

<p>15. ESTIMATED PROJECT FUNDING</p> <p>a. * Total Federal Funds Requested \$1,875,000.00</p> <p>b. Total Non-Federal Funds \$0.00</p> <p>c. * Total Federal & Non-Federal Funds \$1,875,000.00</p> <p>d. * Estimated Program Income \$0.00</p>	<p>16. * IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?</p> <p>a. YES <input type="radio"/> THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:</p> <p>DATE:</p> <p>b. NO <input checked="" type="radio"/> PROGRAM IS NOT COVERED BY E.O. 12372; OR</p> <p> <input type="radio"/> PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW</p>
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17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

* I agree

* The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

18. SFLLL or other Explanatory Documentation. File Name: Mime Type:

19. Authorized Representative

Prefix:	* First Name:	Middle Name:	* Last Name:	Suffix:
	Gregory	S.	Kopf	PhD

* Position/Title: Assoc. Vice Chancellor for Research Admin. * Organization Name: University of Kansas Medical Center Research Institute, Inc.

Department:	Division:	
* Street1: MSN 1039, 3901 Rainbow Boulevard	Street2:	
* City: Kansas City	County/Parish: Wyandotte	* State: KS: Kansas
Province:	* Country: USA: UNITED STATES	* ZIP / Postal Code: 66160-0000
* Phone Number: 913-588-1251	Fax Number: 913-588-3225	* Email: spa@kumc.edu

*** Signature of Authorized Representative**

*** Date Signed**

20. Pre-application File Name: Mime Type:

Project/Performance Site Location(s)

Project/Performance Site Primary Location

Organization Name: University of Kansas Medical Center

* Street1: EVC Office, 3901 Rainbow Boulevard

Street2:

* City: Kansas City

County: Wyandotte

* State: KS: Kansas

Province:

* Country: USA: UNITED STATES

* Zip / Postal Code: 66160-0000

DUNS Number: 016060860 * Project/Performance Site Congressional District: KS-003

File Name

Mime Type

Additional Location(s)

Project Summary/Abstract

Project Summary

SF 424 Guidelines for this section:

The Project Summary must contain a summary of the proposed activity suitable for dissemination to the public. It should be a self-contained description of the project and should contain a statement of objectives and methods to be employed. It should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate lay reader. This Summary must not include any proprietary/confidential information.

This section must be no longer than 30 lines of text. An abstract which exceeds this allowable length may be flagged as an error by the agency upon submission. This would require a corrective action before the application will be accepted.

FONT

- Use an Arial, Helvetica, Palatino Linotype, or Georgia Typeface, a black font color, and font size of 11 points or larger. (A Symbol font may be used to insert Greek letter or special characters; the font size requirement still applies.)

-Type density, including characters and spaces, must be no more than 15 characters per inch.

- Type may be no more than six lines per inch.

PAGE MARGINS

- Use standard paper size (8 1/2" x 11")

- Use at least one-half inch margins (top, bottom, left, and right) for all pages.

UPLOADING THE FINAL FILE DOCUMENT

- File attachment names longer than approximately 50 characters can cause problems processing packages. Please limit attachment names. Also, do not use any special characters (example: %, /, #, &) or spacing in the file and for word separation, use underscore (example: my_Attached_File.pdf) in naming the attachments. Please note that if these guidelines are not followed, your application may be rejected! (Grants.gov guidelines)

- Convert all documents to PDF format before uploading.

COMMON ERRORS IN THIS SECTION:

- Project Summary exceeds the 30 lines of text limit
- Margins are smaller than one-half inch
- Upload the final document as a word document
- Use of special characters in document final names

See next page for example

Example:

Antibiotic resistance is a growing and increasing serious public health problem. Infectious diseases caused by *Escherichia coli* and other bacteria are responsible for millions of deaths each year, and much of the duration of hospital stay, mortality, and morbidity as compared with drug-susceptible infections, economic costs of antibiotic resistance are estimated to be in the billions of dollars. The overall goal of this project is to develop new anti-infectives that are highly effective and refractory to antibiotic resistance using a combinational Genetic Technology (CGT) that allows the identification of new rRNA target sites and the specific nucleotides that are essential for functionality and viability, and RNA Homology Modeling software that allows accurate prediction of mutant RNA structures.

Phase I of this project was highly successful. A functional mutation library of *E. coli* 16S rRNA was constructed and ~5000 viable clones were sequenced. Using CGT, 67 regions of *E. coli* rRNA that contain nucleotides essential for viability were identified. The 67 functionally important regions included known binding sites for antibiotics, tRNAs, proteins, the large ribosome function, but for which no functional role has been identified to date. Some of the individual regions occur near each other in 30S subunit crystal structures and probably contribute to a single functional role.

The Phase II specific aims are 1) to select one RNA subdomain as a prioritized target from the four potential targets chosen from the RNA "regions of interest" identified in Phase I; 2) to use CGT to identify every mutation of the target that could lead to drug resistance, and use multidimensional NMR spectroscopy and homology modeling to determine the essential structural components of the target; 3) to screen compound libraries against the wild type target and its viable mutants; and 4) to carry out structural studies of target/hit complexes to allow optimization of hit compounds, and validate the target/compound using *in vitro* and *in vivo* assays of antibacterial activity. RiboNovix complete the work necessary to develop drug candidates from the leads, and will move qualified candidates into pre-clinical development.

Anti-infectives developed against the target identified in this study will likely be highly effective against microbial pathogens and resistant to target sites mutation, thus resulting in drugs refractory to antibiotic resistance.

PROJECT NARRATIVE

SF 424 Guidelines for this section:

Using no more than two or three sentences, describe the relevance of this research to public health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

EXAMPLE:

Antibiotic resistance is a growing and increasingly serious public health problem. Infectious diseases caused by Escherichia coli and other bacteria are responsible for millions of deaths each year, and much of this mortality is due to the rise of antibiotic resistant organisms. The overall goal of this project is to develop new anti-infectives that are highly effective and refractory to antibiotic resistance.

FONT

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UPLOADING THE FINAL FILE DOCUMENT

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- Convert all documents to PDF before uploading.

Common errors in this section:

- Project Narrative exceeds 2 – 3 sentences
- Margins are smaller than one-half inch
- Upload the final document as a WORD DOC
- Use of special characters in document file names

Bibliography & References Cited

SF 424 Guidelines for this section:

This section (formerly "Literature Cited") should include any references cited in the PHS 398 Research Plan component. The reference should be limited to relevant and current literature. While there is not a page limitation, it is important to be concise and to select only those literature references pertinent to the proposed research. For publicly available citations, URLs or PubMed Central (PMC) submission identification numbers may accompany the full reference. Note copies of these publications are no longer accepted as appendix material.

Each reference must include the names of all authors (in the same sequence in which they appear in the publication), the article and journal title, book title, volume number, page numbers, and year of publication. Include only biographic citations. Be especially careful to follow scholarly practices in providing citations for source materials relied upon when preparing any section of the application.

Facilities and Other Resources

SF 424 Guidelines for this section:

This information is used to assess the capability of the organization resources available to perform the effort proposed. Identify the facilities to be used (Laboratory, Animal, Computer, Office, Clinical and Other). If appropriate, indicate their capabilities, pertinent capabilities, relative proximity and extent of availability to the project. Describe only those resources that are directly applicable to the proposed work. Provide any information describing the Other Resources available to the project (e.g., machine shop, electronic shop) and the extent to which they would be available to the project.

No special form is required but this section must be completed and attached for submissions to NIH and other PHS agencies unless otherwise noted in the FOA. If there are multiple performance sites, then resources available at each site should be described. In describing the scientific environment in which the work will be done, discuss the ways in which the proposed studies will benefit from unique features of the scientific environment, or subject populations or employ useful collaborative arrangements. If research involving Select Agent(s) will occur at any performance site(s), the biocontainment resources available at each site should be described.

Example Template:

Environment: A description of how the scientific environment will contribute to the probability of success of the project, unique features of the environment and, for Early Stage Investigators, the institutional investment in the success of the investigator (e.g. resources, classes, etc.).

Laboratory:

Clinical:

Animal:

Computer:

Office:

Other:

Equipment

SF 424 Guidelines for this section:

List major items of equipment already available for this project and, if appropriate, identify location and pertinent capabilities.

EXAMPLE:

RiboNovix has use of or owns the following equipment: MJ thermacycler, heat blocks, autoclave, 2 variable temperature incubators (RT-50C), -80 freezer, cold box, 2 Eppendorf 5415C centrifuges, Perkin-Elmer VictorIII plate reader, under counter refrigerator, UV camera, New Brunswick shaker incubator, microwave, pH meter, balance, heat/stir plate, -20 freezer, pipetmen, 2 drummond pipettors, 1 large and 1 small water bath, Beckman low and high speed centrifuges, UV Vis, 2 picofuges, BioRad electroprator, BioRad Micropulse, 2 power supplies and gel box equipment. Additional equipment necessary for execution of project is requested in the budget including: a nanodrop spectrophotometer, speedvac, HPLC and columns, water purification equipment, a multidrop, dispenser for 96/384 well plates, and an additional thermal cycler.

Specific major equipment available at Wayne State University includes: Sorvall RC-5 centrifuge with GSA rotor and SS34 rotors, Molecular Devices multi-well plate spectrophotometer and fluorometer, Licor Global IR automated DNA sequencer, French press, Biocomp gradient formation apparatus, 396-well MJ Research PTC200 thermal cyclers, 4 incubators, 3 New Brunswick shaking water baths, 1 New Brunswick air shaker, Perkin-Elmer Lambda Bio UV-Vis spectrophotometer, and Hitachi UV-Vis detector with flow cell. A Bruker Avance-700 MHz spectrometer equipped with cryoprobe 1H, 13C, 15N triple resonance probe with z-axis PFG coil is located in the Chemistry building.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix	* First Name Barbara	Middle Name Frajola	* Last Name Atkinson	Suffix MD
Position/Title: Executive Vice Chancellor		Department: Office of the Exec Vice Chance		
Organization Name: University of Kansas Medical Center		Division:		
* Street1: EVC Office, 3901 Rainbow Boulevard		Street2:		
* City: Kansas City		County: Wyandotte	* State: KS: Kansas Province:	
* Country: USA: UNITED STATES		* Zip / Postal Code: 66160-0000		
*Phone Number 913-588-1440		Fax Number		* E-Mail BATKINSON@kumc.edu
Credential, e.g., agency login: BATKINSON				
* Project Role: PD/PI		Other Project Role Category:		
Degree Type:				
Degree Year:				
		File Name	Mime Type	
*Attach Biographical Sketch		biosketchsample1002290579.pdf	application/pdf	
Attach Current & Pending Support				

PROFILE - Senior/Key Person				
Prefix	* First Name Paul	Middle Name F	* Last Name Terranova	Suffix PhD
Position/Title: Professor		Department: Molecular & Integ Physiology		
Organization Name: University of Kansas Medical Center		Division: School of Medicine		
* Street1: MS 3043, 3901 Rainbow Boulevard		Street2:		
* City: Kansas City		County: Wyandotte	* State: KS: Kansas Province:	
* Country: USA: UNITED STATES		* Zip / Postal Code: 66160-0000		
*Phone Number 913-588-7068		Fax Number 913-588-1412		* E-Mail pterrano@kumc.edu
Credential, e.g., agency login: PTERRANOVA				
* Project Role: Other (Specify)		Other Project Role Category: co-investigator		
Degree Type:				
Degree Year:				
		File Name	Mime Type	
*Attach Biographical Sketch		biosketchsample1002290578.pdf	application/pdf	
Attach Current & Pending Support				

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY

NOTE: The Biographical Sketch may not exceed four pages. Follow the formats and instructions below.

A. Personal Statement

Briefly describe why your experience and qualifications make you particularly well-suited for your role (e.g., PD/PI, mentor, participating faculty) in the project that is the subject of the application.

B. Positions and Honors

List in chronological order previous positions, concluding with the present position. List any honors. Include present membership on any Federal Government public advisory committee.

C. Selected Peer-reviewed Publications

NIH encourages applicants to limit the list of selected peer-reviewed publications or manuscripts in press to no more than 15. Do not include manuscripts submitted or in preparation. The individual may choose to include selected publications based on recency, importance to the field, and/or relevance to the proposed research. When citing articles that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal - In Process." A list of these Journals is posted at: http://publicaccess.nih.gov/submit_process_journals.htm. Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with the full reference (note that copies of publicly available publications are not accepted as appendix material.)

D. Research Support

List both selected ongoing and completed research projects for the past three years (Federal or non-Federally-supported). *Begin with the projects that are most relevant to the research proposed in the application.* Briefly indicate the overall goals of the projects and responsibilities of the key person identified on the Biographical Sketch. Do not include number of person months or direct costs.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Hunt, Virginia Lively	POSITION TITLE Associate Professor of Psychology		
eRA COMMONS USER NAME (credential, e.g., agency login) huntvl			
<i>EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of California, Berkeley	B.S.	05/90	Psychology
University of Vermont	Ph.D.	05/96	Experimental Psychology
University of California, Berkeley	Postdoctoral	08/98	Public Health and Epidemiology

A. Personal Statement

The goal of the proposed research is to investigate the interaction between drug abuse and normal aging processes. Specifically, we plan to measure changes in cognitive ability and mental and physical health across a five-year period in a group of older drug users and matched controls. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a broad background in psychology, with specific training and expertise in key research areas for this application. As a postdoctoral fellow at Berkeley, I carried out ethnographic and survey research and secondary data analysis on psychological aspects of drug addiction. At the Division of Intramural Research at the National Institute on Drug Abuse (NIDA), I expanded my research to include neuropsychological changes associated with addiction. As PI or co-Investigator on several previous university- and NIH-funded grants, I laid the groundwork for the proposed research by developing effective measures of disability, depression, and other psychosocial factors relevant to the aging substance abuser, and by establishing strong ties with community providers that will make it possible to recruit and track participants over time. In addition, I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. As a result of these previous experiences, I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget. The current application builds logically on my prior work, and I have chosen co-investigators (Drs. Gryczynski and Newlin) who provide additional expertise in cognition, gerontology and geriatrics. In summary, I have a demonstrated record of successful and productive research projects in an area of high relevance for our aging population, and my expertise and experience have prepared me to lead the proposed project.

B. Positions and Honors

Positions and Employment

1998-2000	Fellow, Division of Intramural Research, National Institute of Drug Abuse, Bethesda, MD
2000-2002	Lecturer, Department of Psychology, Middlebury College, Middlebury, VT
2001-	Consultant, Coastal Psychological Services, San Francisco, CA
2002-2005	Assistant Professor, Department of Psychology, Washington University, St. Louis, MO
2005-	Associate Professor, Department of Psychology, Washington University, St. Louis, MO

Other Experience and Professional Memberships

1995-	Member, American Psychological Association
1998-	Member, Gerontological Society of America
1998-	Member, American Geriatrics Society
2000-	Associate Editor, Psychology and Aging
2003-	Board of Advisors, Senior Services of Eastern Missouri
2003-04	NIH Peer Review Committee: Psychobiology of Aging, ad hoc reviewer
2005-09	NIH Risk, Adult Addictions Study Section, member

Honors

2003	Outstanding Young Faculty Award, Washington University, St. Louis, MO
2005	Excellence in Teaching, Washington University, St. Louis, MO
2008	Award for Best in Interdisciplinary Ethnography, International Ethnographic Society

C. Selected Peer-reviewed Publications (Selected from 42 peer-reviewed publications)

Most relevant to the current application

1. Merrylye, R.J. & Hunt, V.L. (2004). Independent living, physical disability and substance abuse among the elderly. *Psychology and Aging*, 23(4), 10-22.
2. Hunt, V.L, Jensen, J.L. & Crenshaw, W. (2007). Substance abuse and mental health among community-dwelling elderly. *International Journal of Geriatric Psychiatry*, 24(9), 1124-1135.
3. Hunt, V.L, Wiechelt, S.A. & Merrylye, R. (2008). Predicting the substance-abuse treatment needs of an aging population. *American Journal of Public Health*, 45(2), 236-245. PMID: PMC9162292
4. Hunt, V.L., Newlin, D.B. & Fishbein, D. (2009). Brain imaging in methamphetamine abusers across the life-span. *Gerontology*, 46(3), 122-145.
5. Hunt, V.L. & Sher, K.A. (2009). Successful intervention models for older drug-abusers: Research across the life-span. *American Psychologist*, in press. NIHMSID: NIHMS99135

Additional recent publications of importance to the field (in chronological order)

1. Gryczynski, J., Shaft, B.M., Merrylye, R., & Hunt, V.L. (2002). Community based participatory research with late-life addicts. *American Journal of Alcohol and Drug Abuse*, 15(3), 222-238.
2. Shaft, B.M., Hunt, V.L., Merrylye, R., & Venturi, R. (2003). Policy implications of genetic transmission of alcohol and drug abuse in female nonusers. *International Journal of Drug Policy*, 30(5), 46-58.
3. Hunt, V. L., Marks, A.E., Shaft, B.M., Merrylye, R., & Jensen, J.L. (2004). Early-life family and community characteristics and late-life substance abuse. *Journal of Applied Gerontology*, 28(2),26-37.
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6. Hunt, V.L, Marks, A.E., Venturi, R., Crenshaw, W. & Ratonian, A. (2006). Community-based intervention strategies for reducing alcohol and drug abuse in the elderly. *Addiction*, 104(9), 1436-1606. PMID: PMC9000292
7. Merrylye, R. & Hunt, V.L. (2006). Randomized clinical trial of cotinine in older nicotine addicts. *Age and Ageing*, 38(2), 9-23. PMID: PMC9002364
8. Hunt, V.L., Jensen, J.L. & Merrylye, R. (2008). *The aging addict: ethnographic profiles of the elderly drug user*. NY, NY: W. W. Norton & Company.
9. Hunt, V.L. (2009). Contrasting ethnicity with race in the older alcoholic. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, in press. PMID: PMC Journal – In Process.
10. Hunt, V.L. (2009). Intervening successfully with the older methadone patient. *Journal of Applied Gerontology*, 13(4), 67-79.

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eRA COMMONS USER NAME (credential, e.g., agency login) huntvl			
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University of Vermont	Ph.D.	05/96	Experimental Psychology
University of California, Berkeley	Postdoctoral	08/98	Public Health and Epidemiology

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2005-09	NIH Risk, Adult Addictions Study Section, member

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4. Hunt, V.L., Merrylye, R. & Jensen, J.L. (2005). The effect of social support networks on morbidity among elderly substance abusers. *Journal of the American Geriatrics Society*, 57(4), 15-23.
5. Hunt, V.L., Pour, B., Marks, A.E., Merrylye, R. & Jensen, J.L. (2005). Aging out of methadone treatment. *American Journal of Alcohol and Drug Abuse*, 15(6), 134-149.
6. Hunt, V.L, Marks, A.E., Venturi, R., Crenshaw, W. & Ratonian, A. (2006). Community-based intervention strategies for reducing alcohol and drug abuse in the elderly. *Addiction*, 104(9), 1436-1606. PMID: PMC9000292
7. Merrylye, R. & Hunt, V.L. (2006). Randomized clinical trial of cotinine in older nicotine addicts. *Age and Ageing*, 38(2), 9-23. PMID: PMC9002364
8. Hunt, V.L., Jensen, J.L. & Merrylye, R. (2008). *The aging addict: ethnographic profiles of the elderly drug user*. NY, NY: W. W. Norton & Company.
9. Hunt, V.L. (2009). Contrasting ethnicity with race in the older alcoholic. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, in press. PMID: PMC Journal – In Process.
10. Hunt, V.L. (2009). Intervening successfully with the older methadone patient. *Journal of Applied Gerontology*, 13(4), 67-79.

PHS 398 Cover Page Supplement

1. Project Director / Principal Investigator (PD/PI)

Prefix: * First Name:
Middle Name:
* Last Name:
Suffix:

2. Human Subjects

Clinical Trial? No Yes

* Agency-Defined Phase III Clinical Trial? No Yes

3. Applicant Organization Contact

Person to be contacted on matters involving this application

Prefix: * First Name:
Middle Name:
* Last Name:
Suffix:
* Phone Number: Fax Number:
Email:

* Title:

* Street1:
Street2:
* City:
County:
* State:
Province:
* Country: * Zip / Postal Code:

PHS 398 Modular Budget, Periods 1 and 2

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 1	Start Date: <input type="text" value="12/01/2010"/>	End Date: <input type="text" value="11/30/2011"/>
-------------------------	---	---

A. Direct Costs	Funds Requested (\$)
* Direct Cost less Consortium F&A	<input type="text" value="250,000.00"/>
Consortium F&A	<input type="text"/>
* Total Direct Costs	<input type="text" value="250,000.00"/>

B. Indirect Costs			
	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. <input type="text" value="Research on_campus 50% MTDC"/>	<input type="text" value="50.00"/>	<input type="text" value="250,000.00"/>	<input type="text" value="125,000.00"/>
2. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Cognizant Agency (Agency Name, POC Name and Phone Number) <input type="text" value="Department of Health and Human Services, Theodore Foster, 214-767-3411"/>			
Indirect Cost Rate Agreement Date <input type="text" value="06/05/2008"/>		Total Indirect Costs <input type="text" value="125,000.00"/>	

C. Total Direct and Indirect Costs (A + B)	Funds Requested (\$)
	<input type="text" value="375,000.00"/>

Budget Period: 2	Start Date: <input type="text" value="12/01/2011"/>	End Date: <input type="text" value="11/30/2012"/>
-------------------------	---	---

A. Direct Costs	Funds Requested (\$)
* Direct Cost less Consortium F&A	<input type="text" value="250,000.00"/>
Consortium F&A	<input type="text"/>
* Total Direct Costs	<input type="text" value="250,000.00"/>

B. Indirect Costs			
	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. <input type="text" value="Research on_campus 50% MTDC"/>	<input type="text" value="50.00"/>	<input type="text" value="250,000.00"/>	<input type="text" value="125,000.00"/>
2. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Cognizant Agency (Agency Name, POC Name and Phone Number) <input type="text" value="Department of Health and Human Services, Theodore Foster, 214-767-3411"/>			
Indirect Cost Rate Agreement Date <input type="text" value="06/05/2008"/>		Total Indirect Costs <input type="text" value="125,000.00"/>	

C. Total Direct and Indirect Costs (A + B)	Funds Requested (\$)
	<input type="text" value="375,000.00"/>

PHS 398 Modular Budget, Periods 3 and 4

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 3	Start Date: <input type="text" value="12/01/2012"/>	End Date: <input type="text" value="11/30/2013"/>
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A. Direct Costs	Funds Requested (\$)
* Direct Cost less Consortium F&A	<input type="text" value="250,000.00"/>
Consortium F&A	<input type="text"/>
* Total Direct Costs	<input type="text" value="250,000.00"/>

B. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. <input type="text" value="Research on_campus 50% MTDC"/>	<input type="text" value="50.00"/>	<input type="text" value="250,000.00"/>	<input type="text" value="125,000.00"/>
2. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Cognizant Agency (Agency Name, POC Name and Phone Number)

Indirect Cost Rate Agreement Date Total Indirect Costs

C. Total Direct and Indirect Costs (A + B)	Funds Requested (\$)
	<input type="text" value="375,000.00"/>

Budget Period: 4	Start Date: <input type="text" value="12/01/2013"/>	End Date: <input type="text" value="11/30/2014"/>
-------------------------	---	---

A. Direct Costs	Funds Requested (\$)
* Direct Cost less Consortium F&A	<input type="text" value="250,000.00"/>
Consortium F&A	<input type="text"/>
* Total Direct Costs	<input type="text" value="250,000.00"/>

B. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. <input type="text" value="Research on_campus 50% MTDC"/>	<input type="text" value="50.00"/>	<input type="text" value="250,000.00"/>	<input type="text" value="125,000.00"/>
2. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Cognizant Agency (Agency Name, POC Name and Phone Number)

Indirect Cost Rate Agreement Date Total Indirect Costs

C. Total Direct and Indirect Costs (A + B)	Funds Requested (\$)
	<input type="text" value="375,000.00"/>

PHS 398 Modular Budget, Period 5 and Cumulative

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 5	Start Date: <input type="text" value="12/01/2014"/>	End Date: <input type="text" value="11/30/2015"/>
-------------------------	---	---

A. Direct Costs	Funds Requested (\$)
* Direct Cost less Consortium F&A	<input type="text" value="250,000.00"/>
Consortium F&A	<input type="text"/>
* Total Direct Costs	<input type="text" value="250,000.00"/>

B. Indirect Costs			
	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. <input type="text" value="Research on_campus 50% MTDC"/>	<input type="text" value="50.00"/>	<input type="text" value="250,000.00"/>	<input type="text" value="125,000.00"/>
2. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. <input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Cognizant Agency (Agency Name, POC Name and Phone Number)

Indirect Cost Rate Agreement Date Total Indirect Costs

C. Total Direct and Indirect Costs (A + B) Funds Requested (\$)

Cumulative Budget Information

1. Total Costs, Entire Project Period

* Section A, Total Direct Cost less Consortium F&A for Entire Project Period	\$ <input type="text" value="1,250,000.00"/>
Section A, Total Consortium F&A for Entire Project Period	\$ <input type="text"/>
* Section A, Total Direct Costs for Entire Project Period	\$ <input type="text" value="1,250,000.00"/>
* Section B, Total Indirect Costs for Entire Project Period	\$ <input type="text" value="625,000.00"/>
* Section C, Total Direct and Indirect Costs (A+B) for Entire Project Period	\$ <input type="text" value="1,875,000.00"/>

2. Budget Justifications

Personnel Justification

Consortium Justification

Additional Narrative Justification

Personnel Justification:

SF 424 Guidelines for this section:

"List all personnel, including names, number of person months devoted to the project (indicate academic, calendar, and/or summer) and roles on the project. Do not provide individual salary information. Since the modules should be a reasonable estimate of costs allowable, allocable, and appropriate for the proposed project, you must use the current legislatively imposed salary limitation when estimating the number of modules. For guidance on current salary limitations contact your office of sponsored programs."

"NIH grants also limit the compensation for graduate students. Compensation includes salary or wages, fringe benefits, and tuition remission. This limit should also be used when estimating the number of modules"

Common Errors:

- Effort measured in percentage rather than Calendar Year Months (CYM)
- Graduate Student's effort exceeds 6 CYM (50%)

Example:

Wen Liu, Ph.D., Principle Investigator, (3 CY Mo effort) will oversee development, recruitment, testing, data processing and analysis. He will be responsible for the development of treatment and testing protocol, computer programs for data acquisition and processing, database management, data analysis, and preparation of progress reports, final report and manuscripts. Dr. Liu has a primary appointment as an associate professor in the Department of Physical Therapy and Rehabilitation Science at the University of Kansas Medical Center (KUMC).

Chao Sun, M.D., MPH, consultant, (1 CY Mo effort) will provide advice on the clinical aspects of the project design and acupuncture treatment, and help on the interpretation of results and preparation of final report and manuscripts. Dr. Sun is a physician in Occupational Medicine and a licensed acupuncturist.

Byron Gajewski, Ph.D., co-investigator, (1 CY Mo effort) will help on project design and subject random assignment. Dr. Gajewski will also responsible for statistical analysis of results, and help on the preparation of final report and manuscripts. His expertise in clinical trail studies and statistical analysis is a great resource for the proposed study.

Eric Vidoni, Ph.D., P.T., post-doctoral fellow (6 CY Mo effort) will work as a project manager. He will be responsible for the day-to-day progress of the project, coordinating data collection and database management, helping on data analysis, helping on preparation of progress reports, final report and manuscripts.

TBA, B.S. or M.S. database manager, (6 CY Mo effort) will be responsible for the subject recruitment, stroke registry, database management, and helping on the preparation of clean data set for statistical analysis. This individual will be blind to the subjects' group membership during data collection and analysis period.

Minzhao Huang, M.D. (Chinese medicine), licensed acupuncturist, (5 CY Mo effort) will conduct the acupuncture treatment following the standard procedure. Dr. Huang received her MD degree in Chinese medicine previously in China. She is a licensed acupuncturist and has practiced acupuncture and herb medicine for more than 10 years in the USA.

PHS 398 Research Plan

1. Application Type:

From SF 424 (R&R) Cover Page and PHS398 Checklist. The responses provided on these pages, regarding the type of application being submitted, are repeated for your reference, as you attach the appropriate sections of the research plan.

*Type of Application:

- New Resubmission Renewal Continuation Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

- | | |
|---|--|
| 1. Introduction to Application
(for RESUBMISSION or REVISION only) | <input type="text"/> |
| 2. Specific Aims | <input type="text" value="SPECIFIC_AIMS1002290658.pdf"/> |
| 3. Research Strategy | <input type="text" value="Research_Strategy1002290583.pdf"/> |
| 4. Inclusion Enrollment Report | <input type="text"/> |
| 5. Progress Report Publication List | <input type="text"/> |

Human Subjects Sections

- | | |
|--------------------------------------|--|
| 6. Protection of Human Subjects | <input type="text" value="Protection_of_Human_Subjects1002217368.pdf"/> |
| 7. Inclusion of Women and Minorities | <input type="text" value="Inclusion_of_Women_and_Minorities1002217371.pdf"/> |
| 8. Targeted/Planned Enrollment Table | <input type="text" value="TPETForm1002290659.pdf"/> |
| 9. Inclusion of Children | <input type="text" value="Inclusion_of_Children_12_081002217379.pdf"/> |

Other Research Plan Sections

- | | |
|---|--|
| 10. Vertebrate Animals | <input type="text" value="Vertebrate_Animals1002217377.pdf"/> |
| 11. Select Agent Research | <input type="text" value="Select_Agent_Research1002217378.pdf"/> |
| 12. Multiple PD/PI Leadership Plan | <input type="text"/> |
| 13. Consortium/Contractual Arrangements | <input type="text"/> |
| 14. Letters of Support | <input type="text" value="Letters_of_Support1002217384.pdf"/> |
| 15. Resource Sharing Plan(s) | <input type="text" value="Resource_Sharing_Plan1002217369.pdf"/> |

16. Appendix

SPECIFIC AIMS

State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved.

List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

Specific Aims are limited to one page.

Common errors: Page numbers. Do not page number any part of the application.

RESEARCH STRATEGY

Page Limitation: 12

Research Strategy:

Organize the Research Strategy in the specified order and using the instructions provided below. Start each section with the appropriate section heading—Significance, Innovation, Approach. Cite published experimental details in the Research Strategy section and provide the full reference in the Bibliography and References Cited section (Item 5.5.5). Follow the page limits for the Research Strategy in the Table of Page Limits, unless specified otherwise in the FOA.

a. Significance :

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

b. Innovation:

- Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
- Describe any novel theoretical concepts, approaches or methodologies, instrumentation or intervention(s) to be developed or used, and any advantage over existing methodologies, instrumentation or intervention(s).
- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation or interventions.

c. Approach :

Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Unless addressed separately in Item 5.5.15, include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.

- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.
- Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised. A full discussion on the use of Select Agents should appear in 5.5.11 below.

As applicable, also include the following information as part of the Research Strategy, keeping within the three sections listed above: Significance, Innovation, and Approach.

Preliminary Studies for New Applications. For new applications, include information on Preliminary Studies as part of the **Approach** section. Discuss the PD/PI's preliminary studies, data, and/or experience pertinent to this application. Except for Exploratory/Development Grants (R21, R33), Small Research Grants (R03), Academic Research Enhancement Award (AREA) Grants (R15), and Phase I Small Business Research Grants (R41/R43), preliminary data can be an essential part of a research grant application and help to establish the likelihood of success of the proposed project. Early Stage Investigators should include preliminary data. (However, for R01 applications, reviewers will be instructed to place less emphasis on the preliminary data in applications from Early Stage Investigators than on the preliminary data in applications from more established investigators.)

Progress Report for Renewal and Revision Applications. For renewal/revision applications, provide a Progress Report as part of the Approach section. Provide the beginning and ending dates for the period covered since the last competitive review. Summarize the specific aims of the previous project period and the importance of the findings, and emphasize the progress made toward their achievement. Explain any significant changes to the specific aims and any new directions including changes resulting from significant budget reductions. A list of publications, manuscripts accepted for publication, patents, and other printed materials should be included in 5.5.5; do not include that information here.

Protection of Human Subjects

Not Applicable.

Include only if human subjects are involved in your project.

If human subjects are involved in your project, see next two pages in this PDF attachment for SF 424 Guidelines.

Protection of Human Subjects

(INCLUDE ONLY IF HUMAN SUBJECTS ARE INVOLVED IN YOUR PROJECT)

SF 424 Guidelines for this section:

1. RISKS TO THE SUBJECTS

a. Human Subjects Involvement and Characteristics

- Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status.
- Identify the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special classes of subjects, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that 'prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites in performing the proposed research.

b. Sources of Materials

- Describe the research material obtained from living human subjects in the form of specimens, records, or data.
- Describe any data that will be recorded on the human subjects involved in the project.
- Describe the linkages to subjects, and indicate who will have access to subject identities.
- Provide information about how the specimens, records, or data are collected and whether material or data will be collected specifically for your proposed research project.

c. Potential Risks

- Describe the potential risks to subjects (physical, psychological, social, legal, or other), and assess their likelihood and seriousness to the subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and Informed Consent

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.
- Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. Protection Against Risk

- Describe planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.
- Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral

intervention studies) must include a description of the plan for data and safety monitoring of the research and adverse event reporting to ensure the safety of subjects.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

- Discuss the potential benefits of the research to the subjects and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

NOTE: Test articles (investigational new drugs, devices, or biologicals) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the Food and Drug Administration, and/or the status of requests for an IND or IDE covering the proposed use of the test article in the Research Plan.

5. DATA AND SAFETY MONITORING PLAN

- If your research includes a clinical trial, create a subheading entitled "Data and Safety Monitoring Plan."
- Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the funding I/C, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (<http://www.fda.gov/>) and also see the following websites for more information related to IND and IDE requirements:
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr312_01.html (IND)
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr812_01.html (IDE)
- The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:
 - a. PD/PI (required)
 - b. Independent Individual/Safety Officer
 - c. Designated medical monitor
 - d. Internal Committee or Board with explicit guidelines
 - e. Data and Safety Monitoring Board (DSMB). NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for *multi-site* clinical trials involving interventions that entail potential *risk* to the participants, and generally for Phase III clinical trials. Although Phase I and Phase II clinical trials may also use DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.
 - f. Institutional Review Board (IRB - required)
- A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>). For additional guidance on creating this Plan, see the above reference.

Inclusion of Women and Minorities

Not Applicable.

If human subjects are involved in your project, but not women or minorities, write a brief statement for this section, explaining that women and minorities are not involved in your project.

See next 2 pages of this PDF attachment for SF 424 Guidelines on this section.

Inclusion of Women and Minorities

- If human subjects are involved in your project, but not women or minorities, write a brief statement for this section, explaining that women and minorities are not involved in your project.

SF 424 Guidelines for this section:

"In the attachment for Item 9, include a heading entitled "Inclusion of Women and Minorities." Although no specific page limitation applies to this section of the application, be succinct.

Scientific Review Groups will assess each application as being "acceptable" or "unacceptable" with regard to the protection of human subjects.

In this section of the Research Plan, address, at a minimum, the following four points:

1. The targeted/planned distribution of subjects by sex/gender and racial/ethnic groups for each proposed study or protocol using the format in the Targeted/Planned Enrollment Table. (Instructions for completing this table are provided below.) If you are using existing specimens and/or data that does not meet the criteria for Exemption 4 and you do not have access to information on the distribution of women and minorities, so state and explain the impact on the goals of the research as part of the rationale that inclusion is inappropriate (item 3 below). Alternatively, you may describe the women and minority composition of the population base from whom the specimens and/or data will be obtained. Include the Targeted/Planned Enrollment Table in Item 10.
2. A description of the subject selection criteria and rationale for selection of sex/gender and racial/ethnic group members in terms of the scientific objectives and proposed study design. The description may include, but is not limited to, information on the population characteristics of the disease or condition under study.
3. A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group (see examples below).
4. A description of proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects.

Examples of acceptable justifications for exclusion of:

A. One gender:

1. One gender is excluded from the study because:
 - inclusion of these individuals would be inappropriate with respect to their health;
 - the research question addressed is relevant to only one gender;
 - evidence from prior research strongly demonstrates no difference between genders;
 - sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.
2. One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens).
3. Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

B. Minority groups or subgroups:

1. Some or all minority groups or subgroups are excluded from the study because:
 - Inclusion of these individuals would be inappropriate with respect to their health;

- The research question addressed is relevant to only one racial or ethnic group;
 - Evidence from prior research strongly demonstrates no differences between racial or ethnic groups on the outcome variables;
 - A single minority group study is proposed to fill a research gap;
 - Sufficient data already exists with regard to the outcome of comparable studies in the excluded racial or ethnic groups and duplication is not needed in this study.
2. Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study, and the investigator has satisfactorily addressed this issue in terms of:
- The size of the study;
 - The relevant characteristics of the disease, disorder or condition;
 - The feasibility of making a collaboration or consortium or other arrangements to include representation.
- Some minority groups or subgroups are excluded or poorly represented because the purpose of the research constrains the applicant's selection of study subjects by race or ethnicity (e.g., uniquely valuable cohorts, stored specimens or existing datasets are of limited minority representation, very small numbers of subjects are involved, or overriding factors dictate selection of subjects, such as matching of transplant recipients or availability of rare surgical specimens).
3. Racial or ethnic origin of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens or data sets with incomplete racial or ethnic documentation are used) and this does not compromise the scientific objectives of the research."

Targeted/Planned Enrollment Table

Study Title: _____

Total Planned Enrollment: _____

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino			
Not Hispanic or Latino			
Ethnic Category: Total of All Subjects *			
Racial Categories			
American Indian/Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
Racial Categories: Total of All Subjects *			

* The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

Inclusion of Children

The NIH Policy on Inclusion of Children is referenced and described in [Section 5.7](#). Instructions for Item 11 of the Research Plan are as follows:

- Create a section entitled “Inclusion of Children” and place it immediately following the Targeted/Planned Enrollment Table.
- For the purpose of implementing these guidelines, a *child* is defined as an individual under the age of 21 years (for additional information see <http://grants.nih.gov/grants/funding/children/children.htm> and <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>).
- Provide either a description of the plans to include children, or, if children will be excluded from the proposed research, application, or proposal, present an acceptable justification for the exclusion (see below).
- If children are included, the description of the plan should include a rationale for selecting a specific age range of children. The plan also must include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the age-appropriate inclusion or exclusion of children in the research project.
- When children are involved in research, the Additional Protections for Children Involved as Subjects in Research ([45 CFR Part 46 Subpart D](#)) apply and must be addressed under the Protections Against Risk subheading (4.1.2.b).

Justifications for Exclusion of Children

For the purposes of this policy, all individuals under 21 are considered children; however, exclusion of any specific age group, such as individuals under 18, should be justified in this section. It is expected that children will be included in all clinical research unless one or more of the following exclusionary circumstances can be fully justified:

1. The research topic to be studied is not relevant to children.
2. There are laws or regulations barring the inclusion of children in the research.
3. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be needlessly redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
4. A separate, age-specific study in children is warranted and preferable. Examples include:
 - a. The condition is relatively rare in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or
 - b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
 - c. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some

instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested, or the interventions planned, to allow inclusion of children rather than excluding them.

5. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
6. Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
7. Other special cases can be justified by the investigator and found acceptable to the review group and the Institute Director.

Vertebrate Animals

Not Applicable.

Include this section ONLY if you have animal subjects in your project.

If you have animal subjects in your project, see next page in this PDF attachment for SF 424 Guidelines for this section.

Vertebrate Animals

(INCLUDE THIS SECTION ONLY IF YOU HAVE ANIMAL SUBJECTS IN YOUR PROJECT)

SF 424 Guidelines for this section:

"If you indicated that Vertebrate Animals are involved in this project, address the following five key points. In addition, when research involving vertebrate animals will take place at collaborating site(s) or other performance site(s), provide this information before discussing the five points. Although no specific page limitation applies to this section of the application, be succinct.

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Design and Methods section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the veterinary care of the animals involved.
4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.
5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations."

Select Agent Research

SF 424 Guidelines for this section:

Select Agents are hazardous biological agents and toxins that have been identified by HHS or USDA as having the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal and plant products. CDC maintains a list of these agents. See <http://www.cdc.gov/od/sap/docs/salist.pdf>.

If the activities proposed in your application involve only the use of a strain(s) of Select Agents which has been excluded from the list of select agents and toxins as per 42 CFR 73.4(f)(5), the Select Agent requirements do not apply. Use this section to identify the strain(s) of the Select Agent that will be used and note that it has been excluded from this list. The CDC maintains a list of exclusions at <http://www.cdc.gov/od/sap/sap/exclusion.htm>.

If the strain(s) is not currently excluded from the list of select agents and toxins but you have applied or intend to apply to HHS for an exclusion from the list, use this section to indicate the status of your request or your intent to apply for an exclusion and provide a brief justification for the above exclusion.

If any of the activities proposed in your application involve the use of Select Agents at any time during the proposed project period, either at the applicant organization or at any other performance site, address the following three points for each site at which Select Agent research will take place. Although no specific page limitation applies to this section, be succinct.

1. Identify the Select Agent(s) to be used in the proposed research.

2. Provide the registration status of all entities* where Select Agent(s) will be used.

- If the performance site(s) is a foreign institution, provide the name(s) of the country or countries where Select Agent research will be performed.

*An "entity" is defined in 42 CFR 73.1 as "any government agency (Federal, State, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity.

3. Provide a description of all facilities where the Select Agent(s) will be used.

- Describe the procedures that will be used to monitor possession, use and transfer of Select Agent(s).

- Describe plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

If you are responding to a specific opportunity announcement (e.g., PA or RFA), address any requirements specified by the solicitation.

Letters of Support

Not Applicable.

SF 424 Guidelines for this section:

Attach appropriate letters of support here from all individuals confirming their roles in the project. For consultants, letters should include rate/charge for consulting services.

Resource Sharing Plan

Not Applicable.

SF 424 Guidelines for this section:

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. See Part III, 1.5 Sharing Research Resources.

1) Data Sharing Plan: Investigators seeking \$500,000 or more in direct costs in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible. Specific Funding Opportunity Announcements may also require that all applications include this information regardless of the dollar level. Applicants are encouraged to read the specific opportunity carefully and discuss their data-sharing plan with their program contact at the time they negotiate an agreement with the Institute/Center (IC) staff to accept assignment of their application. See Data-Sharing Policy at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>.

2) Sharing Model Organisms: Regardless of the amount requested, in applications where the development of model organisms is anticipated, the applicant must include a description of a specific plan for sharing or distributing unique model organisms or state why such sharing is restricted or not possible. See NIH Policy on Sharing of Model Organisms at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html>.

APPENDIX

Only one copy of appendix material is necessary. Use the **add attachments** button to the right of this field to complete this entry.

A maximum of 10 PDF attachments is allowed in the Appendix. If more than 10 appendix attachments are needed, combine the remaining information into attachment #10. Note that this is the total number of appendix items, not the total number of publications. When allowed there is a limit of 3 publications that are not publicly available (see below for further details and **check the FOA** for any specific instructions), though not all grant activity codes allow publications to be included in the appendix.

Do not use the appendix to circumvent the page limitations of the research plan.

Appendix material may not appear in the assembled application in the order attached, so it is important to use filenames for attachments that are descriptive of the content. A summary sheet listing all of the items included in the appendix is also encouraged but not required. When including a summary sheet, it should be included in the first appendix attachment. Applications that do not follow the appendix requirements may be delayed in the review process.

New, resubmission, renewal, and revision applications **may** include the following materials in the Appendix:

- **Publications – No longer allowed as appendix materials except in the circumstances noted below.** Applicants may submit up to 3 of the following types of publications:
 - **Manuscripts and/or abstracts accepted for publication but not yet published:** The entire article should be submitted as a PDF attachment.
 - **Manuscripts and/or abstracts published, but a free, online, publicly available journal link is not available:** The entire article should be submitted as a PDF attachment.
 - **Patents directly relevant to the project:** The entire document should be submitted as a PDF attachment.

(Do not include unpublished theses, or abstracts/manuscripts **submitted** (but not yet accepted) for publication.)

- Surveys, questionnaires, and other data collection instruments; clinical protocols and informed consent documents may be submitted in the Appendix as necessary.
- For materials that cannot be submitted electronically or materials that cannot be converted to PDF format (e.g., medical devices, prototypes, DVDs, CDs), applicants should contact the Scientific Review Officer for instructions following notification of assignment of the application to a study section. Applicants are encouraged to be as concise as possible and submit only information essential for the review of the application.

Items that must **not** be included in the appendix:

- Photographs or color images of gels, micrographs, etc., **are no longer accepted as Appendix material.** These images must be included in the Research Plan PDF. However, images embedded in publications are allowed.

Publications that are publicly accessible. For such publications, the URL or PMC submission identification numbers along with the full reference should be included as appropriate in the Bibliography and References cited section, the Progress Report Publication List section, and/or the Biographical Sketch section.

PHS 398 Checklist

1. Application Type:

From SF 424 (R&R) Cover Page. The responses provided on the R&R cover page are repeated here for your reference, as you answer the questions that are specific to the PHS398.

* Type of Application:

New Resubmission Renewal Continuation Revision

Federal Identifier:

2. Change of Investigator / Change of Institution Questions

Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

* First Name:

Middle Name:

* Last Name:

Suffix:

Change of Grantee Institution

* Name of former institution:

3. Inventions and Patents (For renewal applications only)

* Inventions and Patents: Yes No

If the answer is "Yes" then please answer the following:

* Previously Reported: Yes No

4. * Program Income

Is program income anticipated during the periods for which the grant support is requested?

Yes No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period *Anticipated Amount (\$)

*Source(s)

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5. * Disclosure Permission Statement

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

Yes No

PHS 398 Cover Letter

* Mandatory Cover Letter Filename:

Mandatory Cover Letter Filename

SF 424 Guidelines for this section:

“Applicants are encouraged to include a cover letter with the application. The cover letter is only for internal use and will not be shared with peer reviewers. The letter should contain any of the following information that applies to the application:

1. Application title.
2. Funding Opportunity (PA or RFA) title of the NIH initiative.
3. Request of an assignment (referral) to a particular awarding component(s) or Scientific Review Group (SRG). The PHS makes the final determination.
4. List of individuals (e.g., competitors) who should not review your application and why.
5. Disciplines involved, if multidisciplinary.
6. For late applications (see Late Application policy in Section 2.14) include an explanation of the delay as part of the cover letter attachment.
7. When submitting a Changed/Corrected Application after the submission date, a cover letter is required explaining the reason for the Changed/Corrected Application. If you already submitted a cover letter with a previous submission and are now submitting a Changed/Corrected Application, you must include all previous cover letter text in the revised cover letter attachment. The system does not retain any previously submitted cover letters until after an application is verified; therefore, you must repeat all information previously submitted in the cover letter as well as any additional information.
8. Explanation of any subaward budget components that are not active for all periods of the proposed grant.
9. Statement that you have attached any required agency approval documentation for the type of application submitted. This may include approval for applications \$500,000 or more, approval for Conference Grant or Cooperative Agreement (R13 or U13), etc.

Two types of approval documentation are cited as examples in item 6 above: NIH IC approval for an application \$500,000 or more and NIH institute approval for a Conference Grant or Cooperative Agreement application (R13 or U13). To attach the approval documents to this submission, please append those referenced documents to your Cover Letter File, and upload as one attachment.

Suggested Cover Letter Format

The Division of Receipt and Referral (DRR), Center for Scientific Review (CSR) is responsible for assigning applications to ICs and to scientific review groups (SRGs). DRR will be utilizing knowledge management approaches as an adjunct to the work of referral experts as part of an overall plan to shorten the time from submission to review. Analysis has shown that requests made by investigators are a valuable source of information in this process. In order to facilitate the use of these requests in conjunction with knowledge management analysis of the content of the application, applicants are requested to use the following format when assignment requests are contained in a cover letter.”

- List one request per line.
- Place institute/center (IC) and SRG review requests (if both are made) on separate lines.
- Place positive and negative requests (if both are made) on separate lines.
- Include name of IC or SRG, followed by a dash and the acronym. Do not use parentheses.
- Provide explanations for each request in a separate paragraph.

Examples:

Please assign this application to the following Institutes/Centers:

National Cancer Institute - NCI

National Institute for Dental and Craniofacial Research – NIDCR

Scientific Review Groups

Molecular Oncogenesis Study Section – MONC

Cancer Etiology Study Section – CE

Please do not assign this application to the following:

Scientific Review Groups

Cancer Genetics Study Section – CG

The reasons for this request are [provide a narrative explanation for the request(s):