PRIMATE RESEARCH CENTER GRANT **Federal Award Date:** 09/07/2015

Department of Health and Human Services
National Institutes of Health
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 3P51OD011106-54S1
FAIN: P51OD011106

Principal Investigator(s):
MARSHA RUTH MAILICK, PHD

Project Title: Wisconsin National Primate Research Center Support

Brenda A. Egan
Interim Managing Officer
21 N. Park Street, Suite 6401
Madison, WI 537151218

Award e-mailed to: NIH@rsp.wisc.edu

Period Of Performance:
Budget Period: 09/07/2015 – 04/30/2016
Project Period: 06/10/1997 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $407,357 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF WISCONSIN-MADISON in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P51OD011106. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Dawn Walker
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 3P51OD011106-54S1

Award Calculation (U.S. Dollars)

Salaries and Wages	$61,095
Fringe Benefits	$29,020
Personnel Costs (Subtotal)	$90,115
Equipment	$45,000
Other Costs	$174,379
Federal Direct Costs	$309,494
Federal F&A Costs	$97,863
Approved Budget	$407,357
Total Amount of Federal Funds Obligated (Federal Share)	$407,357
TOTAL FEDERAL AWARD AMOUNT	$407,357
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$407,357

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (54)	
GRANT NUMBER	**TOTAL FEDERAL AWARD AMOUNT**
3P51OD011106-54S1	$407,357
5P51OD011106-54	$9,402,376
3P51OD011106-54S2	$382,927
TOTAL	**$10,192,660**

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
54	$407,357	$10,192,660
55	$242,956	$9,799,205

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Research Infrastructure Programs
CFDA Number:	93.351
EIN:	1396006492A1
Document Number:	POD011106J
PMS Account Type:	G (Pooled)
Fiscal Year:	2015

IC	CAN	2015	2016
OD	8014499	$407,357	$242,956

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: CMP01 / **OC**: 414C / **Released** eRA Commons User Name 09/01/2015
Award Processed: 06/15/2015 11:31:44 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 3P51OD011106-54S1

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 3P51OD011106-54S1

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P51OD011106. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 3P51OD011106-54S1

SUBJECT FOA
This award is subject to the conditions set forth in PAR-14-226, "Limited Competition: National Primate Research Centers (P51)," which are hereby incorporated by reference as special terms

and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-14-226.html

ORIP FUNDING PLAN FOR FY2015
This competing award reflects the NIH Fiscal Policy for Grant Awards for FY2015 (see NIH Guide Notice NOT-OD-15-050) and the implementation of the ORIP FY2015 grants funding policy: http://dpcpsi.nih.gov/orip/rf/fyg_fp2015

SUPPLEMENT
This supplemental award provides $407,357 ($309,494 direct costs and $97,863 associated facilities and administrative costs) to support for maintenance and development of common marmosts (Callithrix jacchus) recently acquired from the New England Primate Research Center, in accordance with the grantee's request dated 1/26/15. These funds may not be expended for any other purpose without the written prior approval of the ORIP.

In future years a separate progress report for this Supplement is required as part of the progress report of the parent grant. In addition, unless this award is included under the Streamlined Noncompeting Award Process, a detailed budget page must be submitted.

BUDGET PERIOD/AWARD AMOUNT
This grant has been issued with an 8-month budget period with 8 months of monetary support.

PRE-AWARD AUTHORITY
This award includes 90 day preaward cost authorization to incur costs for approved grant activities.

FUTURE YEAR SUPPORT ADJUSTMENT
Escalation on recurring costs has been removed.

KEY PERSONNEL
In addition to the PI, the following individuals are named as key personnel (individuals who have effort that ORIP staff is tracking):

Excluded by Requester

Written prior approval is required if any of the individuals named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

PRIOR APPROVAL REQUEST
Any prior approval request (e.g., changes to key personnel as noted on the award, changes in human and animal subjects requiring prior approval, carryover requests) must be submitted to the assigned Grants Management Specialist and Programmatic Official. Please refer to Part II Chapter 8 the NIH Grants Policy Statement for the activities and/or expenditures that require NIH approval at http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf

COMMUNICATIONS/PRESS RELEASE
If the grantee plans to issue a press release concerning the outcome of ORIP grant-supported research, it should notify Ms. Patricia Newman, ORIP Communications at 301-435-0744, in advance to allow for coordination.

The ORIP WWW home page is at http://dpcpsi.nih.gov/orip/

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Christina Fleming

Email: fleminch@mail.nih.gov **Phone**: 301-435-0850 **Fax**: 301-480-3777

Program Official: John D. Harding
Email: hardingj@mail.nih.gov **Phone**: 301-435-0776 **Fax**: 30- 480-3819

SPREADSHEET SUMMARY
GRANT NUMBER: 3P51OD011106-54S1

INSTITUTION: UNIVERSITY OF WISCONSIN-MADISON

Budget	Year 54	Year 55
Salaries and Wages	$61,095	$41,415
Fringe Benefits	$29,020	$19,672
Personnel Costs (Subtotal)	$90,115	$61,087
Equipment	$45,000	
Other Costs	$174,379	$116,253
TOTAL FEDERAL DC	$309,494	$177,340
TOTAL FEDERAL F&A	$97,863	$65,616
TOTAL COST	$407,357	$242,956

Facilities and Administrative Costs	Year 54	Year 55
F&A Cost Rate 1	37%	37%
F&A Cost Base 1	$264,494	$177,340
F&A Costs 1	$97,863	$65,616

PI: **MAILICK, MARSHA RUTH**	Title: Wisconsin National Primate Research Center Support	
Received: 01/26/2015	FOA: PAR14-226	Council: 10/2015
Competition ID: FORMS-C	FOA Title: LIMITED COMPETITION: NATIONAL PRIMATE RESEARCH CENTERS (P51)	
3 P51 OD011106-54S1	Dual: RI	Accession Number: 3782082
IPF: 578503	Organization: UNIVERSITY OF WISCONSIN-MADISON	
Former Number: 3P51OD011106-04S3	Department: WAISMAN CENTER	
IRG/SRG: ZRG1 BBBP-T (46)P	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 54: 309,494 Year 55: 180,807 Year 56: 0 Year 57: 0 Year 58: 0	Animals: Y Humans: N Clinical Trial: N Current HS Code: 10 HESC: N	New Investigator: N Early Stage Investigator: N
Senior/Key Personnel:	*Organization:*	*Role Category:*
MARSHA MAILICK PhD	The Board of Regents of the University of Wisconsin System	PD/PI

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

○ Pre-application ○ Application ● Changed/Corrected Application

4.a. Federal Identifier
OD011106

b. Agency Routing Number

2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number
2015-01-26		GRANT11815833

5. APPLICANT INFORMATION **Organizational DUNS*:** 161202122

Legal Name*: The Board of Regents of the University of Wisconsin System
Department:
Division:
Street1*: Suite 6401
Street2: 21 N Park St
City*: Madison
County: Dane
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53715-1218

Person to be contacted on matters involving this application
Prefix: First Name*: BRENDA Middle Name: A Last Name*: EGAN Suffix:
Position/Title: Interim Managing Officer
Street1*: 21 N. Park Street, Suite 6401
Street2:
City*: Madison
County: Dane
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53715-1218
Phone Number*: 608-262-3822 Fax Number: Email: preaward@rsp.wisc.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 396006492

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ○ Women Owned ○ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

○ New ○ Resubmission
○ Renewal ○ Continuation ● Revision

If Revision, mark appropriate box(es).
● A. Increase Award ○ B. Decrease Award ○ C. Increase Duration
○ D. Decrease Duration ○ E. Other *(specify)* :

Is this application being submitted to other agencies?* ○Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*	10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
National Institutes of Health	TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Wisconsin National Primate Research Center Support

12. PROPOSED PROJECT		13. CONGRESSIONAL DISTRICTS OF APPLICANT
Start Date*	Ending Date*	WI-002
04/29/2015	04/30/2017	

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: MARSHA Middle Name: R Last Name*: MAILICK Suffix: PhD

Position/Title: VICE CHANCELLOR
Organization Name*: The Board of Regents of the University of Wisconsin System
Department: WAISMAN CENTER
Division: VC FOR RESEARCH & GRADUATE ED
Street1*: 500 Lincoln Dr
Street2: 333 Bascom Hall
City*: MADISON
County:
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53706-2274
Phone Number*: 6082621044 Fax Number: Email*: mailick@research.wisc.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$655,063.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$655,063.00
d. Estimated Program Income*	$223,970.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

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:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: BRENDA Middle Name: A Last Name*: EGAN Suffix:

Position/Title*: Managing Officer
Organization Name*: The Board of Regents of the University of Wisconsin System
Department: Research & Sponsored Programs
Division:
Street1*: 21 N. Park Street, Suite 6401
Street2:
City*: Madison
County: Dane
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53715-1218
Phone Number*: 608-262-3822 Fax Number: Email*: preaward@rsp.wisc.edu

Signature of Authorized Representative*
BRENDA A EGAN

Date Signed*
01/26/2015

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:

424 R&R and PHS-398 Specific Table Of Contents

Component Summary

Components	Component Project Title	Organization Name	Contact PD/PI Name or Project Lead Name
Overall	Wisconsin National Primate Research Center Support	The Board of Regents of the University of Wisconsin System	MAILICK, MARSHA R
Animal-Resources-001 (001)	Wisconsin National Primate Research Center Support	The Board of Regents of the University of Wisconsin System	Excluded by Requester

Project/Performance
Site Location(s) Summary

Applicant Organization	City	State/Province	Country
The Board of Regents of the University of Wisconsin System	Madison	WI	UNITED STATES

Organization Name	City	State/Province	Country	Component
The Board of Regents of the University of Wisconsin System	Madison	WI	UNITED STATES	Animal-Resources-001 (001)
The Board of Regents of the University of Wisconsin System	Madison	WI	UNITED STATES	Overall

Human Subjects
Clinical Trial
Human Embryonic Stem Cells
Vertebrate Animals
Summary

Components	Human Subjects	Clinical Trial	HESC Involved	Vertebrate Animals
Overall	N		N	Y
Animal-Resources-001 (001)	N		N	Y

Composite Application Budget Summary

Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Salary, Wages and Fringe Benefits	90,115	61,087	0	0	0	151,202
Equipment	45,000	0	0	0	0	45,000
Travel	0	0	0	0	0	0
Participant/Trainee Support Costs	0	0	0	0	0	0
Other Direct Costs (excluding Consortium)	174,379	119,720	0	0	0	294,099
Consortium Costs	0	0	0	0	0	0
Direct Costs	309,494	180,807	0	0	0	490,301
Indirect Costs	97,863	66,899	0	0	0	164,762
Total Direct and Indirect Costs	407,357	247,706	0	0	0	**655,063**

Total Direct Costs less Consortium F&A

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	309,494	180,807	0	0	0	**490,301**

Component Budget Summary

Components	Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Animal-Resources-001 (001)	Salary, Wages and Fringe Benefits	90,115	61,087	0	0	0	151,202
	Equipment	45,000	0	0	0	0	45,000
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	174,379	119,720	0	0	0	294,099
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	309,494	180,807	0	0	0	490,301
	Indirect Costs	97,863	66,899	0	0	0	164,762
TOTALS	Total Direct and Indirect Costs	407,357	247,706	0	0	0	**655,063**
TOTALS		**407,357**	**247,706**	**0**	**0**	**0**	**655,063**

Categories Budget Summary

Categories	Components	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
R&R Budget - Senior/Key Person Funds Requested	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Other Personnel Funds Requested	Animal-Resources-001 (001)	90,115	61,087	0	0	0	151,202
TOTALS		90,115	61,087	0	0	0	**151,202**
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	Animal-Resources-001 (001)	90,115	61,087	0	0	0	151,202
TOTALS		90,115	61,087	0	0	0	**151,202**
R&R Budget - Section C. Total Equipment	Animal-Resources-001 (001)	45,000	0	0	0	0	45,000
TOTALS		45,000	0	0	0	0	**45,000**
R&R Budget - Domestic Travel	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Foreign Travel	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Section D. Total Travel	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**

R&R Budget - Tuition/Fees/Health Insurance	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Stipends	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Trainee Travel	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Subsistence	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Other Participants/Trainee Support Costs	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Section E. Total Participants/Trainee Support Costs	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Materials and Supplies	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Publication Costs	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Consultant Services	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**

R&R Budget - ADP/Computer Services	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Subawards/Consortium/Contractual Costs	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Equipment or Facility Rental User Fees	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Alterations and Renovations	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Other Direct Cost 1	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Other Direct Cost 2	Animal-Resources-001 (001)	174,379	119,720	0	0	0	294,099
TOTALS		174,379	119,720	0	0	0	**294,099**
R&R Budget - Other Direct Cost 3	Animal-Resources-001 (001)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Section F. Total Other Direct Cost	Animal-Resources-001 (001)	174,379	119,720	0	0	0	294,099
TOTALS		174,379	119,720	0	0	0	**294,099**
R&R Budget - Section G. Total Direct Cost (A thru F)	Animal-Resources-001 (001)	309,494	180,807	0	0	0	490,301
TOTALS		309,494	180,807	0	0	0	**490,301**

R&R Budget - Section H. Indirect Costs	Animal-Resources-001 (001)	97,863	66,899	0	0	0	164,762
TOTALS		97,863	66,899	0	0	0	**164,762**
R&R Budget - Section I. Total Direct and Indirect Costs (G +H)	Animal-Resources-001 (001)	407,357	247,706	0	0	0	655,063
TOTALS		407,357	247,706	0	0	0	**655,063**

Senior/Key Personnel
Summary

Name	Organization	Role on Project	Components
MAILICK, MARSHA R	The Board of Regents of the University of Wisconsin System	PD/PI(Contact)	Overall
Excluded by Requester	The Board of Regents of the University of Wisconsin System	Other: Attending Veterinarian	Animal-Resources-001 (001)
	The Board of Regents of the University of Wisconsin System	Other: Project Lead	Animal-Resources-001 (001)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

Excluded by Requester

Page 23 of 97 to Page 33 of 97

Withheld pursuant to exemption

Redacted by agreement

of the Freedom of Information and Privacy Act

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

● I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The Board of Regents of the University of Wisconsin System
Duns Number:	161202122
Street1*:	Suite 6401
Street2:	21 N Park St
City*:	Madison
County:	Dane
State*:	WI: Wisconsin
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	53715-1218
Project/Performance Site Congressional District*:	WI-002

File Name

Additional Location(s)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ○ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ● No

IACUC Approval Date: 09-10-2012

Animal Welfare Assurance Number A3368-01

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Overall_Abstract1017925876.pdf
8. Project Narrative*	Overall_Relevance1017925875.pdf
9. Bibliography & References Cited	Overall_References1017925783.pdf
10.Facilities & Other Resources	
11.Equipment	

SUMMARY/ABSTRACT (Overall). The Wisconsin National Primate Research Center (WNPRC) base operating grant supports services and resources for research addressing human health issues utilizing non-human primate (NHP) models. Located on the campus of the University of Wisconsin-Madison, the WNPRC is fully integrated into the mission of UW-Madison, including research and training links in the several schools and colleges, basic science and clinical departments, and interdisciplinary centers and institutes. In addition, WNPRC investigators have strong research collaborations with scientists across the U.S. and internationally. The WNPRC provides a rich and integrated portfolio of cutting-edge services, resources, and scientific expertise that support NHP research with high impact and direct relevance to human and animal health and disease. This P51 Revision application requests support for maintenance and development of common marmosets (*Callithrix jacchus*) recently acquired from the New England Primate Research Center (NEPRC). Our specific aims to support these animals are as follows:

Aim 1. To provide excellent animal holding facilities and primary enclosures for the marmosets transferred from the NEPRC

Aim 2. To implement exceptional, USDA/PHS/OLAW/AAALAC compliant husbandry and veterinary medical practices for the marmosets transferred from the NEPRC

Aim 3. To implement appropriate genetic and reproductive management for the transferred marmosets

Aim 4. To implement a prudent financial plan to support the transferred marmosets as ORIP support for the animals is progressively reduced

In accomplishing the foregoing Specific Aims, we will then be poised to advance our Center goals to enhance the WNPRC marmoset colony as a national resource—commensurate with demand of investigators—and, develop WNPRC resource initiatives, such as a transgenic marmoset facility.

Relevance (Overall)

The Wisconsin National Primate Research Center (WNPRC) provides a rich and integrated portfolio of cutting-edge services, resources, and scientific expertise that support non-human primate (NHP) research with high impact and direct relevance to human and animal health and disease. With continued support for maintenance and development of common marmosets (*Callithrix jacchus*) recently acquired from the New England Primate Research Center (NEPRC), we will be poised to advance our Center goals to enhance the WNPRC marmoset colony as a national resource—commensurate with demand of investigators—and, develop WNPRC resource initiatives, such as a transgenic marmoset facility.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: MARSHA Middle Name R Last Name*: MAILICK Suffix: PhD

Position/Title*:	VICE CHANCELLOR
Organization Name*:	The Board of Regents of the University of Wisconsin System
Department:	WAISMAN CENTER
Division:	VC FOR RESEARCH & GRADUATE ED
Street1*:	500 Lincoln Dr
Street2:	333 Bascom Hall
City*:	MADISON
County:	
State*:	WI: Wisconsin
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	53706-2274

Phone Number*: 6082621044 Fax Number: E-Mail*: mailick@research.wisc.edu

Credential, e.g., agency login: eRA Commons User Name

Project Role*: PD/PI Other Project Role Category:

Degree Type: Degree Year:

	File Name
Attach Biographical Sketch*:	MailickBio_P51Rev1018025013.pdf
Attach Current & Pending Support:	

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

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

Prefix:	Dr.
First Name*:	MARSHA
Middle Name:	R
Last Name*:	MAILICK
Suffix:	PhD

2. Human Subjects

Clinical Trial?	○ No	○ Yes
Agency-Defined Phase III Clinical Trial?*	○ No	○ Yes

3. 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

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)*

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. 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

7. 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*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	Overall_Introduction1017925775.pdf
2. Specific Aims	Overall_SpecificAimsv21017925865.pdf
3. Research Strategy*	Overall_ResearchStrategyv21018025010.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	Overall_VAS1017925866.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	
13. Resource Sharing Plan(s)	
Appendix (if applicable)	
14. Appendix	

Introduction to the Revised Application (Overall)

This P51 Revision application requests support for maintenance and development of common marmosets (*Callithrix jacchus*) acquired from the New England Primate Research Center (NEPRC). Currently, only two of the existing NPRCs, the WNPRC and the Southwest National Primate Research Center (SNPRC), possess the infrastructure and expertise to maintain common marmoset breeding colonies. The loss of one of these colonies due to closure of the NEPRC would have devastating consequences on the availability and genetic diversity of common marmosets available to U.S. based investigators. Thus, transfer of the existing NEPRC common marmoset colony to the WNPRC and the SNPRC is imperative, and we request funding to establish, maintain, and develop a subset of these animals at the WNPRC.

The WNPRC has maintained a colony of common marmosets (*Callithrix jacchus*) since a founder group of 13 animals was purchased from the Waisman Center (an intellectual and developmental disabilities research center located at the University of Wisconsin-Madison) in 1990. The founder colony was augmented with 170 additional animals acquired from the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP) at New York University in 1991 and 1992 and has been maintained with offspring of the Waisman and LEMSIP founder animals since that time. The census of the WNPRC marmoset colony has ranged from 200 to 350 animals and the animals have historically proven to be critically important in studies of *in vitro* fertilization, stem cell biology, steroid hormone signaling, neuroendocrine mechanisms governing parental behavior, neuroendocrine regulation of fertility, and dietary and hormonal mechanisms controlling body weight and metabolism.

The WNPRC's established colony of common marmosets, which is housed in the Center's Specific Animal Location building in Madison, Wisconsin, currently consists of 203 animals. On August 20, 2013, WNPRC Director Excluded by Requester received a letter from NEPRC Director, Excluded by Requester indicating his desire to Excluded by Requester appropriate sites for the transfer of the NEPRC common marmoset colony. Guidelines for NPRCs interested in accepting the marmosets were outlined in an RFP entitled "Request for Proposals from NPRCs Interested in Receiving the NEPRC Common Marmoset Colony." We determined that it would benefit WNPRC core and affiliate investigators to expand the size of the WNPRC marmoset colony by acquiring a portion of the NEPRC colony. The WNPRC submitted a proposal to the Excluded by Requester and ORIP Health Scientist Administrator Excluded by Requester Excluded by PhD, in response to the RFP, requesting equitable distribution of the NEPRC's established and active breeding groups between the WNPRC and the SNPRC and also requested transfer of several additional marmosets to Wisconsin for proposed studies. On December 23, 2014 Excluded by Requester informed the WNPRC that the NEPRC marmoset population would be divided between the WNPRC and the SNPRC. Additional discussions resulted in a mutual agreement that between 90 and 100 marmosets would be transferred to the WNPRC. Subsequently, ORIP issued a Notice of Grant Award (Direct costs = $309,859, total costs = $424,507) to the WNPRC for an administrative supplement to fund the necessary room renovations and animal enclosures and sufficient to cover salaries and per diems for the period beginning June 30, 2014 and ending April 30, 2015. All renovations and enclosure construction was completed by October 1, 2014 and the WNPRC received 90 marmosets from the NEPRC on November 4, 2014 and an additional 9 marmosets on December 3, 2014. This revised application seeks to continue support for the transferred marmosets for the remaining two years of this P51 grant funding cycle.

Marmosets remain the experimental animal of choice among one or more investigators affiliated with each of the WNPRC Working Groups, which include Neuroscience, Energy Metabolism and Chronic Disease (EMCD), Reproductive and Regenerative Medicine (RRM), and Global Infectious Disease (GID). Current and future demand for marmosets by these WNPRC and UW researchers, as well as by investigators nationwide, appears to be increasing significantly[1-6]. The transfer and development of the NEPRC marmoset colony will thus enhance our capacity to fulfill our specific aim "*To breed and provide animals suitable for research using NHPs*". Marmosets are also being utilized in a major new WNPRC initiative using CRISPR technologies to produce transgenic NHP models of disease, including neurodegenerative and neuropsychiatric disorders. Additionally, we are now employing new imaging-guided stereotaxic surgery and viral vector-mediated gene silencing strategies in marmosets to chronically alter target neural gene expression, permitting cutting-edge studies of neuroendocrine and metabolic disorders. The incorporation of the NEPRC marmoset colony within the WNPRC will therefore also greatly facilitate our efforts to address the specific aim "*To develop NHP models of human disease and facilitate their use.*"

Specific Aims of the Wisconsin National Primate Research Center (Overall)

The Wisconsin National Primate Research Center (WNRPC) is one of eight federally supported National Primate Research Centers (NPRCs). Thousands of scientists – throughout the nation and the world – have conducted research in primate biology with relevance to human and animal health through the Center since its establishment in 1961. The WNPRC maintains a deep commitment to each of the eight objectives of the NPRC Program as originally published by the National Center for Research Resources (NCRR). These Specific Goals are recapitulated below:

- **Goal 1** – Develop and sustain national resources for normative data, consultative and collaborative expertise, biologic and genetic material, and specialized facilities, equipment, and expertise that support NHP-related research.
- **Goal 2** – Breed and provide animals suitable for research using non-human primates (NHP).
- **Goal 3** – Study the biology of NHP species that are of potential research importance for the purpose of enhancing their scientific utility, health, and well-being.
- **Goal 4** – Develop improved practices of NHP breeding, husbandry and genetic definition to help meet research needs for pedigreed, disease-free animals of defined quality, and to ensure the continued availability of species of biomedical research importance whose wild populations are considered threatened or endangered.
- **Goal 5** – Develop NHP models of human disease and facilitate their use.
- **Goal 6** – Conduct pilot (basic and applied) biomedical research projects in areas requiring the use of NHP. Pilot projects are aimed at helping to solve problems related to human health, and they should lead to independent grant support related to the disease or health problem being studied.
- **Goal 7** – Provide opportunities for local, national, and international research involvement and experience in primatology to graduate and undergraduate students, postdoctoral fellows, visiting scientists and faculty members, as well as short-term learning assignments for students of the health professions.
- **Goal 8** – Disseminate the findings of studies and technical advances in NHP research to the scientific community via reports published in internationally-recognized, peer-reviewed journals and other appropriate media.

Specific Aims of the WNPRC Regarding the Newly Acquired NEPRC Marmosets

The common marmoset has been utilized in a variety of basic science, translational, and pre-clinical research studies at the WNPRC for over two decades, addressing scientific and biomedical questions in areas such as stem cell biology, fertility, metabolism, neuroendocrinology, social behavior, and infectious disease. Within the past two years, a major transgenesis initiative has also been launched at the WNPRC, in which new CRISPER technologies are being utilized to develop transgenic marmoset models of human diseases. Our own demand for these animals, as well as those of investigators nationwide, appears to be increasing significantly[1-6]. Currently, only three of the existing eight NPRCs possess the infrastructure and expertise to maintain common marmoset breeding colonies. The loss of one of these colonies due to the impending closure of the New England Primate Research Center (NEPRC) would have devastating consequences on the availability and genetic diversity of common marmosets available to investigators. Thus, transfer of a portion of the existing NEPRC common marmoset colony to the WNPRC is imperative. The Specific Aims of the WNPRC for the transferred NEPRC marmosets are as follows:

- **Specific Aim 1** – To provide excellent animal holding facilities and primary enclosures for the marmosets transferred from the NEPRC
- **Specific Aim 2** – To implement exceptional, USDA/PHS/OLAW/AAALAC compliant husbandry and veterinary medical practices for the marmosets transferred from the NEPRC
- **Specific Aim 3** – To implement appropriate genetic and reproductive management for the transferred marmosets
- **Specific Aim 4** – To implement a prudent financial plan to support the transferred marmosets as ORIP support for the animals is progressively reduced

In accomplishing the foregoing Specific Aims, we will then be poised to advance our Center goals to enhance the WNPRC marmoset colony as a national resource—commensurate with demand of investigators—and, develop WNPRC resource initiatives, such as a transgenic marmoset facility.

Research Strategy (Overall)

Overview of the Wisconsin National Primate Research Center

1. Background and Mission

The scientists and staff of the Wisconsin National Primate Research Center (WNPRC) are pleased to submit this P51 Base Grant Revision application to support a population of common marmosets (*Callithrix jacchus*) recently transferred from the New England Primate Research Center (NEPRC) to the WNPRC. Now in its 53rd year of NIH support, the WNPRC remains an integral component of the national and international NHP research enterprise, serving as a critically important resource for basic and translational biomedical research. From its inception through the present funding period, the WNPRC has been responsive to the overall objective of the NPRC program to provide the animals, facilities, and expertise needed to conduct outstanding basic science and translational research using non-human primates (NHP).

The WNRPC is one of seven federally supported National Primate Research Centers and the only one in the Midwest. Thousands of scientists – from on campus to throughout the nation and the world – have conducted research in primate biology with relevance to human and animal health through the Center since its establishment in 1961. Based in the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE) of the University of Wisconsin-Madison (UW-Madison), the WNPRC currently houses a total of 1,591 monkeys, a population that includes 1,164 rhesus macaques *(Macaca mulatta)*, 122 cynomolgus macaques *(Macaca fascicularis)*, and 305 common marmosets (*Callithrix jacchus*; includes animals recently transferred from the New England Primate Research Center, NEPRC). The Center has strong, long-established research and teaching links to UW Schools or Colleges of Medicine and Public Health (SMPH), Letters and Science (L&S), Agriculture and Life Sciences (CALS), and Veterinary Medicine (SVM).

The administrative, research, and veterinary services of the WNPRC are conducted in Specific Animal Location **Figure 1**, left and right panels respectively) situated Specific Animal Location the UW campus, as well as Specific Animal Location specialized facilities located within the Wisconsin Institute for Medical Research (WIMR) on the SMPH campus, in laboratories located within the UW Research Park, and at a site leased to the UW by Harlan Laboratories in nearby Blue Mounds, WI (**Figure 2**). Personnel offices, Core P.I. research laboratories, service laboratories, and the majority of our monkey colonies and their corresponding veterinary and husbandry Specific Animal Location s are located in WIMR houses a new monkey vivarium, veterinary procedure rooms, ory testing arenas, and state-of-the-art imaging facilities. The AIDS Vaccine Research Laboratory (AVRL) at the UW Research Park houses the laboratories of several of our Core Investigators, as well as three of our Research Service units (Genetics Services, Immunology Services, and Virology Services). The Blue Mounds facility is used as a NHP quarantine unit and holding facility.

Specific Animal Location

Specific Animal Location

The WNPRC supports the studies of a large network of scientists. The Center's scientific portfolio currently includes 103 active doctoral level staff working directly on research projects, as reported in the Center's 2013-2014 Annual Progress Report. Another 39 scientific affiliates and collaborators have conducted research involving the Center since 2008. Hundreds of additional scientists have consulted with its core staff and scientists, or have used its services. This support has been pivotal in attracting a large number of grants that are either administered through the Primate Center or through individual departments or other institutions with cost reimbursement to the Center.

At the national and international levels, we continue to build strong strategic and collaborative links. The WNPRC enjoys open lines of communication and productive working relationships with other members of the NPRC program. We actively participate in the functions of all NPRC consortia and working groups, and several of our specialized service units provide targeted training for our NPRC counterparts. New laboratories regularly join our network from across the United States, and we have collaborations with several international laboratories on five continents.

The fundamental mission of the WNPRC is to increase our understanding of basic primate biology and to improve human health and quality of life through support of outstanding NHP research programs. To accomplish this, the WNPRC:

- Helps discover treatments, preventions, and cures for human disease.
- Accelerates translational research using NHP models.
- Generates new knowledge of primate biology, from the molecular to the organismal levels
- Facilitates research progress by providing the most advanced expertise, resources, and training to scientists worldwide.
- Collects NHP information and disseminates to the research community and to the public.

To realize these objectives, the WNPRC Core and Affiliate Scientists engage in a wide variety of basic science and translational research projects, and Center personnel develop innovative resources and technologies to facilitate these NHP research studies, particularly those funded by the categorical NIH institutes, but also by other federal funding agencies, non-profit biomedical research foundations, and industry. Together, the three service divisions of the WNPRC (Animal Services, Operational Services, and Research Services) work to optimize, tailor, and integrate the animal care, administrative support, and research services that best enhance the scientific endeavors undertaken at the Center, as well as at the home institutions of investigators accessing our services. We strive to provide the most advanced resources and expertise in the most cost-effective manner to the NHP research community, and gauge our progress by the quality and quantity of scientific achievements evidenced in the publications of investigators. **Table 1** lists the core service and resource units that support the scientific studies conducted at the center.

The WNPRC is a leader in several key areas of basic and translational biomedical research, as well as in human care of captive animals. The Center has a history of supporting high-impact research and discovery in regenerative medicine, reproductive biology, immunology, virology, aging and metabolic disease, neuroendocrinology, and behavior. Major advances by WNPRC investigators include insights on:

- Stem cell culture and differentiation. (Monkey and human embryonic stem cells, iPS cells.)
- Beneficial effects of controlled caloric restriction on primate health and longevity.
- How HIV infects the host and escapes the immune system. (Improve current HIV therapies and preventive strategies.)
- Risk factors for endometriosis.
- Causes of polycystic ovary syndrome (PCOS).
- Better enrichment and veterinary care for captive primates. (New diagnostics and treatments.)
- Neuroendocrine triggers of puberty. (Diagnosing and treating disorders of puberty.)

Table 1. Core Service and Resource Units

Division of Research – Director Excluded by Requester
Aging Colony Resource
SIV Elite Controller Resource
Stem Cell Resource
Bone Marrow Transplant Core
Marmoset Transgenesis Resource (in development)
Division of Animal Services – Associate Director Excluded by Requester
Veterinary Services
Colony Management
Compliance and Training
Behavioral Management
Scientific Protocol Implementation (SPI)
Pathology Services
NHP Biological Materials Distribution Core*
Division of Research Services – Associate Director Excluded by Requester
Assay Services
Immunology Services
Virology Services
Genetics Services
Research Computing
Division of Operational Services – Associate Director Excluded by Requester
Administrative Services (includes HR, Grants Management, Purchasing and Business Services)
Facilities, Management and Shop Services
Information Technology and System Services
**** Co-administered by SPI and Pathology Services***

- Improved hormone analysis in wild monkeys. (Monitoring and managing captive and wild primates.)
- Understanding primate family dynamics (Basic knowledge of primates, with insight into human family dynamics.)
- Understanding emotion. (Better treatments for psychological disorders.)
- Improved fMRI and PET techniques for noninvasively studying the primate brain.
- Requirements for early pregnancy success. (Improving natural fertility and understanding causes of miscarriage.)
- Improved IVF techniques (World's first IVF rhesus monkey born in 1984.)

Building on the historical strengths of the WNPRC, and recognizing the progression of collaborative studies in new directions, four ***Working Groups*** of UW investigators were formalized during the most recent period of grant support to address issues central to the following themes:

Global Infectious Disease (GID): Transmission and pathogenesis of Simian Immunodeficiency Virus (SIV), influenza, Dengue, viral escape, vaccine development, MHC-defined animals, influenza, and identification of new viruses with zoonotic and/or pandemic potential.

Regenerative and Reproductive Medicine (RRM): Embryonic/pluripotent stem cell biology including cellular therapies for hematologic, cardiovascular, and neurodegenerative diseases, organ transplant tolerance, stem cell-based therapies for AIDS; assisted reproductive technologies (ART) for NHP transgenesis, maternal-fetal health including pregnancy loss and poor outcomes, intrauterine environment in metabolic and reproductive epigenetic programming, endometriosis, and PCOS.

Energy Metabolism and Chronic Disease (EMCD): Chronic disease and aging research, with an emphasis on the genetic, cellular, and whole animal effects of caloric restriction (CR), as well as excess caloric intake resulting in obesity and metabolic syndrome; diabetes mellitus, osteoporosis, and new studies on post menopausal hormone changes and metabolic disease risks.

Neuroscience: Preclinical Parkinson's disease research, translational studies of glaucoma, as well as stress, anxiety, and depression, and basic studies of central nervous system mechanisms controlling fertility, puberty, menopause, and body weight, and neuroendocrine regulation of reproductive and social behaviors.

2. Relationship to the Grantee Institution

The UW-Madison, founded in 1848 and located on a main campus of 936 acres on the shore of Lake Mendota in the city of Madison, is one of the pre-eminent research universities in the world. It is consistently ranked among the top five U.S. public universities in terms of federally funded research, non-federally funded research, number of doctorates granted, and total research expenditures. The University has a total enrollment of more than 43,275 students, of whom 9,203 are graduate students and 2,701 are enrolled in professional programs (including Medicine and Public Health, Pharmacy, and Veterinary Medicine). The distinguished faculty includes over 40 members of the National Academy of Science, 28 members of the National Academy of Engineering, and recipients of awards from the Private Source and the Private Source Private Source

UW-Madison is a leader in biological research with state-of-the-art facilities and programs that are recognized worldwide. In 2013, external funding awarded to the University totaled $1.141 billion, with $850 million supporting the research enterprise. UW-Madison also has a vibrant academic component, with both undergraduate and graduate students training on an academically diverse campus that includes the SMPH, L&S, SVM, CALS, the College of Engineering, and a School of Pharmacy. The campus hosts 120 doctoral and professional programs and 148 Master's graduate programs, including 42 in the biological and 27 in the physical sciences.

One of the greatest assets of UW-Madison is its strong history of research, curricula, and academic programs that span disciplinary boundaries. The campus atmosphere encourages faculty and students to seek collaborators, share specialized facilities, and explore new research opportunities. Interdisciplinary interactions also are enhanced by activities through the UW-Madison Office of the Vice Chancellor for Research and Graduate Education (OVCRGE), which is dedicated to fostering such endeavors on campus. One component of this commitment is evident through OVCRGE administration of 17 interdisciplinary centers on campus, including the WNPRC. These centers have a range of academic emphases as their focus, and include the Biotechnology Center, the Institute on Aging, the Waisman Center, Wisconsin Institutes for Discovery, and others in addition to the WNPRC.

The WNPRC, along with the other centers under the administrative umbrella of the OVCRGE, largely function autonomously, with the director having responsibility for day-to-day operations and long-term strategic planning in a manner similar to that of the chairs of individual departments in the other schools and colleges at UW-Madison. In support of the activities of the directors, the OVCRGE provides diverse resources to aid in achieving the goals of each center. The Vice Chancellor for Research and Graduate Education (VCRGE), **Dr. Marsha Mailick**, is Principal Investigator on the WNPRC grant application, reflecting her role as Vice Chancellor responsible for global oversight of the Center. Numerous individuals within the VCRGE's office, including Associate and Assistant Vice Chancellors and their staffs, provide support for activities within the WNPRC, reflecting the administrative components available to the WNPRC and other VCRGE centers. The Office of Research and Sponsored Programs in the Office of the Vice Chancellor for Finance and

Administration manages the WNPRC's large portfolio of research grants. In addition to administrative assistance, the OVCRGE supports the scientific activities of the WNPRC through the provision of intramural funds to support faculty across campus via grants supporting faculty research efforts (over $4.44 million in competitively awarded research grants in Biological and Physical Sciences awarded on campus in 2013); funds supporting graduate student recruitment ($2 million in funds awarded to biological physical sciences departments on campus in 2014); monies in support of graduate student training (~$1 million contributed to campus training grants in 2011); and honorific awards to exceptional faculty (over $1.5 million awarded on campus in 2011). These funds are derived primarily from the Private Source During the current funding cycle, the WNPRC has received multiple, specific allocations of funds from the OVCRGE. For example, since 2008, approximately $6,180,000 was provided via the annual Capital Exercise mechanism (indirect cost return).

The WNPRC has extensive interaction with departments and centers in the SMPH, among other schools and colleges on campus. WNPRC scientists engage in research and training collaborations with approximately ten other campus centers and at least eight current training programs. The WNPRC is unique among the NPRCs in that it is located on an academically diverse campus that includes medical, veterinary, and agricultural divisions, along with a broad base of expertise and activity ranging from molecular to ecosystem biological science, translational and clinical medicine, informatics, and behavioral science. All of these aspects are represented in the WNPRC's program and, importantly, comprise a nurturing environment for continued development.

3. Organization and administration of the WNPRC

The **Director,** Excluded by Requester **Ph.D.**, serves as the overall administrative and scientific leader of the WNPRC, overseeing the strategic planning, policymaking, management, and progress of the three major service divisions: **Operational Services**, **Research Services**, and **Animal Services**. The three service divisions are in turn headed by **Associate Directors**, who are delegated operational authority over their respective divisions. The Director and Associate Directors function together as a **Senior Management Team**, meeting weekly to discuss all administrative, scientific, and veterinary matters, including ongoing issues, progress, new initiatives, and immediate, mid-term, and long-range objectives and planning. The Director is also responsible for organizing the scientific programs of the Center (see *Directors Office, Working Group* sections), and fostering new collaborations with national and international investigators engaged in NHP research. Towards these ends, the Director chairs monthly meetings of an **Executive Committee**. The Committee includes the Associate Directors plus PIs who are actively engaged in research using WNPRC resources and services, and whose project funding is administered by WNPRC. They represent the breadth of our primary research areas, and are responsible for the review and approval of research proposals. Each potential project is evaluated against several criteria, including fit with the WNPRC mission, quality of the science, availability of resources and funding source. Approval is obtained through majority vote of an Executive Committee. The Executive Committee additionally plays important roles in advising the Senior Management Team on the long-term and short-term directions of the scientific endeavor, as well as the appointment, promotion, retention, and dismissal of staff scientists in the WNPRC. Other standing WNPRC committees play important roles in space allocation, personnel recruitment, policy reviews, and other important WNPRC administrative matters

4. The External Advisory Board

Per the NPRC Program Guidelines, the role of our External Advisory Board (EAB; the WNPRC National Scientific Advisory Board) is to "provide guidance to the Principal Investigator and Center Director on all aspects of the NPRC, including scientific direction." Our EAB consists of ten experts in the various areas of WNPRC activity. Seven of these are internationally recognized biomedical scientists or primatologists from outside UW-Madison and three are local experts. Included on the EAB is the Director of the UW Institute for Clinical and Translational Research (UW ICTR), who serves as P.I. of the Clinical and Translational Science Award (CTSA) to the UW. All committee members have valuable experience and expertise to share with our Excluded by Requester n. The EAB provides the VCRGE and Director rigorous reviews of progress, priorities, and plans h of our service and scientific components on a semiannual basis and its reports are shared with the

Executive Committee. The first EAB visit of the year is dedicated to evaluations of the scientific programs of Core- and major Affiliate-PIs of WNPRC. The second visit focuses on the progress and plans of the scientific and technical cores and service units. Subsets of the EAB also serve as Research Resource Unit oversight committees, as they specifically critique the planning, progress, and prioritization of work in specific units.

5. Overview of Training and Outreach

Training and outreach activities by the WNPRC include many programs: internal training for all new employees, specific staff in each unit on established protocols, and visiting investigators; training in cooperation with other campus departments for staff, scientists, students, custodial staff, maintenance personnel, police officers; and external training for members of the public or for those who wish to pursue employment at the WNPRC. A summary of the WNPRC training and outreach program follows below.

For staff, the **Compliance and Training Unit** provides mandatory sessions for new employees to address regulatory compliance in all areas. These sessions cover occupational health and safety issues typical to any workplace; however, they also address highly specific concerns for working with NHP, as well as in laboratories with biosafety risks. Staff training includes conveying the importance of compliance with all mandatory Occupational Health and Safety Training, and adhering to all Standard Operating Procedures (SOPs). Our Compliance and Training Unit has continued to set an excellent example for the entire UW-Madison by hiring the first OHSA Compliance Coordinator to ensure the safety of our personnel.

The **Scientific Protocol Implementation** (SPI) **Unit** provides specific training to staff in assisted reproduction procedures, sample procurement, biological imaging, observation, and sample processing and shipping. The Behavioral Management, Colony Management, Pathology and Veterinary Services Units often work together to provide specific training in animal handling, training, enrichment, clinical evaluation, and treatment. Immunology Services, Virology Services, Assay Services and other units provide training on the use of highly specialized biomedical research equipment (flow cytometry, mass spectrometry, gene sequencing, confocal microscopy). Visiting affiliate and collaborating scientists from around the world also benefit from WNPRC shared expertise and training. In addition, all new employees must participate in an orientation session through the Human Resources (HR) Unit. HR also provides training to all staff related to employee benefits, retirement, travel, and other areas.

Because the WNPRC is not a degree-granting department at UW-Madison, WNPRC staff collaborates with other UW schools, colleges and departments to provide undergraduate, graduate student, and post-doctoral research training. Since 2008, Core-PIs have served as mentors for a total of 43 graduate students and 38 postdoctoral fellows. Fields of study for trainees include cellular and molecular biology, immunology, psychology, zoology, anthropology, obstetrics and gynecology, physiology, genetics, neuroscience, veterinary medicine, and other areas. Training programs within each WNPRC division and unit support students' direct contributions to the WNPRC as well as their own professional development. Students benefit from the WNPRC participation in several formal UW-Madison training programs across several schools and institutes. These include the Graduate School, SMPH, SVM, CALS, UW ICTR, Institute on Aging, Institute of Environmental Studies, Center for Neuroscience, Biotechnology Center, Waisman Center, Women's Health Research Institute, Endocrinology and Reproductive Physiology Training Program, Neuroscience Training Program, Stem Cell and Regenerative Medicine Center, School of Library and Information Studies, and training of students. The WNPRC has also hired students trained and certified as animal caretakers by Madison Area Technical College (MATC) on the city's east side, as well as training students who are then hired by private companies, such as the Private Source Research collaborations between undergraduates and WNPRC faculty/scientists are frequent recipients of annual campus awards.

While outreach activities do not directly provide long-term training to students, scientists, and the public, they have served as a critical door opener to the WNPRC for these audiences. Center staff presence and participation at scientific meetings, for example, has led to introductions, recruitment, hiring, and training of enthusiastic and skilled scientific staff and students. Even brief face-to-face connections with intelligent and motivated high school students during school outreach visits and science fairs has led to several such students enrolling at UW-Madison and then pursuing internships and other experiences with WNPRC staff, for example,

in the Public Information Office, in the Animal Services Division, and in various labs at the WNPRC or in affiliated departments.

6. Progress Report for the Period May 1, 2012 – Present

Progress: Research highlights, general. As a part of preparations for our base grant renewal application in 2012, four integrated Working Groups were established in 2011 to convene regularly in "Work-in-Progress" meeting formats, host seminar speakers, and engage in collaborative efforts to design new studies and formulate new grant proposals. The groups include Neuroscience, Reproductive and Regenerative Medicine (RRM), Global Infectious Disease, and Energy Metabolism and Chronic Disease. Each working group has realized major progress in their scientific studies and in the generation of new projects. For example, neuroscientists at the WNPRC found that transplantation of neuronal progenitor cells derived from induced pluripotent stem cells (iPSCs) survive for up to 6 months and differentiate into neurons, astrocytes, and myelinating dendrocytes in hemiparkinsonian rhesus monkeys – a significant step forward for the development of personalized regenerative therapy in Parkinson's disease. In RRM, major cellular pathways leading to specification of hemogenic endothelium and definitive hematopoietic cells from pleuripotent stem cells were identified. Members of the GID working group made major progress in developing new vaccine regimens to curb simian immunodeficiency virus replication, and successfully identifying and characterizing novel RNA viruses from free-living non-human primates. In the EMCD working group, several important studies were published on the effects of caloric restriction on brain development, function, and neuroprotection. In addition, increasing caloric intake was directly linked to early onset of puberty in female monkeys. In concert with the activities of the working groups has been the development of new cores and technical capabilities to advance the capacities of working group members and affiliate P.I.s. to make progress towards these goals. This includes progress in the development of a new Bone Marrow Transplantation Core, in which initial hematopoetic stem cell transplantations have already been performed towards establishing tolerance to kidney graft recipients.

Progress: Research highlights most relevant to the revised P51 application. A non-human primate transgenesis initiative has been launched to develop transgenic animal models of human disease. An initial proof-of-principle project is underway that is designed to generate a transgenic marmoset model of familial Parkinson's disease. Identification of specific alleles of the leucine rich repeat kinase 2 (LRRK2) in familial and sporadic cases of PD prompted WNPRC investigators to first develop a NHP model expressing these variants. Our investigators Excluded by Requester Ph.D.) proposed to advance the development of NHP models of disease by genomic editing with two Specific Aims: 1) To use common marmoset fibroblasts and ESC to optimize targeting vectors for genomic editing of LRRK2 G2019S associated with human Parkinson's Disease, and 2) To define the feasibility and accuracy of LRRK2 genomic editing in IVF-derived common marmoset embryos. The proposed generation and analysis of genomic edited monkeys will provide a platform to assess the impact of LRRK2 mutations in PD, identify and assess biomarkers of prodromal PD and test therapeutic approaches. Marmoset embryonic stem cells differentiate to neural lineages and support midbrain neuron development. Major progress towards these goals during the past year include 1) demonstration that marmoset fibroblasts can be reprogrammed into cells with morphological and molecular characteristics of induced pluripotent cells, 2) establishment of standard protocols for reliable semen collection from male marmoset donors, and 3) demonstration that ovarian stimulation of marmosets with human recombinant hormones will allow oocyte collection for in vitro fertilization and genomic editing.

With the initiation of studies in genomic editing of marmoset embryos Excluded by Requester has also begun a new collaboration with Excluded by Requester and Excluded by Requester of the Department of Pathology and Laboratory Medicine to develop a new nonhuman primate model for AIDS research, utilizing CRISPR/Cas9 approach to introduce the delta32 mutation into the rhesus gene encoding CCR5, an HIV/SIV receptor. The experimental plan will use hematopoietic stem cell transplantation with rhesus macaques to determine the feasibility of HSC modification for protection from, or curing HIV infection.

Progress: Transfer of marmoset colony from the NEPRC to the WNPRC. The WNPRC's established colony of common marmosets, which is housed in the Center's Specific Animal Location in Madison, Wisconsin, currently consists of 203 animals. On August 20, 2013, WNPRC Director Excluded by Requester PhD received a letter

from NEPRC Director [Excluded by Requester] PhD, indicating his desire to identify appropriate sites for the transfer of the NEPRC common marmoset colony. Guidelines for NPRCs interested in accepting the marmosets were outlined in an RFP entitled "Request for Proposals from NPRCs Interested in Receiving the NEPRC Common Marmoset Colony." We determined that it would benefit WNPRC core and affiliate investigators to expand the size of the WNPRC marmoset colony by acquiring a portion of the NEPRC colony. The WNPRC submitted a [Excluded by Requester] al to the [redacted] and ORIP Health Scientist Administrator [redacted] PhD, in response [Excluded by Requester] equesting equitable distribution of the NEPRC's established and active breeding groups betwe WNPRC and the SNPRC and also requested transfer of several additional marmosets to Wisconsin for proposed studies. On December 23 2014 [Excluded by Requester] informed the WNPRC that the NEPRC marmoset population would be divided between the WNPRC and the SNPRC. Additional discussions resulted in a mutual agreement that between 90 and 100 marmosets would be transferred to the WNPRC. Subsequently, ORIP issued a Notice of Grant Award (Direct costs = $309,859, total costs = $424,507) to the WNPRC for an administrative supplement to fund the necessary room renovations and animal enclosures and sufficient to cover salaries and per diems for the period beginning June 30, 2014 and ending April 30, 2015. All renovations and enclosure construction was completed by October 1, 2014 and the WNPRC received 90 marmosets from the NEPRC on November 4, 2014 and an additional 9 marmosets on December 3, 2014. This revised application seeks to continue support for the transferred marmosets for the remaining two years of this P51 grant funding cycle.

Progress: Administrative highlights. The WNPRC has achieved major gains in efficiency, productivity, and optimization or resource utilization and management during past two years. We have combined the human resources/payroll and benefits, finance, purchasing and grants administration units into one cohesive Administrative Services unit, and completed a plan to consolidate all of these offices into a centralized area previously containing our Library's underutilized print research journal collections. The WNPRC library resource was reduced from a physical and electronic service to an electronic resource only, comporting with budgetary restrictions and the need to focus center activities more specifically on those attending to support of biomedical research. With increasing demand for NHPs for research projects, the WNPRC sought to expand quarantine and holding space for monkeys obtained from other sources. A series of strategic planning sessions and negotiations culminated in the signing of a long-term lease agreement for a [Specific Animal Location] animal holding facility in Blue Mounds, WI, owned by Harlan Laboratories. With significant support provided by the University of Wisconsin, the facilities were renovated and then occupied in 2012, providing space for 360 NHPs and allowing the WNPRC to accommodate major new projects on AIDS vaccine development, iPSC preconditioning in solid organ transplantation, and other new areas of study. The WNPRC has also achieved success in the development and launching of a new LabKey Electronic Health Records (EHR) system, which came on-line in full in 2012.

7. Specific accomplishments and their contribution to the mission and goals of the NPRC.

The WNPRC maintains a deep commitment to each of the eight objectives of the NPRC Program as originally published by the NCRR. These specific goals are recapitulated below, accompanied by prime examples of how WNPRC achievements and progress reflect our responsiveness to each during the current funding period, and illustrate WNPRC's unique and diverse contributions to the NPRC program.

Develop and sustain national resources for normative data, consultative and collaborative expertise, biologic and genetic material, and specialized facilities, equipment, and expertise that support NHP-related research.

- The WNPRC is a leader is determining how the animal genetics influences susceptibility to infectious disease and anxious temperament. Specific expertise is made available to the scientific community through the Genetics Services Unit and other NPRC programs.
- NHP research includes work on several species, many of which have regional subpopulations. WNPRC scientists are leaders in understanding the genetic differences between these subpopulations. Researchers considering projects often consult with WNPRC experts to determine which subpopulations are most appropriate for a given study.
- WNPRC investigators help curate NHP genetic databases, publicizing information gained from WNPRC

studies and reducing the redundant discovery of genetic polymorphisms.

- Our new, extremely powerful EHR colony database serves as a resource to qualified investigators in need of normative NHP data from our colony.
- Animals, as well as samples and banked tissues, are available from our aged monkey resource in support of aging research nationwide. Routine clinical data from these animals also forms a unique resource for normative data on aging in rhesus macaques.
- WNPRC is leading a tri-Center, multi-disciplinary, basic-clinical science partnership initiative in determining incidence, traits, and pedigree analysis of naturally-occurring PCOS in female rhesus monkeys at WNPRC and YNPRC, as well as in female cynomolgus monkeys at Wake Forest Primate Center. Identifying inheritance of this prevalent women's cardio-metabolic and infertility syndrome in female NHP holds promise for developing new curative therapeutic approaches
- Utilizing neuroimaging expertise at the Waisman Laboratory for Brain Imaging and Behavior, WNPRC investigators collaborated in development of a 3-D MRI-derived template of the marmoset brain. One of the template's main applications enables neuro-anatomical localization of PET-detectable neuroligands and enhanced or diminished neuroactivity.

Breed and provide animals suitable for research using NHP.

- WNPRC promotes research in embryos and fetuses obtained from time-mated mothers that is providing the foundation for a precise developmental atlas for tissues and organs, especially of the brain and spinal cord, and which is not achievable in humans due to ethical constraints.
- The WNPRC supports core expertise in assisted reproductive technologies to facilitate multi-faceted initiatives in the development and dissemination of approaches for NHP transgenesis.
- In collaboration with Genetics Services, Animal Services focuses its breeding program to maintain important rhesus genotypes, e.g., specific MHC alleles for infectious disease research, while ensuring an appropriate level of genetic diversity.

Study the biology of NHP species that are of potential research importance for the purpose of enhancing their scientific utility, health, and well-being.

- WNPRC investigators help define the biology of NHP that offer improved ways of understanding human biology. For example, WNPRC investigators were among the first to demonstrate the restricted genetic diversity of cynomolgus macaques from Mauritius. This knowledge was used to develop better systems for understanding interactions between genetics and SIV pathogenesis. WNPRC scientists are working with researchers in other disciplines to explore the utility of genetically-defined, outbred animals.
- WNPRC investigators collaborated with a set of international colleagues to demonstrate that Caribbean African green monkeys have restricted genetic diversity like Mauritian macaques. This information helps guide the interpretation of studies that use African green monkeys.
- WNPRC scientists have developed methods for isolating viruses from the blood of captive macaques. These methods can be applied during future disease outbreaks to confirm an infectious origin, categorize the etiologic agent, and develop plans for medical management of outbreaks.
- WNPRC investigators have demonstrated tissue-specific regulation of leukocyte populations in the reproductive tract, which may underlie reproductive efficiency, breeding success, and provide new models for recurrent pregnancy failure.
- Scientists at the WNPRC have revealed trends in the WNPRC colony in the age of menarche associated with nutritional plane that may provide a clue for societal trends towards earlier attainment of puberty.

Develop improved practices of NHP breeding, husbandry and genetic definition to help meet research needs for pedigreed, disease-free animals of defined quality, and to ensure the continued availability of species of biomedical research importance whose wild populations are considered threatened or endangered.

- Scientists at the WNPRC have extensively studied breeding colony animals' MHC genetics. This information can be used to balance genotypes in the colony or specifically breed animals with specific, high-value genetics.

- The WNPRC is working with leading genome centers to study NHP genome biology. Two WNPRC cynomolgus macaques have had their genomes sequenced at the Baylor College of Medicine Center for Human Genome Sequencing, with additional sequencing of WNPRC animals planned in the near future.
- During the last two years, WNPRC scientists, in collaboration with veterinarians and ecologists in Uganda, have begun characterizing pathogens endemic to NHP living in Kibale National Park.
- The WNPRC only breeds rhesus macaques free of Herpes B, STLV, SRV and SIV.

Develop NHP models of human disease and facilitate their use.

- WNPRC researchers are working with colleagues in Australia to characterize hepatitis B prevalence in Mauritian macaques, following a recent report that these animals can be infected with a human-like hepatitis B virus. This could lead to an improved animal model for HBV vaccine optimization and pathogenesis studies.
- WNPRC researchers developed a strategy for sequencing entire SIV genomes using Roche/454 pyrosequencing. This method has been successfully adapted to sequence important human pathogens including HIV, hepatitis C virus, and dengue virus from clinical samples.
- After discovering SHFV in wild primates, WNPRC scientists collaborated with investigators studying Ebola pathogenesis to use the newly discovered virus to optimize BSL-4 containment procedures.
- WNPRC scientists are discussing the possibility of using methods developed to identify novel pathogens in feral primates to look for novel pathogens in people with fevers of unknown origin, such as those people living in close proximity with feral animals and immunosuppressed organ transplant recipients.
- We have been making a concerted effort to further define the rhesus monkey model of obesity and metabolic syndrome and to develop a promising new model, the common marmoset, for these important public health concerns.
- Collaborations with international investigators to develop transgenic nonhuman primate models of devastating diseases, including Parkinson's Disease, and Fragile X Syndrome.
- New initiatives in transplant medicine which builds on cutting-edge understanding of maternal-fetal chimerism and development of tolerance, aimed at improving solid organ transplant success.
- Support for new imaging initiatives to predict and prevent cervical insufficiency and preterm labor, a major risk factor for neonatal morbidity and mortality.
- New initiatives to synthesize leading novel concepts in inflammation and pregnancy success and loss, to develop NHP models of preeclampsia, and to understand the mechanisms of preterm labor and stillbirth arising from *Listeria monocytogenes* infection during pregnancy.
- WNPRC investigators provide overall leadership to a multi-institutional, basic-clinical science, multi-disciplinary team characterizing and experimentally manipulating infant and adult epigenetic, metabolomic, endocrinological, and somatometric traits of an NHP PCOS model to reveal novel mechanistic understanding of developmental origins translatable to human obstetric and pediatric care.
- WNPRC scientists collaborated in the development of a marmoset model of maternal neglect that offers new insight into neuro-mechanisms underlying maternal abuse of children in humans.

Conduct pilot (basic and applied) biomedical research projects in areas requiring the use of NHP. Pilot projects are aimed at helping to solve problems related to human health, and they should lead to independent grant support related to the disease or health problem being studied.

- In 2010, a WNPRC researcher began a pilot project to extend the WNPRC excellence in studying SIV pathogenesis to the study of the pathogenesis of SIV/tuberculosis co-infections.
- Methods developed to determine the MHC genetics in NHP are now being used to rapidly and economically determine the HLA genotypes of participants in human research projects.
- The WNPRC and UW ICTR co-sponsored a pilot project designed to develop the common marmoset model of obesity and metabolic syndrome. This work provided important preliminary data for a recent renewal proposal for a Specialized Center of Research (SCOR) co-directed by Excluded by Requester
- WNPRC and UW ICTR co-sponsored pilot projects were funded for developing new methodologies for NHP transgenesis, and to define immunological biomarkers of pregnancy recognition and loss.

Provide opportunities for local, national, and international research involvement and experience in primatology to graduate and undergraduate students, postdoctoral fellows, visiting scientists and faculty members, as well as short-term learning assignments for students of the health professions.

- The WNPRC routinely hosts visitors who come for a short time to learn specific techniques to collaborate on specific projects. In the past four years, WNPRC has hosted visiting scientists from a variety of national and foreign institutions and foundations, as well as from foreign and domestic pharmaceutical and biotech companies. We have also trained two MD fellows from the UW SMPH Departments of Pediatrics and Pathology
- WNPRC investigators train US and international graduate students and basic science and clinical postgraduate fellows in a broad spectrum of UW-Madison training programs in biomedical sciences.
- As part of an NIH contract, WNPRC investigators have hosted annual training workshops in WNPRC labs, making technologies developed at the WNPRC available to the broader scientific community.
- A team of WNPRC investigators teaches a 100-student undergraduate course on HIV/AIDS at UW-Madison. The course integrates research by WNPRC scientists and collaborators with larger issues about the current state of the HIV pandemic.
- WNPRC investigators are leading novel approaches in a 200-300 student undergraduate biology class, in the sophomore introductory sequence, to integrate contemporary medical issues including obesity, type 2 diabetes, cardiovascular disease, immune responses to infectious disease, and reproductive dysfunction into lecture content and interactive, problem-solving group exercises. A Provost-office initiative captured the essence of these efforts in a short, professional video posted to the UW-Madison Teaching Excellence website for teacher and public access
- The SIV, neurodegenerative, parenting, CR, aging, and PCOS monkey studies routinely attract undergraduate students for opportunities to perform independent study projects utilizing unique NHP resources at the WNPRC. Such research projects frequently garner UW Madison undergraduate research awards.

Disseminate the findings of studies and technical advances in NHP research to the scientific community via reports published in internationally-recognized, peer-reviewed journals and other appropriate media.

- In addition to publishing findings from our studies in high-impact peer-reviewed publications, we frequently welcome appropriate local, national, and international news media to the WNPRC to disseminate our findings to the general public.
- In addition to printed publications, WNPRC researchers are invited to major national and international conferences that disseminate research findings, publicize the advances and opportunities with biomedical NHP research, and directly catalyze collaborative interactions with U.S. and international investigators.

Although not explicitly incorporated into the above NCRR objectives, an overriding mission conferred to the NPRCs is to ***support the conduct of important translational and preclinical studies in NHP.*** *Our progress in this regard includes the following:*

- Following WNPRC studies in NHP models demonstrating that topical applications of actin cytoskeleton-altering compounds to the eye lower intraocular pressure and ameliorate the leading cause of blindness in humans, an initial Phase 1 clinical trial was successfully completed that has since led to the onset of Phase 3 clinical trials.
- A neurodegenerative disease study in parkinsonian NHPs provided crucial evidence to support the first gene therapy trial for Parkinson's Disease (PD). The trial was completed with great success in 2011. The trial tested the safety and feasibility of delivering an adeno-associated viral vector encoding for glutamic acid decarboxylase into the subthalamic nucleus in order to increase the neurotransmitter GABA and balance the damaged neural network.
- A WNRPC study of early PD in NHPs demonstrated the neuroprotective properties of pioglitazone, a PPARgamma agonist currently FDA approved as an antidiabetic treatment. These findings provided the basis for a currently ongoing clinical trial supported and organized by NIH-NINDS Net PD. The NHP

study also showed the interaction between WNPRC Working Groups, as this drug was originally tested by investigators in EMCD for its antidiabetic indication, and then later by investigators in RRM for successful normalization of NHP PCOS signs and symptoms, before its recent engagement by investigators in NS.

- Treatment of male rhesus monkeys with a novel, selective inhibitor of androgen biosynthesis, VT-464, demonstrated clear inhibition of adrenal androgen production without concomitant diminution of adrenal cortisol production and enhanced aldosterone release. These WNPRC results played a key role in initiation of a Phase 1/2 Clinical Trial of VT-464 for Castration-Refractory Prostate Cancer in 2011.

9. Changes in Key Personnel

As of September 1, 2014, Excluded by Requester Ph.D. Personal Info as the Vice Chancellor for Research and the Dean of the Graduate School and returned to his faculty post. Marsha R. Mailick, Ph.D. has been appointed the Interim Vice Chancellor for Research and Graduate Education and, as such, has assumed the role of Program Director on the Primate Center's base grant. Dr. Mailick joined the UW-Madison faculty in 1988. She currently directs the Waisman Center, a large multidisciplinary center with a focus on developmental disabilities and neurodegenerative diseases. A copy of Dr. Mailick's Biosketch is attached to this application.

10. Summary of plans, challenges, and opportunities for the requested period of support

We will capitalize on the forward momentum we have already achieved through new hires, expansion, upgrade and reorganization of facilities, and key resource enhancements. Of highest priority will be the recruitment and expansion of high-impact scientific programs that make use of our unique constellation of resources and s. Shortly after assuming the Directorship Excluded by Requester nitiated a comprehensive assessment of the h and depth of the scientific programs of the Core and UW Affiliate Scientists, and the degree to which collaborative and interactive scientific groups functioned at the WNPRC. This scientific inventory was accomplished in large part by scheduling scientific presentations during the EAB visit in fall 2010, which were then subject to rigorous reviews by the EAB members. Armed with their insightful reports Excluded by Requester Senior Management Team developed a three-pronged plan to further develop and renew the scientific p of the WNPRC – ***the establishment and enhancement of the Working Groups, partnering with key University schools, centers, and departments to recruit strong new NHP researchers, and the development of new and innovative projects with extramural collaborators.***

Collaboration and Interdisciplinarity. We recognize that the increasingly austere NIH funding climate presents a major challenge for investigators at the WNPRC, UW, and all of our peer research institutions. Our approach to maintaining progress will be to utilize our Working Groups as "Centers within the Center" to kindle outstanding new science and collaborations among an increasingly larger group of national and international researchers. We will also continue to utilize and expand the capacities of our SPI unit as a vehicle to engage, plan, and facilitate the conduct of new collaborative projects.

The Director along with the VCRGE and administrators will continue to work to raise internal and external funds for infrastructure improvements and the development and support of new technological facilities and services. We will be enterprising and opportunistic in seeking support from federal and non-federal sources, including both non-profit foundations and commercial institutions. Continued collaboration with UW ICTR, as well as the UW Waisman Center, will also be critically important in leveraging support for new scientific and resource-generating endeavors. Excluded by Requester has established strong working relationships with Excluded by Requester Director of UW ICTR and UW SMPH Senior Associate Dean for Clinical and Translational Res Excluded by Requester Excluded by Requester Director of the Waisman Center. Both of these important administrative figures at UW have committed to continued collaborative efforts with WNPRC in development of new scientific programs. During the current funding period, for example, several Pilot Projects were co-funded by the WNPRC and ICTR to develop new ideas and animal models for translational research in NHP, such as the generation of a marmoset model of human obesity and metabolic syndrome; in the upcoming year, a new project is slated for co-funding that will attempt to produce a new transgenic monkey model of Parkinson's disease. Collaborative project development will also continue between WNPRC and Waisman Center Core-PIs, in which iPSC

technologies are used for transplantation experiments in NHP, to develop iPSC-based therapies for neurodegenerative diseases. The WNPRC will also continue to increase interactions with Excluded by Requester and other leading behavioral neuroscientists at the Harlow Center, a goal that is already being achieved through the launch and initial activities of our Neuroscience Working Group. The participation of both Centers in the hiring of collaborators Excluded by Requester has also cemented a new working relationship between the WNPRC and Harlow Center.

New frontiers in NHP research. In the proposed funding period WNPRC investigators will pursue innovative new avenues of discovery, launching new projects and initiatives that have been energized by new collaborations within and between Working Group, and with their colleagues at other national and international institutions. Below we summarize some of the new directions that are planned.

GID. The next four years promise continued productivity from GID. In the very near future, three projects merit special note. First, the discovery of novel viruses should accelerate with the new acquisition of an Illumina miSeq by Excluded by Requester group. The high throughput of this machine (100x greater than the Roche/454 GS Junior) will dramatically accelerate the screening of plasma samples for new viruses. The throughput will also allow, for the first time, investigation of non-RNA virus pathogens, possibly including DNA viruses and parasites. We are also forging closer collaborations with investigators to examine humans with fevers of unknown origin who live near Ugandan NHP. In February 2012, Excluded by Requester Excluded by Requester will meet in Kibale, Uganda with several of these collaborators to cement these collaborations and develop additional projects. Last, we anticipate forging stronger relationships between GID and RRM, particularly in the realm of marrying adoptive cell transfer research with engineered stem cells to explore curative approaches to SIV, as described below.

GID/RRM. Regenerative Medicine and HIV/AIDS research represent two major components of the WNPRC research program. This provides a unique opportunity to integrate and synergize these resources toward development of novel stem cell-based therapies for AIDS. Provocative advances in HIV 'cure' research showed the need for evaluation of these cell-based curative therapies for AIDS in aNHP. In contrast to current drug therapies, which only decrease viral load and have significant side effects, stem cell therapies have the potential to cure HIV infection. In the next P51 funding period, WNPRC plans to establish a novel Bone Marrow Transplantation unit that will explore hematopoietic stem cell and cellular therapies for AIDS. This project will capitalize on recent advances in reprogramming adult somatic cells to iPSCs by the Thomson lab. Because iPSCs can be expanded indefinitely *ex vivo*, genetically modified using homologous recombination, and differentiated into hematopoietic cells, it may be possible to produce immunologically matched gene-edited HIV-resistant therapeutic cells, including hematopoietic stem cells and T cells. In addition, this approach allows evaluation of HIV resistance mechanisms in NHP. Excluded by Requester an experienced HIV/AIDS researcher Excluded by Requester ecific expertise in NHP cell transfers, and an expert in hematopoiesis from iPSCs, will work her UW-Madison AIDS investigators and hematologists to initiate and develop this exciting new project.

RRM. Studies of the crucial role of the intrauterine environment in healthy fetal development, neonatal outcome, and adult physiology are an opportunity to improve child health in the developing as well as the developed world. For example, Private Source and the Private Source Private Source have committed $50M to fund the International Fetal and Newborn Growth Consortium at worldwide centers to develop a fetal atlas of healthy human development. There is interest in committing additional funds to develop a parallel NHP atlas. and the WNPRC is well-positioned to take advantage of these initiatives. In addition to the demonstration Excluded by Requester lab that intrauterine prenatal androgen treatment Excluded by Requester s a rhesus PCOS model Excluded by Requester lab has demonstrated a negative impact of passive immunization placental MHC class I on placental vascularization and growth, and endometrial maturation in early Excluded by Requester ncy, lab has shown negative fetal outcomes with prenatal anemia and endotoxin exposure. next four years, WNPRC will significantly increase our commitment to using the rhesus model to study the intrauterine environment in healthy and adverse maternal-fetal outcomes and will increase interactions between core investigators and affiliates. In addition to extending the foregoing studies, new initiatives in listeriosis-stimulated pregnancy loss, stillbirth and preterm labor, as well as studies on cervical patency and ripening, will synergize with these ongoing studies of intrauterine antecedents which reprogram postnatal development and health, with the goals of understanding mechanisms and testing therapies.

RRM/Neuroscience. NHP transgenesis specifically requires expertise in embryology and reproductive biology, as well as the collaborative scientific expertise to drive the development of new and innovative models of human disease. The WNPRC will draw on its previous experience with transgenesis and experimental embryology to implement transgenic approaches for the generation of novel NHP models of neurodegenerative and genetic diseases. These studies will be advanced by experienced core scientists working with international collaborators in vector technology, cell biology, reproductive biology, and neurosciences. Specific approaches for Parkinson's disease and Fragile X Syndrome are described further in the RRM section. These efforts will benefit directly from the diverse and strong campus-wide expertise within the Neurosciences group.

Neuroscience. Studies have made it increasingly clear that environmental and experiential factors shape neuronal development and maturation in part via epigenetic mechanisms. For example, molecular modifications to the DNA and the histone core play a key role in regulating gene transcription independent of alterations in gene sequences. These epigenetic phenomena act in concert to signal environmental conditions such as infant rearing conditions and dietary signals. Using a young rhesus monkey model established and Excluded by Requester ed by during the next five years Excluded by Requester and their colleagues will study how nvironmental factors impact the risk of developing anxiety and depressive disorders. Based on the recent finding that feeding juvenile monkeys a high calorie diet results in accelerated body growth with precocious puberty, Excluded by Requester will also investigate the impact of dietary influences on the mechanism of puberty onset. Both groups will use combined approaches of sophisticated behavioral observations and postmortem brain analyses. Neurogenomic approaches include next generation deep RNA sequencing and genome wide DNA methylation analyses in collaboration with the UW Biotechnology Center.

WNPRC researchers will additionally investigate the potential utility of iPS cell-based dopamine replacement therapy for treatment of Parkinson's disease. Excluded by Requester have already been successful in deriving dopamine neurons from individualized monkey iPS cells, and they are now implanting these cells into the respective donor monkeys, in which parkinsonian symptoms were induced. They will continue this project and assess the degree to which symptoms are ameliorated in these animals. Future plans involve expansion of these procedures to assess efficacy for other diseases, such as ALS, Huntington's, and Alzheimer's diseases. Work will also continue on a pilot project supporting development of optogenetic methods to activate specific Excluded by Requester oci in rhesus macaques is collaborating with Excluded by Requester in Medical Physics and rs of the new Department of Neuroscience to deliver viral vectors encoding channel rhodopsin to central neurons. The transduced neurons will be thereafter photoactivated *in vivo* and the impact of neuronal activation on physiological processes will be analyzed to reveal the functional properties of circuitries that govern sensorimotor activity and cognition. This method holds enormous potential to acquire a profound understanding of neural network function in normal and disease states.

Neuroscience/EMCD. A major new investigation has been undertaken by Excluded by Requester to determine the molecular and cellular pathways that mediate estrogen effects in the primate brain. Studies in rodents have revealed that estrogen receptor alpha (ERα) activation in hypothalamic neurons suppresses food intake and increases energy expenditure, and loss of this regulatory mechanism may confer a greatly increased risk of developing metabolic syndrome on postmenopausal women. Little information is available on the cellular mechanisms that may mediate these estrogenic effects in primates. Our studies will make use of novel viral vector-mediated gene transfer methodologies to manipulate the expression and functions of neuronal estrogen receptors, and thereby determine their role in regulating food intake, energy balance, metabolism, and body weight. Information gained in these studies hold great potential for developing selective ERα agonists to reduce the risks of obesity and metabolic disturbances in postmenopausal women.

EMCD. Following over 20 years of study, Excluded by Requester have convincingly shown that many of the well-known benefits of CR in rodents and lower models also occur in primates. This proof of primate efficacy has paved the way for serious study of CR in humans and lucrative development of potential CR mimetics. Excluded by Requester and colleagues now look forward to the much-anticipated finding of the impact of CR on maximum lifespan. These landmark studies have also set the stage for experiments aimed at understanding the mechanisms underlying the beneficial effects of CR in primates. Understanding these mechanisms will not only assist in the translation of CR to humans, but will undoubtedly lead to innovative new approaches to investigation of age-related diseases and conditions. In closely related work, Excluded by Requester Excluded by Requester plan to expand upon their current NHP work on metabolic syndrome to delineate a

predictive diagnostic for metabolic syndrome development and test this diagnostic in human clinical trials. The successful development of this diagnostic tool will not only allow for earlier interventions with known treatments, but will also afford the opportunity to develop novel therapeutics that will be most effective at extremely early disease stages.

Relationship of the marmosets transferred from the NEPRC to the overall function of the WNPRC.
In this P51 Revision application, the WNPRC requests continued support for the maintenance and development of a colony of common marmosets (*Callithrix jacchus*) acquired from the NEPRC. For many years, the NEPRC, SNPRC, and the WNPRC have been the only three of the eight NPRCs that have possessed the infrastructure and expertise to maintain common marmoset breeding colonies. The loss of one of these colonies due to closure of the NEPRC would have devastating consequences on the availability and genetic diversity of common marmosets available to U.S. based investigators. Thus, transfer of the existing NEPRC common marmoset colony to the WNPRC and the SNPRC is imperative, if indeed we are to maintain this NHP resource for the growing needs of the national scientific research community.

The existing marmoset colony at the WNPRC has historically proven to be critically important in studies of *in vitro* fertilization, stem cell biology, steroid hormone signaling, neuroendocrine mechanisms governing parental behavior, neuroendocrine regulation of fertility, and dietary and hormonal mechanisms controlling body weight and metabolism. Marmosets remain the experimental animal of choice among one or more investigators affiliated with each of the WNPRC Working Groups, which include Neuroscience, Energy Metabolism and Chronic Disease (EMCD), Reproductive and Regenerative Medicine (RRM), and Global Infectious Disease (GID). Current and future demand for marmosets by these WNPRC and UW researchers, as well as by investigators nationwide, appears to be increasing significantly[1-6]. The transfer and development of the NEPRC marmoset colony will thus enhance our capacity to fulfill our specific aim "*To breed and provide animals suitable for research using NHPs*".

Present and future support of the collective NPRC marmoset resource has become particularly important to the national research enterprise, inasmuch as exciting new research strategies are being undertaken that take advantage of the special advantages of this experimental animal. Some of these advantages are strategic; the reduced maturation time, propensity for twinning, and ease of social housing dramatically reduces the cost of production and experimental utilization of a non-human primate, and can decrease the time-frame of data acquisition in many studies. These same characteristics of marmosets, when combined with recent technical advances in certain research areas, are now making it feasible to perform experiments in this NHP that until recently were only practical in rodent models. This is particularly true for the study of the genetic determinants of disease. At great cost, very few transgenic NHP models have been developed that have permitted advances to be made in understanding the molecular and genetic determinants of primate-specific physiology and pathophysiological states. With the advent of new genomic editing techniques, transgenesis in NHPs has become a much more feasible endeavor, especially when utilized in the context of the reproductive and developmental advantages offered by the marmoset. One of the most important recent breakthroughs in cell biology methods is the development and refinement of genomic editing with the CRISPR/Cas9 system in mammalian cells and embryos which holds promise for generating animals expressing disease-relevant levels of a mutated protein.

We have launched a new NHP Transgenesis Initiative that will use these genomic editing approaches to produce new NHP models of human disease, and thereby enhance our efforts to address the specific aim "*To develop NHP models of human disease and facilitate their use*." Marmoset monkeys present several advantages for genomic editing approaches compared to macaques, including the ability to routinely carry multiple offspring (rapidly increasing cohort size), facile reproductive management, and a shorter lifespan, which facilitates the study of age-related diseases such as diabetes, arthritis and Parkinson's disease (PD). The WNPRC is the only facility in North America where marmosets, primate embryology, and cutting edge neurological translational models are actively being used to test therapies for human disease. An initial project, which has received P51 supplemental funding, has been underway and significant progress towards the production of an NHP model of familial PD has already been made, as briefly noted in the foregoing progress report.

The WNPRC has maintained a colony of common marmosets (*Callithrix jacchus*) since a founder group of 13 animals was purchased from the Waisman Center (an intellectual and developmental disabilities research center located at the University of Wisconsin-Madison) in 1990. The founder colony was augmented with 170 additional animals acquired from the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP) at New York University in 1991 and 1992 and has been maintained with offspring of the Waisman and LEMSIP founder animals since that time. The census of the WNPRC marmoset colony has ranged from 200 to 350 animals and the animals have historically proven to be critically important in studies of:

- In vitro fertilization
- Stem cell biology
- Steroid hormone signaling
- Neuroendocrine mechanisms governing parental behavior
- Neuroendocrine regulation of fertility
- Dietary and hormonal mechanisms controlling body weight and metabolism

Marmosets remain the experimental animal of choice among one or more investigators affiliated with each of the WNPRC Working Groups, which include Neuroscience, Energy Metabolism and Chronic Disease, Reproductive and Regenerative Medicine, and Global Infectious Disease (GID). Marmosets are also being utilized in a major new WNPRC initiative using CRISPR technologies to produce transgenic NHP models of disease, including neurodegenerative and neuropsychiatric disorders. Additionally, we are now employing new imaging-guided stereotaxic surgery and viral vector-mediated gene silencing strategies in marmosets to chronically alter target neural gene expression, permitting cutting-edge studies of neuroendocrine and metabolic disorders. Current and future demand for marmosets by WNPRC and UW researchers, and similarly by investigators nationwide, thus appears to be increasing significantly[1-6].

The WNPRC's established colony of common marmosets, which is housed in the Center's Specific Animal Location building in Madison, Wisconsin, currently consists of 203 animals. On August 20, 2013, WNPRC Director Excluded by Requester PhD received a letter from NEPRC Director Excluded by Requester PhD, indicating his desire to identify appropriate sites for the transfer of the NEPRC common marmoset colony. Guidelines for NPRCs interested in accepting the marmosets were outlined in an RFP entitled "Request for Proposals from NPRCs Interested in Receiving the NEPRC Common Marmoset Colony." We determined that it would benefit WNPRC core and affiliate investigators to expand the size of the WNPRC marmoset colony by acquiring a portion of the NEPRC Excluded by Requester The WNPRC submitted a proposal to [redacted] and ORIP Health Scientist Administrator Excluded by Requester PhD, in response to the RFP, requesting equitable distribution of the NEPRC's established and active breeding groups between the WNPRC and the SNPRC and also requested transfer of several additional marmosets to Wisconsin for proposed studies. On December 23 2014 Excluded by Requester informed the WNPRC that the NEPRC marmoset population would be divided between the WNPRC and the SNPRC. Additional discussions resulted in a mutual agreement that between 90 and 100 marmosets would be transferred to the WNPRC. Subsequently, ORIP issued a Notice of Grant Award (Direct costs = $309,859, total costs = $424,507) to the WNPRC for an administrative supplement to fund the necessary room renovations and animal enclosures and sufficient to cover salaries and per diems for the period beginning June 30, 2014 and ending April 30, 2015. All renovations and enclosure construction was completed by October 1, 2014 and the WNPRC received 90 marmosets from the NEPRC on November 4, 2014 and an additional 9 marmosets on December 3, 2014.

Vertebrate Animals (Overall)

PLEASE SEE ANIMAL RESOURCES COMPONENT.

References (Overall)

1. Excluded by Requester

Excluded by Requester 3rd. Differential virulence and disease progression following Mycobacterium tuberculosis complex infection of the common marmoset (Callithrix jacchus). Infect Immun. 2013 Aug;81(8):2909-19. doi: 10.1128/IAI.00632-13. PMID: 23716617.

2. Excluded by Requester Common marmoset as a new model animal for neuroscience research and genome editing technology. Dev Growth Differ. 2014 Jan;56(1):53-62. doi: 10.1111/dgd.12109. Epub 2014 Jan 5. Review. PMID: 24387631.

3. Excluded by Requester

Demonstration of marmosets (Callithrix jacchus) as a non-human primate model for secondary dengue virus infection: high levels of viraemia and serotype cross-reactive antibody responses consistent with secondary infection of humans. J Gen Virol. 2014 Mar;95(Pt 3):591-600. doi: 10.1099/vir.0.060384-0. Epub 2013 Dec 9. PMID: 24323638.

4. Excluded by Requester

Excluded by Requester Five-sixth Nephrectomy in Female Common Marmosets (Callithrix jacchus) as a Chronic Renal Failure Model: A Longitudinal Course of Serum Biochemical, Hematological and Histopathological Changes. J Toxicol Pathol. 2014 Oct;27(3-4):183-95. doi: 10.1293/tox.2013-0055. Epub 2014 Jul 3. PMID: 25378803.

5. Excluded by Requester l-DOPA-induced behavioral sensitization of motor activity in the MPTP-treated common marmoset as a Parkinson's disease model. Pharmacol Biochem Behav. 2014 Oct 31;127C:62-69. doi: 10.1016/j.pbb.2014.10.009. PMID: 25449794.

Excluded by Requester On-going elucidation of mechanisms of primate specific synaptic spine development using the common marmoset (Callithrix jacchus). Neurosci Res. 2014 Nov 26. pii: S0168-0102(14)00242-9. doi: 10.1016/j.neures.2014.10.019. [Epub ahead of print] PMID: 25433092.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

5. APPLICANT INFORMATION **Organizational DUNS*:** 161202122

Legal Name*: The Board of Regents of the University of Wisconsin System
Department:
Division:
Street1*: Suite 6401
Street2: 21 N Park St
City*: Madison
County: Dane
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53715-1218

Person to be contacted on matters involving this application

Prefix:	First Name*:	Middle Name:	Last Name*:	Suffix:
	BRENDA	A	EGAN	

Position/Title: Managing Officer
Street1*: 21 N. Park Street, Suite 6401
Street2:
City*: Madison
County: Dane
State*: WI: Wisconsin
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 53715-1218
Phone Number*: 608-262-3822 Fax Number: 608-262-5111 Email: preaward@rsp.wisc.edu

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Wisconsin National Primate Research Center Support

12. PROPOSED PROJECT

Start Date*	Ending Date*
04/29/2015	04/30/2017

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

● I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The Board of Regents of the University of Wisconsin System
Duns Number:	161202122
Street1*:	Suite 6401
Street2:	21 N Park St
City*:	Madison
County:	Dane
State*:	WI: Wisconsin
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	53715-1218
Project/Performance Site Congressional District*:	WI-002

File Name

Additional Location(s)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ○ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number A3368-01

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	AnimalResource_Abstractv21017925880.pdf
8. Project Narrative*	
9. Bibliography & References Cited	AnimalResource_References1017925781.pdf
10.Facilities & Other Resources	
11.Equipment	

SUMMARY/ABSTRACT (Animal Resources). The Animal Services Division of the Wisconsin National Primate Research Center (WNPRC) consists of 6 units (Veterinary Services, Colony Management, Scientific Protocol Implementation, Pathology Services, Compliance and Training, and Behavioral Management) that are dedicated to maintaining the health of the nonhuman primate (NHP) colonies of the WNPRC; supporting the scientific mission of the Center; ensuring regulatory compliance; and, training personnel to work safely with NHP and their tissues. The personnel of the Animal Services Division constantly strive to redefine and expand the responsibilities and goals of each unit in response to the needs of WNPRC investigators, the constructive critiques of ORIP, AAALAC and USDA site visitors, and the evolving regulatory guidelines governing NHP research. While each unit has its own goals and responsibilities, the division is fully integrated into overall WNPRC activities and intra- and inter-divisional activities occur on a daily basis. This P51 Revision application requests support for maintenance and development of common marmosets (*Callithrix jacchus*) recently acquired from the New England Primate Research Center (NEPRC). Our specific aims to support these animals are as follows:

Aim 1. To provide excellent animal holding facilities and primary enclosures for the marmosets transferred from the NEPRC

Aim 2. To implement exceptional, USDA/PHS/OLAW/AAALAC compliant husbandry and veterinary medical practices for the marmosets transferred from the NEPRC

Aim 3. To implement appropriate genetic and reproductive management for the transferred marmosets

Aim 4. To implement a prudent financial plan to support the transferred marmosets as ORIP support for the animals is progressively reduced

In accomplishing the foregoing Specific Aims, we will then be poised to advance our Center goals to enhance the WNPRC marmoset colony as a national resource—commensurate with demand of investigators—and, develop WNPRC resource initiatives, such as a transgenic marmoset facility.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 04-29-2015 **End Date*:** 04-30-2016 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester			Ph.D.	Project Lead	0.00	EFFORT			0.00	0.00	0.00
2.		Excluded by Requester				Attending Veterinarian	0.00				0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Animal Research Technician	12			40,412.00	19,196.00	59,608.00
1	Veterinary Technician	9.6			20,683.00	9,824.00	30,507.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**90,115.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**90,115.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-14-226. Received Date: 2015-01-26T18:02:04.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 04-29-2015 **End Date*:** 04-30-2016 **Budget Period: 1**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
1. Ultrasound machine	45,000.00
Total funds requested for all equipment listed in the attached file	
Total Equipment	**45,000.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 04-29-2015 **End Date*:** 04-30-2016 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Tuition Remission	0.00
9. Animal Per Diem Costs	174,379.00
Total Other Direct Costs	**174,379.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**309,494.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	37	264,494.00	97,863.00
		Total Indirect Costs	**97,863.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, Dallas, 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**407,357.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: AnimalResource_BudgetJustification1017925843.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 05-01-2016 **End Date*:** 04-30-2017 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester			Ph.D.	Project Lead	0.00	EFFORT			0.00	0.00	0.00
2.		Excluded by Requester				Attending Veterinarian	0.00				0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Animal Research Technician	12			27,210.00	13,197.00	40,407.00
1	Veterinary Technician	9.6			13,926.00	6,754.00	20,680.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**61,087.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**61,087.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-14-226. Received Date: 2015-01-26T18:02:04.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 05-01-2016 **End Date*:** 04-30-2017 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs** **0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: The Board of Regents of the University of Wisconsin System

Start Date*: 05-01-2016 **End Date*:** 04-30-2017 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Tuition Remission	0.00
9. Animal Per Diem Costs	119,720.00
Total Other Direct Costs	**119,720.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**180,807.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	37	180,807.00	66,899.00
		Total Indirect Costs	**66,899.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, Dallas, 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**247,706.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: AnimalResource_BudgetJustification1017925843.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION (Animal Resources)

Per Diem Costs

Table 1 below itemizes the per diem support requested from 5/1/2015 through 4/30/2017. Annually, the per diem rate is calculated following the basic principles outlined in the Cost Analysis and Rate Setting Manual for Animal Research Facilities. All costs are categorized into the appropriate account/class codes and cost centers for 39 specific categories/object classifications. Adjustments are made, if applicable, and total expenses for the previous year are tabulated into final figure. This figure is divided by 365 days and an approximate average of animals to determine the per diem rate. If the per diem rate calculation is at or less than the current rate charged the current rate will remain flat or be reduced as applicable. If the calculated rate is higher than the current rate generally the rate will be raised three percent per year to assist in grant budget stabilization. If a larger increase is needed this is advertised at least 6 months in advance to assist in accurate budget proposal building.

Table 1. Requested Per Diem Support (2015-2017)

Year	2015-2016	2016-2017
Per diem	$6.37	$6.56
Animal #	100	100
Annual cost	$232,505	$239,440
ORIP subsidy	75%	50%
Total cost	**$174,379**	**$119,720**

Salary Costs

The WNPRC requests 75% salary support for two full-time animal caretaker positions and one veterinary technician at 80% effort from 5/1/2015 through 4/30/2016; and 50% support for two full-time animal caretaker positions and one veterinary technician at 80% effort from 5/1/2016 through 4/30/2017 (see Tables 2 and 3). WNPRC animal care policy supports the concept that an individual animal caretaker should not be responsible for more than 45 animals, thus two animal caretakers are necessary to perform husbandry for the 90-100 animals transferred from the NEPRC. Additionally, we have found that one veterinary technician utilizes a majority of his/her day traveling to and from BMQH, performing health observations on the NEPRC marmosets, administering treatments (e.g., antibiotics, estrumate), and performing whatever clinical procedures are necessary (e.g., pregnancy checks, post-partum exams, etc.) thus 80% support is requested for one veterinary technician during the funding period

Table 2. Requested Salary Support (2015-2016)

Position	Hourly Rate	Annualized Salary	Fringe	Compensation 5/1/15 – 4/30/16
ART Objective *(100% effort)*	$13.574	$28,343.35	$13,463.09	$41,806 x 0.75 = $31,355
ART Entry *(100% effort)*	$12.231	$25,538.33	$12,130.71	$37,670 x 0.75 = $28,253
Vet Tech 2 *(80% effort)*	$16.509	$27,577.60	$13,099.36	$40,677 x 0.75 = $30,508
				$90,116

Table 3. Requested Salary Support (2016-2017)

Position	Hourly Rate	Annualized Salary	Fringe	Compensation 5/1/16 – 4/30/17
ART Objective *(100% effort)*	$13.709	$28,625.94	$13,883.58	$42,510 x 0.50 = $21,255
ART Entry *(100% effort)*	$12.353	$25,793.92	$12,510.05	$38,304 x 0.50 = $19,152
Vet Tech 2 *(80% effort)*	$16.674	$27,853.38	$13,508.89	$41,362 x 0.50 = $20,681
				$61,088

Capital Equipment

The WNPRC requests funding in 2015-2016 to purchase a GE Loqiq P6 portable ultrasound unit to perform pregnancy checks and fetal measurements on the female marmosets acquired from the NEPRC that will be used as breeding stock. An additional ultrasound unit is necessary as the NEPRC marmosets will be housed at our quarantine and holding facility to maintain separation from the WNPRC's existing Common marmoset colony. The GE Logiq P6 is a lightweight, small footprint portable ultrasound with very good imaging qualities. It is an ideal system to transport and requires minimal storage space. Purchase cost will be $45,000.

Table 4 summarizes the total annual costs for the support of the marmosets from 2015-2017.

Table 4. Overall Requested Support for NEPRC Marmosets (2015-2017)

Year	2015-2016	2016-2017
Capital Equipment	$45,000	
Salary Support	$90,116	$61,088
Per Diems	$174,379	$119,720
Total Directs	**$309,495**	**$180,808**
Total Indirects (F&A Rate = 37.0%)	$97,863	$66,899
Total Costs	**$407,358**	**$247,707**

Total Direct Costs 2015-2017 = **$490,303**
Total Indirect Costs 2015-2017 = **$164,762**
Total Costs 2015-2017 = **$655,065**

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**0.00**
Section B, Other Personnel		**151,202.00**
Total Number Other Personnel	6	
Total Salary, Wages and Fringe Benefits (A+B)		**151,202.00**
Section C, Equipment		**45,000.00**
Section D, Travel		
1. Domestic		
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		**294,099.00**
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2	294,099.00	
10. Other 3		
Section G, Direct Costs (A thru F)		**490,301.00**
Section H, Indirect Costs		**164,762.00**
Section I, Total Direct and Indirect Costs (G + H)		**655,063.00**
Section J, Fee		

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

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

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

Excluded by Requester

2. Human Subjects

Clinical Trial? ○ No ○ Yes
Agency-Defined Phase III Clinical Trial?* ○ No ○ Yes

3. 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

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)*
1	43,163.00	Wisconsin National Primate Research Center Chargeback System
2	180,807.00	Wisconsin National Primate Research Center Chargeback System

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. 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

7. 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*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	AnimalResource_Introduction1017925868.pdf
2. Specific Aims	AnimalResource_SpecificAimsv21017925869.pdf
3. Research Strategy*	AnimalResource_ResearchStrategyv2_rf1017925883.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	AnimalResource_VAS1017925870.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	
13. Resource Sharing Plan(s)	AnimalResource_ResourceSharing1017925872.pdf
Appendix (if applicable)	
14. Appendix	

Introduction to the Application - Animal Services Division (Animal Resources)

The Animal Services Division of the WNPRC has maintained a colony of common marmosets (*Callithrix jacchus*) since a founder group of 13 animals was purchased from the Waisman Center (an intellectual and developmental disabilities research center located at the University of Wisconsin-Madison) in 1990. The founder colony was augmented with 170 additional animals acquired from the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP) at New York University in 1991 and 1992 and has been maintained with offspring of the Waisman and LEMSIP founder animals since that time. The census of the WNPRC marmoset colony has ranged from 200 to 350 animals and the animals have been utilized in a variety of experiments in areas of research that include:

- In vitro fertilization
- Stem cell biology
- Steroid hormone signaling
- Neuroendocrine mechanisms governing parental behavior
- Neuroendocrine regulation of fertility
- Dietary and hormonal mechanisms controlling body weight and metabolism

Marmosets are also currently utilized in major new initiatives using CRISPER technologies to produce transgenic NHP models of disease, including neurodegenerative and neuropsychiatric disorders.

The WNPRC's established colony of common marmosets, which is housed in the Center's Specific Animal Location in Madison, Wisconsin, currently consists of 203 animals.

On August 20, 2013, WNPRC Director Excluded by Requester received a letter from New England Primate Research Center (NEPRC) Director Excluded by Requester PhD, indicating his desire to identify appropriate sites for the transfer of the NEPRC common marmoset colony. Information about the NEPRC's marmoset colony and guidelines for National Primate Research Centers (NPRCs) interested in accepting the marmosets were outlined in an RFP entitled "Request for Proposals from NPRCs Interested in Receiving the New England Primate Research Center (NEPRC) Common Marmoset Colony." Following intensive discussions with his Associate Directors; Excluded by Requester DVM, DACLAM (Animal Services/WNPRC Attending Veterinarian), Excluded by Requester (Research Services), Excluded by Requester (Operational Services) Excluded by Requester determined that it would WNPRC core and affiliate investigators to expand the size of the WNPRC marmoset colony by acquiring a portion of the NEPRC colony.

On September 21, 2013, Excluded by Requester submitted a proposal to Excluded by Requester and ORIP Health Scientist Excluded by Requester strator PhD, in response to the RFP. The WNPRC proposal requested an equitable tion of the NEPRC's established and active breeding groups between the WNPRC and the Southwest National Primate Research Center (SNPRC) and also requested transfer of several additional marmosets to Wisconsin for proposed studies. On December 23 2014 Excluded by Requester informed the WNPRC that the NEPRC marmoset population would be divided between the WNPRC and the SNPRC. Multiple rounds of negotiations ensued between WNPRC and ORIP personnel regarding the following issues:

- Quarantine and per diem costs for the transferred marmosets
- Number of additional personnel required to care for the transferred marmosets
- Animal holding room renovation and caging fabrication costs to house transferred marmosets

Concurrent with the ORIP/WNPRC negotiations Excluded by Requester (Attending Veterinarian of the Excluded by Requester C) and (Attending Veterinarian of the NEPRC) engaged in several discussions to ine which NEPRC marmoset groups and pairs would be appropriate to transfer to Wisconsin. These discussions resulted in a mutual agreement that between 90 and 100 marmosets would be transferred to the WNPRC. Subsequently, ORIP issued a Notice of Grant Award (Direct costs = $309,859, total costs = $424,507) to the WNPRC for an administrative supplement to fund the necessary room renovations and animal enclosures and sufficient to cover salaries and per diems for the period beginning June 30, 2014 and ending April 30, 2015. All renovations and enclosure construction was completed by October 1, 2014 and the WNPRC received 90 marmosets from the NEPRC on November 4, 2014 and an additional 9 marmosets on 12/3/2014.

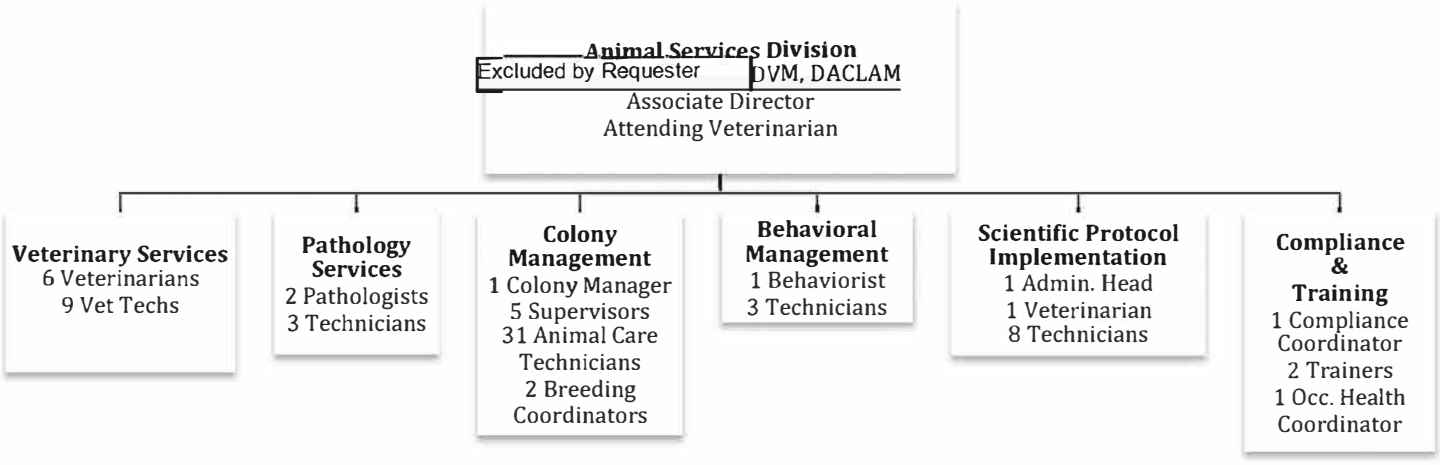
Specific Aims of the WNPRC Animal Service Division (Animal Resources)

The Animal Services Division (See Figure 1) of the WNPRC consists of 6 units (Veterinary Services, Colony Management, Scientific Protocol Implementation, Pathology Services, Compliance and Training, and Behavioral Management). The overall Specific Aims of the Animal Services Division are as follows:

- **Specific Aim 1** – To maintain the physical and psychological health of the nonhuman primate (NHP) colonies of the WNPRC
- **Specific Aim 2** – To support the scientific mission of the WNPRC by providing technical support for the experimental protocols of the Center's investigators
- **Specific Aim 3** – To ensure compliance with all the laws, regulations, and guidelines that govern the use of nonhuman primates in biomedical research
- **Specific Aim 4** – To train personnel to work safely with NHP and their tissues.

The personnel of the Animal Services Division constantly strive to redefine and expand the responsibilities and goals of each unit in response to the needs of WNPRC investigators, the constructive critiques of ORIP, AAALAC and USDA site visitors, and the evolving regulatory guidelines governing NHP research. While each unit has its own goals and responsibilities, the division is fully integrated into overall WNPRC activities and intra- and inter-divisional activities occur on a daily basis.

Figure 1. Animal Services Division Organizational Chart



Specific Aims of the Animal Services Division Regarding the Newly Acquired NEPRC Marmosets

Currently, only three of the existing eight NPRCs possess the infrastructure and expertise to maintain common marmoset breeding colonies. The loss of one of these colonies due to the impending closure of the NEPRC would have devastating consequences on the availability and genetic diversity of common marmosets available to U.S. based investigators. Thus, transfer of the existing NEPRC common marmoset colony to the WNPRC and the SNPRC is imperative, as demand for these monkeys as animal models appears to be increasing significantly[1-6]. The Specific Aims of the Animal Services Division in regards to the NEPRC marmosets to be transferred are as follows:

- **Specific Aim 1** – To provide excellent animal holding facilities and primary enclosures for the marmosets transferred from the NEPRC
- **Specific Aim 2** – To implement exceptional, USDA/PHS/OLAW/AAALAC compliant husbandry and veterinary medical practices for the marmosets transferred from the NEPRC
- **Specific Aim 3** – To implement appropriate genetic and reproductive management for the transferred marmosets
- **Specific Aim 4** – To implement a prudent financial plan to support the transferred marmosets as ORIP support for the animals is progressively reduced

Research Strategy (Animal Resources)

In preparation for the transfer of animals from the NEPRC to the WNPRC, Excluded by Requester had numerous discussions regarding the marmoset husbandry, enrichment, and veterinary practices utilized at the NEPRC. These discussions generally included input from the colony managers, clinical veterinarians, and behavioral specialists of both facilities and greatly facilitated the creation of a plan that would ensure the smooth and safe transfer of a large number of extremely valuable animals between the two facilities. Prior to Excluded by Requester nsfer Excluded by Requester DVM (the WNPRC veterinarian responsible for the daily care of the marmosets rred from the NEPRC) Excluded by Requester (WNPRC marmoset breeding coordinator) spent several days at the NEPRC to review the husbandry and veterinary practices utilized at the center. This trip also provided invaluable information that help shape the plan for the transfer and continuing care of the NEPRC marmosets.

The personnel of the six units of the Animal Services Division will collaborate closely to ensure that the NEPRC marmosets are well cared for when they arrive at the WNPRC and that they are utilized in an efficient manner compliant with all law, regulations, and guidelines governing the use of nonhuman primates in biomedical research. A brief description of the aims and responsibilities of each unit of the Animal Services Division and how they will assist in the care and the utilization of the NEPRC marmosets is provided below.

Veterinary Services

The Veterinary Services Unit of the WNPRC utilizes well-trained and experienced personnel, contemporary equipment, and sound medical policies to provide consistent and excellent clinical care to the NHP colonies housed at the WNPRC. In collaboration with the Scientific Protocol Implementation Unit, the Veterinary Services Unit supports the investigators performing research at the WNPRC by providing them with healthy experimental subjects and supplying clinical care for the NHP assigned to research projects. ***Personnel of the Veterinary Services unit have extensive experience treating the common maladies of captive marmosets and expertise performing and supporting a variety of clinical and research oriented surgical procedures in this species. WNPRC veterinary personnel will be responsible for providing medical care for the NEPRC marmosets from the moment they arrive at the center, through all experimental procedures they will be assigned to, and for the duration of their lives at the center***.

Colony Management

The Colony Management Unit is responsible for all aspects of animal husbandry at the WNPRC including provision of daily care (e.g., feeding and watering), cleaning and sanitization of the animal holding facilities and support areas, maintenance of the rhesus macaque and common marmoset breeding colonies, and rearing of rhesus macaque infants rejected by their dams. Additionally, the personnel of the unit execute a variety of tasks for the Veterinary Services, Behavioral Management, Scientific Protocol Implementation, and Compliance & Training Units of the Center. These tasks include documentation and communication of daily health reports on the NHP colonies, provision of environmental enrichment objects, administration of medical and experimental treatments, collection of blood and other biological samples for experimental and clinical purposes, transport of animals and biological samples, collection of behavioral and scientific data, and maintenance of colony records. ***The personnel of the Colony Management also have extensive experience providing excellent daily care for common marmosets, quickly identifying clinical abnormalities in this species, and providing research support for investigators utilizing these animals.***

Scientific Protocol Implementation

The Scientific Protocol Implementation Unit (SPI) can best be described as an engine for collaborative research and the gateway for conducting studies utilizing WNPRC resources. The Unit is under the supervision of an assistant scientist and a research veterinarian, both with extensive primate research backgrounds. In collaboration with Veterinary Services, SPI attracts collaborations with high quality researchers through the provision of excellent, SOP-standardized technical support that would be difficult or impossible to achieve if individual laboratories employed technicians to accomplish animal-related procedures. Internal and outside investigators choose the level of support desired and utilize the staff as needed. Support varies from simple procedures to functioning as the outside investigators' "laboratory in residence." ***SPI personnel have played a pivotal role in numerous experimental protocols utilizing marmosets and have become adept at performing and supporting delicate and sophisticated procedures with this species. SPI personnel will***

provide research support for all investigators who utilize the NEPRC marmosets in experimental protocols.

Pathology Services

The Pathology Services unit works with clinical veterinary staff to provide rapid disease diagnosis and consistent monitoring of chronic diseases and metabolic conditions affecting animals assigned to long-term research studies. The Unit is integral to the vast majority of research conducted at the WNPRC through advice concerning disease pathogenesis, development of specialized collection protocols, clinical pathology testing, cytology evaluation, surgical biopsy evaluation, gross post mortem examination with research and diagnostic sample collections, and histology with interpretation of lesions in reference to experimental questions and goals and colony health. The unit is responsible for the collection, banking, and distribution of NHP samples to numerous local, national, and internationally located investigators through the Nonhuman Primate Biological Materials Distribution core (NHPBMD) and the National Institute on Aging (NIA) Nonhuman Primate Tissue Bank. ***Pathology Services personnel have a large amount of experience performing a variety of diagnostic assays on marmoset blood and other tissues and performing both gross and histological pathology for the species.***

Compliance and Training

As indicated by its name, the Compliance and Training Unit primarily performs two crucial functions for the Animal Services Division and WNPRC as a whole. The training component of the unit ensures that all personnel who enter the animal areas of the WNPRC and all personnel who handle animals or their tissue are fully educated and trained according to WNPRC standard operating procedures (SOP) and policies. The compliance component of the unit ensures that all WNPRC personnel, procedures, policies, experiments, and facilities remain in compliance with the laws, regulations, and guidelines that govern the use of laboratory animals in research. The compliance component of the unit also assists investigators in the development of IACUC protocols and guides the Occupational Health and Safety Program of the Center. Overall, the unit works in collaboration with the various divisions and investigators of the WNPRC to standardize training and to promote a center-wide atmosphere of regulatory compliance. ***WNPRC compliance personnel will assist investigators with the creation of thorough and detailed IACUC protocols involving marmosets and training personnel will provide extensive training for all investigators who have never handled or utilized marmosets as animal models.***

Behavioral Management

The broad goal of the Behavioral Management Unit (BMU) is to promote animal welfare and facilitate scientific progress by providing exemplary management of the NHP housed at WNPRC. Our approach is team-based, with an emphasis on integration of expertise and efforts across divisions of WNPRC research programs and support services. To promote optimal science and welfare practices, our unit provides animal training, biannual colony-wide assessment of each NHP behavioral welfare, compatibility analyses and socialization, and environmental enhancements. Our specific aims integrate discovery, implementation, and rigorous scientific evaluation of enrichment strategies using a dynamic process of try, evaluate, and modify. The practical employment of any given enhancement incorporates cost:benefit principles to evaluate the short- and long-term benefit of any proposed welfare enhancement. The evaluation of effectiveness and selection criteria for each strategy is determined by striking a balance between positive outcomes for the animals and the practicality with which a strategy can be initiated and maintained. At the level of the animal, our focus is on promoting species-typical behavior; decreasing the expression of abnormal or stereotypic behavior; and facilitating animals' resilience to stress and more rapid adaptation to research and husbandry procedures. Our approach adheres to a lifespan perspective, with consideration of the animals' unique species-typical needs as they mature from infancy to old age. The lifespan perspective requires consideration of the capacities and developmental milestones of the individual NHP as a participant in an interactive social environment. ***Behavioral Management personnel will utilize their expertise to ensure that the relocation of the NEPRC marmosets is as stress-free as possible. Unit personnel will monitor the animals closely upon their arrival and guide behavioral interventions if any abnormal behaviors are noted.***

Specific Aim 1 – To provide excellent animal holding facilities and primary enclosures for the marmosets transferred from the NEPRC

Marmoset Housing Facility

In April of 2012, the Wisconsin National Primate Research Center (WNPRC) leased a Specific Animal Location located in Blue Mounds, Wisconsin to perform nonhuman primate quarantine and holding. The ten-year old Blue Mounds Quarantine and Holding facility (BMQH) was constructed, renovated, and utilized by Harlan Laboratories to quarantine and perform biomedical contract research on macaques, marmosets, and beagles. Harlan decommissioned the facility when they moved all their nonhuman primate activities to Indianapolis, Indiana in 2010. The BMQH floor plan (See Figure 4 at end of Research Strategy text) consists of Specific Animal Location Specific Animal Location animal holding rooms large enough to house approximately 100 macaques each Specific Animal Location large animal holding rooms Specific Animal Location 2 clinical procedure rooms; 2 laboratories, a cage wash suite, a freezer/refrigerator room for sample storage, an animal food prep and storage area, 2 offices, and a large mechanical room.

Specific Animal Location

Specific Animal Location In consultation with the WNPRC Facilities and Shop Supervisor Excluded by Requester o renovate NHP Specific Animal See Figures 4 & 5 at end of Research Strategy text) to house the NEPRC marmosets Specific Animal Location and thus is the easiest to maintain at a temperature range (75°F to 85°F) needed to ensure the wellbeing of callitrichids. Housing the animals at BMQH in NHP Specific Animal Location allows the colony to be quarantined in one large group and also allows it to remain separate e existing WNPRC marmosets until it is determined that neither population is harboring infectious pathogens that may compromise the health of the other colony.

Utilizing funding from the WNPRC and the ORIP administrative supplement Excluded by Requester and personnel from his unit (with assistance from the University of Wisconsin Physical Plant) performed the following renovations and upgrades in NHP Specific Animal Location to prepare for the transfer of the NEPRC marmosets:

- Resurface of the animal holding room cement floor with multiple layers of epoxy paint
- Installed a new double row reheat coil that allows the temperature of NHP Specific Animal Location to be maintained between 75°F - 85°F.
- Installed a room pressurization monitor which provides real time room pressure data to the building automation network
- Installed a stainless steel railing system around the waste trough to prevent marmoset cages from falling into the trough
- Installed "marmoset proof" drain covers in the waste trough
- Installed four separate, equally spaced walkways which span the trough to facilitate easy movement from one side of the trough to the other
- Installed steps to access the waste trough to facilitate cleaning of the trough by WNPRC animal care personnel
- Installed stainless steel diffusers on all the supply air vents and extended exhaust ducts to facilitate filter changes
- Augmented the existing automated watering system with Edstrom coiled water lines

Marmoset Primary Enclosures

In addition to the renovations performed in NHP Specific Animal Location personnel of the WNPRC Facilities and Shop Services unit also constructed enclosures to house the 90-100 marmosets to be transferred to Wisconsin. Rather than acquiring cages from the NEPRC, the decision was made to house the transferred marmosets in cages identical to the ones already used at the WNPRC to promote identical husbandry practices for both colonies of marmosets.

The WNPRC houses breeding pairs of marmosets with multiple offspring in Specific Animal Location Specific Animal Location Specific Animal Location While these enclosures provide less floor space than is required by the Animal Welfare Act for a family of Group 1 species, they are 260% taller than the minimum required height for Group 1 species. The USDA has approved an exemption for these cages since marmosets are an arboreal species that utilize vertical space and the WNPRC cages stimulate species-typical climbing behavior. The IACUC of the Graduate School of the University of Wisconsin-Madison re-approves this space exemption on an annual basis and the WNPRC marmoset colony has thrived in these vertically oriented cages. The following cages were constructed in preparation of the delivery of animals from the NEPRC.

- 13 double cages for breeding pairs + offspring
- 7 change-out double cages
- 12 single cages for pair-housed animals
- 6 change-out single cages

Specific Aim 2 – To implement exceptional, USDA/PHS/OLAW/AAALAC compliant husbandry and veterinary medical practices for the marmosets transferred from the NEPRC

Regulatory Compliance

The WNPRC animal care program complies with all university, local, state, federal (USDA, PHS, OLAW, NIH) and independent (AAALAC) regulations, guidelines, and policies pertaining to animal research and is committed to achieving excellence in animal care and use. Through the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE) of the UW-Madison, the WNPRC is registered with the USDA as a research facility (Certificate # 35-R-001) and has an approved Animal Health Assurance on file with OLAW (A3368-01). The OVCRGE (including the WNPRC) has maintained full AAALAC accreditation (Unit Number 000567) since 1982. The latest AAALAC inspection of the OVCRGE's animal facilities occurred on October 28, 2014. The OVCRGE expects to be notified of continued full accreditation after AAALAC Council meets in January of 2015. The Animal Services Division of the WNPRC, the OVCRGE IACUC, and the Research Animal Resources Center (RARC) of the UW-Madison work in unison to assure that the WNPRC meets all regulatory requirements.

Marmoset Husbandry - SOPs

In preparation for the transfer of 90-100 marmosets from the NEPRC, a team of WNPRC personnel which included Excluded by Requester Staff Veterinarians Excluded by Requester DVM, DACLAM), Colony Manager Excluded by Requester Marmoset Breeding Coordinator Excluded by Requester BMQH Animal Care Supervisor Excluded by Requester Behavioral Management Head Excluded by PhD) Facilities and Shop Supervisor Excluded by Excluded by Requester and Compliance Coordinator Excluded by Requester met repeatedly to review how existing husbandry SOPs have to be amended to apply to housing marmosets at the BMQH facility. The following SOPs required amendments:

- SOP 1.03 - Primate Room Maintenance Schedule
- SOP 1.05 - Animal Feeding and Watering
- SOP 2.01 - Cleaning Animal Areas and Equipment
- SOP 5.01 - Protective Clothing
- SOP 7.02 - Food Enrichment: Fruits, Vegetables, and Treats
- SOP 7.03 - Psychological Well-being: Physical Environment

The WNPRC SOP committee will continue to amend SOPs relevant to work with the transferred marmosets at the BMQH as changes are required.

Marmoset Husbandry - Diet

The NEPRC fed Teklad New World Primate Diet 8794N (Harlan Laboratories, Madison, WI) as the primary staple of their marmoset colony's diet. Teklad 8794N is a fixed formula, non-autoclavable diet manufactured with high quality ingredients and designed to support gestation, lactation, and growth of new-world primates. The diet is produced as a small biscuit that is fortified with taurine and contains vitamin D3 and stabilized

vitamin C (L-ascorbyl-2-polyphosphate), extending the shelf life to six months from date of manufacture. The NEPRC soaked the diet with water as the animals had difficulty chewing the diet in its natural dry state. The NEPRC also augmented their marmosets' diet with a variety of high protein feed items (e.g., hard-boiled eggs, garbanzo beans, cottage cheese, and canned ZuPreem marmoset diet), fruits and vegetables, and a variety of forage items (e.g., peanuts, raisins, cranberries, etc.).

The WNPRC feeds Mazuri Callitrichid High Fiber Gel Diet 5MI6 (Land O'Lakes, St. Paul, MN) as the primary staple of the Center's established marmoset colony's diet. Mazuri 5MI6 is produced as a dry powder that must be mixed with water to form a palatable soft moist gel product that attempts to replicate the type of tree saps and gums that callitrichids consume in their natural habitat. Similar to Teklad 8794N, Mazuri 5mI6 contains vitamin D3 and stabilized vitamin C (L-ascorbyl-2-polyphosphate) to extend it's the shelf life. The WNPRC adds an additional amount of dry vitamin D premix to the Mazuri powder to raise the final Vitamin D content of the diet. Table 1 below compares the major nutrient composition of Teklad 8794N and Mazuri 5MI6. The WNPRC also augments their marmosets' diet with a variety of high protein feed items (e.g., hard-boiled eggs, canned ZuPreem marmoset diet), fruits and vegetables, and a variety of forage items (e.g., peanuts, raisins, etc.).

Table 1. Nutrient Composition of NEPRC and WNPRC Marmoset Diets

Nutrient	Teklad 8794N	Mazuri 5MI6
Vitamin D	8 IU/g	5.7 IU/g*
Vitamin C (ascorbic acid)	910 ppm	520 ppm
Calcium	0.9%	1.1%
Crude Protein	20%	19%
Fat	10%	6%
Energy density	3.2 kcal/g	3.3 kcal/g

*WNPRC adds additional Vitamin D to Mazuri 5MI6 to raise level to 9.7 IU/g

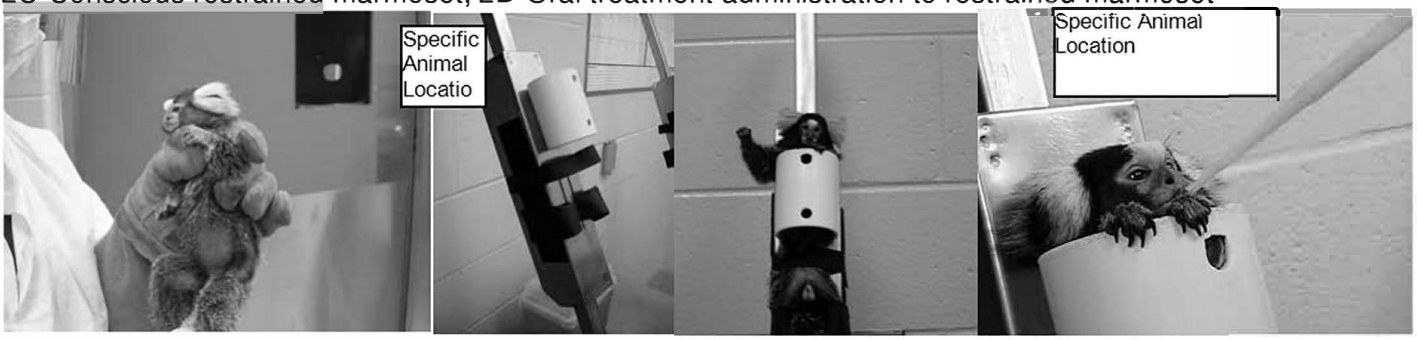
Due to differing nutrient levels between the NEPRC and WNPRC marmoset diets, the WNPRC has chosen to maintain the transferred marmosets on Teklad 8794N to ease the transition to their new environment. Serum samples will be collected from a subset of the animals transferred from the NEPRC and the WNPRC Assay Services Unit will assay these samples for circulating Vitamin D levels. Based on the results, the NEPRC diet may be supplemented with Vitamin D.

The WNPRC provides water to marmosets via lixits connected to an Edstrom automatic watering system. The Town of Blue Mounds Water Utility is in compliance with the Federal Safe Water Drinking Act and monitors the water supply regularly for organic and inorganic contaminants, bacteria, parasites, pesticides, and radionuclides. As noted above, the enclosures constructed for the NEPRC marmosets are identical to the enclosures utilized for the existing WNPRC colony and are equipped with an Edstrom automatic watering system.

Marmoset Husbandry - Restraint

From infancy, all members of the WNPRC marmoset colony are handled while conscious for husbandry and veterinary medical procedures. As animals grow they are acclimated to hand capture and trained to enter a restraint device which consists of a PVC tube (9 cm long x 7 cm in diameter) attached to a stainless steel b race (See Figure 2 below). The restraint device is also equipped with Velcro straps that are placed gently across the abdomen and legs of the animal while the head and arms remain free. The device allows personnel to safely perform procedures such as femoral venipuncture for blood collection, abdominal palpation, abdominal ultrasound, and oral treatment administration while the animal remains conscious. Utilizing the restraint device also significantly decreases the number of times an animal has to be anesthetized throughout the duration of an experimental protocol. All of the NEPRC animals will also be trained to enter this restraint device once they become acclimated to the WNPRC husbandry procedures.

Figure 2. Marmoset Restraint – 2A-Hand restraint of a conscious marmoset, 2B-Marmoset restraint device, 2C-Conscious restrained marmoset, 2D-Oral treatment administration to restrained marmoset



2A 2B 2C 2D

Veterinary Care

To ensure the health of the transferred marmosets, each animal will be evaluated twice daily by a veterinary technician for the evidence of disease or injury (e.g., inappetance, dehydration, diarrhea, depression, inactivity, trauma, etc.). Using paper forms or an iPad, the technician will generate a daily report of animals that need veterinary attention and the veterinary staff will evaluate each animal and treat them accordingly. A current problem and treatment list will be updated daily by the veterinary technicians and veterinarians to ensure that all clinical problems are treated appropriately. All clinical problems, treatments, and case outcomes will be entered into the WNPRC electronic health records database so that complete histories can be generated and ongoing clinical problems can be tracked. All demographic data (e.g., date of birth, gender, dam, sire, weight history, etc.) for each transferred animal will be entered into the WNPRC database upon arrival.

Specific Aim 3 – To implement appropriate genetic and reproductive management for the transferred marmosets

Genetic Management of the NEPRC colony

The NEPRC provided extensive pedigree data (i.e., dams, sires, kinship coefficients, and inbreeding coefficients) to the WNPRC for all the marmosets to be transferred. The WNPRC provided all of the NEPRC pedigree as well as the pedigree data from its existing marmoset colony to Excluded by Requester

Excluded by Excluded by Requester of the Oregon National Primate Research Center's (ONPRC) Colony Genetics Core Unit for analysis. performed an extensive review of the pedigree data utilizing a software package they recently developed to evaluate the genetic diversity of the WNPRC and NEPRC colony to be transferred and the effect that mixing the two colonies would have on the overall genetic diversity of the two populations. The analysis provided by the ONPRC includes the following:

- Curated pedigrees for the individual WNPRC and transferred ONPRC colonies
- A curated pedigree for a potential mixed WNPRC/ONPRC colony
- A variety of genetic value calculations including individual average mean kinship, Z-scores, and genome uniqueness for each member of the WNPRC, NEPRC, and mixed WNPRC/NEPRC colonies
- Overall genetic designation (i.e., high value vs. low value) for each member of the two individual populations of animals and the potential mixed population of animals indicating recommendations for breeding the animals for genetic diversity or simply for research purposes.

All of the genetic data regarding the individual WNPRC and NEPRC colonies will be utilized to make informed breeding decisions that will maintain the genetic diversity of the existing populations if they are maintained separately. Table 2 below provides summary statistics from the ONPRC analysis.

Table 2. Summary Statistics – ONPRC Genetic Analysis of Marmoset Pedigree Data

	WNPRC Colony	NEPRC Colony	Combined Colony
Founders	66	41	105
Founder Equivalents	41.92	32.69	70.91
Grand Mean Kinship	0.030	0.029	0.017

Founder equivalents estimate the expected number of equally contributing founders that would be required to produce the observed genetic diversity in the current population. This acts as a measure of how well genetic diversity has been maintained within the population. The current WNPRC colony was founded by 66 animals, but the number of founder equivalents is lower, at 41.9. This means that genetic diversity has been lost due to unequal reproductive success of the breeding animals. Similar loss of genetic diversity has occurred in the transferred NEPRC colony also. By combining the WNPRC and NEPRC animals into one colony, the number of founders will increase to 105, and the founder equivalents will increase to 70.9; an increase of ~70%.

Grand mean kinship will also improve by combining the two groups. Individual mean kinship is calculated as the average of an individual's pairwise kinship values with all other members of the population. This value acts as a measure of how related an individual is to the rest of the population, on average. The higher the value, the more related an individual is to the other population members. In the current WNPRC colony, individual mean kinship of the animals ranges from 0.004 to 0.050, with the grand mean at 0.030. After combining the WNPRC and NEPRC animals these values will all shift lower, ranging from 0.0027 to 0.033, with a grand mean of 0.017. By combining the two groups, the average inter-relatedness of the animals will decrease, as evidenced by the reduction of the grand mean kinship by nearly half.

The ONPRC analysis verifies that the long-term consequences of maintaining two completely separate colonies without exchange of animals for breeding purposes would result in the inevitable loss of genetic variation over time. Thus, from the perspective of long-term genetic management, a clear case can be made for merging the NEPRC and WNPRC marmoset colonies and managing the population as one combined unit. This would increase the number of potential mates for each breeding individual and reduce average kinship among individuals. However, this possible action must be carefully considered. While the genetic variability within the combined colony and thus future genetic health would be increased by merging the two populations, this may be problematic if the two populations are genetically and taxonomically so different that merging the two would generate hybrid offspring from breeding adults that are too genetically divergent. Therefore Dr. Excluded by Requester PhD (Associate Professor, Human Genome Sequencing Center, Private Source Private Source & WNPRC Genetics Consultant) will collect and assess information necessary to make a decision about the possible colony merge. First, we will collect and evaluate all available records to determine (if possible) where and when the founders of these two marmoset colonies were captured in the wild. This will provide an indication of the likely genetic and taxonomic differences between them. If that investigation does not provide enough information to make a decision, we will pursue molecular genetic studies of the two populations. We would first assess mitochondrial DNA variation within and between the two colony populations and compare those results to published information about mtDNA variability across the geographic range of *Callithrix jacchus*. This will place the two populations in the overall context of genetic and geographic diversity across the species. If that approach is not satisfactory, we will pursue other molecular genetic tests to assess the potential consequences of merging the two breeding populations. Unless there is a strong reason to keep the colonies separate, the long-term genetic health of the animals will be best served by merging the two colonies into one breeding population.

Social and Reproductive Management of the WNPRC and Transferred Marmoset Colonies

Wild groups of common marmosets range in size from three to 15 animals, but usually have about nine members[7]. The wild groups generally consist of three generations of animals and include one or two breeding females with one breeding male and related adults (possibly parents or siblings) and the breeding pairs' offspring[8]. The existing WNPRC marmosets and the NEPRC marmosets are also housed in family groups that closely mimic wild populations.

The WNPRC currently maintains 12 active breeding pairs of marmosets. Kinship coefficients, age, and compatibility are utilized to form male/female pairs and no related individuals are allowed to breed. All reproductively active females are monitored for pregnancy every 28 days by the breeding technician or a member of the veterinary staff using manual palpation and ultrasonography. Several techniques including uterine palpation, previous delivery date, previous prostaglandin administration date, and infant head size are utilized to determine an approximate gestation date. Serial ultrasound exams are performed throughout gestation to verify fetal viability. The offspring of breeding pairs remain in the family until approximately 15 months of age and possibly longer. This familial experience provides offspring with crucial infant care giving

experience as WNPRC colony data demonstrate that offspring that lack experience rearing their younger siblings may become neglectful/abusive parents. Therefore, WNPRC family groups may vary in size from a pair with infants to a larger family with several sets of offspring (usually twins, triplets, or quadruplets) that remain with the family until adulthood.

Pregnancy in the remaining male/female pairs in the colony is controlled by the use of the synthetic prostaglandin analogue cloprostenol sodium (Estrumate®). Estrumate administration consistently causes functional and morphological regression of the *corpus luteum* (luteolysis) in marmosets that leads to abortion[9-11]. Non-breeding colony females are manually palpated and also undergo abdominal ultrasound examination one to two times per month to verify pregnancy status. Females with unwanted pregnancies are treated with 0.75 µg of estrumate administered intramuscularly. In cases where a female marmoset is insensitive to the first dose of estrumate, 1.0 µg of the agent is administered for up to three successive days approximately 5-14 days after the first dose to render effective luteolytic action and subsequent abortion. WNPRC data strongly demonstrates that estrumate treatment has no effect on future breeding success.

The transferred NEPRC females' pregnancy status will be determined upon arrival and animals considered to be at less than 50 days of gestation will have their pregnancies terminated with estrumate. Animals with pregnancies greater than gestation day 50 will be allowed to deliver and raise their offspring. No NEPRC animals will be allowed to carry their pregnancies to term until decisions about combining the colonies are complete.

Specific Aim 4 – To implement a prudent financial plan to support the transferred marmosets as ORIP support for the animals is progressively reduced

WNPRC investigators have several funded and pending grant proposals that call for the use of marmosets (See Table 3 below). A subset of the animals transferred from the NEPRC are aging or are vasectomized and will be utilized by WNPRC investigators within 6 months of their arrival. A subset of the maturing offspring from the mated NEPRC pairs will also be used for funded proposals or will be sold to outside investigators with NIH approved funding to subsidize support of the colony and to maintain the population at an appropriate number based on the capacity of the BMQ facility.

Table 3. Submitted and Funded WNPRC Marmoset Proposals

Investigator	Project Number/Funding Body	Title	Animal Numbers
Excluded by Requester University of Wisconsin	5P01HD021921 NIH	ERA signaling mechanisms regulating ovarian function	150 marmosets over 5 years
Excluded by Requester University of Washington	Dept. of Ophthal. Univ. of Washington	Sequence of Neuronal Generation in Marmoset Visual System	12 marmosets over 3 years
Excluded by Requester University of Wisconsin	P51 supplement 5P51OD011106-53 NIH	Development of genetic altered marmosets for PD model	24 marmosets over 1 year
Excluded by Requester UMass Medical School	K01 CA184388 and WNPRC pilot NIH	Unmasking the role of KSHV glycoproteins in viral entry and vaccine development	24 marmosets over 5 years
Excluded by Requester University of Wisconsin	R24OD019803 NIH	Transgenic marmosets for translational stem cell research	142 marmosets over 4 years
Pending Support			

Pending Support

Progress Report

Animal Delivery and Quarantine

The NEPRC contracted Specific Private Vendor to transport marmosets to the WNPRC. The first shipment, which consisted of 90 animals, arrived safely in Wisconsin on November 4, 2014. One family group destined for the WNPRC was not shipped with the initial group as the matriarch of the group was near-term pregnant and subsequently gave birth to healthy twins on November 9, 2014. While awaiting transport, there was some social unrest in the final family to be transported and two females were removed from the group and paired in another enclosure. The remaining family, which consisted of a mated pair and five offspring, and the newly formed pair, arrived safely at the BMQH on December 3, 2014. Table 4 below provides a synopsis of the NEPRC marmosets transferred to the WNPRC.

Table 4. Social Configuration of Marmosets Transferred from NEPRC to WNPRC

Social Configuration	Number of Animals
Breeding pairs with offspring	8 breeding pairs and 30 offspring (46 animals total)
Breeding pairs without offspring	8 breeding pairs (16 animals total)
Female/female pairs	5 pairs (10 animals total)
Male/male pairs	3 pairs (6 animals total)
Family groups with vasectomized sires	3 groups (11 animals total)
Vasectomized male with sons	1 group (4 animals)
Single females	4
Total	97 animals (52 females, 45 males)

Upon arrival, the NEPRC marmosets were quarantined in their new home enclosures at the BMQH and allowed several days to acclimate. After the acclimation period, each animal was anesthetized and subjected to a thorough physical examination by a WNPRC veterinarian. During the initial physical examination, blood was collected for baseline complete blood counts and chemistry panels on all animals greater than six months of age and each animal greater than 3 months of age was fitted with a subcutaneous ID chip to facilitate future identification. Per WNPRC protocol, each animal over three months of age also underwent a palpebral tuberculin skin test with 0.05 ml of mammalian old tuberculin (Synbiotics Corporation, San Diego) during the initial physical examination and then every two weeks thereafter for a period of 30 days. No positive tuberculin reactions were noted at any time point and the quarantine period for all the animals officially ended on January 6, 2015.

Husbandry Issues

The NEPRC provided water to their marmosets via standard water bottles attached to each enclosure. When the NEPRC animals were transferred to the WNPRC, water bottles were placed in each enclosure to ensure that the animals all had access to water and a small amount of honey was smeared on the lixits in each enclosure to help the animals discover the lixits. Within a week, the NEPRC marmosets discovered the lixits and no cases of dehydration were reported.

Morbidity and Mortality Update

Initially, all of the transferred animals exhibited some inappetence, diarrhea, and subsequent weight loss as they acclimated to their new living conditions at the WNPRC, but a majority of the animals' weights have rebounded to pre-shipment levels and reports of diarrhea have reduced significantly.

Three days after the first group of animals arrived in Wisconsin, one adolescent female had to be euthanized after being severely traumatized by her young adult female cage mate (a half-sister). Eleven days after arrival of the first group, an aging female was treated for evidence of acute or chronic renal failure. Despite intensive fluid therapy, the animal's condition did not improve and euthanasia was elected. No further deaths have occurred among the transferred animals.

Reproductive update

After their acclimation period, all reproductively intact female NEPRC marmosets paired with reproductively intact male marmosets have been manually palpated on a biweekly basis to determine if they are pregnant. Twenty-eight females determined to be less than 50 days pregnant have received estrumate to induce abortion. Three animals that arrived pregnant have spontaneously aborted and two animals that arrived pregnant have given birth to a litter of two infants and three infants, respectively. All infants born just prior to transfer from the NEPRC and all infants born at the WNPRC are alive and appear healthy.

Social Stability and Acclimation Update

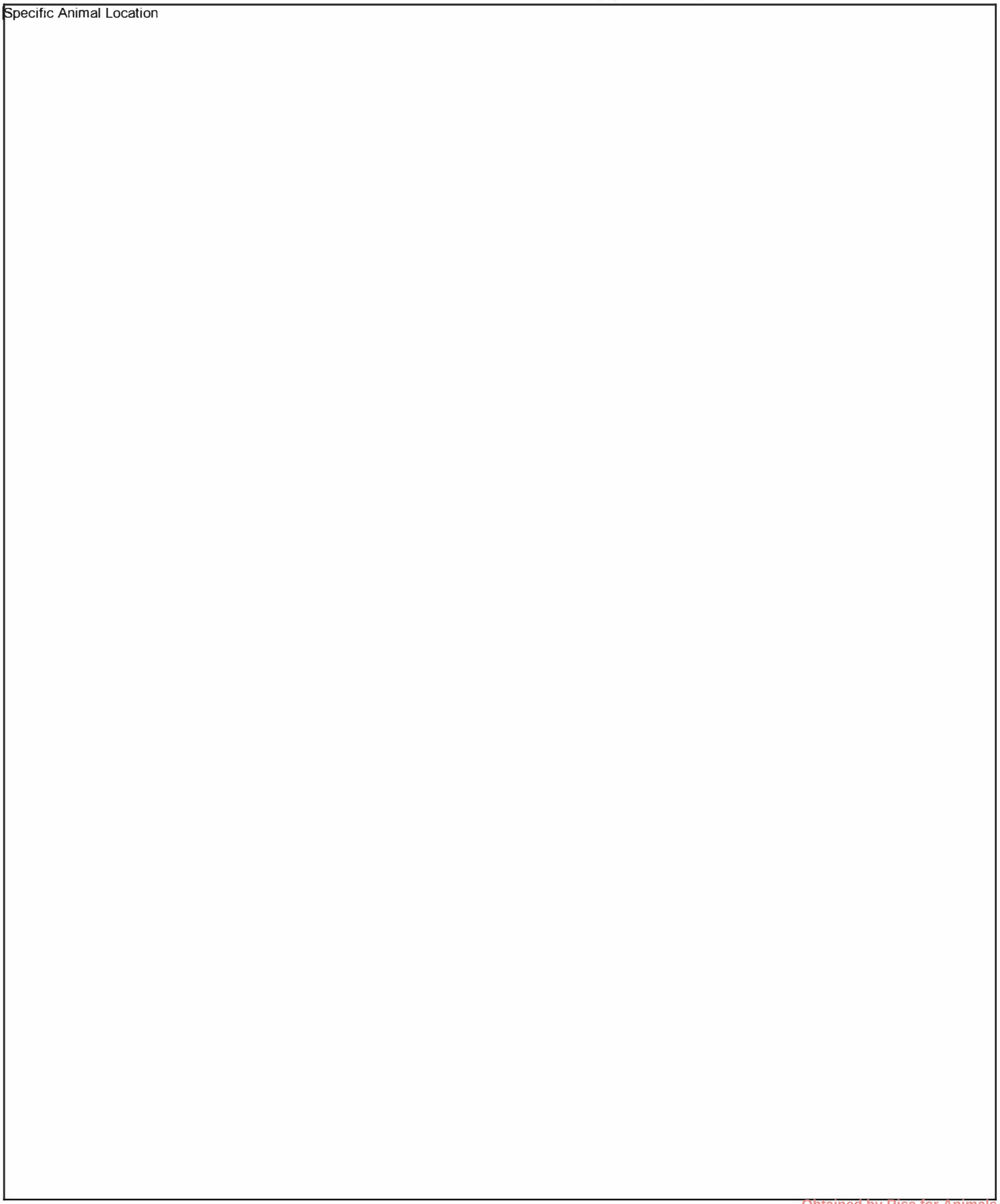
The bachelor group of four males listed in Table 4 above was disbanded and each male was paired with one of the four single females transferred from the NEPRC. The WNPRC utilized the pedigree to data provided by the NEPRC to form these new pairs and to ensure that no inbreeding would occur when the females in these groups are no longer being treated with estrumate. The young adult half-sister of the adolescent animal that was euthanized has been successfully re-paired with an adolescent adult male and is currently on estrumate treatment. The family group (vasectomized male and offspring) of the aging female that was euthanized remains intact.

Figure 3 below depicts an acclimated mated pair of NEPRC animals (Figure 3A), a father with infants who were born at the NEPRC and successfully transferred to the WNPRC (Figure 3B), and a transferred male NEPRC marmoset who is already successfully acclimated to the WNPRC restraint device (3C).

Figure 3. NEPRC Marmosets at BMQH

3A 3B 3C

Figure 4. BMQH Schematic Diagram



Vertebrate Animals (Animal Resources)

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Strategy section. Identify the species, strains, ages, sex and number of animals to be used in the proposed work.

Rhesus macaques (*Macaca mulatta*), Cynomolgus macaques (*Macaca fascicularis*), and Common marmosets (*Callithrix jacchus*) are utilized for a majority of the experimental studies performed at the WNPRC. However, the personnel of the Animal Services Division have the ability to provide appropriate care for all types of Old or New World monkeys and other species may be acquired during the base grant cycle covered by this proposal. Currently, the WNPRC also houses a small group of African Green monkeys (*Chlorocebus aethiops*) that were purchased for a specific experiment.

The personnel of the Animal Services Division also have the ability to provide appropriate care for animals of all age ranges as we maintain infants produced by our SPF macaque breeding colony and geriatric macaques in a long-term calorie restriction project. We expect that animals of all ages will be utilized in the experimental Protocols that will be performed during the base grant cycle covered by this proposal.

All NHP utilized for experimental projects at the WNPRC will be bred at the center or purchased from USDA licensed dealers (e.g., Specific Private Vendor etc.) or directly from other research facilities (e.g., National Primate Research Centers, pharmaceutical companies, universities, etc.).

The WNPRC conducts a wide array of behavioral and biomedical studies utilizing NHP and a majority of experiments that will be performed in the next grant cycle will be focus on one of the four following themes:

Global Infectious Disease: Transmission and pathogenesis of SIV, viral escape, vaccine development, MHC-defined animals, influenza, and a new initiative to identify novel viruses with zoonotic and/or pandemic potential.

Regenerative and Reproductive Medicine: Embryonic/pluripotent stem cell biology including cellular therapy for hematogenic, cardiovascular and neurodegenerative diseases, organ transplant tolerance, stem cell-based therapies for AIDS; assisted reproductive technologies for NHP transgenesis, maternal-fetal health including pregnancy loss, intrauterine environment in metabolic and reproductive programming, endometriosis, and polycystic ovary syndrome (PCOS).

Energy Metabolism and Chronic Disease: Chronic disease and aging research, with an emphasis on the genetic, cellular, and whole animal effects of calorie restriction, as well as excess calorie intake resulting in obesity and metabolic syndrome; diabetes mellitus, osteoporosis, and new studies on post menopausal hormone changes and metabolic disease risks.

Neuroscience: Preclinical Parkinson's disease research, translational studies of glaucoma, as well as stress, anxiety, and depression, and basic studies of central nervous system mechanisms controlling fertility, puberty, menopause, and body weight, and neuroendocrine regulation of reproductive and social behaviors.

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.

All NHP experiments performed at the WNPRC must have a protocol approved by the Institutional Animal Care and Use Committee (IACUC) of the Graduate School of the UW-Madison. The IACUC protocol form requires that investigators specifically justify the use of animals for their research and explain why it is imperative to use animals and why ***non-animal alternatives*** such as computer simulation or in vitro systems are not possible. The species justification section of the IACUC protocol form requires the investigator to specifically justify why they chose the species for their work. Finally the animal number justification section of the IACUC protocol form requires the investigator to explain how the number of animals required was determined, to justify that

need and to include any statistical analysis used (e.g., power calculations) in determining the animal numbers. In addition to having to appropriately answer the questions described above, each protocol must pass the scrutiny of a biomedical statistician before being approved by the ACUC.

Each NHP experiment performed at the WNPRC must also be reviewed and approved by the Executive Committee of the Center. The Committee includes the Associate Directors and PIs who are actively engaged in research using WNPRC resources and services, and whose project funding is administered by the WNPRC. Each potential project is evaluated against several criteria, including fit with the WNPRC mission, quality of the science, availability of resources and funding source. Approval is obtained through majority vote of an Executive Committee.

The number of NHP utilized in each experiment is kept at the minimum number necessary to achieve statistical significance and animals are re-used when possible.

3. Provide information on the veterinary care of the animals involved.

The Veterinary Services Unit of the WNPRC provides veterinary care for all animals housed at the Center. The veterinary staff is led by Excluded by Requester DVM, DACLAM, and consists of six clinical veterinarians, two veterinary pathologists, nine veterinary technicians, and three necropsy technicians. Members of the veterinary staff are present at the center from 7:00AM – 5:00 PM Monday through Friday and are reachable by cell phone at all times during the workday. A clinical veterinarian and a veterinary pathologist are on-call and reachable by cell phone before 7:00AM and after 5:00PM on weekdays and 24 hours per day on weekends. The WNPRC also employs a PhD behaviorist, an enrichment coordinator, and two enrichment technicians to ensure that the psychological well-being of each animal is addressed.

The animal care program of the WNPRC is accredited by AAALAC through the Graduate School of the UW-Madison. The Animal Services Division also utilizes the following documents to ensure that ther animal care program is compliant with all laws, regulations, and guidelines that govern the use of NHP in research:

- The Animal Welfare Act (AWA) and Animal Welfare Regulations (AWR)
- The Guide for the Care and Use Of Laboratory Animals, 8th Edition (NRC 2010)
- The Public Health Service Policy on Humane Care and Use of Laboratory Animals
- US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
- USDA Policy Manual
- AVMA Guidelines for the Euthanasia of Animals: 2013 Edition
- AAALAC International Rules of Accreditation
- AAALAC Position Statements
- Published OLAW Guidance
- NRC's Occupational Health and Safety in the Care and Use of Research Animals
- NRC's Occupational Health and Safety in the Care and Use of Nonhuman Primates
- NRC's Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research

To ensure the health of the NHPs housed at the WNPRC, each animal is evaluated twice daily by an animal research technician or veterinary technician for the evidence of disease or injury (e.g., inappetance, dehydration, diarrhea, depression, inactivity, trauma, etc.). Using paper forms or an Apple iPad, the technician generates a daily report of animals that need veterinary attention and the veterinary staff evaluates each animal and treats them accordingly. A current problem and treatment list is updated daily by the veterinary technicians and veterinarians to ensure that all clinical problems are treated appropriately. All clinical problems, treatments, and case outcomes are entered into the WNPRC electronic health records database so that complete histories can be generated and ongoing clinical problems can be tracked.

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.

Prior to the initiation of any experimental study, the investigator(s) meets with a group of personnel from the Animal Services Division (e.g., veterinarians, veterinary technicians, behaviorists, research technicians, pathologists, trainers, compliance personnel, etc.) to outline their experimental design and hypothesize about the various clinical outcomes that may occur as a result of their experimental manipulations. These meetings strengthen the collaboration between the investigators and Animal Services personnel, highlight the strengths, weaknesses, and predicted problem areas in the proposed study, and allow veterinarians to create detailed clinical plans that are honed to specific studies. For instance, infection with SIV or related viruses results in the development of immunodeficiency disease. Thus, over a period of time, animals are expected to have fever, weight loss, periods of diarrhea, rash, decreased physical activity and possibly pain. SIV infected animals may also contract opportunistic infections (e.g., *Pneumocystis carinii*, *Cryptosporidium sp.*, *Staphylococcus sp.*, etc.). Animals exhibiting signs of disease will be treated with the appropriate therapy (e.g., antibiotics, anti-protozoal agents, analgesics, anti-inflammatories, etc.) at the discretion of a WNPRC veterinarian. Palliative and supportive care (e.g., oral and orogastric supplemental feeding as well as oral, subcutaneous, and intravenous rehydration therapy) will also be administered as needed. Armed with the information from these meetings, Animal Services personnel are more capable of minimizing any discomfort, pain, or distress that may occur due to the planned experimental manipulations.

Anesthetics

The WNPRC Veterinary Staff utilizes an array of agents to anesthetize animals including dissociatives (ketamine), alpha-2-agonists (dexmedetomidine, xylazine), benzodiazepines (diazepam, midazolam), dissociative/benzodiazapine mixtures (tiletamine/zolazepam) and inhalants (isoflurane).

For minor procedures such as physical examinations, blood draws, or lymph node biopsies animals will be anesthetized with an intramuscular dose of ketamine (up to 15 mg/kg) or up to 7 mg/kg ketamine, and up to 0.03 mg/kg of intramuscular dexmedetomidine to be reversed at the conclusion of the procedure by up to 0.25 mg/kg intravenous or intramuscular atipamizole or alternative anesthesia in consultation with a WNPRC veterinarian.

For procedures expected to last longer than 30 minutes or major surgical procedures, animals will be pre-medicated with ketamine (up to 15 mg/kg i.m.) or alternative anesthesia in consultation with a WNPRC veterinarian. Atropine sulfate (0.03-0.05 mg/kg i.m. or s.c.) will be administered. General anesthesia will be maintained during the course of the surgery with isofluorane gas (1-3% isofluorane) delivered via endotracheal tube. Animals will routinely receive isotonic intravenous fluids at the rate of 10ml/kg/hr to avoid dehydration during surgery or the immediate post-operative period. All animals will be monitored using a pulse oximeter. Heart rate, respiration rate, and blood oxygen will be recorded at least every 15 minutes. Adequate anesthesia level will also be assured by checking reflexes and monitoring for any spontaneous movement.

Analgesics

The WNPRC Veterinary Staff utilizes an array of analgesic and anti-inflammatory agents to minimize pain and distress including but not limited to lidocaine, bupivacaine, aspirin, acetaminophen, flunixin meglumine, ketoprofen, keterolac, carprofen, meloxicam, tramadol, buprenorphine, and fentanyl.

Animals exhibiting signs of discomfort or pain post-operatively or due to chronic disease may receive an analgesic such as buprenorphine (0.01 – 0.03 mg/kg, intramuscularly, 2-3 times per day) until a veterinarian determines that their pain has resolved. Animals may also receive meloxicam (0.1-0.3 mg/kg, orally, once per day) or ketoprofen (2-5 mg/kg, 2-3 times per day, intramuscularly) to reduce inflammation and pain. Analgesic and anti-inflammatory treatment regimens are tailored to the level of pain or inflammation an animal is exhibiting or the invasiveness of the experimental procedures they are subjected to.

The Veterinary Services Unit tries to limit the number of anesthetic events each animal must undergo; therefore, they try to perform many minor procedures (e.g., blood collections, experimental drug administrations, ultrasound-aided pregnancy checks) on conscious animals using a table-top restraint device for macaques and a restraint tube for marmosets.

All macaques born at the WNPRC are acclimated to the table-top restraint device from the time they are infants. Animals acquired by the WNPRC become acclimated to the device over time, starting with their quarantine period. The animals will spend no more than a few minutes being restrained for any one procedure. The animal is transported from its home cage in a transport cage, and allowed to enter the device. The gate is adjusted so that the animal is firmly held, but not in discomfort. As soon as the procedure is completed, the gate is released and the animal is allowed to re-enter the transport cage. Each animal always receives a positive reward (e.g., fruit, vegetable, fig cookie, etc.) for entering the device.

All marmosets born at the WNPRC are acclimated to a tube restraint device from the time they are young adults. The marmosets are placed in the 9 cm length x 7 cm diameter PVC tube restraint device with velcro straps across the abdomen and thighs, which allows free movement of the head and arms. Marmosets adapt very readily to this restraint method. Each animal always receives a positive reward (e.g., Ensure, mini-marshmallow etc.) for entering the device.

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 *AVMA Guidelines on Euthanasia*. If not, include a scientific justification for not following the recommendations.

All methods utilized to euthanize NHP at the WNPRC are consistent with the AVMA Guidelines for the Euthanasia of Animals: 2013 Edition.

A majority of the animals euthanized at the WNPRC are sedated with an intramuscular dose of ketamine (up to 15 mg/kg), delivered to necropsy, and euthanized with an intravenous injection of Euthasol®. Euthasol contains two active ingredients (pentobarbitol sodium and phenytoin sodium), which act in a manner to cause humane, painless, and rapid euthanasia. The euthasol is delivered at an appropriate amount to ensure that the animal receives at least 50 mg/kg of pentobarbital sodium.

Many investigators require their animals to be perfused with gluteraldehyde and/or 4% paraformaldehyde at the time of euthanasia. To perform this procedure, animals are sedated with an intramuscular dose of ketamine (up to 15 mg/kg), are delivered to necropsy, and are deeply sedated with an intravenous dose of pentobarbital sodium (Nembutal®). The sternum of the animal is then removed or reflected cranially utilizing sharp dissection and rib cutters. The descending thoracic aorta is isolated and occluded by clamping with 1-2 pairs of hemostats. The pericardium is incised to visualize the heart. The left ventricle is visualized and cannulated, and the right auricle is transected. The animal is then perfused via the left ventricle, first with several liters of physiolocal saline to remove red blood cells from the tissues, followed by perfusion with 2 liters of cold phosphate-buffered saline containing 0.125% glutaraldehyde and 4% peraformaldehyde or other appropriate fixative.

Less often, animals are sedated with an intramuscular dose of ketamine (up to 15 mg/kg), delivered to necropsy, deeply sedated with Euthasol or Nembutal and euthanized via exsanguination using a vacutainer system via the femoral vein or artery or the descending aorta (after an abdominal incision is made).

Rarely, experimental protocols call for the euthanasia of common marmosets via exposure to carbon dioxide. To facilitate this procedure, a mask is held over the nose and mouth of a hand-restrained marmoset and isoflurane is delivered until the animal is unconscious. Once unconscious, the animal is placed in a leak-proof anesthesia box and 100% CO2 is delivered to the box until respiration ceases.

After the euthanasia procedures are performed, death is confirmed by a qualified and experienced person who uses a stethoscope to monitor heart sounds to verify stoppage of the heart. Other vital signs (e.g., respiratory excursions, pupil dilation) are also monitored to ensure death. Complete necropsies are performed on all animals that die naturally or are euthanized at the WNPRC so there is no chance that an animal can awaken after the administration of ketamine and Euthasol or Nembutal.

References (Animal Resources)

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2. Excluded by Requester Common marmoset as a new model animal for neuroscience research and genome editing technology. Dev Growth Differ. 2014 Jan;56(1):53-62. doi: 10.1111/dgd.12109. Epub 2014 Jan 5. Review. PMID: 24387631.

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Resource Sharing Plan (Animal Resources)

As noted in the Introduction to the Animal Services Division, common marmosets are only being bred in two of the seven remaining NPRCs. Consequently, the supply of animals is very small relative to the rapidly increasing demand for this species. Once the NEPRC animals are acclimated and decisions are made about combining the NEPRC and WNPRC colonies, surplus animals will be offered to investigators outside of the University of Wisconsin with funding to perform experimental protocols with marmosets.