CENTERS FOR DIETARY SUPPLEMENT RESEARCH: BOTANICALS

RFA (OD-04-002)
Summary of the Applicant Information Meeting
February 6, 2004 (8:30 AM – 12:30 PM)
Executive Plaza North, 6130 Executive Boulevard
Rockville, MD

Purpose: An Applicant Information Meeting (AIM) was held to improve the quality of applications submitted and to give potential applicants an opportunity to clarify issues or questions concerning the RFA.

This summary of the meeting covers approximately four hours of presentations, discussions, queries and responses. Questions do not appear in the order asked because it was impossible to put questions in context without providing a complete transcript. As an alternative, questions and responses were grouped by topic and usually appear at the end of individual presentations. A number of questions were reworded and many of the responses were expanded with direct references to the RFA.

DISCLAIMER: Applicants may note discrepancies between information provided in this summary and the RFA. If this occurs, the RFA should always be considered the authoritative document.

Information relevant to specific topics (e.g., selection of a center theme, botanical test materials, pilot program) appear throughout the RFA. *Guidance for any of the above topics can be efficiently located in the RFA by copying the RFA to software for word processing (e.g., Word or WordPerfect). With these documents one can use the "find" option (e.g., find "theme") to locate relevant text in the RFA.*

Agenda

Welcome and Opening Remarks
Dr. Paul Coates (Director, ODS)
Dr. Stephen Straus (Director, NCCAM)
Dr. Elizabeth Maull (Program Administrator, NIEHS)

Botanical Research Centers Initiative
Dr. Christine Swanson (Director, Botanical Research Centers Program)

Review Process
Dr. Martin Goldrosen (Director, NCCAM Office of Scientific Review))

Grants Management
Mr. George Tucker (Acting Grants Management Officer, NCCAM)

Technology Transfer*
Dr. Ted Roumel (Assistant Director, Office of Technology Transfer)

* Dr. Roumel's presentation is not summarized, but his PowerPoint presentation is included. Technology transfer issues pertinent to preparation of a grant application can be directed to the Office of Technology Transfer.

AIM SUMMARY

Dr. Coates
Dr. Coates welcomed the meeting participants and thanked them for their interest in the RFA. Dr. Coates expressed his enthusiasm for the Botanical Research Centers Program and noted that it could not exist without the participation of other NIH Institutes, Centers and Offices. NCCAM and NIEHS are the primary funding partners.

Dr. Straus
Dr. Straus welcomed the participants and introduced Dr. Margaret Chesney. Dr. Chesney is the Deputy Director of NCCAM and also serves as the Director of the Division of Extramural Research and Training. Dr. Straus noted that biologically based therapies such as botanicals comprise the largest part of the NCCAM research portfolio. In addition, the NCCAM ratio of clinical to basic research funding has decreased over the last five years, reflecting a need to advance basic science to better inform clinical studies.

Dr. Maull's Presentation (PowerPoint slides provided: http://ods.od.nih.gov/pubs/aim020504maull.ppt)

NIEHS has had an interest in botanicals for a number of years primarily through the efforts of the National Toxicology Program (NTP). In 1998 the NTP held a workshop on Herbal Medicines, resulting in the following recommendations:

- Improve efforts to identify and standardize product ingredients
- Provide additional consumer education
- Conduct additional research on botanicals

The NTP regularly receives nominations for studies of herbal ingredients, many of which are found in dietary supplements. Botanicals and botanical components under study by the NTP are listed below with additional details provided on the following web site: http://ntp-server.niehs.nih.gov/htdocs/liason/factsheets/HerbMedFacts.pdf

Aloe vera gel
Black cohosh
Bladderwrack
Blue green algae extract
Comfrey
Echinacea purpurea
Ephedra
Ginkgo biloba extract
Ginseng and ginsenoides
Goldenseal
Green tea extract
Kava kava extract
Milk thistle extract
Pulegone
Senna
Thujone

NIEHS is interested in the identification of biologically active constituents in botanicals. Several botanical test materials have been selected by NIEHS/NTP for detailed study, including toxicity assessment. To date, NTP has focused on acute high-dose and chronic low-dose studies of toxicity. As warranted, the NTP also assesses reproductive toxicity, neurotoxicity and immunotoxicity of botanicals.

With respect to the Botanical Research Centers, NIEHS is particularly interested in potential botanical/botanical or botanical/drug interactions and responses of sensitive subpopulations, including but not limited to pregnant women, developing fetuses, young, and the elderly. NIEHS is interested in centers structured around a strong central scientific theme and supportive of research that complements ongoing efforts within the NTP.

The NIEHS focus for the RFA resides in two broad areas: agriculturally related issues and biologically related issues. For the agriculturally related issues, NIEHS is interested in the identification of environmental factors that may influence the concentrations of bioactive constituents. These include the impact of harvest time, soil types, optimal growing conditions, use and types of fertilizers. The effect of processing procedures and storage time and conditions on bioactive ingredient concentrations is included in the NIEHS definition of environmental factors. NIEHS is also interested in the localization of bioactive components of a botanical. Finally, NIEHS encourages the development of "fingerprinting" technologies to facilitate unambiguous identification of botanical ingredients in products, including adulterants.

Biologically related issues fall into the following categories listed in the RFA:

- Pharmacokinetic/pharmacodynamic analyses of botanicals
- Mechanisms of action of bioactive ingredients
- Identification of targets for botanicals (molecular, cellular, organ)
- Identification of interactions (antagonistic or synergistic) with other botanical components
- Potential botanical/botanical or botanical/drug interactions
- Study of the role of botanicals as regulators of genetic pathways or epigenetic events
- Identification and validation of biomarkers of botanical intake or biological effects

Dr. Swanson's Presentation (PowerPoint slides provided: http://ods.od.nih.gov/pubs/aim020604swanson.ppt)

I. The Origin of the Botanical Research Centers Program (slides 3-4)

In fiscal year 1999, the Office of Dietary Supplements received additional funding from Congress to establish a botanical research initiative. This provided an opportunity to establish Dietary Supplement Research Centers described in the ODS Strategic Plan for 1998-2003. The RFAs issued in 1999 and 2000 resulted in awards to six centers, all focused on botanicals. Collectively these centers are referred to as the Botanical Research Centers Program. Along with ODS, the primary partners in the Botanical Research Centers Program have been the National Center for Complementary and

Alternative Medicine (NCCAM) and the National Institute of Environmental Health Sciences (NIEHS). The National Institute of General Medical Sciences (NIGMS) and the Office for Research on Women's Health (ORWH) also provided funding. Information about the centers can be found on the ODS and NCCAM web sites listed in the RFA.

II. Expert Panel Review (slides 6-12)

As the first centers approached the end of their 5-year funding cycle, the primary NIH funding partners (ODS, NCCAM, NIEHS) developed a plan to issue a new RFA. As a first step, an expert panel was convened in February of 2003 to review the Botanical Research Centers Program. The panel deliberations and recommendations marked an important milestone. Careful evaluation of the existing program provided an opportunity to consider changes and guided the development of the RFA (OD-04-002). The expert panel report can be found on the ODS and NCCAM web sites.

NIH staff described the development and status of the Botanical Research Centers Program, with emphasis on their purpose, goals and spectrum of research activities. The RFAs issued in 1999 and 2000 had nearly identical required elements (slide 9).

Center Components: A hypothetical organizational chart (slide 10) was presented to provide a framework for discussing key center components and their interactions. As a guiding principle, a center is expected to reach a level of achievement and productivity exceeding that expected on the basis of the sum of its parts. This concept is often referred to as synergy or value added.

Administrative Core: The Center Director is the leader of the core and is responsible for the organization, scientific administration and leadership of the center. An External Advisory Committee functions within this core. The core is responsible for the administration of the pilot research program along with the training and career development components of the center.

Research Cores: These cores are intended to support the research projects. Each research core must support at least two research projects.

Research Projects: The research projects are the centerpiece of the grant application. Research projects are reviewed as R01 level grant applications. The research projects must be hypothesis driven, with relevant preliminary data. In addition, the research projects must be related to the center theme and show evidence of interdisciplinary collaboration. The individual projects must accomplish more as part of a center grant than as isolated R01 awards.

Lessons learned from the first 5 years of the Botanical Program (slide 11): Program staff provided the expert panel with a general subjective assessment of factors contributing to success of the Center Program. First, the RFA is the starting point for the applicant; the RFA requirements must be clearly defined. Key features of the grant application were

emphasized as was the importance of several levels of administrative oversight to monitor scientific progress and allocation of resources.

Program staff asked the expert panel to comment on the importance of a research theme. Recommendations for ways to further promote interdisciplinary collaborative research were sought. The final recommendations of the expert panel to the NIH funding partners are summarized in the panel report. Key recommended elements of future botanical centers are shown in slide 13. All of the recommendations of the expert panel were considered in developing the new RFA.

In considering the recommendations of the expert panel and reflecting on their experience in managing the Botanical Centers Program, program staff concluded that some of the required activities incorporated in the first RFA may have been overly ambitious. For example, in retrospect, it was unreasonable to expect grantees to develop models of both safety and efficacy. Further, it is unlikely that any one model for safety or efficacy would be broadly applicable to the full range of botanicals. The requirement for clinical research has also been problematic. Clinical expertise was beyond the capacity of many otherwise outstanding applicants, particularly those with strengths in basic sciences. Furthermore, some of the current center grantees have found it difficult to complete their clinical research projects, in large part due to time limitations and financial constraints.

Upon further consideration, NIH staff also recognized that the addition of a botanical core requirement had some unintended consequences. Specifically, some of the new botanical cores were not supporting or enhancing the main research projects. In addition, training and career development activities were taking place but not under standard NIH funding mechanisms and progress was difficult to monitor. Finally, time and resources allocated to consumer information activities may have been better applied to research.

The panel noted the importance of quality assurance/quality control of botanical test materials. An NCCAM guidance document noted in the RFA addresses this issue (slide 14).

III. RFA OD-04-002
Dietary Supplement Research Centers: Botanicals

Before discussing the new RFA, Dr. Swanson provided clarification regarding several key terms being used by the meeting participants. Dietary supplements, for example, are defined as commercial products composed of ingredients, including botanicals. The definition of “botanical” as used in the RFA is shown in slide 17.

When the first RFA was issued, it was anticipated (not required) that applicants would focus on botanicals commonly referred to as phytomedicines (see slide 18 for examples). A number of currently funded centers proposed to study botanicals which could be classified either as phytomedicines or foods (e.g., ginger, turmeric, green tea) and some centers study botanicals that are generally regarded as foods (e.g., soy, cranberry). In the current RFA, the term botanical is expanded to include foods of plant origin. Like

phytomedicines many foods of plant origin contain bioactive constituents that may have health promoting properties. Note: Bioactive constituents of interest do NOT include essential nutrients.

According to FDA regulations, dietary supplements (including those that contain botanical ingredients), are not intended to diagnose, cure, mitigate, treat or prevent disease (slide 20). NIH recognizes FDA regulations, but NIH research on botanicals is not necessarily constrained by these boundaries. In other words, investigators responding to the RFA may choose to study biological endpoints or health outcomes that are disease related.

Frequently Asked Questions (slide 22): Decisions related to appropriate test materials, biological processes and health outcomes to be studied must be made by the applicant. Similarly, the applicant must work through the process of developing a center theme. Guidance related to all of these topics is provided in the RFA.

The purpose of the RFA was reviewed. Applicants were reminded of the critical importance of collaborative interdisciplinary research of high potential for being translated into practical benefits for human health.

The objectives of the RFA were summarized. In contrast to the two previous RFAs, there is no requirement for clinical research. Emphasis is now being placed on basic science that will inform clinical studies; appropriate use of contemporary technologies is stressed; and clinical research is optional.

If an applicant chooses to conduct a clinical study, the research should be relatively limited in scope. For example, Phase I or early Phase II trials are appropriate. NCCAM has developed a guidance document for clinical studies. In addition, NCCAM requires review of funded clinical projects through its Office of Clinical and Regulatory Affairs led by Dr. Josh Berman.

QUESTIONS RELATED TO THE RFA COMPETITION

How many of the current centers will be competing for renewal? Five of the six centers are nearing the end of their 5-year cycle.

Six centers are currently funded. How many centers will be funded as a result of this RFA? The current plan is to keep the Botanical Center Research Program at its current size. The number of centers funded will depend on the quality of applications received and availability of funding. It is possible that additional funds will be available; NIH Institutes not listed in the RFA are considering participation.

Will new and re-competing applications be evaluated using the same criteria? No. Currently funded centers have the additional requirement of demonstrating progress and productivity during their initial 5-year funding cycle. The SUPPLEMENTARY

INSTRUCTION section provides a summary of the additional requirements for competing renewals.

Will this RFA be reissued? At this time there are no plans to reissue this RFA.

REQUIRED ELEMENTS OF A CENTER

Note: The length of the RFA reflects an effort to clearly define the RFA requirements (refer to the SPECIAL REQUIREMENTS section).

What is required in terms of institutional commitment? Institutional commitment is very important. Centers represent an important and highly visible NIH investment. It is important to have documentation that the applicant institution will place a center high within its institutional priorities. Guidance regarding institutional commitment is found in the SPECIAL REQUIREMENTS section of the RFA. Dr. Goldrosen comments on institutional commitment in his presentation (below).

ADMINISTRATIVE CORE AND ROLE OF THE CENTER DIRECTOR

The following is a summary of responses to several questions. The information is also provided in the RFA.

The Administrative Core is led by the Center PI who is also the Center Director. The applicant institution may elect to designate a co-PI for the Center. That individual must be affiliated with the applicant institution. If the applicant institution is collaborating with another institution, the leader of the collaborating group may be referred to as the Associate Director of the Center.

There is only one PI (the Center Director) for the center application. The Center Director is expected to devote a minimum of 25% effort to the center (10% as the leader of the Administrative Core and 15% as the project leader of one R01 project). The Center Director is required to be a project leader.

If members of the External Advisory Committee must travel to attend the EAC meetings, can they be paid travel expenses and honoraria? Yes. Those expenses should be included in the budget. Note: Depending on the number of individuals covered, such expenses can add significantly to the budget.

RESEARCH CORES

Note: The RFA indicates that applicants should provide a core utilization table showing an estimate of percent effort devoted to each proposed research project in the first year of the grant.

Can existing resources at a university or other institution serve as cores? Applicants are encouraged to take advantage of existing resources at their institution, particularly

unique resources relevant to botanical research. However, cores are intended to support and enhance the proposed research projects. Not all existing resources at an institution will meet that requirement. As noted in the RFA, proposed core resources should not duplicate resources already available to Center investigators. However, fee-for-service core components (i.e., center use of existing facilities) are acceptable with adequate justification.

NCCAM has proposed to develop an analytical resource center (ARC) that would serve as a resource to NCCAM grantees. Is this currently available to applicants for this RFA? No. NCCAM is proceeding with plans to develop such a resource, but it is not currently available.

RESEARCH PROJECTS

Note: The applicant (center PI) must describe how the individual projects will accomplish more as part of a center grant than as isolated R01 awards. The PI may choose to provide this information as part of the Center Description. The guidelines for the Center Description are described under the SUPPLEMENTARY INSTRUCTIONS section of the RFA.

Must project leaders be affiliated with the applicant institution? Project leaders can be affiliated with either the applicant institution or its collaborating partners. If the collaborating groups are geographically separated, the PI must explain how interactions among the investigators will be established and maintained.

Are scientists working in other countries eligible project leaders?
Foreign institutions are not eligible to apply for this RFA. However, a subcontract with a foreign institution(s) is allowed if the collaboration is needed to accomplish the research objectives of the applicant institution. The PI (Center Director) must justify the need for the collaboration and also describe how a project leader from a foreign institution would be fully integrated into the center activities.

Can preclinical and clinical research be included in one research project?
Yes, however, for any given center application, only one clinical study can be included. As is true of any proposed research project, hypothesis driven research is required. In addition, clear justification of any proposed research strategy is always needed.

Who determines if an IND is needed for clinical research? This is not an NIH decision. The investigator is responsible for contacting the FDA. Guidance is provided in the RFA.

PILOT RESEARCH PROGRAM

What is the purpose of the pilot research program? The pilot program is intended to attract new investigators to the Center and provide them with an opportunity to develop preliminary data in order to apply for independent funding.

Must applicants to the pilot program be from the applicant institution? This is not a requirement, but the intention is to integrate pilot study applicants into the center activities. This is most easily accomplished if the applicants are from the applicant institution. Note: If a center is organized as a consortium of cooperating institutions, pilot studies can be awarded to scientists affiliated with the applicant institution or its collaborating partners. Note: Some key center personnel are not eligible to apply for pilot study funds (see RFA).

Should pilot studies be related to the center theme? Yes, this is a requirement of the RFA.

TRAINING AND CAREER DEVELOPMENT

The following is a summary of responses to questions about the training and career development component of the RFA:

Training is a very important component of a center. R01 projects and even core activities are likely to involve pre-doctoral students, postdoctoral trainees and new investigators. Training will take place as part of these experiences. The expert panel, however, advised the NIH sponsors to consider more structured training circumstances such as those found in established NIH training and career development awards rather than to provide funds specifically for this purpose as part of the center budget. This recommendation was accepted and incorporated into the new RFA. The guidance for the training and career development component of a center application is provided under the SPECIAL REQUIREMENTS section of the RFA.

"ACCEPTABLE" BOTANICAL TEST MATERIALS

There was a lengthy discussion of this topic. Guidance is provided in the RFA. The investigator is responsible for selecting appropriate test materials and providing the rationale for their inclusion.

If a botanical is not currently available as an ingredient in a commercial product, is the botanical acceptable as a topic of research? Yes, but the investigator needs to provide the rationale for studying the material. One might consider such things as, history of human use, prevalence of use, quality and quantity of existing research, potential for translation to human health and the investigator's research experience with the botanical.

Should the research be focused on isolated (active) constituents or less refined extracts or both? Again, the PI must decide. The following guidance is taken from the RFA.

"Botanical test materials ranging from whole fresh plants to isolated bioactive constituents are appropriate test materials for the proposed research. However, botanicals should not be thought of simply as sources of isolated phytochemicals to be studied. A

broader perspective is needed. For example, applicants proposing to study isolated constituents from plants are advised to consider the potential effects of removing bioactive constituents from their original matrix and the potential difference in biological effects and clinical response as one moves from a relatively complex extract to an isolated bioactive constituent."

Dr. Goldrosen's Presentation

Dr. Goldrosen discussed review criteria, including considerations related to topics previously discussed by Dr. Swanson.

I. General Comments

Center Theme: The RFA provides guidance related to this required element. It is incumbent upon an applicant to provide the rationale for the selection of the center theme. The RFA provides numerous examples of areas of interest to the funding partners. The applicant must convince reviewers that the center theme is relevant to the RFA and pursuits of the goals of NIH sponsored research.

Program synergy: As applicants prepare their submissions, they must consider how the individual research components contribute to "value added" of the overall center's program. Most importantly, the applicant is expected to describe the interactions among the proposed research cores and research projects and also explain how the collection of these research activities will result in synergy.

Scoring the Applications: Each research project will receive a score based on the range of scores proposed by the primary, secondary and tertiary reviewers. The overall score should reflect the median of the range of scores of the individual projects if the other elements (e.g. cores, program synergy, institutional commitment) are voted satisfactory. The overall score should be higher than the median range of scores if the other elements are outstanding and lower if the other elements are unsatisfactory.

Quality of Botanical Test Materials: The NCCAM guidance document (NCCAM Policy on the Quality of Natural Products) is distributed to reviewers serving on NCCAM and CSR review panels. The guidance document defines NCCAM standards for botanical test materials.

RFA Format: It is important to follow the instructions for preparing the grant application (see SPECIAL INSTRUCTIONS section). This section was included in the RFA to standardize the format of the applications. All applications will be copied to a CD. An index on the CD will be generated for all applications. Reviewers will be directed to specific sections of the application for their assignments with the aid of the index. In addition, the standard format will allow NIH program staff to more easily locate information.

Letters of Intent: Letters of intent are due May 18. Applicants are not required to submit a letter, but the information is very useful because it helps NIH staff prepared for the receipt and review of applications. Components of the letter of intent are provided in the RFA. In addition, Dr. Goldrosen encouraged applicants to propose a theme (i.e., provide a descriptive title of the proposed research center), list a descriptive title of each project and all investigators involved with the proposed center.

II. Comments on Selected Criteria of the RFA

Institutional commitment: Applicants are expected to document availability of space and resources in addition to a letter of support. Reviewers will look for these items.

R01 Level Projects: The R01 level research projects should be presented as "stand alone" submissions. Each research project will be evaluated by selected reviewers and will receive a score based on criteria listed in the RFA. Each R01 level project must have a hypothesis that relates to the center's theme, and include preliminary data related to the hypothesis.

Research Cores: Each research core will be evaluated by selected reviewers and will receive a merit descriptor (i.e., outstanding, acceptable, unacceptable) according to criteria listed in the RFA (e.g., technical merit, utilization by research projects and contribution to synergy).

Pilot Program: The reviewers will not review pilot projects for scientific merit. They will consider the description of the process used by the applicant to solicit, review, fund and monitor pilot studies.

Competitive Renewals: Applicants submitting competitive renewals have the advantage of previous funding and a history of participation in the Center Program, but they will be held accountable for achieving the goals of their first 5-year funding cycle. Applicants submitting competitive renewals will be evaluated using criteria to assess progress and productivity. Progress will be evaluated against the specific research aims of the original application. If a change in research direction was needed, the success of that modification will be evaluated. Productivity is a reflection of many factors, including but not limited to publications.

QUESTIONS AND RESPONSES TO DR. GOLDROSEN'S PRESENTATION

The Review Process

Will all applications responsive to the RFA be reviewed? As noted in the RFA, responsive applications will be assigned to selected members of the review panel. At a minimum, all research projects will be discussed and scored by the review panel. However, if a large number of responsive applications are received, discussion of the additional elements (cores, institutional commitment, program synergy) will be limited to only those applications deemed to have competitive research projects by the review

panel. A written critique of each application will be prepared and sent to the principal investigator. Applications, will receive a second level of review by the NCCAM and NIEHS Councils.

How are members of the review committee selected? The composition of the review panel will reflect the scientific nature of the submitted applications.

Will the review panel include scientists from industry? Review teams are balanced and those involving botanical research tend to include scientists from industry, academia and government.

Will reviewers with expertise in clinical research be included? Yes, the NCCAM Office of Scientific Review has a dedicated cadre of reviewers with clinical expertise.

Will scientists from other countries serve on the review panel? If an adequate number of reviewers with appropriate expertise cannot be identified among the pool of U.S. scientists, foreign investigators will be invited to serve on the panel.

Should scientists on the External Advisory Committee (EAC) be named in new applications?
Please do NOT identify individuals who might serve on your External Advisory Committee Name the types of scientists who will be on your advisory board committee, emphasizing their expertise and the nature of their participation.

Should scientists on the External Advisory Committee (EAC) be named in competing renewal applications?
Yes. EAC members of existing centers have been identified in required reports submitted to NIH. Past and current members of EACs are likely to be in conflict

The following is a summary of responses to questions related to the overall evaluation of the application and assessment of research cores and projects. Many of the questions are addressed in the RFA under the heading of REVIEW CRITERIA.

If the research projects are reviewed as stand alone R01 level submissions, how does an investigator demonstrate synergy? Each research project should describe how the project fits into the overall theme, its interaction with other projects, the cores used and how these interactions will add to the research project. Note: Reviewers assigned to individual research projects will have access to the entire application and will consider the supporting research cores.

Even though each R01 level research project is reviewed as an independent stand alone project, can the project leader refer to the other research projects? Yes, this is a good approach. Describe how projects and cores are connected. Don't expect the reviewer to hunt for this information in the application.

If the application contains the maximum number of research projects (i.e., four) and one project receives a poor score will that score be reflected in the final score of the entire grant application? Yes. It is not advisable to submit weak or borderline research projects.

I have research experience with botanicals but am considering studying a new test material for which I do not have preliminary data. Is it acceptable to submit preliminary data based on my previous research? Perhaps. Reviewers will decide if those data are relevant to your proposed hypothesis.

Mr. Tucker's Presentation

I. Budget Summary

- The budget should be prepared as outlined in the PHS 398 Application
- Clearly list all projects and prepare categorical budgets
- Identify any significant adjustments, increases, or decreases in the future requested budget
- Each performance site should be identified
- Human and animal assurances will be needed for an award to be issued, if pending at the time of review

II. Detailed Budgets

- A detailed budget for each project should be prepared. The budget page should include only funds requested from NIH. Indicate source of any additional funds elsewhere in the application.
- The effort of all personnel on each project is needed. Concisely describe the role of all staff (professional and nonprofessional) even when not requesting salary. Make sure time estimates do not exceed 100 percent for an individual.
- Salary is currently capped at $174,500. In the application, list the institutional base salary not the capped amount. If the cap is increased, you will be limited to the stated base salary provided in the application.
- Prepare a well-justified budget. Any unique or unusual request should be clearly justified.
- Thoroughly justify consultant activities. Describe exactly what tasks they will do and include a detailed budget for their work.

- Supplies in amounts less than $1,000 do not have to be itemized.

III. Subcontracts/Consortia

- Each participating subcontract must include the face page, budget pages, justification page and checklist page of the application.

- If the contract has not been finalized, a letter of intent will suffice for the review. Once the project has been identified for funding, budget information will be requested before an award is issued.

- The direct cost portion of the subcontract must be included within the budget cap. The indirect costs that exceed the budget limit will be considered on an individual basis.

IV. Implementation of New Salary Limitations

NIH competing grant awards with categorical budgets reflecting salary levels at or above the new cap(s) issued in FY 2004 will reflect adjustments to the current and future years. No funds will be awarded or committed for salaries over the limitation.

An individual's base salary, per se, is NOT constrained by the legislative provision for a limitation of salary. The rate limitation simply limits the amount that may be awarded and charged to NIH grants and contracts. An institution may pay an individual's salary amount in excess of the salary cap with non-federal funds.

The salary limitation does NOT apply to payments made to consultants under an NIH grant or contract. However, as with all costs, those payments must meet the test of reasonableness and be consistent with institutional policy.

The salary limitation provision DOES apply to subawards/subcontracts for substantive work under an NIH grant or contract.

COMPETING grant applications and contract proposals that include a categorical breakdown in the budget figures/business proposal should continue to reflect the actual institutional base salary of all individuals for whom reimbursement is requested. In lieu of actual base salary, however, applicants/offerors may elect to provide an explanation indicating that actual institutional base salary exceeds the current salary limitation. When this information is provided, NIH staff will make necessary adjustments to requested salaries prior to award.

The following are examples of the adjustments that NIH will make when salaries exceed the current salary limitation:

EXAMPLE 1. INDIVIDUAL WITH FULL-TIME APPOINTMENT (based on grant award/contract issued after January 1, 2004 with a $174,500 salary limitation)

Individual's institutional base salary for a FULL-TIME twelve month) appointment	$180,000
Research effort requested in application/proposal - 50%	
Direct Salary requested	$ 90,000
Fringe benefits requested (25% of salary)	$ 22,500
Subtotal	$112,500
Applicant organization's F&A (indirect) costs at a rate of 45% of subtotal	$ 50,625
Amount requested - salary plus fringe benefits plus associated F&A (indirect) costs	$163,125

If a grant/contract is to be funded, the amount included for the above individual will be calculated as follows:

Direct salary - restricted to a RATE of	$174,500
Multiplied by effort (50%) to be devoted to project	$ 87,250
Fringe benefits (25% of allowable salary)	$ 21,813
Subtotal	$109,063
Associated F&A (indirect) costs at 45% of subtotal	$ 49,078
Total amount to be awarded due to salary limitation	$158,141
Amount of reduction due to salary limitation ($163,125 requested minus $158,141 awarded)	$ 4,984

EXAMPLE 2. INDIVIDUAL WITH HALF-TIME APPOINTMENT (based on a grant award/contract issued after January 1, 2004 with a $174,500 salary limitation)

Individual's institutional base salary for a HALF-TIME appointment (50% of a full-time twelve month appointment)	$ 90,000
Research effort requested in application/proposal 30%	
Direct Salary requested	$ 27,000
Fringe benefits requested (25% of salary)	$ 6,750
Subtotal	$ 33,750
Applicant organization's F&A (indirect) costs at a rate of 45% of subtotal	$ 15,188
Amount requested - salary plus fringe benefits plus associated F&A (indirect) costs	$ 48,938

If a grant/contract is to be funded, the amount included in the award for the above individual will be calculated as follows:

Direct salary - restricted to a RATE of	$ 87,250
for a 50% appointment multiplied by 30% effort	$ 26,175
Fringe benefits (25% of allowable salary)	$ 6,544
Subtotal	$ 32,719
Associated F&A (indirect) cost at 45% of subtotal	$ 14,723
Total amount to be awarded due to salary limitation	$ 47,442
Amount of reduction due to salary limitation ($48,938 requested minus $47,442 awarded)	$ 1,495

QUESTIONS & ANSWERS

If a grant award (competing or non-competing) has already been issued in FY 2004, will an adjustment be made? No adjustments will be made. However, rebudgeting (moving funds from one category to another) is allowable.

If an application/proposal fails to provide needed salary information, will an adjustment be made based on the new rates? No adjustment will be made if an application fails to provide adequate information regarding the individual's actual salary level.

Does NIH appropriation language link the salary cap to a Federal Executive Level or to a dollar level? The link is to the Federal Executive Level pay scale (i.e., Executive Level III for FY 1999 and Executive Level II for FY 2000 and Executive Level I for FYs 2001, 2002, 2003 and 2004).

Can grantees/contractors with ongoing awards rebudget/charge to the various salary caps described above, depending on the fiscal year of the award and the time the salary expense is incurred? Yes, salary may be charged in accordance with the FY cap(s), as long as the levels are consistent with the individual's institutional base pay. Please refer to the salary cap summary with times frames for existing salary caps, at http://grants.nih.gov/grants/policy/salcap_summary.htm

Will grantees be permitted to submit revised budgets reflecting higher base salaries? Not as a general rule. NIH policy states that grantees should always reflect actual base salaries in the requested budgets or provide an explanation indicating that actual institutional base salary exceeds the current salary limitation. As a general rule, NIH will use the information available in the existing application and make adjustments for the salary cap based on information available at the time of award.

Dr. Roumel's Presentation (PowerPoint slides provided: http://ods.od.nih.gov/pubs/aimroumel.ppt)