Description of document:	Records related to Department of Health & Human Services (DHHS), National Institute of Allergy and Infectious Diseases (NIAID) Grant awarded to Emergent BioSolutions Inc., Project Title: Development of a Next Generation Anthrax Vaccine, 2008-2010
Requested date:	08-May-2011
Released date:	19-September-2011
Posted date:	16-April-2012
Source of document:	Freedom of Information Act Request National Institute of Allergy and Infectious Diseases (NIAID) Suite 2600 6610 Rockledge Drive, MSC 6605 Bethesda, MD 20892 Fax: 301-480-0904 Email: foia@niaid.nih.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Freedom of Information Office
6610 Rockledge Drive, MSC 6605
Bethesda, Maryland 20892
Tel (301) 451-5109
Fax (301) 480-0904/ Email foia@niaid.nih.gov

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, MD 20892

September 19, 2011

Re: FOI Case No. 38886

This is our final response to your May 8, 2011 Freedom of Information Act (FOIA) request addressed to me. You requested a copy of 1U01AI082224-01 awarded to Emergent Biosolution Inc. by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). Enclosed are 133 electronic pages responsive to your request. This includes:

- Notice of Grant Award [6 pages]
- Original Application [77 pages]
- Revised Budget and Product Development Plan [50 pages]

It is Department of Health and Human Services (DHHS) policy to expunge EIN numbers, percentage of effort, salary and fringe benefit information, cost breakdowns, indirect cost rates, information pertaining to consultants or non-key subcontractor personnel, pending support, source of private support, references to unpublished articles, and any patentable or proprietary material wherever they appear throughout the grant material. This information has been removed from the enclosed material.

Requesters who ask for grant applications usually want to receive only material that will help in understanding the process that led to the awards, or to improve their own methods of drafting grant applications. Requesters usually do not want material that applicants believe would harm them if released. We have found that the spirit of the FOIA can be enhanced through a spirit of cooperation among requesters of materials and those who submitted the materials.

In this instance, we asked the grantee for advice concerning patent rights and other confidential commercial or financial information and the material that we are furnishing reflects that advice. If you feel that materials have been omitted that should have been made available to you, please write to me and I will consult with the NIH Freedom of Information Officer.

In certain circumstances provisions of the FOIA and DHHS FOIA Regulations allow us to recover part of the cost of responding to your request. Because the cost is below the $25 minimum, there is no charge for the enclosed materials.

Sincerely,

Robin L. Schofield-Gruber
Freedom of Information Office
National Institute of Allergy and Infectious Diseases

Enclosure: 133 electronic pages

THIS AWARD IS ISSUED UNDER THE AMERICAN RECOVERY AND REINVESTMENT ACT OF 2009 AND IS SUBJECT TO SPECIAL HHS TERMS AND CONDITIONS AS REFERENCED IN SECTION III

Grant Number: 1U01AI082224-01

Principal Investigator(s):
SUKJOON PARK, PHD

Project Title: Development of a Next Generation Anthrax Vaccine, dmPA7909

GARY S. NABORS, PH.D.
VP OF PRODUCT DEVELOPMENT & SITE OPERATIONS
EMERGENT PRODUCT DEVELOPMENT GAITHERSBURG INC.
300 PROFESSIONAL DRIVE
SUITE 250
GAITHERSBURG, MD 20879

Award e-mailed to: naborsg@ebsi.com

Budget Period: 09/30/2009 – 08/31/2010
Project Period: 09/30/2009 – 08/31/2011

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $2,454,564 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to EMERGENT BIOSOLUTIONS in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 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 that cites results from NIH grant-supported research must include an acknowledgment of NIH grant support and disclaimer such as "The project described was supported by Award Number U01AI082224 from the National Institute Of Allergy And Infectious Diseases. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute Of Allergy And Infectious Diseases or the National Institutes of Health."

Award recipients are required to comply with the NIH Public Access Policy. This includes submission to PubMed Central (PMC), upon acceptance for publication, an electronic version of a final peer-reviewed, manuscript resulting from research supported in whole or in part, with direct costs from National Institutes of Health. The author's final peer-reviewed manuscript is defined as the final version accepted for journal publication, and includes all modifications from the publishing peer review process. For additional information, please visit http://publicaccess.nih.gov/.

Award recipients must promote objectivity in research by establishing standards to ensure that the design, conduct and reporting of research funded under NIH-funded awards are not biased by a conflicting financial interest of an Investigator. Investigator is defined as the Principal Investigator and any other person who is responsible for the design, conduct, or reporting of NIH-funded research or proposed research, including the Investigator's spouse and dependent children. Awardees must have a written administrative process to identify and manage financial conflict of interest and must inform Investigators of the conflict of interest policy and of the Investigators' responsibilities. Prior to expenditure of these awarded funds, the Awardee must report to the NIH Awarding Component the existence of a conflicting interest and within 60 days of any new conflicting interests identified after the initial report. Awardees must comply with these and all other aspects of 42 CFR Part 50, Subpart F. These requirements also apply to subgrantees, contractors,

or collaborators engaged by the Awardee under this award. The NIH website http://grants.nih.gov/grants/policy/coi/index.htm provides additional information.

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

Sincerely yours,

Victoria P. Connors
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 1U01AI082224-01

Award Calculation (U.S. Dollars)

Salaries and Wages	SALARY
Fringe Benefits	Fringe Ben
Consultant Services	$54,342
Supplies	$52,888
Travel Costs	$7,817
Other Costs	$268,847
Consortium/Contractual Cost	$1,741,020
Federal Direct Costs	Direct Costs
Federal F&A Costs	Indirect Costs
Approved Budget	$2,454,564
Federal Share	$2,454,564
TOTAL FEDERAL AWARD AMOUNT	$2,454,564
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$2,454,564

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$2,454,564	$2,454,564
2	$2,481,738	$2,481,738

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

Fiscal Information:

CFDA Number:	93.701
EIN:	EIN
Document Number:	UAI082224Z
Fiscal Year:	2009

IC	*CAN*	*2009*	*2010*
AI	8485145	$2,454,564	$2,481,738

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

NIH Administrative Data:
PCC: M46D B / **OC**: 414L / **Processed**: COATSK 09/21/2009

SECTION II – PAYMENT/HOTLINE INFORMATION – 1U01AI082224-01

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 – 1U01AI082224-01

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 74 or 45 CFR Part 92 as applicable.
d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. 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.)

ARRA TERM OF AWARD: This award is subject to the HHS-Approved Standard Terms and Conditions for the American Recovery and Reinvestment Act of 2009. Approved text for NIH awards can be found at http://grants.nih.gov/grants/policy/NIH_HHS_ARRA_Award_Terms.pdf. Recipients should pay particular attention to the special quarterly reporting requirements required by Section 1512 of the Recovery Act as specified in Term #2.

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

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 – AI Special Terms and Conditions – 1U01AI082224-01

THIS AWARD CONTAINS GRANT SPECIFIC RESTRICTIONS. THESE RESTRICTIONS MAY ONLY BE LIFTED BY A REVISED NOTICE OF AWARD.

Restriction: Funds included in this award for research involving live vertebrate animals are restricted and may not be used for any other purpose without the written prior approval of the NIH awarding component. Under governing PHS Policy no funds may be drawn down from the payment system and no obligations made against federal funds for research involving live vertebrate animals prior to approval by the Office of Laboratory Animal Welfare (OLAW) of an Animal Welfare Assurance in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals. This restriction applies to the applicant organization and all performance sites (e.g., collaborating institutions, sub-contractors, sub-grantees) lacking OLAW-approved Assurances, whether domestic or inter-institutional. If the applicant organization does not have an Animal Welfare Assurance and the animal work will be conducted at an institution with an Assurance, the grantee must obtain an Inter-institutional Assurance from OLAW. Animal Welfare Assurances must be submitted to OLAW not later than November 30, 2009. Failure to submit the Animal Welfare Assurance to OLAW within the required timeframe or to otherwise comply with the above requirements can result in suspension and/or termination of this award, withholding of support, audit disallowances, and/or other appropriate action.

****

The budget period anniversary start date for future year(s) will be September 1.

****

This award provides an allowance of F&A costs of [ ] %F&A rate salaries and wages exclusive of fringe benefits.

****

This award is issued as a Cooperative Agreement, a financial assistance mechanism in which substantial NIH scientific and/or programmatic involvement is anticipated in the performance of the activity. This award is subject to the Terms and Conditions of Award as set forth in Section VI: Award Administrative Information of RFA AI-08-001, ?Title,? release date 02/21/2008, which are hereby incorporated by reference as special terms and conditions of this award.

Copies of the RFA may be accessed at the following Internet address: <http://www.nih.gov/grants/guide/index.html>

As mandated in this RFA, the principal investigator should submit a performance plan to the NIAID program official that details specific milestones and timelines for achieving each milestone. Milestones should be linked to the annual funding cycle and submission of the annual progress report. The plan should include the specific criteria to be used in evaluating the degree of progress made in achieving each milestone.

The timelines and milestones must be approved by the Program Official within 30 days from the issue date of award.

Such timelines and milestones shall be agreed upon by the principal investigator and the NIAID program official before funds may be released.

To receive consideration for funding of each successive year, the annual progress report and an Updated Product Development Plan must be received two months prior to the end of the current funding period, demonstrating that the milestones defined for that funding year have been met.

The award may be adjusted in time or funding, as necessary, if the grantee fails to meet the agreed upon milestones.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens) must complete registration with CDC (or USDA, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

****

The research proposed in this grant may involve Select Agents and/or Highly Pathogenic Agents. NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that, under some circumstances, may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm), your Institutional Biosafety Committee (IBC) or equivalent body, or appropriate designated institutional biosafety official. If there is ambiguity in the BMBL guidelines and/or there is disagreement among the BMBL, an institutional committee or institutional official, the highest recommended containment level must be used.

When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If the work involves Select Agents and/or Highly Pathogenic Agents. Also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

o A list of the new and/or additional Agent(s) that will be studied;
o A description of the work that will be done with the Agent(s);
o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

For domestic work with Select Agents provide documentation of Registration status of all domestic organizations/entities where Select Agent(s) will be used

Please be advised that changes in the use of a Select Agent will likely be considered a change in scope and, therefore, require NIH awarding office prior approval.

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: Kim L. Coats
Email: kcoats@niaid.nih.gov **Phone**: 301-451-4576 **Fax**: 301-493-0597

Program Official: Lanling Zou
Email: lanlingz@niaid.nih.gov **Phone**: 301-451-3757 **Fax**: 301-402-2508

SPREADSHEET SUMMARY
GRANT NUMBER: 1U01AI082224-01

INSTITUTION: EMERGENT BIOSOLUTIONS

Budget	*Year 1*	*Year 2*
Salaries and Wages	SALARY	
Fringe Benefits	Fringe Benefits	
Consultant Services	$54,342	
Supplies	$52,888	$15,000
Travel Costs	$7,817	$10,252
Other Costs	$268,847	$72,667
Consortium/Contractual Cost	$1,741,020	$2,100,988
TOTAL FEDERAL DC	Direct Costs	
TOTAL FEDERAL F&A	Indirect Costs	
TOTAL COST	$2,454,564	$2,481,738

Facilities and Administrative Costs	*Year 1*	*Year 2*
F&A Cost Rate 1	Indirect Costs	
F&A Cost Base 1		
F&A Costs 1		

Form Approved Through 11/30/2010

12144851

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Do not exceed character length restrictions indicated.

PI: **PARK, SUKJOON**
1 U01 AI082224-01
Dual:
IRG: ZAI1 SRC(99)

Council: 01/2009

Received: 06/19/2008

1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*
Development of a Next Generation Anthrax Vaccine, dmPA7909

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☒ YES
(If "Yes," state number and title)
Number: RFA-AI-08-001 Title: Cooperative Research Partnerships for Biodefense and Emerging Infectious Diseases (U01)

3. PROGRAM DIRECTOR/PRINCIPAL INVESTIGATOR — **New Investigator** ☒ **No** ☐ **Yes**

3a. NAME (Last, first, middle)
Park, Sukjoon

3b. DEGREE(S)
Ph.D.

3h. eRA Commons User Name
eRA Commons User Name

3c. POSITION TITLE
Director, Product Development

3d. MAILING ADDRESS *(Street, city, state, zip code)*
300 Professional Drive
Suite 250
Gaithersburg, MD 20879

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

3f. MAJOR SUBDIVISION
Emergent Product Development Gaithersburg Inc.

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: (301) 944-0154 FAX: (301) 590-1252

E-MAIL ADDRESS:
parks@ebsi.com

4. HUMAN SUBJECTS RESEARCH ☒ No ☐ Yes
4a. Research Exempt ☐ No ☐ Yes If "Yes," Exemption No.
4b. Federal-Wide Assurance No.
4c. Clinical Trial ☒ No ☐ Yes
4d. NIH-defined Phase III Clinical Trial ☐ No ☐ Yes

5. VERTEBRATE ANIMALS ☐ No ☒ Yes
5a. Animal Welfare Assurance No.

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
06/01/09	09/30/13	Direct Costs	$2,454,564	Direct Costs	$5,928,440

9. APPLICANT ORGANIZATION
Name Emergent Product Development Gaithersburg Inc.
Address 300 Professional Drive
Suite 250
Gaithersburg, MD 20879

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☒ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
EIN
DUNS NO. 1894885544 Cong. District MD8

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name Michael J. Langford, DVM, Ph.D.
Title Senior V.P., Biodefense
Address Emergent Product Development Gaithersburg Inc.
300 Professional Drive
Gaithersburg, MD 20879
Tel: (301) 944-0144 FAX: (301) 590-1252
E-Mail: langfordm@ebsi.com

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name Michael J. Langford, DVM, Ph.D.
Title Senior V.P., Biodefense
Address Emergent Product Development Gaithersburg Inc.
300 Professional Drive
Gaithersburg, MD 20879
Tel: (301) 944-0144 FAX: (301) 590-1252
E-Mail: langfordm@ebsi.com

14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13: *(In ink. "Per" signature not acceptable.)*

DATE 06/19/08

PROJECT SUMMARY (See instructions):

Emergent BioSolutions Inc. (Emergent) is proposing to advance the development of a novel anthrax vaccine dmPA7909. This next generation vaccine is composed of the double-mutant recombinant Bacillus anthracis protective antigen (dmPA), the aluminum adjuvant Alhydrogel® and the immunostimulatory oligodeoxynucleotide compound CPG 7909 (VaxImmune™) formulated as a dry powder. To ensure that the dmPA7909 vaccine will be stable even at elevated temperatures, Emergent employed proven stabilizing technologies for each of the components in the vaccine formulation. The dmPA has been genetically engineered to remove two major protease cleavage sites within the molecule and, and as a result, its stability is significantly improved. This stable dmPA adsorbed to Alhydrogel has been tested in animal efficacy studies and is currently being used in combination with Alhydrogel in a Phase 1 clinical trial. Alhydrogel (aluminum hydroxide) has a long history of use in vaccines including childhood vaccines and has documented stability at 25 and 37 °C. CPG 7909, unlike other CpG oligonucleotides, has all of its phosphate linkages replaced with phosphorothioate bonds, thus decreasing its sensitivity to nucleases, thus rendering it stable. Additionally, the spray-dried powder formulation dramatically enhances vaccine stability even at extreme temperatures for a extended period of time. CPG 7909 has also been extensively tested in the clinic alone, and in combination with other Alhydrogel-adjuvanted recombinant vaccines.
The characteristics of dmPA7909 that make it an ideal candidate to meet the nation's needs for a next generation anthrax vaccine are:

1. Rapid immune response following 2-3 doses
2. Long-term stability to facilitate ambient temperature storage in the Strategic National Stockpile
3. Ability to be administered in a national emergency without the need for special storage conditions

RELEVANCE (See instructions):

Currently licensed anthrax vaccine, BioThrax®, is efficacious and safe. However, the vaccine requires a cold-chain for storage. In the event of a bioterrorist attack involving aerosolized anthrax spores, there is a need for an effective and stable vaccine that can be stored and distributed without requiring special storage conditions. Emergent's next generation anthrax vaccine, dmPA7909, will fill this unmet need.

PROJECT/PERFORMANCE SITE(S) (if additional space is needed, use Project/Performance Site Format Page)

Project/Performance Site Primary Location			
Organizational Name: Emergent Product Development Gaithersburg Inc.			
DUNS: 1894885544			
Street 1: 300 Professional Drive		Street 2:	
City: Gaithersburg	County: Montgomery		State: MD
Province:	Country: USA		Zip/Postal Code: 20879
Project/Performance Site Congressional Districts:			

Additional Project/Performance Site Location			
Organizational Name: Emergent Biodefense Operations Lansing			
DUNS: 1894885544			
Street 1: 3500 N. Martin Luther King Jr. Blvd.		Street 2:	
City: Lansing	County: Ingham		State: MI
Province:	Country: USA		Zip/Postal Code: 48906
Project/Performance Site Congressional Districts:			

Program Director/Principal Investigator (Last, First, Middle): Park, Sukjoon

Use only if additional space is needed to list additional project/performance sites.

Additional Project/Performance Site Location			
Organizational Name: University of Nebraska- Lincoln Biological Process Development Facility (UNL-BPDF)			
DUNS:			
Street 1: 820 N. 16th Street		Street 2: 304 Othmer Hall	
City: Lincoln	County: Lancaster		State: NE
Province:	Country: USA		Zip/Postal Code: 68588
Project/Performance Site Congressional Districts:			

Additional Project/Performance Site Location
Unfunded

Additional Project/Performance Site Location			
Organizational Name: Bridge Laboratories			
DUNS:			
Street 1: 600 Professional Drive		Street 2:	
City: Gaithersburg	County: Montgomery		State: MD
Province:	Country: USA		Zip/Postal Code: 20879
Project/Performance Site Congressional Districts:			

Additional Project/Performance Site Location			
Organizational Name:			
DUNS:			
Street 1:		Street 2:	
City:	County:		State:
Province:	Country:		Zip/Postal Code:
Project/Performance Site Congressional Districts:			

Additional Project/Performance Site Location			
Organizational Name:			
DUNS:			
Street 1:		Street 2:	
City:	County:		State:
Province:	Country:		Zip/Postal Code:
Project/Performance Site Congressional Districts:			

SENIOR/KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below. Start with Program Director(s)/Principal Investigator(s). List all other senior/key personnel in alphabetical order, last name first.

Name	eRA Commons User Name	Organization	Role on Project
Park, Sukjoon	eRA Commons User Name	Emergent	Principal Investigator
Hughes, Karen		Emergen	Quality Assurance
Pleune, Brett		Emergen	Regulatory Affairs
Savransky, Vladimir		Emergen	Nonclinical Study
Meagher, Michael		UNL	cGMP Manufacturing

OTHER SIGNIFICANT CONTRIBUTORS

Name	Organization	Role on Project
Cureton, Shannon	Emergent	Project Manager
Welch, Richard	Emergent	Process Development
Yang, Huei-Hsing	Emergent	Tech transfer
Chu, Yanfang	Emergent	Tech transfer
Uitz, Catherine	Emergent	Tech transfer
Lyons, Mark	Emergent	Nonclinical Study
TBD	Emergent	Nonclinical Study

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://stemcells.nih.gov/research/registry/. *Use continuation pages as needed.*

If a specific line cannot be referenced at this time, include a statement that one from the Registry will be used.

Cell Line

The name of the program director/principal investigator must be provided at the top of each printed page and each continuation page.

RESEARCH GRANT

TABLE OF CONTENTS

Appendix *(Five identical CDs.)* ☐ Check if Appendix is Included

Program Director/Principal Investigator (Last, First, Middle): Park, Sukjoon

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 06/01/09 THROUGH 05/31/10

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Park, Sukjoon	PD/PI	Effort			Institutional Based Salary	SALARY	Fringe Benefits	SALARY
Hughes, Karen	Quality Assurance							
Welch, Richard	Sr Director Process Dvlp							
Chu, Yanfang	Mgr, Downst Processing							
Uitz, Catherine	Principal Scientist							
Yang, Huei-Hsing	Sr Mgr, Upst Processing							
Savransky, Vladimir	Scientist							
Lyons, Mark	Mgr, Clinical Immunoassa							
TBD	Scientist							
TBD	Project Manager							
Pleune, Brett	Regulatory							
	SUBTOTALS →							

CONSULTANT COSTS		
EQUIPMENT *(Itemize)*		
SUPPLIES *(Itemize by category)*		
TRAVEL 3 trips as detailed in the narrative		$7,790
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		0
OTHER EXPENSES *(Itemize by category)* Unfunded Girindus-Negotiated		$621,613
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	$ Negotiated Costs
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*		$ Subtotal
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	Federal F&A
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$ Direct Costs

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from Form Page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*	SALARY				
CONSULTANT COSTS					
EQUIPMENT					
SUPPLIES					
TRAVEL	$7,790	$4,752		0	
PATIENT CARE COSTS					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES	$621,613	$2,563,260	$58,964	$73,652	$42,334
CONSORTIUM/ CONTRACTUAL COSTS — DIRECT	Negotiated Costs				
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*	Subtotal				
CONSORTIUM/ CONTRACTUAL COSTS — F&A	Federal F&A				
TOTAL DIRECT COSTS	Direct Costs				

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD	$ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

A. Direct labor/Key Personnel

Key Personnel:

Dr. Sukjoon Park — Dr. Park is the PI for this project will be allocated at % Effort for the first two years and at % Effort for the duration thereafter.

Ms. Karen Hughes — Ms. Hughes will provide Quality support for this project. She will be allocated at % Effort for the first two years during cGMP manufacturing activities.

Dr. Brett Pleune — Dr. Pleune will provide Regulatory support for this project. He will be allocated at % Effor for Year 2 to supervise pre-IND regulatory activities.

Dr. Vladimir Savransky — Dr. Savransky will be responsible for nonclinical studies. He will oversee the guinea pig immunogenicity/efficacy study and the repeat-dose toxicology study. He will be allocated a % Effor for the first two years

Dr. Michael Meagher	Dr. Meagher is in charge of the University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF). He will oversee the cGMP manufacturing of bulk cGMP material.

Other Significant Personnel:

Dr. Gary Nabors	Dr. Nabors will provide project oversight. Emergent is not requesting salary for Dr. Nabors.
Ms. Shannon Cureton	Ms. Cureton is the Project Manager for this project will be allocated at % Effort for the first two years and at % Effo rt for the duration thereafter.
Dr. Richard Welch	Dr. Welch will oversee all development and tech transfer activities. He will be allocated at % Effort for the first year.
Dr. Huei-Hsiung Yang	Dr. Yang will provide technical expertise for fermentation and recovery activities during tech transfer. He will be allocated at % Effort for the first year.
Dr. Yanfang Chu	Dr. Chu will provide technical expertise for purification activities during tech transfer. He will be allocated at % Effort for the first year.
Dr. Catherine Uitz	Dr. Uitz will provide technical expertise for purification activities during tech transfer. She will be allocated a % Effort for the first year.
Dr. Mark Lyons	Dr. Lyons will conduct guinea pig immunogenicity/efficacy study. He will be allocated at % Effort for the first year.
TBD	This technical person will be involved in the guinea pig immunogenicity/efficacy study. He/she will be allocated at % Effort for the first year.

B. Justification for Other Major Budget Items

Equipment:

Emergent is not requesting any new equipment in this proposal.

Supplies:

Girindus will supply 30 g of cGMP CPG 7909 adjuvant for this proposal. Girindus is requesting Negotiated Costs for the cGMP material and, since it is a GMP grade, Emergent believes the price is justifiable. Additionally, Emergent is requesting Negotiated Costs to conduct a guinea pig immunogenicity/efficacy study in our Lansing, MI facility. Forty animals will be used in this study and, since the study requires select agent and BSL-3 animal facility, Emergent believes the requested fund is justifiable.

Subcontractors:

University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF)

UNL-BPDF will be a subcontractor for this proposal to Unfunded - ARRA and cGMP dmPA bulk drug substance (BDS). Additionally, UNL-BPDF will also conduct Unfunded - ARRA studies for the Unfunded - ARRA and the BDS. UNL-BPDF is requesting Negotiated Costs for the proposed activities. Since the scope of the study is extensive, Emergent believes the requested fund is fully justifiable.

Unfunded

Bridge Laboratories (Bridge)

Emergent has also selected Bridge Laboratories as a contractor for the toxicology study. Bridge will conduct the animal study portion of the toxicology study. Ninety guinea pigs will be used for the study and extensive tests including, but not limited to, necropsy and histopathology will be conducted in the study. Emergent believes the estimated cost of Estimated Costs is reasonable for the scope of work.

Travel:

Year 1: $7,790

One trip (three days, two nights) for two project team members to Unfunded Unfunded The purpose of this trip is to evaluate and manage the formulation process and assay development activities. Estimated flight costs are Estimated Costs roundtrip from Maryland to Unfunded The 2008 GSA per diem rate for lodging is $198/night, and for meals and incidentals is $118/day. Additionally, the cost for ground transportation is estimated a Estimated Costs Also budgeted is one trip to University of Nebraska in Lincoln, NE for two project team members for two days. The purpose of the trip is to evaluate and manage the cGMP manufacturing activities. Estimated flight costs are Estimated Costs roundtrip from Maryland to Omaha, NE. The 2008 GSA per diem rate for lodging is $70/night, and for meals and incidentals is $39/day. Additionally, the cost for ground transportation is estimated at Estimate d Costs Also budgeted is one trip to Emergent's BSL-3 facility located in Lansing, MI for two project team members for two days, one night. The purpose of the trip is to coordinate the guinea pig immunogenicity/efficacy study. Estimated flight costs are Estimated Costs roundtrip from Maryland to Detroit, MI. The 2008 GSA per diem rate for lodging is $78/night, and for meals and incidentals is $39/day. Additionally, the cost for ground transportation is estimated at Estimated Costs

Year 2: $4,752

One trip (three days, two nights) for two project team members to Unfunded Unfun The purpose of this trip is to coordinate and evaluate the cGMP formulation and fill/finish manufacturing activities. Estimated flight costs are Estimated Costs roundtrip from Maryland to Unfunded The 2008 GSA per diem rate for lodging is $198/night, and for meals and incidentals is $118/day. Additionally, the cost for ground transportation is estimated at Estimated Costs

Facilities and Administrative Costs:

Proprietary Info

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Sukjoon Park	Director, Product Development Emergent Product Development Gaithersburg Inc.
eRA COMMONS USER NAME eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Korea University, Seoul, Korea		1982-1984	Civil Engineering
Ohio University, Athens, Ohio	B.S.	1987-1990	Botany (Honor College)
Ohio State University, Columbus, Ohio	Ph.D.	1990-1996	Graduate Program in Molecular, Cellular & Developmental Biology

A. Positions and Honors.

Positions and Employment

1990 – 1996 Graduate Research Associate, Molecular, Cellular & Developmental Biology, Ohio State University
1997 – 1997 Post-doctoral Researcher, Ohio State University
1997 – 2000 Visiting Fellow, National Institutes of Health, Bethesda, MD
2000 – 2002 Manager Research Dept. Research and Development Group, BioPort Corp., Lansing, MI
2002 – 2003 Senior Manager, Research Department, Research and Development Group, BioPort Corp., Lansing, MI
2003 – 2007 Associate Director, Molecular & Cellular Biology Dept, Emergent Product Development, Gaithersburg, MD
2007 – Present Director, Product Development, Emergent Product Development, Gaithersburg, MD

Other Activities

1998 – 2000 Seminar Committee Member, Nat. Inst. Of Dental and Craniofacial Research, NIH
2003 – 2005 Committee Member, Chemical technology advisory committee, Lansing, MI
2004 – 2004 Scientific Grant Reviewer, Nat. Inst. of Allergy and Infectious Diseases (NIAID), Biodefense Program
2003 – Present Scientific/Technical Reviewer, Defense Threat Reduction Agency (DTRA) Chemical and Biological Defense Core Program

Patents and Inventions

US Patent 7,201,912 Date of Patent: 04/10/2007
Sukjoon Park and Lallan Giri
Recombinant immunogenic compositions and methods for protecting against lethal infections from *Bacillus anthracis*

National Institutes of Health Employee Invention Report (Reference Number: E-296-99/0)
"New system for producing large amounts of pure *Bacillus anthracis* lethal factor"

Scholarships and Awards

1983 – 1984 Music Scholarship, Korea University

1985 – 1987	Two Army Achievement Medals and one Army Commendation Medal, 8th United States Army
1988 – 1990	Honors Scholarship, Ohio University
1994	Excellent Abstract Award in *Pseudomonas* Research, 94th General Meeting, American Society for Microbiology
1996	Graduate Alumni Research Award, Ohio State University
1999	Employee of the Quarter Award, Oral Infection and Immunity Branch, Nat. Inst. of Dental and Craniofacial Research, NIH
2006	Special Achievement Award, Emergent BioSolutions, Inc.

B. Selected Peer-reviewed Publications (in chronological order).

1. Peters, J. E., **S. Park**, A. Darzins, L. C. Freck, J. M. Saulnier, J.M. Wallach and D. R. Galloway (1992). "Further studies on *Pseudomonas aeruginosa* LasA: analysis of specificity." *Molecular Microbiology* 6: 1155-1162.
2. **Sukjoon Park** and Darrell R. Galloway (1995). "Purification and characterization of LasD: a second staphylolytic proteinase produced by *Pseudomonas aeruginosa*." *Molecular Microbiology* 16: 263-270.
3. **Sukjoon Park** and Darrell R. Galloway (1998). "*Pseudomonas aeruginosa* LasD processes the inactive LasA precursor to the active protease form." *Archives of Biochemistry and Biophysics.* 357: 8-12.
4. **Sukjoon Park** and Stephen H. Leppla (2000). "Optimized production and purification of *Bacillus anthracis* Lethal Factor." *Protein Expression and Purification*, 18: 293-302.
5. Brian Price, **Sukjoon Park**, Steve H. Leppla, and Darrell R. Galloway (2001). "Protection against *Bacillus anthracis* lethal toxin challenge by genetic immunization with a plasmid encoding the lethal factor protein." *Infection and Immunity*, 69: 4509-4515.
6. Andrew Pannifer, Thiang Yian Wong, Robert Schwarzenbacher, Martin Renatus, Carlo Petosa, Jadwiga Bienkowska, D. Borden Lacy, R. John Collier, **Sukjoon Park**, Stephen H. Leppla, Philip Hanna & Robert C. Liddington (2001). "Crystal Structure of the Anthrax Lethal Factor." *Nature*, 414: 229-233.

Relevant Abstracts and Presentations

7. **Sukjoon Park** and Darrell R. Galloway (1994). "Purification and characterization of LasD: a novel *Pseudomonas aeruginosa* protease." Abstract for the 94th general meeting of American Society for Microbiology.
8. L. K. Winberry and **S. Park** (2001). "Components of Anthrax Vaccine Adsorbed and Contrast with Merck Vaccine." Oral presentation to Institute of Medicine Anthrax Vaccine Committee (January 29-30, 2001, Washington, DC).
9. B. Price, A. L. Liner, **S. Park**, S. H. Leppla, A. Mateczun, and D. R. Galloway (2001). "Protection Against Lethal Anthrax Toxin Challenge by Genetic Vaccination with Plasmids that Encode *B. anthracis* Protective Antigen and/or a Mutant form of Lethal Factor." Poster presentation for 101st American Society for Microbiology General Meeting (May 20-24, 2001, Orlando, FL).
10. L. K. Winberry, L. Bondoc, **S. Park**, L. Simon, C. N. Shih, and L. Giri (2001). "Characterization of the US-licensed Anthrax Vaccine." Poster presentation for 4th International Conference on Anthrax (June 10-13, 2001, St. John's College, Annapolis, MD).
11. B. Price, A. Liner, **S. Park**, S. H. Leppla, A. Mateczun, and D. R. Galloway (2001). "DNA Vaccine Which Protects Against Anthrax." Poster presentation for 4th International Conference on Anthrax (June 10-13, 2001, St. John's College, Annapolis, MD).
12. **S. Park**, C. Shih, L. Bondoc, L. Simon, B. Price, C. Botezan, P. Hine, and L. Giri (2003). "Development of a dual-component anthrax vaccine." Oral presentation for 5th International Conference on Anthrax (March 30-April 3, Nice, France).
13. D. Willis, **S. Park**, and L. Giri (2003). "Candidate vaccine peptides from Lethal Factor and Protective Antigen of *Bacillus anthracis* using a novel mathematical model." Poster presentation for 5th International Conference on Anthrax (March 30-April 3, Nice, France).
14. M. Cullum, P. Hine, C. Shih, L. Lininger, D. Bienek, J. Ragain, L. Simonson, and S. Park (2003). "Proposed rapid immunoassay of anthrax Protective Antigen in vaccine cultures by fluorescence polarization." Poster presentation for 5th International Conference on Anthrax (March 30-April 3, Nice, France).

C. Research Support

Research Supported by NIH

Project: Development of *Bacillus anthracis* Expression System
Duration: 1997 – 2000
Role: Post-doctoral Project Leader

Project: Development of a DNA Vaccine Against Anthrax
Duration: 1998 – 2000
Role: Post-doctoral Researcher

Project: Development of a Next Generation Anthrax Vaccine, AV7909
Duration: 2008 –
Role: Principal Investigator

Research Supported by Emergent BioSolutions

Project: Next Generation Anthrax Vaccine Project
Duration: 2000–present
Role: Project Leader

Project: Chlamydia Vaccine Development Project
Duration: 2004–present
Role: Project Leader

Project: Non-Typeable Haemophilus influenzae Vaccine Delivery System Development
Duration: 2004–2005
Role: Project Leader

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Hughes, Karen	Senior Director, Development Quality Assurance
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Certificate of Completion, Biochemical Regulatory Engineering Program		1995	GMPs for BioProcess, Quality Control and Quality Assurance for Biotechnology Products
Clarion University of Pennsylvania, Clarion, PA	B.S.	1988	Marketing

Positions and Employment

1988 – 1999	Chesapeake Biological Laboratories, Inc. (CBL), Baltimore MD
1988 – 1991	Sales and Marketing Representative, CBL
1991 – 1994	Quality Assurance Auditor, CBL
1994 – 1996	Quality Assurance Supervisor, CBL
1996 – 1998	Manager, Quality Assurance, CBL
1998 – 1999	Assistant Director, Quality Assurance, CBL
1999 – 2008	MGI Pharma (formerly Guilford Pharmaceuticals Inc.), Baltimore MD
1999 – 2000	Manager, Development Quality Assurance and Quality Control, MGI Pharma
2000 – 2004	Associate Director, Development Quality, MGI Pharma
2004 – 2005	Director, Development Quality, MGI Pharma
2005 – 2008	Senior Director, Development Quality, MGI Pharma
Present	Senior Director, Development Quality Assurance, Emergent BioSolutions Inc.

Professional Membership

American Society for Quality, Certified Quality Auditor from June 1998 to December 2004
American Society for Quality, Member since 1993
Society for Quality Assurance, Member since 2002
Supported the Biotechnology Institute, Baltimore, MD, as an instructor (Topics: Good Documentation Practices: Pharmaceutical Terms) from 1999 – 2004
Participated in the Maryland Center for Quality and Productivity ISO 9000 Consortium as a volunteer speaker

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Brett Martin Pleune	Manager, Regulatory Affairs Department
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Maryland, College Park, MD	Ph.D.	1998	Chemistry
State University of New York at Binghamton, Binghamton, NY	B.S.	1993	Chemistry

A. Positions and Honors.

Positions and Employment

1998–1999 Postdoctoral Research Associate, Arizona State University, Tempe, AZ
1999–2000 Visiting Assistant Professor of Chemistry, Goucher College, Baltimore, MD
2000–2002 Scientist, Sigma-Aldrich Fine Chemicals, Sheboygan Falls, WI
2002–2003 CMC Project Manager, TherImmune Research/Gene Logic Inc., Gaithersburg, MD
2004–2007 Senior Consultant, Salamandra, LLC, Bethesda, MD
2007–Present Manager, Regulatory Affairs Department, Emergent Product Development Gaithersburg, Inc., Gaithersburg, MD

Honors

Graduated cum laude (1993), State University of New York at Binghamton
Sigma Xi Professional Research Society, member since 1998

B. Selected peer-reviewed publications (in chronological order).

1. Fettinger, J.C., **Pleune, B.**, and Poli, R. First Structure of a Cyclopentadienyl Trihydride d^2 System: A Pseudotrigonal Prism Rather than the Expected Pseudooctahedron and its Mechanism of Hydrogen Scrambling. J. Am. Chem. Soc. 1996, 118, 4906-4907.
2. **Pleune, B.**, Fettinger, J.C., and Poli, R. Synthesis, Structure, and Protonation Studies of $Cp^*MH_3(dppe)$ (M = Mo, W). Pseudo-Trigonal Prismatic vs. Pseudo-Octahedral Structures of Half-Sandwich Group 6 M(IV) Derivatives. Organometallics 1997, 16, 1581-1594.
3. **Pleune, B.**, Poli, R., and Fettinger, J.C. Synthesis and Structure of the Stable Paramagnetic Cyclopentadienyl Polyhydride Complexes $[Cp^*MH_3(dppe)]^+$ (M = Mo, W): Stronger M-H Bonds upon Oxidation. J. Am. Chem. Soc. 1998, 120, 3257-3258.
4. **Pleune, B.**, Morales, D., Meunier-Priest, R., Richard, P., Collange, E., Fettinger, J.C., and Poli, R. Stable Paramagnetic Half-Sandwich Mo(V) and W(V) Polyhydride Complexes. Structural, Spectroscopic, Electrochemical, Theoretical, and Decomposition Mechanism Studies of $[Cp^*MH_3(dppe)]^+$ (M = Mo, W). J. Am. Chem. Soc. 1999, 121, 2209-2225.
5. Steffek, C., McMurran, J., **Pleune, B.**, Kouvetakis, J., Concolino, T., and Rheingold, A. Synthesis of Cl_2InN_3, Br_2InN_3, and Related Adducts. Inorg. Chem. 2000; 39, 1615-1617.
6. Williams, D., **Pleune, B.**, Kouvetakis, J., Williams, M., and Andersen, R. Synthesis of $LiBC_4N_4$, BC_3N_3, and Related C-N Compounds of Boron: New Precursors to Light Element Ceramics. J. Am. Chem. Soc. 2000; 122, 7735-7741.

C. Research Support.

Not applicable.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Vladimir Savransky, M.D., Ph.D.	Principal Scientist
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Pavlov's Medical University, Saint-Petersburg, Russia	M.D.	1991	Medicine
Pavlov's Medical University, Saint-Petersburg, Russia	Resident	1991-93	Surgery
Pavlov's Medical University, Saint-Petersburg, Russia	Ph.D.	1994	Medicine/Surgery

ACADEMIC APPOINTMENTS:

1995 - 2000	Assistant Professor	Department of General Surgery, Pavlov's Medical University, Saint-Petersburg, Russia
2001 - 2003	NRC Research Fellow	Department of Experimental Pathology, Division of Pathology, Walter Reed Army Institute of Research, Silver Spring, MD
2003 - 2005	Postdoctoral Research Fellow	Division of Nephrology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
2005 - 2008	Research Associate	Division of Pulmonary and Critical Care Medicine, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
2008 - present	Principal Scientist	In Vivo Testing Unit, Product Development - Gaitherburg Emergent BioSolutions Inc., Gaithersburg, MD

SELECTED PUBLICATIONS (PEER REVIEWED):

1. **Savransky V**, Nanayakkara A, Li J, Bevans S, Smith PL, Rodriguez A, Polotsky VY. Chronic Intermittent Hypoxia Induces Atherosclerosis. Am J Respir Crit Care Med. 2007; 175(12):1290-7.
2. **Savransky V**, Nanayakkara A, Vivero A, Li J, Bevans S, Smith PL, Torbenson MS, Polotsky VY. Chronic intermittent hypoxia predisposes to liver injury. Hepatology. 2007; 45(4):1007-13.
3. **Savransky V**, Bevans S, Nanayakkara A, Li J, Smith PL, Torbenson MS, Polotsky VY. Chronic intermittent hypoxia causes hepatitis in a mouse model of diet-induced fatty liver. Am J Physiol Gastrointest Liver Physiol.2007; 293(4):G871-7.
4. Li J, Nanayakkara A, Jun J, **Savransky V**, Polotsky VY. The Effect of Deficiency in SREBP Cleavage-Activating Protein (SCAP) on Lipid Metabolism during Intermittent Hypoxia. Physiol Genomics. 2007;31 (2):273-80.
5. Li J, **Savransky V**, Nanayakkara A, Smith PL, O'Donnell CP, Polotsky VY. Hyperlipidemia and lipid peroxidation are dependent on the severity of chronic intermittent hypoxia. J Appl Physiol. 2007; 102(2):557-63.
6. Ascon DB, Lopez-Briones S, Liu M, Ascon M, **Savransky V**, Colvin RB, Soloski MJ, Rabb H. Phenotypic and functional characterization of kidney-infiltrating lymphocytes in renal ischemia reperfusion injury. J Immunol. 2006; 177(5):3380-7.
7. **Savransky V**, Molls RR, Burne-Taney M, Chien CC, Racusen L, Rabb H. Role of the T-cell receptor in kidney ischemia-reperfusion injury. Kidney Int. 2006; 69(2):233-8.

8. Molls RR, **Savransky V**, Liu M, Bevans S, Mehta T, Tuder RM, King LS, Rabb H. Keratinocyte-derived chemokine is an early biomarker of ischemic acute kidney injury. Am J Physiol Renal Physiol. 2006; 290(5):F1187-93.
9. Li J, Bosch-Marce M, Nanayakkara A, **Savransky V**, Fried SK, Semenza GL, Polotsky VY. Altered metabolic responses to intermittent hypoxia in mice with partial deficiency of hypoxia-inducible factor 1 {alpha}.Physiol Genomics. 2006; 25(3):450-7.
10. **Savransky V**, Pinelis D, Korolev S, Ionin B, Fegeding K. Immunogenicity of the histidine-to-tyrosine staphylococcal enterotoxin B mutant protein in C3H/HeJ mice. Toxicon. 2004; 43(4):433-8.
11. **Savransky V**, Rostapshov V, Pinelis D, Polotsky Y, Korolev S, Komisar J, Fegeding K. Murine lethal toxic shock caused by intranasal administration of staphylococcal enterotoxin B. Toxicol Pathol. 2003; 31(4):373-8.
12. Korolev S, Pinelis D, **Savransky V**, Komisar J, Vogel P, Fegeding K. Toxicity of the staphylococcal enterotoxin B mutants with histidine-to-tyrosine substitutions. Toxicology. 2003; 187(2-3):229-38.
13. Potashov LV, Vasil'ev VV, **Savransky VM**, Semenov DIu, Osmanov ZKh. [The immediate results of laparoscopic treatment in perforated gastroduodenal ulcers]Vestn Khir Im I I Grek. 1999; 158(6):9-11.
14. Potashov LV, Vasil'ev VV, **Savransky VM**, Semenov DIu, Osmanov Zkh. [A methods of laparoscopic suturing of perforated pyloro-bulbar ulcers]Vestn Khir Im I I Grek. 1999; 158(5):62-4.Potashov LV, Morozov VP, **Savransky VM**, Arutiunian AA, Did-Zurabova ES, Safonova NV. [Characteristics of Helicobacter infections in gastroduodenal ulcers and their complications]Vestn Khir Im I I Grek. 1999; 158(4):22-4.
16. Potashov LV, Semenov DIu, **Savransky VM**, Smolina EN. [The comparative hemodynamic characteristics in the lower extremities during laparoscopic and traditional interventions on the abdominal cavity organs]Vestn Khir Im I I Grek. 1999; 158(2):22-6.
17. Potashov AV, Morozov VP, **Savransky VM**, Kudrevatykh IP, Did-Zurabova ES, Kimkov AV. [Prognosis of bleeding from duodenal ulcers]Khirurgiia (Mosk). 1998; (7):4-6.
18. Potashov LV, Vasil'ev VV, **Savransky VM**, Semenov DIu, Levitina EI, Klener EG, Smolina EN. [Use of laparoscopic methods in combined surgery]Vestn Khir Im I I Grek. 1997; 156(6):16-8.Potashov LV, Morozov VP, Bubnova LN, **Savransky VM**, Kabakov AB, Boriskova ME, Did-Zurabova ES. [The HLA phenotype and duodenal ulcers in patients following kidney transplantation] Vestn Khir Im I I Grek. 1997; 156(5):23-8.
20. Potashov LV, Morozov VP, Did-Zurabova ES, **Savransky VM**, Kudrevatykh IP, Arutiunian AA, Boriskova ME. [The pathophysiological basis of vagotomy in perforated duodenal ulcers]Vestn Khir Im I I Grek. 1997; 156(1):17-9.
21. Potashov LV, Morozov VP, Kudrevatykh IP, **Savransky VM**, Aurtiunian AA, Did-Zurabova ES, Zhebrun AB, Safonova NV, Dovgal' SG. [The diagnosis of Helicobacter infections in patients with gastric and duodenal peptic ulcers]Zh Mikrobiol Epidemiol Immunobiol. 1996; (6):11-3.
22. Potashov LV, Morozov VP, **Savransky VM**, Arutiunian AA, Kudrevatykh IP, Did-Zurabova ES, Popova VF, Safonova NV, Nutfullina GM. [Patient Helicobacter pylori infectivity after gastric resection]Vestn Khir Im I I Grek. 1996; 155(6):17-20.
23. Potashov LV, **Savransky VM**, Morozov VP. [Blood flow and free radical oxidation of lipids in gastric and duodenal mucosa in complicated duodenal ulcers]Khirurgiia. 1996; (5):40-2.
24. Potashov LV, Morozov VP, **Savransky VM**, Arutiunian AA, Did-Zurabova ES, Cherkashina LG. [Detection of Helicobacter pylori in stomach cancer]Vopr Onkol. 1996; 42(3):30-2.
25. Potashov LV, **Savransky VM**, Berkos AS, Bubnova LN, Morozov VP. [The association of HLA antigens with gastric and duodenal peptic ulcer]Vestn Khir Im I I Grek. 1994; 152(1-2):14-7.
26. Morozov VP, Perelygin VG, **Savransky VM**, Shabunevich LV. [Lipid peroxidation in the blood and tissues of patients with peptic ulcer]. Klin Med. 1992; 70(2):75-7.

RESEARCH SUPPORT

University of Maryland Subcontract
Pilot and Feasibility Grant of the Clinical Nutrition Research Unit (DK72488)
Sleep Apnea and Lipid Metabolism in Obesity
$25,000/year, 11/01/2005 – 10/30/2007

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Michael M. Meagher, Ph.D.	Professor and Director of the UNL Biological Process Development Facility
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Colorado State University, Fort Collins, CO	B.S.	1981	Engineering Science
Iowa State University, Ames, IA	M.S.	1984	Chemical Engineering
Ohio State University, Columbus, Ohio	Ph.D.	1987	Chemical Engineering

A. POSITIONS AND HONORS

Positions and Employment

1981-87 Graduate Research Assistant, Iowa State University
1987-89 Senior Scientist/Biochemical Engineer, Hoffmann-LaRoche
1989-95 Assistant Professor, University of Nebraska-Lincoln
1995-03 Associate Professor, University of Nebraska-Lincoln
2003-present Professor, Donald and Mildred Othmer Distinguished Professor, University of Nebraska-Lincoln

Other Experience and Professional Memberships

Member, American Institute of Chemical Engineering and American Chemical Society

B. SELECTED PEER-REVIEWED PUBLICATIONS (2003 - 2007)

1. Johnson, S.K., Zhang, W., Smith, L.A., Hywood-Potter, K.J., Swanson, T.S., Schlegel V.L., **Meagher, M.** Scale-up of the Fermentation and Purification of the Recombinant Heavy Chain Fragment C of Botulinum Neurotoxin Serotype F Expressed in *Pichia pastoris*, *Protein Express. Purif.*, 32(1):1-9, 2003.
2. Sinha, J., Plantz, B.A., Zhang, W., Gouthro, M., Schlegel, V.L., Liu, C.-P., **Meagher, M.** Improved Production of Recombinant Ovine Interferon-□ by Mut$^+$ Strain of *Pichia pastoris* Using an Optimized Methanol Feed Profile, *Biotechnol. Prog.*, 19(3):794-802, 2003.
3. Zhang, W., Liu, C.P., Inan, M., **Meagher, M.** Optimization of Cell Density and Dilution Rate in *Pichia pastoris* Continuous Fermentations for Production of Recombinant Proteins, *J.Ind.Microbiol Biotechnol.*, 31(7):330-4, 2004.
4. Zhang, Wenhui; Sinha, Jayanta; Smith, Leonard A.; Inan, Mehmet; **Meagher, Michael M**. Maximization of Production of Secreted Recombinant Proteins in Pichia pastoris Fed-Batch Fermentation. Biotechnology Progress (2005), 21(2), 386-393.
5. Sinha, J., Plantz, B.A., Inan, M., **Meagher, M.** Causes of Proteolytic Degradation of Secreted Recombinant Proteins Produced in Methylotrophic Yeast *Pichia pastoris*: Case Study with Recombinant Ovine Interferon-tau, *Biotechnol. Bioeng.*, 89(1):102-12, 2005.
6. Dux, M.P., Barent, R., Sinha, J., Gouthro, M., Swanson, T., Barthuli, A., Inan, M., Ross, J.T., Smith, L.A., Smith, T.J., Webb, R., Loveless, B., Henderson, I., **Meagher, M.M.** Purification and Scale up of a Recombinant Heavy Chain Fragment C of Botulinum Neurotoxin Serotype E [rBoNTE(H_c)] in *Pichia pastoris GS115, Protein Express. Purif.*, 45:357-367, 2006.
7. Inan, Mehmet; Aryasomayajula, Dinesh; Sinha, Jayanta; **Meagher, Michael M.** Enhancement of protein secretion in *Pichia pastoris* by overexpression of protein disulfide isomerase. Biotechnology and Bioengineering (2006), 93(4), 771-778.

8. Sinha, Jayanta; Inan, Mehmet; Fanders, Sarah; Taoka, Shinichi; Gouthro, Mark; Swanson, Todd; Barent, Rick; Barthuli, Ardis; Loveless, Bonnie M.; Smith, Leonard A.; Smith, Theresa; Henderson, Ian; Ross, John; **Meagher, Michael M.**. Cell bank characterization and fermentation optimization for production of recombinant heavy chain C-terminal fragment of botulinum neurotoxin serotype E (rBoNTE(Hc): Antigen E) by Pichia pastoris. Journal of Biotechnology (2007), 127(3), 462-474.

Ongoing Research Support

U01-AI056514-01 09/02/2003 – 09/01/2007
NIH
Fast Track Development of a Heptavalent Vaccine Against the Botulinum Neurotoxin
Overall project goal: The goal of this project is to complete all aspects of process development for a recombinant vaccine against the botulinum neurotoxin. This includes molecular biology, fermentation, purification, analytical methods development, and technology transfer for cGMP production of serotypes C, D, E, F, and G of the botulinum neurotoxin.
Role: Co-PI

Completed Research Support

DAMD17-02-C-0107 01/01/2002 – 01/01/2007
USAMRMC
Process Research and Development for Therapeutic Agents and Vaccines as Countermeasures Against Biological Warfare Agents
Overall project goal: The goal of this project is the research and development of processes to produce vaccines and therapeutic agents against biological threats. The Army needs countermeasures to protect combat and non-combat personnel against biological threats.
Role: P.I.:

DAMD17-02-1-0659 03/15/2002-03/14/2005
UAMRMC
Process Research and Development of Antibodies as Countermeasures for *C. botulinum*
Overall Project Goal: The goal of this project is to express and optimize expression in CHO cells of human antibodies against the the botulinum neurotoxin. The goal of the this project is to fill out laboratory space on third floor of Othmer Hall, new home for the UNL Biological Process Development Facility
Role: P.I.

DAMD17-98-C8034 01/01/1998 – 12/30/2001
USAMRMC
Fermentation Process Development for the Production of the Hc Fragment of the Botulinum Neurotoxin Serotype A
Overall project goal: This is part of the project "Fermentation, Recovery, and Purification of the Hc Fragment of the Botulinum Neurotoxin from *Pichia pastoris*" contracted with USAMRMC. The goal is to develop a workable and scalable fermentation and purification process research and development of botulinum vaccine candidates.
Role: P.I.

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Nabors, Gary S.	V.P., BioDefense Product Development
eRA COMMONS USER NAME eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Wake Forest University, Winston-Salem, NC	B.A.	1985	Biology
University of Georgia, Athens, GA	Ph.D.	1991	Immunology
University of Pennsylvania, Philadelphia, PA	Post-Doc	1991–1995	Immunology

A. Positions and Honors

Positions and Employment

1995–1998 Research Scientist, Immunology Platform, Pasteur Mérieux Connaught (now Sanofi Pasteur), Swiftwater, PA
1998–2001 Immunology Platform Manager (department head), Research, Aventis Pasteur, Swiftwater, PA
2001–2004 Director, Immunology, Antex Biologics, Inc., Gaithersburg, MD (now Emergent Product Development Gaithersburg Inc.)
2004–2005 Director, Product Development, Emergent ImmunoSolutions, Gaithersburg, MD
2005–present V.P., Biodefense Product Development, Emergent Product Development Gaithersburg Inc.

Other Experience and Professional Memberships

Infectious Disease Society of America, American Association of Immunologists, International Cytokine Society, International Society for Vaccines

B. Selected Peer-reviewed Publications (in chronological order)

1. Tarleton RL, **Nabors GS**. Regulation of cytokine production in Chagas' disease, in *Molecular and Immunological Aspects of Parasitism*, AAAS Press, New York, C.C. Wang, ed. p. 15-30;1991.
2. **Nabors GS**, Tarleton RL. Differential control of IFN-γ and IL-2 production during *Trypanosoma cruzi* infection. *J. Immunol.* 1991; 146: 3591-3598.
3. **Nabors GS**, Farrell JP. Site-specific immunity to *Leishmania major* in SWR mice: the site of infection influences susceptibility and the expression of the antileishmanial immune response. *Infect. Immun.* 1994; 62: 3655-3662.
4. **Nabors GS**, Farrell JP. Depletion of interleukin-4 in BALB/c mice with established *Leishmania major* infections increases the efficacy of Pentostam therapy and promotes Th1-like responses. *Infect. Immun.* 1994; 62: 5498-5504.
5. **Nabors GS**, Afonso LCC, Farrell JP, Scott P. A switch from a Th2 to Th1 type response and cure of established *Leishmania major* infection in mice is induced by combined therapy with interleukin-12 and Pentostam. *Proc. Nat. Acad. Sci. U.S.A.* 1995; 92: 3142-3146.
6. **Nabors GS**, Farrell JP. Activity of Pentostam (sodium stibogluconate) against cutaneous leishmaniasis in mice treated with neutralizing anti-interferon-gamma antibody. *Am. J. Trop. Med. Hyg.* 1995; 53: 55-60.

7. **Nabors GS**, Nolan T, Croop W, Li J, Farrell JP. The Influence of the site of parasite inoculation on the development of Th1 and Th2 type immune responses in (BALB/c x C57BL/6) F1 mice infected with *Leishmania major. Parasite Immunol.* 1995; 17: 569-579.
8. **Nabors GS**, Farrell JP. Successful chemotherapy in experimental leishmaniasis is influenced by the polarity of the T cell response before treatment. *J. Infect. Dis.* 1996;173:979-986.
9. **Nabors GS**. Modulating ongoing Th2 responses in experimental leishmaniasis. *Parasitology Today* 1997; 13: 76-79.
10. Becker RS, Gray ML, Biscardi KS, Pyle DJ, Huebner RC, **Nabors GS**. Recombinant engineering of PspA antigen from *Streptococcus pneumoniae* as a PAM_3Cys-lipidated protein potentiates immunogenicity for both parenteral and mucosal routes of administration. In *Vaccines* 97. F. Brown, D. Burton, P. Doherty, J. Mekalanos, and E. Norrby, eds. Cold Spring Harbor Press, Cold Spring Harbor Laboratory. 1997.
11. Briles DE, Hollingshead S, Brooks-Walter A, **Nabors GS**, Ferguson L, Schilling M, Gravenstein S, Braun P, King J, Swift A. The potential to use PspA and other pneumococcal proteins to elicit protection against pneumococcal infection. *Vaccine* 2000; 18: 1707-1711.
12. **Nabors GS**, Braun PA, Herrmann DJ, Heise ML, Pyle DJ, Gravenstein S, Schilling M, Ferguson LM, Hollingshead SK, Briles DE, Becker RS. Immunization of healthy adults with a single recombinant pneumococcal surface protein A (PspA) variant stimulates broadly cross-reactive antibodies to heterologous PspA molecules. *Vaccine* 2000; 18: 1743-1754.
13. Briles DE, Hollingshead S, King J, Swift A, Braun P, Ferguson LM, Nahm M, **Nabors GS**. Immunization of human volunteers with recombinant PspA elicits antibodies which passively protect mice from fatal infection with *Streptococcus pneumoniae* expressing heterologous PspA molecules. *J. Infect Dis.* 2000; 182: 1694-1701.
14. Briles DE, Hollingshead S, **Nabors GS**, Paton J, Brooks-Walter A. The potential for using protein vaccines to protect against otitis media caused by *Streptococcus pneumo*niae. *Vaccine* 2001; S87-95.
15. Swiatlo E, King J, **Nabors GS**, Mathews B, Briles DE. Pneumococcal surface protein A (PspA) is expressed in vivo and monoclonal antibodies to PspA are effective therapy in a murine model of pneumococcal sepsis. *Infect Immun* 2003; 71(12): 7149-7153
16. McKenzie R, Walker RI, **Nabors GS**, Verg LL, Carpenter C, Gomes G, Forbes E, Tian JH, Yang HH, Pace JL, Jackson WJ, Bourgeois AL. Safety and immunogenicity of an oral, inactivated, whole-cell vaccine for *Shigella sonnei:* preclinical studies and a Phase I trial. *Vaccine* 2006; 24: 3735-45.
17. Gu M, Hine PM, James Jackson W, Giri L, **Nabors GS**. Increased potency of BioThrax® anthrax vaccine with the addition of the C-class CpG oligonucleotide adjuvant CPG 10109. *Vaccine* 2007; 25(3): 526-534.

C. Research Support

Ongoing Research Support Supported by NIH/NIAID

Project: Grant U01AI070486-01 Nabors (PI) 08/15/2006–12/31/2009
Anthrax Immune Globulin to Prevent & Treat Anthrax: Advanced Product Development
Goal: The goal of this grant is to develop assays for anthrax immune globulin and test the product in rabbit models of inhalation anthrax.
Role: Principal Investigator

Project: Grant U01AI060624-01 Nabors (PI) 06/01/2004–06/30/2008
Developing an Inactivated Whole Cell *Helicobacter pylori* Vaccine.
Goal: The goal of this study is the development of a prophylactic and/or therapeutic vaccine against *Helicobacter pylori*
Role: Principal Investigator

Project: Grant UO1AI056452-02 Clements (PI) 07/01/2003–06/30/2008
Novel Adjuvants for Biodefense Vaccines
Goal: The goal of this study is to determine whether mucosal boosting augments pre-existing immune responses generated by parenteral priming using tetanus Toxoid as a model antigen.

Role: Technical Project Leader at Emergent site

Research Supported by DARPA

Project: Contract DAAD1903C0124, "Studies to evaluate the immunostimulatory effect of CpG 10103 ODN when added as an adjuvant to Anthrax Vaccine Adsorbed (BioThrax®)." Period of award: September 2003–December 2005.
Goal: Increase the immunogenicity of licensed anthrax vaccine by the use of CpG adjuvants; determine whether use of CpG adjuvants allows for reduced dosage of licensed anthrax vaccine
Role: Technical Project Leader

Research Supported by Private Source **/Emergent Product Development Gaithersburg Inc.**

Goal: Development of a prophylactic and/or therapeutic vaccine against *Helicobacter pylori*
Role: Project Leader

Goal: Development of next-generation vaccines against *Bacillus anthracis*
Role: Design and oversight of non-clinical studies

Goal: Development of botulinum toxoid vaccine, recombinant botulinum toxoid vaccine, and botulinum immune globulin
Role: Design and oversight of non-clinical studies, programmatic oversight

Goal: Development of anthrax immune globulin for the treatment of *Bacillus anthracis*
Role: Design and oversight of non-clinical studies, programmatic oversight

Goal: Development of a prophylactic vaccine against *Chlamydia trachomatis*
Role: Design and oversight of non-clinical studies

Goal: Development of a multi-component travelers' vaccine to protect against *Campylobacter jejuni, Shigella* sp. and enterotoxigenic *E. coli* (ETEC)
Role: Design and oversight of non-clinical studies

Research Supported by Private Source

Immunology Platform Manager

Goal: Development of protein-based vaccine for PspA/PsaA pneumococcal infection
Role: Project team member responsible for proof of concept experiments in animal models and potency test development; participation in clinical trial design, clinical sample analysis and interpretation

Goal: Development of pneumococcal and menignococcal conjugate vaccines for infants, adolescents and young adults
Role: Oversight of non-clinical studies including formulation studies and those directed towards the development of potency and stability tests

Goal: Development of a second generation Lyme disease vaccines
Role: Evaluation of adjuvants for their ability to increase protective capacity of candidate Lyme disease vaccines in animal models

Goal: Development of human interleukin-1 as an intranasal adjuvant
Role: Project Leader

Goal: Initiative on replacing existing animal-based vaccine potency tests for licensed vaccines with *in vitro* tests
Role: Project Leader

BIOGRAPHICAL SKETCH

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

NAME	POSITION TITLE
Cureton, Shannon M.	Project Manager
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Maryland, College Park, Maryland	B.S.	1997-2001	Biochemistry
University of Utah, Salt Lake City, Utah	M.S.	2002-2004	Organic Chemistry
Project Management Professional Certification	PMP	2006	Project Management

C. Positions and Honors.

Positions and Employment

1998-2000 Laboratory Technician, National Cancer Institute, Fort Detrick, Maryland
1999-2001 Undergraduate Teaching Assistant, University of Maryland at College Park, Department of Chemistry and Biochemistry, College Park, Maryland
2001-2002 Chemistry Lecturer, University of Maryland at College Park, Department of Chemistry and Biochemistry, College Park, Maryland
2003-2005 Chemistry Laboratory Manager, Thatcher Company, Salt Lake City, Utah
2005-2007 Project Manager, Dynport Vaccine Company, Frederick, Maryland
2007-Present Project Manager, Emergent Biosolutions, Gaithersburg, Maryland

Other Experience and Professional Memberships

1997-2001 Chemistry Tutor, University of Maryland at College Park, Department of Chemistry and Biochemistry, College Park, Maryland
1997-2001 Section Leader/Instructor, Freshman Honors Seminar, University of Maryland at College Park, Department of Chemistry and Biochemistry, College Park, Maryland
1997-2001 Guided Study Director for Organic Chemistry, University of Maryland at College Park, Department of Chemistry and Biochemistry, College Park, Maryland
2002-2004 Cheves Walling Fellowship, University of Utah, Salt Lake City, Utah
2002-2004 Graduate Teaching Assistantship, University of Utah, Salt Lake City, Utah
2002-2004 Henry Eyring Summer Research Fellowship, University of Utah, Salt Lake City, Utah

Honors

1997-2001 University Honors Program
1997-2001 Alpha Lambda Delta
1997-2001 Phi Kappa Phi
1997-2001 Golden Key National Honors Society
1997-2001 National Collegiate Scholars
1997-2001 University of Maryland Honors Scholarship
1997-2001 George Cowan Junior Scholarship
1997-2001 Senior Merck Index Award
2001 Bachelor of Science: Summa Cum Laude

B. Selected peer-reviewed publications (in chronological order).

1. Danilkovitch A, **Donley S,** Skeel A, and Leonard EJ. Two independent signaling pathways mediate the antiapoptotic action of macrophage-stimulating protein on epithelial cells. Mol Cell Biol Vol 2000; 6:2218-2227.
2. Danilkovitch-Miagkova A, Angeloni D, Skeel A, **Donley S,** Lerman M, and Leonard E. Integrin-mediated RON Growth Factor Receptor Phosphorylation Requires Tyrosine Kinase Activity of Both the Receptor and c-Src. J Biol Chem 2000; 275(20):14783-14786.

C. Research Support

Completed Research Support

NIAID Grant Number 1 UC1 AI062531-01 Ian Henderson (PI) Period of Involvement 6/05 – 7/27/07

Development of a Stabilized Recombinant Botulinum Vaccine Formulation: The work aimed to embed the seven different botulinum vaccine antigens within stable glass microspheres suspended in an anhydrous fluorocarbon liquid, enabling the development of a single ready-to-inject multivalent vaccine against botulism.

Role: Project Manager

RESOURCES: Emergent Product Development Gaithersburg, Inc. (Emergent)

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. If research involving Select Agent(s) will occur at any performance site(s), the biocontainment resources available at each site should be described. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

Emergent Product Development Gaithersburg Inc. (300 Professional Drive, Gaithersburg, MD 20879) contains a 24,000 sq. ft. fully-functional research and development laboratory. Scientists and staff at this location are providing R&D, product development, clinical development and regulatory support of existing and new product entities. Within this area are dedicated laboratories that provide services for media preparation, fermentation, product analysis, freeze drying, raw material storage, equipment preparation & cleaning, cold storage and autoclaving. The laboratory is HVAC supported with single-pass conditioned air, compressed air, house vacuum, gas distribution and RO/DI water.

Clinical:

N/A

Animal:

Emergent operates a fully-validated Biosafety Level 3 (BSL-3) animal facility in Lansing, MI (Emergent Biodefense Operations, Lansing). This facility will be used for the proposed guinea pig immunogenicity/efficacy study.

Computer:

Emergent's information technology system consists of a local network of PCs and servers. All servers are programmed for automatic data backup during off-business hours. The company also has high-speed internet access for literature searches and other Web-based research needs. The data network is configured using Microsoft Windows Server 2003 with an Active Directory authentication system.

Office:

Emergent occupies 24,000 square feet of office space in Gaithersburg, MD.

Other:

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

RESOURCES: University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF)

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. If research involving Select Agent(s) will occur at any performance site(s), the biocontainment resources available at each site should be described. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

The University of Nebraska-Lincoln Biological Process Development Facility has on the third floor of Othmer Hall a multipurpose cGMP suite used for production Master Cell Banks (MCB) and Working Cell Banks (WCB) and biotherapeutic derived from recombinant yeast or bacteria. The GMP suite is a uni-suite that is designed around a 60 L fermentor with all associated downstream processing equipment to produce Purified Drug Substance (bulk) expressed as either as a secreted or intracellular product. The GMP uni-suite includes a 150 ft^2 cold room, a clean staging area and a gowning airlock.

The GMP uni-suite has three different areas with access controlled using an electronic card access system

Proprietary Info

Personal and raw materials enter the GMP uni-suite through a 600 ft^2 clean staging area, which is the primary entrance into facility. Individuals are required to gown-up before entering the clean staging area. The clean staging area is unclassified clean space with the supply air HEPA filtered and this space meets ISO 8 standards.

Next is the gowning airlock (40 ft^2) which meets ISO 8 requirements. Staff entering the GMP uni-suite are required to put on additional gowning.

The GMP uni-suite (600 ft^2) meets ISO 8 standards and under static conditions exceeds ISO7 standards. The GMP uni-suite includes a 150 ft^2 cold room. The HVAC system has its own control system and is supplied air from the main building air handler. The room pressure differentials and the air flow in both clean staging and the GMP uni-suite is monitored real time.

Support space for the GMP uni-suite includes a 250 ft^2 quarantine, release and reject handling area that includes an upright freezer and refrigerator and an area with a chemical hood and a clean and dirty autoclave.

All classified areas are under an environmental monitoring (EM) program for viable and non-viable particles that is run by the QC group and overseen by QA.

The BPDF also has a Quality Assurance Unit (QAU) that is responsible for quality oversight of both the GMP uni-suite and the QC laboratory.

Clinical:

N/A

Computer:

Office:

Other:

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

New Brunswick Scientific Mobile Pilot Plant 80

The New Brunswick Scientific Mobile Pilot Plant 80 (NBS MPP-80) is a 60 L working volume Steam-In-Place (SIP) fermentor with a 2:1 aspect ratio and two rushton turbines.

NCSRT Chromatography Skid

The NCSRT 316L SS process chromatography skid is controlled by an Allen Bradley SLC 5/05 PLC with a Panel View 1000 HMI. The system is capable of 100 to 6,000 ml/min gradient flow rate and 100 to 12,000 ml/min isocratic flow rate. The gradient is generated by varying the speed of pump A and pump B. There are two sets of American Lewa dual diaphragm pumps (100 to 500 ml/min and 400 to 6,000 ml/min) that can be changed out depending on the flow range requirements. The system has on-line $UV_{280\,nm}$, conductivity, pH, pressure, mass flow rate, temperature and an inline bubble trap (plastic). The system uses only sanitary diaphragm valves and all wetted parts are 316L stainless steel. The system has 3 inlets per pump and 5 outlets for collecting fractions.

NCSRT Model 10 CrossFlow Filtration System

The NCSRT Model 10 is a 316L SS sanitary system equipped with a vertically mounted Alpha Laval Model SRU-2 rotary lobe pump capable of a recirculation rate upto 60 L/min at 60 psig. The unit is equipped with a mag flow meter, pressure transducers to measure the inlet and outlet pressure across the membrane module, temperature, pH and conductivity. The unit has a 10 L jacketed recirculation tank that sits directly above the pump and a return line that is below the 4 L liquid level. There is a drain line at the lowest point of the system. The minimum process volume is 4 L.

NCSRT Model 5 CrossFlow Filtration System

The NCSRT Model 5 is a 316L SS sanitary system equipped with a vertically mounted Quatroflo pump capable of a recirculation rate up to 10 L/min at 60 psig. The unit is equipped with a mag flow meter, pressure transducers to measure the inlet and outlet pressure across the membrane module, temperature, and an inline shell and tube heat changer. The unit has a 4 L plastic recirculation tank that sits directly above the pump and a return line that is below the 1 L liquid level. There is a drain line at the lowest point of the system. The minimum process volume of the unit is approximately 1 L.

M-110EH-30 Microfluidics Microfluiderizer

The Microfluidics M-110EH-30 is a sanitary microfluidizer designed to operate from 2,500 psig to 30,000 psig and is used primarily for cell disruption. The system has a flow rate of 450 ml/min at 25,000 psig and is equipped with a heat exchanger for cooling immediately after the disruption chamber. The minimum process volume is approximately 400 ml.

Sorvall Evolution RC Floor Model Centrifuge

The Evolution RC centrifuge is a refrigerated floor model batch centrifuge and is equipped with a fixed angle SLC-6000 rotor which holds 6 by 1 L bottles. The maximum speed of the SLC-6000 rotor is 8,500 rpm generating 15,180xg.

SterilGARD Class II Type A2 Biosafety Cabinet

A 4 foot class 100 SterilGARD Class II Type A2 biosafety cabinet is located in the CGMP suite

RESOURCES—Bridge Global Pharmaceutical Services

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. If research involving Select Agent(s) will occur at any performance site(s), the biocontainment resources available at each site should be described. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

Clinical:

N/A

Animal:

Bridge Global Pharmaceutical Services is fully committed to conducting the GLP guinea pig toxicology study as described in SA6 and has provided a Letter of Commitment for inclusion in this submission. Although Bridge will house the animals and be responsible for all aspects of the in life portion of the GLP tox study, once histopathology slides are prepared, Bridge will ship them to Summit Drug Development Services for evaluation.

The Bridge facility located at 620 Professional Drive in Gaithersburg is a vivarium dedicated to small animal work. It is fully equipped with 49 animal rooms. This facility is also equipped with a fully functional loading/receiving dock, storage space, and various administrative offices and cubicles. There is backup power in place for critical equipment and refrigerators and freezers are monitored by the R&D system.

The Histology Suite has the necessary equipment for tissue processing, embedding, microtomy, slide and cassette labeling and staining. Space is also available for temporary slide and tissue storage, as well as a dedicated archive holding room. The Clinical Pathology Suite has all the necessary equipment to perform tests associated with the following areas: Hematology (Advia 120), Osmolality (VAPRO), Urinalysis (Clintek 100 and Clintek Atlas), Clinical Chemistry (Vitros 250 and Vitros 950) and Coagulation (ACL 1000 and ACL 10,000).

The AAALAC has given the site a letter of endorsement and full accreditation as of November 2004. OLAW Certification was renewed in October 2002. The site's Animal Welfare Assurance number is A3889-01.

Computer:

Office:

Other:

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

CHECKLIST

TYPE OF APPLICATION *(Check all that apply.)*

☒ NEW application. *(This application is being submitted to the PHS for the first time.)*

☐ RESUBMISSION of application number: _____
(This application replaces a prior unfunded version of a new, renewal, or revision application.)

☐ RENEWAL of grant number: _____
(This application is to extend a funded grant beyond its current project period.)

☐ REVISION to grant number: _____
(This application is for additional funds to supplement a currently funded grant.)

☐ CHANGE of program director/principal investigator.

Name of former program director/principal investigator: _____

☐ CHANGE of Grantee Institution. Name of former institution: _____

☐ FOREIGN application ☐ Domestic Grant with foreign involvement List Country(ies) Involved:

INVENTIONS AND PATENTS *(Renewal appl. only)* ☐ No ☐ Yes

If "Yes," ☐ Previously reported ☐ Not previously reported

1. PROGRAM INCOME ***(See instructions.)***
All applications must indicate whether program income is anticipated during the period(s) for which grant support is request. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)

2. ASSURANCES/CERTIFICATIONS ***(See instructions.)***
In signing the application Face Page, the authorized organizational representative agrees to comply with the policies, assurances and/or certifications listed in the application instructions when applicable. Descriptions of individual assurances/certifications are provided in Part III and listed in Part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS. See specific instructions.

☐ DHHS Agreement dated: _____ ☐ No Facilities And Administrative Costs Requested.

☒ DHHS Agreement being negotiated with NIH, DFAS Regional Office.

☐ No DHHS Agreement, but rate established with _____ Date _____

CALCULATION* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information.)*

a. Initial budget period:	Amount of base $		Federal F&A
b. 02 year	Amount of base $		
c. 03 year	Amount of base $		
d. 04 year	Amount of base $		
e. 05 year	Amount of base $		

*Check appropriate box(es):

☐ Salary and wages base ☐ Modified total direct cost base ☒ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.):*

EPDG: Total project costs, excluding subcontractors and other direct costs for this application

4. DISCLOSURE PERMISSION STATEMENT: If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)? ☐ Yes ☒ No

RESEARCH PLAN

A. SPECIFIC AIMS

A.1 Introduction

Emergent BioSolutions Inc. (Emergent) is proposing to advance the development of the anthrax vaccine dmPA7909. This vaccine is composed of the double-mutant recombinant *Bacillus anthracis* protective antigen (dmPA), the aluminum adjuvant Alhydrogel and the immunostimulatory oligodeoxynucleotide compound CPG 7909 (VaxImmune™) formulated as a dry powder. The characteristics of dmPA7909 that make it an ideal candidate to meet the nation's needs for anthrax vaccine are:

1. **Rapid immune response following 2-3 doses**: In guinea pigs, dmPA7909 provided protection against a lethal dose of anthrax spores after 2 doses. Alhydrogel and CPG 7909 as an adjuvant system when combined with rPA produced a more rapid and greater immune response than Alhydrogel alone.
2. **Long-term stability to facilitate ambient temperature storage in the Strategic National Stockpile**: Results of Emergent's stability studies with the dmPA demonstrate that the dmPA is significantly more stable than other recombinant *B. anthracis* protective antigens (rPAs). Additionally, dry powder vaccine formulations consisting of recombinant proteins and Alhydrogel have been demonstrated to be stable for years at elevated temperatures such as 25 °C and 37 °C.
3. **Ability to be administered in a national emergency without the need for special storage conditions**: The spray-dried powder formulation of dmPA7909 markedly enhances vaccine stability even at extreme temperatures such as Proprie tary Inf.

To ensure that the dmPA7909 vaccine will be stable to meet the U.S. Government's needs for a vaccine with a prolonged shelf-life that is easy to store and administer at elevated temperatures, Emergent employed proven stabilizing technologies for each of the components in the vaccine formulation. The dmPA has been genetically engineered to remove two major protease cleavage sites within the molecule and, and as a result, its stability is significantly improved. This stable active ingredient (dmPA protein) has been tested in animal efficacy studies and is currently being used in combination with Alhydrogel in a Phase 1 clinical trial. Alhydrogel (aluminum hydroxide) has a long history of use in vaccines including childhood vaccines and has documented stability at 25 °C and 37 °C. CPG 7909, unlike other CpG oligonucleotides, has all of its phosphate linkages replaced with phosphorothioate bonds, thus decreasing its sensitivity to nucleases. CPG 7909 has also been extensively tested in the clinic in combination with other Alhydrogel-adjuvanted recombinant vaccines.

A.2 Specific Aims

Emergent has been developing the third generation anthrax vaccine dmPA7909 for the last year. The dmPA was licensed by Emergent from the National Institutes of Health (NIH), and CPG 7909 was licensed by Emergent from Pfizer for use in an anthrax vaccine. Process development and formulation studies are in progress, and proof-of-concept has been demonstrated in guinea pig efficacy studies. As the manufacturer of BioThrax®, the only FDA-licensed anthrax vaccine, Emergent is leveraging over 40 years of experience in anthrax vaccine research and development expertise to expedite development of dmPA7909. As a part of the comprehensive development plan, Emergent is proposing the following specific aims in the current proposal: The work proposed in this application encompasses: 1) completion of formulation method and assay development; 2) cGMP manufacture of dmPA7909; 3) Unfunded - ARRA and 4) completion of a guinea pig repeat-dose toxicology study.

Specific Aim 1 (SA1): Finalize the formulation for dmPA7909 Anthrax Vaccine

Proprietary Info

Specific Aim 2 (SA2): Manufacture and Release Vaccine Suitable for a Phase 1 Clinical Trial

Emergent will manufacture and release one cGMP lot of dmPA bulk drug substance (BDS) and one cGMP lot of dmPA7909 final drug products (FDP) for use in a Phase 1 clinical trial. The FDP lot will contain dmPA Proprietary Info Proprietary Info μg), CPG 7909 μg), and Alhydrogel μg) per dose. The FDP lot will be formulated and filled in a dry powder form and will be reconstituted to a liquid form before vaccination with water for injection (WFI).

Proprietary Info

Specific Aim 3: Examine Long-term Stability of dmPA7909 Anthrax Vaccine

Unfunded - ARRA Both BDS and lots will be evaluated for their stability for Unfunded - ARRA Stability testing of the BDS will be

Proprietary Info Unfunded - ARRA

Specific Aim 4: Establish Nonclinical Safety of dmPA7909 Anthrax Vaccine

A repeat-dose toxicity study will be performed by Bridge Laboratories, who routinely conduct IND-enabling toxicity studies for vaccines and biologic-based therapeutics. This study will be conducted in Hartley guinea pigs following GLP guidance utilizing the FDP lot.

B. BACKGROUND AND SIGNIFICANCE

B.1 Anthrax – The disease

Anthrax is a fatal bacterial infection caused when *B. anthracis* spores enter the body through the skin, by inhalation, or through ingestion. Historically, human anthrax has been a disease of those having close contact with animals or animal products contaminated with *B. anthracis* spores. For example, in the mid-1800s, inhalational anthrax related to the textile industry became known as "woolsorters' disease" in England and "ragpickers' disease" in Germany and Austria because of the frequency of infection in mill workers exposed to imported animal fibers contaminated with *B. anthracis* spores (Brachman et al., 1966). Anthrax was the first disease to fulfill Koch's postulates and, in 1881, it became the first bacterial disease for which immunization was available (Hambleton et al., 1984).

There are three forms of anthrax disease—cutaneous, inhalational, and gastrointestinal. Most endemic anthrax cases are cutaneous and are contracted by close contact of abraded skin with products contaminated with *B. anthracis* spores (Dixon et al., 1999). Inhalational anthrax is rare but nearly uniformly fatal. Inhalational anthrax generally occurs after an incubation period of 12 hours to several days (Vasconcelos et al., 2003). After the incubation period, a nonspecific flu-like illness ensues, characterized by fever, cough, headache, and mild chest discomfort (Cieslak and Eitzen, Jr., 1999). Sometimes, an intervening period of improvement is observed after 1 to 3 days of the initial symptoms. However, rapid deterioration follows the intervening period, leading to a 95% case fatality rate among untreated patients. A third form of anthrax, gastrointestinal anthrax, is exceedingly rare. The symptoms appear 2 to 5 days after the ingestion of undercooked meat contaminated with *B. anthracis* spores. Pathological studies on gastrointestinal anthrax indicate that ulcerations with edema and mucosal necrosis can be detected in the affected area (Dixon et al., 1999). The symptoms of the infection include nausea and vomiting. Since these symptoms are common to other abdominal conditions, it is very difficult to diagnose gastrointestinal anthrax.

The real danger of anthrax disease derives from the fact that it represents the single greatest biological warfare threat owing to its ease of production and the lethality of inhaled anthrax spores. A World Health Organization report estimated that 95,000 people would die in a city of 500,000 if 50 kg of anthrax spores were released under the appropriate conditions (Cieslak and Eitzen, Jr., 1999). In a real example of the lethality of anthrax spores, an accident at a former Soviet military compound in Sverdlovsk resulted in 66 confirmed deaths caused by inhalational anthrax (Abramova et al., 1993; Jackson et al., 1998; Meselson et al., 1994; Walker et al., 1994). Another case of the use of anthrax as a weapon of bioterrorism is the well-known letter attacks that occurred in the United States in the fall of 2001 (Dewan et al., 2002; Jernigan et al., 2001). In this case, fortunately, the survival rate of the first 10 patients with inhalational anthrax was much higher (60%) than previous cases mainly because of the fact that all patients received combinational antimicrobial therapy with more than one countermeasure against *B. anthracis* (Jernigan et al., 2001).

B.2 Organism and virulent factors

Bacillus anthracis is a gram-positive, spore-forming organism well characterized as a causative agent of anthrax. The bacterium is a facultative anaerobe and grows in most rich media with an optimal growth temperature of 37°C (Thorne, 1993). Under most culture conditions, the rod-shaped cells form long chains and sporulating cells carry elliptic, centrally located spores. Taxonomically, *B. anthracis* is most closely related to *B. cereus* based on physiological and genetic similarities (Ash and Collins, 1992; Ash et al., 1991; Castanha et al., 2007). For example, almost all of the putative chromosomal virulence factors and surface proteins in *B. anthracis* have homologues in *B. cereus*, highlighting the similarities between the two species (Read et al., 2003).

The virulence factors of *B. anthracis* are a poly-D-γ-glutamic acid capsule and a three-component anthrax toxin (Keppie et al., 1963; Smith et al., 1955; Smith and Keppie, 1954; Smith and Stanley, 1962; Smith and Stoner, 1967; Stanley and Smith, 1961). Studies of virulent strains of *B. anthracis* have revealed that the genes for the virulence factors are located on two large plasmids, pXO1 and pXO2. Plasmid pXO1 is 182-kb in length and contains more than 140 open reading frames (ORFs) (Okinaka et al., 1999b). The genes encoded by pXO1 include structural genes for all three toxin proteins - *pagA* (protective antigen), *lef* (lethal factor), and *cya* (edema factor) - as well as other genes such as a regulatory element (*atxA*) and a topoisomerase (*topA*) (Fouet et al., 1994). Plasmid pXO2 is 93-kb in length and contains genes required for synthesis of the capsule structure such as *capA*, *capB*, and *capC* (Okinaka et al., 1999a; Pannucci et al., 2002; Robertson et al., 1990). Similar to pXO1, pXO2 also contains regulatory genes including genes associated with capsule regulation (*acpA*) and depolymerization (*dep*).

The principal virulence factor of *B. anthracis* is a secreted three-component toxin consisting of three separate gene products designated protective antigen (PA), lethal factor (LF) and edema factor (EF) (Duesbery and Vande Woude, 1999; Leppla, 2000). None of the three proteins has a toxic effect when administered alone. However, when either LF or EF is combined with PA, they form active and potent toxin complexes (Leppla, 1999). Lethal toxin (LT), the combination of LF and PA, is sufficient to induce many laboratory manifestations of anthrax disease in animal models (Beall et al., 1962; Beall and Dalldorf, 1966; Fish et al., 1968; Klein et al., 1962; Klein et al., 1966). Edema toxin (ET) is formed when EF and PA are combined and, when injected, ET induces edema by accumulation of cyclic AMP due to stimulation of adenylate cyclase activity (Leppla, 1982; Duesbery and Vande Woude, 1999).

B.3 Scientific Basis for the Selection of the Proposed Candidate Anthrax Vaccine

The proposed vaccine candidate was selected to focus on three critical attributes of an anthrax vaccine - safety, efficacy, and stability. To achieve all these goals, Emergent chose the following vaccine components for its anthrax vaccine.

B.3.1 Antigen: Protease resistant, double mutant recombinant protective antigen (dmPA)

One of the major issues of an rPA-based vaccine is the molecule's poor stability. After the PA gene (*pagA*) was cloned in 1983 (Vodkin and Leppla, 1983), it soon became apparent that there are two predominant protease cleavage sites in PA. The first site is a furin cleavage site located at ^{164}RKKR^{167} of the mature 83 kDa PA (Klimpel et al., 1992). Furin is a trypsin-like protease found on the surface of eukaryotic cells. The cleavage of the 83 kDa PA at the furin site generates a functional 63 kDa PA for subsequent heptamerization. Without the cleavage, the PA molecule is not functionally active and, therefore, cannot contribute to formation of Lethal Toxin (LT) when combined with LF. The second site, located at residues ^{313}FF^{314}, can be cleaved by chymotrypsin yielding 37 and 47 kDa PA fragments (Novak et al., 1992). It was demonstrated that mutations in this region reduce PA's ability to translocate LF into the cytoplasm (Singh et al., 1994). Due, in part, to the presence of these well-characterized protease cleavage sites within the molecule, rPA naturally degrades to smaller fragments over time.

To address the stability issues, Emergent has been evaluating a protease resistant, double mutant recombinant rPA (dmPA) expressed from an avirulent strain of *B. anthracis*

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Proprietary Info The double-mutant molecule mentioned above was designed to delete the two protease cleavage sites and, therefore, increase the stability of the 83 kDa PA. In this molecule, the sequence of the

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Because of the mutations in the PA molecule at critical sites, dmPA is not functionally active.

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As described below, Emergent is planning to use a different adjuvant system and a unique dry formulation technology to address all critical needs described in the previous section.

B.3.2 Adjuvant: Combination of CPG 7909 and Alhydrogel

Emergent is using two adjuvants in the dmPA7909 vaccine formulation. It was demonstrated that, when combined, these adjuvants have a synergistic effect and accelerate and/or enhance the immune response (Rynkiewicz et al., 2005; Cooper et al., 2005; Cooper et al., 2004a; Gu et al., 2006). These adjuvants, Alhydrogel and CPG 7909, have a documented history of safety.

Alhydrogel is an aluminum hydroxide adjuvant with a solid safety record, which is known to induce strong humoral immune responses. Aluminum-containing adjuvants have historically served as immunopotentiators in vaccines including those used in routine pediatric vaccines, and continue to be the most widely used adjuvants. Billions of doses of aluminum-adsorbed vaccines have been administered dating back to the 1930s when aluminum-adjuvanted diphtheria and tetanus vaccines were demonstrated to have superior efficacy to non-adjuvanted vaccines. For infections that can be prevented by induction of serum antibodies, aluminum adjuvants are the adjuvants of choice and will continue to be used with human vaccines for many years as a result of their excellent track record of safety and adjuvanticity. Currently, at least 15 FDA-licensed vaccines contain aluminum compounds as adjuvants including Daptacel® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed), Twinrix® (Hepatitis A Inactivated and Hepatitis B Vaccine), COMVAX® (Haemophilus influenzae Type b Conjugate and Hepatitis B Vaccine) BioThrax (Anthrax Vaccine Adsorbed), and Prevna® (Pneumococcal 7-valent Conjugate Vaccine).

CPG 7909 is a completely synthetic, single-strand oligodeoxynucleotide (ODN) consisting of 24 nucleotide bases in length (**Figure 01**). In CPG 7909, the phosphodiester (PO) backbone has been replaced with a phosphorothioate (PS) backbone providing the molecule with increased stability and resistance to nucleases. The mammalian immune system can be stimulated by DNA containing six base motifs consisting of unmethylated CpG dinucleotides flanked by two 5'-purines and two 3'-pyrimidines (CpG motifs) (Krieg, 2002; Pisetsky, 1996).

The nucleotide sequence of CPG 7909 has been optimized for potent immune stimulation acting through the Toll-like receptor 9 (TLR9) and, as a result, CPG 7909 is a potent agonist of TLR9. Three classes of CpG ODN have been identified, with distinct structures and immune effects. Based on its mode of action and on pre-clinical pharmacology model data, CPG 7909 belongs to the B class of CpG ODNs. CpG-B ODNs have a fully phosphorothioate-modified backbone and induce the production of modest levels of IFN-γ, with weak NK cell activation but with profound B cell activation. CpGs with a fully phosphorothioate-modified backbone are more nuclease resistant than CpGs that have only a partially phosphorothioate-modified backbone (Temsamani et al., 1993).

To date, multiple nonclinical and clinical studies have shown that CPG 7909 is safe and can accelerate and/or enhance the immune response to Alhydrogel-containing vaccines, such as BioThrax and hepatitis B vaccine (Engerix-B®), when administered to animals and humans (Cooper et al., 2004b; Cooper et al., 2005; Cooper et al., 2004a; Link et al., 2006; Rynkiewicz et al., 2005; Speiser et al., 2005).

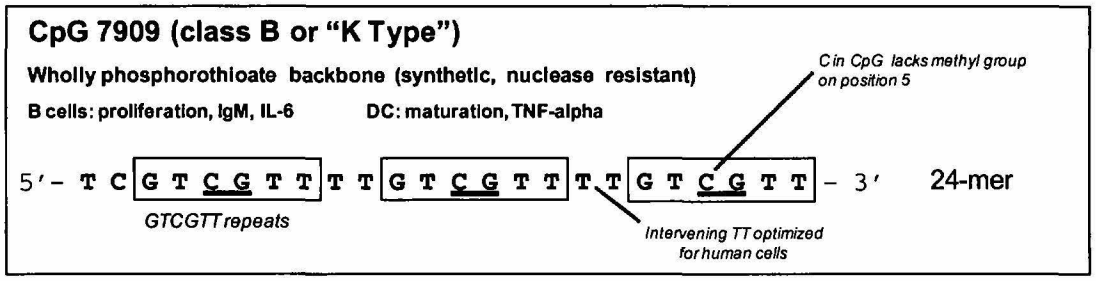

Figure 01: Structure of CPG 7909

To date, multiple nonclinical and clinical studies have shown that CPG 7909 is safe and can accelerate and/or enhance the immune response to Alhydrogel-containing vaccines, such as BioThrax and hepatitis B vaccine (Engerix-B®), when administered to animals and humans (Cooper et al., 2004b; Cooper et al., 2005; Cooper et al., 2004a; Link et al., 2006; Rynkiewicz et al., 2005; Speiser et al., 2005).

B.3.3 Formulation: Dry powder formulation

One of the key factors of Emergent's new anthrax vaccine is its ability to be stored at ambient or even higher temperatures. To achieve this level of stability, Emergent has partnered with Cambridge Biostability LTD (CBL) for the development of a thermostable formulation process. With this state-of-art spray dry formulation technology, Emergent has demonstrated that proteins can be stable for an extended time even at extreme temperature such as Proprietary Info Using this technology, dmPA7909 will be filled and stored at room temperature in a dry powder form in single-dose vials. The vaccine then will be reconstituted to a liquid form before vaccination with water for injection (WFI).

C. PRELIMINARY STUDIES/PROGRESS REPORT

C.1 Prior Clinical and Nonclinical Studies

C.1.1 Clinical studies

C.1.1.1 AV7909 Phase 1/2 human safety study

dmPA7909 is a novel next generation anthrax vaccine and, therefore, no clinical trial has been conducted with the vaccine. However, Emergent has evaluated the immune-enhancing effects of CPG 7909 on the FDA-approved BioThrax in a Phase 1 clinical trial (Rynkiewicz et al., 2005). Similar to dmPA7909, the principal active ingredient in BioThrax is *B. anthracis* protective antigen (PA), and the vaccine contains Alhydrogel. This study was a double blind, randomized, multi-center, parallel group, controlled trial comparing AV7909 (BioThrax + CPG7909) to BioThrax alone and to CPG 7909 alone. In this study AV7909 was formulated by mixing 0.5 ml of BioThrax (the licensed dose) and 1.0 mg of CPG 7909 per dose.

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Additionally, based on toxin neutralizing antibody (TNA) data shown in **Figure 02**, immunogenicity results observed in this study indicated that antibody levels achieved after three doses (0, 2, 4 weeks) of BioThrax alone could be achieved after only two doses of AV7909 (0, 2 weeks). This suggests that the addition of CPG 7909 has tremendous potential to provide more rapid protection against infection – a characteristic that is of particular importance for post-exposure prophylaxis.

C.1.2 Nonclinical studies

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component dmPA7909 vaccine: dmPA, CPG 7909 and Alhydrogel.

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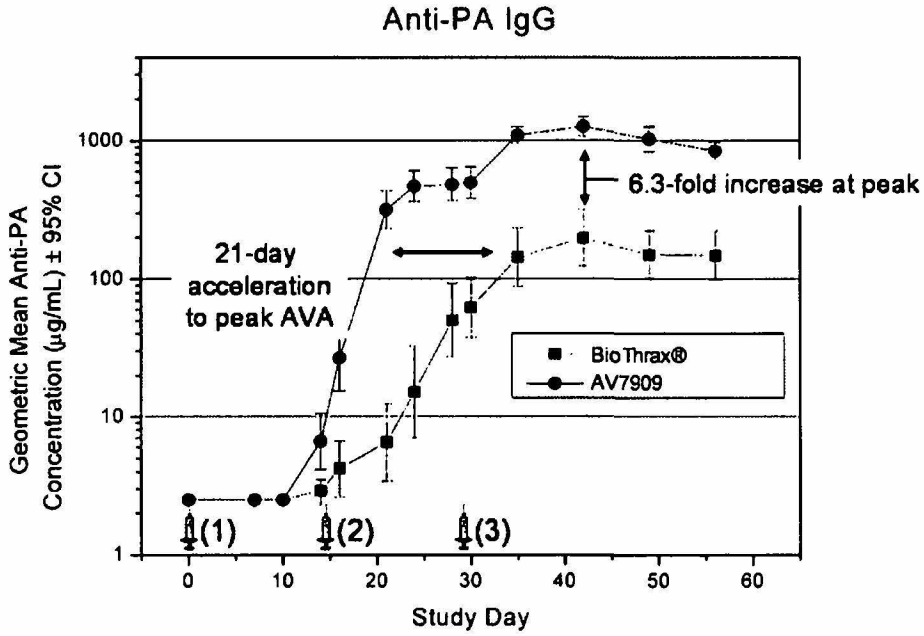

Figure 02: Levels of toxin neutralizing antibodies after vaccination

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C.2 Process Development

C.2.1 Host strain – B. anthracis Proprietary Info

The host strain used in the production of dmPA, *B. anthracis* Proprietary Info is an avirulent,

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C.2.2 Production of dmPA

The fermentation and purification processes utilized a combination of processes developed by Proprietary Info The process scheme for dmPA production is illustrated in **Figure 04.**

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The current fermentation and purification processes have been specifically developed to be scalable, transferable to and compliant with cGMP manufacturing requirements.

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C.2.3 dmPA bulk formulation process

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current development process has been designed to be scalable and transferable to a cGMP manufacturing

facility, it has also been demonstrated to be superior with respect to

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While Emergent currently has a scalable process which can be transferred to production for cGMP manufacturing, we are currently executing a development plan to improve the processes prior to award. Key targets of the ongoing development plan are improving final fermentation yield, further development of clarification of the bacterial broth to decrease risk during technology transfer, and a limited investigation of process ranges for the transfer of the purification process to manufacturing.

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C.2.4 Synthesis of CPG 7909: Girindus

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C.2.5 Formulation process:

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C.3 Status of Assays

Most of the characterization, in-process, and release assays have been developed and are in use. The few remaining assays currently in development will be ready by the time the award period starts in June 2009. Assays required for the release of the Unfunded - ARRA are described in **Table 04**. **Table 05** describes the assays, the test methods and utilization of those assays for the dmPA production process. The release assays described in **Table 05** will be used by Emergent for release of the Bulk Drug Substance (BDS) manufactured by University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF). **Table 06** contains the assays which will be used by Emergent to release the FDP formulated and filled by Unfun ded. All assays with the exception of those noted have been developed and will be qualified for their intended use per ICH guidelines prior to transfer to UNL-BPDF or Unfun ded

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C.4 Stability profile of dmPA7909

Emergent has conducted Prop stability studies on bulk dmPA.

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C.4.1 Simulated Bulk Drug Substance Study

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C.4.2 Simulated Final Drug Product Study

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D. RESEARCH DESIGN AND METHODS

D.1 Specific Aim 1 (SA1): Finalize the Formulation for dmPA7909 Anthrax Vaccine

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D.1.2 Specific Aim 1.2 (SA1.2): Formulation-specific assay development

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D.1.3 Specific Aim 1.3 (SA1.3): Guinea pig immunogenicity and efficacy study

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D.2. Specific Aim 2 (SA2): Manufacture and Release Vaccine Suitable for a Phase 1 Clinical Trial

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D.2.1 Specific Aim 2.1 (SA2.1): Tech transfer to UNL-BPDF

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D.2.3 Specific Aim 2.3 (SA2.3): Manufacturing and Release of cGMP dmPA BDS

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D.2.4 Specific Aim 2.4 (SA2.4): Manufacturing and Release of cGMP CPG 7909

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D.2.5 Specific Aim 2.5 (SA2.5): Formulation process/Assay tech transfer

Once developed, the formulation process and assays will be transferred from Unfunded Laboratories for cGMP manufacture of the dmPA7909 FDP lots. Unfunded subcontractor for cGMP spray-drying process and final fill/finish.

D.2.6 Specific Aim 2.6 (SA2.6): Manufacturing and Release of cGMP dmPA7909 FDP

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D.2.6.1 Formulation/Spray Drying

The formulation/spray-drying process will be performed at Unfunded Unfunded owns a cGMP-compliant pilot-scale spray dryer (ASD-1) which is housed at Unfunded has agreed to house the ASD-1 and provide a fully operational cGMP spray drying facility exclusively available for the production of Unfunded materials at any time including, but not limited to spray drying development batches and production batches, fill/finish activities, qualification/validation work, process development and media fills.

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finished product store.

D.3. Specific Aim 3 (SA3): Examine Long-term Stability of dmPA7909 Anthrax Vaccine

D.3.1 Specific Aim 3.1 (SA3.1): dmPA BDS Unfunded - ARRA *stability study*

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D.4. Specific Aim 4 (SA4): Establish Nonclinical Safety of dmPA7909 Anthrax Vaccine

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F. HUMAN SUBJECTS RESEARCH

Since the proposed program does not involve human subject research, this section is not applicable.

G. VERTEBRATE ANIMALS

The guinea immunogenicity and efficacy study will be conducted at Emergent's BSL-3 facility located in Lansing, MI (Emergent Biodefense Operations Lansing, Lansing, MI). The guinea pig repeat-dose toxicity study will be conducted at Bridge laboratories located in Gaithersburg, MD. Study designs for both studies are described in Sections D.1 and D.4, respectively.

G.1 Outline of Animal Studies

Proprietary Info

G.2 Justification of Animal Use

Proprietary Info

Proprietary Info

G.3 Veterinary Care of Animals

The guinea pig studies will be conducted at the following locations:

- The immunogenicity and efficacy studies and potency studies will be performed at Emergent's Lansing, MI facility (Emergent Biodefense Operations Lansing).
- The guinea pig toxicology study will be conducted at Bridge Laboratories located in Gaithersburg, MD.

All facilities have full and current accreditation by AAALAC and OLAW and have similar animal handling procedures subject to IACUC oversight. The general practices described below are followed by all vendors.

The general practices described below are followed by all vendors.

G.3.1 Quarantine

Species and strain selection is based upon the research goals of the individual project. Consultation with the client, literature review, cost and availability are the major factors in the selection of a specific model. Animal health status, availability, and previous experience with a particular vendor are the primary criteria in the final selection of the animal source. All animals are purchased from established commercial colonies. Health status reports supplied by these breeders are reviewed regularly to assure that animals are acceptable for use. A health status report is required for all incoming animals. All animals are subject to a one week quarantine/acclimation period. All incoming animals are held in a separate quarantine suite serviced by its own HVAC system.

Upon receipt, each shipment is verified against the approved animal ordering records. All animal shipments are recorded in a general incoming log, located in the receiving area. Animals are unpacked as soon as possible after receipt. All shipments are checked for the following information: 1) Supplier; 2) Animal strain; 3) Sex; 4) Number of animals; 5) Date of birth; 6) Order number; 7) Purchase order number and 8) Investigator's name.

At no time are animals of a different strain, sex, or source mixed in the holding cages. Each animal or shipment of animals is identified and the information is recorded as they are unloaded. Shipping boxes are immediately removed from the quarantine room and discarded. Cage cards, containing all identifying information, are attached to each cage. Each shipment of animals received is entered on a separate quarantine sheet. The quarantine sheet is kept as a permanent record and includes the following information: 1) Species/Strain; 2) Number of males/Number of females; 3) Source; 4) Date of birth; 5) Date received; 6) Date released and 7) Investigator.

Each cage is checked daily for dead or moribund animals. Any such animal found is recorded and brought to the attention of the Project Manager who notifies the Project Officer. If requested, a necropsy is performed and, where appropriate, specimens are preserved and sent to the pathologist for evaluation. Upon completion of the quarantine period, healthy animals are transferred to holding cages and transported to the holding room. Sick animals are held in quarantine until treated and cured, or euthanized.

G.3.2 Animal Husbandry

Guinea pigs are either housed singly (when weighing > 350g) or in pairs in cages measuring 11"x 19"x 8" with stainless steel wire bar lids and filter tops. These microisolator cages are supplied with autoclaved food,

pelleted paper or low dust hardwood bedding, and water. The light/dark cycle will be approximately 12 hours each per day, using fluorescent lighting. Animal room temperatures and humidity will be maintained according to SOP requirements. All cages are changed three to four times per week or more frequently when needed. Cages are changed in AniGARD II cabinets (The Baker Company), which are designed to provide protection to the animals by delivering HEPA filtered air in a vertical down flow within the workspace. Guinea pigs are transferred to clean cage units, containing bedding, fresh food and a fresh water bottle. Soiled cages are removed to the cage washing area prior to dumping. This practice minimizes the potential spread of airborne infection.

All cage units are sanitized once per week or as needed in the cage washer with a final rinse of 180°F. Shelf racks are sanitized weekly using a pressure washer and quaternary ammonia disinfectant with 140°F water. Animal room floors are swept and mopped daily. Walls and ceilings are washed every two weeks with a quaternary ammonia disinfectant. After removal of all animals and equipment from the room, the floor is completely swept. A disinfectant is mixed according to directions, and the ceilings, floor and walls are wiped down with a sponge mop and allowed to dry.

G.3.3 Animal Identification

Animals will be uniquely identified with ear tags and corresponding information on cage cards. The cage cards will indicate: species and/or strain, number and sex of animals, ID numbers, investigator ID, date of birth or receipt, and origin or source of the animal. Manipulations of the animal such as blood sampling and injections will be also recorded on the cage card. Room logs and study control logs will be located outside of each room. Animal care personnel record all information pertaining to the animals on study in these logs.

G.3.4 Health Observations

All animals are checked daily by animal technicians/caretakers who have been trained to recognize aberrant behavior and to look for signs of injury and illness. The animal technician/caretaker assigned to the room will immediately report sick or injured animals to the Project Manager and veterinarian and complete a Health Incident Report. Daily health observations are recorded on the Health Incident Report until the problem has been resolved. Completed Health Incident Reports are maintained in the Central Files. Animals that have been found dead in the cage are noted on the cage card and if the death is unexpected, the Investigator is notified.

Procedures have been established to ensure that the animal colonies are maintained specific pathogen free. This has been accomplished by isolating the colonies in a part of the facility where access is limited to only those staff members assigned to the program. Personnel change into clean laboratory clothing prior to entering the facility and all manipulations involving the guinea pigs are conducted within AniGARD II cabinets (cage changing) or Biological Safety Cabinets. Routine serological testing on sentinel animals is conducted quarterly for a battery of infectious agents. Samples are taken from either study guinea pigs or sentinel guinea pigs. Positive results are reported to the Investigator as soon as test results are received.

G.3.5 Veterinary Care

The veterinarian who directs the Animal Care Program performs the following functions:

- Advise and implement procedures to prevent, control and treat disease occurrence and animal injuries.
- Respond to animal health problems as seen or as reported by animal caretakers or technical staff.
- Oversee all diagnostic testing, interpret results.
- Train employees in proper animal handling, restraint, and other techniques as needed.
- Train animal caretakers to perform and respond to daily health observations when required.
- Suggest and assist in the development of new training programs.
- Advise management of potential employee hazards and improper practices.
- Provide guidance in proper animal handling, restraint, anesthesia, analgesia, and other techniques.
- Monitor surgical procedures as required.
- Ensure that animal pain and distress is alleviated humanely and is of the shortest duration possible.
- Serve on the IACUC.

G.3.6 Criteria for Euthanasia

The following criteria have been pre-established for euthanasia: moribund, respiratory distress, ≥20% body weight loss, and seizures. All animals that are judged to be moribund by a highly trained life sciences technician, veterinarian, or by the Study Director will be euthanized immediately. Animals that are euthanized will be anesthetized using an appropriate dose of xylazine hydrochloride and ketamine hydrochloride or other anesthetic agent approved by the American Veterinary Medical Association (AVMA) and then administered an overdose of a euthanasia agent containing pentobarbital or other AVMA-approved method of euthanasia.

H. SELECT AGENT RESEARCH

Select agent will be used in this proposal. Specifically, virulent *Bacillus anthracis* Proprietary Info strain will be used in the guinea pig efficacy studies. The Proprietary Info strain will be used at Emergent's Lansing facility in Michigan as a challenge strain during the guinea pig potency test. Emergent is currently operating a GLP BSL-3 facility in Lansing for the test. The corporation is registered (CDC registration number C20060911-0531) in accordance with 42 CFR Parts 72 and 73 with the Select Agent program and has implemented a written security program, which addresses the safeguards of the select agents or toxins against unauthorized access, theft, loss, or release. The security plan was designed according to a site-specific risk assessment and cannot be shared because of national security. The CDC has reviewed the plan.

I. MULTIPLE PI LEADERSHIP PLAN

There is one Principal Investigator for this program: Sukjoon Park, Ph.D.

J. CONSORTIUM / CONTRACTUAL ARRANGEMENTS

Emergent Product Development Gaithersburg Inc., the applicant organization, is a biopharmaceutical company that develops medical countermeasures to fight bioterrorism. With its affiliated companies under the parent Emergent BioSolutions, Inc., Emergent is uniquely positioned to contribute to the global biodefense effort. Emergent will provide overall program direction, project management, oversight of subcontractors, regulatory support and direct interaction with the U.S. Government and regulatory authorities.

J.1 Subcontractors

In the execution of the proposed program, Emergent will engage highly qualified subcontractors. University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF, Lincoln, NE), Unfunded Unfunded Bridge Laboratories (Gaithersburg, MD) will serve as subcontractors.

UNL-BPDF

University of Nebraska-Lincoln Biological Process Development Facility will manufacture and release cGMP dmPA bulk drug substance.

Unfunded

Bridge

Emergent has selected Bridge Laboratories as a contractor for the guinea pig repeat-dose toxicology study.

J.2 Program Management

J.2.1 Project Management Tools

The lead role in the overall program management will be provided by Emergent under the supervision of the PI. A product development team for the project has already been organized and is actively working on the

project. Immediately after grant award, the team will refine the product development plan, following interactions with NIAID. This project implementation plan will contain detailed information on schedules and budgets, along with the materials and resources required to complete the statement of work.

The proper use of project management tools will ensure efficient and expeditious execution of the program minimizing cost and optimizing schedule. Microsoft Project® will be used as the primary program management software supplemented by Microsoft Office® applications and JMP™ (SAS) for project communications and data analysis. These tools enable the Project Manager to capture and analyze cost and performance data; generate standard government reports; and provide detailed task scheduling, critical path analyses, and presentation graphics capabilities. Resource data (personnel, supplies, materials, and facilities) are inputs into the Microsoft Project and Microsoft Office applications. To capitalize on the strengths of each tool, we will also employ features within Microsoft applications and JMP for electronic project data interchange.

J.2.2 Communication and Reporting

The project team acknowledges and welcomes NIAID's wish to be closely involved with this program. The PI will be available for communication with NIAID as and when requested to do so including during Milestone review and any revision or renegotiation of milestones. The PI will provide a periodic Technical Progress Report detailing progress on key goals and milestones to the designated NIAID Program Manager. During Milestone Review NIAID personnel will be invited to meet with the PI, scientific lead and any other key personnel to discuss progress on meeting the agreed deliverables. Following this meeting the PI will submit a final Milestone Report which will contain details of progress against project goals, identify any successes or issues, supplemented with budgetary information and an updated project plan.

Finally, the PI will work closely with the NIAID Program Officer to organize the annual progress review meeting at which key personnel will present progress updates.

J.2.3 Subcontract Management

Although Emergent intends to engage highly qualified subcontractors to perform cGMP manufacturing and non-clinical studies, it does so with the full knowledge that Emergent retains full responsibility for their performance. As such, Emergent will closely manage the subcontractors' performance to ensure cost-effective and timely delivery of agreed scopes of work. The subcontractor will be viewed as a valuable member of the project team and key elements of subcontract management will include firm and clear definition of scopes of work, close communication and progress monitoring, and assistance wherever necessary with problem resolution.

K. LETTERS OF SUPPORT

University of Nebraska Lincoln

Biological Process Development Facility
College of Engineering

June 9, 2008

Sukjoon Park, Ph.D.
Director, Product Development Group
Project Manager, Chlamydia & Next Generation Anthrax Vaccines
Emergent Product Development Gaithersburg Inc.
300 Professional Drive, Suite 100
Gaithersburg, MD 20879

Dr. Park,

The University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF) is willing to participate in Emergent's U01 proposal titled, "Development of a Next Generation Anthrax Vaccine, dmPA7909." The UNL-BPDF will provide support to produce Unfunded - ARRA Proprietary Info Unfunded - ARRA. The UNL-BPDF is willing to commit the time and resources needed to complete this work. Emergent understands that the timeline proposed in the grant is tentative with respect to scheduling and the UNL-BPDF will commit to a firm schedule once an award is made and a contract is signed.

Sincerely,

Dr. Michael Meagher
Donald F. and Mildred T. Othmer Distinguished Professor of Chemical and Biomolecular Engineering
Director, UNL Biological Process Development Facility

304 Othmer Hall / 820 N 16th Street / Lincoln NE 68588-0668
Phone (402) 472-1983 / FAX (402) 472-4985 / BPDF.UNL.EDU

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Fax: +1 (513) 679 3053
E-Mail: info@girindus.com
Internet: www.girindus.com

June 12, 2008

Dear Dr. Park,

Girindus is please to commit to Emergent Product Development Gaithersburg Inc. in connection with its proposal submission to the National Institutes of Allergy and Infectious Diseases (NIAID) in response to RFA-AI-08-001, "Cooperative Research partnerships for Biodefense and Emerging Infectious Diseases (U01)". The title of the proposal is "Development of a Next Generation Anthrax Vaccine, mdPA7909".

Girindus recognizes the project to be of critical national importance and, subject to the execution of a definitive contract between us with respect to the matters referred to in this letter, would commit to the success of this initiative by dedicating the necessary resources and maintaining the appropriate level of oversight in performing the following services:

- Manufacture and release of CPG 7909 (30 g)
- Perform all necessary QC, QA, and analytical work

Girindus acknowledges that its facilities and capabilities would be subject to GLP, cGMP, GCP and QC/QA audits. We would agree to comply with requests to make necessary records available in response to any pre-award visit or audit by the NIAID or its designee.

Girindus agrees to enter into negotiations in good faith with Emergent Product Development Gaithersburg Inc. for the purpose of establishing a contract between us in accordance with the principles set forth above.

Sincerely yours,

Non-Keys PERS

Unfunded

June 9, 2008

Vladimir Savaransky, MD, PhD
Principal Scientist, In Vivo Testing Unit
Emergent Product Development Gaithersburg, Inc.
300 Professional Drive
Gaithersburg, MD 20879

Dear Dr. Savaransky,

Bridge Global Pharmaceutical Services, Inc. (Bridge) is pleased to commit to Emergent Product Development Gaithersburg Inc. in connection with its proposal submission to the National Institute of Allergy and Infectious Diseases (NIAID) in response to RFA-AI-08-001, "Cooperative Research Partnership for Biodefense and Emerging Infectious Diseases. Bridge will participate as a subcontractor. Bridge is a small business, as defined under NAICS code 541712, with facilities and corporate headquarters in Gaithersburg, Maryland.

Proprietary Info The studies that we are including for price purposes are representative of the type of studies that may be required for the completion of this program. Final pricing will reflect the final protocols to be implemented.

We recognize the importance of this project, and are prepared to provide the necessary facilities, personnel, resources, and technical assistance required for its successful completion.

Proprietary Info We are prepared to perform the following program-related duties:

- Protocol Development
- Preclinical Toxicology Study Execution
- FDA Compliant Reporting

These studies have a high priority status within Bridge and all necessary and available resources will be allocated to accomplish this work within the time constraints of the schedule, as dictated by the statement of work.

Our cognizant field audit office is the National Institutes of Health. We maintain current CCR registration, and our current Representations and Certifications are available on line at ORCA. Our DUNS number is 048532902.

610 Professional Drive, Gaithersburg, MD 20879 • t 888.364.7710 • f 240.364.6231 • www.bridgelaboratories.com

Bridge agrees to recognize the source of funding of the awarded contract in all public releases, subject to U.S. Government restrictions on publicity.

Proprietary Info

Bridge agrees to participate in an audit of specific facilities as well as GLP and QC/QA capabilities. It is understood that such audits will be scheduled with reasonable advance notice, and that Bridge will have the opportunity to approve audit by any entity not composed of NIAID or Emergent personnel. We agree to comply with requests to make all records, including previous regulatory inspection reports, and staff, available in response to a pre-award site visit or audit by the NIAID.

Sincerely,

Non-Keys PERS

L. RESOURCE SHARING

L.1 Data Sharing Plan

Emergent plans to present the progress of the proposed non-clinical studies at professional conferences, and to publish our findings in peer-reviewed journals. Within these presentations and publications would be descriptions of the animal models developed and used as funded by this grant. Emergent will release and share data created with grant funds in a timely manner, in accordance with the NIH definition of "timely release of sharing" of data. This includes data resulting from completed experiments performed in the course of grant performance. This does not include any proprietary methods or data created with funds from sources other than the U.S. Government. Emergent will provide data at the time of acceptance for publication of any research results as of the main findings of the final data set. Emergent will provide the appropriate data and appropriate documentation on CD-ROM, under its own auspices, in a commonly used data format (such as ASCII file, Excel, or Access) to those that request the data for the purpose of furthering scientific knowledge and the improvement of human health. The nature of the data makes the provision of analytical tools unnecessary.

Emergent and its subcontractors retain all intellectual property rights arising from work performed outside the scope of the proposal, including, but not limited to, prior (1) product development experiments, (2) assay development, and (3) production methods. A data sharing agreement will be required for those requesting data to ensure that the intellectual property rights of Emergent and its subcontractors are protected. As required by NIAID, this data sharing agreement will not place limits on questions or methods as a precondition of the provision of the data. Data sharing will be under the auspices of the principal investigator and subject to the execution of one or more confidential disclosure agreements (CDAs) between Emergent and other interested parties. However, proprietary information and trade secrets will not be shared.

L.2 Sharing Model Organisms

The sharing of model organisms is not appropriate under this grant because model organisms are not being developed with Grant funds. Any model organisms were developed prior to the initiation of the grant.

L.3 Genome-Wide Association Studies (GWAS)

Not applicable.

ADDITIONAL SUBMISSION REQUIREMENTS

1. MILESTONES AND TIMELINE

Milestones

Table 13 provides the milestones and timeline for the dmPA7909 project during the 5-year plan we have specified in this proposal. Except the spray-dry formulation method and the formulation-specific assay development, all other process and assay development activities will be completed pre-award and, therefore, are not included in the specific aims for this proposal. As shown in the table, the first three milestones are the spray-dry formulation process/assay development followed by a guinea pig study to confirm the immunogenicity and efficacy of the formulated dmPA7909. In parallel to the formulation method development, Emergent will perform tech transfer of process and assays to UNL-BPDF for manufacturing of dmPA BDS (Milestone 4). Milestones 5-9 are related to manufacturing of dmPA BDS and subsequent Unfunde d - ARR stability study. Milestones 10-11 are related to the cGMP manufacturing of CPG 7909. Since Girindus has already successfully produced cGMP CPG 7909 for Emergent, 4 months should be enough to manufacture and release 30 g of CPG 7909. Milestones 12-15 are associated with activities for manufacturing of a dmPA7909 FDP lot and Unfunded - ARRA Finally, Emergent will perform a repeat-dose toxicology study with the FDP lot (Milestone 16)

Table 13: dmPA7909 Project Milestones for Award Time Period

Milestone Number	Milestone Description	Start Date	Completion Date
1	Complete formulation process development	Unfunded - ARRA	
2	Complete formulation –specific assay development and qualification		
3	Conduct guinea pig immunogenicity and efficacy study		
4	Tech transfer dmPA process/assays to UNL-BPDF		
5	Unfunded - ARRA		
6			
7	Manufacture cGMP dmPA BDS		
8	Release cGMP dmPA BDS lot		
9	Complete dmPA BDS Unfunde d - ARR stability test		
10	Manufacture cGMP CPG 7909 adjuvant		
11	Release cGMP CPG 7909		
12	Tech transfer formulation process and assays to Nova		
13	Manufacture cGMP dmPA7909 FDP lot		
14	Release cGMP dmPA7909 FDP lot		
15	Unfunded - ARRA		
16	Conduct a GLP repeat-dose toxicity study		

In addition to the project milestones, **Figure 15** provides a timeline based on Specific Aims.

Quantitative Assessment Criteria

Table 14 describes assessment criteria by which milestone achievement will be assessed.

Go/No-Go Criteria

Specific decision points and "Go/No Go" criteria for the dmPA7909 vaccine development project is list in **Table 15**.

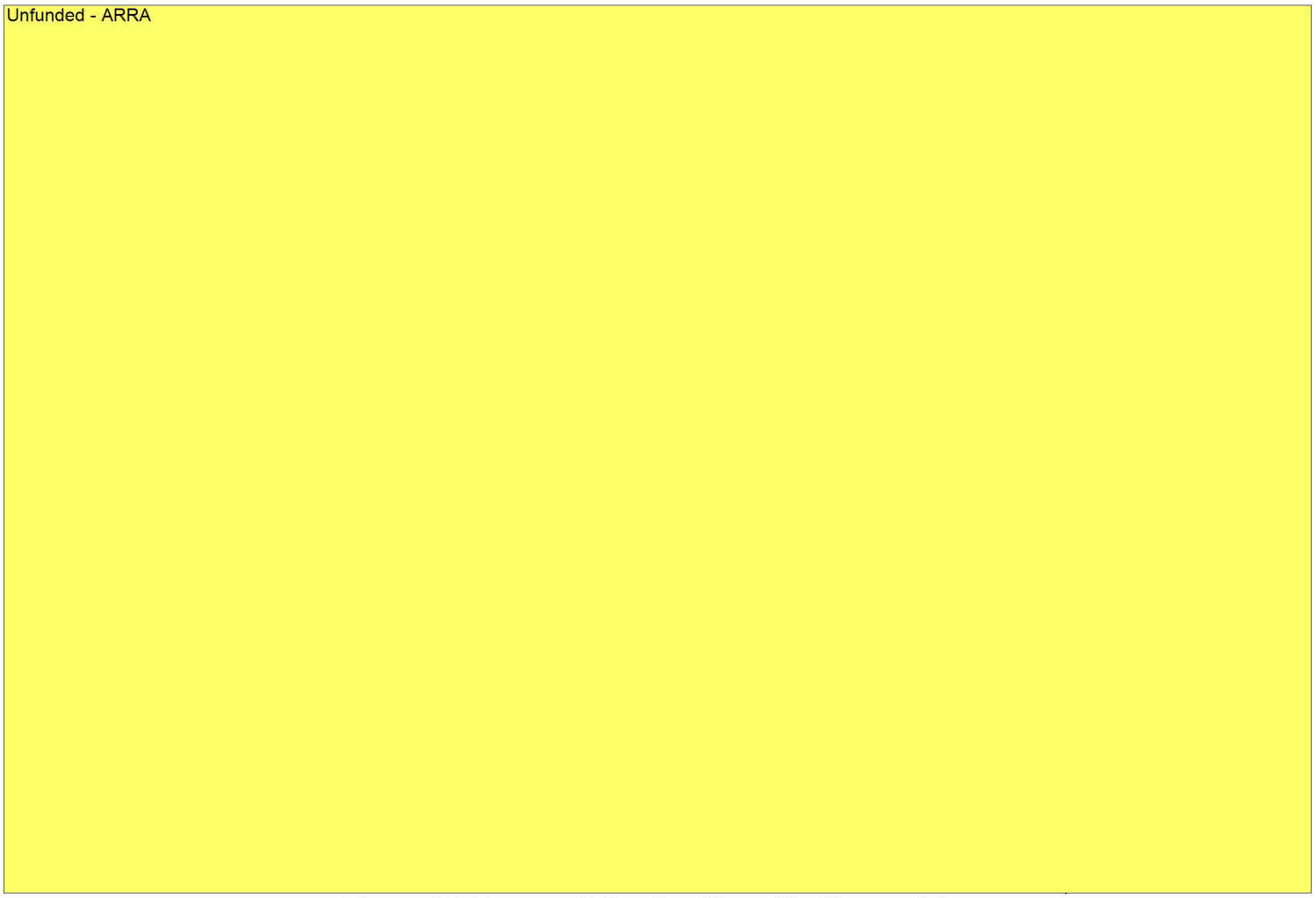

Figure 15: Proposal Timeline (Specific Aims only)

Table 14: Quantitative Milestone Assessment Criteria

Milestone 1-3: Formulation process/assay development and guinea pig study	
Tasks	Complete spray dry process development using Proprietary Info
	Identify necessary characterization, in-process, and release assays related to the formulation process
	Conduct the guinea pig immunogenicity/efficacy study with the formulated dmPA7909
Assessment Criteria	Proprietary Info
Milestones 4-8 & 10-14: Manufacture Phase 1 cGMP dmPA7909 FDP	
Tasks	Unfunded - ARRA
	Transfer dmPA production process to UNL-BPDF and scale up to process to 60L
	Manufacture and release cGMP dmPA BDS
	Manufacture and release cGMP CPG 7909
	Transfer dmPA and CPG 7909 to CBL
	Transfer formulation process and assays to Nova

	Perform formulation and final fill/finish at CBL
	Release phase I cGMP dmPA7909 FDP
Assessment Criteria	Proprietary Info
Milestones 9 & 15: Complete Phase 1 BDS Unfunded - ARRA stability studies	
Tasks	Develop stability study protocols
	Complete Unfund stability studies on cGMP BDS Unfunded - ARRA
	Prepare draft reports
	Issue final reports
Assessment Criteria	Proprietary Info
Milestone 16: Complete a repeat-dose toxicology study	
Tasks	Execute contract with Charles River
	Prepare toxicity study protocol
	Conduct the toxicity study
	Prepare draft report
	Issue the final report
Assessment Criteria	Proprietary Info

Table 15: Go/No-Go Criteria

Project Stage	Task Description	"No-Go" Criteria
Proprietary Info		

Patent Status

dmPA is developed by

Proprietary Info

Unfunded

Gantt Chart

Figure 16 on the following page presents a high-level Gantt chart of the major activities of the project.

Proprietary Info,Unfunded - ARRA

2. PRODUCT DEVELOPMENT PLAN

Emergent is proposing to advance the development of the anthrax vaccine dmPA7909. The characteristics of dmPA7909 that make it an ideal candidate to meet the nation's needs for anthrax vaccine are:

1. **Rapid immune response following 2-3 doses**: In guinea pigs, dmPA7909 provided protection against a lethal dose of anthrax spores after 2 doses. Alhydrogel and CPG 7909 as an adjuvant system when combined with rPA produced a more rapid and greater immune response than Alhydrogel alone.
2. **Long-term stability to facilitate ambient temperature storage in the Strategic National Stockpile**: Results of Emergent's stability studies with the dmPA demonstrate that the dmPA is significantly more stable than other recombinant *B. anthracis* protective antigens (rPAs). Additionally, dry powder vaccine formulations consisting of recombinant proteins and Alhydrogel have been demonstrated to be stable for years at elevated temperatures such as 25 °C and 37 °C.
3. **Ability to be administered in a national emergency without the need for special storage conditions**: The spray-dried powder formulation of dmPA7909 markedly enhances vaccine stability even at extreme temperatures such as Prop °C.

To ensure that the dmPA7909 vaccine will be stable to meet the U.S. Government's needs for a vaccine with a prolonged shelf-life that is easy to store and administer at elevated temperatures, Emergent employed proven stabilizing technologies for each of the components in the vaccine formulation. The dmPA has been genetically engineered to remove two major protease cleavage sites within the molecule and, and as a result, its stability is significantly improved. This stable dmPA has been tested in animal efficacy studies and is currently being used in combination with Alhydrogel in a Phase 1 clinical trial. Alhydrogel (aluminum hydroxide) has a long history of use in vaccines including childhood vaccines and has documented stability at 25 °C and 37 °C. CPG 7909, unlike other CpG oligonucleotides, has all of its phosphate linkages replaced with phosphorothioate bonds, thus decreasing its sensitivity to nucleases. CPG 7909 has also been extensively tested in the clinic in combination with other Alhydrogel-adjuvanted recombinant vaccines.

The overall Product Development Plan for dmPA7909 leading to FDA licensure is shown in **Figure 17** with the activities that Emergent is proposing in response to this BAA indicated in different colors as specified in the figure.

Between submission of this proposal and contract award, additional activities are planned including process and assay development. Those activities are scheduled to be completed before the initiation of the proposed contract. The initial goal of the work proposed herein is to complete the cGMP manufacture of dmPA7909 suitable for a Phase 1 clinical trial.

Proprietary Info

The rationale for the specific studies proposed herein and a description of how they fit into the overall development plan for dmPA7909 are described in more detail below.

Nonclinical Development Plan

An overview of the nonclinical development plan is summarized in **Figure 18**. In contrast to non-biodefense vaccines, the efficacy of vaccines for life-threatening biowarfare agents cannot ethically be tested in humans. For diseases that are not life-threatening, challenge studies are sometimes used to evaluate the efficacy of vaccine candidates in humans, where the therapeutic is tested for its ability to prevent or treat infection in study subjects exposed experimentally to the infectious agent. Demonstration of efficacy in late-stage clinical testing relies on the case-controlled field trial, which compares natural infection rates between individuals treated and untreated with the experimental therapeutic. These methods of efficacy assessment are not feasible for biodefense vaccines because it is unethical to intentionally expose humans to deadly biowarfare agents in an experimental setting, and natural human exposures to biowarfare agents such as anthrax are rare. For such agents, regulations for licensure have been established which allow pivotal animal efficacy studies where human efficacy

studies are not feasible or ethical (21 CFR Part 610, Subpart H). FDA will rely on animal studies to determine efficacy of the product when: 1) there is a reasonably well understood pathophysiological mechanism of the toxicity of the substance and its prevention or substantial reduction by the product, 2) the effect is demonstrated in more than one animal species expected to react with a response that is predictive for humans, 3) the animal study endpoint is clearly related to the desired benefit in humans, and 4) the data or information on the kinetics and pharmacodynamics of the product allows selection of an effective dose in humans.

Proprietary Info

Figure 17: Comprehensive development plan for dmPA7909[1]

Rabbits and non-human primates (NHP) are generally considered the preferred animal models for anthrax infection and have been widely used in anthrax vaccine efficacy studies (Phipps et al., 2004). CpG-containing ODN molecules are generally active in a variety of vertebrate species, although a given CpG sequence may be highly active in certain species and not in others. In the case of CPG 7909, its activity in rabbits has generally been observed to be significantly weaker compared to the level of activity seen in monkeys, humans, mice, and other vertebrates (Rankin et al., 2001).

Proprietary Info

Proprietary Info

Proprietary Info

Clinical Development Plan

The clinical program for the dmPA7909 third generation anthrax vaccine candidate will include a Phase 1, Phase 2 and Phase 3 studies in healthy adult populations. Subsequently, clinical studies will evaluate pediatric, elderly and immunosuppressed populations.

The Phase 1 study will evaluate Proprietary Info

The Phase 2 study will evaluate Proprietary Info

The Phase 3 study will evaluate the Proprietary Info

3. Biosafety and Biocontainment

Environmental Health and Safety (EHS) Program

Emergent's corporate EHS program is designed to ensure compliance with all applicable regulations. The following details Emergent's EHS Management System:

- The system is based in part upon federal, state and local law, and regulations, MIOSHA, ISO 14000, OHSAS 18001 and ANSI/AIHA Z10 2005 Occupational Health and Safety Management System.
- The EHS Committee and the Biosafety Committee are active and have charters.
- Changes to or new biological work must be reviewed by the Biosafety Committee.
- Any changes that involve biological work with animal models must be reviewed by the IACUC as well.

EHS Written Programs and cGMP SOPs govern and document the company's processes, covering the following areas:

- EHS Written Programs address the compliance issues and include but are not limited to the Biosafety Manual (which was based on the CDC BMBL) monitoring procedure to ensure compliance with OSHA/MIOSHA, EPA and CDC.
- SOPs supply the information necessary to perform a given task, including information on the potential EHS hazards and necessary precautions and means to control the hazard.
- SOPs are developed and followed to ensure that the corporation's requirements for testing engineering controls—such as, but not limited to, biological safety cabinets, high-efficiency particulate air (HEPA) filters, and autoclaves—are followed and documented.
- SOPs are in place to address a potential exposure to biological and chemical materials.
- Access to the manufacturing area is restricted. SOP governing the access to the manufacturing area as well as approval for access the area.
- Accesses to the biosafety level 2 (BSL-2) laboratories are limited. The laboratory manager, building owner, Security, and EHS manager must at the very minimum all agree to approve access to a restricted or limited access area.
- Access to biosafety level 2, where work with Select Agents is conducted, is limited and will be addressed in the Section on Select Agent.

Training

All individuals who work directly with biological, chemical, mechanical, or any other recognized hazard are required to take training courses. Those training courses include laboratory practices, personal protective equipment, use of engineering controls, waste disposal and handling, incident reporting requirements labeling and signage, emergency procedures, processes that may be used to disinfect and sterilize, as well as task specific training. Other policies related to training are as follows:

- Task specific training includes packaging, transporting and shipping of etiological material when necessary.
- Training is provided in the handling of etiological agents, which may include Select Agents if applicable to the tasks involved.
- MSDS for the potentially hazardous chemicals are made available.
- Individuals who work with biological material must demonstrate their skills in the form of a skill assessment prior to performing the testing method without supervision. Skill assessments are conducted on a routine basis.

Medical Surveillance

Immunization requirements are established and are based on an analysis of the type of work the individual will perform, the engineering controls in place and potential for exposure. Individuals within the immunization program are subject to medical surveillance histories on a yearly basis.

Select Agent

Select Agents are used in the guinea pig challenge testing of dmPA7909. The corporation is registered in accordance with 42 CFR Parts 72 and 73 with the Select Agent program and has implemented a written security program, which addresses the safeguards of the select agents or toxins against unauthorized access, theft, loss or release. The security plan was designed according to a site-specific risk assessment and cannot be shared because of national security. The CDC has reviewed the plan.

NIAID Grant Number: 1U01AI082224-01
PI Name: Sukjoon Park
Grant Title: Development of a Next Generation Anthrax Vaccine, dmPA7909

Revised Budget

1. Emergent Product Development Gaithersburg (EPDG)
2. University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF)
3. Aridis and Aeras
4. Emergent BioDefense Operations Lansing (EBOL)
5. Bridge Laboratories

Program Director/Principal Investigator (Last, First, Middle): Park, Sukjoon

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 10/01/09 THROUGH 09/30/10

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Park, Sukjoon	PD/PI	Effort			Institutional Based Salary	SALARY	Fringe Benefits	SALARY
Bosse, Wilma	Quality Assurance							
Williams, Lee	Director Process Dvlp							
TBD	Process Dvlpt							
Chu, Yanfang	Mgr, Downst Processing							
Uitz, Catherine	Principal Scientist							
Yang, Huei-Hsing	Sr Mgr, Upst Processing							
Savransky, Vladimir	Scientist							
TBD	Project Manager							
Pleune, Brett	Regulatory							
	SUBTOTALS →							

CONSULTANT COSTS GMP Quality Audit and GMP manufacturing oversight		61,650
EQUIPMENT *(Itemize)*		
SUPPLIES *(Itemize by category)* As detailed in the narrative		60,000
TRAVEL 4 trips as detailed in the narrative		8,868
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		0
OTHER EXPENSES *(Itemize by category)* Girindus		Negotiated Costs
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	Negotiated Costs
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*	$	Subtotal
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	Federal F&A
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD	$	Direct Costs

Program Director/Principal Investigator (Last, First, Middle): Park, Sukjoon

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from Form Page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*	SALARY				
CONSULTANT COSTS	Negotiated Costs				
EQUIPMENT					
SUPPLIES	60,000	15,000			
TRAVEL	8,868	10,252			
PATIENT CARE COSTS					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES	Negotiated Costs				
CONSORTIUM/ CONTRACTUAL COSTS	Negotiated Costs				
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*	Subtotal				
CONSORTIUM/ CONTRACTUAL COSTS	Federal F&A				
TOTAL DIRECT COSTS	Direct Costs				
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD					$ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

A. Direct labor/Key Personnel

Key Personnel:

Dr. Sukjoon Park — Dr. Park is the PI for this project will be allocated at % Effo for the entire duration of the grant.

Ms. Wilma Bosse — Ms. Bosse will provide Quality support for this project during the cGMP manufacturing campaign. She will be allocated at % Effor for the year and % Effort for the second year.

Dr. Brett Pleune — Dr. Pleune will provide Regulatory support for this project. He will be allocated at % Effor for the first year and % Effor for the second year to supervise pre-IND regulatory activities.

Dr. Vladimir Savransky — Dr. Savransky will be responsible for nonclinical studies. He will oversee the guinea pig immunogenicity/efficacy study and the repeat-dose toxicology study. He will be allocated at % Effor for the two year grant period.

Dr. Michael Meagher — Dr. Meagher is in charge of the University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF). He will oversee the cGMP manufacturing of bulk cGMP material. His labor cost will be covered as a part of the UNL subcontract cost.

Dr. Vu Truong	Dr. Truong is in charge of the formulation and manufacturing activities at Aridis. He will oversee formulation process development, scale up process development, tech transfer, and cGMP manufacturing of the final drug product.

Other Significant Personnel:

Dr. Gary Nabors	Dr. Nabors is the business official for the grant and will provide project oversight. Emergent is not requesting salary for Dr. Nabors.
TBD	TBD Project Manager for this project will be allocated at % Effor for both years.
Mr. Lee Williams	Mr. Williams will oversee all development and tech transfer activities. He will be allocated at % Effor for both grant years.
Dr. Huei-Hsiung Yang	Dr. Yang will provide technical expertise for fermentation and recovery activities. He will be allocated at % Effort for both years.
Dr. Yanfang Chu	Dr. Chu will provide technical expertise for purification activities. He will be allocated at % Effor for both years.
Dr. Catherine Uitz	Dr. Uitz will also provide technical expertise for purification activities. She will be allocated at % Effo for both years.
Dr. Mark Lyons	Dr. Lyons from EBOL will conduct guinea pig immunogenicity/efficacy study. He will be allocated at % Effort for the first year.
TBD	This technical person will be involved in the purification process development. The person will be allocated % Effort for the first year and % Effor for the second year.

B. Other Major Budget Items

Equipment:

Emergent is not requesting any new equipment in this proposal.

Supplies:

$75,000 ($60,000 in the first year and $15,000 in the second year) is budgeted for general supplies. Due to extensive formulation and process development work, we anticipate consuming Breakdown/Itemi a month for columns, media, and other laboratory supplies.

C. Subcontractors

University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF):

UNL-BPDF will be a subcontractor for this proposal to manufacture cGMP dmPA bulk drug substance (BDS). Additionally, UNL-BPDF will also conduct 12 month stability studies for GMP cell banks and the BDS. UNL-BPDF is requesting [redacted] for the proposed activities, including all necessary supplies. Since the scope of the study is extensive, Emergent believes the requested funds are fully justifiable.

Negotiated Costs

Aridis:

Aridis will be a subcontractor for dmPA7909 formulation process development. The scope of work includes spray drying and foam freeze drying formulation process development, process scale up development, and tech transfer of the drying process to the contract manufacturer (Aeras). In addition, Emergent and Aridis will oversee the production of cGMP final drug product (FDP) at Aeras. Aeras will be a subcontractor to Aridis. Their total cost for an 18 month period is [redacted] Since the scope includes extensive process development and a GMP manufacturing campaign, Emergent believes that the proposed budget is appropriate.

Negotiated Costs

Emergent BioDefense Operations Lansing (EBOL):

EBOL will be performing immunological assays and in vivo guinea pig immunogenicity and efficacy tests. This will consist of [redacted] in supplies and guinea pigs to conduct the in vivo tests. Up to 600 animals will be used in this study and, since the study requires select agent and BSL-3 animal facility, Emergent believes the requested fund is justifiable.

Negotiated Costs

% Effort

Mark Lyons (in year one) & TBD Scientist (% Effort in year one) will perform immunological assays. Bob Merriman % Effort in year two), Amanda Schneider in year two), and Anya Chamberlain in year two) will perform in vivo guinea pig immunogenicity and efficacy tests. EBOL is requesting for the proposed activities. % Effort Subcontract Money

% Effort

Bridge Laboratories (Bridge):

Emergent has also selected Bridge Laboratories as a contractor for the GLP toxicology study. Ninety guinea pigs will be used for the study and extensive tests including, but not limited to, necropsy and histopathology will be conducted in the study. Emergent believes the estimated cost of Estimated is reasonable for the extensive GLP safety study. The proposed cost is fixed price and is also consistent with other contracts Emergent awarded to Bridge.

D. Other Expenses:

Negotiated Costs

Girindus:

Girindus will supply 100 g of cGMP CPG 7909 adjuvant for this proposal. Girindus is requesting or the cGMP material and, since it is a GMP grade, Emergent believes the price is justifiable. The same fixed price contract was previously awarded to Girindus for one of Emergent's vaccine development programs funded under a NIAID contract. Girindus will also charge Negotiated Costs in year two to conduct a stability study of the GMP material.

E. Consultants:

Consultant Info

F. Travel:

Year 1: $8,868 Estimated Costs

Emergent is requesting two trips to University of Nebraska in Lincoln, NE for three project team members for three days (two nights). The purpose of the trip is to evaluate and manage the cGMP manufacturing activities. Estimated flight costs are roundtrip from Maryland to Omaha, NE. The 2009 GSA per diem rate for lodging is $70/night, and for meals and incidentals is $39/day. The cost for ground transportation is estimated at Additionally, Emergent is Estimated Costs requesting one trip to the new cGMP formulation and vialing facility (TBD) for three team members. The purpose of the trip is to finalize the facility selection and conduct a quality audit. Since we have not identified the facility, we are using the same estimate for airfare, lodging, meals and ground transportation as above. Also budgeted is one trip to Emergent's BSL-3 facility located in Lansing, MI (subcontractor-EBOL) for two project team members for two days (one night). The purpose of the trip is to coordinate the guinea pig immunogenicity/efficacy study. Estimated flight costs are roundtrip from Maryland to Detroit, MI. The 2009 GSA per diem rate for lodging is $81/night, and for meals and incidentals is $39/day. Additionally, the cost for ground transportation is estimated at Estimated Costs

Estimated Costs

Year 2: $10,252

Estimated Costs

Estimated Costs

We are proposing one trip (three days and two nights) to University of Nebraska in Lincoln, NE for three project team members. The purpose of the trip is to complete the GMP manufacturing campaign. Estimated flight costs are roundtrip from Maryland to Omaha, NE. The 2009 GSA per diem rate for lodging is $70/night, and for meals and incidentals is $39/day. Additionally, the cost for ground transportation is estimated at . Additionally, Emergent is requesting two trips to the new cGMP formulation and vialing facility (TBD) for three team members. The purpose of these trips is to oversee the GMP formulation and vialing activities. Since we have not identified the facility, we are using the same estimate for airfare, lodging, meals and ground transportation as above. Also budgeted are two trips to Emergent's BSL-3 facility located in Lansing, MI (subcontractor-EBOL) for two project team members for two days (one night). The purpose of the trip is to coordinate the guinea pig immunogenicity/efficacy study. Estimated flight costs are roundtrip from Maryland to Detroit, MI. The 2009 GSA per diem rate for lodging is $81/night, and for meals and incidentals is $39/day. The cost for ground transportation is estimated at

Estimated Costs

Estimated Costs

G. Facilities and Administrative (F&A) Costs:

Proprietary Info

Program Director/Principal Investigator (Last, First, Middle): Meagher, Michael (UNL-BPDF)

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 10/01/09 THROUGH 09/30/10

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Dr. Michael Meagher	Co-PI	Effort			Institutional Based Salary	SALARY	Fringe Benefits	SALARY
Subcontractor Personnel								
SUBTOTALS →								

CONSULTANT COSTS		
EQUIPMENT *(Itemize)*		
SUPPLIES *(Itemize by category)* See justification for detailed listing		Breakdown/Itemization by categ
TRAVEL		
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		Breakdown/Itemization by categ
OTHER EXPENSES *(Itemize by category)* See justification for detailed listing		Breakdown/Itemization by categ
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*		$ Subtotal
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	Federal F&A
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$ Direct Costs

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS		INITIAL BUDGET PERIOD (from Form Page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*		SALARY				
CONSULTANT COSTS						
EQUIPMENT						
SUPPLIES		Breakdown/Itemization by categ				
TRAVEL						
PATIENT CARE COSTS	INPATIENT					
	OUTPATIENT					
ALTERATIONS AND RENOVATIONS		Breakdown/Itemization by				
OTHER EXPENSES		Breakdown/Itemization by categ				
CONSORTIUM/ CONTRACTUAL COSTS	DIRECT					
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*		Subtotal				
CONSORTIUM/ CONTRACTUAL COSTS	F&A	Federal F&A				
TOTAL DIRECT COSTS		Direct Costs				
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD						$ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

A. Direct labor

Senior/Key Personnel:

Dr. Michael M. Meagher, Project Director and PI of the project at UNL. (Project Management), (total 24 month effort = Effort calendar months) will be responsible for overseeing the technical aspects of the project. Dr. Meagher's salary exceeds the NIH salary cap, therefore the latest cap rate was used as his base salary. (Benefits calculated at Fringe Benefits

Subcontractor Personnel

Subcontractor Personnel

B. Benefits

Faculty and Staff benefits are estimated at Fring of salary unless specifically indicated. The actual cost of benefits for each person will be charged to the project.

C. Equipment

No new equipment will be necessary to perform the experiments for the direct benefit of the project.

D. Travel

No travel at this time is anticipated.

E. Materials and Supplies

Costs are estimated at Negotiated Costs in year 1 and Negotiated Costs in year 2 to purchase consumable materials and supplies for the proposed experiments, as well as other expenses necessary to complete the project. The following is a breakdown of supplies by BPDF tasks.

Year 1:

Yr 1 Supplies	
Further Development	
Fermentations for media optimization Itemized Cost	Negotiated Costs
Analytics for fermentations (30 X SDS and WESTERN ELISA)-Cover QC staff and supplies	
Flat Sheets	
Fermentation TT	
2 fermentations Itemized Cost	
Purification TT	
Chromatography Resin	
General Laboratory Supplies (reagents, SDS-PAGE Gels, columns, resins, etc.)	
Cross flow membranes	
AML TT	
ID Western Blot	
ID ELISA	
PURITY RP HPLC	
PURITY SDS	
PURITY DNA	

PH USP 791		Negotiated Costs
Host cell protein		
Concentration A280		
Aggregates SEC HPLC		
Bioburden Plates		
Appearance USP 1		
Plasmid stability (end of run and final)		
Conductivity		
Residual kanamycin PAD HPLC		
Residual antifoam (RP HPLCE DAD Spect)		
Residual EDTA (Ion exchange Cu Chelating HPLC DAD spec)		
Endotoxin LAL		
General laboratory chemicals		
QA for SOP Review		
Archiving		
Document Processing		
PCL		
HPLC columns - 3 columns Itemized Cost each, guard columns Itemized Cost each		
HPLC solvents - high purity acetonitrile, methanol, and ion pairing agents		
Assay Reagents - proteases, HPLC grade chemicals, standards		
General Laboratory Chemicals		
General Laboratory Supplies (towels, garbage/biohazard bags, lab coats)		
General Operating (mailing expenses, etc.)		
Mass Spectrometry Supplies - capillary tubing, Liq N2 dewars, connections, fittings, etc.		
QA BPR		
Archiving		
Document Processing		
Shake Down Run		
Hyclone Bags		
Buffer Chemicals		
Media and chemicals		
Probes		
Resins		
Membranes		
WFI		
Disposables (filters, tubing, PDS bottles, etc)		
QCC for Shake Down Run		
In-Process Assays for BDS		
ID By ELISA		
Purity by SDS-PAGE (Reducing and Non-Reducing) Itemized Cost		
ID byWestern Blot Itemized Cost 2 blots)		
PH USP 791		
Purity by RP-HPLC		
Plasmid stability		
Bioburden		
BCA Total protein		
Residual Kanamycin		
Residual EDTA		
Endotoxin (Itemized Cost 1 sample)		

Peptide mapping mass spec		Negotiated Costs
IEF		
Conductivity		
Release Assays for BDS		
ID By ELISA		
Purity by SDS-PAGE (Reducing and Non-Reducing) Itemized		
ID byWestern Blot Itemized Cost 2 blots)		
PH USP 791		
Purity by RP-HPLC		
Residual Host protein (Itemized Cost 1 sample)		
Concentration A280		
Aggregation by SEC-HPLC		
Appearance USP 1		
NaCL Colorimetric		
Plasmid stability		
Total protein BCA		
Peptide mapping mass spec		
IEF		
Conductivity		
Endotoxin (Itemized Cost 1 sample)		
QA for Shake Down Run		
Archiving		
Document Processing		
QCM Shake Down Run		
Riboprinter Supplies		
Enviromental Monitoring (number of tests)		
Disposables (pipettes, plates, etc)		
GMP Run		
Hyclone Bags		
Media and chemicals		
Probes		
Resins		
Membranes		
WFI		
Disposables (Hyclone bags, filters, tubing, PDS bottles)		
QA for GMP		
Archiving		
Document Processing		
QCC for GMP		
In-Process Assays for BDS		
ID By ELISA		
Purity by SDS-PAGE (Reducing and Non-Reducing) Itemized		
ID byWestern Blot (Itemized y 2 blots)		
PH USP 791		
Purity by RP-HPLC		
Plasmid stability		
Bioburden		
BCA Total protein		

Residual Kanamycin		Negotiated Costs
Residual EDTA		
Endotoxin (Itemized Cost : 1 sample)		
Peptide mapping mass spec		
IEF		
Conductivity		
Release Assays for BDS		
ID By ELISA		
Purity by SDS-PAGE (Reducing and Non-Reducing) Itemized Cost		
ID byWestern Blot (Itemized Cost , 2 blots)		
PH USP 791		
Purity by RP-HPLC		
Residual Host protein Itemized Cost 1 sample)		
Concentration A280		
Aggregation by SEC-HPLC		
Appearance USP 1		
NaCl Colorimetric		
Plasmid stability		
Total protein BCA		
Peptide mapping mass spec		
IEF		
Conductivity		
Endotoxin Itemized Cost 1 sample)		
QCM for GMP		
Riboprinter Supplies		
Enviromental Monitoring (number of tests)		
Disposables (pipettes, plates, etc)		
FM		
Maintenance supplies		
Maintenance supplies		
PM		
none		
Forced Deg		
Bioanalyzer analyses (including standard curves and controls)		
Strong Cation Exchange HPLC analyses (including standard curves and controls)		
Reverse Phase HPLC analyses (including standard curves and controls)		
Peptide mapping by UV-HPLC		
LC-MS intact Mass characterization		
LC-MS-MS peptide mapping characterization		
Total Yr 1 Supplies		

Other Expenses Yr 1	
Further Development	
Maintenance Fee	
Fermentation TT	
none	

Purification TT	
PDL Maintenance Fee	Negotiated Costs
AML TT	
Milli-Q water system x 2	
Microplate UV/VIS Reader Maintenance Cost	
General laboratory calibrations (pipettes)	
HPLC Maintenance Costs	
QA for SOP Review	
none	
PCL	
Milli-Q water systems	
HPLC Maintenance Cost	
General laboratory calibrations (pipettes)	
TOF MS Maintenance Costs	
QA BPR	
none	
Shake Down Run	
Elastomer Changeout	
Milli Q water maintenance	
QCC for Shake Down Run	
QC Laboratory Usage Fee	
QA for Shake Down Run	
QCM Shake Down Run	
QC Microbiology Lab Usage Fee	
GMP Run	
QA for GMP	
QCC for GMP	
QC Laboratory Usage Fee	
QC Microbiology Lab Usage Fee	
PM	
General Operating (mailing expenses, etc.)	
General Operating (mailing expenses, etc.)	
Forced Deg	
Milli-Q water system	
General laboratory calibrations (pipettes)	
MS Maintenance Fees	
Total Expenses	
FM	
Alterations and Renovations	

Year 2:

Yr 2 Supplies	
General Laboratory Supplies	
Peptide Mapping - BDS at real time and end to end - 12 samples@ Itemized Cost	

BioBurden (8 tests@ Itemize d Cost		Negotiated Costs
RP HPLC (12 tests@ Itemized Cost		
CEX HPLC (12 tests@ Itemized Cost		
Size Exclusion HPLC (12 tests (Itemized Cost		
Western (12 assays@ Itemize		
pH (12 tests @ Itemiz		
SDS (12 tests@ Itemized		
Concentration (UV) (12 tests(Itemize		
Intact Mass Analysis (12 samples Itemized Cost		
Archiving		
Document Processing		
Maintenance supplies		
Total		
Yr 2 Other Expenses		
General Operating (mailing expenses, etc.)		
Set up 2 protcols		
Calibration of Stability Chambers		
Total		

F. Facilities and Administrative Costs

UNL's federally negotiated rate for organized research is [ ] of Direct Costs.

Federal F&A

Program Director/Principal Investigator (Last, First, Middle): Truong, Vu (Aridis)

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 10/01/09 THROUGH 09/30/10

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Vu Truong	Principal Investigator	Effort			Subcontract Money	SALARY		SALARY
Subcontractor Personnel								
	SUBTOTALS →							

CONSULTANT COSTS		
EQUIPMENT *(Itemize)*		
SUPPLIES *(Itemize by category)*		Breakdown/ Itemization by categ
TRAVEL		Breakdown/ Itemization by categ
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		0
OTHER EXPENSES *(Itemize by category)*		

CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*		$ Subtotal
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	Federal F&A
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$ Direct Costs

Program Director/Principal Investigator (Last, First, Middle): Truong, Vu (Aridis)

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD *(from Form Page 4)*	ADDITIONAL YEARS OF SUPPORT REQUESTED 2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*	SALARY				
CONSULTANT COSTS		Negotiated Costs			
EQUIPMENT					
SUPPLIES	Breakdown/Itemization by categ				
TRAVEL	Breakdown/Itemization by categ				
PATIENT CARE COSTS					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES					
CONSORTIUM/ CONTRACTUAL COSTS		Negotiated Costs			
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*	Subtotal				
CONSORTIUM/ CONTRACTUAL COSTS F&A	Federal F&A				
TOTAL DIRECT COSTS	Direct Costs				

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD $ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

A. Labor

Vu Truong-Le-Principal Investigator will be responsible for the scientific management of the project at % Effort for the first year and % Effort for the next 6 months.

Subcontractor Personnel

B. Supplies

Year 1:

Line Item Costs

General laboratory supplies -
Supplies for spray drying and foam freeze drying supplies - Reagents for analytical assays - $10,000
Columns for analytical assays -
TOTAL = Breakdown/Itemizati

Line Item Costs Line Item Costs Line Item Costs

Year 2:

General laboratory supplies -
Supplies for spray drying and foam freeze drying supplies - Line Item Costs
Reagents for analytical assays -
Columns for analytical assays - Line Item Costs
TOTAL = Breakdown/Itemizati

C. Travel

In the first year, Aridis (3 people) will travel to Anhydro in Columbia, MD for scale up process development. They will take 2 trips at 7 nights/8 days each trip. Airfare is estimated at lodging is based on Columbia, MD per diem rate as per the GSA website, which is $125/night. Meals are $49/day. Incidentals are estimated at 15% of total lodging (these are lodging taxes). Ground transportation is estimated at per trip. First year total travel is

Estimated Costs Estimated Costs

Breakdown/Item ization by categ

In the next six months, Aridis (3 people) will travel to Anhydro in Columbia, MD for scale up process development. They will take 1 trip at 7 nights/8 days each trip. Airfare is estimated at lodging is based on Columbia, MD per diem rate as per the GSA website, which is $125/night. Meals are $49/day. Incidentals are estimated at 15% of total lodging (these are lodging taxes). Ground transportation is estimated at per trip. Four people will also travel to Aeras in Rockville, MD for tech transfer for manufacturing and to oversee the manufacturing campaign. They will take 1 trip at 7 nights/8 days each trip. Airfare is estimated at lodging is based on Rockville, MD per diem rate as per the GSA website, which is $209/night. Meals are $64/day. Incidentals are estimated at 15% of total lodging (these are lodging taxes). Ground transportation is estimated at per trip. Total travel for next 6 months is

Estimated Costs Estimated Costs Estimated Costs

Breakdown/Item ization by categ

Estimated Costs Estimated Costs

D. Consortium/Contractual Costs

Negotiated Costs

Aeras Global TB Vaccine Foundation will charge for formulation process/assay tech transfer and manufacture and release of cGMP dmPA7909 FDF in year two of the grant.

E. F&A COSTS

Overhead at is applied to all direct costs except consortium/contractual costs.

Overhead Rates

Program Director/Principal Investigator (Last, First, Middle): Lyons, Mark (EBOL)

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM 10/01/09 THROUGH 09/30/10

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Lyons, Mark	PD/PI	Effort			Institutional Based Salary	SALARY	Fringe Benefits	SALARY
TBD	Scientist							
	SUBTOTALS →							

CONSULTANT COSTS		
EQUIPMENT *(Itemize)*		
SUPPLIES *(Itemize by category)*		
TRAVEL		
PATIENT CARE COSTS	INPATIENT	0
	OUTPATIENT	0
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		0
OTHER EXPENSES *(Itemize by category)*		

CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*		$ Subtotal
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$ Direct Costs

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD (from Form Page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED			
		2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*	SALARY				
CONSULTANT COSTS					
EQUIPMENT					
SUPPLIES		Breakdown /Itemizatio n by categ			
TRAVEL					
PATIENT CARE COSTS					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES					
CONSORTIUM/ CONTRACTUAL COSTS					
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*	Subtotal				
CONSORTIUM/ CONTRACTUAL COSTS					
TOTAL DIRECT COSTS	Direct Costs				
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD					$ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

A. Direct Labor

Mark Lyons (% in year one) & TBD Scientist (% in year one) will perform immunological assays. Bob Merriman % in year two), Amanda Schneider % Eff in year two), and Anya Chamberlain (% in year two) will perform in vivo guinea pig immunogenicity and efficacy tests.

Dr. Mark Lyons — Dr. Lyons will conduct guinea pig immunogenicity/efficacy studies. He will be allocated at % for the first year.

Scientist (TBD) — The Scientist will assist Dr. Lyons with guinea pig immunogenicity/efficacy studies for % for the first year.

Bob Merriman — Will perform immunological assays at % Eff in year two.

Amanda Schneider — Will perform immunological assays at % in year two.

Anya Chamberlain — Will perform immunological assays at % in year two.

B. Justification for Other Major Budget Items

EBOL will be performing immunological assays and in vivo guinea pig immunogenicity and efficacy tests. This will consist of Breakdown n/Itemizati in supplies and guinea pigs to conduct the in vivo tests. Up to 600 animals will be used in this study and the study requires select agent and BSL-3 animal facility.

Program Director/Principal Investigator (Last, First, Middle): Engelke, Kory (Bridge)

DETAILED BUDGET FOR ~~INITIAL~~ BUDGET PERIOD
DIRECT COSTS ONLY (SECOND BUDGET PERIOD)

FROM 10/1/2009 THROUGH 9/30/2010

PERSONNEL *(Applicant organization only)*		Months Devoted to Project				DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Kory Engelke, PhD	PD/PI							SALARY
Subcontractor Personnel								
SUBTOTALS →								

CONSULTANT COSTS
Subcontractors — Breakdown/Itemization by cate

EQUIPMENT *(Itemize)*

SUPPLIES *(Itemize by category)*
all — Breakdown/Itemization by cate

TRAVEL

PATIENT CARE COSTS — INPATIENT

OUTPATIENT

ALTERATIONS AND RENOVATIONS *(Itemize by category)*

OTHER EXPENSES *(Itemize by category)*
Room Charge — Breakdown/Itemization by

CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS

SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)* — $ Subtotal

CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS

TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD — $ Direct Costs

Program Director/Principal Investigator (Last, First, Middle): Engelke, Kory (Bridge)

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS		INITIAL BUDGET PERIOD *(from Form Page 4)*	ADDITIONAL YEARS OF SUPPORT REQUESTED			
			2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*			SALARY			
CONSULTANT COSTS			Breakdown/Itemization by categ			
EQUIPMENT						
SUPPLIES			Breakdown/Itemization by categ			
TRAVEL						
PATIENT CARE COSTS	INPATIENT					
	OUTPATIENT					
ALTERATIONS AND RENOVATIONS						
OTHER EXPENSES			Breakdown/Itemization by			
CONSORTIUM/ CONTRACTUAL COSTS	DIRECT					
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*						
CONSORTIUM/ CONTRACTUAL COSTS	F&A					
TOTAL DIRECT COSTS			Direct Costs			

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD $ Direct Costs

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

Memo

protected by emergent biosolutions

Lanling Zou, MD. Ph.D.
Bacteriology Program Officer
Chief, Translational Sciences Section
BMB/DMID/NIAID/NIH/DHHS
6610 Rockledge Drive, Rm 4225
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August 28, 2009

NIAID Grant Number: 1U01AI082224 - 01
PI Name: Sukjoon Park
Grant Title: Development of a Next Generation Anthrax Vaccine, dmPA7909

Dear Dr. Zou,

Enclosed is the revised product development plan for the grant proposal referenced above. We made following changes in this revision:

1. Identified a new formulation partner (Aridis) and a fill/finish CMO (Aeras)
2. Included detailed product development plans for the new partners
3. Included a period of performance for each subcontractor by quarters
4. Updated budget information for each subcontractor by quarters
5. Revised the total budget based on the new scope of work
6. Included letter of supports from Aridis and Aeras

We plan to submit a revised budget to the grant management office no later than Tuesday, September 1, 2009. Please let me know if you have any questions. Thank you.

Best Regards,

Gary S. Nabors, Ph.D.
VP Product Development & Site Operations

Emergent BioSolutions
Emergent Product Development Gaithersburg Inc.
300 Professional Drive, Suite 250
Gaithersburg, MD 20879

t 301-944-0150
f 301-590-1252
c 240-643-5943
e naborsg@ebsi.com

cc: Ms. Kim Coats

NIAID U01 Grant Proposal

Revised Product Development Plan

Grant Title: Development of a Next Generation Anthrax Vaccine, dmPA7909

Grant Number: 1U01AI082224-01

August 28, 2009

Principal Investigator: Sukjoon Park, Ph.D.
Address: Emergent Product Development Gaithersburg Inc.
300 Professional Drive, Suite 250

A. Introduction

On June 19, 2008, Emergent Product development Gaithersburg Inc (Emergent) submitted a U01 grant proposal to NIAID (Title: Development of a next generation anthrax vaccine, dmPA7909) to advance the development of the anthrax vaccine dmPA7909. This vaccine is composed of the double-mutant recombinant *Bacillus anthracis* protective antigen (dmPA), the aluminum hydroxide adjuvant Alhydrogel® and the immunostimulatory oligodeoxynucleotide compound CPG 7909 (VaxImmune™) formulated as a dry powder. The characteristics of dmPA7909 that make it an ideal candidate to meet the nation's needs for anthrax vaccine are:

1. **Rapid immune response following 2-3 doses**: In guinea pigs, dmPA7909 provided protection against a lethal dose of anthrax spores after 2 doses. Alhydrogel and CPG 7909 as an adjuvant system when combined with dmPA produced a more rapid and greater immune response than Alhydrogel alone.
2. **Long-term stability to facilitate ambient temperature storage in the Strategic National Stockpile**: Results of Emergent's stability studies with dmPA demonstrate that the dmPA is significantly more stable than other recombinant *B. anthracis* protective antigens (rPAs). Additionally, dry powder vaccine formulations consisting of recombinant proteins and Alhydrogel have been demonstrated to be stable for years at elevated temperatures such as 25 °C and 37 °C.
3. **Ability to be administered in a national emergency without the need for special storage conditions**: The spray-dried powder formulation of dmPA7909 markedly enhances vaccine stability even at extreme temperatures such as Propriet

Emergent has been developing the third generation anthrax vaccine dmPA7909 since Proprietary Info and CPG 7909 was licensed by Emergent from Coley Pharmaceutical Group (purchased by Pfizer in 2008) for use in an anthrax vaccine. As the manufacturer of BioThrax®, the only FDA-licensed anthrax vaccine, Emergent is leveraging over 40 years of experience in anthrax vaccine research and development expertise to expedite development of dmPA7909. As a part of the comprehensive development plan, Emergent proposed the following specific aims in the original proposal:

Specific Aim 1 (SA 1): Finalize the formulation for dmPA7909 anthrax vaccine

Emergent planned to conduct extensive formulation process development studies to finalize the spray-dry formulation process for the final drug product (FDP). Unfunded Unfunded was chosen to perform the proposed studies.

Specific Aim 2 (SA 2): Manufacture and release vaccine Suitable for a Phase 1 clinical trial

Emergent proposed to manufacture and release one cGMP lot of dmPA bulk drug substance (BDS) and one cGMP lot of dmPA7909 final drug product (FDP) for use in a Phase 1 clinical trial. The FDP lot will contain dmPA Proprietary Info CPG 7909 Proprietary Info, and Alhydrogel Proprietary Info per dose. The FDP lot will be formulated and filled in a dry powder form and will be reconstituted to a liquid form before vaccination.

Specific Aim 3 (SA 3): Examine long-term stability of dmPA7909 anthrax vaccine

Both BDS and Unfunded lots will be evaluated for their stability for Stability testing of Unfunded - ARRA the BDS will be conducted at Proprietary Info Stability testing of the Unfunded - ARRA Unfunded - ARRA

Specific Aim 4 (SA 4): Establish non-clinical safety of dmPA7909 anthrax vaccine

A repeat-dose toxicity study will be performed in Hartley guinea pigs following GLP guidance utilizing the FDP lot (engineering lot).

To successfully complete the proposed scope of work, Emergent proposed following partners for Specific Aims 1, 2 and 4 (**Table 1**)

Table 1: Performance Site for Each Specific Aim in the Original Proposal

Specific Aims	Tasks	Performance Site
1.1	Formulation process development	Unfunded
1.2	Formulation-specific assay development	
1.3	Guinea pig immunogenicity and efficacy study	EBOL[2]
2.1	Tech transfer to UNL-BPDF	Emergent[3]/UNL-BPDF[4]
Unfunded - ARRA		
2.3	Manufacture and release cGMP dmPA BDS	UNL-BPDF
2.4	Manufacture and release cGMP CPG 7909	Girindus[5]
2.5	Formulation process/assay tech transfer	Unfunded
2.6	Manufacture and release cGMP dmPA7909 FDF	Unfunded
3.1	dmPA BDS Unfunded - ARRA stability study	UNL-BPDF
Unfunded - ARRA		
4	Guinea pig repeat-dose toxicology study	Bridge[7]

[1] Unfunded
[2] EBOL: Emergent BioDefense Operations Lansing (Lansing, Michigan)
[3] Emergent: Emergent Product Development Gaithersburg Inc (Gaithersburg, Maryland)
[4] UNL-BPDF: University of Nebraska-Lincoln Biological Process Development Facility (Lincoln, Nebraska)
[5] Girindus (Cincinnati, Ohio)
[6] Unfunded
[7] Bridge: Bridge Global Pharmaceutical Services, Inc. (Gaithersburg, Maryland)

In the original proposal, Unfunded was chosen to perform the spray drying formulation process development activities based on their expertise in the spray drying technology. Unfunded also owned a GMP spray-drier housed at Unfund. Therefore, Unfund was a logical choice for manufacturing of the spray-dried Unfund However, Unfunded went out of business recently and, as a result, we are unable to use Unfunded as a formulation partner. Due to the uncertainty of the legal ownership of the GMP stray-drier housed at Unfund it is also unlikely that we can use the Unfund facility for the Unfu GMP manufacturing.

During the last 6 weeks, Emergent has been conducting extensive search and evaluation exercises to identify a new partner in order to replace the Unfunded consortium. At the

same time, we also have been evaluating compatible technologies to substitute the spry drying technology as a backup strategy.

As a result of the extensive efforts, Emergent is happy to report that we have chosen a new partner to initiate the proposed scope of work without deviating from the original proposal. The new partner is Aridis Pharmaceuticals (Aridis). Aridis' expertise includes, but is not limited to, spray drying and foam freeze drying technologies. Aridis will conduct all tasks proposed in the original proposal. In addition, Proprietary Info Emergent also identified a new contract manufacturing organization (CMO) to manufacture the GMP FDP. The manufacturer, Aeras, has a GMP spry drying manufacturing facility which is validated to process biologics under aseptic conditions. Letters of support from both organizations are attached (**Appendices 1** and **2**, respectively)

Table 2 describes an updated performance site for each specific aim. It is noteworthy to mention that, Unfunded - ARRA Immediately after the submission of the proposal in June, 2008, Emergent established a partnership with the University of Nebraska-Lincoln Biological Process Development Facility (UNL-BPDF) and they have manufactured the GMP cell banks. Unfunded - ARRA

Due to the fact that the duration of the award is now reduced from 5 years to 2 years, Emergent Unfunded - ARRA

Table 2: Revised Performance Sites and Specific Aims

Original SA	Revised SA	Tasks	Performance Site
1.1	1.1	Formulation process development	Aridis[1]
N/A	1.2	Scale-up formulation process development	Aridis
1.2	1.3	Formulation-specific assay development	Aridis
1.3	1.4	Guinea pig immunogenicity and efficacy study	EBOL
2.1	2.1	Tech transfer to UNL-BPDF	Emergent/UNL-BPDF
2.2	N/A	Unfunded - ARRA	Completed at UNL-BPDF
2.3	2.2	Manufacture and release cGMP dmPA BDS	UNL-BPDF
2.4	2.3	Manufacture and release cGMP CPG 7909	Girindus
2.5	2.4	Formulation process/assay tech transfer	Aridis/Aeras[2]
2.6	2.5	Manufacture and release cGMP dmPA7909 FDF	Aeras
3.1	3	dmPA BDS 12-month stability study	UNL-BPDF
3.2	N/A	Unfunded - ARRA	Not proposed under the current grant
4	4	Guinea pig repeat-dose toxicology study	Bridge

[1] Aridis: Aridis Pharmaceuticals (San Jose, California)
[2] Aeras: Aeras Global TB Vaccine Foundation (Rockville, Maryland)

B. New Formulation Process Development Partner – Aridis

1. Background information on Aridis and relevant experience

Aridis has a strong track record of developing advanced room temperature stable formulations for proteins and vaccines. Aridis is the recipient of numerous grant and contract awards related to its formulation technologies, including three primary NIH grant awards, two NIH subawards, two PATH/Gates Foundation awards, a NIH Regional Centers of Excellence (RCE) subaward, a USAID subaward, and five contract research awards from other private organizations. Aridis' technology portfolio comprises formulation Proprietary Info, superior process technology (Proprietary Info spray drying and foam freeze drying), and convenient delivery systems (dry powder inhalers and oral quick dissolving wafers) to produce high-quality, room-temperature stable and easy to handle therapeutics. Aridis' proprietary formulation and drying technologies, including Proprietary Info spray drying, and foam freeze drying, have been applied to produce heat resistant vaccines, including live attenuated anthrax vaccine, live respiratory syncytial virus (RSV), live parainfluenza virus, live *S. typhi* Ty21a, live listeria-vectored vaccine, live attenuated rotavirus, live attenuated adenovirus and live measles virus.

Aridis Pharmaceuticals is located at the San Jose Biocenter, 5941 Optical Court, suite 206, San Jose, CA 95138. Aridis has a combined area of Square Footage for its exclusive use consisting of laboratory space Square Footage and office space Square Foota Aridis also has access to the following shared areas: reception area; conference rooms Square two (2) meeting rooms Square ; library/breakroom Square ; administrative/copy room Square Foot ; shared equipment room Squar sq ft); coldroom Square tissue culture rooms Square . The San Jose Biocenter (SJBC) occupies approximately 20,000 sq ft of laboratory, office and common use space including a receiving area. SJBC provides receptionist, security, janitorial and routine maintenance services.

2. Technical Background

The stability of the vaccine will determine the cost of pre-anthrax stockpiling and logistic of distribution for vaccine deployment. Vaccines with a long shelf life will provide greater potency assurance and reduce the cost of the stockpiling program by minimizing the stockpile turn-over. In addition, stable anthrax vaccines stored under ambient conditions can be rapidly deployed for mass immunization to control an anthrax outbreak without being constrained by the cold chain.

a. Limitations of Conventional Lyophilization Process

Lyophlization has always been the method of choice for heat-labile vaccines when a reasonable shelf life cannot be achieved with liquid formulations. All lyophilized vaccines, due to constraints of the formulation design and processing stress, still require refrigerated storage. The conventional formulation approach stabilizes vaccines with sugar or other excipients that form a crystal or glassy state when dried, providing more rigid, dynamically stable structures. However, recent neutron and x-ray scattering studies revealed that these excipient matrices and the encased antigen undergo high frequency molecular and sub-molecular vibrations that cause instability, denaturation and activity loss of the vaccine, which are more pronounced at elevated temperatures.

The stress to vaccine during the lyophilization process is another cause of vaccine instability. Lyophilization involves three sequential steps: freezing, primary drying, and secondary drying. The freezing step, which separates water from the vaccine and excipients by immobilizing the

water as crystals, poses the most stress to the vaccine. The ice crystals formed may not only denature proteins and inactivate live vaccines, but also cause phase separation with the aluminum adjuvant, resulting in an unstable preparation. Additionally, the freeze concentrate (concentrated formulation left behind after the water crystallizes) often causes an osmotic and pH shock to the vaccine.

b. Proprietary Info glass formulation technology

In the proposed project, Aridis will apply an advanced formulation technology to produce thermostable dry formulations of the dmPA7909 vaccine. The formulation technology, called

Proprietary Info

formulation represents a new paradigm in pharmaceutical stabilization that is applicable to a wide variety of drying processes (including lyophilization) and products.

Proprietary Info

c. Manufacturing Process of Proprietary Info Spray Drying

Spray drying is a cost-effective, scalable drying method that can directly produce pharmaceutical powders that is increasingly finding its way into the biopharmaceutical industry. Because this process does not involve subjecting the vaccine to a freezing regime, as with freeze drying,

spray drying may be more compatible with alum containing vaccine preparations. Another potential advantage of the spray drying process is the ability Proprietary Info The resulting vaccine powder will be comprised of a homogeneous mixture of formulated and stabilized dmPA7909 vaccine that can be filled into any container closure for subsequent reconstitution and injection.

Conventional spray drying involves significant Proprietary Info For example, an IgG1 monoclonal antibody was stabilized at 37 °C for months without significant loss in monomer content (**Figure 2**). In another example, a live rotavirus vaccine was stabilized at room temperature (25 °C) for over one year with no detectable loss in potency (**Figure 3**).

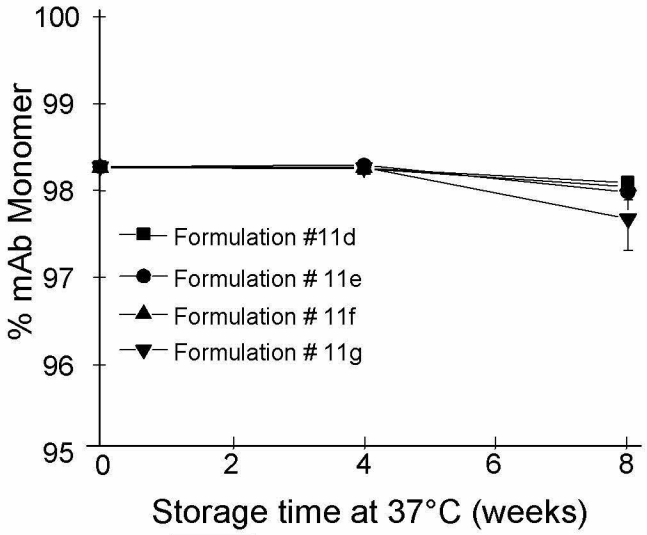

Figure 2: Proprie spray dried IgG1 mAb could be stabilized for months at 37 °C without significant monomer loss

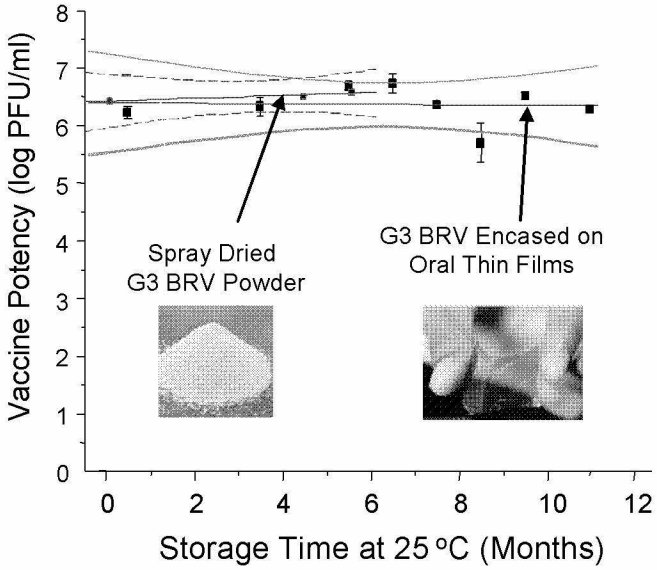

Figure 3: Stabilization of live rotavirus vaccine by Propriet spray drying

d. Manufacturing Process of Plasticized Glass Formulation: Foam Freeze Drying

An alternative drying process that could be more compatible with alum containing vaccines is a modified freeze drying process which we call foam freeze drying. This process uses conventional freeze dryers and standard pharmaceutical excipients and subjects the product to very brief (minutes rather than hours), transient sublimation states resulting in maximal activity recovery, while minimizing protein-adjuvant phase separation problems that could occur with a conventional freeze drying process. The resulting glassy foam cake can be quickly reconstituted and delivered as a liquid for parenteral injection. With optimal stabilizer selection, foam freeze

drying could be used to stabilize proteins, inactivated vaccines, and live bacterial and viral vaccines.

While the foam freeze drying process is essentially a freeze drying process, the superior stability to conventionally freeze dried processes is attributed to lower process stress (foam freeze drying process does not involve prolonged transition to the freezing step) and the solid state properties of the foam cake as compared to the conventional lyophilization cake. Some of the stability impacting solid state properties of the foam cake include lower specific surface area, more homogeneous distribution of vaccine to and from the surface of the solid, longer glassy state relaxation kinetics (i.e. lower energy state), and lower molecular motions. For example, as shown in **Figure 4**, foam freeze dried monoclonal antibody exhibited the longest glass relaxation time and lowest molecular motions, as compared to the same formulation processed by spray drying or conventional freeze drying. Such solid state properties correlated with superior stability, as determined by the protein aggregation rate, of the foam freeze dried antibody.

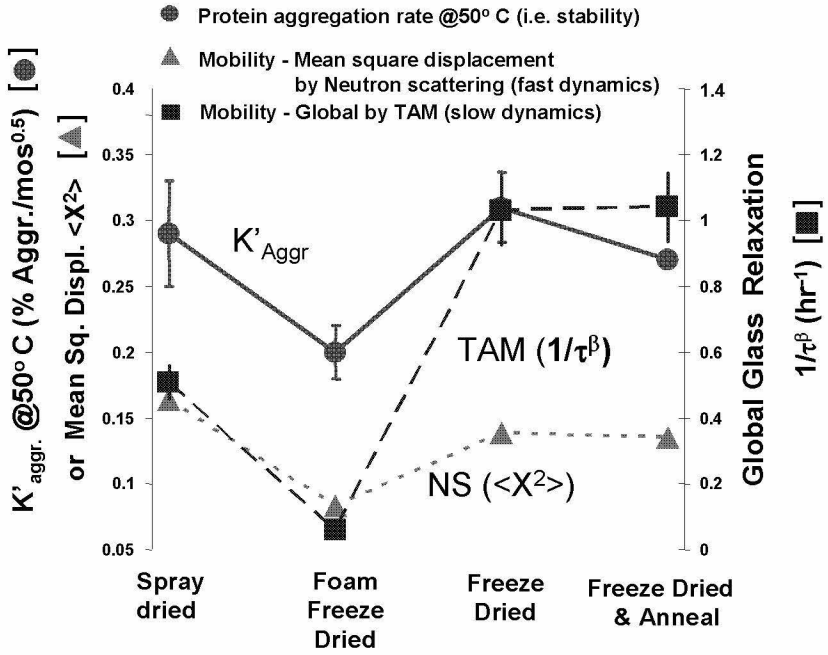

Figure 4: Correlation of protein stability to global glass relaxation kinetics

Proprietary Info

3. Aridis Project Management and Key Personnel

a. Management of the Proposed Project

Aridis will direct and coordinate the activities of the in-house research team and other external collaborators, and will coordinate with Emergent to support the project. Aridis will be responsible for deliverables to and communications with Emergent. The technical lead for the subproject, Dr.

Vu Truong, will be responsible for the scientific management of the subproject.

Subcontractor Personnel

b. Summary of Qualifications for Key Aridis Personnel

Vu Truong, Ph.D., Chief Scientific Officer, Aridis Pharmaceutical: Dr. Truong has more than 10 years experience in formulation and stabilization of macromolecules. He was the lead researcher responsible for completing all room temperature stabilization technology development related objectives during the first phase of the SBIR grant R43AI063829 'Live Oral Heat Stable S. typhi Ty21a Vaccine'. He is one of the leading researchers on biopreservation of live vaccines and human monoclonal antibodies and holds five patents related to these technologies. His accomplishments include the development of room temperature stable live virus and bacterial vaccine formulations using lyophilization, spray freeze drying, spray drying, and foam freeze drying. He is also an expert in process development and engineering of powders for optimal oral, nasal, and pulmonary delivery. Dr. Truong led a Formulation Department at Medimmune for five years with $1.8M annual budget and over 5 different intramural and extramural collaborations at any one time. He has been the head of R&D at Aridis for the past 2 years where he is managing a similar size budget with seven active R&D collaborations. In 2003, Dr. Truong co-founded Aridis Pharmaceuticals LLC, to develop simple, convenient and effective therapeutics initially focused on live attenuated vaccines that can be delivered in simple oral or nasal dosage forms that do not need a cold chain (i.e., are stable at room temperature and above). Dr. Truong, Subcontractor Personnel are collaborating on vaccines based on expression of antigens in a live attenuated Ty21a vector. Dr. Truong received his Ph.D. in Pharmacology and Molecular Sciences from the Johns Hopkins School of Medicine.

Subcontractor Personnel

Subcontractor Personnel

C. Specific Aims

1. Specific Aim 1 (SA1): Finalize the Formulation for dmPA7909 Anthrax Vaccine

Aridis will perform an optimization study before manufacturing the cGMP material. During this period of work the spray drying and the foam freeze drying conditions will be identified. These conditions will produce a product with similar characteristics to that obtained in the previous studies at Unfunded Aridis' experience of successfully stabilizing proteins and a number of inactivated and live vaccines provides a strong baseline for developing a room temperature stable dmPA7909 vaccine.

a. Specific Aim 1.1 (SA1.1): Formulation process development

Proprietary Info

To accomplish the goal, Aridis Proprietary Info the dmPA7909 vaccine to Proprietary Info

Proprietary Info

temperature.

Proprietary Info

time of use. However, we believe it is very likely that we can find a suitable formulation for the dmPA7909 vaccine. Emergent has previously demonstrated that the dmPA7909 vaccine can be stably spray-dried and our immunogenicity and efficacy non-clinical studies demonstrated that the spray-dried vaccine is highly immunogenic and efficacious.

Because it is known that the shelf life of dried vaccines is dependent on residual moisture content, we will ensure that the process can generate powders with consistently low (1-3%) moisture content. Key characteristics of the spray dried powders that will be tested using U.S. Pharmacopeia (USP)-based methods include the following tests: Karl Fisher titration for moisture content and differential scanning calorimetry (DSC) for glass transition temperature. Additional powder properties that affect powder filling such as tap density and powder dispensability will also be tested.

Proprietary Info

b. Specific Aim 1.2 (SA 1.2): Scale-up formulation process development

Proprietary Info

Proprietary Info

Our pilot plant scale spray drying process will subsequently be transferred to Aeras for GMP manufacturing of the clinical material.

Proprietary Info

c. *Specific Aim 1.3 (SA1.3): Formulation-specific assay development*

Except assays specific to the final spray drying formulation (or foam freeze drying formulation), all other characterization, in-process, release, and stability indicating assays appropriate for Phase 1 GMP manufacturing will be developed by Emergent. The formulation-specific assays will be developed and qualified by Emergent and Aridis in parallel with the formulation method development.

d. *Specific Aim 1.4 (SA1.4): Guinea pig immunogenicity and efficacy study*

The formulated dmPA7909 vaccine candidate will be tested for its immunogenicity and efficacy at Emergent's BSL-3 facility (Emergent Biodefense Operations Lansing, Lansing, MI) utilizing a guinea pig anthrax challenge model. In this non-GLP study, adult guinea pigs (equal number of males and females) will be randomly assigned to Pr groups as described in **Table 3**.

Table 3: Guinea Pig Immunogenicity and Efficacy Study Design

Proprietary Info

Proprietary Info

2. Specific Aim 2 (SA2): Manufacture and Release Vaccine Suitable for a Phase 1 Clinical Trial

Proprietary Info

The FDP manufacturing campaign will be conducted at Aeras. Aridis' pilot plant scale spray drying process will be transferred to Aeras for GMP manufacturing of clinical material. Aeras is a US based vendor that has GMP pilot plant spray drying equipment and a facility validated to process biologics under aseptic conditions. We have confirmation from Aeras that they will participate in the contract work and will work in parallel with Aridis to transfer the process into their GMP suite. In addition, we also identified Proprietary as a backup vendor. Aridis will manage

Proprietary Info

a. Specific Aim 2.1 (SA2.1): Tech transfer to UNL-BPDF

Emergent will transfer all processes and assays necessary to manufacture and release cGMP

dmPA BDS to UNL-BPDF. The targeted production volume for the cGMP dmPA BDS for the

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b. Specific Aim 2.2 (SA2.2): Manufacturing and Release of cGMP dmPA BDS

The BDS manufacturing effort will involve the following major components:

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Certain aspects of different milestones may run concurrently in order to meet project timelines. These concurrent aspects will be agreed upon in writing by both Emergent and UNL-BPDF upon finalization of the award.

Following is the scope of work for the proposed tasks:

i) **Task 1: Process and assay development**

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ii) **Task 2: Generate Master Production Record (MPR) and any additional product-specific SOPs.**

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iii) **Task 3: Confirm the process and the batch records in the cGMP suite – 60 L engineering run**

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iv) **Task 4: Produce, test and release a Phase I cGMP lot of dmPA BDS**

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v) **Task 5: Forced degradation study of dmPA**

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c. Specific Aim 2.3 (SA2.3): Manufacturing and Release of cGMP CPG 7909

CPG 7909 is considered a raw material, utilized during the formulation of the FDP. Proprietary Info Proprietary Info grams of CPG 7909 will be supplied by Girindus. Girindus is one of the leading

manufacturers of oligonucleotides. Girindus has already manufactured two cGMP lots of CPG 7909 for Emergent's AV7909 anthrax vaccine program which is currently funded by two NIAID awards (U01 grant: 5 U01 AI078169-02, contract: HHSN272200800051C). CPG 7909 will be released to Emergent by Girindus based on the release specifications outlined in **Table 6**.

Table 6: Proposed Specifications and Test Methods for CPG 7909

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After manufacturing the cGMP CPG 7909 lot, Girindus will perform a Unfunded - ARRA stability study at various temperatures as described in **Table 7**. The tests to be performed at the various time points are appearance, ion exchange HPLC, reverse phase HPLC, water content, pH, and bioburden. However, only 12 months of the Unfunded - ARRA study can be performed during the 2-year grant period. Since there are a total of [redacted] time points and 10 of them are within the first 12 months of the study, Emergent will request reimbursement for the 10 time points Negotiated Costs of Negotiated Costs to NIAID. The cost for the additional [redacted] time points will be funded by Emergent.

Unfunded - ARRA

Unfunded - ARRA

Table 7: Proposed CPG 7909 Stability Time Points

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d. Specific Aim 2.4 (SA2.4): Formulation process/Assay tech transfer

Once developed, the formulation process and assays will be transferred from Aridis to Aeras for cGMP manufacturing of the dmPA7909 FDP lots. Aeras is Aridis' subcontractor for cGMP spray-drying process and the final fill/finish.

e. Specific Aim 2.5 (SA2.5): Manufacturing and Release of cGMP dmPA7909 FDP

Emergent will formulate and fill one FDP lot for use in a Phase 1 clinical trial. The FDP lot will contain dmPA Proprietary Info CPG 7909 Proprietary Info and Alhydrogel Proprietary Info per dose. The proposed dose combination is based on the current Phase 1 clinical trial design to evaluate the safety and immunogenicity of the dmPA7909 vaccine. The FDP lot will be stored at room temperature in a dry powder form in single-dose vials and will be reconstituted to a liquid form before vaccination with water for injection (WFI).

After development of the pilot plant scale manufacturing processes, we will have feasibility data demonstrating the production of stabilized dmPA7909 vaccine at clinical production scale. Consequently, the dosage presentation for the initial Phase 1 clinical trial will be dried stable vaccine in glass vials that will be reconstituted with WFI prior to administration as a liquid. The goal of this phase of the work is to manufacture, test and release one lot of dried stable dmPA7909 vaccine under cGMP conditions for future clinical trials.

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3. Specific Aim 3 (SA3): Examine Long-term Stability of dmPA BDS

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4. Specific Aim 4 (SA4): Establish Nonclinical Safety of dmPA7909 Anthrax Vaccine

Emergent is planning on conducting a guinea pig repeat-dose toxicity study to ensure that dmPA7909 is safe to use in clinical trials, and to satisfy anticipated FDA requirements. The study will be conducted by Bridge Global Pharmaceutical Services, Inc., who routinely conducts IND-enabling toxicity studies for vaccines and biologic-based therapeutics.

This repeat dose, pre-clinical, GLP toxicology study will investigate any adverse effects of a new vaccine prior to the initiation of clinical trials. This study is aimed at evaluating the toxicity of the dmPA7909 vaccine candidate in Hartley guinea pigs as shown in **Table 11**. Emergent currently plans to use the engineering FDP lot in this study.

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D. Period of Performance

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E. Budget

Table 13 describes the budget for Emergent and each subcontractor specified in the previous sections.

Table 13: Period of Performance for All Specific Aims

Emergent and Subcontractor/ supplier	Budget by Quarter ($)								Total Budget ($)
	Year 1				Year 2				
	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	
Emergent	Direct Costs								
EBOL									
Aridis									
UNL-BPDF									
Girindus[1]									
Aeras[2]									
Bridge									
Total Budget (Direct Cost)									

[1] Girindus is a GMP material supplier.
[2] Aeras is a subcontractor of Aridis.

ARIDIS
Pharmaceuticals

Sukjoon Park, Ph.D.
Emergent Product Development Gaithersburg Inc.
300 Professional Drive, Suite 250
Gaithersburg, MD 20879

August 28, 2009

RE: Letter of Commitment for NIAID U01 Grant # 1U01AI082224 - 01

Dear Dr. Park,
Aridis Pharmaceuticals is pleased to commit certain of its resources to Emergent Product Development Gaithersburg Inc. (Emergent) in connection with the proposed National Institute of Allergy and Infectious Diseases (NIAID) U01 grant (Grant # 1U01AI082224 - 01, Title: Development of a next generation anthrax vaccine, dmPA7909). Aridis recognizes this project to be of critical national importance. Upon awarding, Aridis will commit to assisting the success of this project by dedicating the necessary resources and maintaining the appropriate level of oversight on this effort and is ready to perform the following activities:

- Task 1: Develop a stable formulation
  - Develop a stable spry-dry formulation process for dmPA7909
  - Develop a foam freeze-dry formulation process for dmPA7909
  - Conduct stability testing of both technologies for downselction
- Task 2: Complete process development and tech transfer to manufacturer
  - Complete scale-up process development
  - Tech transfer the process to the GMP final drug product (FDP) manufacturer
- Task 3: Manufacture a GMP lot of dried dmPA7909 vaccine

This work will have high priority status within Aridis, and necessary and available resources will be allocated to accomplish the work within the time constraints of the agreed-upon schedule.

Aridis agrees to recognize the source of funding of the proposed grant in all public releases, subject to U.S. Government restrictions on publicity. Rights to data, materials, information and inventions will be outlined in the Services Agreement between Emergent and Aridis.

Aridis agrees to participate in an audit of specifically-agreed facilities as well as applicable GXP and QC/QA capabilities. We agree to comply with requests to make all records, including previous regulatory inspection reports, and staff, available in response to an audit by the NIAID or its designee.

I will serve as the Principal Investigator for the Aridis activities on this project and the main point of contact. I can be contacted at 408-385-1742 (address below).

Sincerely,

Vu L. Truong, Ph.D.
Chief Scientific Officer

5941 Optical Court, San Jose, CA 95138
Tel: 408-385-1742 Fax: 408-960-3822
www.aridispharma.com

Appendix 1

Aridis Pharmaceuticals

Letter of Support

Appendix 2

Aeras Global TB Vaccine Foundation

Letter of Support

AERAS

August 24, 2009

Vu L. Truong, Ph.D.
Founder & CSO,
Aridis Pharmaceuticals
5941 Optical Ct.
San Jose, CA 95138

Dear Dr. Truong,

This is a letter of support for your grant application "Development and Clinical Manufacturing of Stable rPA Anthrax Vaccine"

As you know, Aeras is located in Rockville, Maryland and has qualified staff in Process Development, Manufacturing, Quality Control and Quality Assurance departments required for the production of human clinical material. The organization occupies a Square Footage research building with laboratories for vaccine design, construction, assessment, development and manufacturing. A core capability of Aeras is our current Good Manufacturing Practice (cGMP) manufacturing capability. A Square Footage cGMP cleanroom facility on the third floor, the Upstream Vaccine Manufacturing Area (VMA-U), has been in operation since the first Quarter of 2007. It has produced recombinant biologics that have been used in clinical trials in the United States, Europe, and other countries. It has a Water for Injection (WFI) generation system. We have the quality control systems in place to handle raw materials and quarantined areas for storage of raw materials and finished bulk. The facility has unidirectional flow of materials, waste, people and product. This facility can produce Biosafety level II (BSL2) vaccines for Phase I through Phase III clinical trials. This facility has established changeover procedures.

A Square Footage cGMP cleanroom facility on the second floor, the Downstream Vaccine Manufacturing Area (VMA-D), is mechanically complete and is being commissioned and validated. It is a BSL-2 facility that has up to Grade A cleanroom space that is designed for the purification and Fill/Finish of biologic vaccines.

A Grade-B cleanroom in the VMA-D has a BSL-2, sterilizable, cGMP, 35 Kg/hr. spray dryer. The spray dryer has been designed to produce cGMP spray dried material for human clinical testing and has been designed to be compliant with US FDA requirements for GMP manufacture of biological products, including live vaccines. The spray dryer can be operated in a Grade A Biological Safety Cabinet in the room.

Our facility and staff are ready and able to engage in this project. We would like to invite you to visit our facility and see first hand our capabilities. We look forward to working with Aridis on this exciting project. Should you have any questions, please do not hesitate to contact me.

Sincerely,

Non-Keys PERS

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