) interactions includes studies of the interactions among cognition, emotion, personality, social relationships, and health. Many underlying processes affect the emotional and medical outcome of patients with chronic and life-threatening diseases. NCCAM scientists are interested in exploring a range of CAM techniques, including hypnosis, acupuncture, massage, psychotherapy, guided imagery, yoga, and relaxation, that may help enhance the physical and psychological well-being of patients.

To broaden and strengthen its research on brain-body interactions, NCCAM initiated a two-tiered research program in FY 2003. The first component of the program, *Mind-Body Interactions and Health: Exploratory/Developmental Research Program*, will foster interdisciplinary collaboration and innovation in mind-body and health research and provide essential and cost-effective core services to support the development, conduct, and translation into practice of mind-body and health research. NCCAM has announced a partner initiative, *Research on Mind-Body Interactions and Health*, to be awarded in FY 2004. The program will encourage interdisciplinary collaboration and innovation towards understanding the processes underlying mind-body interactions and health, and to help translate basic knowledge into interventions and clinical practices that promote health and prevent or treat disease and disabilities.

Scientific Advances in Research on Brain-Body Interactions
The combination of exercise and meditation has been recommended by ancient Chinese and Indian physicians to improve health. In recent decades these types of therapies have been said to improve performance, at least in part by boosting one's immunity. Yet, there has been little formal evidence for this assertion until now. In FY 2003, NCCAM-funded researchers completed a study to determine whether a form of the Chinese exercise regimen Tai Chi could improve physical

performance and boost immunity, as measured by lymphocyte responses to the virus that causes chickenpox , the varicella zoster virus (see box below). As we age, our immunity to this common virus wanes, until the infection can reactivate from its dormant state in nerves, to cause the painful eruption known as shingles. The results of the study indicate that older adults who participated in a form of Tai Chi for 15 weeks showed a statistically significant increase in specific immune responses against varicella zoster virus and improved physical health.

TAI CHI Improves Virus-Specific Immunity in Elderly with Shingles

In a remarkable melding of an ancient healing practice and modern science, NCCAM grantees at the University of California, San Diego showed that Tai Chi significantly boosts the body's immunity to a debilitating viral infection and enhances one's overall feeling of health and level of activity. Tai Chi is a traditional Chinese exercise that combines disciplined exercise and meditation. Sometimes described as "yoga in motion," it has long been held to promote health and resistance to illness. The grantees tested whether Tai Chi can enhance specific immunity to the herpesvirus that causes shingles and whether that increase would correlate with overall improvement in measures of health. Shingles, or herpes zoster, is a painful skin infection that develops in about 20 percent of people who previously had chickenpox, about 300,000 Americans a year. The virus that causes chickenpox the varicella zoster virus (VZV) remains in the body in a dormant, or latent, state for life after the initial infection, but the immune system helps keep it from reactivating. As people age, the immunity to VZV declines, gradually increasing the chances that the virus will reemerge and cause shingles. Thus, most people with shingles are over 60 years old. The reemergence of VSV correlates directly with a decrease in the number and activity of specific immune system cells. Although there are antiviral drugs to lessen the duration and pain of shingles, the infection cannot be prevented or cured. The pain of shingles generally recedes in a few weeks or months, but about 10 percent of older patients experience prolonged and debilitating discomfort. The aging of the Baby Boomer generation means that the population at highest risk of painful shingles is expanding rapidly.

In the recent NCCAM study, 36 individuals over age 60 agreed to take either 15 weeks of classes in Tai Chi Chih (a highly structured version of tai chi designed with older people in mind) or to remain on a waiting list for those classes, acting as the study's control group. Blood tests showed that those participating in the classes developed more than a 50 percent increase in the immune system cells that suppress shingles as compared with controls. More important, the Tai Chi group members also showed significant improvements in everyday physical activities, such as carrying packages, walking, and climbing stairs. Those participants who before Tai Chi had the greatest impairments in physical activity experienced the greatest gains from the program. No significant changes in physical performance were evident in the control group who had not yet received Tai Chi instruction.

This is the first scientific study to demonstrate that a complementary or alternative medical therapy is responsible both for improvements in physical function and in virus-specific immunity. Although immunity to VZV was tested specifically in this study, the cells responsible for immune system memory are critical in defense against a wide range of viral infections. Consequently, the findings of this research may be relevant to resistance against an array of infections that challenge the health of aging Americans. Because this study was relatively small and of short duration, additional research is needed to verify the benefits of Tai Chi on the immune system and its potential for improving immunity and functioning in the elderly. These promising followup studies are being supported by NIH.

Irwin MR, Pike JL, Cole JC, and Oxman MN. Effects of a behavioral intervention, tai chi chih, on varicella-zoster virus specific immunity and health functioning in older adults. Psychosom Med. 2003 Sep-Oct;65(5):824-30

FY 2003 Awards: Quantifying Brain-Body Interactions

NCCAM awarded grants to examine various aspects of brain-body interactions, spanning an array of interventions that include yoga, home-based massage, and shamanic healing, as well as the effects of spirituality on health. The goal of one project, an international collaboration, is to fund the planning, assessment, and resource development needed to conduct Phase I pilot trials and Phase II clinical trials on the efficacy of yoga-based interventions, as well as two pilot studies of yoga as a behavioral intervention. Another study will investigate whether spirituality and religiosity have a significant influence on immune system functioning.

CAM Therapies and HIV/AIDS

Recent advances in antiviral therapies have dramatically prolonged the lives of patients with HIV/AIDS, but the disease continues to be emotionally devastating and relentlessly progressive; many people taking antiviral drugs experience adverse side effects. A study conducted at the NIH Clinical Center showed that as many as 91% of people with HIV/AIDS use various forms of CAM for many reasons. Persons with HIV/AIDS may use massage and energy therapies to lessen the emotional and psychological impact of the disease. Some reports indicate that stress management techniques or aerobic and resistance exercise improve the quality of life and sense of well-being. Some preliminary recent reports suggest the possibility of using CAM to treat HIV infection more directly, possibly by modulating immune system function. To address these and other issues, NCCAM is supporting a range of studies to identify potential roles for CAM in the treatment of HIV/AIDS and its complications, and to ameliorate the adverse effects of antiviral drug therapy.

FY 2003 Awards in Research on HIV/AIDS
NCCAM awarded a range of HIV/AIDS research projects. Three studies aim to identify CAM therapies, such as acupuncture, that will help improve the quality of life for people with HIV/ AIDS by relieving debilitating symptoms. Another study will investigate whether alpha-lipoic acid, a naturally occurring chemical that acts as an antioxidant at high doses, helps alleviate the painful neuropathy that occurs in 70 percent of people with advanced AIDS. Another award will fund a collaboration between U.S. scientists and investigators in India.

Two projects will explore the interactions of commonly used botanicals with drugs that are part of the HAART regimen now prescribed for many HIV/AIDS patients. One study will evaluate whether olive leaf extract, taken to reduce the side effects of HAART, affects the activity of three anti-HIV drugs. Researchers will also examine whether olive leaf extract alone has antiviral effects and, if so, by what mechanism of action. The second project will determine whether three botanicals—piperine, silymarin, and glucarate—that modulate glucuronidation interfere with the metabolism of anti-HIV drugs. Glucuronidation is a key step in the biochemical pathway that metabolizes drugs, including those used in the management of HIV/AIDS.

FY 2005: Future Research Directions in Research on HIV/AIDS
In FY 2005, NCCAM plans to make awards under a new multidisciplinary research initiative, *Use of Complementary and Alternative Medicine (CAM) in the Management of HIV/AIDS,* to determine mechanisms of action, safety, pharmacology, and potential clinical utility of CAM approaches to treat HIV/AIDS. The project, a new partnership between NCCAM and the National Institute of Allergy and Infectious Diseases, will support experienced and new investigators in institutions that have a history of HIV/AIDS research and have a record of developing programs in basic, translational, and early-phase clinical research for promising CAM therapies. The research will investigate the range of potential uses as well as the risks of CAM in the treatment of HIV/AIDS.

Restructuring NCCAM Research Centers Program

In response to the recommendations of an expert panel convened in 2002 to review its Research Centers Program, NCCAM refined its approach to organizing and funding research centers in FY 2003. NCCAM now offers a range of support mechanisms that will provide funding for the first time for centers at both research-intensive and CAM institutions.

For investigators with proven research records, NCCAM initiated a program of Centers of Excellence in CAM Research to study the mechanisms and clinical potential of CAM practices. These centers will undertake multiple research projects organized around a specific, CAM-related scientific theme. NCCAM awarded two centers of excellence in FY 2003, one focusing on the neurobiological basis of acupuncture and acupuncture analgesia using neuroimaging techniques, and a second on the effects of antioxidant therapies. NCCAM anticipates funding additional centers of excellence each year through FY 2005.

For CAM institutions with emerging research expertise, NCCAM has introduced a program of developmental research centers to strengthen the research capacity of these institutions by forging partnerships between them and research-intensive institutions. NCCAM established two developmental research centers in FY 2003, one focusing on effects and mechanisms of chiropractic manipulation, and a second looking at Oriental medical systems, particularly acupuncture. NCCAM hopes to fund additional such centers in FY 2004 and 2005.

For international CAM investigators with limited research experience, NCCAM awarded planning grants to assist in developing applications for a research center. In FY 2003, NCCAM awarded 10 planning grants to U.S. and international institutions that are collaborating to design and implement research on CAM approaches that have emerged from traditional indigenous medical systems. These two-year partnerships will create the infrastructure and scientific foundation for multidisciplinary research on CAM; it is anticipated that in FY 2005 one or more of these collaborations will be named NCCAM’s first International Centers for CAM Research.

In addition to these newly established centers, NCCAM continues to support two exploratory program grants for research on frontier medicine—CAM practices for which no conventional biomedical explanation exists. These centers are conducting pilot and feasibility studies, which will be completed in FY 2005. It is anticipated that with the substantial developmental funding they received, investigators at these centers will be better prepared to design and submit meritorious applications to extend their work.

Across the NIH, research centers are supported through a variety of funding mechanisms, some of which are reflected in the 'centers' line of the NIH budget and some of which are not. Originally, almost all of NCCAM's centers were funded using the specialized research centers mechanism (P50) that is reflected in the centers line. An expert panel reviewed the centers program and recommended that NCCAM use a wider variety of mechanisms to support its centers programs. In particular, this panel noted that institutions that specialize in complementary and alternative medicine (CAM) were either not competitive for or lacked the infrastructure to succeed as P50 centers. Thus, as many of NCCAM's current P50 centers conclude their work, comparable levels of investments are being

diversified using U19 developmental centers awards for CAM institutions, P01 awards for research intensive centers of excellence, and R21planning grants for international research centers. While these mechanisms provide a comprehensive, multi-level centers program, none of them appear in the 'centers' line of budget mechanism tables. This action affirms NCCAM's commitment to strong research centers by taking measured steps to enhance their effectiveness and diversity.

Future Directions in NCCAM Research

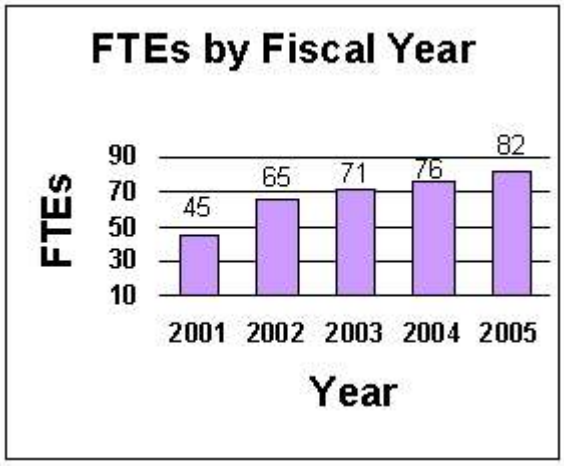
Future decisions about NCCAM-sponsored programs will be guided by a set of principles developed to fill gaps in NCCAM's research portfolio, capitalize on emerging opportunities to advance CAM research, and leverage the expertise and resources of other NIH institutes and centers. The guiding principles are to: (1) elucidate CAM mechanisms of action; (2) conduct small, well-developed Phase I and II clinical trials as preludes to more definitive studies; (3)
build critical research infrastructure in CAM institutions; and (4) encourage collaborations between conventional and CAM institutions.

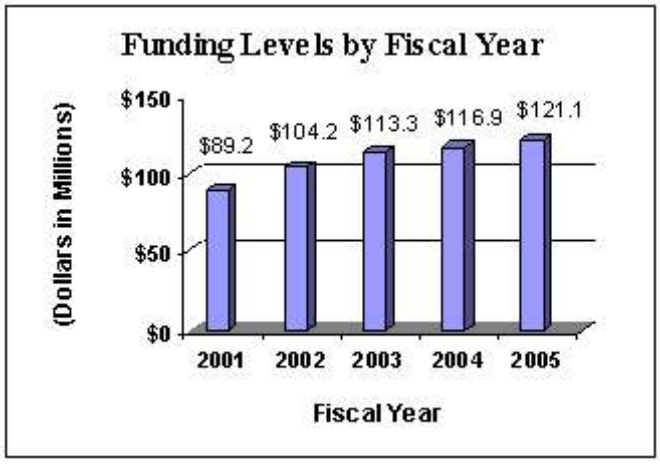
NCCAM will continue to build its research portfolio with a focus on priority areas of science, such as those described for FY 2005—obesity, botanicals, acupuncture, brain-body interactions, neurodegenerative conditions, and HIV/AIDS. NCCAM will also continue to pursue activities that correspond to the NIH Roadmap efforts. This will benefit NCCAM grantees in a variety of ways: by providing an interdisciplinary collective for increased training and research opportunities, and widening access to research tools, services, and patient communities. Thus, by adhering to guiding principles, focusing on high-priority research, and supporting a balanced portfolio of awards to individual investigators, research centers, and international programs, NCCAM will verify the safety and effectiveness of a range of CAM products and practices to meet public health needs.

Budget Policy

The Fiscal Year 2005 budget request for the NCCAM is $121,116,000, an increase of $4,173,000 and 4.0 percent over the FY 2004 Final Conference Level. Also included in the FY 2005 request is NCCAM's support for the trans-NIH Roadmap initiatives, estimated at 0.63% of the FY 2005 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 NIH Overview.

A five year history of FTEs and Funding Levels for NCCAM are shown in the graphs below. Note that the Fiscal Year 2001 FTE figure is not comparable to the figures in the succeeding years due to NIH's consolidation of its Human Resources function in FY 2003.

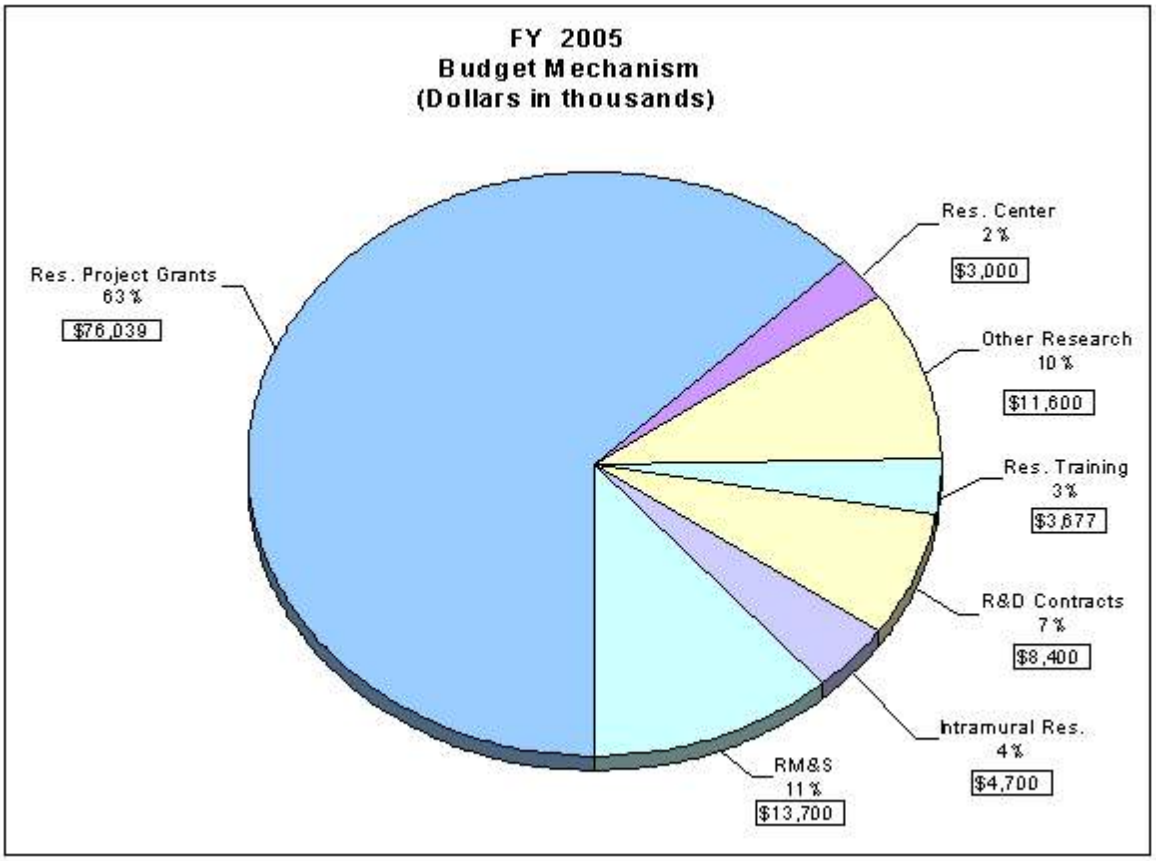


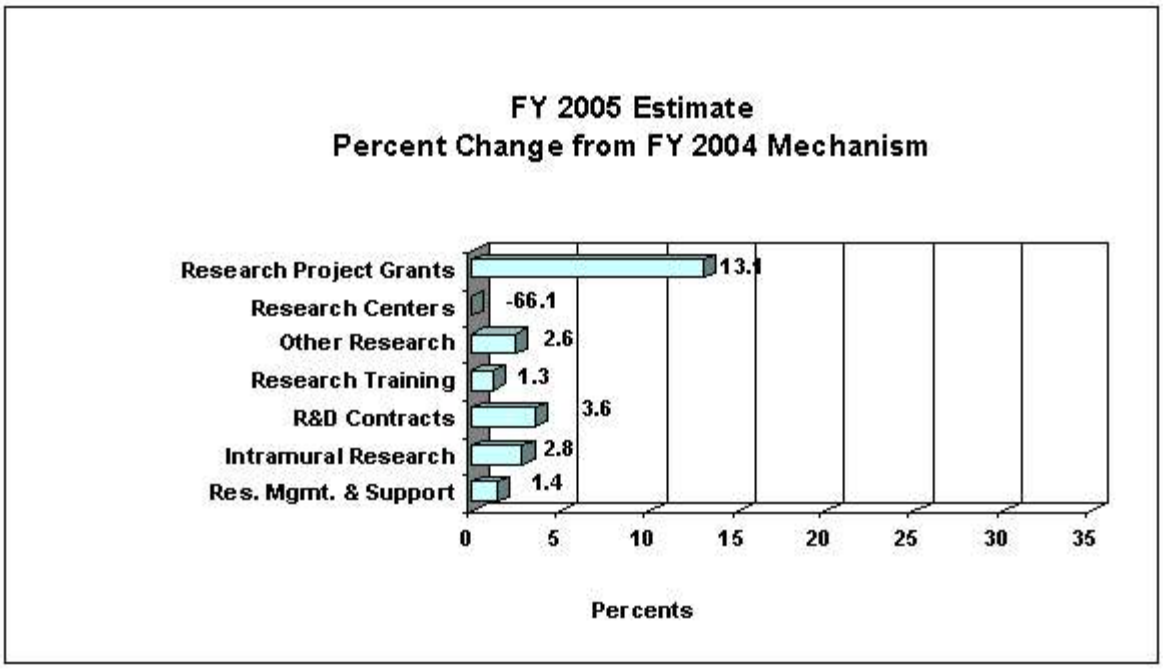


NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The FY 2005 NIH request provides for an aggregate 1.3 percent increase in average cost for Research Project Grants, consistent with the Gross Domestic Product Deflator. The NCCAM is providing an average cost increase of 1.9 percent for direct recurring costs in noncompeting continuation awards. Competing RPGs are based on an average cost increase of 1 percent.

Advancement in medical research is dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2005 request, NCCAM will support 79 pre- and post-doctoral trainees in full-time training positions. Stipend levels for pre-doctoral and post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will remain at FY 2004 levels.

The Fiscal Year 2005 request includes funding for 6 research centers, 59 other research grants, including 17 clinical career awards, and 13 R&D contracts. Intramural Research and Research Management and Support receive increases of 2.8% and 1.4% respectively to support increased pay and estimated inflationary increases in FY 2005.
The mechanism distribution by dollars and percent change are displayed below:


FY 2005
Budget Mechanism
(Dollars in thousands)
Res. Center
2%
$3,000
Other Research
10%
$11,600
Res. Training
3%
$3,677
R&D Contracts
7%
$8,400
Intramural Res.
4%
$4,700
RM&S
11%
$13,700
Res. Project Grants
63%
$76,039


FY 2005 Estimate
Percent Change from FY 2004 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
13.1
-66.1
2.6
1.3
3.6
2.8
1.4
0
5
10
15
20
25
30
35
Percents

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Budget Mechanism - Total

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	87	$34,023,000	98	$39,089,000	113	$43,442,000
Administrative supplements	(10)	1,394,000	(10)	1,000,000	(10)	1,000,000
Full funded	1	125,000	1	125,000	1	126,000
Single year	65	18,232,000	83	24,073,000	98	28,706,000
Renewal	1	222,000	1	228,000	2	460,000
New	64	18,010,000	82	23,845,000	96	28,246,000
Supplements	0	0	0	0	0	0
Subtotal, competing	66	18,357,000	84	24,198,000	99	28,832,000
Subtotal, RPGs	153	53,774,000	182	64,287,000	212	73,274,000
SBIR/STTR	11	2,543,000	11	2,670,000	12	2,765,000
Subtotal, RPGs	164	56,317,000	193	66,957,000	224	76,039,000
Research Centers:						
Specialized/comprehensive	14	16,460,000	9	8,857,000	6	3,000,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	14	16,460,000	9	8,857,000	6	3,000,000
Other Research:						
Research careers	31	4,714,000	33	4,973,000	33	5,100,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	1,000,000	0	0	0	0
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	25	6,168,000	26	6,338,000	26	6,500,000
Subtotal, Other Research	56	11,882,000	59	11,311,000	59	11,600,000
Total Research Grants	234	84,659,000	261	87,125,000	289	90,639,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	14	463,000	14	479,000	14	479,000
Institutional awards	63	3,013,000	64	3,152,000	65	3,198,000
Total, Training	77	3,476,000	78	3,631,000	79	3,677,000
Research & development contracts	13	8,440,000	13	8,110,000	13	8,400,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	13	3,659,000	16	4,570,000	19	4,700,000
Research management and support	58	13,033,000	60	13,507,000	63	13,700,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NCCAM	71	113,267,000	76	116,943,000	82	121,116,000
(RoadMap Support)		(0)		(402,000)		(762,000)
(Clinical Trials)		(38,980,769)		(40,200,000)		(41,500,000)

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Extramural Research and Training		$96,575		$98,866		$102,716		$3,850
Subtotal, Extramural research		96,575		98,866		102,716		3,850
Intramural research	13	3,659	16	4,570	19	4,700	3	130
Res. management & support	58	13,033	60	13,507	63	13,700	3	193
Total	71	113,267	76	116,943	82	121,116	6	4,173

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Summary of Changes

FY 2004 Final Conference				$116,943,000
FY 2005 Estimated Budget Authority				121,116,000
Net change				4,173,000
	FY 2004 Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$1,253,000		$20,000
b. Annualization of January 2004 pay increase		1,253,000		13,000
c. January 2005 pay increase		1,253,000		14,000
d. One less day of pay		1,253,000		(5,000)
e. Payment for centrally furnished services		798,000		24,000
f. Increased cost of laboratory supplies, materials, and other expenses		2,519,000		10,000
Subtotal				76,000
2. Research Management and Support:				
a. Within grade increase		6,345,000		106,000
b. Annualization of January 2004 pay increase		6,345,000		65,000
c. January 2005 pay increase		6,345,000		73,000
d. One less day of pay		6,345,000		(24,000)
e. Payment for centrally furnished services		1,609,000		47,000
f. Increased cost of laboratory supplies, materials, and other expenses		5,553,000		37,000
Subtotal				304,000
Subtotal, Built-in				380,000

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Summary of Changes--continued

CHANGES	FY 2004 Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	98	$40,089,000	15	$4,353,000
b. Competing	84	24,198,000	15	4,634,000
c. SBIR/STTR	11	2,670,000	1	95,000
Total	193	66,957,000	31	9,082,000
2. Research centers	9	8,857,000	(3)	(5,857,000)
3. Other research	59	11,311,000	0	289,000
4. Research training	78	3,631,000	1	46,000
5. Research and development contracts	13	8,110,000	0	290,000
Subtotal, extramural				3,850,000
	FTEs		FTEs	
6. Intramural research	16	4,570,000	3	54,000
7. Research management and support	60	13,507,000	3	(111,000)
Subtotal, program		116,943,000		3,793,000
Total changes	76		6	4,173,000

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Budget Authority by Object

	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease	Percent Change
Total compensable workyears:				
Full-time employment	76	82	6	7.9
Full-time equivalent of overtime & holiday hours	0	0	0	0.0
Average ES salary	$0	$0	$0	0.0
Average GM/GS grade	11.9	12.0	0.1	0.8
Average GM/GS salary	$74,259	$76,784	$2,525	3.4
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$85,032	$86,648	$1,616	1.9
Average salary of ungraded positions	$128,342	$130,781	$2,439	1.9

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease	Percent Change
Personnel Compensation:				
11.1 Full-Time Permanent	$4,204,000	$4,619,000	$415,000	9.9
11.3 Other than Full-Time Permanent	1,372,000	1,510,000	138,000	10.1
11.5 Other Personnel Compensation	121,000	134,000	13,000	10.7
11.7 Military Personnel	218,000	242,000	24,000	11.0
11.8 Special Personnel Services Payments	121,000	134,000	13,000	10.7
Total, Personnel Compensation	6,036,000	6,639,000	603,000	10.0
12.1 Civilian Personnel Benefits	1,434,000	1,574,000	140,000	9.8
12.2 Military Personnel Benefits	128,000	142,000	14,000	10.9
13.0 Benefits for Former Personnel	0	0	0	0.0
Subtotal, Pay Costs	**7,598,000**	**8,355,000**	**757,000**	**10.0**
21.0 Travel & Transportation of Persons	145,000	148,000	3,000	2.1
22.0 Transportation of Things	35,000	37,000	2,000	5.7
23.1 Rental Payments to GSA	0	0	0	0.0
23.2 Rental Payments to Others	4,000	5,000	1,000	25.0
23.3 Communications, Utilities & Miscellaneous Charges	105,000	107,000	2,000	1.9
24.0 Printing & Reproduction	60,000	62,000	2,000	3.3
25.1 Consulting Services	0	0	0	0.0
25.2 Other Services	5,100,000	5,026,000	(74,000)	-1.5
25.3 Purchase of Goods & Services from Government Accounts	8,347,000	8,420,000	73,000	0.9
25.4 Operation & Maintenance of Facilities	35,000	37,000	2,000	5.7
25.5 Research & Development Contracts	3,346,000	3,136,000	(210,000)	-6.3
25.6 Medical Care	130,000	132,000	2,000	1.5
25.7 Operation & Maintenance of Equipment	80,000	83,000	3,000	3.8
25.8 Subsistence & Support of Persons	0	0	0	0.0
25.0 Subtotal, Other Contractual Services	**17,038,000**	**16,834,000**	**(204,000)**	**-1.2**
26.0 Supplies & Materials	750,000	775,000	25,000	3.3
31.0 Equipment	450,000	475,000	25,000	5.6
32.0 Land and Structures	0	0	0	0.0
33.0 Investments & Loans	0	0	0	0.0
41.0 Grants, Subsidies & Contributions	90,756,000	94,316,000	3,560,000	3.9
42.0 Insurance Claims & Indemnities	0	0	0	0.0
43.0 Interest & Dividends	2,000	2,000	0	0.0
44.0 Refunds	0	0	0	0.0
Subtotal, Non-Pay Costs	**109,345,000**	**112,761,000**	**3,416,000**	**3.1**
Total Budget Authority by Object	**116,943,000**	**121,116,000**	**4,173,000**	**3.6**

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Salaries and Expenses

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$4,204,000	$4,619,000	$415,000
Other Than Full-Time Permanent (11.3)	1,372,000	1,510,000	138,000
Other Personnel Compensation (11.5)	121,000	134,000	13,000
Military Personnel (11.7)	218,000	242,000	24,000
Special Personnel Services Payments (11.8)	121,000	134,000	13,000
Total Personnel Compensation (11.9)	**6,036,000**	**6,639,000**	**603,000**
Civilian Personnel Benefits (12.1)	1,434,000	1,574,000	140,000
Military Personnel Benefits (12.2)	128,000	142,000	14,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**7,598,000**	**8,355,000**	**757,000**
Travel (21.0)	145,000	148,000	3,000
Transportation of Things (22.0)	35,000	37,000	2,000
Rental Payments to Others (23.2)	4,000	5,000	1,000
Communications, Utilities and Miscellaneous Charges (23.3)	105,000	107,000	2,000
Printing and Reproduction (24.0)	60,000	62,000	2,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	0	0	0
Other Services (25.2)	5,100,000	5,026,000	(74,000)
Purchases from Govt. Accounts (25.3)	5,349,000	5,310,000	(39,000)
Operation & Maintenance of Facilities (25.4)	0	0	0
Operation & Maintenance of Equipment (25.7)	80,000	83,000	3,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**10,529,000**	**10,419,000**	**(110,000)**
Supplies and Materials (26.0)	750,000	775,000	25,000
Subtotal, Non-Pay Costs	11,628,000	11,553,000	(75,000)
Total, Administrative Costs	**19,226,000**	**19,908,000**	**682,000**

NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

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

FY 2004 House Appropriations Committee Report Language (H. Rpt. 108-188)

Item

Liver disease – The Committee is aware of efforts to synthesize and calibrate the production of milk thistle for use in clinical trials to demonstrate its value to slow the progression of nonalcoholic steatohepatitis and to reduce the side effects of hepatitis C interferon treatments. The Committee encourages NCCAM to support research into milk thistle. (Page 87)

Action taken or to be taken

Nearly one in ten Americans suffer with the devastating effects of liver disease during their lifetimes. Milk thistle (*Silybum marianum*) is the most frequently used dietary supplement in patients with these disorders. In 2001, milk thistle products ranked 12th in the list of supplements sold in the United States.

In 1999, NCCAM, in conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), held a symposium to review the use of milk thistle in chronic liver disease. While the hepatoprotective properties of milk thistle against a variety of liver toxins seems to be supported by some experimental data, the mechanisms of action and the clinical benefits of milk thistle are not yet well understood. For this reason, current evidence is not sufficient to determine whether milk thistle is safe or effective to treat or prevent liver disease.

Before conducting the required basic and clinical investigations on milk thistle, it is critical that research-grade product is available in quantities large enough to support this research. In FY 2001, to encourage the development of appropriately standardized milk thistle, NCCAM, in collaboration with NIDDK, released a Request for Applications, using the Small Business Innovation Research and Small Business Technology Transfer mechanisms, to provide a reliable, on-going supply of milk thistle for research. Awards were made in 2001 and well-characterized milk thistle product is expected to be available in June 2004. Once this material is available, basic and clinical research studies can be conducted, including studies to elucidate the mechanism of action of milk thistle and randomized, controlled, double-blind studies to test its safety and efficacy for the prevention and treatment of liver disease in humans.

In anticipation of the availability of research-grade milk thistle, NCCAM will explore further collaborations with other NIH Institutes and Centers to better understand the biological effects

and mechanisms of action of milk thistle as well as the safety and efficacy of milk thistle in animals and humans for liver disease. Before conducting large-scale, human clinical trials, it will be incumbent first to study pharmacokinetics, bioavailability, dosing effects, different product delivery formulations, and the safety and efficacy of milk thistle through Phase II studies in humans.

FY 2004 Senate Appropriations Committee Report Language (S. Rpt. 108-81)

Item

Evaluation of data on alternative therapies – The Committee expects that funding of new and existing 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 AHRQ's literature reviews and data-analysis efforts and to develop and disseminate a comprehensive set of fact sheets on CAM therapies to inform the public and health professionals of the state of scientific knowledge about these therapies.

(Page 161)

Action taken or to be taken

While millions of Americans are using complementary and alternative medicine (CAM), few of these practices have been rigorously tested for safety and effectiveness. The National Center for Complementary and Alternative Medicine (NCCAM) is committed to a strong, multifaceted centers program as a keystone for providing meaningful and definitive research on CAM to address this critical public health need.

The study of CAM therapies and modalities presents unique challenges to address, including increasing the visibility and credibility of CAM research and studying whether CAM products that are already used widely by the public are safe and effective. To enhance the level of experience and scientific rigor required to transform the promise of CAM into proven treatments and therapies, in FY 2002, NCCAM convened an expert panel to review the CAM research centers that were established shortly after the Center's creation. Based on the lessons learned from these first centers and, and in response to the evolving scientific opportunities and challenges in CAM research, the expert panel recommended that NCCAM adopt a flexible approach to structuring and supporting research centers and encourage a greater focus on centers' pursuit of original science.

In response to the expert panel's recommendations and consistent with the goals outlined in NCCAM's strategic plans, NCCAM has designed three innovative new programs to build its next generation of research centers: (1) the Centers of Excellence for Research on CAM (CERC) program for established, highly accomplished research institutions; (2) the Developmental Centers for Research on CAM (DCRC) program to support collaborations among CAM institutions and

conventional medical research institutions; and (3) Planning Grants for International Research on CAM (PICRC) to stimulate novel partnerships among international and U.S. institutions. Awards were made under each of these programs in October 2003. The studies that will be undertaken by theses centers should yield more definitive information about the safety, efficacy, and therapeutic potential of CAM practices than was previously available. Additional new awards are planned under the CERC and DERC initiatives in FY 2004 and FY 2005.

NCCAM remains strongly committed to soliciting innovative alternative approaches to the treatment and prevention of disease from CAM practitioners in the field. For example, at the June 2003 meeting of the National Advisory Council for Complementary and Alternative Medicine (NACCAM), NCCAM presented a plan to develop a Cancer Working Group, to be composed of NACCAM members, basic and clinical investigators, practitioners, clinicians, and patient advocates. The Working Group will evaluate CAM practitioners' evidence, including medical records, medical imaging (e.g., x-ray or ultrasound), and pathology reports, in support of a CAM treatment's therapeutic effect on a group of cancer patients. The Working Group, which will hold its initial meeting in June 2004, will continue the work of the Cancer Advisory Panel for Complementary and Alternative Medicine (CAPCAM), whose charter was withdrawn in 2002 during a Federal reduction of chartered advisory committees. NCCAM also conducts multiple outreach activities to encourage and solicit CAM research applications through professional society meetings, workshops, town meetings, targeted advertisements in CAM and conventional scientific periodicals, and web site announcements.

NCCAM fosters productive collaborations with the Centers for Disease Control and Prevention (CDC) and the Agency for Healthcare Research and Quality (AHRQ) through the NIH Trans-Agency CAM Research Coordinating Committee, which NCCAM chairs. NCCAM looks forward to working with the CDC on relevant field investigations, and is exploring potential research partnerships with the CDC Division of Nutrition and Physical Activity. NCCAM continues to support AHRQ's literature reviews and data-analysis efforts. For example, NCCAM, in conjunction with the NIH Office of Dietary Supplements, co-sponsored with AHRQ the largest-ever review of existing scientific literature on ephedra efficacy and safety in weight loss an athletic performance enhancement. The review, released in February 2003, will assist NIH in developing an appropriate research agenda, identifying gaps in knowledge, and suggesting study designs to yield more definitive answers regarding ephedra's safety. NCCAM and AHRQ also are currently funding a literature review and analysis of the safety and efficacy of the hormone and dietary supplement melatonin for sleep disorders. In FY 2003, NCCAM renewed its contract with AHRQ to support these activities.

Providing the public and health care providers with authoritative information on CAM remains a critical element of NCCAM's mission. In FY 2003, NCCAM published numerous fact sheets to inform the public on CAM issues including, *What's in the Bottle? An Introduction to Dietary Supplements*; *Questions and Answers About Homeopathy; and Herbal Supplements: Consider Safety, Too*, which are posted to NCCAM's web site (www.nccam.nih.gov). In FY 2004, NCCAM will publish additional fact sheets to address the scientific evidence for popular CAM

topics including the use of chiropractic to treat back pain and CAM to ameliorate the symptoms of menopause. NCCAM also continues to collaborate with the NIH ODS and the National Cancer Institute (NCI) to develop fact sheets. For example, in FY 2004, NCCAM partnered with ODS to publish a fact sheet, *Botanical Dietary Supplements: Background Information*. In addition, NCCAM and NCI recently updated a fact sheet on the use of CAM in treating cancer.

Item

Chiropractic Research Center – The Committee strongly urges NCCAM to increase support for the chiropractic research center. (Page 161)

Action taken or to be taken

NCCAM remains committed to forging new partnerships between complementary and alternative medicine (CAM) institutions and major research universities. In October 2003, in an innovative effort to advance research on widely used CAM practices, including chiropractic care, NCCAM funded two awards to inaugurate Developmental Centers for Research on Complementary and Alternative Medicine (DCRC), to foster a collaborative CAM research community and to enhance the scientific quality of CAM research.

Through collaborations between established scientific investigators and scientists in CAM institutions, the DCRC initiative will allow the conduct of rigorous exploratory and developmental research projects on CAM. The DCRCs will assist CAM institutions conducting high-quality research, promote research expertise and infrastructure within the CAM community, and support enhanced communication and partnerships between CAM and conventional medical research institutions to enable established researchers to gain the clinical and cultural perspectives required to engage in CAM research. The dynamic DCRC partnerships also are expected to develop and strengthen preliminary CAM research studies that could lead to the submission of competitive R01 grant applications to NIH, the hallmark of a mature scientific research program.

One of first two grants under the DCRC initiative was awarded to the Palmer Center for Chiropractic Research in Davenport, Iowa. Under the award, scientists at the Palmer Chiropractic University will collaborate with investigators at the University of Iowa, Kansas State University, the State University of New York at Stony Brook, and the National University of Health Sciences in Illinois to examine the mechanisms of action and effects of chiropractic manipulation, focusing on the common problem of lower back pain.

Item

Office of Dietary Supplements – The Committee is supportive of the efforts of NCCAM and the Office of Dietary Supplements (ODS) in the study of the beneficial effects of botanical dietary supplements as alternative medical therapies, and especially in the efforts to promote development and employment of reference standards and analytical methods. The Committee strongly encourages the continued cooperation of NCCAM and ODS with the programs of FDA/CFSAN to ensure the safety of botanical dietary supplements. **(**Page 161)

Action taken or to be taken

Botanicals and other natural products, such as dietary supplements, are widely employed by Americans as alternative therapies in the treatment of numerous diseases and conditions. Recent studies, however, affirm great variability in the quality and composition of these commercially available biologic and biologically active products.

The National Center for Complementary and Alterative Medicine (NCCAM) has developed an extensive portfolio of research designed to examine questions regarding the safety and efficacy of dietary supplements, as well as characterizing their basic biochemical activities. As part of this mission, NCCAM continues its productive collaborations with the NIH Office of Dietary Supplements (ODS) and other NIH Institutes and Centers. For example, NCCAM currently is supporting the development of research-grade cranberry products for use in basic and clinical research. In FY 2004, NCCAM, in conjunction with the NIH ODS, National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK), and the National Institute of Dental and Craniofacial Research, will award new grants for basic and clinical studies of these highly characterized products. Also, NCCAM, in collaboration with NIDDK, is supporting the development of clinical-trial grade botanicals (milk thistle, feverfew, and *Echinacea*) through Small Business Innovation Research and Small Business Technology Transfer programs.

As of July 2003, NCCAM requires grant applicants who are interested in studying botanicals and other biologic of biologically active products to certify that the products that they will study are stable and of high quality. This is to elevate the quality and reproducibility of research results on botanical and other dietary supplements and to improve the likelihood that these products studied will prove safe and effective. In addition, NCCAM strongly encourages applicants to seek testing of their products by an independent laboratory. Furthermore, to ensure the safety of the materials tested, NCCAM's terms of awards for clinical trials require applicants to submit human subject research proposals involving biologically based interventions, including botanicals, to the Food and Drug Administration (FDA) to determine whether an Investigational New Drug application is needed.

By mandating evidence of product quality that manufacturers are only voluntarily required ensure, NCCAM has substantially raised the bar for prospective grantees. For this reason, NCCAM, in partnership with the NIH ODS, has developed a comprehensive strategy for analyzing botanicals and developing standardized products for use in rigorous clinical and basic studies. In FY 2004, NCCAM will initiate a program to ensure the character, quality, and purity of biologically active agents used in NCCAM-supported studies. As part of this program, in FY 2005, NCCAM and ODS plan to establish a Pharmacokinetic Assay Resource Center (PARC) to conduct *in vivo* testing of dietary supplements, including botanical products, and functional foods, such as studies of dose ranging, pharmacokinetics, and CAM-drug interactions. The PARC would allow quick and reliable screening for product manufacturers and information on dosing and formulations for researchers' use of products in Phase II and III clinical trials.

As members of the NIH Trans-Agency CAM Research Coordinating Committee, NCCAM, the FDA, and the NIH ODS, maintain productive collaborations regarding botanicals and other research on complementary and alternative medicine. NCCAM will continue to explore opportunities for collaboration with the NIH ODS as well as the FDA.

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2004 Amount Authorized	2004 Final Conference	2005 Amount Authorized	2005 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$113,312,000	Indefinite	$117,439,000
National Center for Complementary and Alternative Medicine	Section 485D	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	3,631,000	b/	3,677,000
Total, Budget Authority				116,943,000		121,116,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

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	114,149,000	114,149,000
Rescission				(742,000)
2004	116,202,000	116,202,000	117,902,000	117,752,000
Rescission				(774,000)
2005	121,116,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

NATIONAL INSTITUTES OF HEALTH

National Center for Complementary and Alternative Medicine

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Office of the Director	8	8	8
Office of Administrative Operations	16	16	16
Office of Communications and Public Liaison	7	7	7
Office of Science Policy and Operations	8	8	8
Division of Extramural Research and Training	12	14	17
Office of Scientific Review	6	6	6
Division of Intramural Research	14	17	20
Total	71	76	82
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2001	10.7
2002	11.2
2003	11.9
2004	11.9
2005	12.0

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

Detail of Positions

GRADE	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	0	0	0
ES-3	0	0	0
ES-2	0	0	0
ES-1	0	0	0
Subtotal	0	0	0
Total - ES Salary	$0	$0	$0
GM/GS-15	8	8	8
GM/GS-14	14	16	18
GM/GS-13	4	4	4
GS-12	15	15	15
GS-11	6	6	7
GS-10	0	0	0
GS-9	3	4	4
GS-8	4	4	4
GS-7	5	5	5
GS-6	0	0	0
GS-5	1	1	1
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	60	63	66
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	3	2	1
Senior Grade			
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	3	2	1
Ungraded	26	30	35
Total permanent positions	62	74	75
Total positions, end of year	89	95	102
Total full-time equivalent (FTE) employment,end of year	71	76	82
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$0	$0	$0
Average GM/GS grade	11.9	11.9	12.0
Average GM/GS salary	$71,817	$74,259	$76,784

NATIONAL INSTITUTES OF HEALTH
National Center for Complementary and Alternative Medicine

New Positions Requested

	FY 2005		
Title	Grade	Number	Annual Salary
Staff Clinician	AD	1	$82,000
Clinical Fellow	AD	1	$42,000
Health Scientist Administrator	GS-14	2	$86,112
Health Program Specialist	GS-11	1	$51,129
Technician	GS-9	1	$42,257
Total Requested		6	