



Case No. 2021-00092-FOIA-PHS

December 01, 2020

Sent via email:

Ms. Elizabeth A Brehm
Attorney
Siri & Glimstad
200 Park Avenue
Floor 17
New York, NY 11786
Foia@sirillp.comm

Dear Ms. Brehm:

This letter is the final response to your October 11, 2020, Freedom of Information Act (FOIA) request. Specifically, you requested the following records:

“1. Any and all documents and communications concerning Grant Number R18 HS017045, given to Principal Investigator Ross Lazarus from Harvard Pilgrim Health Care, Inc., by the AHRQ (the “Grant”). This should include, but is not limited to, any and all documents and communications concerning proposals for the Grant, awarding of the Grant, and evaluation of the Grant.

2. Any and all documents and communications with Ross Lazarus, Michael Klompas, or Steve Bernstein, (the “Grant Personnel”) concerning the Vaccine Adverse Event Reporting System (“VAERS”). This request should include, but is not limited to, any documents or communications concerning giving the Grant Personnel access to, permission to use, permission to interact with, or permission to submit data to VAERS.

3. Any and all documents and communications concerning both (a) the Grant or the Grant Personnel, and (b) the VAERS. This request should include, but is not limited to, any internal documents or communications concerning giving the Grant Personnel access to, permission to use, permission to interact with, or permission to submit data to VAERS.

4. Any and all documents and communications concerning the report entitled “ELECTRONIC SUPPORT FOR PUBLIC HEALTH: VALIDATED CASE FINDING AND REPORTING FOR NOTIFIABLE DISEASES USING ELECTRONIC MEDICAL DATA,” by Lazarus R., Klompas M., Campion FX, et al. published in the Journal of the American Medical Informatics Association’s Jan-Feb 2009 edition; 16(1):18-24, available at <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf> (the “Report”).

The Agency for Healthcare Research and Quality (ARHQ) conducted a search and located 446 pages of responsive records. After a careful review of these pages, I have determined to release 428 pages in part, with portions redacted, pursuant to Exemptions (b)(4), (b)(5), and (b)(6) of the FOIA (5 U.S.C. §552 (b)(4)(b)(5)(b)(6)) I have also determined to withhold 18 pages in their entirety, pursuant to Exemptions (b)(6), of the FOIA (5 U.S.C. §552 (b)(6)).

FOIA exemption (b)(4) permits the withholding of trade secrets and commercial or financial information that is privileged or confidential. The information withheld consists of pricing and commercial information.

FOIA exemption (b)(5) protects inter-agency or intra-agency memoranda or letters which would not be available by law to a party other than an agency in litigation with the agency. This exemption protects documents that would be covered by any privilege an agency could assert in a civil proceeding. These privileges include, among others, the deliberative process privilege, the attorney-client privilege, and the attorney work-product privilege. In this instance, the process privilege applies.

FOIA exemption (b)(6) permits a Federal agency to withhold information and records about individuals in "personnel and medical files and similar files, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy." The definition of "similar files" has historically been broadly interpreted to include a wide variety of files, and the United States Supreme Court has held that Congress intended the term "similar files" to be interpreted broadly, rather than narrowly. I have analyzed these records and find they meet the threshold requirement of this exemption. Additionally, I have reviewed and weighed the public interest in disclosure of this information against the privacy interest in nondisclosure, and found that the privacy interest outweighs the public's interest in disclosure.

If you believe the information withheld should not be exempt from disclosure, or this response constitutes an adverse determination, you may appeal. By filing an appeal, you preserve your rights under FOIA and give the agency a chance to review and reconsider your request and the agency's decision.

Your appeal must be postmarked or electronically transmitted within 90 calendar days of the date of this letter, to

Mr. Mark Weber
Acting Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, S.W.
Washington, DC 20201

Please clearly mark both the envelope and your letter "Freedom of Information Act Appeal."
You may also e-mail your appeal to: HHS.ACFO@hhs.gov.

If you would like to discuss our response before filing an appeal to attempt to resolve your dispute without going through the appeals process, you may contact the HHS FOIA Public Liaison for assistance at:

HHS FOIA/PA Public Liaison
FOI/Privacy Acts Division
Assistant Secretary for Public Affairs (ASPA)
Office of the Secretary (OS)
U.S. Department of Health and Human Services (HHS)
200 Independence Avenue, SW, Suite 729H
Washington, DC 20201

Telephone: (202) 690-7453
Fax: (202) 690-8320
E-mail: HHS_FOIA_Public_Liaison@hhs.gov

If you are unable to resolve your FOIA dispute through our FOIA Public Liaison, the Office of Government Information Services (OGIS), the Federal FOIA Ombudsman's office, offers

mediation services to help resolve disputes between FOIA requesters and Federal agencies. The contact information for OGIS is:

Office of Government Information Services
National Archives and Records Administration
8601 Adelphi Road-OGIS
College Park, MD 20740-6001

Telephone: 202-741-5770
Toll-Free: 1-877-684-6448
E-mail: ogis@nara.gov
Fax: 202-741-5769

There are no charges in this instance because the billable costs are less than our threshold of \$25.

Sincerely yours,

Wakema Williams for

Brandon J. Gaylord
Director
FOI/Privacy Acts Division

Enclosure(s)

AWARD BACKER

GRANT NUMBER:

1-R18-HS017045-01

FILE CONTENTS:

File Tab Number	File Tab Section Label	Document Examples
T-5 GRANT (1 file) folders	Front Cover	Financial Status Report(s)
	1	Application/Appendix/Pre-Award Materials
	2	Funding Documents
	Back Cover	Miscellaneous
T-4 GRANT (3-11) files folders	Front Cover	Financial Status Report(s)
	1	Application/Appendix
	2	Pre-Award Material
	3	Summary Statement & Related Documents
	4	Funding Documents
	5	Institutional Information
	Back Cover	Miscellaneous

RFA HS-07-002

OFFICIAL FILE

Agency for Healthcare Research and Quality

NOTICE OF AWARD

RESEARCH
Department of Health and Human Services
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

Issue Date: 12/07/2007



Grant Number: 1R18HS017045-01 REVISED

Principal Investigator:
ROSS LAZARUS, MBBS

Project Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES

BARBARA RICHARD
Director, Office of Sponsored Programs
Harvard Pilgrim Health Care
133 Brookline Ave
6th Floor
Boston, MA 02215

Award e-mailed to: research_admin@harvardpilgrim.org

Budget Period: 09/30/2007 – 09/29/2008

Project Period: 09/30/2007 – 09/29/2009

Dear Business Official:

The Agency for Healthcare Research and Quality hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to HARVARD PILGRIM HEALTH CARE in support of the above referenced project. This award is pursuant to the authority of 42 USC 299a 42 CFR 67, PL 101-239 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.

All investigators and directors of research projects supported by grants from the Agency for Healthcare Research and Quality are expected to make their research results promptly and widely available to the health professions, public administrators, and the scientific community. All published reports, both formal and informal, should acknowledge grant support with the following footnote: "This project was supported by grant number R18HS017045 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality." When a manuscript resulting from this grant is accepted for publication, the principal investigator must promptly notify the project officer of its acceptance and the date it is scheduled to be published.

Award recipients are also responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. For additional information, please visit <http://www.iedison.gov>.

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

Sincerely,


Joan R. Metcalfe
Grants Management Officer
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

Additional information follows

SECTION I – AWARD DATA – 1R18HS017045-01 REVISED**Award Calculation (U.S. Dollars)**

Salaries and Wages	(b)(4);
Fringe Benefits	(b)(6)
Personnel Costs (Subtotal)	
Consultant Services	
Supplies	\$200
Travel Costs	\$1,470
Consortium/Contractual Cost	(b)(4)

Federal Direct Costs	(b)(4)
Federal F&A Costs	
Approved Budget	\$499,809
Federal Share	\$499,809
TOTAL FEDERAL AWARD AMOUNT	\$499,809

AMOUNT OF THIS ACTION (FEDERAL SHARE) \$0

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

YR	Total Cost
02	\$499,405

Fiscal Information:

CFDA Number:	93.226
EIN:	1042452600A1
Document Number:	RHS017045A
Fiscal Year:	2007

IC	CAN	2007	2008
HS	K72PS53	\$499,809	\$499,405

AHRQ Administrative Data:

PCC: CP3 / OC: 4145

SECTION II – PAYMENT/HOTLINE INFORMATION – 1R18HS017045-01 REVISED

For payment and HHS Office of Inspector General Hotline information, see the AHRQ Home Page at <http://www.ahrq.gov/fund/awdrsrc.htm>.

SECTION III – TERMS AND CONDITIONS – 1R18HS017045-01 REVISED

This award is based on the application submitted to, and as approved by, AHRQ on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following: (see AHRQ Home Page at <http://www.ahrq.gov> for certain references cited below)

- The grant program legislation and program regulation cited in this Notice of Grant Award.
- The restrictions on the expenditure of federal funds in appropriations acts to the extent those restrictions are pertinent to the award.
- 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- The HHS Grants Policy Statement, including addenda, in effect as of the beginning of the budget period. NOTE: For budget periods beginning before October 1, 2006, the PHS Grants Policy Statement (last revised 4/94) remains applicable in accordance with the original award for that budget period.
- Standard terms and conditions can be found at <http://www.ahrq.gov/fund/awdrsrc.htm>.
- Additional terms and conditions:

AHRQ POLICY REGARDING PRE-AWARD COSTS

The following applies to all AHRQ awards except for NRSA Fellowship Awards (F31 or F32) and AHRQ Dissertation (R36) awards, which do not allow pre-award costs:

Unless otherwise indicated by term of award, the grantee may, at its own risk, incur obligations and expenditures to cover project-related costs prior to the effective date of an award provided the following criteria are met:

1. The costs incurred are considered reasonable, allocable, and necessary to the conduct of the project.
2. The costs are allowable under the potential award.
3. When required for specific expenditures or activities, AHRQ prior approval was obtained.

For new and competing continuation awards, the costs must be incurred within 90 days prior to the effective date of the award, otherwise AHRQ prior approval is required.

In allowing the applicant/grantee this flexibility, AHRQ expects the applicant/grantee to be fully aware that such borrowing against future year support must not impair its ability to accomplish the project objectives within the approved timeframe or in any way adversely affect the conduct of the project. Additionally, the incurrence of costs prior to the award of a grant imposes no obligation on the Federal Government to either make the award or increase the amount of the approved budget.

Treatment of Program Income: Additional Costs

SECTION IV – AHRQ Special Terms and Condition – 1R18HS017045-01 REVISED

This revised award removes the restricted term on the award issued on September 24, 2007, and reflects AHRQ's acceptance of IRB approval for this project. Costs associated with human subjects research may be charged to the project as of the IRB approval date.

THE FOLLOWING TERMS OF AWARD FROM THE PREVIOUS NOTICE OF AWARD ISSUED ON SEPTEMBER 24, 2007, ALSO APPLY TO THIS AWARD:

This grant is included under expanded authorities.

As proposed in the application, the Principal Investigator, Dr. Ross Lazarus, will devote 20% effort to this grant. Any reduction in this level of effort requires the written prior approval of AHRQ.

The grantee is required to participate in an annual patient safety and health IT conference sponsored or supported by AHRQ. The date and location of the conference will be communicated to the grantee after grant award. The Principal Investigator and at least one program staff member from the project are required to attend the annual conference.

Awardees are required to fully cooperate with AHRQ contractors in promoting the Agency's patient safety and health IT initiative activities.

AHRQ strongly encourages grantees to submit quarterly reports on project status, lessons learned, and challenges encountered. This will support AHRQ's mission and enable AHRQ to tailor its interactions with grantees to be most supportive of the individual projects in the Health IT portfolio. These reports will be submitted electronically to the AHRQ National Resource Center for Health IT, the AHRQ coordination center for the HIT program. More information on this submission will be provided at a later date.

The grantee institution has been identified as a non-profit organization and as such is subject to OMB Circular A-122 Cost Principles for Non-Profit Organizations (http://www.whitehouse.gov/omb/circulars/a122/a122_2004.html). If the grantee believes this designation is incorrect, contact the grants management specialist named on the Notice of Grant Award immediately. NOTE: A subawardee or contractor under this grant is subject to the cost principles applicable to its type of organization.

Recipients of Federal funds are subject to annual audit requirements as specified in OMB Circular A-133 (<http://www.whitehouse.gov/omb/circulars/a133/a133.html>). Grantees should refer to the above Circular for the current annual Federal fund expenditure threshold level which requires audit. Note that for-profit organizations and foreign entities have the option of conducting a Single Audit (using OMB Circular A-133) or a program-specific audit as provided in 45 CFR 74.26 (http://a257.g.akamaitech.net/7/257/2422/05dec20031700/edocket.access.gpo.gov/cfr_2003/octqtr/pdf/45cfr74.26.pdf).

No individual may be committed to more than 100% professional time and effort. In the event that an individual's commitment exceeds 100%, the grantee must make adjustments to reduce effort. For AHRQ-sponsored projects, significant reductions in effort (i.e., in excess of 25% of the originally proposed level of effort) for the Principal Investigator and key personnel named on this Notice of Grant Award must receive written prior approval from AHRQ.

None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of executive level I of the Federal Executive pay scale (currently at a level of \$186,600). If applicable, this award and future years have been adjusted.

This award includes at least one future year commitment. A complete non-competing continuation application (PHS Form 2590) to request funding for each future year is to be submitted to AHRQ four (4) months prior to the start date of each budget period. AHRQ will no longer send separate notification of application deadlines to Principal Investigators and/or institutional business officials.

Please note that AHRQ's Policy on the Inclusion of Priority Populations in Research (<http://grants.nih.gov/grants/guide/notice-files/NOT-HS-03-010.html>), indicates that AHRQ will monitor the implementation of the policy during the development, review, award, and conduct of research. To facilitate this monitoring, grantees whose projects were funded based on a competing application submitted on or after the October 1, 2003, application receipt date are required to include in each non-competing continuation application a report of progress related to the inclusion of AHRQ priority populations.

It is the grantees' responsibility to ensure that non-competing continuation applications are submitted to AHRQ on time. Late submission of applications may jeopardize funding. Please refer to AHRQ's website, www.AHRQ.gov, Funding Opportunities, Grants Process, Noncompeting

Continuation Funding (Multiyear Grants), for details regarding application submission, including priority population reporting. If instructions on the AHRQ website contradict instructions for the PHS 2590 form, follow the instructions on the AHRQ website.

AHRQ requires the grantee to submit annual Financial Status Reports (FSRs; Standard Form 269). Forms are available on-line. The preferred form is SF 269 (the long form): http://grants.nih.gov/grants/fsr_sf269_long.pdf; however, SF 269A (the short form) may be filed if the grantee has no program income to report: http://grants.nih.gov/grants/fsr_sf269a_short.pdf.

A hard copy of the annual FSR must be submitted to the attention of FSR Coordinator no later than 90 days after the end date of the budget period. FSRs are to be mailed to the address listed below. AHRQ is NOT currently able to accept FSRs electronically via the NIH Commons.

Please note that for grants including restricted funds the grantee should state the status of the restricted funds in the Remarks section of the FSR (total restricted, total spent in accordance with the restriction, total unexpended restricted funds). Also, for grants under expanded authorities, the Remarks section must indicate whether or not non-restricted unobligated funds are being carried forward under expanded authorities (EA) to the next budget period (restricted funds may not be carried forward under EA).

Mail FSRs to:

AHRQ Grants Management
540 Gaither Road
Rockville, MD 20850

SPECIAL NOTICE: AHRQ is in the process of transitioning to the new SF424 Research & Related (R&R) grant application form and to electronic submission through www.Grants.gov for competing awards. The transition will occur by individual research funding mechanism. Funding Opportunity Announcements (FOAs, formally referred to as RFAs or PAs) have been/will be issued in the NIH Guide for Grants and Contracts and will be posted on the Grants.gov website as mechanisms are transitioned. The transition by mechanism will include all active FOAs for that mechanism. Applications in response to these announcements will require electronic submission via Grants.gov. See <http://grants.nih.gov/grants/guide/notice-files/NOT-HS-06-003.html> for additional information.

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 submitted via e-mail or may be mailed to:

AHRQ
OPART / Grants Management
540 Gaither Road

Rockville, MD 20850

Grants Management Specialist: SUZANNE HOLMAN

Email: suzanne.holman@ahrq.hhs.gov **Phone:** (301) 427-1460 **Fax:** (301) 427-1462

Program Official: MARYBETH FARQUHAR

Email: mfarquha@ahrq.gov **Phone:** (301) 427-1317 **Fax:** (301) 427-1341

SPREADSHEET SUMMARY

GRANT NUMBER: 1R18HS017045-01 REVISED

INSTITUTION: HARVARD PILGRIM HEALTH CARE

<i>Budget</i>	<i>Year 1</i>	<i>Year 2</i>
Salaries and Wages	(b)(4); (b)(6)	
Fringe Benefits		
Personnel Costs (Subtotal)		
Consultant Services		
Supplies	\$200	\$205
Travel Costs	\$1,470	\$1,600
Consortium/Contractual Cost	(b)(4)	
TOTAL FEDERAL DC		
TOTAL FEDERAL F&A		
TOTAL COST	\$499,809	\$499,405

<i>Facilities and Administrative Costs</i>	<i>Year 1</i>	<i>Year 2</i>
F&A Cost Rate 1	(b)(4)	
F&A Cost Base 1		
F&A Costs 1		

REVISED AWARD CHECKLIST

GRANT NUMBER: 1 R18 H5017045-01
 GRANTEE INSTITUTION: Harvard Pilgrim Health Care
 PI: Ross Lazarus
 PO: Marybeth Farquhar
 GMS: Suzanne Holman

REASON FOR REVISION	
Finalize provisional award	<input checked="" type="checkbox"/>
Remove/modify restrictive term(s)	<input checked="" type="checkbox"/>
Administrative supplement	
Add funds (adjustment) (Prior year funds? Y N)	
No-cost extension (1 st _____ 2 nd _____)	
Carry over funds from _____ year	
Partial pay funds from _____ year	
Other (see remarks):	

ITEMS 1 – 7 TO BE COMPLETED BY GMS, NOT BY 1ST LEVEL REVIEWER

1. Required business official endorsement in place? ☒
2. Required FSR in file and reviewed? N/A
3. For Extension, Partial Payment, or Carryover, FSR and FCO-E report (PMS) reconciled? N/A
4. PO recommendation obtained via: memo _____ e-mail _____ N/A ☒
5. Terms, as applicable:

Explanation of revision ☒ "Terms of Original Award" stmt ☒

[Make sure the following, as appropriate, appear under the terms of original award; check below if they have been added because they were missing]:

EA or not EA ☒; Salary cap ☒;
 Cost principles ☒; Audit requirements ☒;
 T5 applic requirements ☒; FSR requirements ☒;
 Other support ☒; Human Subjects ☒;
 Inquiries N/A; Terms of cooperation ☒;
 "Final Year" reports N/A; E-NGA establishment ☒;
 SF424 R&R transition ☒; Other _____

6. Is e-mail NGA de-activated? Y ☒ N/A (not e-mail enabled)
7. Addresses (PI, Grantee, etc.) confirmed/updated in IMPAC II? ☒ Y ☐ N

REMARKS:

IRB approval — 10/18/07

PREPARED BY: Suzanne Holman DATE: 12/4/07 Con't? no

1ST LEVEL REVIEWER: J Metcalf DATE: 12/4/07

Holman, Suzanne (AHRQ/OPART/GM)

From: Julie_Dunn@harvardpilgrim.org
Sent: Tuesday, December 04, 2007 11:40 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Subject: Re: IRB approval for 1 R18 HS017045-01
Attachments: ESP_VAERS_Submission_Approval_3.10.07.pdf

Hello Suzanne,

Apologies for this delay - we have had some grant deadlines during these last few weeks. Attached on pg 2, please find our formal IRB approval dated 11/13.

Thanks,

Julie

Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
www.dacp.org

emails

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

12/04/2007 10:49 AM

To: Julie_Dunn@harvardpilgrim.org
 cc
 Subject: IRB approval for 1 R18 HS017045-01

Dear Julie Dunn,

Please let me know the latest about your IRB approval. Thanks.

Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management
 Agency for Healthcare Research and Quality
 540 Gaither Road, Room 4202
 Rockville, Maryland 20850
 301-427-1460 (phone)
 301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

12/4/2007

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Harvard Pilgrim Health Care

November 13, 2007

HPHC IRB#00000882

Ross Lazarus, MBBS, MPH, Mmed
DACP
133 Brookline Ave
Boston, MA 02215

NOTICE OF HUMAN STUDIES COMMITTEE ACTION

HSC#: 3.10.07
Study: Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)
Item: Response to Review
Risk Assignment: Minimal-46.110(b)
Type of Review: Subcommittee

Decision: Study Approved
Approval Date: October 18, 2007
Expiration Date: October 17, 2008
Next Review Due: September 1, 2008

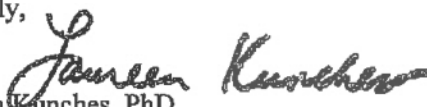
Comments: The subcommittee has reviewed the minor revisions requested by the HSC and approves activation of the study. The conditions for a waiver of authorization and consent have been met and approved for the use and disclosure of PHI from the HealthOne database. A data use agreement is required for use or disclosure of limited datasets.

Please retain this letter with your research records. Research records include all Institutional Review Board submissions and responses which must be kept in the principal investigator's file for a minimum of six (6) years after completion of the study.

Any changes, modifications, or amendments to the study or study procedures require prior written approval from the Human Studies Committee (HSC). Serious adverse events or unanticipated problems involving risks to subjects or others must be reported immediately by telephone to the HSC at 617 509-9587, followed by a written report. The HPHC Human Studies Committee Policies and Procedures and forms are available for reference on the HPHC website (<http://www.harvardpilgrim.org>).

Please remember to use the HSC file number on all documents or correspondence relating to your study.

Sincerely,


Lauren Kunches, PhD
Chair
Human Studies Committee

Harvard Pilgrim Health Care
Office of Sponsored Programs
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Telephone (617) 509-9843 • Fax (617) 509-9859

IRB



Harvard Pilgrim Health Care

25 September 2007

Ross Lazarus
Director of Bioinformatics
Channing Laboratory, Brigham & Women's Hospital
181 Longwood Avenue
Boston, MA 02215

Dear Dr. Lazarus,

Your study, entitled **Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP: VAERS)** and funded by **the Agency for Healthcare Research and Quality (AHRQ)**, has been approved by the Harvard Pilgrim Health Care Office of Sponsored Programs.

As the HPHC Principal Investigator your responsibilities include:

- being aware of and adhering to HPHC's research policies,
- representing the study within HPHC and serving as the principal contact for the study,
- obtaining all required approvals,
- ensuring the study is conducted as stated in the approved protocol,
- assuring that all personnel involved in the study adhere to Harvard Pilgrim's policies regarding confidentiality, scientific integrity, conflict of interest, use of human subjects, and HIPAA privacy rule compliance.
- assuring that all information provided will be used only for the purpose described in this proposal. Any other uses will require the written approval of the HPHC Office of Office of Sponsored Programs,
- reporting any breaches of Harvard Pilgrim's confidentiality or HIPAA privacy policies (or any other policies) to OSP and Harvard Pilgrim's Privacy Officer..

Please contact the office if you have any questions or need any assistance.

Sincerely,

Dennis Ross-Degnan, Sc.D.
Director of Research

Harvard Pilgrim Health Care
Office of Sponsored Programs

133 Brookline Avenue, 5th Floor
Boston, MA 02215

Telephone (617) 509-9843 • Fax (617) 509-9859

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Tuesday, December 04, 2007 10:49 AM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: IRB approval for 1 R18 HS017045-01

Dear Julie Dunn,

Please let me know the latest about your IRB approval. Thanks.

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
301-427-1460 (phone)
301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

12/4/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Monday, November 05, 2007 2:27 PM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: RE: IRB Approval for 1 R18 HS017045-01

Thanks for letting me know and following up so quickly!

Suzanne Holman

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Monday, November 05, 2007 2:24 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: ross.lazarus@channing.harvard.edu
Subject: Re: IRB Approval for 1 R18 HS017045-01

Hello Suzanne,

Thank-you for this follow-up. We are currently responding to a few questions that the IRB posed during the 10/18 meeting. Following the submission to address these questions (which will hopefully happen this week), we will expect to receive a final approval letter shortly, at which time I will send along to you.

Regards,

Julie

Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

11/05/2007 02:12 PM

To Julie_Dunn@harvardpilgrim.org
 cc ross.lazarus@channing.harvard.edu
 Subject IRB Approval for 1 R18 HS017045-01

Dear Julie Dunn,

The last correspondence I had from you said that there was an IRB meeting scheduled for October 18, 2007. Please let me know any information about IRB approval you have from that meeting. Thanks!

Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management

11/5/2007

Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
301-427-1460 (phone)
301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

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11/5/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Wednesday, October 10, 2007 11:56 AM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: RE: IRB Approval for Award Number 1 R18 HS017045-01

Thanks for letting me know.

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Wednesday, October 10, 2007 11:51 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: ross.lazarus@channing.harvard.edu
Subject: Re: IRB Approval for Award Number 1 R18 HS017045-01

Hello Suzanne,

As I stated in a prior e-mail concerning this topic, as we did not receive the official NGA until after the September 6th HSC / IRB meeting at our institution, this project will be reviewed at the next meeting, scheduled for October 18th, after which time I will provide you with the IRB approval letter, once I have received it.

Thank You,

Julie

 Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

10/10/2007 11:16 AM

To: Julie_Dunn@harvardpilgrim.org
 cc: ross.lazarus@channing.harvard.edu
 Subject: IRB Approval for Award Number 1 R18 HS017045-01

Dear Julie,

An email I have from you from the end of August 2007 stated that IRB approval would happen on September 6. However, you later informed me that it didn't happen.

Could you please update me on when you anticipate IRB approval will occur so that I can revise the award and lift the restriction from the award?

Thank you so much!

10/10/2007

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
301-427-1460 (phone)
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10/10/2007

First Level Review of Competing and Noncompeting Applications

Reviewer, check yes if OK; check NO if not; if not applicable, check N/A
After 1st level review and correction of identified issues. GMS should forward file to GMO for release

	Yes	No	Corrected	NA				
Grant # : <u>1R18 HS 17045-01</u>								
Organization in letter and address matches (NGA face page)	✓							
Award includes categorical budget	✓							
Awarded level no more than committed level/appropriate level	✓							
If UC1, federal share is no more than non-federal share				✓				
EIN matches either application face page (competings) or previous NGA (non-competings)	✓							
Document number appropriate	✓							
CAN # verified	✓							
If grantee is for-profit, program income is deductive alternative				✓				
PO and GMS listed on NGA	✓							
<table border="0" style="width: 100%;"> <tr> <td style="width: 15%;">Terms include:</td> <td style="width: 30%;"> <input checked="" type="checkbox"/> A-133 Audit <input checked="" type="checkbox"/> Correct Cost Principles <input checked="" type="checkbox"/> EA or <input type="checkbox"/> not EA </td> <td style="width: 30%;"> <input checked="" type="checkbox"/> Salary Cap <input checked="" type="checkbox"/> Other Support <input checked="" type="checkbox"/> Program-specific <input type="checkbox"/> Terms of Cooperation </td> <td style="width: 25%;"> <input checked="" type="checkbox"/> T-5 and <input checked="" type="checkbox"/> FSR OR <input type="checkbox"/> Close Out Term </td> </tr> </table>					Terms include:	<input checked="" type="checkbox"/> A-133 Audit <input checked="" type="checkbox"/> Correct Cost Principles <input checked="" type="checkbox"/> EA or <input type="checkbox"/> not EA	<input checked="" type="checkbox"/> Salary Cap <input checked="" type="checkbox"/> Other Support <input checked="" type="checkbox"/> Program-specific <input type="checkbox"/> Terms of Cooperation	<input checked="" type="checkbox"/> T-5 and <input checked="" type="checkbox"/> FSR OR <input type="checkbox"/> Close Out Term
Terms include:	<input checked="" type="checkbox"/> A-133 Audit <input checked="" type="checkbox"/> Correct Cost Principles <input checked="" type="checkbox"/> EA or <input type="checkbox"/> not EA	<input checked="" type="checkbox"/> Salary Cap <input checked="" type="checkbox"/> Other Support <input checked="" type="checkbox"/> Program-specific <input type="checkbox"/> Terms of Cooperation	<input checked="" type="checkbox"/> T-5 and <input checked="" type="checkbox"/> FSR OR <input type="checkbox"/> Close Out Term					
File Contents Include:								
GMS worksheet signed by FM	✓							
Specialist checklist completed, signed and dated	✓							
Funding memo/PO review and approval documentation	✓							
Signed/dated face page								
IRB within 12 months of budget period start date <input type="checkbox"/> OR appropriate exemption # designated <input type="checkbox"/>		★ ✓						
Evidence of cost analysis of budget and budget justification	✓							
Skip year FSR annotated, initialed and dated				✓				
Resolution of excessive unobligated balance issues				✓				
Issues from prior year resolved and any revision necessary done				✓				

Detail any problems identified, and return to GMS for resolution

★ H.S term requiring followup.

Reviewer: *M. Metcalf*

Date: 9/19/07

AHRQ COMPETING GRANT / COOPERATIVE AGREEMENT AWARD CHECKLIST

GRANT NUMBER: <u>1 R18 H5017045-01</u>		RFA/PA # or name: _____	
GRANTEE INST'N: <u>Harvard Pilgrim Health Care</u>		Budget limits or other special requirements of RFA/PA: _____	
PI: <u>Ross Lazarus</u>			
PO: <u>Jon White</u>			
GMS: <u>Suzanne Holman</u>			
BACK-UP GMS, if applicable: _____			

A. FUNDING / CODING	Y	N	N/A
1. Funding approval in file? Date of funding approval: <u>8/15/07</u>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Funding memo in file? <u>Received 9/18/07</u>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Summary Statement in file?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. MIN code: <u>1A</u> GEN code: <u>1A</u> If "U," issue resolved?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
5. Complete application (i.e. checklist _____; signature _____; appendices _____)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Program income anticipated? If Yes, use program income term on NGA.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

B. ORGANIZATIONAL INFORMATION	Y	N	N/A
1. New grantee (no previous Federal grant or contract support)? If Yes, OCR Assurance (HHS 690), stmt of non-profit status and balance sheets and/or audit reports obtained? [GMS should also conduct separate managemt rvw]	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
2. Valid EIN on file or established if needed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Grantee's DUNS number: <u>071721088</u>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. For-profit grantee? If Yes, use "Deductive Alternative" for Program Income (for-profits are only eligible for cooperative agreements).	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
5. Foreign grantee? If Yes, date State Dept. clearance received on: _____	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
6. Grantee organization on HHS Alert List <u>Under Reconstruction</u> (http://intranet.grantsinfo.hhs.gov/AlertList.cfm?id=300&CFID=5386&CFTOKEN=41244888)?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
7. PI on GSA Debarment List (http://epls.arnet.gov/) ?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
8. PI on ORI Scientific Misconduct List (http://silk.nih.gov/public/cbz1bje.@www.orilist.html) and http://www.fda.gov/ora/compliance_ref/bimo/dis_res_assur.htm) ?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
9. PI on DGM delinquent final report list?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

C. COLLABORATIVE INFORMATION	Y	N	N/A
1. Consortium(s) involved in project?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
2. Foreign involvement? If involvement is "substantial," date State Dept. clearance received: _____; If not "substantial," documentation of such in file _____	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

D. HUMAN SUBJECTS	Y	N	N/A
1. Human Subjects involved? (Sum. Stmt code: <u>30</u>) If Yes, complete as appropriate: Exemption #: _____ Grantee's Assurance #: <u>FWA00000100</u> IRB approval date: <u>pending</u>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Human Subject involvement at any other site(s)? Does each site have an Assurance? <u>(See email dated 8/27/07)</u>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
HS NOTES: _____ _____ _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

1 R18 H5017045-01

9/7 - Emailed PO, Jon White, who is now Marybeth Farquhar, that PO funding memo is missing

9/11 - PO Memo still missing. It is in the Director of CP3's office for signature

9/13 - PO Funding Memo still needed.

9/18 - PO Funding Memo received. GMS reviewed it and ~~it~~ had no additional concerns.

Grant No: 1R18HS017045-01

PI Name : LAZARUS, ROSS

DESCRIPTION (provided by the applicant): Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Every patient receiving a vaccine will be automatically identified, and for the next 30 days their health care diagnostic codes, laboratory tests, and medication prescriptions will be evaluated for values suggestive of an adverse event. When a possible adverse event is detected it will be recorded, and the appropriate clinician will be notified electronically. Clinicians will be able to preview a pre-populated report with information from the electronic medical record about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment about whether they wish to send a report. Clinicians will have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. Approved reports will be securely transferred to VAERS as electronic messages in an interoperable health data exchange format (HL7). We will evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

PI: LAZARUS, ROSS		Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES)	
Received: 02/12/2007		FOA: HS07-002	Council: 10/2007
		FOA Title: AMBULATORY SAFETY AND QUALITY PROGRAM: ENABLING QUALITY MEASUREMENT THROUGH HEALTH IT (R18)	
1 R18 HS017045-01		Dual:	Accession Number: 2969517
IPF: 444701		Organization: HARVARD PILGRIM HEALTH CARE, INC.	
Former Number:		Department:	
IRG/SRG: ZHS1 HSR-O (01)		AIDS: N	Expedited: N
Subtotal Direct Costs <u>(excludes consortium F&A)</u> Year 1: 318,498 Year 2: 312,705		Animals: N Humans: Y Clinical Trial: N Exemption: 30 HESC: N	New Investigator: N
<i>Senior/Key Personnel:</i>		<i>Organization:</i>	<i>Role Category:</i>
Ross Lazarus		Channing Laboratory, Brigham & Women's Hospital	PD/PI
Jeffrey Brown		HPHC	Co-PD/PI
(b)(6)		Harvard Vanguard Medical Association	Co-PD/PI
		Harvard Pilgrim Health Care	Co-PD/PI
		Harvard Pilgrim Healthcare	Co-PD/PI
		Harvard Pilgrim Health Care	Co-PD/PI

SF 424 (R&R)Tracking Number:

16. ESTIMATED PROJECT FUNDING		17. * IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?	
a. * Total Estimated Project Funding \$999,995.00 b. * Total Federal & Non-Federal Funds \$999,995.00 c. * Estimated Program Income \$0.00		a. YES <input type="radio"/> THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON: DATE: b. NO <input checked="" type="radio"/> PROGRAM IS NOT COVERED BY E.O. 12372; OR <input type="radio"/> PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW	
18. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001) <input checked="" type="radio"/> * I agree <small>* The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.</small>			
19. Authorized Representative			
Prefix:	* First Name:	Middle Name:	* Last Name:
	Barbara		Richard
* Position/Title: Director		* Organization Name: Harvard Pilgrim Health Care	
Department: Office of Sponsored Programs		Division:	
* Street1: 133 Brookline Ave		Street2: 6th Floor	
* City: Boston		County:	* State: MA: Massachu- setts
Province:	* Country: USA: UNITED STATES		* ZIP / Postal Code: 02481
* Phone Number: 617-509-9950	Fax Number: 617-509-9859		* Email: Research_Admin@hphc.org
* Signature of Authorized Representative		* Date Signed	
Barbara W Richard		02/12/2007	
20. Pre-application File Name: Mime Type:			
21. Attach an additional list of Project Congressional Districts if needed.			
File Name: Mime Type:			

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Appendix

Number of Attachments in Appendix: 4

RESEARCH & RELATED Project/Performance Site Location(s)

Project/Performance Site Primary Location

Organization Name: Harvard Pilgrim Healthcare - DACP

* Street1: 133 Brookline Ave

Street2: 6th Floor

* City: Boston

County:

* State: MA: Massachusetts

Province:

* Country: USA: UNITED STATES

* Zip / Postal Code: 02215

Project/Performance Site Location 1

Organization Name: Brigham & Women's Hospital - Channing Laboratory

* Street1: 181 Longwood Avenue

Street2:

* City: Boston

County:

* State: MA: Massachusetts

Province:

* Country: USA: UNITED STATES

* Zip / Postal Code: 02215

Project/Performance Site Location 2

Organization Name: Harvard Vanguard Medical Associates (HVMA)

* Street1: 275 Grove Street

Street2: Suite 3-300

* City: Newton

County:

* State: MA: Massachusetts

Province:

* Country: USA: UNITED STATES

* Zip / Postal Code: 02466

File Name

Mime Type

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? <input checked="" type="radio"/> Yes <input type="radio"/> No		
1.a. If YES to Human Subjects		
Is the IRB review Pending? <input checked="" type="radio"/> Yes <input type="radio"/> No		
IRB Approval Date:		
Exemption Number: — 1 — 2 — 3 — 4 — 5 — 6		
Human Subject Assurance Number 00000100		
2. * Are Vertebrate Animals Used? <input type="radio"/> Yes <input checked="" type="radio"/> No		
2.a. If YES to Vertebrate Animals		
Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No		
IACUC Approval Date:		
Animal Welfare Assurance Number		
3. * Is proprietary/privileged information <input type="radio"/> Yes <input checked="" type="radio"/> No included in the application?		
4.a. * Does this project have an actual or potential impact on <input type="radio"/> Yes <input checked="" type="radio"/> No the environment?		
4.b. If yes, please explain:		
4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No		
4.d. If yes, please explain:		
5.a. * Does this project involve activities outside the U.S. or <input type="radio"/> Yes <input checked="" type="radio"/> No partnership with International Collaborators?		
5.b. If yes, identify countries:		
5.c. Optional Explanation:		
6. * Project Summary/Abstract	7148-ESP_VAERS_Abstract.pdf	Mime Type: application/pdf
7. * Project Narrative	346-ESP_VAERS_Project_Narrative.pdf	Mime Type: application/pdf
8. Bibliography & References Cited	8337-ESP_VAERS_References.pdf	Mime Type: application/pdf
9. Facilities & Other Resources	161-ESP_VAERS_Resources.pdf	Mime Type: application/pdf
10. Equipment		

ESP:VAERS Abstract

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Every patient receiving a vaccine will be automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions will be evaluated for values suggestive of an adverse event. When a possible adverse event is detected, it will be recorded, and the appropriate clinician will be notified electronically. Clinicians will be able to preview a pre-populated report, with information from the electronic medical record about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgement about whether they wish to send a report. Clinicians will have the option of adding free-text comments to pre-populated VAERS reports, or to document their decision not to send a report. Approved reports will be securely transferred to VAERS as electronic messages in an interoperable health data exchange format (HL7). We will evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project, and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

ESP:VAERS Project Narrative

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). We will use electronic medical records available from all ambulatory care encounters in a large multi-specialty practice to achieve this goal.

Harvard Pilgrim Health Care

RESOURCES AND ENVIRONMENT

Harvard Pilgrim Health Care (HPHC) is the largest non-profit HMO in New England. It currently serves more than 800,000 members in Massachusetts, New Hampshire, and Maine in a variety of organizational settings. These include medical groups, community health centers, independent physician practices, and a preferred provider network.

HPHC's research mission is to encourage high quality, public domain research. Currently, HPHC researchers have grants, cooperative agreements and contracts for studies of quality improvement, clinical process, clinical practices, and education on patient outcomes within the HMO environment. The NIH is the largest single source of research funds at HPHC, with grants from NCI, NIAAA, NIAID, NIA, NIMH, and NLM. Research funding has also been obtained from AHCPR, FDA, HCFA, HRSA, and CDC, as well as the Robert Wood Johnson Foundation and the Pew Charitable Trusts. HPHC is deeply committed to collaborative research, and currently has 10 active research collaborations that use joint protocols and data sharing with other HMO's, most of whom are members of the HMO Research Network. There are also strong research collaborations with investigators at Harvard Medical School, Harvard School of Public Health, the Dana Farber Cancer Institute, Brigham and Women's Hospital, the Massachusetts General Hospital, and the University of Rhode Island.

Office Space:

The Department of Ambulatory Care and Prevention (DACP) at Harvard Medical School and Harvard Pilgrim Healthcare (prime grantee) has over 30,000 square feet of office and conference space, and maintains 3 floors at the Harvard Vanguard Medical Associates Kenmore Center, 133 Brookline Avenue, Boston, MA. DACP had access to the clinical and program evaluation resources of Harvard Pilgrim Healthcare (HPHC), one of the nation's largest mature health maintenance organizations.

Computing Resources:

The computer systems at HPHC are well equipped for creating custom databases and performing analyses on the data. Searches for study populations based on ambulatory and hospital-based care are conducted on the host clinical computers, maintained by a large staff in the Information Technology Department. HPHC claims data (including inpatient and outpatient services, outpatient prescription drug dispensings, outside referrals, home care and long-term care records) are stored on an 8 node NCR-Teradata 5300 MPP computer system. All computer systems are linked through a network allowing authorized users to access many systems from a single workstation. To facilitate research, an in-house data services group, the Research Support Data Center with a staff of 10 programmer/analysts prepare custom research datasets that combine data from all these sources while maintaining systems to ensure patient privacy and confidentiality. Harvard Medical School staff within RSDC also have access to Harvard Vanguard Medical Associates (HVMA) data warehouse and EpicCare, electronic medical record systems for approved research projects. EpicCare and the data warehouse reside on Hewlett Packard computers running a UNIX operating system. EpicCare runs on a Cache database and the data warehouse is on an Oracle platform. Data extracts derived from EpicCare are used to create a service level database containing detailed information on internal office visits, diagnostic and laboratory orders, drug orders and some laboratory test results, this is called Clarity. The HVMA data warehouse also contains claim data from insurers (including outside referrals, outpatient prescription drug dispensings, hospital, emergency, home care and long-term care records for capitated patients).

Channing Laboratory, Brigham & Women's Hospital

RESOURCES AND ENVIRONMENT

Channing Laboratory:

The Channing Laboratory is located at 181 Longwood Avenue within easy access to other Harvard and Brigham and Women's facilities in the area. The Channing Laboratory occupies floors 3 through 8, a total of 65,185 square feet, including 20,835 square feet of wet laboratory space. The Respiratory Epidemiology offices and computer facility are located in 4000 square feet of space on the 4th floor. An additional 1500 square feet of genetic epidemiology lab space where DNA extraction and genotyping are performed is located in the LMRC building, connected directly to the Channing Lab via a tunnel. The lab is equipped with centrifuges, -80 degree freezers, and a walk-in 4-degree cold room. A freezer farm of liquid nitrogen freezers is adjacent to the lab. An automated bar code labeling system is in place, as well as a separate area for PCR. PCR machines (MJ Research), Biorad gel boxes, and a Spectromax Plus DNA quantitator (Molecular Devices) are located here. Two ABI-3100 (Applied Biosystems) machines, an ABI-7900 (Applied Biosystems), an ABI 3730, a Hydra Robot (Robbins), a fluorimeter, a Sequenom mass spectrometry system, and an Illumina BeadStation 500G are available in our laboratory for use on this project.

Computers:

This study will share the use of the Channing Laboratory Sun 690MP computer system, utilized by the Laboratory's Respiratory Epidemiology Group for primary data management and analysis operations. The system includes forty (40) gigabytes disk storage, 320MB main memory, tape drives, and printers. Available software includes SAS, ISML, BMDP, Splus, and extensive custom software programs needed for management and analyses of large, complex datasets. We maintain access to an extensive collection of genetic analysis programs, including FBAT, PBAT, SAS GENETICS, PEDCHECK, S.A.G.E., SDT, LINKAGE, ALLEGRO, and SOLAR. This facility is fully integrated with the LMRC Genetics Laboratory.

Office Space:

The Channing Laboratory facility at 181 Longwood Avenue has 38,135 square feet of research and administrative office space distributed over six floors.

Other:

We have access to the Francis A. Countway library, one of the largest medical and health libraries in the United States. Countway Library contains over ½ million books and receives 4,000 journal titles. The library has public access to Medline. The Channing Laboratory is part of the Harvard Medical School complex and is located adjacent to Harvard Medical School, the Harvard School of Public Health, and the Francis A. Countway Library of Medicine. Professional personnel have Brigham and Women's Hospital and Harvard Medical School and/or Harvard School of Public Health appointments. The Laboratory is within one block of the Children's Hospital, Beth Israel Deaconess Medical Center, Brigham and Women's Hospital as well as the Dana Farber Cancer Center and the Joslin Diabetes Center. There is ongoing collaboration among the Respiratory Epidemiology Group investigators both through an ongoing seminar series on work-in-progress and through informal discussions of current work.

Harvard Vanguard Medical Associates

RESOURCES AND ENVIRONMENT

Harvard Vanguard Medical Associates is a multispecialty, non-profit medical group practice of approximately 500 physicians with 17 office locations, serving 350,000 patients. HVMA has recently joined with four other leading physician groups in the Boston area to form a non-profit organization called the HealthOne Care System. HealthOne Care System provides services to patients in the Metro Boston area and throughout eastern Massachusetts. Corporate offices are located in Newton Massachusetts. HealthOne is presently the largest independent physician network in the Commonwealth of Massachusetts with approximately 700 physicians in the greater Boston area. More than 500,000 patients presently receive their care at one of these practices. This collaboration will allow all HealthOne affiliates to share Harvard Vanguard's advanced electronic medical records system. All groups will complete installation of the common EpicCare electronic medical record system by 2008.

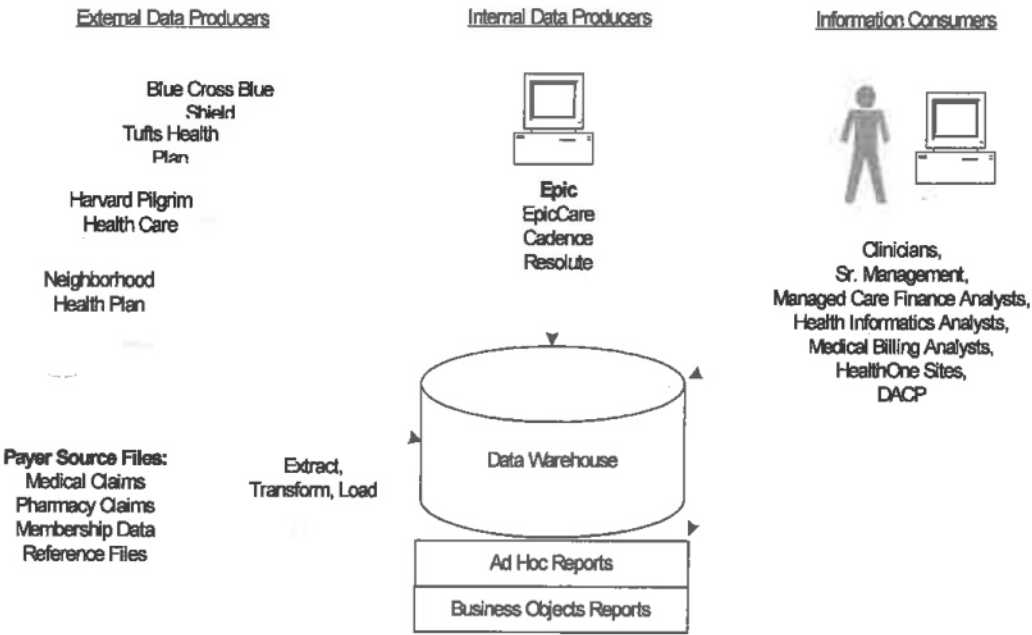
Electronic Medical Records:

HVMA has used an automated ambulatory record system since it was founded in 1969. Since 1999 all clinical services at HVMA are documented in the EpicCare Electronic Medical Record System (Epic Systems, Inc, Verona, Wisconsin). EpicCare is inherently flexible, accommodating specialty providers and facilities while ensuring that clinical information is stored in a seamless ambulatory care record. An active clinical decision support system works at every point of the care process to minimize medical errors, encourage formulary compliance, and ensure that patients receive recommended health maintenance and disease management services. This computerized record is the only record used for the day-to-day care of HVMA patients; no paper copies are retained. All provider notes and other information from services at HVMA centers are included, with the exception of selected items such as X-rays which are stored as hard copy. Clinicians order immunizations, laboratory tests, and write and transmit prescriptions on the computer, either while in the clinic room with the patient or at their desks. The pharmacy, lab, and radiology systems all interface with EpicCare. Test results are linked with the patient encounter during which they were ordered. In some instances, documentation is received from external sources where electronic interfaces do not exist (e.g. outside referrals, consults, test results, or discharge summaries); these documents are all scanned into the EpicCare. The scheduling (Cadence™) and billing (Resolute™) systems are both Epic Systems products and are integrated with the EpicCare medical record system. Electronic clinical data acquired prior to 1999 was converted from the former system called the Automated Medical Record System (AMRS).

Computer Hardware: Harvard Vanguard Medical Associates and the HealthOne Care System maintain a large, modern data center at 133 Brookline Avenue, Boston. The system is fully redundant and is staffed 24 hours per day. The help-desk staff support over 3,000 users including the electronic medical record system, company-wide email, financial systems and other IT components. There are over 70 fulltime IT staff managing all aspects of information systems operations across the organization. HealthOne maintains a testing environment for EpicCare that mirrors the functionality of the production system, but does not contain actual patient data. All clinical examination rooms are equipped with a networked computer for patient care.

HealthOne Data Warehouse:

The HealthOne Data Warehouse resides in an Oracle 9i environment and consists of the Clarity and Payer databases. The Clarity database, from Epic Systems, Inc., is a relational database which contains clinical and financial information from the Epic Suite of products; including the electronic medical record system (EpicCare), the appointment scheduling system (Cadence), the patient accounting system (Resolute), the Patient Web Portal (MyChart) and the master patient index (Identity). The various tables within the Clarity database are refreshed on a daily, weekly or monthly basis. The Payer database contains medical claims, pharmacy claims and membership managed-care data from the 4 payers with whom we have capitated contracts. The various tables within the Payer database are refreshed on a monthly basis. Data Marts have been created to improve performance and for ease-of-use while integrating the Clarity and Payer data and Business Objects Crystal reports was implemented for standard web-based reporting. There are also approximately a dozen "power users" who use SQL tools to access the data directly.



RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix Dr.	* First Name Ross	Middle Name	* Last Name Lazarus	Suffix
Position/Title: Director of Bioinformatics		Department:		
Organization Name: Channing Laboratory, Brigham & Women's Hospital		Division:		
* Street1: 181 Longwood Ave		Street2:		
* City: Boston	County:	* State: MA: Massachusetts	Province:	
* Country: USA: UNITED STATES		* Zip / Postal Code: 02215		
*Phone Number 617-525-2730		Fax Number 617-525-0958	* E-Mail ross.lazarus@channing.harvard.edu	
Credential, e.g., agency login (b)(4); (b)(6)				
* Project Role: PD/PI		Other Project Role Category:		
*Attach Biographical Sketch		File Name 3240-RLazarus_Bio.pdf	Mime Type application/pdf	
Attach Current & Pending Support				

PROFILE - Senior/Key Person				
Prefix Dr.	* First Name (b)(6)	Middle Name	* Last Name	Suffix
Position/Title: Data Manager		Department: DAPC		
Organization Name: HPHC		Division:		
* Street1: 133 Brookline Ave		Street2: 6th Floor		
* City: Boston	County: Suffolk	* State: MA: Massachusetts	Province:	
* Country: USA: UNITED STATES		* Zip / Postal Code: 02215		
*Phone Number (b)(6)		Fax Number (b)(6)	* E-Mail (b)(6)@harvardpilgrim.org	
Credential, e.g., agency login (b)(4); (b)(6)				
* Project Role: Co-PD/PI		Other Project Role Category:		
*Attach Biographical Sketch		File Name (b)(6).pdf	Mime Type application/pdf	
Attach Current & Pending Support				

PROFILE - Senior/Key Person				
Prefix Dr.	* First Name (b)(6)	Middle Name	* Last Name	Suffix
Position/Title: Director of Clinical Informatics		Department:		
Organization Name: Harvard Vanguard Medical Association		Division: HealthOne Care System		
* Street1: 275 Grove Street		Street2:		

* City: Newton	County:	* State: MA: Massachusetts	Province:
* Country: USA: UNITED STATES	* Zip / Postal Code: 02466		
*Phone Number (b)(6)	Fax Number (b)(6)	* E-Mail (b)(6)@vmed.org	
Credential, e.g., agency login: (b)(4); (b)(6)			
* Project Role: Co-PD/PI		Other Project Role Category:	
*Attach Biographical Sketch Attach Current & Pending Support	File Name (b)(6).pdf	Mime Type application/pdf	

PROFILE - Senior/Key Person				
Prefix Dr.	* First Name (b)(6)	Middle Name	* Last Name	Suffix
Position/Title: Associate Professor		Department: DACP		
Organization Name: Harvard Pilgrim Health Care		Division:		
* Street1: 131 Brookline Ave		Street2: 3rd Floor		
* City: Boston	County:	* State: MA: Massachusetts	Province:	
* Country: USA: UNITED STATES	* Zip / Postal Code: 02215			
*Phone Number (b)(6)	Fax Number	* E-Mail (b)(6)@harvardpilgrim.org		
Credential, e.g., agency login: (b)(4); (b)(6)				
* Project Role: Co-PD/PI		Other Project Role Category:		
*Attach Biographical Sketch Attach Current & Pending Support	File Name (b)(6).pdf	Mime Type application/pdf		

PROFILE - Senior/Key Person				
Prefix Dr.	* First Name (b)(6)	Middle Name	* Last Name	Suffix
Position/Title: Chairman		Department: DACP		
Organization Name: Harvard Pilgrim Healthcare		Division:		
* Street1: 133 Brookline Ave		Street2: 6th Floor		
* City: Boston	County:	* State: MA: Massachusetts	Province:	
* Country: USA: UNITED STATES	* Zip / Postal Code: 02215			
*Phone Number (b)(6)	Fax Number	* E-Mail (b)(6)@harvard.edu		
Credential, e.g., agency login: (b)(4); (b)(6)				
* Project Role: Co-PD/PI		Other Project Role Category:		
*Attach Biographical Sketch Attach Current & Pending Support	File Name (b)(6).pdf	Mime Type application/pdf		

PROFILE - Senior/Key Person				
Prefix Dr.	* First Name	Middle Name	* Last Name	Suffix
	(b)(6)			
Position/Title: Research Fellow in Medicine		Department: DACP		
Organization Name: Harvard Pilgrim Health Care		Division:		
* Street1: 133 Brookline Ave		Street2: 6th Floor		
* City: Boston	County:	* State: MA: Massachusetts	Province:	
* Country: USA: UNITED STATES		* Zip / Postal Code: 02215		
*Phone Number (b)(6)		Fax Number (b)(6)	* E-Mail (b)(6)@partners.org	
Credential, e.g., agency login		(b)(4); (b)(6)		
* Project Role: Co-PD/PI		Other Project Role Category:		
*Attach Biographical Sketch		File Name (b)(6).pdf	Mime Type application/pdf	
Attach Current & Pending Support				

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

Additional Senior/Key Person Form Attachments

When submitting senior/key persons in excess of 8 individuals, please attach additional senior/key person forms here. Each additional form attached here, will provide you with the ability to identify another 8 individuals, up to a maximum of 4 attachments (32 people).

The means to obtain a supplementary form is provided here on this form, by the button below. In order to extract, fill, and attach each additional form, simply follow these steps:

- Select the "Select to Extract the R&R Additional Senior/Key Person Form" button, which appears below.
- Save the file using a descriptive name, that will help you remember the content of the supplemental form that you are creating. When assigning a name to the file, please remember to give it the extension ".xfd" (for example, "My_Senior_Key.xfd"). If you do not name your file with the ".xfd" extension you will be unable to open it later, using your PureEdge viewer software.
- Using the "Open Form" tool on your PureEdge viewer, open the new form that you have just saved.
- Enter your additional Senior/Key Person information in this supplemental form. It is essentially the same as the Senior/Key person form that you see in the main body of your application.
- When you have completed entering information in the supplemental form, save it and close it.
- Return to this "Additional Senior/Key Person Form Attachments" page.
- Attach the saved supplemental form, that you just filled in, to one of the blocks provided on this "attachments" form.

Important: Please attach additional Senior/Key Person forms, using the blocks below. Please remember that the files you attach must be Senior/Key Person Pure Edge forms, which were previously extracted using the process outlined above. Attaching any other type of file may result in the inability to submit your application to Grants.gov.

- 1) Please attach Attachment 1
- 2) Please attach Attachment 2
- 3) Please attach Attachment 3
- 4) Please attach Attachment 4

	Filename
ADDITIONAL SENIOR/KEY PERSON PROFILE(S)	MimeType

	Filename
Additional Biographical Sketch(es) (Senior/Key Person)	MimeType

	Filename
Additional Current and Pending Support(s)	MimeType

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 Ross Lazarus		POSITION TITLE	
eRA COMMONS USER NAME (b)(4); (b)(6)		Director of Bioinformatics, Channing Laboratory Brigham and Women's Hospital	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Melbourne, Australia	M.B.B.S.	1974	Medicine
University of Melbourne, Australia	M.Med.	1985	Epidemiology
Monash University, Australia	M.P.H.	1985	Public Health
Royal Melbourne Institute of Technology, Australia	G.Dip.	1988	Computer Science

A. POSITIONS AND HONORS:**POSITIONS AND EMPLOYMENT**

1975 Resident Medical Officer, Royal Princess Alexandra Hospital
 1976-1979 Physician, Collingwood Community Health Center
 1979-1994 Occupation Physician, State Electricity Commission of Victoria
 1988-1995 Lecturer, University of Sydney
 1994-1998 Manager, Information Systems, Bundoora Extended Care Center
 1995-1998 Senior Lecturer, University of Sydney
 1998-present Sub-Dean for Information Technology, University of Sydney
 1998-present Association Professor, University of Sydney
 2000-2004 Visiting Associate Professor in Medicine, Harvard Medical School
 2000- Director of Bioinformatics, Channing Laboratory, Brigham and Women's Hospital

AWARDS AND OTHER PROFESSIONAL ACTIVITIES

1975 Medical Board of Victoria, Registered
 1980 Fellow of the Royal Australian College of General Practitioners
 1988 Medical Board of New South Wales, Registered Medical Practitioner
 1991 Fellow of the Faculty of Public Health Medicine of the Royal Australian College of Physicians

B. SELECTED PUBLICATIONS (ORIGINAL REPORTS):

1. **Lazarus R**, Sparrow D, Weiss ST. Effects of Obesity and fat distribution on ventilatory function: The Normative Aging Study. *Chest*, 1997;111:891-898.
2. **Lazarus R**, Sparrow D, Weiss ST. Alcohol intake and insulin levels in men: Evidence for lower insulin resistance in moderate drinkers from the Normative Aging Study. *Am J Epidemiol*, 1997;145(10):909-916.
3. Lee MT, **Lazarus R**. Meta-analysis of drug safety data with logistic regression. *Drug Information J*, 1997;31(4):1189-1193.
4. **Lazarus R**, Sparrow D, Weiss S. Hand-grip strength and insulin levels: cross-sectional and prospective associations in the Normative Aging Study. *Metabol Clin Exper*, 1997;46(11):1266-1269.
5. **Lazarus R**, Colditz G., Berkey C. and Speizer F. Effects of body fat on ventilatory function in children and adolescents: cross-sectional findings from a random population sample of school-children. *Pediatr Pulmonol*, 1997; 24(3):187-194.

6. **Lazarus R**, Sparrow D, Weiss ST. Temporal relationships between obesity and Insulin: longitudinal data from the Normative Aging Study. *Am J Epidemiol*, 1998;147:173-9.
7. Tsang CW, **Lazarus R**, Smith W, Mitchell P, Burnett L, Koutts J. Hematological Indices in an older population sample: Derivation of healthy reference values. *Clin Chem*, 1998;44(1):96-101.
8. Paleologos M, Cumming RG, **Lazarus R**. Cohort study of Vitamin C intake and cognitive impairment. *Am J Epidemiol*, 1998;148:45-50.
9. **Lazarus R**, Sparrow D, Weiss S. Baseline ventilatory function predicts the development of insulin resistance: the Normative Aging Study. *Eur Respir Rev*, 1998; 12: 641-645.
10. **Lazarus R**, Sparrow D, Weiss S. Insulin resistance is associated with impaired ventilatory function in non-diabetic men: The Normative Aging Study. *Eur Respir Rev*, 1998; 12: 635-640.
11. Smith W, Mitchell P, **Lazarus R**. Carrots, carotene and seeing in the dark. *Australian and New Zealand Journal of Ophthalmology*, 1999; 27:204-207.
12. Sinn JKH, Lloyd J, Todd D, **Lazarus R**, Maesel A, John E. Umbilical cord blood lactate in normal infants: Comparison between two methods of measurement. *J Ped Child Health*, 2001;37:24-27.
13. Lawson JA, **Lazarus R**, Kelly JJ. Prevalence and prognostic significance of malnutrition in chronic renal insufficiency. *Journal of Renal Nutrition*, 2001;11(1):16-22.
14. **Lazarus R**, Kleinman K, Dashevsky I, DeMaria A, Platt R. Using automated medical records for rapid identification of illness syndromes: the example of lower respiratory infection. *BMC Public Health*, 2001;1:9.
15. Arora, SC, Mudaliar YM, Lee C, Mitchell D, Iredell J, **Lazarus R**. Non-bronchoscopic Bronchoalveolar Lavage in the Microbiological Diagnosis of Pneumonia in Mechanically Ventilated Patients. *Anaesthesia and Intensive Care*, 2002;30(1):11-20.
16. **Lazarus R**, Klimecki W, Palmer L, Kwiatkowski D, Silverman E, Brown A, Martinez F, Weiss ST. Single nucleotide polymorphisms in the Interleukin 10 gene: Differences in frequencies, linkage disequilibrium patterns and haplotypes in three US ethnic groups. *Genomics*, 2002;80(2):223-228.
17. **Lazarus R**, Kleinman K, Dashevsky I, Adams C, Kludt P, DeMaria A. Detection of acute illness clusters, including potential bioterrorism events, using automated ambulatory care encounter records. *Emerging Infectious Diseases*, 2002;8(8):753-760.
18. Raby BA, Klimecki T, Laprise C, Renaud Y, Faith J, Lemire M, Greenwood C, Lange C, Palmer L, **Lazarus R**, Vercelli D, Kwiatkowski D, Silverman E, Martinez F, Hudson TJ, Weiss ST. Common functional polymorphisms in Toll-Like Receptor 4 (TLR4) are not associated with asthma or atopy-related phenotypes. *Am J Respir Crit Care Med*, 2002;166(11):1449-56.
19. **Lazarus R**, Vercelli D, Palmer L, Klimecki W, Silverman EK, Richter B, Riva A, Ramoni M, Martinez FD, Weiss ST, Kwiatkowski DJ. Single Nucleotide Polymorphisms in Innate Immunity Genes: Abundant Variation and Potential Role in Complex Human Disease. *Immunol Rev*, 2002;190:9-25.
20. Barlow-Stewart K, Burnett L, Proos A, Howell V, Huq F, **Lazarus R**, Aizenberg H. A Genetics Screening Program for Tay-Sachs Disease and Cystic Fibrosis for Australian Jewish High School Students. *J Med Gen*, 2003;40:E45.
21. **Lazarus R**, Klimecki W, Raby B, Vercelli D, Palmer L, Kwiatkowski D, Silverman E, Brown A, Martinez F, Weiss ST. Single nucleotide polymorphisms in the Toll-like receptor 9 gene (TLR9): Frequencies, pairwise linkage disequilibrium and haplotypes in three US ethnic groups and exploratory case-control disease association studies. *Genomics*, 2003;81:85-91.
22. Raby BA, Silverman EK, **Lazarus R**, Lange C, Kwiatkowski DJ, Weiss ST. Chromosome 12q harbors multiple genetic loci related to asthma and asthma-related phenotypes. *Hum Mol Genet*, 2003;12:1973-7.
23. Sebastiani P, **Lazarus R**, Weiss ST, Kunkel LM, Kohane IS, Ramoni MF. Minimal haplotype tagging. *Proc Natl Acad Sci*, 2003;100:9900-9905.
24. Kleinman K, **Lazarus R**, Platt R. A generalized linear mixed models approach for detecting incident clusters of disease in small areas, with an application to biological terrorism. *Am J Epidemiol*, 2004;159(3):217-24.
25. Ramsey CD, **Lazarus R**, Camargo CA Jr, Weiss ST, Celedón JC. Polymorphisms in the interleukin 17F gene (IL17F) and asthma. *Genes Immunol* 2005 May; 6(3): 236-41.
26. Litonjua AA, Tantisira KG, Lake S, **Lazarus R**, Richter BG, Gabriel S, Silverman ES, Weiss ST. "Polymorphisms in signal transducer and activator of transcription 3 and lung function in asthma". *Respir Res*. 2005 Jun 3;6(1):52
27. Chen Y.C., Giovannucci E., **Lazarus R.**, Kraft P., Ketkar S., Hunter D.S. "Sequence variants of Toll-Like Receptor 4 (TLR4) and susceptibility to prostate cancer", *Cancer Research* 2005 65(24):11771-11778

28. Raby B., Van Steen K., **Lazarus R.**, Celedón J., Silverman E., Weiss S. "Eotaxin polymorphisms and serum total IgE levels in children with asthma." *Journal of Allergy and Clinical Immunology*, 2006, 117(2):298-305
29. Hersh C.P., DeMeo D.L., **Lazarus R.**, Celedón J., Raby B., Benditt J.O., Criner G., Make B., Martinez F.J., Scanlon P.D., Sciurba F.C., Utz J.P., Reilly J.J., Silverman E.K. "Genetic Association Analysis of Functional Impairment in Chronic Obstructive Pulmonary Disease." *American Journal of Respiratory and Critical Care Medicine*, 2006, doi:10.1164/rccm.200509-1452OC
30. Zeng Q.T., Goryachev S., Weiss S.T., Sordo M., Murphy S.N., **Lazarus R.** "Extracting principal diagnosis, co-morbidity and smoking status for asthma research: evaluation of a natural language processing system", *BMC Medical Informatics and Decision Making*, 2006 6:30
31. Rakovski C.S., Xu X., **Lazarus R.**, Blacker D., Laird N.M. "A New Multimarker Test for Family-Based Association Studies", *Genetic Epidemiology*, in press (accepted July 2006)
32. **Lazarus R.**, Yih K. Platt R., "Distributed data processing for public health surveillance", *BMC Public Health* 2006, 6:235

C. RESEARCH SUPPORT:

Ongoing Research Support

2 U01 HL065899-05 (Weiss)

NIH/ NHLBI

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. Overlap: None.

08/01/05 – 06/30/10

Role: Co-Investigator

UR8 / CCU115079-08 (Platt)

CDC

National Bioterrorism Syndromic Surveillance Program

02/01/05 – 01/31/07

Role: Principal Investigator (subcontract)

This work will demonstrate the feasibility of a national bioterrorism syndromic surveillance program using minimally identifiable data derived from ambulatory care records. This includes development of standards, protocols, and infrastructure for securely transmitting de-identified count data, detecting and reporting unusual geographic and temporal clusters of daily counts of syndromes that might represent the initial manifestations of a bioterrorism event. No overlap.

Number Not Available (Platt)

Centers for Excellence in Public Health Informatics (ESP)
(subcontract)

Using Electronic Medical Records to Support Core Public Health Needs

01/01/06 – 12/31/08

Role: Principal Investigator

This work will build directly on this group's accomplishments in developing the CDC National Bioterrorism Syndromic Surveillance Demonstration Project. ESP will serve three major functions: 1) Completely transparent reporting of conditions where all required information can be extracted from EMRs, 2) Initiation of reporting that triggers an automated query to clinicians if non-extractable information, and 3) Automatic responses to electronic queries by health authorities regarding demographic and treatment status of individuals with positive laboratory tests. Overlap: None

1 U54 LM008748 (Kohane)

NIH/NHLBI

Genetics and Pharmacogenetics of Common Complex Diseases

09/15/04 – 07/31/09

Role: Co-Investigator

This work will perform as part of the Informatics for Integrating Biology and the Bedside (I²B²) project and will lead to the development and implementation of methods and tools to improve genetic epidemiological and pharmacogenetic research in complex disease.
No overlap.

Ongoing Research Support (continued)

Industry Grant (Kwiatkowski)
D.W. Reynolds

07/01/03 – 06/30/08
Role: Co-Investigator

Human Genetics of Inflammation in Atherosclerosis

This work examines the hypothesis that individuals with high C-reactive protein, low cholesterol, and atherosclerotic events have genetic risk factors that predispose them to a particular set of clinical features and pursues the identification of strong single gene effects that cause high C-reactive protein, low cholesterol, and atherosclerotic event phenotype by a linkage analysis and positional cloning approach. No overlap.

1 R01 HG003646-01A1 (Lazarus)
NIH

12/01/05 – 11/30/10
Role: Principal Investigator

A Genetic Association Research Statistical Framework (BISTI)

The specific aims of this project include software support for importing experimental data and genomic annotation; methods for statistical power calculations and for selecting maximally informative subsets of markers during experimental design; methods for visualizing and summarizing experimental results; established and recently developed methods supporting statistical inference on single markers, multiple markers and on the epistatic and gene by environment interactions characteristic of these diseases and needed for emerging fields of study such as pharmacogenetics. Overlap: None.

Completed Research Support

5 U01 HL066795 (Weiss)
NHLBI

10/01/00 – 07/31/05
Role: Co-Investigator

Innate Immunity in Heart, Lung, and Blood Disease

This PGA will develop and expand genomic knowledge within the heart, lung, and blood community and to apply that knowledge to the pathobiology of asthma, chronic obstructive pulmonary disease, myocardial infarction, and deep vein thrombosis. No overlap.

5 U01 HL065899 (Weiss)
NIH/NIGMS/NHLBI

04/01/03 – 07/31/05
Role: Co-Investigator

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. No overlap.

Assignment Number Pending (Platt)

09/01/04 – 08/31/05

Massachusetts Department of Public Health (MDPH) Role: Principal Investigator (subcontract)

Public Health Preparedness and Response to Bioterrorism

The specific aims of this project include: (1) the continued development and evaluation of syndromic surveillance for the early detection of bioterrorism events; and (2) the utilization of untapped sources of data for infectious disease surveillance purposes by developing linkages to new data sources, systems, and partners. No overlap.

Withheld pursuant to exemption

(b)(6)

of the Freedom of Information Act

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2007

* End Date: 06-30-2008

Budget Period: 1

Fringe Rates need to be verified.

A. Senior/Key Person							Base Salary (\$)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits (\$)	* Funds Requested (\$)
Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role								
1. Dr.	Ross		Lazarus		PD/PI	(b)(4); (b)(6)							
2. Dr.	(b)(6)				Co-I								
3. Dr.					Co-I								
4. Dr.					Co-I								
5. Dr.					Statistician								
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:					File Name:	Mime Type:	Total Senior/Key Person			(b)(4); (b)(6)			

B. Other Personnel		* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
* Number of Personnel								
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical	(b)(4); (b)(6)				(b)(4); (b)(6)		
1	Julie Dunn, MPH - Project Manager							
1	TBN - Programmer							
1	(b)(6) BS - Research Assistant							
3	Total Number Other Personnel							
Total Salary, Wages and Fringe Benefits (A+B)							(b)(4); (b)(6)	

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

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2007

* End Date: 06-30-2008

Budget Period: 1

C. Equipment Description

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

Equipment Item

* Funds Requested (\$)

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment:

File Name:

Mime Type:

D. Travel

Funds Requested (\$)

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

1,470.00

2. Foreign Travel Costs

0.00

Total Travel Cost

1,470.00

E. Participant/Trainee Support Costs

Funds Requested (\$)

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other: 0

0.00

0 Number of Participants/Trainees

Total Participant/Trainee Support Costs

0.00

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

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2007

* End Date: 06-30-2008

Budget Period: 1

F. Other Direct Costs		Funds Requested (\$)
1. Materials and Supplies		200.00
2. Publication Costs		
3. Consultant Services		(b)(4)
4. ADP/Computer Services		(b)(4)
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. n/a		0.00
Total Other Direct Costs		320,502.00

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	432,861.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. Modified Total Direct Costs	(b)(4)		
Total Indirect Costs			(b)(4)
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)

K. * Budget Justification	File Name: 7908-HPHC__justification.pdf	Mime Type: application/pdf
	(Only attach one file.)	

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

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2008

* End Date: 06-30-2009

Budget Period: 2

A. Senior/Key Person												
Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary (\$)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits (\$)	* Funds Requested (\$)
1.	Dr.	Ross	Lazarus		PD/PI	(b)(4); (b)(6)						
2.	Dr.	Jeffery	Brown		Co-I							
3.	Dr.	Michael	Klompas		Co-I							
4.	Dr.	Richard	Platt		Co-I							
5.	Dr.	Ken	Kleinman		Statistician							
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:		Mime Type:		Total Senior/Key Person			(b)(4); (b)(6)		

B. Other Personnel											
* Number of Personnel					* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
	Post Doctoral Associates										
	Graduate Students										
	Undergraduate Students										
	Secretarial/Clerical										
1	Julie Dunn, MPH - Project Manager								(b)(4)		
1	Johanna Vostok, BS - Research Assistant										
1	TBN - Programmer										
3	Total Number Other Personnel										
Total Salary, Wages and Fringe Benefits (A+B)										(b)(4)	

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

Budget Period 2

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2008

* End Date: 06-30-2009

Budget Period: 2

C. Equipment Description

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

Equipment Item	* Funds Requested (\$)
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment:	File Name:
	Mime Type:

D. Travel

Funds Requested (\$)

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,600.00
2. Foreign Travel Costs	
Total Travel Cost	1,600.00

E. Participant/Trainee Support Costs

Funds Requested (\$)

1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
0 Number of Participants/Trainees	Total Participant/Trainee Support Costs
	0.00

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

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

* ORGANIZATIONAL DUNS: 0717210880000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Harvard Pilgrim Health Care

* Start Date: 07-01-2008

* End Date: 06-30-2009

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)
1. Materials and Supplies	205.00
2. Publication Costs	
3. Consultant Services	(b)(4)
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	(b)(4)
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	311,896.00

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	430,306.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. Modified Total Direct Costs		(b)(4)	
		Total Indirect Costs	(b)(4)
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)
	0.00

K. * Budget Justification	File Name: 7908-HPHC__justification.pdf	Mime Type: application/pdf
(Only attach one file.)		

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

Harvard Pilgrim Health Care Budget Justification

Ross Lazarus, M.B.B.S., M.P.H, Principle Investigator (2.4 calendar months - salary to be provided via Channing Laboratory Subcontract)

Dr Ross Lazarus, Director of Bioinformatics at the Channing Laboratory, will be the PI and will dedicate one day each week to this project. Dr Lazarus will provide direction and leadership for the programmer-analyst and the administrative support, meeting with the Project Manager and Programmer-analyst each week to review progress to date and to discuss and modify the work plan. He will be the technical lead for the project, providing advice on the design of the overall system, and will ensure that widely adopted infrastructure is used to enhance application transportability. He will be responsible for specifying the overall design, testing and development strategy for all application development and play a major role in application testing and implementation. Dr Lazarus will meet every 2 weeks with staff from the DACP including Drs (b)(6) and (b)(6) to ensure that work at the Channing and HVMA are proceeding in an orderly fashion, and to discuss progress and plan work on the HVMA side.

(b)(6) MD, PhD, Co-Investigator (0.36 calendar months)

Dr. (b)(6) will serve as a Co-Investigator for this project. Dr. (b)(6) is a principal investigator for the CDC-funded Center for Excellence in Public Health Informatics, a widely respected pioneer in the use of EMR for public health, and Departmental Chair in the Department of Ambulatory Care and Prevention. His extensive experience in vaccine and medication safety research and practice will provide guidance for the project, and external liaison with potential partners, to ensure that our systems are widely adopted.

(b)(6) MD, Co-Investigator (4.20 calendar months)

Dr. Klompas is an Infectious Disease physician who led the development of algorithms for the ESP project of the Center for Excellence. In collaboration with Dr. Lazarus, Dr. (b)(6) will be responsible for the design, monitoring and refinement of algorithms for detecting Adverse Events of interest.

(b)(6) MA, PhD, Co-Investigator (1.20 calendar months in Year 1, 1.08 in Year 2)

Dr. (b)(6) an experienced pharmaco-epidemiologist and collaborator on the ESP project, will contribute his substantial expertise in insurance claims data analysis related to the project.

(b)(6) ScD, Senior Statistician (0.24 calendar months in Year 1, 0.84 in Year 2)

Dr. (b)(6) specializes in repeated measures, cluster statistics, and longitudinal data analysis with a focus on infectious diseases epidemiology and bioterrorism surveillance. He will lead all data analysis activities, which will be focused on formal statistical tests to determine the impact of ESP:VAERS on the rate, completeness and accuracy of resulting VAERS reports.

(b)(6) MPH, Project Manager (1.8 calendar months in Year 1, 1.44 in Year 2)

Ms. (b)(6) will be responsible for overall project management and documentation, budget management, IRB reporting functions, and other coordinating tasks relating to the infrastructure of the project. She will supervise the research assistant and oversee all activities and communications with participating hospitals and collaborators. She will manage the design of the data collection tools, creation of operations manuals and record review guidelines, as well as maintain IRB approval, etc.

(b)(6) BS, Research Assistant (4.44 calendar months in Year 1, 4.5 in Year 2)

Ms. (b)(6) will perform administrative duties, such as IRB/HIPAA documentation and project documentation, under the supervision of the Project Manager. She will be available to the investigators for project assistance.

TBN, Programmer (1.20 calendar months in Year 1, 0.84 in Year 2)

The computer programmer will be responsible for developing and implementing the data analysis strategy for this project.

Office Supplies

Standard office supplies, toner cartridges and photocopying costs are requested to support staff working on this project, in addition to support for routine conference calls and additional correspondence between HVMA, BWH, HPHC and the MDPH.

Travel

As required within the RFP, funding is requested to allow at least two members of the project team to attend at least three days of an annual AHRQ grantee meeting in the Washington DC area.

Epic Consulting Services

Funds are requested to support necessary consulting services provided by EpicCare, the EMR vendor through which ESP:VAERS will be operationalized within the HVMA / HealthOne system.

Subcontract Costs

These costs reflect the subcontracting sites as described in the technical proposal. These costs cover the costs of the Channing Laboratory at Brigham and Women's Hospital and the Harvard Vanguard Medical Association (HVMA).

Facilities and Administration costs for HPHC are calculated at 57.4% of modified total direct costs.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		(b)(4); (b)(6)
Section B, Other Personnel		
Total Number Other Personnel	6	
Total Salary, Wages and Fringe Benefits (A+B)		
Section C, Equipment		
Section D, Travel		3,070.00
1. Domestic	3,070.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		632,398.00
1. Materials and Supplies	405.00	
2. Publication Costs	0.00	
3. Consultant Services	(b)(4)	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	(b)(4)	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		863,167.00
Section H, Indirect Costs		(b)(4)
Section I, Total Direct and Indirect Costs (G + H)		
Section J, Fee		0.00

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

* ORGANIZATIONAL DUNS: 0433974500000

* Budget Type: ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* Start Date: 07-10-2007

* End Date: 06-30-2008

Budget Period: 1

Fringe Rate
Used -

A. Senior/Key Person

Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary (\$)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits (\$)	* Funds Requested (\$)
1.	Dr.	(b)(6)			Co-I	(b)(4); (b)(6)						
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:												
File Name:						Mime Type:		Total Senior/Key Person				(b)(4); (b)(6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	TBN - Programmer						
1	Total Number Other Personnel						
							Total Salary, Wages and Fringe Benefits (A+B)
							(b)(4); (b)(6)

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

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

* **ORGANIZATIONAL DUNS:** 0433974500000

* **Budget Type:** ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* **Start Date:** 07-10-2007

* **End Date:** 06-30-2008

Budget Period: 1

C. Equipment Description

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

Equipment Item

*** Funds Requested (\$)**

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment:

File Name:

Mime Type:

D. Travel

Funds Requested (\$)

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

2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs

Funds Requested (\$)

1. Tuition/Fees/Health Insurance

2. Stipends

3. Travel

4. Subsistence

5. Other:

0 **Number of Participants/Trainees**

Total Participant/Trainee Support Costs

0.00

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

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

* ORGANIZATIONAL DUNS: 0433974500000

* Budget Type: ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* Start Date: 07-10-2007

* End Date: 06-30-2008

Budget Period: 1

F. Other Direct Costs	Funds Requested (\$)
Total Other Direct Costs	

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	53,885.00

H. Indirect Costs				
	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. Modified Direct Cost		(b)(4)		
Total Indirect Costs				(b)(4)
Cognizant Federal Agency				
(Agency Name, POC Name, and POC Phone Number)				

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)
	0.00

K. * Budget Justification	File Name: 8711-HVMA_justification.pdf	Mime Type: application/pdf
(Only attach one file.)		

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

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

* ORGANIZATIONAL DUNS: 0433974500000

* Budget Type: ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* Start Date: 07-01-2008

* End Date: 06-30-2009

Budget Period: 2

A. Senior/Key Person

Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary (\$)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits (\$)	* Funds Requested (\$)
1.	Dr.	Francis	X.	Campion	Co-I	(b)(4); (b)(6)						

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

Additional Senior Key Persons:

File Name:

Mime Type:

Total Senior/Key Person

(b)(4); (b)(6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	TBD - Senior Programmer						
1	Total Number Other Personnel						
Total Salary, Wages and Fringe Benefits (A+B)							(b)(4); (b)(6)

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

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

* **ORGANIZATIONAL DUNS:** 0433974500000

* **Budget Type:** ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* **Start Date:** 07-01-2008

* **End Date:** 06-30-2009

Budget Period: 2

C. Equipment Description		
List items and dollar amount for each item exceeding \$5,000		
Equipment Item		* Funds Requested (\$)
Total funds requested for all equipment listed in the attached file		
Total Equipment		
Additional Equipment:	File Name:	Mime Type:

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

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

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

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

* ORGANIZATIONAL DUNS: 0433974500000

* Budget Type: ☐ Project ☒ Subaward/Consortium

Enter name of Organization: HVMA

* Start Date: 07-01-2008

* End Date: 06-30-2009

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)
Total Other Direct Costs	

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	54,570.00

H. Indirect Costs				
	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. Modified Total Direct Costs		(b)(4)		
			Total Indirect Costs	(b)(4)
Cognizant Federal Agency				
(Agency Name, POC Name, and POC Phone Number)				

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)
	0.00

K. * Budget Justification	File Name: 8711-HVMA_justification.pdf	Mime Type: application/pdf
	(Only attach one file.)	

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

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		(b)(4)
Section B, Other Personnel		
Total Number Other Personnel	2	
Total Salary, Wages and Fringe Benefits (A+B)		
Section C, Equipment		
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other		
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		0.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		108,455.00
Section H, Indirect Costs		(b)(4)
Section I, Total Direct and Indirect Costs (G + H)		
Section J, Fee		0.00

**Harvard Vanguard Medical Association
Budget Justification**

PERSONNEL

(b)(6) **MD, Co-Investigator** (1.2 calendar months)

Dr. (b)(6) is a practicing physician with Harvard Vanguard Medical Associates (HVMA) and Director of Research for HVMA. He will provide leadership and experience that will play a vital role in liaison with HVMA staff, ensuring that the project serves the needs of patients and clinicians appropriately.

TBN, Senior Epic Programmer (3.2 calendar months)

The senior programmer will be responsible for programming to ensure compatibility of the ESP-VARES system and the current EMR system used across HVMA sites. They will also provide EMR-specific technical consult to members of the BWH programming team, and assist in any necessary trouble-shooting in regards to this system across participating HVMA sites.

Facilities and Administration Costs for HVMA are calculated at (b)(4) of modified total direct costs.

GRANT NUMBER: <u>1 R18 H5017045-01</u>		<u>Y</u>	<u>N</u>	<u>N/A</u>
E. FINANCIAL INFORMATION				
1. Copy of F&A agreement for Grantee & any consort. requesting F&A in file?	1. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. Cost analysis completed (budget justification, etc. adequate)? [Use "Remarks" section to explain additional information requested from Grantee. Show adjustments on budget page or explain in "Remarks."]	2. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. Updated other support obtained and acceptable for all key personnel?	3. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. Identifiable CMS Data required? If yes, ensure costs/funds are not included in award.	4. <input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
5. For Competing Continuation, appropriate FSR (___ year) reviewed & in file?	5. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
6. Any annualized salaries over Executive Level I salary cap (\$186,600 for FY2007 CR)? If Yes, complete 'multiyear personnel chart' and adjust budget accordingly.	6. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
F. AWARD				
1. Cost adjustments documented in this file and contained in the attached spreadsheet reflect: Reviewers' recommendations _____; PO's recommendations _____; GMS's administrative adjustments <input checked="" type="checkbox"/> ; None, awarded as requested _____				
2. Award negotiated with _____ on _____ and above adjustments discussed. [NOTE: if this award is < 12 months, notify the grantee that it is only eligible for a no-cost extension of up to the duration of the original project period.]	2. <input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
3. TERMS OF AWARD (TOA in bold are required on all/most NGAs): HHS policy stmt (1 st term) <u>N/A</u> ; EA or not EA <input checked="" type="checkbox"/> Cost principles <input checked="" type="checkbox"/> ; Audit Requirements <input checked="" type="checkbox"/> Other Support <input checked="" type="checkbox"/> ; Salary Cap <input checked="" type="checkbox"/> T5 application requirements <input checked="" type="checkbox"/> ; FSR Requirements <input checked="" type="checkbox"/> SF424 R&R transition <input checked="" type="checkbox"/> ; Inquiries <u>N/A</u> ; Negotiation of Award _____; Terms of Cooperation _____; Human Subjects _____; Program Income _____; Need to negotiate F&A rate _____; "Final Year" reports _____; Co-funding _____; E-NGA establishment _____; Provisional Award _____; 12-18 mo bud per interim reports _____; "Spreadsheets" term (grantee can request ss from GMS) _____; Need progress reports more frequently than annually _____; Other reason(s) _____				
4. NGA E-mail notification disabled? For: terms _____; spreadsheets _____; N/A bec. Grantee is not E-NGA enabled _____ (note: use E-NGA TOA).	4. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
5. Addresses (PI, Grantee, etc.) confirmed/updated in IMPAC II?	5. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. IMPAC II Award Worksheet Report signed by FM and in file?	6. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
G. REMARKS <u>8/15 - Approved for funding</u> <u>8/18 - Initial email sent to BO & PI</u> PREPARED BY: <u>Suzanne Holman</u> DATE: <u>9/7/07</u> Con't? <input checked="" type="checkbox"/> PAGE 2 of <u>3</u>				

GRANT NUMBER: 1-R18-H5017045-01

REMARKS - CONTINUED

- 8/20 - BO emailed and asked to get back to me by 8/31/07 instead of 8/27/07. GMS agreed.
- 8/24 - BO promised to work on request. GMS needed to know about IRB approval, Fringe Rates used; Base Salaries for all Other Personnel; Office Supplies; Travel, Consultants, Equipment & ADP Computer Services. All needed to be itemized; MTDC explained; and Other Support provided.
- 8/28 - F&A rate agreement for Brigham and Women's Hospital sent to GMS. Also, base salaries and itemized budgets and Other Support. IRB approval planned for Sept. 6.
- 8/30 - Sent email that OS was still an issue. OS sent again by BO. w/s approved by Janet Jordan.
- 8/31 - Problem just with PI's OS.
- 9/4 → 9/7 - Problem was finally fixed on 9/7.
- 9/7 - IRB approval has not occurred. GMS will print NoA with IRB restrictive term.

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2007* **End Date:** 06-30-2008**Budget Period:** 1**A. Senior/Key Person**

Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary	Cal.	Acad.	Sum.	* Requested	* Fringe	* Funds Requested (\$)
						(\$)	Months	Months	Months	Salary (\$)	Benefits (\$)	
1.	Dr.	Ross	Lazarus		PI	(b)(4); (b)(6)						
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:				File Name:		Mime Type:				Total Senior/Key Person		
										(b)(4); (b)(6)		

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical						
1	Xuanlin Hou - Programmer						
1	Jody Senter Sylvia - Information Technology Manager						
3	Total Number Other Personnel						
							Total Other Personnel
							(b)(4); (b)(6)
							Total Salary, Wages and Fringe Benefits (A+B)
							(b)(6)

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

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2007* **End Date:** 06-30-2008**Budget Period:** 1

C. Equipment Description		
List items and dollar amount for each item exceeding \$5,000		
	Equipment Item	* Funds Requested (\$)
1.	Dual processor (4 core) SunFire X4300	15,000.00
Total funds requested for all equipment listed in the attached file		
		Total Equipment 15,000.00
Additional Equipment:	File Name:	Mime Type:

D. Travel	Funds Requested (\$)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,500.00
2. Foreign Travel Costs	
Total Travel Cost	2,500.00

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2007* **End Date:** 06-30-2008**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)
1. Materials and Supplies	1,000.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	6,774.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	7,774.00

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	147,654.00

H. Indirect Costs		Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
Indirect Cost Type				
1. Modified Total Direct Costs		(b)(4)		
Total Indirect Costs				(b)(4)
Cognizant Federal Agency		DHHS, Joseph Guarnieri, (212) 264-2069		
(Agency Name, POC Name, and POC Phone Number)				

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)

K. * Budget Justification	File Name: 476-Budget_Justification_Lazarus.pdf	Mime Type: application/pdf
(Only attach one file.)		

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

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2008* **End Date:** 06-30-2009**Budget Period:** 2**A. Senior/Key Person**

Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary (\$)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits (\$)	* Funds Requested (\$)
1.	Dr.	Ross	Lazarus		PI	(b)(4); (b)(6)						
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:		Mime Type:		Total Senior/Key Person					(b)(4); (b)(6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary (\$)	* Fringe Benefits	* Funds Requested (\$)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical						
1	Jody Senter Sylvia - Programmer						
1	Xuanlin Hou - Information Technology Manager						
3	Total Number Other Personnel						
Total Other Personnel							(b)(4); (b)(6)
Total Salary, Wages and Fringe Benefits (A+B)							(b)(6)

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

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2008* **End Date:** 06-30-2009**Budget Period:** 2

C. Equipment Description		
List items and dollar amount for each item exceeding \$5,000		
Equipment Item		* Funds Requested (\$)
Total funds requested for all equipment listed in the attached file		
Total Equipment		
Additional Equipment:	File Name:	Mime Type:

D. Travel	Funds Requested (\$)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,575.00
2. Foreign Travel Costs	
Total Travel Cost	2,575.00

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2* **ORGANIZATIONAL DUNS:** 0308112690000* **Budget Type:** ☐ Project ☒ Subaward/Consortium**Enter name of Organization:** The Brigham and Women's Hospital* **Start Date:** 07-01-2008* **End Date:** 06-30-2009**Budget Period:** 2

F. Other Direct Costs		Funds Requested (\$)
1. Materials and Supplies		1,030.00
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		6,977.00
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
Total Other Direct Costs		8,007.00

G. Direct Costs	Funds Requested (\$)
Total Direct Costs (A thru F)	136,720.00

H. Indirect Costs				
	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	* Funds Requested (\$)
1. MTDC		(b)(4)		
Total Indirect Costs				(b)(4)
Cognizant Federal Agency		DHHS, Joseph Guarnieri, (212) 264-2069		
(Agency Name, POC Name, and POC Phone Number)				

I. Total Direct and Indirect Costs	Funds Requested (\$)
Total Direct and Indirect Institutional Costs (G + H)	(b)(4)

J. Fee	Funds Requested (\$)

K. * Budget Justification	File Name: 476-Budget_Justification_Lazarus.pdf Mime Type: application/pdf
	(Only attach one file.)

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

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		(b)(4); (b)(6)
Section B, Other Personnel		
Total Number Other Personnel	6	
Total Salary, Wages and Fringe Benefits (A+B)		15,000.00
Section C, Equipment		5,075.00
Section D, Travel		
1. Domestic	5,075.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		15,781.00
Section F, Other Direct Costs		
1. Materials and Supplies	2,030.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services	13,751.00	
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		284,374.00
Section H, Indirect Costs		(b)(4)
Section I, Total Direct and Indirect Costs (G + H)		
Section J, Fee		

BUDGET JUSTIFICATION	ASSIGNMENT NUMBER N/A
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Adverse Event Ambulatory Care Surveillance System

Channing Laboratory, Brigham and Women's Hospital

Personnel

Fringe benefits are calculated at 35.0% for professionals (M.D.s, Ph.D.s, and other doctoral level degree holders, excluding post-doctoral fellows), 31.0% for non-professionals (non-doctoral degree holders), and 24.0% for post-doctoral fellows. Salaries are adjusted each year at 3.0% above the previous year's figures.

Professional Personnel

Ross Lazarus, M.B.B.S., M.P.H., Principle Investigator, 2.4 calendar months.

Dr Ross Lazarus, Director of Bioinformatics at the Channing Laboratory, will be the PI and will dedicate one day each week to this project. Dr Lazarus will provide direction and leadership for the programmer-analyst and the administrative support, meeting with the Project Manager and Programmer-analyst each week to review progress to date and to discuss and modify the work plan. He will be the technical lead for the project, providing advice on the design of the overall system, and will ensure that widely adopted infrastructure is used to enhance application transportability. He will be responsible for specifying the overall design, testing and development strategy for all application development and play a major role in application testing and implementation. Dr Lazarus will meet every 2 weeks with staff from the DACP including Drs Klompas and Campion to ensure that work at the Channing and HVMA are proceeding in an orderly fashion, and to discuss progress and plan work on the HVMA side.

Non Professional Personnel

(b)(6) **Laboratory Manager**, 0.30 calendar months. (b)(6) Information Technology Manager, at the Channing Laboratory will be the Project Manager for the Channing subcontract, maintaining documentation and records of meetings, supervising the Programmer-analyst, ensuring that all effort and spending are within the budget for the project, and advising on technical aspects of the project as needed. She will join the weekly meeting with Dr Lazarus and the Programmer-analyst and will meet with the Programmer-analyst as needed for supervision of the project.

(b)(6) **Programmer**, 8.0 calendar months effort. (b)(6) will be the programmer-analyst, working under the supervision of the Project manager and the technical direction of the PI. Ms (b)(6) will be responsible for detailed documentation and system design, database design, programming of the application software and web application, and all testing. Ms (b)(6) will meet regularly each week with Dr Lazarus and Ms (b)(6) and individually with other team members as needed, and will spend time as needed to maintain the application server installed at HVMA using a workstation in the DACP.

(b)(6) **Administrative Assistant**, 0.30 calendar months. Mr. (b)(6) will assist Dr. Lazarus and the Study Team with preparation of human subject protocols, annual reviews, and manuscript preparation. He will prepare progress reports and facilitate communication between the laboratories involved in the project.

Equipment

1. A dual processor (4 core) SunFire X4300 with 10TB of disk storage will be required for the project. This will be purchased and initially configured at the Channing Laboratory and installed behind the HVMA firewall in the secured HVMA computer facility.

Total Equipment (Year 1): \$15,000

Supplies

1. Funds in amount of \$1000 are requested annually with 3% increase to cover the office and computer supplies necessary to conduct the study.

Total Supplies (Year 1): \$1,000

Travel

1. Dr. Lazarus will travel to the scientific meeting. Per-trip cost will be \$2,500 with 3% annual increase.

Total Travel Expenses (Year 1): \$2,500

Other Expenses – Computing

The Channing Laboratory computer facility provides access to two components: UNIX based system for data storage and analysis and; System support for desktop network of PCs. Charges for each component is based on FTE effort on each grant. Channing Laboratory computing infrastructure will be used for all development and testing, and Channing web server and web services infrastructure will provide the primary site for software and documentation distribution. All current research grants at the Channing pay a fixed annual contribution per FTE to the computing budget. The fee has been a component of every NIH grant submitted from the Channing over the past 5 years, and has always been accepted by NIH reviewers to date. The Channing Laboratory computer facility provides access to Linux and Solaris based servers for centralized authentication, email, security, audit, automated backup and recovery, web servers, data storage and analysis. The Channing computer system includes a grid of more than 20 Sun servers and blades (including two 4 CPU and one 8 core main servers) and a 12TB SAN, three Oracle (2 production and 1 development) Sunfire v440 and Sun Enterprise 450 servers, and a 32 CPU Linux cluster, together with duplicated failover Sun server redirectors and multiple redundant backend web servers. Each individual study contributes to the overall costs of the UNIX based data storage and analysis component. Current annual costs for system administration, data storage and processing including software licenses (such as the EMC Legato backup suite, Veritas Foundation Suite, SAS and SPlus statistical packages), security auditing and administration, automated backup systems, software programming and hardware maintenance, and planned replacement of obsolete hardware are more than \$600,000 for approximately 250 users in 35 projects in areas of chronic disease epidemiology, respiratory epidemiology, pharmacoepidemiology, and statistics. Each study is charged on an as per FTE basis at a rate of \$4,013 per FTE. $0.917 \text{ FTE} @ 4,013 = \$3,679$. The annual increase of 3% has been applied for the following year.

PC Desktop system support: The Channing computer system operates a network of desktop computers for investigators to use in their daily work activities. Services supported include word processing, graphical presentations, and spreadsheets. The costs of maintaining the network include software licenses, service contracts on desktops and printers and personnel to maintain the hardware as well as replacement of obsolete equipment. Annual costs are \$300,000 serving 90 users within the Channing Laboratory at 181 Longwood Avenue. Each study is charged on a per FTE basis at a rate of \$3,377 located at 181 Longwood Avenue. $0.917 \text{ FTE} @ 3,377 = \$3,096$. The annual increase of 3% has been applied for the following year.

Total Other Expenses – Computing (Year 1): \$6,774

PHS 398 Cover Page Supplement

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

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

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

* New Investigator? ☒ No ☐ YesDegrees:

2. Human Subjects

Clinical Trial? ☒ No ☐ Yes* Agency-Defined Phase III Clinical Trial? ☐ No ☐ Yes

3. Applicant Organization Contact

Person to be contacted on matters involving this application

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

* Phone Number: Fax Number:
Email:

* Title:

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

PHS 398 Cover Page Supplement

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

4. Human Embryonic Stem Cells

* Does the proposed project involve human embryonic stem cells?

☒ No ☐ Yes

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

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

PHS 398 Research Plan**1. Application Type:**

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

*Type of Application:

☒ New ☐ Resubmission ☐ Renewal ☐ Continuation ☐ Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

- | | |
|---|---|
| 1. Introduction to Application
(for RESUBMISSION or REVISION only) | <input type="text"/> |
| 2. Specific Aims | <input type="text" value="5629-ESP_VAERS_Specific_Aims.pdf"/> |
| 3. Background and Significance | <input type="text" value="3128-ESP_VAERS_Background.pdf"/> |
| 4. Preliminary Studies / Progress Report | <input type="text" value="5365-ESP_VAERS_Preliminary_Studies.pdf"/> |
| 5. Research Design and Methods | <input type="text" value="6185-ESP_VAERS_Research_Design.pdf"/> |
| 6. Inclusion Enrollment Report | <input type="text"/> |
| 7. Progress Report Publication List | <input type="text"/> |

Human Subjects Sections

Attachments 8-11 apply only when you have answered "yes" to the question "are human subjects involved" on the R&R Other Project Information Form. In this case, attachments 8-11 may be required, and you are encouraged to consult the Application guide instructions and/or the specific Funding Opportunity Announcement to determine which sections must be submitted with this application.

- | | |
|---------------------------------------|---|
| 8. Protection of Human Subjects | <input type="text" value="122-ESP_VAERS_HumanSubjects_Protection.pdf"/> |
| 9. Inclusion of Women and Minorities | <input type="text" value="6606-ESP_VAERS_Women_Minorities.pdf"/> |
| 10. Targeted/Planned Enrollment Table | <input type="text" value="6377-ESP_VAERS_Targeted_enrollment.pdf"/> |
| 11. Inclusion of Children | <input type="text" value="4686-ESP_VAERS_Inclusion_Children.pdf"/> |

Other Research Plan Sections

- | | |
|---|---|
| 12. Vertebrate Animals | <input type="text"/> |
| 13. Select Agent Research | <input type="text"/> |
| 14. Multiple PI Leadership | <input type="text"/> |
| 15. Consortium/Contractual Arrangements | <input type="text"/> |
| 16. Letters of Support | <input type="text" value="4730-ESP_VAERS_LOS.pdf"/> |
| 17. Resource Sharing Plan(s) | <input type="text"/> |

18. Appendix

Attachments

IntroductionToApplication_attDataGroup0

File Name**Mime Type**

SpecificAims_attDataGroup0

File Name

5629-ESP_VAERS_Specific_Aims.pdf

Mime Type

application/pdf

BackgroundSignificance_attDataGroup0

File Name

3128-ESP_VAERS_Background.pdf

Mime Type

application/pdf

ProgressReport_attDataGroup0

File Name

5365-ESP_VAERS_Preliminary_Studies.pdf

Mime Type

application/pdf

ResearchDesignMethods_attDataGroup0

File Name

6185-ESP_VAERS_Research_Design.pdf

Mime Type

application/pdf

InclusionEnrollmentReport_attDataGroup0

File Name**Mime Type**

ProgressReportPublicationList_attDataGroup0

File Name**Mime Type**

ProtectionOfHumanSubjects_attDataGroup0

File Name

122-ESP_VAERS_HumanSubjects_Protection.pdf

Mime Type

application/pdf

InclusionOfWomenAndMinorities_attDataGroup0

File Name

6606-ESP_VAERS_Women_Minoroties.pdf

Mime Type

application/pdf

TargetedPlannedEnrollmentTable_attDataGroup0

File Name

6377-ESP_VAERS_Targeted_enrollment.pdf

Mime Type

application/pdf

InclusionOfChildren_attDataGroup0

File Name

4686-ESP_VAERS_Inclusion_Children.pdf

Mime Type

application/pdf

VertebrateAnimals_attDataGroup0

File Name**Mime Type**

SelectAgentResearch_attDataGroup0

File Name**Mime Type**

MultiplePILeadershipPlan_attDataGroup0

File Name**Mime Type**

ConsortiumContractualArrangements_attDataGroup0

File Name**Mime Type**

LettersOfSupport_attDataGroup0

File Name

4730-ESP_VAERS_LOS.pdf

Mime Type

application/pdf

ResourceSharingPlans_attDataGroup0

File Name	Mime Type
Appendix	
File Name	Mime Type
184-AppendixIII_Vaccine_Safety_Publication.pdf	application/pdf
1735-AppendixI_Funding_Preferences.pdf	application/pdf
9955-AppendixII_ESP_Disease_Surveillance_Manuscript.pdf	application/pdf
2008-AppendixIV_Letters_of_Support.pdf	application/pdf

A. SPECIFIC AIMS

Routine vaccination is a cornerstone of modern primary preventative care in the ambulatory setting, and has dramatically decreased many serious diseases among Americans of all ages, races, and genders.¹ However, vaccines occasionally cause important adverse effects that are only discovered after widespread use. The continued public health success of comprehensive vaccination efforts depends on building and maintaining public confidence in vaccine safety. Public and professional trust in vaccination programs can be assured with rigorous and complete post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) have created the Vaccine Adverse Event Reporting System (VAERS) so clinicians and patients can report possible adverse events. VAERS relies on clinician initiative to spontaneously document suspected adverse events. There are few incentives for busy clinicians, and no widespread, automated mechanisms supporting uniform and complete detection and electronic reporting of adverse events to VAERS. Consequently, the utility of VAERS data is diminished by substantial physician under-reporting, and by incomplete documentation of reported adverse event cases.²

The Institute of Medicine and the Agency for Healthcare Research and Quality have advocated the use of health information technology to improve the monitoring and detection of adverse events in healthcare.^{3,4} Electronic medical record (EMR) systems offer an exciting and increasingly available opportunity for low cost access to comprehensive clinical data, clinician interfaces, and electronic communications, potentially supporting the automated identification and reporting of adverse events. **Our goal is to create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.** We will achieve this by extending the Electronic Support for Public health (ESP) system recently deployed by our group. ESP is a portable, generalizable, integrated information system that scans electronic ambulatory encounter data each day, to identify patients with notifiable diseases, and electronically report cases to public health authorities. We will modify ESP to perform near real-time safety monitoring and electronic VAERS reporting for all vaccines administered in an ambulatory care setting. Specifically, we propose:

Aim 1: Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.

Aim 2: Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).

Aim 3: Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

Aim 4: Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

This proposal builds on our group's nationally recognized leadership in querying electronic health databases for vaccine and medication adverse events, and in the design and implementation of large-scale electronic systems for near real-time public health surveillance using ambulatory care EMR data. The development of adverse event detection algorithms will be informed by our experience as one of CDC's eight national Vaccine Safety Datalink sites. We will also draw on our expertise as an AHRQ and FDA sponsored Center for Education and Research in Therapeutics with a proven track record in querying managed care databases to explore medication adverse effects. The robust electronic surveillance and reporting system we create will be built on our currently deployed ESP framework. ESP:VAERS will be implemented and tested in collaboration with the same multi-site, multi-specialty medical practice with over 500,000 patients, where ESP is already deployed. The health care information systems we propose will lead to better measurement of the safety profile of vaccines, and improve available measures of the quality and safety of existing and future vaccination programs in health care.

B. BACKGROUND & SIGNIFICANCE

B.1. Importance of vaccines and their safety for public health

Vaccines have been instrumental in the near elimination of diseases that once afflicted hundreds of thousands of Americans.⁵ The United States has vigorously pursued a program of universal immunizations for more than fifty years. In 2005, more than 95% of children entering kindergarten had been immunized against at least ten different pathogens⁶ and the list of disease targets is constantly expanding. Within the last year alone, the Advisory Committee on Immunization Practices broadened its recommendations to include three new vaccines (rotavirus, human papillomavirus, and *Herpes zoster*) and broader use of existing vaccines (varicella acellular pertussis, and influenza).^{1,6,7} More than 200 million vaccine doses are administered each year.⁸ Public health preparedness for the control of potential pandemic outbreaks of rapidly evolving organisms such as H5N1 influenza, hinges on a capacity to quickly deliver millions of doses of new vaccines.⁹

While vaccination forms a cornerstone of modern public health by preventing many of the once common and dangerous infectious diseases, there is a small risk of adverse effects after vaccination. Since the majority of vaccines are given to healthy children and adolescents, there is a widespread and reasonable expectation that the risks of routine vaccination should be as small as possible. The continued quality and effectiveness of immunization programs depends heavily on public and professional confidence in vaccine safety. Accurate safety profiles of vaccines are crucial to guiding patients, parents, clinicians and policy makers on the rational approval, marketing, and use of specific vaccines.

B.2 Vaccine safety and adverse events

New medicines and vaccines undergo rigorous, mandatory evaluation by the Food and Drug Administration (FDA) prior to approval. These studies are typically limited to selected, healthy subjects and have relatively low statistical power for detecting very rare adverse effects. Consequently, the true safety and adverse effect risk profile of vaccines only becomes apparent after FDA approval, when the agent is administered to large numbers of patients. Unexpected adverse effects of vaccines that only came to light after broad post-approval deployment have included intussusception associated with rhesus-human rotavirus vaccine, myopericarditis associated with smallpox vaccine, alopecia associated with hepatitis B vaccine, and seventh cranial nerve palsies associated with intranasal influenza vaccine.¹⁰⁻¹³ In addition, since vaccines are biological agents there is constant risk of manufacturing batch specific variability that may affect large numbers of patients exposed to a specific lot.^{14,15} **The fundamental importance of robust safety surveillance systems to detect post-marketing adverse effects of vaccines arises as a consequence of their widespread use, their central importance to public health, and well-recognized limitations of pre-approval trials.** Current systems for gathering, integrating, and studying post-marketing safety data are insufficient to fully satisfy the needs of patients, parents, clinicians and policy makers .

B.2.1 Passive surveillance systems for vaccine related adverse events: The CDC and FDA rely heavily on passive surveillance systems to identify unsuspected adverse effects of approved products. The Vaccine Adverse Event Reporting System (VAERS) accepts spontaneous reports from clinicians, pharmaceutical companies, and the public. The companion system for drugs is AERS, the Adverse Event Reporting System. In addition to mandatory reporting of specific events by manufacturers, VAERS and AERS rely upon clinician initiative to spontaneously report possible adverse events via telephone, fax, or internet notification form either directly to VAERS/AERS, or to manufacturers who are required to report on their behalf. Since there are few incentives for busy physicians to submit these reports, information capture by VAERS and AERS is idiosyncratic and case documentation may be incomplete.² CDC officials estimate that the completeness of reporting varies widely. Well-described, serious events such as paralytic disease after oral polio vaccine might be reported more than 60% of the time,¹⁶ while fewer than 5% of cases of less commonly known, but nonetheless severe events, such as idiopathic thrombocytopenia after measles-mumps-rubella vaccine or hypotonic-hyporesponsive episodes after diphtheria-tetanus-pertussis vaccine¹⁶ might be reported. For drugs, officials estimate that only about 1% of adverse reactions are reported to AERS.¹⁷ Moreover, many VAERS reports are poorly documented particularly with regard to vaccine lot number and precise date of administration. The lack of reliable and complete adverse effect case

descriptions and counts is mirrored by paucity of data on the precise number of patients exposed to each vaccine, making it impossible to reliably estimate adverse event incidence rates from the currently available passive surveillance systems.

B.2.2 Surveillance using ambulatory care data: Large medical practices using electronic medical record (EMR) systems offer an exciting and relatively low-cost opportunity to improve adverse event surveillance by automated processing of coded EMR data, with electronic tools to systematically monitor a defined population. The Institute of Medicine has specifically advocated that the FDA take advantage of large automated healthcare databases to improve post-marketing surveillance of pharmaceuticals.³ CDC's recognition of the value of large databases covering defined population led to the creation of the Vaccine Safety Datalink (VSD) project in 1990.¹⁸ Our research group has participated in the VSD since 2000. VSD investigators prospectively gather vaccination and medical encounter information using a common protocol from eight health maintenance organizations distributed around the country, including our own. Data collected by VSD is regularly surveyed for associations between vaccines and a shortlist of defined, serious adverse events as well as to explore novel vaccine safety hypotheses.² VSD analyses have helped confirm the improved safety profile of the new acellular pertussis vaccine and the low likelihood of an association between the meningococcal conjugate vaccine and Guillain-Barré syndrome.^{15,19} However, VSD is an extremely resource intensive research collaboration that is never intended to be extended beyond the 3% of the U.S. population that it currently covers. VSD uses a combination of claims and EMR data but most other extant U.S.-based large databases that have been used to evaluate safety hypotheses primarily rely upon insurance claims.

B.3 Opportunities to improve adverse event surveillance

We hypothesize that EMR systems offer three potential synergies for existing passive and claims based systems: 1) EMRs have access to much richer data streams, including vital signs and laboratory test results, 2) EMR data streams are updated in real-time, permitting more timely adverse event detection compared to claims databases, and 3) EMR systems can query the relevant care provider, regarding specific events in near-real time, adding further richness and specificity to adverse event detection. As with claims data, EMR systems servicing defined populations can record population level vaccine exposure in order to enable calculation of adverse event incidence densities, rather than simply counts. EMR systems are in increasingly widespread use, particularly in larger group practices, so a generalizable and portable automated adverse event surveillance approach based on existing EMR systems offers the possibility of quickly ramping up surveillance for adverse effects to millions of exposed patients at relatively low marginal cost.

B.3.1 Frameworks and components to support EMR based adverse event surveillance: Vaccine safety surveillance would be greatly strengthened by automated systems that monitor coded EMR data from ambulatory encounters in near real-time in order to detect possible vaccine adverse events, seek clinician confirmation, and facilitate immediate electronic reporting to VAERS. Such systems will need vaccine adverse event detection algorithms such as those developed by our group for VSD, and algorithms developed by other investigators to survey ambulatory encounter electronic medical records for possible medication adverse events.^{20,21} By fusing electronic algorithms to detect possible cases with clinician review, it may be possible to overcome the two major limitations of extant, purely automated adverse event detection models: limited capability to capture idiosyncratic events, and the high false positive rate of purely rule-based systems.²¹⁻²³ A web-based semi-automated work-flow system that facilitates a clinician review and approval step before transmission of case details, has recently been deployed in a notifiable disease reporting system described below (see C.2.2). Convenient, automated support systems are likely to substantially improve clinician case reporting rates as well as report completeness, and report reliability. Electronic messaging is a core requirement for large scale, systematic data collection, and CDC is currently working to introduce electronic VAERS messaging to the nation. CDC contractors have created an infrastructure for VAERS to accept electronic reports. Currently, one pilot site is working to develop EMR interfaces to send VAERS reports. The CDC's Immunization Safety Office is enthusiastic about leveraging our group's experience creating and securely transmitting electronic health messages in order to refine the development, implementation, and activation of their new capacity to accept electronic reports (see letter of support from Dr. Robert Davis of CDC).

B.3.2 Frameworks and components available for EMR based adverse event surveillance: Our proposal builds on the work of our CDC-supported Center of Excellence in Public Health Informatics (CDC P01 CD000260-02). The Electronic Support for Public health (ESP)²⁴ system already created by our group provides an existing, stable EMR data base, regularly refreshed with data extracted from a commercial EMR system (see Figure 1). All ambulatory care records are analysed for cases of notifiable communicable diseases and secure electronic reporting of cases to public health authorities is currently operating. The ESP architecture already implements many desirable features required for vaccine safety surveillance described above, as it efficiently loads, and consolidates, all relevant ambulatory care EMR encounter data into an independent database. The purpose of this database is to remove additional load from the host EMR system, analyze encounter data for conditions of interest, and then securely communicates its findings to an external authority. The ESP system is currently deployed in a large multi-specialty physician practice with over 400,000 patients, but has been specifically designed to work with any EMR system capable of exporting demographic, diagnostic, laboratory, and prescription records in an agreed format on a regular basis (see Figure 1).

Our group has also built a prototype computer-assisted vaccine adverse event elicited surveillance system for pediatric vaccines. The existing system electronically flags every child who is given a vaccine. If the child presents for further care within 14 days of immunization and is given a diagnostic code that is not on an exclusion list of benign diagnoses, the EMR automatically queries the child's clinicians as to whether they think the new presenting condition could be related to the child's recent vaccine. Clinicians who answer in the affirmative are invited to submit a pre-populated paper report to VAERS via facsimile.²⁵ We plan to transfer this work to the ESP platform in order to: 1) expand the coverage of the system to include all vaccines administered rather than just routine pediatric vaccines, 2) increase the sophistication of adverse event detection by incorporating more data streams for analysis, 3) make the vaccine adverse event detection and reporting generalizable beyond the proprietary EMR system in which the prototype currently resides, and 4) take advantage of ESP's ability to construct and send HL7 messages so as to begin automatic electronic reporting to VAERS.

B.4 Summary

The urgent need to develop comprehensive and automated methods to improve systematic surveillance and reporting of adverse effects from vaccines is widely recognized. Adding value to existing ambulatory care EMR data streams offers a practical and efficient means to survey large numbers patients. Expanding the algorithms of the existing ESP system in order to perform adverse event monitoring after every vaccination can be achieved at relatively low marginal cost, and could be quickly generalised to multiple large group practices to provide national coverage of millions of patients in a relatively short time frame. Creating a fully functional EMR based system that transparently identifies vaccine adverse events, prompts clinician input for those that require individual judgment, and automatically submits secure electronic reports when indicated, would be a substantial contribution to the safety of vaccination in ambulatory care. Testing such a system's performance against the CDC's Vaccine Safety Datalink, the nation's gold standard vaccine adverse event surveillance system, would provide objective benchmarks and validation. While it may seem ambitious to propose that such a system could be fully operational by the end of the grant period, a substantial portion of the infrastructure including the EMR data interface, database backend, case management web application prototype, and HL7 libraries, is already deployed. Attached letters of support demonstrate widespread recognition of the value and importance of the work that we propose, willingness and commitment to collaborate with us, and confidence in our capacity to deliver. The ESP design described below is adaptable to any modern EMR system, so if our deliverables are freely available, flexible, and reliable, the systems we propose are likely to be in sustainable, widespread use, and under ongoing development long after the end of the requested funding period.

C. PRELIMINARY STUDIES

The capacity of the team assembled for this project to successfully undertake the research proposed is illustrated using specific examples and preliminary data from current research collaborations. Relevant research in drug safety and vaccine adverse event detection using large claims-based databases, syndromic surveillance and reporting using ambulatory care EMR data, notifiable disease detection and reporting using ambulatory care EMR data, and computer-assisted clinician-endorsed reporting of vaccine adverse events within an EMR system are described. This is followed by a summary of some specific technical issues underlying the large scale, transportable software systems we developed to support these systems, highlighting specific examples of standards, informatics, engineering, methods and tools.

C.1 Research and collaborations on drug and vaccine safety using integrated EMR and claims based databases

C.1.1 Center for Education and Research in Therapeutics (CERT)

The Center for Research and Therapeutics (CERT) is a national initiative authorized by the FDA Modernization Act of 1997 and administered by the Agency for Healthcare Research and Quality (AHRQ) in consultation with FDA to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research. The HMO Research Network (HMORN) is a consortium of 15 healthcare delivery systems that work collaboratively to conduct research in the public interest.^{26,27} The HMORN CERT was established in 2000 under the leadership of ESP:VAERS co-investigator Dr. Richard Platt, in order to conduct population-based investigations and activities relevant to therapeutics in accordance with the national CERT program. Our center has substantial expertise conducting pharmacoepidemiologic and drug safety research using administrative claims and medical encounter data.^{15,19,28-33} The HMORN CERT holds an FDA contract to perform post-marketing drug safety and utilization studies to support regulatory decision-making (FDA HHSF223200510010C) and has close ties to the CDC Vaccine Safety Datalink (VSD – see section C.1.2), for which Dr. Platt is site-PI at Harvard. The HMORN CERT and VSD are currently collaborating to adapt the VSD rapid cycle surveillance methods from vaccines to drugs (see Section C.1.3). In addition, the FDA and CDC are jointly funding work on the development of capacity for near real-time evaluation for serious rare adverse reactions after influenza vaccination with the goal of supporting regulatory decision making if/when a pandemic influenza vaccine becomes widely used. This work was recently highlighted by the FDA in its response to the Institute of Medicine's 2006 report on improving drug safety throughout a product's lifecycle.³⁴ The HMO Research Network CERT fully endorses the development of ESP:VAERS (see letter of support from HMO Research Network and National CERTs).

C.1.2 Vaccine Safety Datalink Project

CDC initiated the Vaccine Safety Datalink Project (VSD) in 1990 to improve the nation's assessment of vaccine safety through active surveillance.¹⁸ VSD uses automated, large linked databases from 8 health maintenance organizations (HMO) or multispecialty provider groups covering approximately 3% of the US population to evaluate vaccine safety. VSD's population-based system allows for follow up investigation of VAERS signals via rigorous epidemiological studies, and for calculation of incidence rates of adverse events. Four VSD sites include data from all age groups. The other four sites, including ours, only include data on children less than 18 years of age. Harvard joined the VSD in 2000 under the leadership of Dr. Richard Platt as Principal Investigator. Dr. Platt is a co-investigator on this ESP:VAERS proposal. Harvard's VSD data files include automated demographic, vaccination, and inpatient and outpatient encounter data, enrolment, and claims data from 1991-2005 on 223,263 children ages 0-17 years that have been part of the Harvard Vanguard Medical Associates (HVMA) population. HVMA was a precursor organization to HealthOne, the system in which ESP:VAERS will be developed and tested. Our site has led VSD studies to assess adverse events related to multiple vaccinations, the impact of changes in the childhood immunization schedule on vaccination coverage, and the incidence of outpatient visits that are associated with influenza among young children, among others.³⁵⁻³⁷ We participated in a multi-site study on the association between thimerosal exposure from vaccines and neuro-developmental outcomes in children, and we currently participate in a case-control study of the association between thimerosal

exposure and autism spectrum disorders. We are leading a study on the validation of codes used to identify seizures, and studies on the safety of meningococcal conjugate vaccine and influenza vaccine.

C.1.3 Rapid Cycle Analysis Vaccine Safety Surveillance

The VSD Rapid Cycle Analysis Project (RCA) builds upon the VSD infrastructure by producing weekly aggregate data files from the VSD dynamic data files, and analyzes them for pre-specified adverse outcomes by comparing observed and expected rates of serious adverse events.¹⁵ RCA utilizes maximized sequential probability ratio testing (maxSPRT) as a signal detection mechanism for serious, rare outcomes.¹⁵ This sequential analysis methodology enables near-continuous looks at the data while minimizing false positive signals. Signals detected by RCA must then be investigated further via chart review and/or systematic epidemiological studies. The Harvard VSD site serves as the rapid cycle analysis (RCA) data coordinating center, in conjunction with CDC and the Northern California Kaiser VSD site. The Harvard VSD Team currently leads an RCA study on meningococcal conjugate vaccine and supports an RCA study on rotavirus vaccine. As the RCA data coordinating center, we support protocol development and preliminary analyses for sequential analysis of new vaccines, including measles-mumps-rubella-varicella, Tdap, Herpes zoster and human papillomavirus.

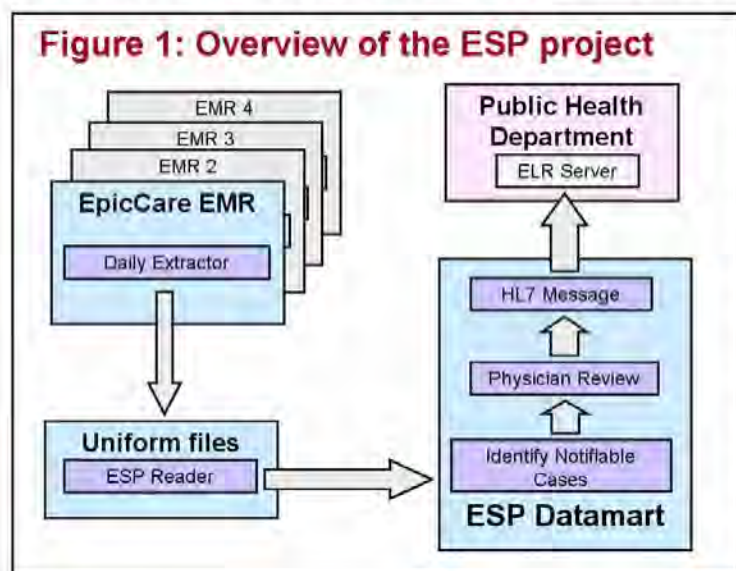
C.1.3.2. Ongoing RCA Studies: Our current RCA studies have examined outcomes potentially associated with Menactra® (meningococcal conjugate vaccine) since May 2005, and RotaTeq® (pentavalent rotavirus vaccine) since May 2006 using data from 7 of the 8 VSD sites. Pre-specified outcomes for the Menactra analyses are Guillain-Barré Syndrome, facial paralysis, thrombocytopenia and seizure within 42 days of vaccination in adolescents aged 11 to 17.99 years of age. Pre-specified outcomes for the RotaTeq® analyses are intussusception, gastrointestinal bleeding, meningitis and encephalitis, myocarditis, gram-negative sepsis and seizure within 30 days of vaccination in children from 4 to 52 weeks of age. To date, we have analyzed 144,432 visits following Menactra® vaccination and 20,511 visits following RotaTeq® vaccination. Preliminary analyses have not detected a signal indicating an increased risk for any of the pre-specified outcomes for either of these vaccines.

C.1.3.3 Expansion of RCA to assess drug safety: synergies between CERT and RCA: HMORN CERT investigators, including Drs. Platt and Brown, are working with the VSD investigators to develop and implement a prospective drug safety surveillance system based on the sequential testing methodology (maxSPRT) developed by VSD for rapid cycle vaccine safety surveillance.^{19,38,39} To test the methodology in drug safety, we first identified the key drug safety methodological and implementation challenges beyond those encountered in vaccine safety studies and then performed a retrospective evaluation of maxSPRT to identify known adverse drug reactions under conditions similar to real-time monitoring. The key challenges in conducting drug safety surveillance beyond those in vaccine safety include the need to define patterns of medication use (e.g., new, chronic, intermittent); allowance for misclassification of exposure due to suboptimal adherence to therapy; and adjustment for comorbidities, disease severity, and concurrent medication use. In addition, because drugs treat specific conditions, the pool of users for a new medication is limited and unique and users may differ from non-users in important ways, both observable and nonobservable. Other complications of drug safety studies include use of a drug for multiple indications, off-label drug use, and potential differences between early and late adopters. Our experience in addressing these unique drug safety problems will be crucial in supporting our long-term plans to expand ESP:VAERS to incorporate drug safety surveillance.

C.1.3.4 ESP:VAERS and RCA synergies: We envision ESP:VAERS as complementing rather than replacing RCA. RCA has proven to be a valuable tool to assess vaccine safety routinely and in near real-time, and includes claims data that are not available in ESP:VAERS, covers a larger population than ESP:VAERS, and is geared to population level systematic surveillance rather than creating individual case reports. RCA does not, however, obtain clinicians' assessments of individual events or supplemental information from them as ESP:VAERS will be able to do while their recollection of the case is still fresh. In addition, ESP:VAERS includes identifiable health information and real-time messaging capability to enable immediate submission of case reports to VAERS. Finally, ESP:VAERS is designed to be portable and easily scalable to new practice sites whereas the VSD activities are limited to its current eight centers.

C.2 Research in syndrome, notifiable disease, and vaccine adverse event detection and reporting using EMR systems

C.2.1 Notifiable disease surveillance in EMR and secure reporting



Electronic medical record Support for Public health (ESP)²⁴ is the EMR monitoring system we have created for notifiable disease detection and reporting in Massachusetts as part of our CDC supported Center of Excellence in Public Health Informatics. This system receives a daily extract from the unified EMR system of HealthOne, a 500,000 patient multi-specialty practice in the greater Boston area, as shown in Figure 1. The daily extract includes comprehensive data from every patient encounter at HealthOne over the preceding 24 hours including patient demographics, visit type, vital signs, diagnostic codes, laboratory orders and results, medication prescriptions, immunization details, and pregnancy status. As indicated in the top left quadrant of Figure 1, any EMR system able to regularly extract data as text

files in the required format for the current ESP Reader could be used in place of the HealthOne EpicCare EMR system. ESP analyzes this data for evidence of notifiable diseases that clinicians are mandated by state law to report to the Department of Public Health. Taking the case of Pelvic Inflammatory Disease (PID) as an example, ESP scans extracted EMR data for encounters with an ICD9 code for PID and a positive genetic probe for *Chlamydia trachomatis* within a 30-day window. When a case is detected, ESP assembles an HL7 message and securely transmits it to the Massachusetts Department of Public Health. The message contains the patient's name and demographics, the detected condition, treatment prescribed, pregnancy status, and clinical symptoms.

As illustrated in Figure 1, ESP is decoupled from the host EMR system and runs on a separate server, allowing for the following advantages: 1) ESP is readily adapted to different host EMR systems, making it portable, 2) the analytical computational load is offloaded from the clinical EMR system to minimize interfering with routine operation, and 3) we are able to modify our disease detection algorithms without requiring EMR platform-specific programming or asking over-burdened health-plan IT staff to regularly implement new algorithms on our behalf. The database is secured inside the health plan IT infrastructure, ensuring that the same confidentiality and proprietary protections apply to these data as to all other clinical information they protect.

Table C.2 Comparison of Chlamydia, gonorrhea, and PID cases retrospectively identified by ESP algorithms versus manual reports from HVMA, 2000-2004.

	Manual Reports	ESP Algorithms
Chlamydia	1,629	1,824
Gonorrhea	502	531
Pelvic Inflammatory Disease	1	74

At present, ESP detects and reports cases of chlamydia, gonorrhea, and PID. The algorithms used to detect these diseases were validated by applying them to a five year historical cohort of data from HVMA (a subset of HealthOne patients). Case detection by ESP

was compared to the number of cases manually reported to the Massachusetts Department of Public Health during the same historical period. Despite the fact that HVMA employed dedicated infection control personnel to find and report notifiable diseases during the test period, ESP algorithms consistently detected more cases than had been manually reported (see Table C.2). This was especially striking in the case of

PID, a disease that can be very challenging to diagnose, and hence difficult for non-clinician infection control practitioners to identify for reporting.

C.2.2 Distributed syndromic surveillance from EMR: The CDC funded National Bioterrorism Syndromic Surveillance Program (NBSSP), led by Drs. Platt and Lazarus, demonstrated the potential utility of ambulatory care EMR for real-time public health surveillance in 2001 (CDC: UR8/CCU115079-08/2).⁴²⁻⁴⁵ The project gathers data from 6 health plans and large group practices across 5 states in collaboration with local health departments to detect localized disease outbreaks and to facilitate rapid public health authority follow-up of clusters of illness suggestive of a potential event of public health importance.⁴⁰ Data are extracted nightly on patient encounters occurring during the previous 24 hours at each of the participating data provider sites from a variety of EMR systems, and processed with software written, supported and distributed by the data center. Office visits or telephone encounters with diagnostic codes corresponding to syndromes of interest are counted; repeat encounters are excluded. Only de-identified daily counts of syndromes by zip code are transferred to the data center where they are statistically analyzed for unusual clustering by using a model-adjusted SaTScan.⁴¹ The CDC PHIN-MS secure messaging software is used to transfer counts from each data provider to the data center.⁴² Statistical results and the count data are available to authenticated users on a secured website maintained by the data center (<http://btsurveillance.org>).

NBSSP is a distributed system, where identifiable, patient-level information stays at the originating health-care organization unless required by public health authorities, thus minimizing the risk of inadvertent disclosure of protected health information.⁴³ If a cluster of syndrome counts surpasses a threshold of statistical aberration chosen by the corresponding public health department, an electronic alert is sent. In Massachusetts, when an agreed threshold has been exceeded, the system automatically sends an electronic alert to the state Health Alert Network, where it is automatically routed to the appropriate public health officials. The system is flexible, allowing for changes in participating organizations, syndrome definitions, and alert thresholds. The statistical results and automated alerts are usable by local and national health agencies and the software has been built using freely distributable software infrastructure that can run on both Linux and Windows operating systems. Both CDC and state/local health authorities are full partners in the development, implementation, and evaluation of this system.

C.2.3 Computer-assisted, clinician-verified vaccine adverse event surveillance integrated into a proprietary EMR system: As part of the VSD, we initiated an elicited surveillance and reporting system of pediatric vaccine adverse events within the HealthOne EMR EpicCare system.²⁵ The purpose of this system was to flag potential vaccine adverse events for the clinician and to facilitate reporting of these events to VAERS. We designed this system to overcome some of the limitations of passive reporting, including underreporting and incomplete reports. Our system improves upon completely automated reporting systems in that it asks clinicians to consider conditions as potential vaccine adverse events, and facilitates reporting by providing clinicians with the option to have a pre-populated report faxed to VAERS.

C.2.3.1 Implementation: When a clinician enters a diagnosis into the EMR during an office visit or telephone encounter within 14 days following any pediatric vaccination, an alert appears within the EMR. It presents information on the vaccine and the outcome to the clinician, allows the clinician to provide additional details, and simplifies reporting by allowing the clinician to request that a report be submitted to VAERS. If the clinician chooses to submit a report, an electronic file is automatically sent to a designated HealthOne clinician who prints it and submits it via facsimile to VAERS. In order to capture unanticipated types of adverse reactions, alerts were presented for all diagnoses unless they appear on an "exclusion list" of ICD-9 diagnosis codes that we categorized as being relatively common and/or very unlikely to be vaccine adverse events. We included relatively common diagnoses on this list to minimize the number of alerts sent to clinicians.

C.2.3.2 Preliminary Data: During five months, a total of 33,420 pediatric vaccinations were administered during 14,466 encounters. There were 5,914 follow-up contacts by vaccines within 14 days of the vaccination visits; 686 (11.6%) generated an alert. Clinicians submitted VAERS reports for 23 of these (0.69 per 1,000 immunizations). Our system has proven useful within HealthOne as clinicians have continued to use it as part of routine practice. However, it is based in a proprietary EMR system, and thus is not easily

portable to other EMR systems at other institutions. In addition, we utilized an electronic-to-paper method to avoid the resource investment that would have been required to establish a PHIN-MS compliant messaging system that would allow fully electronic reporting from the EMR to VAERS.

C.3 Informatics supporting data abstraction, analysis, and communication of EMR data for public health surveillance and reporting

Our team has a long track record of successful collaboration, as indicated in the major informatics achievements mentioned above, and the PI has wide experience integrating and supervising component activities and of collaboration with co-investigators. This will ensure that the end results are not only sound from a health services and epidemiological perspective, but also well engineered in terms of design, systems architecture and software quality. In this section we describe some technical aspects of recent relevant and successful large scale projects. We then we highlight specific examples of each of the major specific informatics activities proposed in our specific aims, including ambulatory care EMR data access and data manipulation, developing, testing and implementing case identification algorithms, secure messaging, and adoption of interoperable standards.

C.3.1 Successful, large scale, collaborative informatics deployments:

The ESP system described above (see C.2.1), integrates a scaleable database, case management workflow application web server, and messaging applications, which are deployed on a pre-configured server provided by the Channing informatics group, led by Dr. Lazarus. The server is installed in the HealthOne computing facility, and is fully protected by their internet firewall and physical security. The server was installed in December 2006, and ESP has been operating continuously since that time, loading and analysing new data as it becomes available from EpicCare (see Figure 1). During development and testing, we loaded more than 7 months of daily HealthOne EMR data into the ESP database. Based on these records, we project approximately 360,000 immunization records, 4,400,000 encounter records, 1,700,000 prescription records, and more than 20,000,000 laboratory results each year, from about 413,000 individual patients. Source code licensed under the LGPL is freely available from the project web site⁴⁴ and we are collaborating with the Massachusetts eHealth Collaborative in order to plan testing and deployment to their member sites.

The NBSSP,^{43,45-47} described in more detail in C.2.2 above, is an ongoing research collaboration between our group and 6 health plan sites. The system was designed to automatically identify statistical evidence of unusual spatial and temporal clusters of cases of predefined syndromes. Results are presented on a secured web site, and alerts are securely transmitted to appropriate public health officials automatically.

Dr. Lazarus is the PI on an NIH funded R01 research grant (1R01HG003646-01A1) that is currently developing an open-source, community supported, application development project called Rgenetics. Source code for software and applications produced by the project is available through the BioConductor source code repository (see <http://bioconductor.org>), and there is a SourceForge⁴⁸ site, where development archives are maintained. There are 38 registered Rgenetics project members⁴⁹ including a subset of 9 core developers, of whom about half are from the academic community. Four core developers are full time employees from a diverse mix of commercial entities, including both software and pharmaceutical companies, who permit their employees to contribute effort, presumably because they believe that supporting the Rgenetics collaboration is in their strategic commercial interests.⁵⁰ Details of these collaborations are at <http://rgenetics.org>.⁴⁹

C.3.2 Distribution and support of public health EMR based systems: ESP (see Figure 1) operates inside the health plan secured IT environment, so the risk of inadvertent disclosure of PHI from the system is entirely controlled and managed by health plan IT staff. This design feature,⁴³ based on the distributed processing model of the NBSSP, makes the system more attractive to organizations wishing to ensure that they comply fully with statutory obligations while at the same time ensuring patient privacy. Source code for the entire application licensed under the LGPL,⁵¹ is freely available for anonymous Subversion⁵² checkout to any developer wishing to obtain a copy, as documented on the project web site.⁵³

Similarly, the NBSSP uses a distributed informatics model to support statistical processing while protecting patient privacy.⁴³ Given the choice, our collaborators would likely choose not to take the risks associated with central collection of their identifiable patient data, so pre-processing is done under their

control and no central repository of PHI is needed. In a distributed model, identifiable patient data can be restricted to the secured systems of the health plan. A daily extract from the local EMR system is processed with software designed, written, tested, maintained, distributed and supported by our group, and this takes place entirely within the secured environment of the health plan. Summary (count) data are then automatically transferred to the data center web services server using CDC distributed PHIN-MS messaging software.⁴² The benefits of this approach come at the price of substantial additional technical and remote application software support challenges for the data center and research team, particularly since we are not allowed to see the remote input data our software is processing, but instead, must rely on comprehensive input error checking and reporting, while dealing with multiple sources of EMR data. We have successfully operated this model for more than 5 years.

C.3.3 Design, deployment and maintenance of software and systems for processing EMR: In the ESP system shown in Figure 1, the ESP database tables contain all of the host EMR system transactions, including all identifiable patient demographic details, all daily encounters and associated ICD9 codes, all prescription records, all laboratory orders and results, all immunization records and details of all providers involved in each episode of care. These transactions are read from text files containing copies of each transaction extracted each night from the previous day's EpicCare EMR data, and formatted into in an agreed and portable manner, as illustrated in Figure 1. Any EMR system capable of reformatting transaction data into the same standard text format could be used as the ESP data source without alteration to the current ESP Reader. At HealthOne, the ESP server checks to see if new data files are available from the HealthOne server every hour. If any new input files are found, they are downloaded, and read into MySQL database tables shown as the ESP Datamart in Figure 1. Patient data matching a set of case criteria are presented for evaluation by a physician in a secured case management workflow web application, visible only within the HealthOne firewall. The reviewer confirms that they notifiable cases or seeks further information if appropriate. This review step is optional and can be bypassed if desired.

In the NBSP^{43,45-47} described in C.2.2 above, EMR data are extracted nightly for all patient encounters that occurred during the previous 24 hours. This occurs independently at each of the participating data provider sites. This extraction occurs from a wide variety of EMR systems and was made practicable by requiring all participating data providers to produce a set of uniform files meeting standards set by the Channing data center. These uniform input files are plain ASCII text files, containing all required data items as delimited text fields in a specific order. At each remote site, these uniform files are created each night from the previous day's encounters, and then processed at the remote site into relational database tables,⁴³ using software written, supported and distributed by the data center. The entire updated source code base is always distributed with each new revision of the software that we ask remote sites to install and run, in order to allow local informatics staff to check that the code poses no potential security threat to their secured computing environments. If a cluster of syndrome counts surpasses a threshold of statistical aberration⁵⁴ chosen by the corresponding public health department, an electronic alert is sent. In Massachusetts, when an agreed threshold has been exceeded, the system automatically sends an electronic alert to the state Health Alert Network for routing to the appropriate public health officials. The statistical results and automated alerts are usable by local and national health agencies, and the software has been built using freely distributable software infrastructure, which enables the program to run on both Linux and Windows operating systems.

C.3.4 Adoption of interoperable standards: In the ESP system, notifiable disease case definitions and logic use ANSI-HITSP recommended vocabularies, including ICD9, SNOMED, CPT and LOINC⁵⁵, and ANSI-HITSP recommended security standards⁵⁶ including SSH and SSL, SOAP for web services protocols and HL7 for representing patient data transferred to the health department server, have been used. The NDBSP project uses PHIN-MS secure messaging,⁴² ANSI-HITSP recommended security standards including SSL,⁵⁶ and interoperable XML for all data transfer.

C.3.5 Development and testing of case identification algorithms: In the ESP system, cases of notifiable conditions, currently including Gonorrhoea, Chlamydia and Pelvic inflammatory disease, are automatically detected using logic based on specific diagnostic and demographic criteria. Diagnoses are defined in terms of ANSI-HITSP recommended vocabularies.⁵⁵ The NDBSP groups ICD9 diagnostic codes into like groups,

termed syndromes.^{40,45,47} Ambulatory care cases are grouped and counted in syndrome, zip code and date categories. Syndrome definitions were developed in a multi-center collaboration facilitated by the CDC.⁴⁶

C.3.6 Valid message generation: In the ESP system, physician approved cases are notified to the Massachusetts Department of Public Health directly from the health plan as HL7 messages conforming to the Massachusetts electronic laboratory reporting (ELR) HL7 specification. The configuration of these HL7 messages are based on the 1997 CDC specification,⁵⁷ with some additional extensions for this particular application (see Letter of Support from James Daniel, Massachusetts Department of Public Health). In the NDBSP system, PHIN-MS is used to securely transmit syndrome by zip code by date count data as XML messages to the data center each day for storage, statistical processing and display.⁴²

C.3.7 Maintaining security and patient privacy: Protection of patient privacy is a primary goal in all of our work. We describe below some of our innovations and experience in deploying and securing applications that deal with complex patient data, and in secure, accurate messaging using interoperable standards. All of our research collaborations involving protected health information (PHI) require prior approval, and ongoing oversight, from our Institutional Review Board (IRB) to ensure compliance with all applicable legal and other requirements and standards. All staff requiring access to patient data on our secured systems are trained in their obligations under HIPAA and other relevant legislation, and are certified to the standards required by the IRB. Our systems are designed, engineered and maintained specifically to ensure the absolute minimum possible risk of inadvertent disclosure of or unauthorized access to PHI. Our research team has particular expertise in innovative, distributed designs, avoiding any requirement to move PHI outside the health plan's secured infrastructure. The PI and all of the programmers and system administrators working under his leadership have extensive expertise in application and server security, authentication, and access control. This is particularly important for securing information exposed through highly accessible channels such as the public internet, and our systems all employ best-practice methods to ensure web application security, strong message encryption, and other techniques to ensure that these data are protected at or beyond standards consistent with ANSI-HITSP recommendations.^{55,56}

Security is a major focus and goal for all of the systems that we have deployed. The ESP project was designed to be installed and operational inside the protected computing environment of the health care provider in order to minimise the risk of PHI being exposed, and using secure, strongly encrypted end-to-end messaging systems, for the transport of identifiable PHI in HL7 sent to the health department server over the public internet. The design of our NBSSP^{43,45-47} started from the concept of a distributed system,⁴⁰ with data-center provided and supported software that performed aggregation over PHI on hardware secured within the provider's computing environment, coupled with encrypted transmission of aggregated data to the data-center, as described in more detail in C.3.2 above. We use the recommended ANSI-HITSP approach⁵⁶ for secure transmission of data over the public internet. Access to our servers is restricted to secure encrypted connections through SSH logins and we ensure that our servers do not offer insecure plain-text password based protocols such as telnet or ftp. Our operating systems and all of our application software packages are regularly patched and updated as vulnerabilities are discovered and fixed. All of our server logs are routinely monitored for unusual activity, and external internet access is restricted through professionally maintained hardware firewalls. User accounts for individuals who are no longer employees are routinely inactivated as part of the termination process and all of our professional staff are well aware of the importance of, and best practice for, protecting patient data.

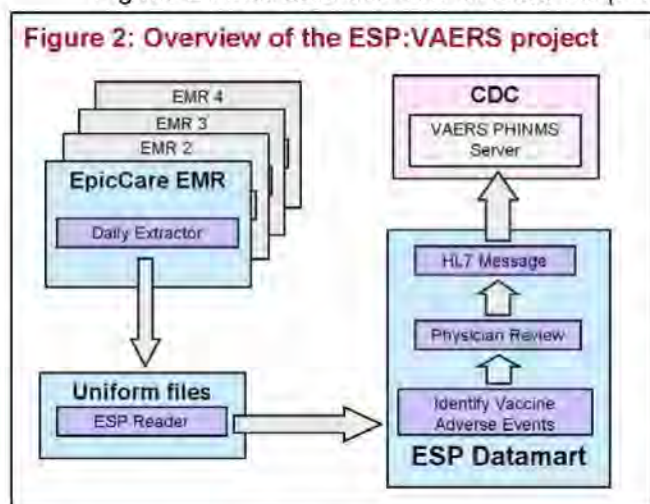
C.3.8 Workflows for clinicians: Although the ESP project was designed to optionally operate without any intervention, it offers a case management workflow system through a secured web application, visible only within the health plan firewall protected internal network. An authorized clinician can use their desktop internet browser to review notifiable disease cases before they are approved for transmission to the health department. This system was designed and prototyped by the PI (Dr. Ross Lazarus), an experienced clinician and informatician, and refined in collaboration with the target clinician users of the system. It is described in more detail on the ESP web site.⁵³

D. RESEARCH DESIGN AND METHODS

ESP will provide a large part of the infrastructure needed for our proposal, and is already deployed and available. It has been described above, thus not detailed again here, but we propose to build upon our deliverables within that existing system and data flow. Below, we describe our research plan and methods for each of our specific aims in turn, followed by a timeline illustrating how the resources we request and the activities we propose will be efficiently matched and coordinated. This will ensure that our research aims are achieved and that our deliverables are available by the end of the proposed funding period.

D.1. Identify required data elements, and deploy systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration

Figure 2 illustrates the flow of data we propose for our first two Aims. Existing and functioning ESP components are shown on the left, and Aims 1 and 2 on the right. ESP:VAERS will flag every vaccinated patient, and prospectively accumulate that patient's diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions. We will develop algorithms to detect potential adverse event cases using diagnostic codes, and we will test methods to identify prescriptions or abnormal laboratory values that might be suggestive of an adverse effect. These algorithms will be designed to seek both expected and unexpected adverse effects. When a potential adverse effect is identified it will be recorded in a registry database table, and the clinician will be contacted electronically to ask if this event should be reported to VAERS (see D.2 below). The clinician will be invited to review the case details. While viewing the patient's



data, the clinician will be offered the option to add comments and to submit an immediate electronic case report to VAERS with a mouse click, or alternatively to decline notifying, and provide a brief explanation for later evaluation. The HL7 message automatically generated for approved notifications will be a physician approved VAERS report containing all appropriate information about the patient, vaccine, lot number, date of vaccination, possible adverse effect, and date of adverse effect extracted from the ESP Datamart. Details of the existing ESP Datamart, the methods by which it is updated daily, the methods used to identify events of interest, and how HL7 messages are securely transmitted are described in section C2 above. We hypothesize that the combination of computer-assisted adverse event detection and clinician endorsed event reporting will substantially increase the number, quality, and timeliness of case reports compared to the existing spontaneous reporting system and we will test this as described in D.3 below. In addition, nesting this monitoring and reporting system within a defined patient population will permit calculation of adverse event incidence by assessing the population for total exposure to each vaccine.

D.1.1 Study setting: ESP:VAERS will be implemented at HealthOne, a multi-specialty medical group practice based in Eastern Massachusetts (see Letter of Support). HealthOne currently employs approximately 700 physicians to serve 500,000 patients at more than 18 office sites spread throughout the greater Metropolitan Boston area. The majority of HealthOne physicians are primary care internal medicine physicians or pediatricians but the network also includes physicians from every major specialty. The entire practice is served by an integrated EMR system, the EpicCare Ambulatory suite (Epic Care, Epic Systems Corporation, Verona, WI) certified by the Certification Commission for Health Information Technology.⁵⁸ See Letter of Support from Dr. Richard Marshall, the chief medical officer of HVMA on behalf of HealthOne.

D.1.2 Study Population: The entire adult and pediatric population served by HealthOne will be included in our adverse event surveillance system. HealthOne serves a full spectrum of patients that reflects the broad

diversity of Eastern Massachusetts. A recent analysis suggests that the population served by HealthOne is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the HealthOne population is under age 18.

D.1.3 Patient identification: The HealthOne unique patient identifier will be used to identify individual patients in our database. Daily patient encounter data received by ESP:VAERS will be analyzed each night to detect all patients given vaccines over the past 24 hours. Newly vaccinated patients will be entered into a registry database table for prospective follow-up for adverse reactions and for counting the total number of doses administered and patients exposed for each vaccine. Code based on the existing ESP notifiable disease case logic will be written to update the ESP:VAERS Datamart with a record of the patient, date of vaccination, vaccine type, lot number, site of administration, and responsible clinician.

D.1.4 Vaccine Adverse Event Detection Logic: Every time a patient is given a vaccine, ESP will begin 30 days of prospective surveillance for possible adverse effects. If the patient has a medical encounter (office visit, urgent care visit, telephone encounter) within the 30 day period, then ESP will analyze laboratory tests, medication prescriptions, allergy data, and ICD9 diagnostic codes associated with the encounter.

Possible adverse events will be stratified into high-suspicion and low-suspicion events. High-suspicion events will be reported to the clinician as high probability adverse reactions that will be reported to VAERS by default unless the clinician explicitly disagrees (“opt-out reporting”). Clinicians will be able to view all the information that will be reported to VAERS including patient demographics; vaccine type, date, and lot number; and suspected adverse reaction. Clinicians will be invited to add their own comments to the case report form. Clinicians that opt-out of reporting will be asked to give their reason for doing so from a coded list and optionally provide a brief text explanation.

Low-suspicion adverse events will also be presented to clinicians but as possible rather than probable events. Clinicians will be asked to comment on whether the identified event is possibly related to recent vaccination. Those who answer in the affirmative will be invited to submit an immediate electronic report to VAERS (“opt-in reporting”), so in contrast to high suspicion events, these will only be reported to VAERS with explicit clinician endorsement. All electronic reports will be formatted as HL7 and will include patient demographics, vaccine information, the adverse event, and optional clinician comments. Details of the research plan for clinician interaction, HL7 generation and messaging to VAERS are presented in D.3 below.

D.1.4.1 Abnormal biochemical tests: We will assess white blood cell count, haemoglobin, platelet count, creatinine, alanine aminotransferase, alkaline phosphatase, and bilirubin. If the patient has an abnormal value for one of these parameters then ESP will query the patient’s encounters in the 12 month period prior to vaccination to see if the abnormal value is new or not. New abnormal values will be considered high-suspicion adverse events. If the patient has no record of the specific parameter being tested before then, the new abnormal value will be considered a possible adverse effect and will be presented to the clinician for opt-out reporting as described above. If the patient has had the specific test done before within the preceding 12 months then ESP will assess the most recent historical value of the test. If the current lab value is within 50% of the most recent historical parameter then no further action will be taken. If the value in question is significantly worse (i.e. a rise in creatinine or a fall in platelets) then it will be considered a possible adverse effect and will be presented to the patient’s clinician as described above for opt-in reporting. The specific threshold for a deleterious change will be tailored to each lab test during testing to ensure that clinicians are not over-burdened.

D.1.4.2. Suggestive new prescription: If a patient is prescribed prednisone (or another steroid) within 30 days of vaccination then ESP will query each of the patient’s recorded prescriptions over the past 12 months to determine if this is a new prescription or not. If it appears that this is the patient’s first exposure to steroids within the past year then ESP will query the clinician on whether the steroid therapy is for a possible vaccine adverse effect. New prescription for prednisone will be considered a low-suspicion adverse event.

D.1.4.3 New allergy to vaccine: ESP will follow the patient’s coded allergy list for 30 days after immunization. The appearance of a new allergy to the recently administered vaccine will be considered

suggestive of an adverse effect and the clinician will be prompted for comment. New allergy to recently given vaccine will be considered a high-suspicion adverse event.

D.1.4.4 Diagnostic codes: ESP will evaluate each ICD9 diagnostic code entered on a patient within 30 days of immunization. Diagnostic codes will be divided into Black List codes, White List codes, and all other ICD9 codes (referred to here as Gray List codes). The Black List will constitute ICD9 codes consistent with the most characteristic and most serious adverse effects classically associated with vaccines such as Guillain-Barré syndrome, seizures, and thrombocytopenia. The core ICD9 codes for the Black List will be those currently being surveyed by the VSD rapid cycle analysis program (see Table D1). As with the VSD code set, we will pair each blacklist code with exclusion criteria codes for the same visit in order to decrease false positive signals from confounding conditions (for example, if a post-vaccine encounter is coded with ICD9's for both encephalitis *and* Herpes simplex instead of just encephalitis alone, the case will be discarded - see Table D.1.1). Additional Black List codes will be assigned to correspond to the consensus vaccine adverse effect case definitions published by the International Brighton Collaboration.⁵⁹ We will seek input and consensus on the full Black List of codes from the CDC Office of Immunization Safety prior to activation (see Letter of Support from Dr. Robert Davis). All Black List codes will be considered high-suspicion events that will be presented to the clinician using the “opt-out” reporting model.

White List codes will be the diagnoses of routine care that are highly unlikely to represent medication adverse effects such as periodic health examination, well baby visit, blood pressure check, routine gynaecological examination, lacerations, fractures, and others. If a White List code is detected no further action will be taken by ESP.

Gray List codes will be all codes that appear on neither the Black List nor the White List. This category is designed to detect hitherto unknown adverse effects of vaccination. The Gray List will not be literally assembled but will rather be indicative of a visit in which there was no diagnosis consistent with a classic vaccine adverse event (Black List Codes) but also no evidence that the visit was simply for routine care (White List Codes). ESP will first query the body of ICD9 diagnoses entered on the patient in the 12 months prior to vaccination to determine if the Gray List diagnosis had been entered on the patient before or not. If it appears that the diagnosis is new then the diagnosis will be treated as a evidence of a possible idiosyncratic, unexpected adverse effect of the recent vaccination. The diagnosis will be presented to the clinician as a low-probability event using the “opt-in” reporting model whereby a report will only be sent to VAERS if the clinician chooses to endorse an association between the novel diagnosis and the patient's recent vaccine.

Table D.1.1 Example adverse event Black List definitions

Condition	INCLUSIONS		EXCLUSIONS	
	ICD9	ICD9 Explanation	ICD9	ICD9 Explanation
Intussusception	543.9	Other & unspecified appendiceal disease	--	--
	560.0	Intussusception		
GI Bleeding	569.3	Hemorrhage of rectum and anus	004	Shigellosis
	578.1	Blood in stool	008	Intestinal infections due to other organisms
	578.9	Hemorrhage of GI tract, unspecified	204-208	Leukemia
			286	Coagulation defects
			287	Purpura and other hemorrhagic conditions
			558.3	Allergic gastroenteritis and colitis
			800-998	Injury and poisoning
Meningitis/encephalitis	047.8	Other specified viral meningitis	047.0	Coxsackie virus
	047.9	Unspecified viral meningitis	047.1	ECHO virus
	049.9	Unspecified non-arthropod-borne viral diseases of CNS	048	Other enterovirus diseases of central nervous system
	321.2	Meningitis due to virus not elsewhere classified	049.0-049.8	Specified non-arthropod borne viral diseases of the central nervous system
	322	Meningitis of unspecified cause	053-056	Herpes zoster, simplex, measles, rubella
	323.5	Encephalitis following immunization	320	Bacterial meningitis
	323.9	Unspecified cause of encephalitis		

Seizures	780.3	Convulsions	--	--
	779.0	Other and ill-defined conditions originating in the peri-natal period		
	333.2	Myoclonus		
	345	Epilepsy		
Myocarditis	429.0	Myocarditis, unspecified	--	
	422	Acute myocarditis		
Gram-negative sepsis	038.4	Septicaemia due to other gram-negative organisms	--	
	038.9	Unspecified septicaemia		

D.1.4.5 Validation of adverse event detection algorithms: Prior to implementation, each proposed adverse event detection algorithm will be validated by applying it to historical data. We will assess the number of suspected events per clinician per week and then do chart reviews to assess the likelihood that the identified patients did suffer an adverse event temporally related to recent vaccination. Wherever possible, we will use the case definitions developed by the Brighton Collaboration, an international effort to develop standardized case definitions for adverse events following immunization.^{2,60} This process will be designed to assure algorithm accuracy and limit the number of alerts per clinician per week to levels acceptable to clinicians.

D.1.5 Target Vaccines and Roll Out Strategy: The ESP:VAERS surveillance and reporting system will be progressively implemented to cover all vaccines administered at HealthOne. Initially, we will use a subset of pediatric vaccines for testing and development. A small number of volunteer pediatricians will be recruited at this point to trial the system prior to further deployment. Subsequently coverage will be extended include all routine childhood vaccines, and novel adolescent and adult vaccines, namely Gardasil and Zostavax. As with the pediatric vaccines, we will recruit a small number of volunteer internists to pilot and refine the system before these are rolled out into production. Finally, we will expand the system to cover all physicians and all vaccines administered in HealthOne including annual influenza vaccinations, pneumovax, and travel associated vaccinations, after a pilot and refinement test process.

D.1.5.1 Physician education: We will work with the HealthOne clinician liaison (a co-investigator on this grant) to assure maximum acceptance of ESP:VAERS by HealthOne clinicians. Prior to implementation we will test and validate our algorithms on historical data to refine algorithm accuracy and to ensure that the volume of projected alerts per clinician per week will be reasonable. The system will then be trialed with a small volunteer group of pediatricians and internists (see D.1.5). Prior to widespread deployment of ESP:VAERS we will meet with the pediatric and internal medicine service chiefs to describe our system and elicit their support. We will prepare written documentation describing how to use the system that will be emailed and posted to each clinician. We will then visit a group meeting at each office site at least once to demonstrate the system to physicians and answer questions. Finally, we will establish a dedicated email and telephone help lines for clinicians to contact a member of the research group when questions arise. Based on the positive reception of our existing pediatric vaccine elicited surveillance system (see C.2.3) where physicians elected to keep the system operational despite completion of its trial period, we anticipate ESP:VAERS will likewise be accepted by clinicians.

D.1.6 Data Collection: ESP:VAERS will keep registries of all vaccines administered throughout the practice, high suspicion events presented to clinicians as opt-out reports with annotation of which reports physicians permitted to be sent to VAERS and those that were declined, and the Gray list events presented to clinicians as opt-in reports with annotation of which events clinicians chose to report and those that they did not. Analysis of these reporting counts and patterns will be presented in D.3 below.

D.1.7. Potential Pitfalls: ESP:VAERS will be limited by the quality of its adverse event detection algorithms, the willingness of clinicians to participate in reviewing potential case reports, and the limitations of clinicians' intuition in associating vaccines with unexpected adverse events. Work done by other investigators on medication adverse event rate detection in the ambulatory setting suggested that EMR data alone failed to capture all adverse events and had generated a large number of false negative reports.^{21,23}

We anticipate that ESP:VAERS will overcome some of these difficulties by extensive use of baseline, pre-exposure data to increase the likelihood that identified events are truly novel and by implementation of an efficient mechanism for clinician review of suspected events to confirm and report, or to reject as false-positives and not report. Additionally, our initial focus on vaccines rather than medications will also reduce the problem of false positive alerts by allowing us to focus on predominantly healthy patients with relatively brief, well-defined risk periods following immunization.

Our success will also be largely contingent upon physician acceptance and participation in clinician review and reporting of suspected events. In order to promote physician acceptance we have included HealthOne physician leadership in our study design and implementation staff. Moreover, we will validate our algorithms and monitor their implementation to assure that clinicians are not “bombarded” with an excessive number of case reports. If the daily possible adverse event rates exceed a reasonable level, we will batch each clinicians’ potential cases and present them periodically, in order to minimize clinician fatigue. The success of our pilot program of physician prompting for adverse event reporting at HealthOne leads us to believe that we can also obtain sustainable clinician acceptance with ESP:VAERS.

Finally, our ability to detect unexpected, idiosyncratic adverse events will be limited by clinician’s judgment. This inclusion of clinicians’ judgment is an intended feature that will not affect our ability to perform separate analyses of all detected events without regard to the clinicians’ views.

D.1.8 Significance and sustainability: Implementation of ESP:VAERS and acceptance by clinicians, will represent a substantial advance in vaccine adverse event detection and reporting. The rapid pace of introduction of new major vaccines reminds us that vaccines remain essential and central pillars of our public health system. Vigorous post-marketing surveillance to detect rare adverse effects and characterise vaccine safety profiles under “real world” conditions is essential to assure continued public safety and broad acceptance of new vaccines. ESP:VAERS is likely to increase the number, breadth, and completeness of information reaching VAERS. Moreover, ESP:VAERS is designed to be applicable to any ambulatory care practice that uses a contemporary electronic medical record system capable of exporting data to ESP, and has ready access to the appropriate technical expertise. This creates the potential for very widespread computer-assisted clinician centered VAERS reporting in the coming years. Enriching the data streams feeding VAERS can only bolster the speed and confidence with which VAERS can evaluate current and forthcoming vaccines with a view to assuring that the public will realise the full health potential of these essential interventions.

D.2 Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS)

In this section, we describe our approach to Aim 2, as seen in Figure 2. We describe the specific technical methods we will use to develop software systems to communicate cases detected by the logic developed in Aim 1, to the appropriate clinician for review, how approved cases will be formatted as valid HL7 messages for VAERS, and how these messages will be securely transmitted to the CDC VAERS using PHIN-MS.⁴² Note that technical details about the general infrastructure and engineering approach we will use to support all our aims are provided in D.4 below.

D.2.1 Physician notification and case management: Automated, efficient electronic communication with HealthOne physicians is central to this aim. The EpicCare system user interface includes an electronic “In Basket,” where system and external messages can be stored, ready for action when the physician has time to review and deal with them. HealthOne EpicCare liaison personnel have made documentation available indicating that access to this In Basket is available to external applications through appropriately formatted HL7 messages through the EpicCare interface engine server. The deployment server will have access to the interface engine because it is within the HealthOne firewall. The physician identifier for every encounter is already available in the data stream currently provided from EpicCare EMR to our ESP application, enabling us to readily identify and locate the appropriate primary care physician for any adverse event we detect. Some implementation details will be specific to EpicCare at HealthOne, however we will ensure that all the code we develop is as flexible to as possible. The transcription HL7 message is a common mechanism in commercial EMR systems, so our implementation should prove relatively easily to adapt for interoperable EMR system HL7 interface engines. This approach can readily be adapted to use html mime-

type e-mail attachments instead of HL7 messages, for communication to clinicians in situations where direct interface with an EMR system is not feasible.

D.2.1.1 EMR application (EpicCare) “In Basket” access: We will derive code from our existing HL7 code base to prepare an HL7 transcription message on the ESP:VAERS server, containing a transcription message segment containing a MIME encoded HTML formatted notification, formatted with a header identifying the physician ID, and sent to the HealthOne HL7 interface engine, from where it will be transferred to a holding area. A time-date stamped notification will be automatically created in the designated recipient’s In Basket, by existing EpicCare infrastructure without any additional programming.

D.2.1.2 Clinician message details: The potential adverse event message sent to the patient’s physician will be formatted as HTML, so hyperlinks to the ESP:VAERS internal web application can be created by the code preparing the message. The code to do this will be based on currently deployed ESP web form generating modules. Use of a web form for communication will help to minimize the need for training and to make it quicker and more convenient for participating clinicians to respond to a potential adverse event. The message will contain a brief summary of the patient, the vaccination and the suspected adverse event. Three options will be offered to the physician in their “in-basket” message – approve and send the notification, cancel the notification, or view more details before making a decision. Choosing the hyperlink for either of the first two options will open a web form with a coded list of decision categories and space for an optional comment from the clinician. Clinicians can add further details concerning the adverse event or can give an explanation for not sending the notification. The third option will lead to a case review screen showing all available details about the suspected case, with hyperlinks for the same first two options provided in the original message. All comments and decisions will be stored in the ESP:VAERS server with the case details for evaluation, as described in D.3 below.

D.2.1.3 Clinician training, evaluation and support: Following implementation and testing by co-investigators and clinician collaborators, HealthOne physicians involved in the ESP:VAERS trial will receive a brief hands-on training session followed by test messages to ensure that they are familiar with the project and comfortable managing the notifications. Participants will be asked to complete a short, anonymous evaluation questionnaire to gather feedback such as ease-of-use and overall burden. Support for clinicians using the ESP:VAERS system will be provided through a help-line telephone number for urgent matters, and the online trouble ticket system (see D.4.4), linked at the end of every ESP:VAERS message, and on the ESP:VAERS internal web site.

D.2.2 Automated HL7 message creation: We will work with CDC and their vendors to ensure that messages we prepare conform to the required HL7 specification, and are interoperable with the vendor’s implementation. The current HL7 message specification for VAERS notifications has been provided the vendor through CDC staff assisting us in preparing our proposal. The collaboration already in place will allow us to work quickly once funding is available. Code to generate these messages will be adapted from the existing, ESP HL7 messaging code (<http://esphealth.org/trac/browser/trunk/ESP/utlis/hl7XML.py>). Since we already have working code compatible with the ELR HL7 specification,⁵⁷ we do not anticipate any major difficulties in constructing VAERS HL7 messages. A development, testing and an acceptance testing plan negotiated with our CDC collaborators will be followed to ensure that our HL7 messages are correctly formatted and interoperable with the vendor’s systems. When the system is operational, once a case is approved for transmission by the physician, details from the EMR records plus any clinician comments will be extracted from the database, formatted into an HL7 message by ESP:VAERS code, and placed in the ESP:VAERS PHIN-MS ⁴² queue for secure transmission to the CDC VAERS server.

D.2.3 PHIN-MS client implementation: CDC PHIN-MS⁴² software will be used for all VAERS transmission. A PHIN-MS client certificate will be obtained for HealthOne from the CDC vendor through our existing contacts. A PHIN-MS client compatible with the CDC vendor VAERS PHIN-MS server will be installed on the ESP:VAERS server at HealthOne, and tested in collaboration with the vendor through CDC staff partners. We anticipate that this will be straightforward, based on nearly 5 years experience we have had working with PHIN-MS software.⁴⁷ The vendor is currently installing the most recent (2.7) version of PHIN-MS for this purpose.

D.2.4 Creating messages and managing physician responses: We will build a new web application module, based on the existing ESP code base,⁴⁴ to provide the destination web forms for the hyperlinks formatted into physician electronic notifications described above. Based on existing ESP code, the web form will automatically store physician decisions, and text responses, in tables that we will add to the existing ESP database schema. These recorded decisions will drive the logic selecting adverse events for notification to the CDC, and will later be used for evaluation as described in D.3 below.

D.2.5. Sustainability: HealthOne is committed to supporting our proposal because it offers a mechanism to improve patient care through automated alerts to physicians of potential adverse events (see Letter of Support from HVMA chief medical officer Richard Marshall on behalf of HealthOne). This support will likely continue even after the end of the funding period for this proposal, since the costs of maintaining it are likely to be small. We anticipate that EMR vendors will adopt some or all of our software because it is very likely to be the first accessible module that will be freely available to use with their systems to support this important public health need. The CDC Center of Excellence in Public Health Informatics, which the current investigators lead, will provide an organizational home for continued maintenance and dissemination. Additionally, the Center for Education and Research on Therapeutics, also led by these investigators, has substantial capabilities for dissemination.

D.2.6. Potential pitfalls: Major potential risks for this aim are failure in design, failure in infrastructure, failure in collaboration, and failure in implementation. Our team is very experienced, with an established record of collaboration, and of successful HL7 development, and we have been running PHIN-MS for more than 5 years. The proposal will build and extend an existing system that already provides working database infrastructure and EMR connectivity. Existence of this functional infrastructure alone implies that the team and the proposal are at relatively low risk of misadventure in terms of deliverables for this aim. Collaboration and support is well established with CDC and is unlikely to be at risk of failure.

D.3. Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Data.

We plan two evaluations of ESP:VAERS performance. The primary evaluation (see D.3.2) will be a cluster randomized trial in which ESP:VAERS enhanced reporting will be compared to standard practice, i.e., spontaneous detection and VAERS reporting by HealthOne clinicians. The secondary evaluation (see D.3.3) will be a comparison of ESP:VAERS to suspected adverse events identified in VSD research files.

Before conducting our primary and secondary evaluations we will undertake a detailed assessment and reporting of the performance characteristics of ESP:VAERS (see D.3.1). This assessment of all ESP:VAERS elicited reports detected and reviewed by clinicians will include analysis of report severity, timing of detection, vaccinee and provider characteristics, and vaccine type(s). The number, rate of elicited reports per vaccine visit, and type of elicited reports transmitted electronically to VAERS after clinician review also will be described and contrasted with those events that clinicians elected not to submit to VAERS.

D.3.1 Performance characteristics of ESP:VAERS: Our initial evaluation will describe all elicited reports identified by ESP:VAERS and their resolution. An important aspect of this research will be to fully describe the events that are identified by ESP:VAERS and also the resolution of the clinician feedback loop. The key evaluation parameters will include:

1. *Number of elicited reports during the study period:* Total count of all reports identified by ESP:VAERS.
2. *Reports per vaccine visit and per vaccination:* Number of reports divided by the number of vaccine visits, and by individual vaccinations since a vaccine visits may include one or more vaccine doses
3. *Report severity:* Indicator of the resolution of the event as specified in the VAERS report form, including the following: emergency room visit; hospitalization; disability; life threatening condition; and death.
4. *Patient characteristics:* Age and sex.
5. *Provider characteristics:* Age, sex, specialty, location.
6. *Vaccine type(s):* Vaccine(s) associated with the report.

7. *Report timing*: Time between vaccine administration and suspected event (date of medical care associated with the suspected adverse event).
8. *Report completeness*: Given concerns over incomplete VAERS reporting² we will assess the completeness of key data elements sent electronically to VAERS, including relevant dates, demographic information, clinician resolution, diagnostic information, and clinician comments. The completeness of each data element will be calculated as the percentage of reports with missing, incomplete, or complete data.
9. *Report accuracy*: We also will assess the accuracy of the reports submitted to VAERS using a series of logic checks design to identify inconsistent data (e.g., vaccination dates after the date of the suspected adverse event, vaccine dates before birth dates). This metric will be calculated as the percentage of reports with one or more inaccurate data elements as defined by our logic checks.
10. *Report type*: Flag to identify if the report was generated from the Black or Gray list.
11. *Report resolution*: Reported electronically to VAERS or rejected by the clinician.

A parallel evaluation will describe clinician comments as elicited by ESP:VAERS regarding their reasons for requesting that an electronic VAERS report **not** be sent to FDA. The information from this evaluation will add substantially to our understanding of the performance of ESP:VAERS.

D.3.2. Primary trial evaluation: Cluster randomized trial to assess ESP:VAERS: We will implement a cluster-randomized trial (CRT) to assess the effect of ESP:VAERS on the probability of a report, and the completeness and accuracy of ESP:VAERS reporting as compared to standard passive surveillance among control group clinicians. We will use an analysis appropriate to the interventional trial design, rather than interrupted time-series or other methods suited to non-interventional experiments.

D.3.2.1 Randomization and implementation: Each of the HealthOne medical group practices will be matched into pairs. Matches will be based on features of patient population which are most likely to affect reporting: average patient income; makeup of primary care providers at the sites by panel size and years since medical training; and make-up of patient panel in terms of age and gender. The study team has experience with this type of matching (Personal Communication, Dr Ken. Kleinman). After grouping, one site in each pair will be randomly assigned to the intervention and the other will be assigned to the control group. The randomization program will be written and executed using SAS software.⁶¹ Our current pilot elicited surveillance system will be suspended at least six months before the beginning of the randomized trial. After this washout period, ESP:VAERS will be implemented as described above (Section D.1) at each intervention site. To the extent possible, clinicians at the control sites will be shielded from communication regarding the intervention.

D.3.2.2 Data sources: In collaboration with CDC (see Letter of Support from Dr. Robert Davis) we will identify all VAERS reports submitted by HealthOne clinicians for the year before randomization (pre-intervention) and during the 12 month study period (post-intervention). The data will be supplied by FDA once at the end of the study period. A preliminary review by CDC staff (Personal Communication, Robert L. Davis, Director, Immunization Safety Office, Centers for Disease Control and Prevention) of the completeness of 2006 VAERS reports from Massachusetts found substantially complete data (e.g., 90% for street address, 91% for telephone number, 88% with non-missing street, city, and zip code) for the data elements we would need in order to match VAERS reports to clinicians, indicating that this plan is feasible.

After we obtain an appropriate data-use agreement, the CDC has agreed to extract all VAERS reports submitted from Massachusetts clinicians to maximize the likelihood that the extracted listings include all HealthOne associated reports generated via ESP:VAERS or passive surveillance. Based on the data provided by the FDA we will match the VAERS reports to HealthOne clinicians and categorize the reports into 4 categories: 1) pre intervention control group; 2) pre intervention ESP:VAERS group; 3) post intervention control group; and 4) post intervention ESP:VAERS group. As a check of validity and reliability, a listing of reports sent by ESP:VAERS maintained by the study team will be compared to those identified by FDA. Using the VAERS system as the primary data source will ensure consistency in reporting across the intervention and control sites and in the pre and post periods.

D.3.2.3 Analysis plan: Our primary analysis will focus on 3 formal statistical tests to determine the impact of ESP:VAERS on the rate, completeness, and accuracy of VAERS reports. Each test will effectively be a difference-in-differences analysis based on the pre and post probability of a VAERS report per vaccine visit in the intervention and control sites. Heuristically, the test assesses whether a larger change is seen in the intervention sites than in the control sites. Technically, we will use logistic regression to conduct the formal testing, using generalized linear mixed models to account for clustering within sites.⁶² An exact logistic regression approach may be required to assess differences between ESP:VAERS and passive reporting in the completeness and on the accuracy of VAERS reports (see section D.3.1 for definitions of completeness and accuracy.). This approach will work even if the ESP:VAERS reports in the post period are 100% complete and accurate. The specific mixed model to be employed in the main analysis of report probability could be expressed as:

$$\text{logit}(p_{ij}) = \log\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_0 + \beta_1 * \text{post}_{ij} + \beta_2 * \text{int}_{ij} + \gamma * (\text{post}_{ij} * \text{int}_{ij}) + b_i \quad (1)$$

where p_{ij} is the probability that vaccine visit j at site i results in a VAERS report, post_{ij} indicates whether the visit occurred in the post period ($\text{post}_{ij} = 1$) or not ($\text{post}_{ij} = 0$), and int_{ij} denotes whether site i is an intervention site ($\text{int}_{ij} = 1$) or not ($\text{int}_{ij} = 0$). The b_i term is a random effect unique to each site and assumed to have a Normal distribution. For simplicity here we omit an index for repeat visits within subject; since few visits generate reports, nearly all subjects will not generate a report for any visit. The b_i effectively introduce correlation between the subjects at a given site, and it is this accommodation of the intracluster correlation that allows the mixed effects model to incorporate all of the individual-level data. The uniformity with respect to the outcome within person noted above means that adjusting for correlation within subject will probably not be possible. The post_{ij} effect allows for a secular difference between the pre and post periods affecting both intervention and control sites; the int_{ij} effect allows for baseline differences between the intervention and control sites. The test of interest concerns γ , the estimated effect of the intervention on the pre-post change. Under the null hypothesis it is 0; a larger value suggests a greater probability in the intervention sites during the intervention period than would be suggested by the secular change seen in the control group. In the example above, we consider only simple pre and post effects, but the model can easily include, e.g., linear trends over time within the pre and post periods and whether the linear trend is affected by the intervention. Data will be analyzed using SAS[®].⁶¹

D.3.2.4 Power and sample size considerations: Power and sample size needs for mixed models are an active area of research for statisticians. In light of this, we will use a less precise technique developed for use when sites are of equal size. Effectively, the correlation of individuals within a site reduces the actual information provided by each additional individual. Heuristically, if the correlation was perfect, knowing the result for one person would make any additional person redundant. A more typical intra-cluster correlation for doctor-diagnosed outcomes in cluster-randomized trials is no more than 0.0011.⁶³ The analysis here was generated by PASS software.⁶⁴ Assuming 20,000 vaccine visits per practice per year (see C.3.1) and a conservative intra-cluster correlation of 0.001, the smallest reporting rate difference detectable with 80% power for a 5% error level and a control group report rate probability of 0.00005 (1 per 20,000 vaccine visits) is 0.0011 (22 per 20,000 visits). With a more plausible intra-class correlation of 0.0001 and a control group report rate of 0.00005 (1 per 20,000 vaccine visits), a rate of 0.00025 (5 per 20,000 visits) can be detected with 80% power. Note that results are not very sensitive to the number of vaccine visits per site; with only 5,000 visits per site, smallest detectable differences increase by only about 0.0001 per vaccine visit. The above discussion considers a test for comparing two proportions; this is the most complex analysis for which power assessment is readily available. The study design calls for a pre-post analysis. The power in pre-post analyses typically exceeds that of simple differences, since variability between sites with respect to starting level is removed by the pre-post difference. More technically, the random intercept in the mixed model absorbs variability that would attenuate power in the post-only differences assessment above. The net result of this is that the above power assessment is conservative. Power should be greater for the model discussed in section D.3.2.4 than for the simple differences presented here. Power assessment for exact logistic regression is more complex and will not be essayed here for the secondary outcomes.

D.3.3 Compare ESP:VAERS elicited reports to those identified by the CDC's Vaccine Safety Datalink:

The goal of this comparison is to test the accuracy of the ESP:VAERS data files and the implementation of its logic against the permanent, research quality, data files created by the Vaccine Safety Datalink. These VSD files are considered a national gold standard for vaccine safety research; their creation entails extensive data cleaning and quality checks, including cross-checks against similar files created by other VSD sites. ESP:VAERS' performance characteristics will be tested against that of the CDC's Vaccine Safety Datalink, the nation's gold standard vaccine adverse event surveillance system. Due to the time-lag in the availability of VSD data, this evaluation will be conducted retrospectively in 2008 using data from 2006 and 2007. To generate the required counts of ESP:VAERS elicited reports, ESP:VAERS algorithms will be applied retrospectively to data collected from June 2006 through December 2007 at all HealthOne sites. This will provide a listing of all ESP:VAERS potential adverse events that would have been generated during that time. The count of suspected vaccine adverse events from VSD will be based on VSD annual files. The 2007 file will be available in late 2008. The ESP:VAERS potential events to events identified by having a separate VSD programmer apply the ESP:VAERS logic to the VSD data. The ESP:VAERS and VSD data will be based on the same patient population and original clinical files, thereby providing a perfect testing group to assess the performance of the ESP:VAERS system. The specific comparisons are described below.

D.3.3.1 Comparison of the rate of adverse event identification: This assessment will compare the rate of potential adverse events per vaccine visit identified by the ESP:VAERS and VSD algorithms. This measure will be the same one used in the CRT and descriptive analyses. The results will be described overall and stratified by vaccine type and diagnosis (e.g., seizure).

D.3.3.2 Concordance of identified events, ESP:VAERS versus VSD: Concordance tables for each outcome will be constructed to illustrate any differences in the two approaches. Findings will be reported descriptively. If the evaluation identifies potential adverse events that were detected by VSD but not detected by ESP:VAERS we will conduct a comprehensive review to determine why the event was not identified by the system.

D.4 Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

Our final specific aim requires that the deliverables we produce to achieve our specific aims 1 and 2 are interoperable, widely accessible, and useful to other groups working in this domain. To facilitate this, we will ensure that there are as few practical and legal barriers as possible that might prevent or inhibit other groups, including commercial entities, from taking advantage of our work. In addition, interoperable standards, high levels of security, and solid engineering will be used. Finally, our work will be made well known to potential users through appropriate partnerships, widely published, and readily accessible to potential collaborators. Our goal is to make it as easy as possible for interested and technically competent groups to reuse, adapt, and improve our work, requiring at most modest programmer effort to reconfigure our HealthOne EpicCare adapter for each new EMR system. Under the LGPL, source code for any of these adapters distributed by any vendor, must be shared. We hope and anticipate that these distributors would become collaborators, writing a library of adapters for a wide range of EMR systems, and supporting a community of users, as is the case with BioConductor^{65,66} and more recently Rgenetics,⁴⁹ and many other vigorous open-source projects such as the thousands based at SourceForge.⁴⁸ For practical reasons, we specifically do not propose resources to support naive end users. Although installing, configuring and running the code we make available will always be possible, it will never be trivial, so substantial in-house or purchased support will always be required. Large health plan and large group practices with consolidated EMR systems offer the best return on any given installation investment.

D.4.1 Engineering, operating system and software infrastructure: Our deliverables will be developed, and will run efficiently, on freely distributable software infrastructure using interoperable standards because proprietary engineering standards or costly software infrastructure would be a barrier to widespread adoption and interoperability. The infrastructure components we will use (detailed below) are widely used and freely available for both Windows and Linux operating systems. They were used in our successful

development and deployment of the ESP system, so they are familiar to our team and are known to work well. We will build upon the existing ESP code base since it is mature, and provides an established mechanism for maintaining and querying an independent database of all daily EMR transactions.

For reasons of security, performance, and cost, our development environment and the recommended operating system for server deployment is the freely distributable Linux operating system – in particular, CentOS⁶⁷ v4.4. However, at all stages during development, at least one developer will regularly test our code using the Windows operating system on a workstation desktop.

The CDC Public Health Information Messaging System⁴² (PHIN-MS) package will be used for secure HL7 message transmission. The Python language (<http://python.org>) will be used for most general programming, with Java (<http://java.sun.com/>) components as needed for PHIN-MS interfaces and messaging. Developers will regularly check in code and documentation changes to our current Subversion⁵² infrastructure, used to manage all of our source code development and for versioning and release management.⁴⁴ All system automation will be deployed using timed batch (cron) jobs, with automated forwarding of error logs to our system administrator for attention in case of problems arising at the remote site. The web application framework we will use is Django (<http://djangoproject.com>), written mostly in Python and providing an Object Relational Mapper (ORM) interface that works transparently with most of the widely used relational database management systems (RDBMS), including freely distributable PostgreSQL, SQLite and MySQL, together with the commercial Oracle package if needed for extremely large and high volume environments. Our preferred web server is Apache v2 (<http://apache.org>). For medium to high volume sites, of the order of tens to hundreds of millions of records each year such as HealthOne (see C.4.1), the RDBMS we will use for development and recommend for production deployment is MySQL v4.2 (<http://www.mysql.com/>), since in our experience with ESP, it works very well at these scales on commodity hardware. SQLite (<http://www.sqlite.org/>) is an embedded, “zero configuration” RDBMS. In developing the ESP system, our tests demonstrated that SQLite provides satisfactory performance to and beyond 10 million total records on recent high-end Windows desktop machines, offering a relatively simple, and low cost solution, for small practices.

D.4.2 Licensing: We will use freely distributable software infrastructure. All code we write will be distributed under the Lesser General Public License,⁵¹ chosen because it is compatible with commercial exploitation under specific conditions. The terms of the license under which this is permitted essentially oblige anyone distributing derived products (defined in the text of the license) to make all bug fixes and improvements available as source code. We have had considerable success with this arrangement in creating viable and mutually beneficial partnerships with commercial organizations such as those between the Rgenetics⁴⁹ project and commercial vendors such as InforSense⁵⁰ described in C.3.1 above.

D.4.3 Source code distribution: Subversion⁵² is a widely adopted as an interoperable standard for anonymous source code distribution in community supported projects, including Bioconductor,⁶⁵ Rgenetics⁴⁹ and all projects hosted at SourceForge.⁴⁸ Source code versioning will be managed in our Subversion repository,⁵² from where it will be freely available for download in the same way as is currently available for the ESP project⁴⁴ for any developer with access to Subversion⁵² software, packaged with almost all Linux installations and freely available for Windows workstations.⁶⁸

D.4.4 Support for distributed software: Although we will have limited resources available to provide support outside HealthOne, we will use the Trac (<http://trac.edgewall.org/>) software package to provide a publicly accessible resource in order to manage software source code and documentation distribution, trouble tickets, and announcements for any collaborators working with our source code. In the longer term, a community of users can use this resource to collaborate and provide additional mechanisms for support, as is the case with the BioConductor^{65,66} and more recently Rgenetics⁴⁹ open-source communities. We will extend the existing ESP public support infrastructure⁴⁴ to include ESP:VAERS as an optional module, authorizing collaborating developers to post and manage trouble tickets and commit code and documentation changes.

D.4.5 Partnerships and partners: In addition to our established collaborations with HealthOne (see Letter of Support from Dr. Richard Marshall), external collaborations are vital to the success of our project. Technical contacts, vendor contacts, and essential documentation enabling us to plan and prepare this

proposal were kindly made available by officials from the CDC (see Letter of Support from Dr. Robert Davis). With their help, the current HL7 specification being used in the pilot project in Michigan has been provided to us by the vendor involved in that project, and we have established direct communication with appropriate technical contacts to work with us when we design, test, and deploy our HL7 VAERS reports and PHIN-MS messaging systems as described above.

D.4.6 Standards and Interoperability: All data structures, engineering and infrastructure will be to applicable ANSI-HITSP standards where these have been proposed⁵⁵ or ratified. For example, our security infrastructure will rely on SSH and SSL.⁵⁶ HL7 will be used where appropriate for patient and related data exchange.⁵⁵ Where specific ANSI-HITSP recommendations or endorsed standards are not available, we will use widely used open standards supported by the open-source communities that provide the software infrastructure we have chosen.

D.4.7 Publication and dissemination: We will publish details and results from our proposal in peer-reviewed literature, in order to ensure that other potential users of our work are made aware of its availability. Installation and configuration will require appropriate technical expertise, and access to the host EMR, so our targets for dissemination will primarily be commercial vendors and IT groups who support clinician users of EMR systems. We will ensure that these groups are aware of the location and accessibility of the source code and documentation on the project web site that will be added to the ESP site,⁵³ and Subversion repositories⁵² as described in D.4.4 above. We intend specifically to work with EMR vendors to facilitate their linking ESP:VAERS to the their products. The specific license we will release under permits commercial entities to use and improve our code, but ensures that this is an equitable arrangement, so all users benefit.

D.4.8 Potential pitfalls: Risk of technical failure for this proposal are relatively low since the team has a long track record of technical success. Similarly, we have worked together as a team for nearly 6 years and have a longstanding relationship with CDC staff, so failure of collaboration seems unlikely to occur. Whether any of the major EMR system or other vendors will collaborate is not clear at this stage. Although our deliverables will be readily available, vendor uptake cannot be guaranteed. Our proposal will lower the price of entry into a potentially expanding service and support market. As described above in the Rgenetics project for example, vendors are willing to work with the LGPL licensed collaborative model that we propose, particularly if it is in their strategic interests.⁵⁰ A working system such as the one we will create and distribute would obviate the substantial business risk associated with software development, so it seems reasonable to be optimistic and assume that they may choose to collaborate.

D.4.9 Significance: We have chosen well tested and well supported freely redistributable infrastructure components that can be readily transported to a wide variety of informatics environments. Our proposed dissemination web presence will be an extension of the current ESP site.⁵³ All of these components, and our informatics approaches, have been developed, and proven to work well, in similar large-scale systems that we have already deployed. We will ensure that our deliverables function reliably, comply with all relevant informatics standards to enhance interoperability, provide appropriate protection of patient privacy, are licensed and available in a manner that facilitates broad partnerships, and are built to best practice design and engineering standards. Achieving these aims would lead to very great gains in the quality and completeness of vaccine safety data, enabling ongoing improvement in the safety of vaccination programs, and lead to improved quality of health care.

D.5 Timeline

D.5	ESP:VAERS Project Dissemination Timeline	Year 1 (2007 - 2008)				Year 2 (2008 - 2009)			
		July- Sept	Oct- Dec	Jan- Mar	Apr- June	July- Sept	Oct- Dec	Jan- Mar	Apr- June
D.1. identify the data elements, and refine algorithms to detect vaccine adverse events in electronic medical records from routine ambulatory encounter data									
- develop, custom tailor, validate & test AE criteria to assess these parameters for new or abnormal values that might be suggestive of an adverse effect		X	X						
- development of HL7 messages code for ESP:VAERS to ensure secure transmission to CDC via PHIN-MS			X	X					
- setup of HealthOne PHIN-MS server				X	X				
- design case-management website			X	X	X				
- begin VAERS code implementation within ESP				X	X				
- HI7 'live' message testing within selected sites, begin data collection					X				
D.2 Automatically prepare and securely submit clinician approved electronic VAERS reports									
- refine secure, automated HL7 message specifications & complete test-phase with CDC					X	X			
- implement acceptance testing for VAERS within ESP					X	X			
- development of clinician alert system within EpicCare system user interface					X	X	X		
- go-live with case management website, ongoing monitoring, data collection					X	X	X	X	X
- HealthOne clinician training, evaluation & ongoing support						X	X		
- refine rules for non-statutory AE								X	X
D.3. Evaluate the performance of ESP:VAERS									
- comprehensive evaluation of overall ESP:VAERS performance characteristics							X	X	X
- comparison of ESP:VAERS to suspected adverse events as identified by the VSD via ongoing vaccine safety research								X	X
- formal data analysis, manuscript preparation								X	X
- cluster randomized trial for comparison of passive vaccine safety surveillance by affiliated clinicians via review of VAERS reports					X	X	X	X	X
- formal data analysis, manuscript preparation									X
-distribution of HealthOne provider survey to obtain clinician & administrator system feedback								X	X
- descriptive reporting of results & incorporation of feedback into final version of ESP:VAERS								X	X
D.4 Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.									
- widespread dissemination of ESP:VAERS offered through MA-SHARE									X
- establish and maintain accessible resource for distribution of software source code		X	X	X	X	X	X	X	X

PROTECTION OF HUMAN SUBJECTS

ESP:VAERS will receive full IRB approval via Harvard Pilgrim Healthcare, as well as through the individual IRB mechanisms at all participating institutions prior to the start of proposed research activity.

1. Risks to the subjects

A. Human Subjects Involvement and Characteristics

- Involvement of human subjects in the work outlined in the Research Design and Methods section

Patient information used in this proposal is already being collected as part of routine medical care and no interviews, questionnaires or other collection of new data from any patient is proposed.

- Characteristics of the subject population

The goal of the proposed project is to include all ethnic/racial and sex/gender categories within the scope of study. ESP:VAERS will the entire adult and pediatric population served by HealthOne will be included in our adverse event surveillance system. **However, since these cases have yet to be identified, the exact distribution of this information is unknown.** HealthOne serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by HealthOne is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the HealthOne population is under age 18.

- Criteria for inclusion or exclusion of any subpopulation

Inclusion will involve receiving a vaccine during the study period. Those excluded from this study will be individuals who do NOT receive a vaccine during the study period. In collaboration with Federal authorities, we will conduct a trial of vaccine safety reporting mechanisms, but this will involve randomization of physician reporting methods for vaccine adverse events, and will have no direct impact on usual medical care for individual patients that may, or may not, be included in reports to the appropriate Federal authorities.

- Rationale for the involvement of vulnerable populations, such as fetuses, neonates, pregnant women, children, or others who may be considered

We are confident that our IRB will find that the proposed research presents a reasonable opportunity to further the understanding, prevention, or alleviation of serious vaccination adverse events affecting the health or welfare of children and other vulnerable populations.

In addition, all of our research protocols will be approved and our research will be overseen by the Institutional Review Boards of the relevant institutions, and we will follow all established regulatory and other procedures including HIPAA, required to ensure patient privacy.

B. Sources of Materials

- Describe the research material obtained from living human subjects in the form of specimens, records, or data.

Our research will be conducted using data already present within existing patient electronic medical records (EMR's) only. **No direct patient contact and no interventions to alter usual medical care are proposed in any of our research.** Patient information used in this proposal is already being collected as part of routine medical care and no interviews, questionnaires or other collection of new data from any patient is proposed.

- Describe any data that will be recorded on the human subjects involved in the project, including when specimens, records, or data are collected and whether new material or data will need to be collected specifically for this proposed research project

Those patients who have been given a vaccine within the study period will be entered into a registry database table for prospective follow-up for adverse reactions and for counting the total number of doses administered. If one of these vaccinated patients has a medical encounter (office visit, urgent care visit, telephone encounter) within the 30 day period after the vaccine has been administered, then ESP:VAERS will analyze laboratory tests, medication prescriptions, allergy data, and ICD9 diagnostic codes associated with the encounter.

- Linkages to subjects, and indicate who will have access to subject identities

All identifiable patient information will be retained under the control of HealthOne staff already responsible for securing electronic medical records. Data on study subjects will be handled by authorized individuals operating under strict confidentiality protocols. These staff-persons are familiar with the procedures for handling PHI, as they must adhere to them in their routine handling of patient data for other purposes and have all signed active confidentiality agreements. Only specific staff needing access to identifiable data for record review purposes will be authorized viewers of this information, and all staff work under a strict set of rules established to protect patient confidentiality. Strong encryption will be used to protect patient privacy when transmitting electronic notification of individual patient adverse events to the appropriate Federal authorities. In addition, all computing involving patient-level data is performed on a secure password and firewall protected system.

C. Potential Risks

At most, minimal risks to the subjects are envisioned. The only risk, that of revelation of PHI, is expected to be no greater than it is under current VAERS reporting practices and is reasonable compared to the importance of improving vaccine safety and other adverse event reporting and surveillance.

2. ADEQUACY OF PROTECTION AGAINST RISKS

Security measures are in place at HPHC and HealthOne and the Channing Laboratory at Brigham & Women's Hospital in order to protect patient privacy. The proposed work, intended to improve reporting and surveillance, includes robust physical, programming, and personnel-training security measures, making unintentional disclosure of PHI highly unlikely.

A. Recruitment and Informed Consent

No subjects will be recruited, as all study population data is routinely collected as collected as part of the patients electronic medical record (EMR) .

B. Protection Against Risk

As previously stated, all identifiable patient information will be retained under the control of HealthOne staff already responsible for securing electronic medical records. Data on study subjects will be handled by authorized individuals operating under strict confidentiality protocols. These staff-persons are familiar with the procedures for handling PHI, as they must adhere to them in their routine handling of patient data for other purposes and have all signed active confidentiality agreements. Only specific staff needing access to identifiable data for record review purposes will be authorized viewers of this information, and all staff work under a strict set of rules established to protect patient confidentiality. Strong encryption will be used to protect patient privacy when transmitting electronic notification of individual patient adverse events to the appropriate Federal authorities. In addition, all computing involving patient-level data is performed on a secure password and firewall protected system.

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

Given that the CDC will be the recipient of all VAERS reports resulting from the proposed research and has explicitly stated support for collaboration with this study, we believe that an increase in the volume, timeliness, and accuracy of these reports will serve to only further benefit the ultimate mission of VAERS reporting as it pertains to overall public health & safety.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Inclusion of Women and Minorities

The entire adult and pediatric population served by HealthOne will be included in our vaccine adverse event surveillance system, ESP:VAERS. However, since these cases (all patients receiving a vaccine within the study period) have yet to be identified, the exact distribution of this information is unknown.

HealthOne serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by HealthOne is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the HealthOne population is under age 18.

Targeted/Planned Enrollment Table

This report format should NOT be used for data collection from study participants.

Study Title: Electronic Support for Public health: Vaccine Adverse Event Reporting System (ESP:VAERS)

Not yet determined – dependent on distribution of HealthOne patients receiving a

Total Planned Enrollment: vaccine during the study period.

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

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

Inclusion of Children

Any child receiving a vaccination during the ESP:VAERS study period will be included within the study population. Those children excluded from this study will be individuals who do NOT receive a vaccine during the study period since there is no risk of an adverse reaction resulting from a vaccination.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

February 2, 2007

Ross Lazarus, MD, MBBS, MPH
Department of Ambulatory Care
and Prevention
Harvard Medical School
Boston, MA

Dear Dr. Lazarus,

This letter confirms the strong interest and enthusiastic support of the Center for Disease Control's Immunization Safety Office (ISO) for your proposed project, ESP-VAERS "Electronic Support for Public Health - Vaccine Adverse Event Reporting System". Your intention to create software to prospectively identify potential vaccine adverse effects in electronic medical records, and to facilitate clinicians' evaluation and electronic reporting to VAERS, will constitute an important, exciting, and long-awaited advance in the field of vaccine safety. The capability you hope to create will serve both individual clinicians as well as national efforts.

I see several important strengths to your work. First, I am pleased to see that you plan to study the effects of an advance in technology by using a randomized clinical trial. This study design will provide the strongest evidence to clinicians and policy makers alike as to the benefit of this system. Second, by and large this system will be transparent to clinicians – that is, it will not impede the clinician's day-to-day clinical practice. However, in the event that there is a suspect vaccine adverse event, clinicians can submit reports with very little effort (in fact, this system will likely save time compared with the more cumbersome system currently in place). Third, the ability of this system to gather (in the background, using available electronic data), more complete information about the vaccinated individuals, and the ability of the system to provide data on the entire population of persons who were immunized, will be important enhancements to current reporting systems. Fourth and finally, the fact that your software will be open source and is designed work in a wide range of software environments will create the right conditions for its widespread adoption. All of these are important additions to your earlier work on elicited surveillance "reference here".

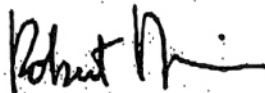
It is important for me to note that conducting this work in clinical practices that currently participate in the CDC's Vaccine Safety Datalink (VSD), (which the Immunization Safety Office leads), means there will be substantial opportunities for the VSD to collaborate in ensuring the success of this new research. Your plan to use VSD information as the gold standard for assessing the performance characteristics of your software is one excellent example of this collaboration, and I expect there will be others.

In addition to encouraging further alignment of the VSD to facilitate your work, I will be having VAERS staff work with you to address the wide range of technical issues that are

sure to arise, to develop standards governing which events should be reported, and to support the randomized clinical trial that you will conduct to evaluate the impact of this system.

Finally, I will mention that it makes great sense to me to build this work on the existing programs and activities of Harvard's CDC-supported Center of Excellence in Public Health Informatics. Combining the accumulated resources and expertise of the Center of Excellence and VSD will allow you to make great strides quickly.

Sincerely yours,



Robert L. Davis, MD, MPH
Director, Immunization Safety Office
Centers for Disease Prevention and Control



Centers for
Education &
Research on
Therapeutics

a program of the Agency for Healthcare Research and Quality

February 2, 2007

Ross Lazarus, MBBS, MPH, MMED
Department of Ambulatory Care & Prevention
Harvard Medical School / Harvard Pilgrim Healthcare
133 Brookline Ave., 6th Floor
Boston, MA 02115

Dear Ross:

This letter is to document the enthusiastic support of the Steering Committee of the Centers for Education & Research on Therapeutics (CERTs) for your proposed study entitled "Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)."

Your proposed study addresses a crucial area in therapeutics: the need to improve adverse event detection and reporting for vaccines. The ESP:VAERS has the potential to substantially increase the number, completeness, and timeliness of case reports submitted to the CDC compared to the existing spontaneous reporting system. Your initiative to provide electronic monitoring of adverse events for vaccines is an important one.

As you know, CERTs is a program administered by the Agency for Healthcare Research and Quality (AHRQ), in consultation with the Food and Drug Administration. It was authorized by Congress as part of the Food and Drug Administration Modernization Act of 1997 (Public Law 105-115). The vision of the CERTs program is to serve as a trusted national resource for people seeking to improve health through the best use of medical therapies. The mission of the CERTs is to conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products.

Your aim – to determine if electronic monitoring will improve the detection and reporting of adverse events for vaccines – will clearly advance the CERTs mission. Therefore, the Steering Committee wholeheartedly supports your application.

Sincerely,

Hugh H. Tilson, MD, DrPH
Chairman, CERTs Steering Committee

CERTs Coordinating Center
Duke University Medical Center

P.O. Box 17969 • Durham, NC 27715 • FAX: (919) 668-7166 • PHONE: (919) 668-8543
www.certs.hhs.gov



The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
250 Washington Street, Boston, MA 02108-4619

DEVAL L. PATRICK
GOVERNOR

TIMOTHY P. MURRAY
LIEUTENANT GOVERNOR

JUDYANN BIGBY, MD
SECRETARY

PAUL J. COTE, JR.
COMMISSIONER

Ross Lazarus, MD, MBBS, MPH
Department of Ambulatory Care and Prevention
Harvard Medical School

Dear Dr. Lazarus,

This letter is to express my strong support of your AHRQ Enabling Quality Measurement through Health IT proposal entitled ESP:VAERS. Your intention to create software to prospectively identify potential vaccine adverse effects in electronic medical records, and to facilitate clinicians' evaluation and electronic reporting to VAERS, will constitute an important advance in vaccine safety. The capability you will create will serve individual clinicians as well as state and national programs.

The very high level of public health experience and academic expertise along with the technical and informatics skills of your group has formed a solid foundation for the success of our collaborations over the past 6 years. Your group has been critical not only in the success of our syndromic surveillance projects, but also in integrating the alerts from this system with our Health Alert Network (HAN). This effort helped define the standards for electronic HAN to HAN communications across states.

As described in your proposal, the ESP software produced by your group, as part of our CDC Center of Excellence in Public Health Informatics project, is currently deployed at HealthOne, securely reporting statutory notifiable disease cases as HL7 messages, to our ELR system, for immediate transfer to appropriate officials, providing a new and efficient source of accurate and complete case reports. Your team quickly delivered valid HL7 messages and batch wrappers, to our ELR SOAP server, according to our specifications, and worked with our vendor on extensions we needed for ESP to report treatment to the ELR, in a very proficient, deft and professional manner.

Your proposal has our support, because our experience has shown your team has the range of skills needed and is capable of successfully integrating and completing the public health, validation, technical, and informatics tasks described in your proposal. In addition, our long collaborative experience suggests that your proposed collaboration with the CDC, FDA and their vendors, will proceed smoothly and professionally.

Additional functions will make the whole ESP software base even more sustainable and flexible, helping us and others to improve public health surveillance from electronic ambulatory care records in Massachusetts and elsewhere. The ESP system appears to be technically sound, stable and mature and source code is readily available. Since your systems are, and will be, adaptable, freely distributable, available for commercial vendors, and designed work in a wide range of software environments, there are no obvious barriers to their widespread adoption and prolonged sustainability.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Ja B. Daniel", written in a cursive style.

James Daniel, MPH
Chief Information Officer
Massachusetts Department of Public Health



**Harvard
Vanguard**
Medical Associates

A major teaching affiliate of Harvard Medical School

January 31, 2007

Ross Lazarus, MBBS, MPH, MMED
Department of Ambulatory Care & Prevention
Harvard medical School / Harvard Pilgrim Healthcare
133 Brookline Ave, 6th Floor
Boston, MA 02115

Dear Dr. Lazarus:

On behalf of the HealthOne Care System, I should like to confirm our enthusiastic support for your proposal to develop ESP-VAERS, a near real-time vaccine adverse event detection, clinician query, and automated reporting system that will be implemented in our practices. As you know, HealthOne is the largest independent physician network in Massachusetts with approximately 600 physicians serving 600,000 patients from across the greater Boston area. We now completing system-wide deployment of EpicCare, a sophisticated electronic medical record system that is used to document every patient encounter. HealthOne has always been a leader in harnessing clinical information systems to improve the care of both individuals and our patient population at large. We see your proposed ground breaking work in automated vaccine adverse event detection and reporting as continued progress for patient safety and physician practice.

We have a had very productive relationship with your research team on other projects and know that this proposal will be successful. To date, we have worked together to use automated data streams from our electronic medical record system for syndromic disease surveillance and for communicable disease detection and public health reporting. We also are currently using a simplified clinician-elicited vaccine adverse event surveillance system created by your group for our pediatric patients. This shared experience augurs well for further fruitful collaboration on the design, data interfacing, and elicitation of clinician participation in this new venture.

In particular, HealthOne anticipates being able to provide the following (pending Institutional Review Board approval of your planned activities):

- Continued timely access to the full range of codified EpicCare data that is currently being sent to the ESP server located within the HVMA firewall at the Kenmore Computing Center.
- Information Systems expertise to support creation of an interactive interface between ESP and EpicCare in order to enable ESP to communicate suspected adverse events to the responsible clinician via EpicCare's secure internal clinician mail system
- Permission to pilot ESP-VAERS on a small subset of clinicians and vaccines in order to validate your algorithms and informatics structures

- Permission for scaled deployment of ESP-VAERS across HealthOne once you have demonstrated smooth functioning of the system and minimal interference with clinician workflow.
- We will work with you to inform HealthOne clinicians about ESP-VAERS and to win their agreement to participate in reviewing personalized alerts about possible adverse effects suffered by their patients
- Permission to retain one year's worth of patient data on the ESP server at any one time and permanent records of all cases reported to the Vaccine Adverse Event Reporting System (VAERS)

We are confident that you and your team will continue to use our data in a responsible manner that respects all applicable patient privacy laws. We look forward to a mutually beneficial collaboration on this exciting new project.

Yours Sincerely,

A handwritten signature in cursive script that reads "R Marshall MD".

Richard Marshall, MD
Chief Medical Officer
Harvard Vanguard Medical Associates

PHS 398 Checklist

OMB Number: 0925-0001

Expiration Date: 9/30/2007

1. Application Type:

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

* Type of Application:

☒ New ☐ Resubmission ☐ Renewal ☐ Continuation ☐ Revision

Federal Identifier: **2. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix: * First Name: Middle Name: * Last Name: Suffix: ☐ Change of Grantee Institution

* Name of former institution:

3. Inventions and Patents (For renewal applications only)* Inventions and Patents: Yes ☐ No ☐

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

* Previously Reported: Yes ☐ No ☐

4. * Program Income

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

☐ Yes

☒ No

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

*Budget Period *Anticipated Amount (\$)

*Source(s)

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5. Assurances/Certifications (see instructions)

In agreeing to the assurances/certification section 18 on the SF424 (R&R) form, the authorized organizational representative agrees to comply with the policies, assurances and/or certifications listed in the agency's application guide, when applicable. Descriptions of individual assurances/certifications are provided at: <http://grants.nih.gov/grants/funding/424>

If unable to certify compliance, where applicable, provide an explanation and attach below.

Explanation:

--

Attachments

CertificationExplanation_attDataGroup0

File Name

Mime Type

Appendix III: Active surveillance of vaccine safety: a system to detect early signs of adverse events.

Citation

Davis RL, Kolczak M, Lewis E, Nordin J, Goodman M, Shay DK, Platt R, Black S, Shinefield H, Chen RT. Active surveillance of vaccine safety: a system to detect early signs of adverse events. *Epidemiology*. 2005 May;16(3):336-41.

Abstract

BACKGROUND: There currently are no population-based systems in the United States to rapidly detect adverse events after newly introduced vaccines. To evaluate the feasibility of developing such systems, we used 5 years of data from 4 health maintenance organizations within the Centers for Disease Control and Prevention (CDC) Vaccine Safety Datalink. **METHODS:** Within every year, each week's vaccinated children were followed for 4 weeks, and rates of adverse events were compared with rates among children of similar ages before the introduction of the new vaccine. We assessed risks for intussusception after rotavirus vaccination and risks for fever, seizures, and other neurologic adverse events after the change from whole cell diphtheria-tetanus-pertussis (DTPw) to acellular DTP vaccine (DTPa). We used sequential probability ratio testing, adjusted for age, sex, calendar time, season, and HMO, and with a stopping value based on the probability of an adverse event under the null hypothesis and under a preset alternative hypothesis. **RESULTS:** We detected an increase in intussusception after 2589 vaccine doses of rotavirus vaccine, about the same time initial reports of intussusception were made to the Vaccine Adverse Events Reporting System. Decreases in risk for fever, seizures, and other abnormal neurologic events became detectable within 12 weeks, 42 weeks, and 18 months, respectively, after the change from DTPw to DTPa. **CONCLUSIONS:** We conclude that it is feasible to develop systems for rapid and routine population-based assessments of new vaccine safety.

Online

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15824549&dopt=Abstract

Appendix I: Qualifications for funding preferences

No funding preferences requested.

Appendix II: Electronic medical record Support for Public health (ESP): Automated Detection and Reporting of Statutory Notifiable Diseases to Public Health Authorities; (submitted to *Advances in Disease Surveillance*)

Electronic medical record Support for Public health (ESP): Automated Detection and Reporting of Statutory Notifiable Diseases to Public Health Authorities

Michael Klompas MD,^{1,2} Ross Lazarus MBBS,² James Daniel MPH,³ Gillian Haney MPH,³ Francis Campion MD,⁴ Benjamin Kruskal MD PhD,⁴ Xuanlin Hou MSc,² Alfred DeMaria MD,³ and Richard Platt MD MSc^{1,2}

¹Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA; ²Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; ³Massachusetts Department of Public Health, Boston, MA; ⁴Harvard Vanguard Medical Associates, Boston, MA.

Contact: Michael Klompas
Harvard Medical School
Department of Ambulatory Care and Prevention
133 Brookline Ave, Boston, MA 02215
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Word Count: 2,475

Abstract

Clinician initiated reporting of notifiable conditions is often delayed, incomplete, and lacking in detail. We report on the deployment of **Electronic medical record Support for Public health (ESP)**, a system we have created to automatically screen electronic medical record (EMR) systems for evidence of reportable diseases, to securely transmit disease reports to health authorities, and to respond to queries from health departments for clinical details about laboratory detected cases. ESP consists of software that constructs and analyzes a temporary database that is regularly populated with comprehensive codified encounter data from a medical practice's EMR system. The ESP database resides within the host medical practice's firewall, configured on either a central workstation to service large multi-site, multi-physician practices or as a software module running alongside a small practice's EMR system on a personal computer. The encounter data sent to ESP includes patient demographics, diagnostic codes, laboratory test results, vital signs, and medication prescriptions. ESP regularly analyzes its database for evidence of notifiable diseases. When a case is found, the server initiates a secure Health Level 7 (HL7) message to the health department. The server is also able to respond to queries from the health department for demographic data, treatment information, and pregnancy status on cases independently reported by electronic laboratory systems. ESP is designed to be compatible with any EMR system with export capability: it facilitates translation of proprietary local codes into standardized nomenclatures, shifts the analytical burden of disease identification from the host electronic medical record system to the ESP database, and is built from open source software. The system is currently being piloted in Harvard Vanguard Medical Associates, a multi-physician practice serving 350,000 patients in eastern Massachusetts. Disease detection algorithms are proving to be robust and accurate when tested on historical data. In summary, ESP is a secure, unobtrusive, flexible, and portable method for bidirectional communication between EMR systems and health departments. It is

currently being used to automate the reporting of notifiable conditions but has promise to support additional public health objectives in the future.

MEDICAL SUBJECT HEADINGS (MeSH):

Public Health Practice

Epidemiologic Measurements

Disease Notification

Medical Records Systems, Computerized

"No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring."

Introductory statement printed each week in *Public Health Reports* from 1913 through 1951

INTRODUCTION

For over 100 years, public health authorities have actively tracked the incidence and geography of communicable diseases as a first step towards understanding and preventing their spread.¹ The adoption of direct electronic reporting by clinical laboratories has increased the breadth and efficiency of reporting for many diseases.^{2,3} Laboratory reporting systems, however, have not obviated the need for clinician participation in reporting. Some reportable diseases are only established by a clinical impression, such as pelvic inflammatory disease or culture negative tuberculosis. Other diseases require clinician interpretation of laboratory results; examples include Lyme disease and acute hepatitis C. In addition, electronic laboratory reporting systems do not provide detailed demographic data on patients or pertinent clinical details such as symptoms, treatment rendered, and pregnancy status. Clinician reporting, however, is dependent upon clinician initiative and is still largely done manually by mail, fax, or telephone. Some jurisdictions have instituted web-based reporting systems but these continue to depend upon clinician initiative to report.⁴ Unfortunately, clinician initiated health reporting suffers from incomplete capture of incident infections, incomplete descriptions of case data, delay between detection and processing of reports, and substantial administrative cost for manual processing of reports.^{5,6,7} In light of these limitations of current reporting, we have created an electronic system to automate the detection and reporting of notifiable conditions by leveraging the information coded into electronic medical record (EMR) systems. The name of the system is *Electronic medical record Support for Public health* (ESP). It supports secure, bidirectional communication between EMR systems and health departments. It detects and reports notifiable conditions identified from clinician's medical records. It can also report specific

patient level clinical information to health authorities in response to health department queries about patients identified independently by electronic laboratory reporting. The system has been developed using the EpicCare EMR system⁸ at Harvard Vanguard Medical Associates (HVMA), a multipractice physician group serving 350,000 patients in Eastern Massachusetts. It has been designed, however, to be compatible with any EMR system that has export capability.

Conceptual framework

ESP is designed to embody the following principles:

1. Automatic – shifts the initiative for reporting from health care providers to electronic systems.
2. Unobtrusive – invisible to clinicians during routine clinical care; transfers analytical workload away from the host EMR server so as not to interfere with clinical computing.
3. Secure – employs stringent measures to protect sensitive clinical data.
4. Universal – designed to be compatible with almost any electronic medical record system.
5. Flexible – easily accommodates rule modifications to detect new conditions or improve the detection of existing conditions.
6. Provider controlled – clinical data is stored on the provider's premises and cases can be reviewed for approval prior to transmission.

METHODS

Architecture

ESP consists of a database and analytical software placed within a medical practice. The database is regularly populated with specific data elements extracted from each encounter recorded in the practice's EMR system. ESP analyzes the database nightly for evidence of notifiable conditions. When notifiable conditions are identified, ESP formats Health Level 7 (HL7) message and initiates a secure, encrypted electronic message to the state health department. ESP is also able to respond to HL7 messages from the health department

containing queries for clinical details about cases reported directly by laboratories. Practices with multiple locations that share an integrated EMR system can be accommodated by a single central ESP server. Our initial deployment, for example, uses a single server located in the practice's central data center to serve 16 different clinical sites. ESP can also be configured for small practices as an independent software module that can run on a practice's microcomputer.

The model of an independent database and analytical software system housed on a practice's premises and secured by the practice's staff was selected for the following reasons: 1) to avoid interference with clinical operations by offloading analytical and processing burden from the host EMR system; 2) to permit flexibility to frequently modify ESP case detection algorithms without interfering with the host EMR system; 3) to secure confidential patient information by retaining all data behind the practice's electronic firewall until a message is sent to the health department; and 4) to allow portability of ESP to a wide array of EMR systems with different internal structures, proprietary codes, and analytical capabilities.

The ESP database is regularly populated with data extracts of encounter data sent by the host EMR system via ftp protocol. The source EMR system formats the clinical data into a defined sequence of delimited text fields containing patient demographics, diagnostic codes, laboratory orders, laboratory results, medication prescriptions, vital signs, and pregnancy status. Clinician notes and other free text entries are not currently included. ESP has a built-in code remapping tool to convert local codes into standardized nomenclatures that can be analyzed by ESP. Laboratory test codes are translated into logical object identifier names and codes (LOINC), result names are translated into systematized nomenclature of medicine (SNOMED) codes, diagnoses are translated into ICD9 codes, and prescribed medication codes are translated into national drug code (NDC) numbers. The ESP code remapping tables are maintained and managed by authorized practice staff using a local ESP web application.

When a case is identified, ESP queries the database for additional clinical information of importance to the health department including pregnancy status and relevant prescriptions. The

system also assesses recent ICD9 codes and vital signs to determine whether the patient was symptomatic (for example, recorded temperature for presence of fever; ICD9 codes for urethritis or vaginal leukorrhea).

ESP preferentially sends an immediate case report to the health department. If a clinician wishes to review cases prior to transmission, however, ESP can queue cases for manual approval before they are sent. Cases queued for confirmation are reviewed by authorized personnel using a secure, web-based case management system within the practice's firewall. The case management system presents the user with a list of patients with suspected reportable diseases. When the reviewer selects a patient, ESP displays a summary of recent encounters types and dates, ICD9 diagnoses, lab test results, medication prescriptions, and ordering clinicians. The particular data terms that led to ESP flagging the case for reporting are highlighted. The reviewing clinician can choose to reject the case (false positive), to authorize transmission (true positive), or to place the case on hold while further information is being gathered. The web interface also has links to contact information for each ordering clinician and to the CDC website with criteria for notifiable disease identification.⁹ A demonstration version of the ESP case management interface using fictional patient data can be viewed at esphealth.org.

When a case is ready for transmission, ESP generates a standardized HL7 message. The initial deployment sends encrypted HL7 messages to the Massachusetts Department of Public Health server using a simple object access protocol (SOAP) web-service, but the ESP messaging sub-system is also able to send messages using the Centers for Disease Control's PHIN-MS secure messaging protocol. Any authorized health authority capable of receiving HL7 messages can potentially receive ESP messages. ESP also supports queries initiated by authorized health departments to provide clinical context for positive lab tests they have received independently from their electronic lab reporting system. Patient matching is done using test accession numbers, patient names, and test dates. As with conditions first identified by ESP, the system assesses for pregnancy status, patient symptoms, and relevant

prescriptions. Response messages are transmitted back to the health department in HL7 format following the same protocol as ESP initiated cases, including optional case review by a practice designee.

The ESP database is purged of all patient encounter data after 90 days other than the data relevant to confirmed cases. Data from these cases are retained to permit the generation of reports that detail the system's notification activity.

The ESP server runs custom software built from the following open-source applications: MySQL RDBMS (MySQL AB, Uppsala, Sweden), CDC PHIN-MS (Centers for Disease Control and Prevention, Atlanta, GA), and the Python language (Python Software Foundation, Ipswich, MA). It can run upon both Linux (Red Hat, Raleigh, NC) and Windows (Microsoft Corporation, Redmond, WA) operating systems.

Security

Confidential patient data is protected by keeping it under the physical and logical control of the practice until the point of message transmission. ESP does require outbound access to the public internet in order to communicate with the health department server but it is protected from external access behind an internet firewall. Messages are preferentially transmitted using PHIN-MS over 128 bit encrypted communication channels, but the messaging protocol can be tailored to suit the requirements of different health departments. Public key encryption infrastructure (PKI) certificates are required of both the sending and receiving machines before patient data is transmitted.

Case identification logic

Cases are identified by analyses of diagnostic codes, laboratory tests and results, and medication prescriptions. The case definitions are based upon those published by the Centers for Disease Control, but can be customized for local users.⁹ They run the gamut from simple to

complex. A positive DNA probe for *Chlamydia trachomatis* from a urethral swab, for example, is sufficient to establish a case of Chlamydia. Other conditions require more sophisticated analysis of multiple laboratory tests. Acute Hepatitis C, for example, is diagnosed when the patient has a concurrent positive Hepatitis C ELISA, confirmatory RIBA, negative IgG and/or IgM for Hepatitis A, negative core and surface antigens of Hepatitis B, and a serum alanine aminotransferase level seven times above the upper limit of normal for the assay. The system can also assess for suggestive changes in laboratory tests over time. Acute hepatitis C can also be diagnosed by serial negative followed by a positive hepatitis C ELISA; or by the combination of a negative ELISA paired with a positive Hepatitis C RNA PCR assay. Conditions that are diagnosed on clinical grounds alone are sought by looking for suggestive combinations of ICD9 codes, laboratory test orders, and medication prescriptions. Lyme disease, for example, can be diagnosed from the combination of 1) an ICD9 code 088.81 [erythema chronicum migrans] or positive Lyme serology, and 2) prescription for at least 14 days of doxycycline or other suggestive antibiotic.

Portability

ESP has been designed to enable broad adoption by minimizing technical and processing demands on source EMR systems, by embracing standardized nomenclatures, by easily permitting custom case identification algorithms, and by reliance on low cost software components. The ESP input data files extracted from source EMR systems consist only of unformatted text delimited into our specified field sequence. The EMR system can export encounter data using its own internal codes since the ESP data load tool includes user-configurable translation tables to map proprietary local codes into standardized vocabularies. Local users are responsible for building, maintaining and confirming the accuracy of their proprietary to standard code mapping tables, but this task is made easier by the ESP remapping table web application. Case identification algorithms within ESP can be modified to conform to

particular specifications from different health departments. Source code for ESP can be downloaded under a lesser general public license from esphealth.org.

RESULTS

Validation

Case identification algorithms were validated by applying each one to a five year span of historical data from HVMA. The total number of patients identified by each algorithm was compared with the Massachusetts Department of Public Health's historical counts for HVMA patients manually reported to have the disease of interest. A subset of 50 randomly chosen charts of patients who met the rule's conditions was then manually reviewed to assess the rule's accuracy. These 50 patients were then matched to individuals in the health department records using limited identifiers (gender, date-of-birth, HVMA office site, and test date) in order to assess congruity between patients identified electronically and those reported manually. For example, between 2000 and 2004, HVMA reported 1629 cases of Chlamydia to the health department. Application of the ESP Chlamydia detection algorithm to electronic records from this period identified 1927 episodes. Review of 50 randomly selected charts confirmed that all cases were true positives (100% specificity). We were able to match 90% of these 50 cases to individuals in health department records, a percentage that reassuringly mirrors the ratio of manually reported cases to electronically identified cases from our five year cohort.

Current Status

ESP has been implemented at HVMA, a large multisite, multispecialty group practice with over 350,000 patients based in Eastern Massachusetts. Messages are sent to the Massachusetts Department of Public Health. The system currently detects and reports chlamydia, gonorrhea, and pelvic inflammatory disease. We will add reporting next for pertussis, acute hepatitis C, and Lyme disease, and then, for the remaining 75 conditions that

are reportable in Massachusetts. The State health department anticipates initiating queries to ESP triggered by their Electronic Lab Reporting system in March 2007. We have also formed a partnership with the Massachusetts eHealth Collaborative to pilot ESP in the community-wide electronic medical record system being deployed in North Adams, Massachusetts.

DISCUSSION

Potential Future Applications

The ESP model of a time-limited database, refreshed daily with comprehensive clinical data and capable of bidirectional communication with health departments, has potential to serve many additional public health functions beyond identification and reporting of notifiable diseases. These include syndromic surveillance (including the distributed data model used by the National Bioterrorism Syndromic Surveillance Demonstration Program^{10,11}), vaccine registries, clinical decision support for management of notifiable conditions, auditing of mandated screening programs such as lead assays in children, assessment for spatial clusters of environmentally linked diseases such as asthma, and population level surveillance for non-notifiable diseases. We anticipate also building modules to generate reports for clinicians' or practices' use that tally the number of notifiable conditions detected and reported for a given period relative to the denominator of their choice (e.g. total ambulatory visits, total number of patients tested for the condition, total number of patients with an ICD9 code suggestive of the presenting clinical syndrome, etc) in order to assist with internal quality control and education.

Conclusion

We have created a system to automatically identify and report individual patients with notifiable conditions using routine data collected by electronic medical record systems. Electronic medical record Support for Public health (ESP) also supports queries initiated by health departments for clinical data to guide management of positive laboratory reports received

independently from electronic laboratory reporting systems. ESP uses industry standard nomenclature. The system is designed to be secure, unobtrusive to clinicians, and compatible with most electronic medical record systems. The system also has the potential to support additional public health objectives including syndromic surveillance, vaccine registries, and auditing of mandated screening programs. It is currently being deployed and actively tested in Massachusetts.

Acknowledgements: The development of ESP is supported by a grant from the Centers for Disease Control (CDC-05-109).

¹ Centers for Disease Control and Prevention (CDC). Notifiable disease surveillance and notifiable disease statistics—United States, June 1946 and June 1996. 1996;45:530-6.

² Effler P, Ching-Lee M, Bogard A, leong MC, Nekomoto T, Jernigan D. Statewide system of electronic notifiable disease reporting from clinical laboratories. Comparing automated reporting with conventional methods. *JAMA* 1999; 282:1845-50.

³ Panackal AA, M'ikanatha N, Tsui FC, et al. Automatic electronic laboratory-based reporting of notifiable infectious diseases at a large health system. *Emerg Infect Dis* 2002; 7:685-91.

⁴ Centers for Disease Control and Prevention (CDC). Progress in improving state and local disease surveillance—United States, 2000-2005. *MMWR Morb Mortal Wkly Rep* 2005; 54:822-5

⁵ Thacker SB, Choi K, Brachman PS. The surveillance of infectious diseases. *JAMA* 1983; 249:1181-85.

⁶ Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev* 1988; 10:164-90.

⁷ Standaert SM, Lefkowitz LB Jr, Horan JM, Hutcheson RH, Schaffner W. The reporting of communicable diseases: a controlled study of *Neisseria meningitidis* and *Haemophilus influenzae* infections. *Clin Infect Dis* 1995; 20:30-6.

⁸ EpicCare Ambulatory. Available at <http://www.epicsystems.com/Software/EnterpriseClinical.php#ambulatory>. Accessed December 3, 2006.

⁹ Centers for Disease Control and Prevention (CDC). Summary of notifiable diseases - United States, 2003. *MMWR Morb Mortal Wkly Rep* 2005;52:1-85. Available at http://www.cdc.gov/epo/dphsi/casedef/case_definitions.htm. Accessed November 30, 2006.

¹⁰ Yih WK, Caldwell B, Harmon R, et al. National Bioterrorism Syndromic Surveillance Demonstration Program. *MMWR Morb Mortal Wkly Rep* 2004;53 Suppl:43-9.

¹¹ Lazarus R, Yih K, Platt R. Distributed data processing for public health surveillance, *BMC Public Health*. 2006; 6: 235. Published online 2006 September 19. doi: 10.1186/1471-2458-6-235.

PROGRAM CONTACT:

Jon White
(301) 427-1171
jwhite@ahrq.gov

**SUMMARY STATEMENT
(Privileged Communication)****Release Date: 08/08/2007****Application Number: 1 R18 HS017045-01****Principal Investigator****LAZARUS, ROSS MBBS****Applicant Organization: HARVARD PILGRIM HEALTH CARE, INC.****Review Group: ZHS1 HSR-O (01)****AHRQ Special Emphasis Panel****AMBULATORY SAFETY AND QUALITY PROGRAM: ENABLING QUALITY
MEASUREMENT THROUGH HEALTH IT SEP****Meeting Date: 06/27/2007****RFA/PA: HS07-002****Council: OCT 2007****PCC: CP3****Requested Start: 07/01/2007****Project Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System
(ES)****SRG Action: Priority Score: (b)(5)****Human Subjects: 30-Human subjects involved - Certified, no SRG concerns****Animal Subjects: 10-No live vertebrate animals involved for competing appl.****Gender: 1A-Both genders, scientifically acceptable****Minority: 1A-Minorities and non-minorities, scientifically acceptable
Clinical Research - not NIH-defined Phase III Trial**

Project Year	Direct Costs Requested	Estimated Total Cost
1	(b)(4)	501,478
2		498,517
TOTAL		999,995

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Agency grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

Withheld pursuant to exemption

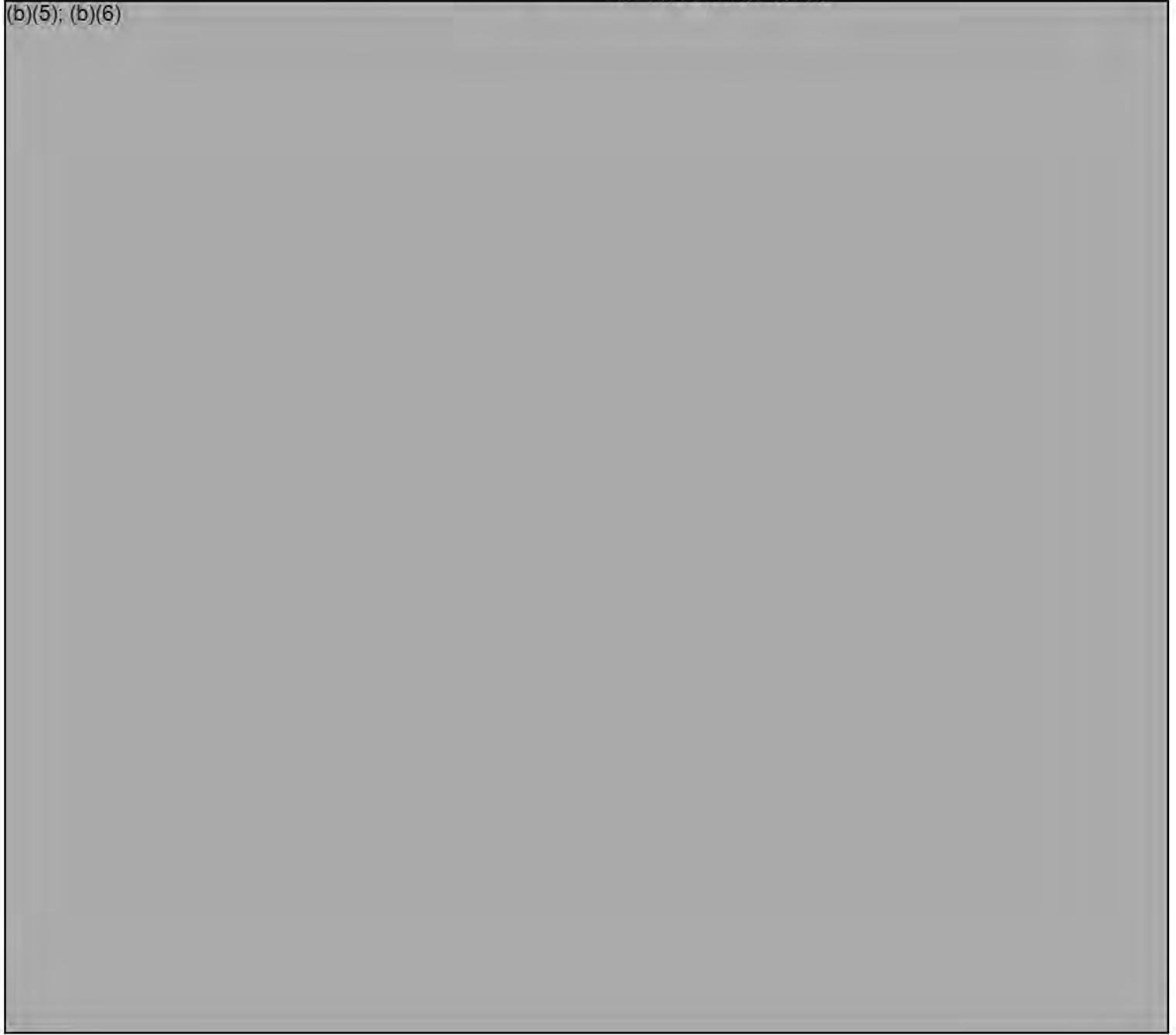
(b)(5)

of the Freedom of Information Act

MEETING ROSTER

**AHRQ Special Emphasis Panel
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY
ZHS1 HSR-O (01) 1
June 27, 2007 - June 28, 2007**

(b)(5); (b)(6)



Withheld pursuant to exemption

(b)(5); (b)(6)

of the Freedom of Information Act

Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.

DOMESTIC INSTITUTIONS/COMPONENTS

CONTAINING 'Pilgrim' (4)

[NEW SEARCH](#)

Find institution/component in table below and click corresponding 'Detail' link to view assurance:

Assurances/Components Found					
Assurance	Institution/Component	Type	City	State or Country	
FWA00005782	G. F. Pilgrim, Inc.	F	Brockton	MASSACHUSETTS	Detail
T3411	HARVARD PILGRIM Hlth CARE (DEACTIVATED)	T	BROOKLINE	MASSACHUSETTS	Detail
FWA00000100	Harvard Pilgrim Hlth Care	F	Boston	MASSACHUSETTS	Det
FWA00007255	Pilgrim Tower East Associates	F	PASADENA	CALIFORNIA	Detail

* Here Type: 'F' = FWAs 'M' = MPAs 'C' = Components 'T' = CPAs

If you have questions about human subject research, click ohrp@osophs.dhhs.gov
 If you have questions/suggestions about this web page, click [WEBMASTER](#)

Updated August 5, 2004

ASSURANCE INFORMATION

ASSURANCE: - Harvard Pilgrim Hlth Care

NEW SEARCH

Located at: Boston, MASSACHUSETTS

Expires: December 22, 2009

No Assurance Components Identified

IRBS LINKED TO THIS ASSURANCE				
Ident	Name	City	State or Country	
IRB00000064	Brigham & Women's Hosp IRB #1	Boston	MASSACHUSETTS	Detail
IRB00000065	Brigham & Women's Hosp IRB #2	Boston	MASSACHUSETTS	Detail
IRB00000433	Massachusetts General Hosp IRB #1	Boston	MASSACHUSETTS	Detail
IRB00000668	Group Hlth Cooperative IRB #1	Seattle	WASHINGTON	Detail
IRB00000673	Marshfield Clinical Rsch Foundation (MCRF) IRB #1(A)	Marshfield	WISCONSIN	Detail
IRB00000695	Westat, Inc. IRB #1	Rockville	MARYLAND	Detail
IRB00000882	Harvard Pilgrim Hlth Care IRB #1	Boston	MASSACHUSETTS	Detail
IRB00000931	Massachusetts General Hosp IRB #2	Boston	MASSACHUSETTS	Detail
IRB00002610	Massachusetts General Hosp IRB #3	Boston	MASSACHUSETTS	Detail
IRB00003985	Brigham & Women's Hosp IRB #3	Boston	MASSACHUSETTS	Detail

Agency Only Access

SEP. 25. 2006 1:59PM

NO. 0717 P. 2/1



DEPARTMENT OF HEALTH & HUMAN SERVICES

Program Support Center
Financial Management Service
Division of Cost Allocation

28 Federal Plaza-Room 41-122
New York, New York 10278
PHONE: (212)-264-2069
FAX: (212)-264-5478

September 25, 2006

Ms. Barbara B. Bierer, M.D.
Senior Vice President, Research
Brigham and Women's Hospital
Office of Research Administration
75 Francis Street
Boston, MA 02115

Dear Dr. Bierer:

A negotiation agreement is being faxed to you for signature. This agreement reflects an understanding reached between your institution and a member of my staff concerning the rates or amounts that may be used to support your claim for costs on grants and contracts with the Federal Government. The agreement must be signed by a duly authorized representative of your institution and faxed to me; retain a copy for your file. Our fax number is (212) 264-5478. We will reproduce and distribute the agreement to awarding agencies of the Federal Government for their use.

Requirements for adjustments to costs claimed under Federal Grants and Contracts resulting from this negotiation are dependent upon the type of rate contained in the negotiation agreement. Information relating to these requirements is enclosed.

In consideration of this agreement, the following was agreed to:

1. The following carry-forward amounts are from the finalization of fringe benefits for fiscal year ended September 30, 2005. The carry-forwards are to be included with your actual fringe benefit rate calculations for the fiscal year specified below:

Fringe Benefit RateFYE 09/30/07

Professional
Non-Professional
Intern, Residents,
and Fellows

(b)(4)

() Denotes Over-Recovery

2. The fringe benefit proposal for fiscal year ending September 30, 2006 is due to be submitted to our office by March 31, 2007.

SEP. 25. 2006 1:59PM

NO. 0717 P. 3/7

Ms. Barbara E. Bierer, M.D.

-2-

September 25, 2006

A proposal encompassing all activities of your institution together with the required supporting information must be submitted to my office at the address shown below for each fiscal year your institution claims costs under grants and contracts awarded by the Federal Government. This proposal is due within six months after the close of your fiscal year. Therefore, a proposal for fiscal year ending September 30, 2007 will be due in my office not later than March 31, 2008. The proposal will be used to establish rates/amounts for the fiscal year subsequent to the last period covered by an approved final, fixed, or predetermined rate(s). Failure to submit a timely proposal will be interpreted as a forfeiture of reimbursement for indirect costs. Therefore, unless a proposal is received by March 31, 2008, future awards made by the Department of Health and Human Services will be for direct costs only and will not provide for the recovery of costs contained in this agreement. In addition, the costs claimed against awards already made may be subject to disallowances.


If you are unable to submit your proposal by the prescribed date, you may request an extension. This request must be submitted prior to the due date of the proposal and must contain a justification for the extension and the date the proposal will be submitted.

Your proposal and relevant correspondence should be addressed to:

Department of Health and Human Services
Division of Cost Allocation
26 Federal Plaza, Room 41-122
New York, New York 10278
(212) 264-1823

In addition, please acknowledge your concurrence with the comments and conditions cited above by signing this letter in the space provided below and FAX (212-264-5478) it to me with the enclosed negotiation agreement.

Sincerely,


Robert I. Aaronson
Director, Division of
Cost Allocation

Enclosures
Concurrence:


Name

Title

Date

Senior Vice President Research, BWH

September 27, 2006

SEP. 25. 2006 1:59PM

NO. 0717 P. 4/7

HOSPITAL RATE AGREEMENT

ORIGINAL

EIN #: 1042312909A1

DATE: September 25, 2006

HOSPITAL:
Brigham And Women's Hospital
Office of Research Administration
75 Francis Street
Boston

MA 02115-

FILING REF.: The preceding
Agreement was dated
August 22, 2005

The rates approved in this agreement are for use on grants, contracts and other
agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES*

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

TYPE	EFFECTIVE PERIOD		RATE(%)	LOCATIONS	APPLICABLE TO
	FROM	TO			
PRED.	10/01/05	09/30/08	(b)(4)	On-Site	Research
PRED.	10/01/04	09/30/08		Off-Site	Research
PROV.	10/01/08 UNTIL AMENDED			Use same rates and conditions as those cited for fiscal year ending September 30, 2008.	

*Base: Total direct costs less items of equipment, major subcontracts, alterations
and renovations, animal charges, hospitalization and other fees related to patient
care.

Brigham
Women's
Hospital

(1)

H10517

SEP. 25, 2006 2:00PM

PAGE 05/01

NO. 0717 P. 5/7

HOSPITAL;
Brigham And Women's Hospital
Office of Research Administration

AGREEMENT DATE: September 25, 2006

SECTION I: FRINGE BENEFITS RATES**

RATE TYPES: FIXED		FINAL	PROV. (PROVISIONAL)	FRED. (PREDETERMINED)	
TYPE	EFFECTIVE PERIOD		RATE (%)	LOCATIONS	APPLICABLE TO
	FROM	TO			
FIXED	10/01/06	09/30/07	(b)(4)	All	Professional
FIXED	10/01/06	09/30/07		All	Non-Professional
FIXED	10/01/06	09/30/07		All	Intern&Residents, Fel
PROV.	10/01/07	UNTIL AMENDED		Use same rates and conditions as those cited for fiscal year ending September 30, 2007.	

**DESCRIPTION OF FRINGE BENEFITS RATE BASE:
Salaries and wages.

(2)

HOSPITAL:
Brigham And Women's Hospital
Office of Research Administration

AGREEMENT DATE: September 25, 2006

SECTION XIX: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions: (1) only costs incurred by the organization were included in its indirect cost pool as finally accepted; such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) the same costs that have been treated as indirect costs are not claimed as direct costs; (3) similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Change to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement requires prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from indirect to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the cost principles promulgated by the Department of Health and Human Services, and should be applied to the grants, contracts and other agreements covered by these regulations subject to any limitations in A above. The hospital may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing indirect costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of indirect costs allocable to these programs.

BY THE HOSPITAL:

Brigham And Women's Hospital

Office of Research Administration

(HOSPITAL)

Robert I. Larson

(SIGNATURE)

Robert I. Larson, MD

(NAME)

Senior Vice President, Research

(TITLE)

September 27, 2006

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

Robert I. Larson

(SIGNATURE)

Robert I. Larson

(NAME)

DIRECTOR, DIVISION OF COST ALLOCATION

(TITLE)

September 25, 2006

(DATE) 0517

THIS REPRESENTATIVE: *Joseph Guarnieri*

telephone: *(212) 264-2069*

Rate Agreements

Agreement Text for: n2055805.txt

Agreement Date: 04/27/2005

NPrfMA Harvard Pilgrim Health Care Inc 1042452600A1 04 27 05 0558

NONPROFIT RATE AGREEMENT

EIN 1042452600A1

DATE April 27 2005

ORGANIZATION

Harvard Pilgrim Health Care Inc

FILING REF The preceding

Agreement was dated

Boston

MA

02215

January 15 2002 133 Brookline Avenue 6th Floor

The rates approved in this agreement are for use on grants contracts and other agreements with the Federal Government subject to the conditions in Section III

RATE TYPES FIXED FINAL PROV PROVISIONAL PRED PREDETERMINED

SECTION I

TYPE	EFFECTIVE PERIOD		RATE	LOCATIONS	APPLICABLE TO
	FROM	TO			
PRED	01 01 05	12 31 07	(b)(4)	On Site	Research
PRED	01 01 05	12 31 07	(b)(4)	Off Site	Research
PROV	01 01 08	UNTIL AMENDED			

Use same rates and conditions as those cited for fiscal year ending December 31 2007

Harvard
Pilgrim
Health Care
F&A

BASE

Total direct costs excluding capital expenditures buildings individual items of equipment alterations and renovations and subawards

ORGANIZATION

Harvard Pilgrim Health Care Inc

AGREEMENT DATE April 27 2005

TREATMENT OF PAID ABSENCES

Vacation holiday sick leave pay and other paid absences are included in salaries and wages and are claimed on grants contracts and other agreements as part of the normal cost for salaries and wages Separate claims for the costs of these paid absences are not made

Treatment of Fringe benefits Fringe benefits applicable to direct salaries and wages are treated as direct costs except incentive compensation which is treated as an indirect cost

Equipment means an article of nonexpendable tangible personal property having a useful life of more than one year and an acquisition cost of 1 000 or more per unit

ORGANIZATION

Harvard Pilgrim Health Care Inc

AGREEMENT DATE April 27 2005

A LIMITATIONS

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant contract or other agreement only to the extent that funds are available Acceptance of the rates is subject to the following conditions

1 Only costs incurred by the organization were included in its indirect cost pool as finally accepted such costs are legal obligations of the organization and are allowable under the governing cost principles 2 The same costs that have been treated as indirect costs are not claimed as direct costs 3 Similar types of costs have been accorded consistent accounting treatment and 4 The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government In such situations the rates would be subject to renegotiation at the discretion of the Federal Government

B ACCOUNTING CHANGES

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period Changes to the method of accounting for costs which affect

INQUIRY: Partial EIN or PIN Search Provides Full EIN DATE: 08/17/2007 TIME: 11:57:03 AM

*** SEARCH PARAMETERS *****

EIN: 1042452600A1

PIN has the following matches in PMS:

****EIN****	****DUNS****	****TYPE****	**PIN**	HHS USER	***NAME***
*****	*****	*****	*****	IND CODE	
1042452600A1		PAYEE EIN FOR 4715	Y	F21	HARVARD PILGRIM HEALTH CARE, INC

Hits: 1

***** Inquiry Results Complete *****

You may now make another selection from the Menu

PMS

IMPAC II: EIN Name Search Results

Note only EIN numbers that are valid for Grant payments are displayed.

August 17, 2007 10:20 AM Search String = 'HARVARD PILGRIM HEALTH CARE'

EIN	Organization	FDP 3	FDP 4
1042452600A1	HARVARD PILGRIM HEALTH CARE INC		



Holman, Suzanne (AHRQ/OPART/GM)

From: Burr, Michelle (AHRQ)
Sent: Monday, June 18, 2007 4:34 PM
To: AHRQ - OPART-GRANTS MANAGEMENT
Subject: Alert list is still under reconstruction

FYI – as of today the Alert List is still under reconstruction, therefore please continue to note the green sheet and include a copy of my 4/17/07 (or this) e-mail in each FY2007 award to document why we are not able to check the alert list.

From: Burr, Michelle (AHRQ)
Sent: Tuesday, April 17, 2007 1:41 PM
To: AHRQ - OPART-GRANTS MANAGEMENT
Subject: Alert list

Per the HHS website (screen shot, below), HHS is reconstructing the Alert list. Until the list is reinstated (timeline unknown), we will not be able to check the Alert list prior to issuing awards. In the interim, where the greensheet asks if the grantee is on the Alert list please make a note that the Alert list is not currently available and include a copy of this e-mail in the file. When/if the Alert list is reconstructed we'll return to checking it as usual.

Thanks.

GrantsInfo Microsoft Internet Explorer provided by AHRQ

Address <http://intrinet.grantsinfo.hhs.gov/AlertList.cfm?id=300>

United States Department of Health & Human Services

Alert List

UNDER RECONSTRUCTION!

HHS INTERNAL ALERT LIST

SPECIAL CONDITIONED AWARDS

NOTICE: The HHS Internal Alert List is undergoing reconstruction. This listing identifies grantees that have been designated as high risk and have special award conditions to protect the government's interests, grantees with acute audit findings and/or delinquent audits.

Based on feedback from various sources, the Office of Grants (OG) is reviewing: (1) the process by which awardees are added to this listing, (2) supporting documentation requirements, and (3) duplication with other centralized listings. The OG intends to develop mechanisms to enable OPDIV data input, OG on-line validation, and posting on-line guidance regarding the appropriate and prohibited uses of this information by HHS staff and management. The timing of the projected systems development effort will determine when the reconstructed listing will be available for use. Until that time, please continue to share useful post-award information within your OPDIV and with other HHS OPDIVs.

8/17/07 ALERT LIST
still not available
-slh

U.S. Department of Health & Human Services • 200 Independence Avenue, S.W. • Washington, D.C. 20201

Opening page <http://intrinet.grantsinfo.hhs.gov/AlertList.cfm?id=300>

12:28 PM

List Updated on 04/16/2007

DEBARMENT LIST

The following is a public list of firms or persons debarred pursuant to **sections 306(a) and (b)** of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 335(a) and (b)) as published in the **FEDERAL REGISTER (FR)**:

Firms

NAME OF FIRM	EFFECTIVE DATE	END/TERM OF DEBARMENT	FR DATE.txt (MM/DD/YY)	VOLUME PAGE.pdf
None as of this date				

Persons

NAME OF PERSON	EFFECTIVE DATE	END/TERM OF DEBARMENT	FR DATE.txt (MM/DD/YY)	VOLUME PAGE.pdf
Chang, Charles Y.	03/08/1993	Permanent^	03/08/1993	58FR12967
		FR Correction	04/26/1993	58FR21983
Mannan, Muhammad Z.	04/06/1993	Permanent^	04/06/1993	58FR17896
Rivers, Jacob H.	04/12/1993	Permanent^	04/12/1993	58FR19128
Vegesna, Raju	04/12/1993	Permanent^	04/12/1993	58FR19129
Finelli, Gena R.	04/21/1993	Permanent^	04/21/1993	58FR21469
Kalidindi, Sanyasi Raju	04/21/1993	Permanent^	04/21/1993	58FR21470
Azeem, Mohammed	04/26/1993	Permanent^	04/26/1993	58FR21982
		FR Correction	05/05/1993	58FR26814
Schetlick, Gloria H.	04/26/1993	Permanent^	04/26/1993	58FR21983
Colton, Steven F.	06/17/1993	Permanent^*	06/17/1993	58FR33446
Sturm, Jan T.	06/22/1993	Permanent^	06/22/1993	58FR33941
		FR Correction	07/06/1993	58FR36252
Prasad, Kumar	06/30/1993	Permanent^	06/30/1993	58FR35006

Fogari, Robert A.	07/08/1993	Permanent^*	07/08/1993	58FR36691
Rodriquez, Juan Manuel	07/26/1993	Permanent^	07/26/1993	58FR39819
Shulman, Robert NMI	08/27/1993	Permanent^	08/27/1993	58FR45340
Shah, Dillip	08/31/1993	Permanent^*	08/31/1993	58FR45899
Desai, Kanubhai C.	10/06/1993	Permanent^	10/06/1993	58FR52111
Matkari, Rajaram K.	10/20/1993	Permanent^*	10/20/1993	58FR54156
	06/13/2000	Withdrawn++	06/13/2000	65FR37154
Dicola, Charles G.	11/05/1993	Permanent^*	11/05/1993	58FR59044
Hossain, Liaquat	11/05/1993	Permanent^*	11/05/1993	58FR59046
Pai, Daphne (aka Lau, Daphne)	11/05/1993	Permanent^*	11/05/1993	58FR59048
Bansal, Padam C.	11/29/1993	Permanent^*	11/29/1993	58FR62674
	03/11/1997	Sp.Trmnation+	03/11/1997	62FR11212
Donnelly, Mary	11/29/1993	Permanent^	11/29/1993	58FR62675
Perkal, Mark B.	11/29/1993	Permanent^	11/29/1993	58FR62676
	09/11/1998	Sp.Trmnation+	09/11/1998	63FR48733
Long, Susan M.	12/23/1993	Permanent^*	12/23/1993	58FR68147
Bae, Kun Chae	12/30/1993	Permanent^*	12/30/1993	58FR69368
Brancato, David J.	01/06/1994	Permanent^*	01/06/1994	59FR00751
Shah, Satish R.	08/01/1994	Permanent^*	08/01/1994	59FR38983
Patel, Ashok	11/08/1994	Permanent^*	11/08/1994	59FR55670
Kletch, Walter S.	11/29/1994	Permanent^*	11/29/1994	59FR60989
Ryan, Patrick T.	11/29/1994	Permanent^	11/29/1994	59FR60992
		FR Correction	01/17/1995	60FR03451
Shah, Atul	12/05/1994	Permanent^*	12/05/1994	59FR62399

	03/11/1997	Sp.Trmnation+	<u>03/11/1997</u>	<u>62FR11212</u>
Mendell, Arnold S.	12/21/1994	Permanent^*	<u>12/21/1994</u>	59FR65773
Quamruzzaman, Abu	11/18/1993	Permanent^#	<u>12/30/1994</u>	59FR67709
Morris, Andrew	05/16/1994	Permanent^#	<u>01/11/1995</u>	<u>60FR02767</u>
Shainfeld, Frederick Jay	03/10/1995	Permanent^#	<u>02/28/1996</u>	<u>61FR07521</u>
Copanos, John D.	03/11/1996	Permanent^*	<u>03/11/1996</u>	<u>61FR09711</u>
		FR Correction	<u>04/18/1996</u>	<u>61FR16975</u>
Bushlow, John W.	03/22/1996	Permanent^*	<u>03/22/1996</u>	<u>61FR11846</u>
Chatterji, Dulal C.	11/01/1995	Permanent^#	<u>01/22/1997</u>	<u>62FR03297</u>
	06/11/1998	Sp.Trmnation+	<u>06/11/1998</u>	<u>63FR32013</u>
Mays, Gary D.	01/24/1997	5 years%	<u>01/24/1997</u>	<u>62FR03703</u>
Garfinkel, Barry D.	04/02/1997	Permanent^*	<u>04/02/1997</u>	<u>162FR1573</u>
Elbert, Robert	04/03/1997	Permanent^*	<u>04/03/1997</u>	<u>62FR15902</u>
Sacher, Robert E.	08/11/1997	Permanent^	<u>08/11/1997</u>	<u>62FR42998</u>
Islam, Amirul	08/27/1997	Permanent^#	<u>08/27/1997</u>	<u>62FR45423</u>
	10/09/2003	Sp. Trmnation+	<u>10/09/2003</u>	<u>68FR58352</u>
Banks, Norma D.	08/28/1997	Permanent^	<u>08/28/1997</u>	<u>62FR45667</u>
Herman, Hedviga	10/17/1997	Permanent^	<u>10/17/1997</u>	<u>62FR54117</u>
Rana, Nandlal	10/20/1997	Permanent^	<u>10/20/1997</u>	<u>62FR54462</u>
Anthony, James Michael	11/07/1997	Permanent^	<u>11/07/1997</u>	<u>62FR60249</u>
Feuer, Scott	06/02/1998	5 years%	<u>06/10/1998</u>	<u>63FR31789</u>
Kostas, Constantine I.	06/25/1998	Permanent^*	<u>06/10/1998</u>	<u>63FR34652</u>
Girdhari, Premchand	01/21/2000	Permanent^*	<u>01/21/2000</u>	<u>65FR03454</u>

Elsharaiha, Rami	09/29/2000	Permanent^	<u>09/29/2000</u>	<u>65FR58555</u>
Marcus, Jay	09/29/2000	5 years%	<u>09/29/2000</u>	<u>65FR58556</u>
Uddin, Mohammad NMI	09/29/2000	Permanent^	<u>09/29/2000</u>	<u>65FR58557</u>
Petrik, Craig H.	04/30/2002	Permanent^	<u>04/30/2002</u>	<u>67FR21255</u>
Fiddes, Robert A.	11/06/2002	20 years%	<u>11/06/2002</u>	<u>67FR67628</u>
	01/21/2003	FR Correction	<u>01/21/2003</u>	<u>58FR2784</u>
One person removed from list	11/06/2002	Rescission!!!	<u>01/16/2003</u>	<u>68FR2339</u>
Lai, Elaine Yee-Ling	11/13/2002	5 years%	<u>11/13/2002</u>	<u>67FR68877</u>
		FR Correction	<u>11/23/2003</u>	<u>68FR03264</u>
Charpentier, Laverne M.	12/02/2002	5 years%*	<u>12/02/2002</u>	<u>67FR71574</u>
Peugeot, Renee	01/13/2003	Permanent^	<u>01/13/2003</u>	<u>68FR1619</u>
Snyder, Jr., Harry W.	01/13/2003	Permanent^	<u>01/13/2003</u>	<u>68FR1619</u>
Kokes, Edwin	04/30/2003	Permanent^	<u>04/30/2003</u>	<u>68FR23138</u>
Theodore, Thomas Ronald	08/05/2003	Permanent^	<u>08/05/2003</u>	<u>68FR46197</u>
Borison, Richard L.	09/30/2003	10 years%	<u>09/30/2003</u>	<u>68FR56298</u>
Sardesai, Suhas V.	09/30/2003	Permanent^	<u>09/30/2003</u>	<u>68FR56299</u>
Striefsky, Edmund J.	09/30/2003	Permanent^	<u>09/30/2003</u>	<u>68FR56300</u>
Courtney, Robert Ray	10/20/2003	Permanent^	<u>10/20/2003</u>	<u>68FR59942</u>
Bhutani, Baldev Raj	12/02/2004	Permanent^	<u>12/02/2004</u>	<u>69FR70148</u>
Caro Acevedo, Eduardo	03/24/2005	5 years%	<u>03/24/2005</u>	<u>70FR15107</u>
Rodgers, Jr., Thomas M.	07/28/2005	5 years%	<u>07/28/2005</u>	<u>71FR43699</u>

Butkovitz, Anne L.	10/17/2006	Permanent^	<u>10/17/2006</u>	<u>71FR61061</u>
Kimball, James T.	01/30/2007	Permanent ^	<u>01/30/2007</u>	<u>72FR4269</u>

NOTATIONS:

- ^ Mandatory Debarment (Sec. 306(a))
- % Permissive Debarment (Sec. 306(b))
- * Hearing requested and denied.
- # Acquiesced to Debarment.
- + Special Termination of Debarment (Sec. 306(d)(4)(C) and (d)(4)(D))
- ++ Order to Withdraw Order of Debarment (debarment terminated) (Sec. 306(d)(3)(B)(i))
- !!! Rescission of Debarment Order

aka Also known as

NMI No Middle Initial known to be used

This public list is compiled in accordance with **21 U.S.C. 335a(e)** from notices published in the FEDERAL REGISTER. Firm or individual names appearing for the first time in a FR notice of debarment are added to the end of the list. Subsequent FR debarment notices concerning the same firm or person are posted after the first listing of the firm or individual.

This list is prepared by the Office of Enforcement, Division of Compliance Policy (HFC-230), 5600 Fishers Lane, Rockville, Maryland 20857; telephone 240.632.6860; FAX 240.632.6861.

"The Disqualified/Restricted/Assurance List for Clinical Investigators," is located at:

http://www.fda.gov/ora/compliance_ref/bimo/dis_res_assur.htm
and,

"The Public Health Service Administrative Actions Listing," is located at:

<http://silk.nih.gov/public/cbz1bje.@www.orilist.html>


FEDERAL REGISTER publications from 1994 to date are located on the internet at:

http://www.access.gpo.gov/su_docs/aces/aces140.html

Debarment certification statements: **Draft guidance for industry** (PDF) and Notice of Availability **63 FR 53060 10/02/1998** (Text)

Background information on Debarment: **["FDA Consumer" magazine March 1997 "Inside FDA:Barring People from the Drug Industry"]**

Hyperlinks to **FEDERAL REGISTER** statements are provided where available. Debarments prior to 1994 are **not available** online.

 Entries marked with this logo are PDF documents. You will need "Acrobat Reader" to view it. If you do not have it installed on your computer, click on the following link to download a free copy.



dbar053foi.doc [lstsv/rqst2web 07/28/2005 tc]

dbar054foi.doc [lstsv/rqst2web 10/17/2006 ca]

dbar055foi.doc [lstsv/rqst2web 04/16/2007 ca]

Irrelevant characters removed from explanatory text [06/25/2007 pmb]

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- > Advanced Archive Search
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Contact Information

- > Email: support@epls.gov
eplscomments@epls.gov
- > Phone: 1-866-GSA-EPLS
1-866-472-3757

Search Results for Parties Excluded by

Partial Name : Lazarus

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Page: 1

Lemon, Lazarus

Classification: Individual ; Exclusion Type: Reciprocal ; Address 1:
{ Pittsburgh, PA, 15221 ; DUNS: none } ; Action 1 { CT Code: R,
Agency: OPM } ; Action 2 { CT Code: Z1, Agency: HHS } ;
Description: none

Long, Richard Lazarus, Jr.

Classification: Individual ; Exclusion Type: Reciprocal ; Address 1:
{ Santa Barbara, CA, 93110 ; DUNS: none } ; Action 1 { CT Code: R,
Agency: OPM } ; Action 2 { CT Code: Z1, Agency: HHS } ;
Description: none

Page: 1

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021

DGM

vwPIDelinquentList



GRANT_NUMBER	PI_NAME
1UC1HS015316-01	A Blair
5P01HS010856-05	A Washington
5U18HS012021-03	Ajit Sachdeva
5R01HS007538-02	Alan White
1F32HS013985-01	Amy Kaji
5F31HS011929-04	Andrea Ireland
5K08HS000004-05	Andrew Siderowf
5K02HS011294-04	Anthony Losasso
5R24HS011673-03	Anthony Wutoh
1U01HS014355-01	Aram Dobalian
5R01HS010153-07	Barbara Mark
7R01HS011983-03	Bradley Evanoff
5K08HS013007-05	Brent Asplin
5R01HS010596-03	Carol Simon
5U18HS013721-02	Carole Lannon
5F32HS013108-02	Catherine Milch
1UC1HS015359-01	Charles Bryant
5U01HS007399-05	Charles Francis
1R13HS016360-01	Charles Homer
5R01HS010884-04	Christopher Callahan
5K08HS013333-03	Christopher Landrigan
5R01HS013328-03	Christopher Schmid
1R13HS016490-01	Constantine Gatsonis
5R24HS013353-03	Daniel Howard
5P20HS011550-03	David Hickam
5R18HS007095-03	David Kanouse
1R13HS016288-01	Dorothy Naylor
5U54HS008633-03	Edward Brandt
1R03HS009357-01	Elisha Atkins
1R21HS014862-01A1	Ellen Wald
5R01HS011431-03	Eric Schneider
1R03HS013230-01	Frederick Connell
5R01HS009948-03	Frederick Connell
1R01HS015054-01	Gail Keenan
1U01HS014337-01	Gary Green
5R01HS010623-03	Gillian Sanders
5R01HS011966-04	Ginette Pepper
5R24HS014034-03	Gordon Belcourt
1R03HS07531-01	Herbert Fillmore
5R01HS007035-03	Jack Froom
5R24HS011618-03	Jean Freeman
5T32HS000076-02	Jeanne Miranda
1R03HS014105-01	Jennifer Carroll
1R03HS010789-01	Jennifer Miglionico
1R13HS010089-01	Jo Powell
5T32HS000052-11	Jody Sindelar
5U18HS013685-03	John Combes
1R03HS009599-01	John Schneider
1R13HS010104-01	Karen Goldman
5U18HS013690-04	Karen Kmetik
5R13HS013368-03	Kay Dickersin

7/19/07

1K08HS000012-01	Kenley Chin
7R01HS011088-06	Laura Mccloskey
5R01HS011444-03	Laura Morlock
5R01HS013152-04	Laura Siminoff
1F32HS015773-01	Leslie Boxer
1R13HS016312-01	Linda Lesky
1R01HS015941-01A1	Lisa Iezzoni
5K08HS014062-03	Lisa Strate
5R01HS010315-03	M Hawes
1U18HS016093-01	Maria Suarez-Almazor
5K08HS000008-05	Marielena Lara
1R13HS014385-01	Mary Auld
1U18HS016378-01	Michael Bordelon
5U18HS013718-04	Michael Callahan
1R13HS015757-01	Michael Devita
5R01HS013654-03	Michael Yedidia
5R01HS013329-02	Nananda Col
1UC1HS016143-01	Nancy Shank
1R03HS008481-01	Patricia Caulfield
1R03HS014633-01A1	Patricia Coon
1R03HS013977-01A1	Pei-Shu Ho
5F31HS014586-02	Rashida Dorsey
5U18HS010385-07	Raymond Woosley
5T32HS000026-12	Richard Scheffler
5K02HS013299-03	Rita Mangione-Smith
5R01HS013131-02	Rita Snyder-Halpern
5R01HS010630-04	Robert Friedman
5R24HS011617-03	Robert Mayberry
5R24HS014060-03	Roberto Torres-Zeno
5K08HS011644-04	Saul Weingart
5U18HS011885-03	Scott Williams
1R36HS015528-01	Shannon Flood
5R01HS006897-04	Sherrie Kaplan
5R01HS009507-03	Stephen Downs
5R24HS011845-05	Steven Fleming
5U18HS013716-04	Steven Ornstein
1R13HS016305-01	Thomas Stripling
1R03HS07512-01	Verita Custis
1R13HS010076-01	Virginia Paganelli
5K02HS013655-03	William Adams

HS 07-002

FUNDING LIST FOR SPECIAL EMPH...IS PANEL 2007/10 ZHS1 HSR-O (01)

07/13/2007

REVIEW CYCLE 0710

PAGE 1 OF 3

P.I.	FUNDED APPL. NO.	TITLE	INSTITUTION	ST	PROJECT OFFICER	SCORE	PCT	BGT YEAR TOTAL COST	DIRECTOR'S SIGN OFF
(b)(4); (b)(5); (b)(6)									

LAZARUS, ROSS	N	R18 HS17045-01	Electronic Support for Public Health - Vaccine Adverse E	HARVARD PILGRIM HEALTHCARE INC	MA	WHITE, JON	169	100	\$501,478	MAX	X
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(b)(4); (b)(5); (b)(6)											
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HYGIENE

* Pay list signed 8/15/07

FUNDING LIST FOR SPECIAL EMPHASIS PANEL 2007/10 ZHS1 HSR-O (01)

07/13/2007

REVIEW CYCLE 0710

PAGE 2 OF 3

P.I.	FUNDED APPL. NO.	TITLE	INSTITUTION	ST	PROJECT OFFICER	SCORE	PCT	BGT YEAR TOTAL COST	DIRECTOR'S SIGN OFF
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(b)(4); (b)(5); (b)(6)

**paylist signed 8/15/07*

FUNDING LIST FOR SPECIAL EMPHASIS PANEL 2007/10 ZHS1 HSR-O (01)

07/13/2007

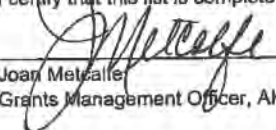
REVIEW CYCLE 0710

PAGE 3 OF 3

P.I.	FUNDED APPL. NO.	TITLE	INSTITUTION	PROJECT ST OFFICER	SCORE	PCT	BGT YEAR TOTAL COST	DIRECTOR'S SIGN OFF
(b)(4); (b)(5); (b)(6)								

TOTAL NUMBER OF APPLICATIONS: 37

I certify that this list is complete and correct

 7/16/07
Joan Metcalfe
Grants Management Officer, AHRQ

FUNDING RECOMMENDATION

Ambulatory Safety and Quality: Enabling Quality Measurement through Health IT (RFA # HS-07-002)

I. Background

Ambulatory Safety and Quality Initiative:

The purpose of the Agency for Healthcare Research and Quality's (AHRQ) Ambulatory Safety and Quality (ASQ) program is to improve the safety and quality of ambulatory health care in the United States. The scope of ambulatory care has increased over the past decade as the volume and complexity of interventions have burgeoned. Safe, high quality ambulatory care requires complex information management and coordination across multiple settings, especially for patients with chronic illnesses. The opportunity to turn the potential of health IT towards improving safety and quality in the ambulatory care setting, especially within care transitions, forms the cornerstone of the proposed Ambulatory Safety and Quality (ASQ) Program.

Enabling Quality Measurement through Health IT:

The purpose of this FOA is to develop safety and quality measures in ambulatory care settings, automate quality measurement, demonstrate the ability of electronic data systems (such as EHRs or claims data merged with EHR data) to expand potential safety and quality measures, and demonstrate improved ability to export data for reporting performance on measures and improvement. Projects that explore the roles of health information exchange in support of public reporting of quality measures and emerging transparency initiatives are also encouraged.

Applicants were encouraged to consider projects that focus on a variety of aspects of quality measurement. Some aspects of interest include process, data elements, value and accuracy, creation of meaningful information, and timeliness of data integration. Additional areas of interest include demonstration of the ability of interoperable electronic data systems and health information exchanges to provide data for measurement and for public reporting, EHRs that include the capacity and increased efficiency to export data for measurement, and the impact of feedback to clinicians and public reporting on outcomes including provider satisfaction, provider performance, patient satisfaction and/or patient outcomes.

Available funds and funding priorities:

AHRQ has designated \$6.8 million in FY07 to fund approximately 15 applications under this FOA. \$5 million is from the health IT portfolio, with a \$1.8 million set aside for non-HIT projects funded from the patient safety portfolio.

Response to the FOA: The FOA was published on December 5, 2006. AHRQ received 81 letters of intent, and 59 applications were received in response to the FOA. Of these, 3 applications were returned after administrative review. The SEP met on June 28-29, 2007, triaged 22 applications and discussed the remaining 34 applications.

II. Core Funding Recommendation

The health IT and patient safety teams considered applications with scores under 245 for funding. They closely examined these 20 applications taking into consideration their scores and the diversity they would bring to the program.

The teams recommend funding 15 proposals.

	Funding Obligation and Outgoing Years	
	FY 07	FY 08
Recommended Applications	\$6,506,123	\$6,454,669

Recommendations for ASQ-EQM FOA Awards**Health IT Funding**

Rank Order	PI Name	Title	FY 07	Score
(b)(5)				
(b)(5)	LAZARUS, ROSS	Electronic Support for Public Health - Vaccine Adverse Event Reporting System	\$499,995	(b)(5)
(b)(5)				
Total			\$4,676,016	

Patient Safety Funding

Rank Order	PI Name	Title	FY 07	Score
(b)(5)				
Total			\$1,830,107	

Considered for Funding

Rank Order	PI Name	Title	FY 07	Score
(b)(5)				

III. Funding Preference

This FOA included an opportunity for the applicant to designate a funding preference for the Patient Safety set-aside which did not include a health IT component. Notably, none of the applicants requested consideration for the patient safety set-aside.

IV. Program Overview

The following table summarizes key descriptors for each of the applications recommended for funding. Strengths of this recommendation include robust projects addressing significant chronic conditions such as cardiovascular disease, diabetes and asthma. There is prominent involvement of national organizations and initiatives such as the American Medical Association, NCQA, the American Gastroenterological Association, and the AQA. A variety of ambulatory settings and organizations are addressed, from large integrated delivery systems to small provider practices; and from urban settings to small rural communities. Several applications address underserved populations through involvement of community health centers. The projects target a good geographic spread including 11 sites in the Northeast, 7 in the Midwest, 2 in the South, and 11 in the West. Of particular note and mild concern is that three Harvard applications and three Kaiser Foundation applications are in the top eight scores.

ASQ-EQM Program Overview:

PI Name	IOM Priority Condition*	Measure Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
(b)(5); (b)(6)	DM, IHD, MM	Medication safety monitoring for ACEI/ARB, Digoxin, Diuretics and Statins	EMR	CHC	Baltimore, MD	low income, minorities (African American), women, chronic care
	Multiple	AQA starter set for primary care (26 measures)	EMR	Primary care practices	Boston, MA	women, children
	HTN, IHD, MM	Cardiovascular disease process and outcome measures	EMR	Multi-specialty practice	Oakland, CA	minorities (African American, Hispanic, Asian), women, chronic care, rural
LAZARUS, ROSS	Immunization	Vaccine adverse effects	EMR	Multi-specialty practice	Boston, MA	women, children
(b)(5); (b)(6)	Asthma	19 asthma care quality measures from the RAND Quality Assessment Tools	EMR, automated data extraction system	CHC, Multi-specialty practice	Portland, OR	low income, women, children, chronic care, rural
	IHD, Tobacco, HTN, DM, Obesity	Prevention Index and Disease Management Index	EMR	Primary care practices	Honolulu, HI	minorities (Asian, Pacific Islander), women, chronic care
	DM	Diabetes care measurement techniques accounting for differences in patient populations.	EMR	Primary and specialty care practices	Philadelphia, PA	women, children, chronic care
	DM, IHD	Development of new diabetes quality-of-care process measures.	EMR	Primary care practices	Boston, MA	minorities (African American, Hispanic), women, chronic care
	Cancer Screening	Colonoscopy pre-procedure, procedure and post-procedure measures	Data repository	Specialty practices	Portland, OR	women

PI Name	IOM Priority Condition*	Measure Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
(b)(5); (b)(6)		Ambulatory quality metrics responsive to the effects of health IT and HIE	HIE	Primary care practices	New York City, Fishkill, and Albany, NY	women, rural
	Children (sickle cell, CF, cancer)	Adverse drug events for pediatric patients in ambulatory settings, emergency departments, and transitions of care	Electronic records, automated surveillance system	ED, Primary care practices	St. Louis, MO	minorities (African American), children, chronic care
	IHD, CHF	Coronary Artery Disease and Heart Failure measures	EMR	Primary care practices	Chicago, Saint Charles, and Lombard, IL; Des Moines, IA; Pittsburgh, PA; Avon, OH; Lexington, MA; Washington, DC	chronic care, rural
	DM, HTN, IHD, CHF	PQRI	EMR, automated data extraction system	Hospital Outpt and Primary care practices	Bolivar, MO	rural
	DM	Specific measures to be determined.	HIE, EMR	CHC, Hospital Outpt, Primary care practices	Denver, Lafayette, Glenwood Springs, Greeley, Englewood, Lamar, and Colorado Springs, CO	low income, minorities (Hispanic), chronic care, rural
	Obesity, IHD, Depression,	Ambulatory care screening measures	HIE, EMR	CHC, Hospital Outpt, Primary care practices	New York City and Lake Success, New York	low income, minorities (African American, Hispanic) women

*Key:

- DM: Diabetes mellitus
- IHD: Ischemic heart disease
- MM: Medication management
- HTN: Hypertension
- CF: Cystic fibrosis
- CHF: Congestive heart failure

Rank/ScoreRecommended for Health IT Funding – Brief Project Description:

(b)(5)

(b)(5)

Lazarus (1R18HS017045-01):**Electronic Support for Public Health - Vaccine Adverse Event Reporting System**

The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. The researchers will evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project, and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

Rank/Score

(b)(5)

(b)(5)

(b)(5)

Rank/Score

Recommended for Patient Safety Funding – Brief Project Description:

(b)(5)

(b)(5)

Rank/Score **V. Application Skipped Over for Funding**

(b)(5)

(b)(5)

Rank/Score VI. Additional Applications Considered for Funding

(b)(5)

(b)(5)

(b)(5)

(b)(5)

IOM Priority Condition	Measures Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
DM, HTN, CAD, CHF, Asthma	Standardized measures in five ambulatory care-sensitive chronic conditions	EMR	Primary care practices	Cleveland, OH	low income, minorities (African American), women

VI. Discussion Items

1. Institutional funding concentration

VII. Action Item

1. Approve applications 1-14 and 16 for funding.

FUNDING RECOMMENDATION**Ambulatory Safety and Quality: Health IT Sweep-up Funding****I. Background****Ambulatory Safety and Quality Initiative:**

The purpose of the Agency for Healthcare Research and Quality's (AHRQ) Ambulatory Safety and Quality (ASQ) program is to improve the safety and quality of ambulatory health care in the United States. The scope of ambulatory care has broadened over the past decade as the volume and complexity of interventions have increased. Safe, high quality ambulatory care requires coordination across multiple settings and presents complex information management challenges, especially for patients with chronic illnesses. The opportunity to use the potential of health IT for improving safety and quality in the ambulatory care setting, especially across care transitions, forms the cornerstone of the Ambulatory Safety and Quality (ASQ) Program.

Available funds:

AHRQ has set aside \$21 million in FY07 to fund ASQ applications. In prior funding recommendations, we have already committed \$19.5 million. Additionally, we have been made aware that one of our previously recommended applications (Marcin) has already been funded by HRSA, leaving a total of \$1.8 million uncommitted. Therefore, we are recommending four new applications for funding which will bring our total commitment to \$20.9 million for FY2007.

The Health IT team recommends funding four additional applications.

	Funding Obligation and Outgoing Years		
	FY 07	FY 08	FY 09
Recommended Applications	\$1,771,959.00	\$1,633,830.00	\$796,501.00

II. Funding Recommendation

Enabling Patient-Centered Care through Health IT (RFA # HS-07-007)

No priority score order skip is required to fund this application.

(b)(5)

Rank/Score: (b)(5)

(b)(5)

Area of Patient-Centered Care	Intervention/ Type of HIT	Settings of Care	Location	Priority Populations
Patient self-management, Shared decision-making, Patient-clinician communication, Access to Medical Information	Clinical Decision Support (Medication Management)	Primary care practices	Chicago, IL	women, minority (African American)

Enabling Quality Measurement through Health IT (RFA # HS-07-002)

One priority score order skip is required make this recommendation.

(b)(5)

Rank/Score: (b)(5)

(b)(5)

IOM Priority Condition	Measures Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
No focus	Diagnostic errors	Operational Decision Support (Quality of Care)	Primary care practices	Temple and Houston, TX	rural

(b)(5)

Rank/Score: (b)(5)

(b)(5)

(b)(5)

IOM Priority Condition	Measures Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
Medication Management	Appropriateness of prescriptions	Clinical Decision Support	ED, Primary care practices	Birmingham, AL; Jacksonville, FL	low income, minorities (African American), women, disabilities, chronic care

Improving Quality through Clinician Use of Health IT (RFA # HS-07-006)

Three priority score order skips are required make this recommendation.

(b)(5)

Rank/Score: (b)(5)

(b)(5)

Area of Interest	Disease	Intervention/ Type of HIT	Settings of Care	Location	Priority Populations
Impact of Health IT on outcomes in ambulatory settings; Improved use of effective alert strategies for decision support	hypertension	Registries, Clinical Decision Support	Primary care practices (inc. CHCs)	New York, Ossing, Sleepy Hollow, Mt. Kisco, and Port Chester, NY	low-income, minorities (Hispanic), women, chronic care

III. Applications Skipped Over for Funding

Enabling Quality Measurement through Health IT (RFA # HS-07-002)

(b)(5)

Rank/Score: (b)(5)

(b)(5)

IOM Priority Condition	Measures Areas Addressed	Type of Health IT	Settings of Care	Geographic Locations	Priority Populations
HTN	Lifestyle behavior recommendations role in changes in blood pressure	EMR, natural language processing	Primary care practices	Atlanta, GA; Portland, OR	Minorities (African American), women

Improving Quality through Clinician Use of Health IT (RFA # HS-07-006)

(b)(5)

Rank/Score: (b)(5)

(b)(5)

Area of Interest	Disease	Intervention/ Type of HIT	Settings of Care	Location	Priority Populations
Impact of health IT across transitions in care; Care for pts with multiple chronic conditions		Telehealth (provider focused)	Primary care practices, Specialty	Denver, CO	women, minority (African American, Hispanic, Asian)

(b)(5)

Rank/Score: (b)(5)

(b)(5)

(b)(5)

Area of Interest	Disease	Intervention/ Type of HIT	Settings of Care	Location	Priority Populations
Relationship between health IT and workflow redesign	Rheumatic diseases	EMR, dashboard	Specialty	Danville and State College, PA	women, chronic care

(b)(5)

Rank/Score: (b)(5)

(b)(5)

Area of Interest	Disease	Intervention/ Type of HIT	Settings of Care	Location	Priority Populations
Improved use of effective alert strategies for decision support		practice-individualized clinical reminders for meds	Primary care practices	Ann Arbor and East Lansing, MI	chronic care

VII. Action Item

Approve recommended applications for funding.

Prepared for AHRQ SLT by Jon White and AHRQ health IT team members (b)(5)

(b)(5)

Submitted: August 10, 2007

COE
Funding
Memo

MEMORANDUM

Date: August 17, 2007

From: Grants Management Officer

Subject: Decisions from August 14, 2007, Funding Meeting

To: Director, COE
Director, CDOM
Director, CQUIPS
Director, CP3
Director, CFACT
Director, OCKT
Director, OPART
Director, OEREP

On August 15 the Director signed the paylists for the K08, K02, F31, R01, R21, R36, R03, and large and small conference grant applications listed below. Paylists for five additional applications submitted under ASQ FOAs were also signed. Grants management staff will initiate pre-award administrative review and budget negotiations with business officials of applicant organizations. Awards will be issued upon completion of pre-award review. Please refer the PIs to the grants management specialists should they have questions regarding the status of the award.

Project officers may contact the PIs to (a) inform them that their applications are being processed for possible award actions; (b) immediately discuss and resolve pending issues (if any) including those relating to human subjects, minority subjects, women, children, priority populations, and other programmatic concerns *either* expressed by the reviewers in the summary statement *or* discussed at the funding meeting; (c) if revised budget is required, alert them that grants management will be requesting it from their business officials; (d) if applicable, explore co-funding immediately and initiate MOU if the grant is to be co-funded. Please forward all relevant information (e.g., responses to summary statements) to grants management staff as soon as it is received.

PIs should be informed that funding decisions are not final until they receive a Notice of Grant Award from the grants management office. This cautionary approach will protect the Agency's interests if, for any reason, an award cannot be made.

Withheld pursuant to exemption

(b)(5)

of the Freedom of Information Act

1 K02 HS017013-01	Bennett	Chronic Care Quality Improvement Learning Laboratory (cQuILL)	Anderson	Hornbeak
1 K08 HS017014-01	Wetterneck	Assessing Risk in Ambulatory Medication Use after Hospital Transitions	Anderson	Deal
1 R36 HS016959-01A1	Allen	Geographic Patterns in Recurrent Stroke Rates by Gender and Race	Harding	Holman
1 R36 HS016836-01A1	Nicholas	Medicare Advantage?	Harding	Holman
1 R36 HS017382-01	Smith, Laura	Home Health Agency Quality: Profit Orientation, Competition and Rehospitalization	Harding	Holman
1 R36 HS017387-01	Stellefson	Efficacy of DVD Technology in COPD Self-Management Education of Rural Patients	Harding	Holman
1 R36 HS017379-01	Golberstein	Essays on Long-Term Care Dynamics	Harding	Holman
1 R36 HS017388-01	Brennan	Error and Near-Miss Reporting of Infection-Related and Other Pediatric Events	Harding	Holman
1 R36 HS016951-01A1	Keuffel	The Economics of Physical Activity	Harding	Holman
1 R36 HS017375-01	Sandler	The Effects of Maternal Labor Supply on Child Health	Harding	Holman
1 R36 HS017381-01	Bellebaum	The Relationship between Nurses Work Hours, Fatigue, and Medication Administration	Harding	Holman
1 R18 HS017045-01	Lazarus	Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES)	White	Holman
1 R18 HS017244-01	Thomas	Using Electronic Records to Detect and Learn from Ambulatory Diagnostic Errors	White	Adeniyi
1 R18 HS017060-01	Berner	Closing the Feedback Loop to Improve Diagnostic Quality	White	Deal
1 F31 NR010294-01	Brooks	We Will Not be Moved: the Black Church Health Movement, 1900-1935	Harding	Deal

Joan Metcalfe

cc: Project Officers
K. Murray
S. Prasad
OCKT-Division of Public Affairs
Office/Center grant coordinators
OPART - Financial Management
OPART- Grants Management
OPART- Performance Management

**Funding Recommendation Memo
(New Grant)**

RFA/PA Number: HS07-002

RFA/PA Title: AMBULATORY SAFETY AND QUALITY PROGRAM: ENABLING QUALITY MEASUREMENT TH

Grant Number: R18 HS17045-01

Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES)

Institution: HARVARD PILGRIM HEALTH CARE, INC.

Principal Investigator: LAZARUS, ROSS **New Investigator?** No

Priority Score: 169 **Percentile:**

Reporting Requirement: Quarterly

Project Officer: FARQUHAR, MARYBETH

Center: CP3

Budget Year	Applicant Requested		Project Officer Recommended	
	Direct Costs	Total Costs	Direct Costs	Total Costs
01	(b)(4)			\$501,478
02				\$498,517
Total				\$999,995

Coding Selections			
Strategic Goal Area:	Safety/Quality	Activity Code(s):	New Knowledge
Portfolio:	Health Information Technology		
Outcome Goal(s):	- By 2008, increase the # of providers using the system from none to over 50%		

Complementary Portfolio(s):	Q/S of Patient Safety	Departmental Coding Theme(s):	Patient Safety, Quality, and Reducing Medical Errors
Field of Science Code:	Medical Sciences		
Cross Cut Code(s):	Health Information Technology		

P.O. Signature:

Marybeth Langhew

Date:

9/10/07

Director Signature:

BMeyer

Date:

9/17/07

Identifiable Data Needed ?:

No

Clinical Trials Registry ?:

No

Data and Safety Monitoring Plan ?:

Yes

Involvement of Priority Populations:

Children

PO Recommendation:

Recommended

Enthusiasm Indicator:

High

PO Comments:

This is a well-designed and well-thought out study submitted by an excellent research team that has had previous success in developing similar project. There is also strong support for this project from Federal agencies including in particular the CDC, and this could be critical in the eventual dissemination of the study findings.

PHS 398 Abstract:

DESCRIPTION (provided by the applicant): Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality

of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Every patient receiving a vaccine will be automatically identified, and for the next 30 days their health care diagnostic codes, laboratory tests, and medication prescriptions will be evaluated for values suggestive of an adverse event. When a possible adverse event is detected it will be recorded, and the appropriate clinician will be notified electronically. Clinicians will be able to preview a pre-populated report with information from the electronic medical record about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment about whether they wish to send a report. Clinicians will have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. Approved reports will be securely transferred to VAERS as electronic messages in an interoperable health data exchange format (HL7). We will evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

Aims of the Project: The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System. The applicants will apply a comprehensive information management system to the task of improving both the accuracy and timeliness of vaccination adverse reaction reporting.

Scientific Significance: Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified.

Anticipated or Actual Impact on Decision Makers: This project will evaluate the system by comparing adverse events findings to those in the Vaccine Safety Datalink project and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number,

completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

**Issues Raised by
Reviewer:**

None

Partnerships:

The researchers will be working with electronic medical records available from all ambulatory care encounters in a large multi-specialty practice.

Principal Investigator/Program Director LAZARUS, ROSS	Degree MBBS	Grant 1-R18-017045-01	IRG ZHS1	CFDA 93 226	Appl ID 7356601
Grantee Organization HARVARD PILGRIM HEALTH CARE INC	Entity No 1042452600A1	Total Project Period from: 09/30/07 thru: 09/29/08			

GM checklist status: Completed by Suzanne Holman 09/18/2007

Award Worksheet Report

Title/Tr.area

Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES)

For Budget Period

from: 09/30/07 thru: 09/29/08

FY FUNDS: 2007
PROG CLASS: CP3
CAN: K72PS53 (SINGLE-CAN)
CNCL: 200710 **PCNTL:** PS: 169
CNCL Action: **CNCL Priority:**
MISCONDUCT IN SCIENCE: **EXP DATE:** 04/30/08
RFA NO: HS07-002
IPF NO: 444701
KIND OF ORG: Other health, human resrces, environmen/community
OWNERSHIP: serv org
Private, Nonprofit Independent
CARRYOVER AUTHORITY:
FEDERAL DEMONSTRATIONS:

AIDS RELATED: N
GENDER: 1A
MINORITY: 1A
CHILD: 1A
EXCEPTION TRACKING: IC
HUMAN SUBJECT: 30
VERT ANIMAL: 10
PHASE III CODE: N
PROGRAM INCOME: Additional Costs
EXPEDITED REVIEW: N
INST. ASSURANCE FILED? Y
IRB CERTIFICATION FILED? Y
ASSURANCE NO. 00000100
DATE 10/01/07
SPEC SUPLMNT INDICATOR:
NGA RELEASE DATE
APPL RECEIVED DATE: 02/12/07 **CURR. ISSUE DATE:** 09/21/07
SNAP AWARD: **ESNAP?:** N
FOREIGN INVOLVEMENT:
CLINICAL TRIAL CODE: No Clinical Trial

Budget

Direct

	Year 1	Year 2
Salaries and Wages	(b)(4); (b)(6)	
Fringe Benefits		
Personnel Costs (Subtotal)		
Consultant Services		
Equipment	\$0	\$0
Supplies	\$200	\$205
Travel Costs	\$1,470	\$1,600
Patient Care (Inpatient)	\$0	\$0
Patient Care (Outpatient)	\$0	\$0
Alterations and Renovations	\$0	\$0
Other Costs	\$0	\$0
Consortium/Contractual Cost	\$315,716	\$308,298
	\$432,675	\$429,713
Direct Costs	(b)(4)	
Indirect Costs		
Total Approved	\$499,809	\$499,405
Fee	\$0	\$0
Non-Federal	\$0	\$0
Unob. bal. Prior Budget	\$0	\$0
Increase/Decrease Amount	+\$0	+\$0
Award Amount	\$499,809	\$499,405

F&A

	Year 1	Year 2
FA Cost Base 1	(b)(4)	
FA Cost Rate 1		
FA costs 1		

GM Comments

Authorized Officials

Principal Investigator/Program Director LAZARUS, ROSS	Degree MBBS	Grant N° 1-R18-1	7045-01	IRG ZHS1	CFDA 93 226	AppI ID 7356601
Grantee Organization HARVARD PILGRIM HEALTH CARE, INC.	Entity No	Total Project Period from: 09/15/07 thru: 09/14/09				

Program Official: Marybeth Farquhar
e-Signature By:
e-Signature Date:

Specialist Name: Suzanne Holman
e-Signature By: Suzanne Holman
e-Signature Date: 08/30/2007

GM Officer: Joan Metcalfe
e-Signature By:
e-Signature Date:

X

X

X

Signature (Optional)

Date

Signature (Optional)

Date

Signature (Optional)

Date

Signature Notes

- a. Grants Management Officer Sign Note:
- b. Specialist Sign Note: 8/30 - Checklist sent to Janet Jordan for her approval.
- c. Program Official Sign Note:

Janet Jordan
8/30/07

GRANT NUMBER: 1 R18 HS017045-01
 GRANTEE INSTITUTION: Harvard Pilgrim Health Care
 P.I.: Ross Lazarus

COMMITTED LEVELS

BUDGET	YEAR 01	YEAR 02
Salaries	(b)(4); (b)(6)	
Fringe Benefits		
PERSONNEL		
CONSULTANTS		
EQUIPMENT	0	0
SUPPLIES	200	205
TRAVEL	1,470	1,600
INPATIENT	0	0
OUTPATIENT	0	0
ALTERATIONS	0	0
3RD PARTY DIRECT	(b)(4)	
TUITION REMISSION	0	0
OTHER	0	0
DIRECT COSTS*	(b)(4)	
3RD PARTY F&A		
TOTAL DIRECT COSTS		
F&A COSTS		
TOTAL COSTS	499,809	499,405

F&A UPDATE DATE

F&A CALCULATION

MTDC? Y

EQUIPMENT	0	0
TOTAL 3RD PARTY	(b)(4)	
PATIENT CARE	0	0
ALTERATIONS	0	0
TUITION	0	0
OTHER	0	0
TOTAL EXCLUSIONS	(b)(4)	
TOTAL BASE		

1st SPLIT IN MONTHS=

12

12

BASE 1	(b)(4)	
RATE 1		
SUBTOTAL 1		
BASE 2	0	0
RATE 2	0.00%	0.00%
SUBTOTAL 2	0	0
TOTAL	(b)(4)	

GRANT NUMBER: **1 R18 HS017045-01****AWARD WORK-UP**GRANTEE INSTITUTION: **Harvard Pilgrim Health Care**P.I.: **Ross Lazarus**

Budget Start Date:

Budget End:

APPROVED BUDGET	Rec Level	Award
Salaries	(b)(4); (b)(6)	
Fringe Benefits		
PERSONNEL		
CONSULTANTS		
EQUIPMENT	0	0
SUPPLIES	200	200
TRAVEL	1,470	1,470
INPATIENT	0	0
OUTPATIENT	0	0
ALTERATIONS	0	0
THIRD PARTY DC	(b)(4)	
THIRD PARTY F&A		
TUITION REMISSION	0	0
OTHER	0	0
TOTAL DC	(b)(4)	

Number of Consortiums= 2

100.00% FY 00 funding level

- Total "Other"

AWARD CALCULATION		Amount
DIRECT COSTS		(b)(4)
F&A COSTS		
Base(s)	Rate(s)	
(b)(4)		
0	0.00%	0
0	0.00%	0
0	0.00%	0
TOTAL F&A COSTS		(b)(4)
TOTAL COSTS		
Unobligated Balance		0
AMOUNT OF AWARD-->		499,809

Project Period Total Rec Costs:

\$630,617

Future Years	YEAR 02
Total Direct Costs	(b)(4)
F&A Costs	
Total Cost Award	499,405

PROJECT PERIOD TOTAL COSTS

9/18/2007

017045-0

GRANT NUMBER: **1 R18 HS017045-01**
GRANTEE INSTITUTION: **Harvard Pilgrim Health Care**
P.I.: **Ross Lazarus**

File Name: 017045-0

GMS Date: Not Saved

<- DO NOT USE
SAVE BUTTON

CORRECTED RECOMMENDED LEVELS

MAIN BUDGET	YEAR 01	YEAR 02
Salaries	(b)(4); (b)(6)	
Fringe Benefits		
PERSONNEL		
CONSULTANTS		
EQUIPMENT	0	0
SUPPLIES	200	205
TRAVEL	1,470	1,600
INPATIENT	0	0
OUTPATIENT	0	0
ALTERATIONS	0	0
3RD PARTY DIRECT	(b)(4)	
TUITION REMISSION	0	0
OTHER	0	0
DIRECT COSTS*	318,251	312,366

* does not include 3rd party F&A. These costs appear on the COMMITTED budget sheet

ENTER DOLLAR FIGURES HERE FIRST FOR ALL BUDGET CATEGORIES EXCEPT 3RD PARTY DIRECT, WHICH SHOULD BE ENTERED ON EACH CONSORTIUM BUDGET AND WILL FEED BACK TO THIS BUDGET.

Figures from this CORRECTED RECOMMENDED LEVELS budget will feed into the COMMITTED budget sheet.

GRANT NUMBER: 1 R18 HS017045-01

CONSORTIUM

Harvard Vanguard Medical Association Harvard Vanguard Medical Association

P.I: (b)(6)	REC	REC
Harvard Vanguard Medical Association	YEAR 01	YEAR 02
Salaries	(b)(4)	
Fringe		
Personnel		
Consultants	0	0
Equipment	0	0
Supplies	0	0
Travel	0	0
Inpatient Costs	0	0
Outpatient Costs	0	0
Alterations	0	0
Third Party	0	0
Tuition Remission	0	0
Other Expenses	0	0
Total Direct Costs	(b)(4)	

COMMITTED LEVELS	YEAR 01	YEAR 02
Salaries	(b)(4); (b)(6)	
Fringe		
Personnel		
Consultants	0	0
Equipment	0	0
Supplies	0	0
Travel	0	0
Inpatient Costs	0	0
Outpatient Costs	0	0
Alterations	0	0
Third Party	0	0
Tuition Remission	0	0
Other Expenses	0	0
TOTAL DIRECT COSTS	(b)(4)	
F&A COSTS		
TOTAL COSTS	68,757	69,631
F&A COST CALCULATION	MTDC? Y	
EQUIPMENT	0	0
TOTAL 3RD PARTY	0	0
PATIENT CARE	0	0
ALTERATIONS	0	0
TUITION	0	0
OTHER	0	0
TOTAL EXCLUSIONS	0	0
TOTAL BASE	(b)(4)	
FIRST BASE SPLIT=	12	12
BASE 1	(b)(4)	
RATE 1		
SUBTOTAL 1		
BASE 2	0	0
RATE 2	0.00%	0.00%
SUBTOTAL 2	0	0

GRANT NUMBER: 1 R18 HS017045-0

CONSORTIUM

The Brigham and Women's Hospital

P.I. Lazarus	REC	REC
The Brigham and Women's Hospital	YEAR 01	YEAR 02
Salaries	(b)(4); (b)(6)	
Fringe		
Personnel		
Consultants	0	0
Equipment	15,000	0
Supplies	1,000	1,030
Travel	2,500	2,575
Inpatient Costs	0	0
Outpatient Costs	0	0
Alterations	0	0
Third Party	0	0
Tuition Remission	0	0
Other Expenses	(b)(4)	
Total Direct Costs	147,407	136,381

COMMITTED LEVELS	YEAR 01	YEAR 02
Salaries	(b)(4); (b)(6)	
Fringe		
Personnel		
Consultants	0	0
Equipment	15,000	0
Supplies	1,000	1,030
Travel	2,500	2,575
Inpatient Costs	0	0
Outpatient Costs	0	0
Alterations	0	0
Third Party	0	0
Tuition Remission	0	0
Other Expenses	(b)(4)	
TOTAL DIRECT COSTS	147,407	136,381
F&A COSTS	(b)(4)	
TOTAL COSTS	246,712	238,667

F&A COST CALCULATION	MTDC? Y	
EQUIPMENT	15,000	0
TOTAL 3RD PARTY	0	0
PATIENT CARE	0	0
ALTERATIONS	0	0
TUITION	0	0
OTHER	0	0
TOTAL EXCLUSIONS	15,000	0
TOTAL BASE	132,407	136,381

FIRST BASE SPLIT=	12	12
BASE 1	(b)(4)	
RATE 1		
SUBTOTAL 1		
BASE 2	0	0
RATE 2	0.00%	0.00%
SUBTOTAL 2	0	0

1 R18 HS017045-01

\$186,600 Cap

IF YOU NEED TO ADD A CHART,

MULTI YEAR SALARY CALCULATION CHART

DO SO BEFORE ENTERING ANY FIGURES

Harvard Pilgrim Health Care, Prime or ParentHarvard Pilgrim Health Care, Prime or Parent

PERSON OR POSITION	YEAR 01		YEAR 02	
	%	SALARY	%	SALARY
Lazarus	(b)(4); (b)(6)			
Brown				
Project Manager				
Programmer				
Research Assistant				
Salary				
Fringe at 30%				
Subtotal Salary				
Klompas				
Platt				
Kleinman				
Salary				
Fringe at 25.3%				
Subtotal Salary				
SALARY				
FRINGE*				
TOTAL				

* FB calculation is composite rate calculated based on Personnel figures entered on CORRECTED RECOMMENDED page

Harvard Vangaurd Medical Association (HVMA)Harvard Vangaurd Medical Association (HVMA)

PERSON OR POSITION	0		0	
	%	SALARY	%	SALARY
Campion	(b)(4); (b)(6)			
Fringe				
Funds Requested				
Programmer				
Fringe				
Funds Requested				
SALARY				
FRINGE*				
TOTAL				

* FB calculation is composite rate calculated based on Personnel figures entered on CORRECTED RECOMMENDED page

The Brigham and Women's HospitalThe Brigham and Women's HospitalThe Brigham and Women's Hospital

PERSON OR POSITION	0		0	
	%	SALARY	%	SALARY
Lazarus	(b)(4); (b)(6)			
Fringe				
Funds Requested				
Admin Assistant				
Programmer				
Manager				
Salaries for O.P.				
Fringe				
Funds Requested				
SALARY				
FRINGE*				
TOTAL				

* FB calculation is composite rate calculated based on Personnel figures entered on CORRECTED RECOMMENDED page

Holman, Suzanne (AHRQ/OPART/GM)

From: Julie_Dunn@harvardpilgrim.org
Sent: Tuesday, September 18, 2007 3:30 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: (b)(6)@harvardpilgrim.org; ross.lazarus@channing.harvard.edu;
 (b)(6)@harvardpilgrim.org
Subject: Re: 1 R18 HS017045-01 (Lazarus)
Importance: High

Hello Suzanne,

This is unfortunate since we were under the impression that things had all been settled! To address your questions:

1. Other Support for Dr. Platt: Award 1 U18 HS016955-01 was not listed under his Other Support. This award started on September 1, 2007. His level of effort for this grant is 15%. He is already at 99.82%. Therefore, this one will put him over. If 5 U18 HS010391-07 truly ends this month which is at 19%, then it will be fine. However, I do need his Other Support updated.

YES, 5 U18 HS010391-07 truly ends this month so Dr. Platt will be fine. I am not at liberty to change his Other Support Page until / unless we have received an official NGA from you, so I can provide you an updated version when the NGA is received.

2. Is the (b)(4) F&A (Indirect) Cost Rate one that HVMA negotiated with HPHC? If so, it needs to be stated in writing.

As HVMA does not have a federally-approved IDC rate, the (b)(4) is the approved HPHC off-site rate which HVMA has been using over multiple projects for multiple years. Exactly how would you like this stated in writing & who should sign this document? I have cc'd Nicholas Mulherin, our Grants manager for this submission to please advise & correspond with you on this point.

3. For some reason, I used (b)(4) Fringe Rate for Year 1 and (b)(4) for Year 2 for instead of the negotiated Fringe Rate of (b)(4). Therefore, I'll need to fix it unless you can justify why it should remain the way I currently have it.

I guess that you will need to fix it.

Thank you,

Julie

 Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

09/18/2007 02:08 PM

To: Julie_Dunn@harvardpilgrim.org
 cc: (b)(6)@channing.harvard.edu,
 (b)(6)@harvardpilgrim.org, ross.lazarus@channing.harvard.edu
 Subject: 1 R18 HS017045-01 (Lazarus)

9/18/2007

Dear Julie,

I was finally able to submit the proposed subject award to the Grants Officer this morning for signature. She had three questions that need to be addressed before the proposed award is signed:

1. Other Support for Dr. Platt: Award 1 U18 HS016955-01 was not listed under his Other Support. This award started on September 1, 2007. His level of effort for this grant is 15%. He is already at 99.82%. Therefore, this one will put him over. If 5 U18 HS010391-07 truly ends this month which is at 19%, then it will be fine. However, I do need his Other Support updated.
2. Is the (b)(4) F&A (Indirect) Cost Rate one that HVMA negotiated with HPHC? If so, it needs to be stated in writing.
3. For some reason, I used (b)(4) Fringe Rate for Year 1 and (b)(4) for Year 2 for instead of the negotiated Fringe Rate of (b)(4). Therefore, I'll need to fix it unless you can justify why it should remain the way I currently have it.

Please get back to me as soon as possible with a response so I can resubmit this one for signature. Thanks!

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
301-427-1460 (phone)
301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

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9/18/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Farquhar, Marybeth (AHRQ)
Sent: Tuesday, September 11, 2007 5:05 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: White, Jonathan (AHRQ)
Subject: RE: 1 R18 HS017205-01 (Davidson)

(b)(5)



MB

Marybeth Farquhar, RN, M.S.N., C.A.G.S.
Senior Advisor, Quality Indicators Initiative
Center for Delivery, Organization, & Markets
Agency for Healthcare Research & Quality
540 Gaither Road
Rockville, MD 20850
Phone: 301-427-1317
Fax: 301-427-1430
E-Mail: marybeth.farquhar@ahrq.hhs.gov

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Tuesday, September 11, 2007 4:32 PM
To: Farquhar, Marybeth (AHRQ)
Cc: White, Jonathan (AHRQ)
Subject: 1 R18 HS017205-01 (Davidson)

Dear Marybeth Farquhar,

(b)(5)



Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
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301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

9/11/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Friday, September 07, 2007 3:41 PM
To: White, Jonathan (AHRQ)
Subject: Funding Memo needed for 1 R18 HS017045-01 (Lazarus)
Importance: High

Dear Jon White,

This one is all ready to go. In fact, I printed out the Notice of Grant Award just now. Then I realized that there is no PO Funding Memo.

Please get this to me as soon as you can. Thanks!

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
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Rockville, Maryland 20850
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Suzanne.Holman@ahrq.hhs.gov

9/7/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Friday, September 07, 2007 2:39 PM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: RE: IRB Approval for 1 R18 HS017045-01 (Lazarus)

Then that is what I'll do since you don't know about IRB yet.

Suzanne

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Friday, September 07, 2007 2:35 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: (b)(6) (b)(6)@harvardpilgrim.org; ross.lazarus@channing.harvard.edu
Subject: Re: IRB Approval for 1 R18 HS017045-01 (Lazarus)

Also, (to follow-up) we initially thought that we would be receiving the NGA before 9/6, hence why I thought we would be granted approval, which is now not the case. We are fine with receiving the award with this IRB restriction, since this is what usually occurs.

Thanks,

Julie

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

09/07/2007 02:28 PM

To: Julie_Dunn@harvardpilgrim.org, (b)(6)@harvardpilgrim.org
 cc: (b)(6)@channing.harvard.edu, ross.lazarus@channing.harvard.edu
 Subject: IRB Approval for 1 R18 HS017045-01 (Lazarus)

Dear All,

I was putting the award package together and I came across an email dated Monday, August 27, which stated that IRB submission was going to be made on September 6 which was yesterday. My question is: Did the IRB review / approval happen yesterday as planned? If so, could I have a copy of your approval letter from the meeting? If not, could you please let me know when you anticipate IRB approval? I will not be able to print off the award package until I know about IRB. The reason is, if IRB approval has occurred as planned, I need to include that approval date in the award submission that is done on the computer. If not, I need to add a restrictive term to the award which restricts funds until IRB approval has occurred.

Please let me know what you know today or early next week. Thanks so much!

Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management
 Agency for Healthcare Research and Quality
 540 Gaither Road, Room 4202
 Rockville, Maryland 20850
 301-427-1460 (phone)

9/7/2007

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Holman, Suzanne (AHRQ/OPART/GM)

From: Julie_Dunn@harvardpilgrim.org
Sent: Friday, September 07, 2007 2:32 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: (b)(6)@harvardpilgrim.org; ross.lazarus@channing.harvard.edu
Subject: Re: IRB Approval for 1 R18 HS017045-01 (Lazarus)
Importance: High

Hello Suzanne,

Until we receive an official Notice of Grant Award from AHRQ, we are unable to receive full IRB approval (which usually occurs within 2 weeks of award). Once that is granted, we will send a copy of the approval letter directly to you. Will this suffice?

Thanks,

Julie

 Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
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"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

09/07/2007 02:28 PM

To: Julie_Dunn@harvardpilgrim.org, (b)(6)@harvardpilgrim.org
 cc: (b)(6)@channing.harvard.edu, ross.lazarus@channing.harvard.edu
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Dear All,

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Please let me know what you know today or early next week. Thanks so much!

Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management

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9/7/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: (b)(6)@channing.harvard.edu]
Sent: Friday, September 07, 2007 10:38 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: (b)(6)@harvardpilgrim.org; Julie_Dunn@harvardpilgrim.org;
ross.lazarus@channing.harvard.edu
Subject: Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification
Attachments: dean.katica.vcf

(b)(6)

Dear Suzanne,

Yes, this TBA (We put TBA until we got the grant number) is the same grant as 1 R18 HS017045-01. Dr. Lazarus does not have effort exceeding more than 100%. The \$ amount is just an estimate because we don't have the notice of award yet and this grant is practically still pending until we receive the notice of award. Also, the award amount shown on the other support is suppose to be just the direct cost for that particular year and not the total project award amount.

Please let us know if you have any further questions.

Thank you,

(b)(6)
Administrative Assistant to Dr. Lazarus
Channing Laboratory

(b)(6)

Holman, Suzanne (AHRQ/OPART/GM) wrote:

>
> Dear Johanna,
>
> Good Morning! I believe that TBA (Platt) is not the same grant as this
> one, even though they have the same project title, because the
> approved funding is only for \$247,144 and this proposed award (1 R18
> HS017045-01) is for almost a million dollars for 2 years. Also,
> Davidson is the PI on this one and Platt is the PI on whatever other
> one TBA (Platt) is.
>
> It would probably be best if Dr. Lazarus got back to me directly to
> straighten this out because he should know first hand what projects he
> is directly involved and not involved in. Also, Dr. Lazarus should
> understand that his Level of Time and Effort cannot be more than 100%
> total, including this award.
>
> It would be sad if this continues to be the only item that holds up
> this proposed grant award from being funded this fiscal year.
>
> Suzanne Holman
>
> * From: *(b)(6)@harvardpilgrim.org
> [mailto:(b)(6)@harvardpilgrim.org]
> *Sent:* Thursday, September 06, 2007 11:25 AM
> *To:* Holman, Suzanne (AHRQ/OPART/GM)
> *Cc:* Julie_Dunn@harvardpilgrim.org; ross.lazarus@channing.harvard.edu
> ;(b)(6)@channing.harvard.edu
> *Subject:* RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other
> Support clarification

>
>
> Suzanne,
>
> It looks as though you may have counted this new grant twice-- on Dr.
> Lazarus' Other Support Page it is listed as a current project. (b)(6)
> (b)(6) Dr. Lazarus' admin, has added the grant award number to the
> listed project to eliminate the confusion.
>
> Thanks,
> Johanna
>
>
>
>
> * "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov> *
>
> 09/05/2007 03:09 PM
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> To
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>
> (b)(6)@harvardpilgrim.org
>
> cc
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>
> Julie_Dunn@harvardpilgrim.org, ross.lazarus@channing.harvard.edu
>
> Subject
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>
> RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support
> clarification
>
>
>
>
>
> Dear (b)(6)
>
> Attached is the revised other support page I created based on what you
> sent me - Dr. Lazarus' other support.
>
> It appears that Dr. Lazarus eliminated one award that had 24% effort
> that made him at 120% and then added one that had 20% effort so now
> instead of being 120%, he is now at 116%. His total level of effort
> cannot be more than 100%.
>
> Please make have Dr. Lazarus adjust his Level of Time and Effort so we
> can expedite this award. This is the only things that I see that is
> holding up this award from being prepared for the Grants Officer's
> signature.
>
> Suzanne Holman
>
>
> * From: * (b)(6)@harvardpilgrim.org
> [mailto:(b)(6)@harvardpilgrim.org] *
> Sent: * Tuesday, September 04, 2007 12:14 PM*

> To:* Holman, Suzanne (AHRQ, OPART/GM) *

> Cc:* Julie_Dunn@harvardpilgrim.org*

> Subject:* Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other

> Support clarification

>

>

> Hi Suzanne,

>

> I hope you had a nice Labor Day weekend! Attached is Dr. Lazarus'

> Other Support page. Please let Julie and I know if you need anything

> else.

>

> Thanks!

> (b)(6)

>

> * Julie Dunn/CORP/HPHC *

>

> 09/04/2007 11:00 AM

>

>

>

> To

>

>

> "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>

>

> cc

>

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>

> (b)(6)@hphc.org

>

> Subject

>

>

>

> Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support

> clarification Link

> <Notes:///852572580072070C/38D46BF5E8F08834852564B500129B2C/E2E63BCA51

> F495DF8525734700460F37>

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>

> Hello Suzanne,

>

> I have seen the correspondence that occurred last week during my

> vacation & believe that Johanna has provided you with most of the

> outstanding documents that you have requested. Could you please let us

> know if there are any additional elements that you still need & we

> will be sure to get them to you ASAP?

>

> Many Thanks,

>

> Julie

>

> *****

> Julie D. Dunn, MPH

> Project Manager - PharmacoEpidemiology / Health IT Department of

> Ambulatory Care and Prevention Harvard Medical School / Harvard

> Pilgrim Healthcare
> 133 Brookline Ave , 6th Floor
> Boston , MA 02215
> Phone: (617) 509-9880 / Fax: (617) 509-9857 www.dacp.org
>
> * "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov> *
>
> 08/30/2007 08:44 AM
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> To
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> Julie_Dunn@harvardpilgrim.org
>
> cc
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>
> ross.lazarus@channing.harvard.edu ,
> (b)(6)@harvardpilgrim.org , (b)(6)@harvard.edu ,
> (b)(6)@hphc.org , (b)(6)@partners.org , (b)(6)@vmed.org
>
> Subject
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>
> Proposed Grant Award Number 1 R18 HS017045-01 - Other Support
> clarification
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>
> Dear Julie Dunn,
>
> Everything seems to be in order administratively based on the
> information you sent me.
>
> The only item I need clarified is that for the five researchers (Dr.
> Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael
> Klompas, and Dr. R. Platt) you sent me regarding their Other Support,
> that none of the projects listed under "Pending" are "Active." The
> reason I ask this is because under Dr. Brown, it looks like at least 2
> listed under "Pending" should be "Active" and under Dr. Kleinman, one
> might be "Active" instead of "Pending". Please clarify.
>
> Also, I still need Other Support for Dr. Francis Campion.
>
> Thank you in advance for your cooperation.
>
> Suzanne Holman
> Grants Management Specialist
> Office of Performance, Accountability, Resources, and Technology;
> Grants Management Agency for Healthcare Research and Quality 540
> Gaither Road , Room 4202 Rockville , Maryland 20850 301-427-1460
> (phone)
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> Suzanne.Holman@ahrq.hhs.gov <mailto:Suzanne.Holman@ahrq.hhs.gov>
>
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>

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Friday, September 07, 2007 8:06 AM
To: (b)(6)@harvardpilgrim.org
Cc: Julie_Dunn@harvardpilgrim.org; 'ross.lazarus@channing.harvard.edu'; (b)(6)@channing.harvard.edu
Subject: RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear (b)(6)

Good Morning! I believe that TBA (Platt) is not the same grant as this one, even though they have the same project title, because the approved funding is only for \$247,144 and this proposed award (1 R18 HS017045-01) is for almost a million dollars for 2 years. Also, Davidson is the PI on this one and Platt is the PI on whatever other one TBA (Platt) is.

It would probably be best if Dr. Lazarus got back to me directly to straighten this out because he should know first hand what projects he is directly involved and not involved in. Also, Dr. Lazarus should understand that his Level of Time and Effort cannot be more than 100% total, including this award.

It would be sad if this continues to be the only item that holds up this proposed grant award from being funded this fiscal year.

Suzanne Holman

From: (b)(6)@harvardpilgrim.org [mailto:(b)(6)@harvardpilgrim.org]
Sent: Thursday, September 06, 2007 11:25 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org; ross.lazarus@channing.harvard.edu; (b)(6)@channing.harvard.edu
Subject: RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Suzanne,

It looks as though you may have counted this new grant twice-- on Dr. Lazarus' Other Support Page it is listed as a current project. Dean Katica, Dr. Lazarus' admin, has added the grant award number to the listed project to eliminate the confusion.

Thanks,
 Johanna

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

09/05/2007 03:09 PM

To: (b)(6)@harvardpilgrim.org
 cc: Julie_Dunn@harvardpilgrim.org, ross.lazarus@channing.harvard.edu
 Subject: RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear (b)(6),

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It appears that Dr. Lazarus eliminated one award that had 24% effort that made him at 120% and then added one that had

9/7/2007

20% effort so now instead of being 40%, he is now at 116%. His total level of effort cannot be more than 100%.

Please make have Dr. Lazarus adjust his Level of Time and Effort so we can expedite this award. This is the only things that I see that is holding up this award from being prepared for the Grants Officer's signature.

Suzanne Holman

From: (b)(6)@harvardpilgrim.org [mailto:(b)(6)@harvardpilgrim.org]
Sent: Tuesday, September 04, 2007 12:14 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Hi Suzanne,

I hope you had a nice Labor Day weekend! Attached is Dr. Lazarus' Other Support page. Please let Julie and I know if you need anything else.

Thanks!

(b)(6)

Julie Dunn/CORP/HPHC

09/04/2007 11:00 AM

To "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
 cc (b)(6)@hphc.org
 Subject Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification [Link](#)

Hello Suzanne,

I have seen the correspondence that occurred last week during my vacation & believe that Johanna has provided you with most of the outstanding documents that you have requested. Could you please let us know if there are any additional elements that you still need & we will be sure to get them to you ASAP?

Many Thanks,

Julie

 Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor

9/7/2007

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"Holman, Suzanne (AHRQ/OPART/GM)"
<Suzanne.Holman@AHRQ.hhs.gov>

08/30/2007 08:44 AM

To Julie_Dunn@harvardpilgrim.org
cc ross.lazarus@channing.harvard.edu, (b)(6)@harvardpilgrim.org,
(b)(6)@harvard.edu, (b)(6)@hphc.org, (b)(6)@partners.org,
(b)(6)@vmed.org
Subject Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie Dunn,

Everything seems to be in order administratively based on the information you sent me.

The only item I need clarified is that for the five researchers (Dr. Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael Klompas, and Dr. R. Platt) you sent me regarding their Other Support, that none of the projects listed under "Pending" are "Active." The reason I ask this is because under Dr. Brown, it looks like at least 2 listed under "Pending" should be "Active" and under Dr. Kleinman, one might be "Active" instead of "Pending". Please clarify.

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9/7/2007

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Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Wednesday, September 05, 2007 3:09 PM
To: (b)(6)@harvardpilgrim.org'
Cc: Julie_Dunn@harvardpilgrim.org; 'ross.lazarus@channing.harvard.edu'
Subject: RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification
Attachments: Revised Other Support.xls

Dear Johanna,

Attached is the revised other support page I created based on what you sent me – Dr. Lazarus' other support.

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Sent: Tuesday, September 04, 2007 12:14 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

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Thanks!

(b)(6)

Julie Dunn/CORP/HPHC

09/04/2007 11:00 AM

To "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
cc (b)(6)@hphc.org
Subject Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification [Link](#)

Hello Suzanne,

I have seen the correspondence that occurred last week during my vacation & believe that Johanna has provided you with most of the outstanding documents that you have requested. Could you please let us know if there are any additional elements that you still need & we will be sure to get them to you ASAP?

9/5/2007

Many Thanks,

Julie

 Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

08/30/2007 08:44 AM

To Julie_Dunn@harvardpilgrim.org
 cc ross.lazarus@channing.harvard.edu, (b)(6)@harvardpilgrim.org,
 (b)(6)@harvard.edu, (b)(6)@hphc.org, (b)(6)s@partners.org,
 (b)(6)@vmed.org

Subject Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie Dunn,

Everything seems to be in order administratively based on the information you sent me.

The only item I need clarified is that for the five researchers (Dr. Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael Klompas, and Dr. R. Platt) you sent me regarding their Other Support, that none of the projects listed under "Pending" are "Active." The reason I ask this is because under Dr. Brown, it looks like at least 2 listed under "Pending" should be "Active" and under Dr. Kleinman, one might be "Active" instead of "Pending". Please clarify.

Also, I still need Other Support for Dr. Francis Campion.

Thank you in advance for your cooperation.

Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management
 Agency for Healthcare Research and Quality
 540 Gaither Road, Room 4202
 Rockville, Maryland 20850
 301-427-1460 (phone)
 301-427-1462 or 1464 (fax)
 Suzanne.Holman@ahrq.hhs.gov

9/5/2007

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9/5/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: (b)(6)@harvardpilgrim.org
Sent: Tuesday, September 04, 2007 12:14 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification
Attachments: LAZARUS-OTHER SUPPORT-September 2007.pdf

Hi Suzanne,

I hope you had a nice Labor Day weekend! Attached is Dr. Lazarus' Other Support page. Please let Julie and I know if you need anything else.

Thanks!

(b)(6)

Julie Dunn/CORP/HPHC

09/04/2007 11:00 AM

To "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
 cc (b)(6)@hphc.org
 Subject Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification [Link](#)

Hello Suzanne,

I have seen the correspondence that occurred last week during my vacation & believe that Johanna has provided you with most of the outstanding documents that you have requested. Could you please let us know if there are any additional elements that you still need & we will be sure to get them to you ASAP?

Many Thanks,

Julie

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 Phone: (617) 509-9880 / Fax: (617) 509-9857
www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

To Julie_Dunn@harvardpilgrim.org

9/4/2007

08/30/2007 08:44 AM

cc: ross.lazarus@channing.harvard.edu, (b)(6)@harvardpilgrim.org,
(b)(6)@harvard.edu, (b)(6)@hphc.org, (b)(6)@partners.org,
(b)(6)@vmed.org

Subject Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie Dunn,

Everything seems to be in order administratively based on the information you sent me.

The only item I need clarified is that for the five researchers (Dr. Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael Klompas, and Dr. R. Platt) you sent me regarding their Other Support, that none of the projects listed under "Pending" are "Active." The reason I ask this is because under Dr. Brown, it looks like at least 2 listed under "Pending" should be "Active" and under Dr. Kleinman, one might be "Active" instead of "Pending". Please clarify.

Also, I still need Other Support for Dr. Francis Campion.

Thank you in advance for your cooperation.

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
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Suzanne.Holman@ahrq.hhs.gov

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9/4/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Tuesday, September 04, 2007 11:05 AM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: RE: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie,

The only problem is that Ross Lazarus' Other Support is now at 120%. It cannot be above 100%. Please send me a revised Other Support for Dr. Lazarus as soon as possible. Thanks!

Suzanne

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Tuesday, September 04, 2007 11:01 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: (b)(6)@hphc.org
Subject: Re: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Hello Suzanne,

I have seen the correspondence that occurred last week during my vacation & believe that Johanna has provided you with most of the outstanding documents that you have requested. Could you please let us know if there are any additional elements that you still need & we will be sure to get them to you ASAP?

Many Thanks,

Julie

Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
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 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

08/30/2007 08:44 AM

To: Julie_Dunn@harvardpilgrim.org
 cc: ross.lazarus@channing.harvard.edu, (b)(6)@harvardpilgrim.org,
 (b)(6)@harvard.edu, (b)(6)@hphc.org, (b)(6)@partners.org,
 (b)(6)@vmed.org
 Subject: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie Dunn,

Everything seems to be in order administratively based on the information you sent me.

9/4/2007

The only item I need clarified is that for the five researchers (Dr. Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael Klompas, and Dr. R. Platt) you sent me regarding their Other Support, that none of the projects listed under "Pending" are "Active." The reason I ask this is because under Dr. Brown, it looks like at least 2 listed under "Pending" should be "Active" and under Dr. Kleinman, one might be "Active" instead of "Pending". Please clarify.

Also, I still need Other Support for Dr. Francis Campion.

Thank you in advance for your cooperation.

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9/4/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Friday, August 31, 2007 7:59 AM
To: (b)(6)@harvardpilgrim.org
Cc: Julie_Dunn@harvardpilgrim.org
Subject: RE: Other Support for 1 R18 HS017045-01 (Lazarus)

Dear Johanna,

Thank you for the additional information and updated Other Support; however, the real issue remains Dr. Lazarus.

If I do not get an updated Other Support for Dr. Lazarus next week, we'll have to issue the award with restriction funds until we receive that information because, as it stands now, it appears that Dr. Lazarus does not have sufficient time to devote to this award with everything else on his plate!

Suzanne Holman

From: (b)(6)@harvardpilgrim.org [mailto:(b)(6)@harvardpilgrim.org]
Sent: Thursday, August 30, 2007 4:21 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Other Support for 1 R18 HS017045-01 (Lazarus)

Suzanne,

Attached is Dr. Campion's Other Support.

Thanks,

(b)(6)

(b)(6) CORP/HPHC

08/30/2007 01:52 PM

To "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
cc Julie_Dunn@harvardpilgrim.org
Subject Re: Other Support for 1 R18 HS017045-01 (Lazarus) [Link](#)

Suzanne,

Attached are the updated Other Support pages for Dr. Brown and Dr. Kleinman along with the updated Other Support Excel file. I'm still waiting to hear back from Dr. Campion and Dr. Lazarus.

Thank you,

(b)(6)

(b)(6)

8/31/2007

Research Assistant - Pharmacoepidemiology,
 Department of Ambulatory Care and Prevention
 Harvard Med School / Harvard Pilgrim Health Care
 133 Brookline Ave
 Boston, MA 02215
 617.509.9796

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

08/30/2007 11:57 AM

To Julie_Dunn@harvardpilgrim.org, (b)(6)@hphc.org
 cc ross.lazarus@channing.harvard.edu
 Subject Other Support for 1 R18 HS017045-01 (Lazarus)

Dear All,

According to the attached Excel spreadsheet which I created based on what Julie Dunn sent me, the only researcher who is over 100% is Dr. Lazarus when you include this proposed award. (Of course, I am still awaiting Dr. Campion's Other Support before I can give a final OK on this area).

Please review the attached spreadsheet for any errors and, of course, necessary adjustments for Dr. Lazarus.

Thank you so much for your continued cooperation.

Suzanne Holman
 Grants Management Specialist
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 Agency for Healthcare Research and Quality
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 Rockville, Maryland 20850
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Suzanne.Holman@ahrq.hhs.gov

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8/31/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: (b)(6)@harvardpilgrim.org
Sent: Thursday, August 30, 2007 1:52 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Other Support for 1 R18 HS017045-01 (Lazarus)
Attachments: Other Support.xls; Brown_Other_Support_8.30.07.pdf; Kleinman_Other_Support_8.30.07.pdf; Other Support_Updated.xls

Suzanne,

Attached are the updated Other Support pages for Dr. Brown and Dr. Kleinman along with the updated Other Support Excel file. I'm still waiting to hear back from Dr. Campion and Dr. Lazarus.

Thank you,

(b)(6)

(b)(6)

Research Assistant - Pharmacoepidemiology
 Department of Ambulatory Care and Prevention
 Harvard Med School / Harvard Pilgrim Health Care
 133 Brookline Ave
 Boston, MA 02215

(b)(6)

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

08/30/2007 11:57 AM

To Julie_Dunn@harvardpilgrim.org, (b)(6)@hphc.org

cc ross.lazarus@channing.harvard.edu

Subject Other Support for 1 R18 HS017045-01 (Lazarus)

Dear All,

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Suzanne Holman
 Grants Management Specialist
 Office of Performance, Accountability, Resources, and Technology; Grants Management
 Agency for Healthcare Research and Quality
 540 Gaither Road, Room 4202

8/30/2007

Rockville, Maryland 20850
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8/30/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Thursday, August 30, 2007 11:57 AM
To: Julie_Dunn@harvardpilgrim.org; (b)(6)@hphc.org'
Cc: 'ross.lazarus@channing.harvard.edu'
Subject: Other Support for 1 R18 HS017045-01 (Lazarus)
Attachments: Other Support.xls

Dear All,

According to the attached Excel spreadsheet which I created based on what Julie Dunn sent me, the only researcher who is over 100% is Dr. Lazarus when you include this proposed award. (Of course, I am still awaiting Dr. Campion's Other Support before I can give a final OK on this area).

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Suzanne.Holman@ahrq.hhs.gov

8/30/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: (b)(6)@harvardpilgrim.org
Sent: Thursday, August 30, 2007 10:08 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: Re: Fringe Rate Used for Other Personnel at BWH needs to be verified
Attachments: BWH_Budget_Justification.pdf; ESP_VAERS_Other_pers_base_sal&fringe_Updated.doc

Suzanne,

Thank you for sending these e-mails along to me. Attached is the Budget Justification for BWH that explains the fringe rates as well as an updated version of the document "ESP_VAERS_Other_pers_base_sal&fringe.doc"

Please let me know if this is sufficient. I will get you the updated Other Support pages by the afternoon.

Thanks!

(b)(6)

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

To Julie_Dunn@harvardpilgrim.org (b)(6)@hphc.org

cc

08/30/2007 09:03 AM

Subject Fringe Rate Used for Other Personnel at BWH needs to be verified

It calculates out to be (b)(4) however, I have no documentation to show that is what the Fringe Rate should be. Thanks.

Suzanne Holman
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8/30/2007

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8/30/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Thursday, August 30, 2007 8:50 AM
To: (b)(6)@hphc.org
Subject: FW: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

FYI – since Julie Dunn is out of the office.

Suzanne Holman

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Thursday, August 30, 2007 8:45 AM
To: 'Julie_Dunn@harvardpilgrim.org'
Cc: 'ross.lazarus@channing.harvard.edu'; (b)(6)@harvardpilgrim.org; (b)(6)@harvard.edu; (b)(6)@hphc.org; (b)(6)@partners.org; (b)(6)@vmed.org
Subject: Proposed Grant Award Number 1 R18 HS017045-01 - Other Support clarification

Dear Julie Dunn,

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The only item I need clarified is that for the five researchers (Dr. Ross Lazarus, Dr. Jeffrey Brown, Dr. Ken Kleinman, Dr. Michael Klompas, and Dr. R. Platt) you sent me regarding their Other Support, that none of the projects listed under "Pending" are "Active." The reason I ask this is because under Dr. Brown, it looks like at least 2 listed under "Pending" should be "Active" and under Dr. Kleinman, one might be "Active" instead of "Pending". Please clarify.

Also, I still need Other Support for Dr. Francis Campion.

Thank you in advance for your cooperation.

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 301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Tuesday, August 28, 2007 2:14 PM
To: 'Julie_Dunn@harvardpilgrim.org'
Subject: RE: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Strange. This time, everything came out normal. Now I can actually read it! However, I probably will not get to it today.

Suzanne

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Tuesday, August 28, 2007 1:26 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Subject: RE: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Hi Suzanne,

Interesting - things looks fine on my end - are you referring to the font within the e-mail or on the attached PDF files? I can attempt to re-send either / all of these in a different font if you'd like...

Thanks,

Julie

"Holman, Suzanne (AHRQ/OPART/GM)"
<Suzanne.Holman@AHRQ.hhs.gov>

To Julie_Dunn@harvardpilgrim.org
cc

08/28/2007 01:14 PM

Subject RE: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Yes. Just curious why the font came out so small.

Suzanne

From: Julie_Dunn@harvardpilgrim.org [mailto:Julie_Dunn@harvardpilgrim.org]
Sent: Tuesday, August 28, 2007 12:33 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Subject: Re: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Hello Suzanne,

I just wanted to follow-up to ensure that you had, in fact, received the following e-mail with attachments that I submitted to you yesterday?

Many Thanks,

Julie

8/28/2007

Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
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 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
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Julie
 Dunn/CORP/HPHC

08/27/2007 04:22 PM

To Suzanne.Holman@AHRQ.hhs.gov
 cc ross.lazarus@channing.harvard.edu (b)(6) @harvard.edu, (b)(6) @hphc.org (b)(6) @partners.org,
 (b)(6) @vmed.org (b)(6) /CORP/HPHC@HPHC
 Subject Re: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus) Link

IRB
 Pending

→ Didn't happen -
 see email dated
 9/7/07
 sel

Hello Suzanne,

Per your request, please find documentation attached in order to complete the administrative review for our ESP:VAERS proposal. Please confirm receipt of this e-mail, as we have been experiencing problems with e-mail attachments as of late.

To answer your questions specifically:

1. When do you anticipate receiving IRB approval?

We are unable to obtain IRB approval until we have received formal award from AHRQ. Assuming that this is received in a timely manner, we would be able to submit for full internal IRB review / approval on September 6th. Otherwise we expect to receive approval at the October meeting of the IRB.

>

> 2. The Fringe Rates used for Harvard Pilgrim Health Care and Harvard
 > Vanguard Medical Associates (Subaward 1) need to be verified. I
 > only have them in the Budget Justification for Channing Laboratory,
 > Brigham and Women's Hospital (Subaward 2).

See fringe rates for these institutions listed within the "Other Personnel" salary document.

>

> 3. The Base Salaries used for all Other Personnel needs to be provided.

See attached file.

>

> 4. Office Supplies, Travel, Consultant Service, Equipment, and
 > ADP/Computer Services all need to be itemized for the budgets.

See attached file.

>

> 5. Documentation is needed for Modified Total Direct Cost Indirect Rate of 75%

> The current F&A Rate Agreement shows rates of (b)(4)

To clarify, the MTDC rate for HPHC (the Prime site) is, in fact, (b)(4) for HVMA. I have attached the official MTDC rate agreement for BWH / Channing Laboratory, which is set at 75%.

Please let me know if this information is sufficient or if you require additional documentation.

8/28/2007

> 6. A listing of Other Research Support for all Senior/Key Personnel
 > in calendar months and/or percentage is needed. This proposed award
 > needs to be included plus any pending awards slated to start within
 > the next one - two months.

See attached Zip file.

Many Thanks,

Julie

Julie D. Dunn, MPH
 Project Manager - PharmacoEpidemiology / Health IT
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 509-9857
 www.dacp.org

> ----- Forwarded by Nwenna Swan/CORP/HPHC on 08/20/2007 10:17 AM -----

>
 > "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
 > 08/18/2007 03:50 PM

> To

> Research_Admin@hphc.org

> cc

> ross.lazarus@channing.harvard.edu

> Subject

> Proposed Award Number 1 R18 HS017045-01 (Lazarus)

> Dear Ms. Richard,

> I have been assigned to perform the administrative review on the
 > proposed subject award.

> Here is a list of items that I need to be addressed in order to
 > complete my administrative review:

> 1. When do you anticipate receiving IRB approval?

> 2. The Fringe Rates used for Harvard Pilgrim Health Care and Harvard
 > Vanguard Medical Associates (Subaward 1) need to be verified. I
 > only have them in the Budget Justification for Channing Laboratory,
 > Brigham and Women's Hospital (Subaward 2).

8/28/2007

>
> 3. The Base Salaries used for all Other Personnel needs to be provided.
>
> 4. Office Supplies, Travel, Consultant Service, Equipment, and
> ADP/Computer Services all need to be itemized for the budgets.
>
> 5. Documentation is needed for Modified Total Direct Cost Indirect Rate of 75%
> . The current F&A Rate Agreement shows rates of (b)(4)
>
> 6. A listing of Other Research Support for all Senior/Key Personnel
> in calendar months and/or percentage is needed. This proposed award
> needs to be included plus any pending awards slated to start within
> the next one - two months.
>
> If possible, please have all this information to me no later than
> COB on Monday, August 27, 2007.
>
> Thank you in advance for your cooperation.
>
> Suzanne Holman
> Grants Management Specialist
> Office of Performance, Accountability, Resources, and Technology;
> Grants Management
> Agency for Healthcare Research and Quality
> 540 Gaither Road, Room 4202
> Rockville, Maryland 20850
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> 301-427-1462 or 1464 (fax)
> Suzanne.Holman@ahrq.hhs.gov
>
> [attachment "ESP_VAERS_Other_pers_base_sal&fringe.pdf" deleted by Julie Dunn/CORP/HPHC] [attachment
"HPHC_itemized_justification.pdf" deleted by Julie Dunn/CORP/HPHC] [attachment "ESP_VAERS_Other_Support.zip"
deleted by Julie Dunn/CORP/HPHC] [attachment "BWH_Rate_Agreement_09-25-06.pdf" deleted by Julie
Dunn/CORP/HPHC]

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8/28/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Nicholas_Mulherin@harvardpilgrim.org
Sent: Friday, August 24, 2007 1:46 PM
To: Holman, Suzanne (AHRQ/OPART/GM)
Subject: Re: Fw: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Hi, Suzanne. I just wanted to let you know that I received this request today (I was away from my office at a conference for the last four days) and will get working on it immediately so you can have it by COB on Monday — I don't anticipate this being a problem, but I will let you know if I encounter any hold-ups in getting the information (I don't know who else may not be in the office today or Monday).

best regards,
 Nick

--
 Nick Mulherin
 Grants Manager, Sponsored Programs
 Harvard Pilgrim Health Care
 133 Brookline Avenue, 5th Floor
 Boston, MA 02215
 Ph. 617.509.9933, Fx. 617.509.9859
 nicholas_mulherin@hphc.org

```
> ----- Forwarded by Nwenna Swan/CORP/HPHC on 08/20/2007 10:17 AM -----
>
> "Holman, Suzanne (AHRQ/OPART/GM)" <Suzanne.Holman@AHRQ.hhs.gov>
> 08/18/2007 03:50 PM
>
> To
>
> Research_Admin@hphc.org
>
> cc
>
> ross.lazarus@channing.harvard.edu
>
> Subject
>
> Proposed Award Number 1 R18 HS017045-01 (Lazarus)
>
> Dear Ms. Richard,
>
> I have been assigned to perform the administrative review on the
> proposed subject award.
>
> Here is a list of items that I need to be addressed in order to
> complete my administrative review:
>
> 1. When do you anticipate receiving IRB approval?
>
> 2. The Fringe Rates used for Harvard Pilgrim Health Care and Harvard
> Vanguard Medical Associates (Subaward 1) need to be verified. I
> only have them in the Budget Justification for Channing Laboratory,
> Brigham and Women's Hospital (Subaward 2).
>
> 3. The Base Salaries used for all Other Personnel needs to be provided.
>
> 4. Office Supplies, Travel, Consultant Service, Equipment, and
> ADP/Computer Services all need to be itemized for the budgets.
>
> 5. Documentation is needed for Modified Total Direct Cost Indirect Rate of 75%
> The current F&A Rate Agreement shows rates of (b)(4)
>
> 6. A listing of Other Research Support for all Senior/Key Personnel
> in calendar months and/or percentage is needed. This proposed award
> needs to be included plus any pending awards slated to start within
> the next one - two months.
>
> If possible, please have all this information to me no later than
> COB on Monday, August 27, 2007.
```

8/25/2007

>
> Thank you in advance for your cooperation.
>
> Suzanne Holman
> Grants Management Specialist
> Office of Performance, Accountability, Resources, and Technology;
> Grants Management
> Agency for Healthcare Research and Quality
> 540 Gaither Road, Room 4202
> Rockville, Maryland 20850
> 301-427-1460 (phone)
> 301-427-1462 or 1464 (fax)
> Suzanne.Holman@ahrq.hhs.gov
>
>

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8/25/2007

Holman, Suzanne (AHRQ/OPART/GM)

From: Holman, Suzanne (AHRQ/OPART/GM)
Sent: Monday, August 20, 2007 11:00 AM
To: 'Research_Admin@harvardpilgrim.org'
Subject: RE: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

That is fine. **COB Friday, August 31, 2007**, is fine to get back to me, in this case.

Suzanne Holman

From: (b)(6)@harvardpilgrim.org [mailto:(b)(6)@harvardpilgrim.org] **On Behalf Of** Research_Admin@harvardpilgrim.org
Sent: Monday, August 20, 2007 10:15 AM
To: Holman, Suzanne (AHRQ/OPART/GM)
Subject: Re: Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Good morning,

I wanted to let you that know that we rec'd your email. Our grant manager, Nick Mulherin (he's on vacation and returns later this week), will respond to your requests when he gets back.

Thank you.

(b)(6)
 Administrative Assistant
 Office of Sponsored Programs
 Harvard Pilgrim Healthcare
 133 Brookline Avenue, 5th Flr.
 (b)(6) (phone)
 (b)(6) (fax)

"Holman, Suzanne (AHRQ/OPART/GM)"
 <Suzanne.Holman@AHRQ.hhs.gov>

08/18/2007 03:50 PM

To Research_Admin@hphc.org
 cc ross.lazarus@channing.harvard.edu
 Subject Proposed Award Number 1 R18 HS017045-01 (Lazarus)

Dear Ms. Richard,

I have been assigned to perform the administrative review on the proposed subject award.

Here is a list of items that I need to be addressed in order to complete my administrative review:

1. When do you anticipate receiving IRB approval?
2. The Fringe Rates used for Harvard Pilgrim Health Care and Harvard Vanguard Medical Associates (Subaward 1) need to be verified. I only have them in the Budget Justification for Channing Laboratory, Brigham and Women's Hospital (Subaward 2).

8/20/2007

3. The Base Salaries used for all Other Personnel needs to be provided.
4. Office Supplies, Travel, Consultant Service, Equipment, and ADP/Computer Services all need to be itemized for the budgets.
5. Documentation is needed for Modified Total Direct Cost Indirect Rate of 75%. The current F&A Rate Agreement shows rates of (b)(4)
6. A listing of Other Research Support for all Senior/Key Personnel in calendar months and/or percentage is needed. This proposed award needs to be included plus any pending awards slated to start within the next one – two months.

If possible, please have all this information to me no later than **COB on Monday, August 27, 2007**.

Thank you in advance for your cooperation.

Suzanne Holman
Grants Management Specialist
Office of Performance, Accountability, Resources, and Technology; Grants Management
Agency for Healthcare Research and Quality
540 Gaither Road, Room 4202
Rockville, Maryland 20850
301-427-1460 (phone)
301-427-1462 or 1464 (fax)
Suzanne.Holman@ahrq.hhs.gov

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Harvard Pilgrim Health Care Itemized Budget Justification

Office Supplies

\$200 Year 1

\$205 Year 2

Standard office supplies are calculated at approximately .2% of subtotal Direct Costs for HPHC. This includes toner cartridges and photocopying to support staff working on this project, in addition to support for routine conference calls and additional correspondence between HVMA, BWH, HPHC and the MDPH.

Travel

\$1,470 Year 1

\$1,600 Year 2

As required within the RFP, funding is requested to allow at least two members of the project team to attend at least three days of an annual AHRQ grantee meeting in the Washington DC area. Approximate costs were calculated as follows:

2 round trip flights from Boston, MA to Washington, D.C. @ \$200/each ($\$200 * 2 = \400.00)

2 nights stay for 2 rooms @ \$250 / night ($\$250 * 2 = \$500 * 2 = \$1,000$)

Additional incurred costs (taxes, meals, etc) make up the additional balance for each year, estimated cost inflation/increase factored in for Year 2.

Epic Consulting Services

(b)(4) Year 1

Year 2

Funds are requested to support necessary consulting services provided by EpicCare, the EMR vendor through which ESP:VAERS will be operationalized within the HVMA / HealthOne system.

Costs were calculated at a consulting rate of (b)(4) allowing for (b)(4) hours (b)(4) of service during Year 1, and (b)(4) hours (b)(4) during Year 2.

Facilities and Administration costs for HPHC are calculated at (b)(4) of modified total direct costs.

Itemized
Budget

ESP:VAERS
Year 1 Institutional Base Salary Information for all Other Personnel*

NAME <u>HPHC (Prime)</u>	TITLE	BASE SALARY
Julie Dunn, MPH (b)(6)	Project Manager	(b)(4); (b)(6)
	Research Assistant	
TBN	Senior Programmer	

HPHC FRINGE RATES:

(b)(6) = (b)(4)
 All Other = (b)(4)

BWH

(b)(6)	Laboratory Manger	(b)(4); (b)(6)
	Programmer	
	Administrative Asst.	

BWH FRINGE RATES:

Lazarus = (b)(4)
 All Other = (b)(4)

HVMA

TBN	Senior EPIC Programmer	(b)(4); (b)(6)
-----	------------------------	----------------

HVMA FRINGE RATES:

(b)(6) = (b)(4)
 Programmer = (b)(4)

** all salaries for year 2 were estimated incorporating (b)(4); increase from those listed above*

Base Salaries

BUDGET JUSTIFICATION	ASSIGNMENT NUMBER N/A
----------------------	--------------------------

Adverse Event Ambulatory Care Surveillance System
Channing Laboratory, Brigham and Women's Hospital

Personnel

Fringe benefits are calculated at (b)(4) for professionals (M.D.s, Ph.D.s, and other doctoral level degree holders, excluding post-doctoral fellows), (b)(4) for non-professionals (non-doctoral degree holders), and (b)(4) for post-doctoral fellows. Salaries are adjusted each year at (b)(4) above the previous year's figures.

Professional Personnel

Ross Lazarus, M.B.B.S., M.P.H., Principle Investigator, 2.4 calendar months.

Dr Ross Lazarus, Director of Bioinformatics at the Channing Laboratory, will be the PI and will dedicate one day each week to this project. Dr Lazarus will provide direction and leadership for the programmer-analyst and the administrative support, meeting with the Project Manager and Programmer-analyst each week to review progress to date and to discuss and modify the work plan. He will be the technical lead for the project, providing advice on the design of the overall system, and will ensure that widely adopted infrastructure is used to enhance application transportability. He will be responsible for specifying the overall design, testing and development strategy for all application development and play a major role in application testing and implementation. Dr Lazarus will meet every 2 weeks with staff from the DACP including Drs Klompas and Campion to ensure that work at the Channing and HVMA are proceeding in an orderly fashion, and to discuss progress and plan work on the HVMA side.

Non Professional Personnel

(b)(6) **Laboratory Manager**, 0.30 calendar months. (b)(6) Information Technology Manager, at the Channing Laboratory will be the Project Manager for the Channing subcontract, maintaining documentation and records of meetings, supervising the Programmer-analyst, ensuring that all effort and spending are within the budget for the project, and advising on technical aspects of the project as needed. She will join the weekly meeting with Dr Lazarus and the Programmer-analyst and will meet with the Programmer-analyst as needed for supervision of the project.

(b)(6) **Programmer**, 8.0 calendar months effort. (b)(6) will be the programmer-analyst, working under the supervision of the Project manager and the technical direction of the PI. Ms (b)(6) will be responsible for detailed documentation and system design, database design, programming of the application software and web application, and all testing. Ms (b)(6) will meet regularly each week with Dr Lazarus and Ms (b)(6) and individually with other team members as needed, and will spend time as needed to maintain the application server installed at HVMA using a workstation in the DACP.

(b)(6) **Administrative Assistant**, 0.30 calendar months. Mr. (b)(6) will assist Dr. Lazarus and the Study Team with preparation of human subject protocols, annual reviews, and manuscript preparation. He will prepare progress reports and facilitate communication between the laboratories involved in the project.

Equipment

1. A dual processor (4 core) SunFire X4300 with 10TB of disk storage will be required for the project. This will be purchased and initially configured at the Channing Laboratory and installed behind the HVMA firewall in the secured HVMA computer facility.

Total Equipment (Year 1): \$15,000

Supplies

1. Funds in amount of \$1000 are requested annually with 3% increase to cover the office and computer supplies necessary to conduct the study.

Total Supplies (Year 1): \$1,000

Travel

1. Dr. Lazarus will travel to the scientific meeting. Per-trip cost will be \$2,500 with 3% annual increase.

Total Travel Expenses (Year 1): \$2,500

Other Expenses – Computing

The Channing Laboratory computer facility provides access to two components: UNIX based system for data storage and analysis and; System support for desktop network of PCs. Charges for each component is based on FTE effort on each grant. Channing Laboratory computing infrastructure will be used for all development and testing, and Channing web server and web services infrastructure will provide the primary site for software and documentation distribution. All current research grants at the Channing pay a fixed annual contribution per FTE to the computing budget. The fee has been a component of every NIH grant submitted from the Channing over the past 5 years, and has always been accepted by NIH reviewers to date. The Channing Laboratory computer facility provides access to Linux and Solaris based servers for centralized authentication, email, security, audit, automated backup and recovery, web servers, data storage and analysis. The Channing computer system includes a grid of more than 20 Sun servers and blades (including two 4 CPU and one 8 core main servers) and a 12TB SAN, three Oracle (2 production and 1 development) Sunfire v440 and Sun Enterprise 450 servers, and a 32 CPU Linux cluster, together with duplicated failover Sun server redirectors and multiple redundant backend web servers. Each individual study contributes to the overall costs of the UNIX based data storage and analysis component. Current annual costs for system administration, data storage and processing including software licenses (such as the EMC Legato backup suite, Veritas Foundation Suite, SAS and SPlus statistical packages), security auditing and administration, automated backup systems, software programming and hardware maintenance, and planned replacement of obsolete hardware are more than \$600,000 for approximately 250 users in 35 projects in areas of chronic disease epidemiology, respiratory epidemiology, pharmacoepidemiology, and statistics. Each study is charged on an as per FTE basis at a rate of (b)(4) The annual increase of (b)(4) has been applied for the following year.

PC Desktop system support: The Channing computer system operates a network of desktop computers for investigators to use in their daily work activities. Services supported include word processing, graphical presentations, and spreadsheets. The costs of maintaining the network include software licenses, service contracts on desktops and printers and personnel to maintain the hardware as well as replacement of obsolete equipment. Annual costs are \$300,000 serving 90 users within the Channing Laboratory at 181 Longwood Avenue. Each study is charged on a per FTE basis at a rate of (b)(4) located at 181 Longwood Avenue. 0.917 (b)(4) The annual increase of (b)(4) has been applied for the following year.

Total Other Expenses – Computing (Year 1): (b)(4)

18
Assigned

Grant	PI	Institution	Title	PO Assigned
1 R18 HS017060-01	BERNER, ETA S	UNIVERSITY OF ALABAMA AT BIRMINGHAM	Closing the Feedback Loop to Improve Diagnostic Quality	Bob Mayes
1 R18 HS017205-01	DAVIDSON, ARTHUR	DENVER HEALTH AND HOSPITAL AUTHORITY	Colorado Associated Community Health Information Exchange (CACHIE)	Marybeth Farquhar
1 R18 HS017022-01	HAZLEHURST, BRIAN L	KAISER FOUNDATION RESEARCH INSTITUTE	Automating Assessment of Asthma Care Quality	Marybeth Farquhar
1 R18 HS017067-01	KAUSHAL, RAINU	WEILL MEDICAL COLLEGE OF CORNELL UNIV	Developing and Using Valid Clinical Quality Metrics for HIT with HIE	Marybeth Farquhar
1 R18 HS017045-01	LAZARUS, ROSS	HARVARD PILGRIM HEALTH CARE, INC.	Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES	Marybeth Farquhar
1 R18 HS017094-01	MCCOLM, DENNI	CITIZENS MEMORIAL HOSPITAL DISTRICT	Standardization and Automatic Extraction of Quality Measures in an Ambulatory EMR	Marybeth Farquhar
1 R18 HS017018-01	MILLER, MARLENE ROSEMARY	JOHNS HOPKINS UNIVERSITY	Medication Monitoring for Vulnerable Populations via IT	Marybeth Farquhar
1 R18 HS017059-01	MOSTASHARI, FARZAD	NEW YORK CITY HEALTH/MENTAL HYGIENE	Bringing Measurement to the Point of Care	Marybeth Farquhar
1 R18 HS017048-01	SCHNEIDER, ERIC CARL	HARVARD UNIVERSITY (SCH OF PUBLIC HLTH)	Massachusetts Quality E-Measure Validation Study	Marybeth Farquhar
1 R18 HS017244-01	THOMAS, ERIC J	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	Using Electronic Records to Detect and Learn from Ambulatory Diagnostic Errors	Bob Mayes
1 R18 HS017030-01	TURCHIN, ALEXANDER	BRIGHAM AND WOMEN'S HOSPITAL	Monitoring Intensification of Treatment for Hyperglycemia and Hyperlipidemia	Marybeth Farquhar
1 R18 HS017016-01	VOGT, THOMAS M.	KAISER FOUNDATION RESEARCH INSTITUTE	Using IT to Improve the Quality of CVD Prevention & Management	Marybeth Farquhar
1 R18 HS017099-01	WEINER, MARK G	UNIVERSITY OF PENNSYLVANIA	Crossing the Quality Assessment Chasm: Aligning Measured and True Quality of Care	Bob Mayes

THE FOLLOWING GRANTS ARE ALSO BEING FUNDED BUT THEY WILL BE FUNDED USING PATIENT SAFETY \$ - CQUIPS IS RESPONSIBLE FOR ASSIGNING THE PO

1 R18 HS017010-01	KILBRIDGE, PETER MATTHEW	WASHINGTON UNIVERSITY	SURVEILLANCE FOR ADVERSE DRUG EVENTS IN AMBULATORY PEDIATRICS	check with CQUIPS
1 R18 HS017160-01	KMETIK, KAREN	AMERICAN MEDICAL ASSOCIATION	Cardio-Hit Phase II	check with CQUIPS
1 R18 HS017017-01	LOGAN, JUDITH R	OREGON HEALTH & SCIENCE UNIVERSITY	Improving Quality In Cancer Screening: The Excellence Report For Colonoscopy	check with CQUIPS
1 R18 HS017031-01	SELBY, JOE V	KAISER FOUNDATION RESEARCH INSTITUTE	Feedback of Treatment Intensification Data to Reduce Cardiovascular Disease Risk	check with CQUIPS

Revised Other Support for 17045 dated 9/7/07				
Personnel	Award Number	Dates of Award	Percentage	
Lazarus	Active			
	2 U01 HL065899-05	08/01/05 - 06/30/10	5%	
	P01 CD000260	01/01/06 - 12/31/08	10%	
	1 R01 HG003646-01A1	12/01/05 - 11/30/10	33%	
	1 P01 HL083069	12/01/06 - 11/30/11	20%	
	1 R01 HL066289	04/01/07 - 03/31/11	5%	
	R01 HL086601-01	12/01/06 - 11/30/10	3%	
	1 R18 HS017045-01	09/30/07 - 09/29/09	20%	new AHRQ one
			96%	
	Pending			
	1 R01 HL092197-01	04/01/08 - 03/31/13	2.50%	
Brown	Active			
	LCF030207	03/01/07 - 02/28/08	10%	
	2 U18 HS10391	09/28/06 - 09/30/07	20%	
	200-2002-00732	10/01/06 - 09/30/07	20%	
	HHSN268200425216C	09/30/04 - 09/29/07	15%	
	HHSF223200510012C C.O.A. #3	05/01/06 - 12/31/07	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	10%	new AHRQ one
			85%	
	Pending			
	HPHC PI (Lazarus)	TBD	9.50%	
	HPHC PI (Brown)	07/01/07 - 06/30/11	13%	
	HPHC PI (Brown)	09/30/07 - 09/29/11	30%	
	HPHC PI (Fletcher)	05/01/07 - 04/30/12	7%	
Kleinman	Active			
	K24 HL 068041	09/30/01 - 06/30/11	4%	
	K24 HD 047667	07/01/04 - 06/30/09	5%	
	R01 HL 075504	08/01/04 - 04/30/08	2%	
	R21 LM 008707	06/01/05 - 05/31/08	24%	
	R01 HD 050966	08/01/05 - 07/31/10	4%	
	P01 CD 000260	09/30/05 - 09/29/08	10%	
	U01 GM 076672	02/01/06 - 01/31/11	15%	
	R01 HD034568	08/01/06 - 06/30/10	8%	
	R01 A1 066304	08/01/06 - 07/31/10	2%	
	R01 PH 000032	09/30/06 - 09/29/08	10%	
	R21 DK 073739	09/30/06 - 08/31/08	5%	
	R01 HL064925	05/15/07 - 03/31/11	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	2%	new AHRQ one
			96%	
	Pending			
	R18 (Simon)	07/01/07 - 06/30/10	5%	
	R01 (Oken)	12/01/07 - 11/30/11	5%	
	R01 (McCray)	02/01/08 - 01/31/11	5%	
	G13 (Kleinman)	04/01/08 - 03/31/11	14.16%	
	(Oken)	01/01/08 - 12/31/10	5%	
Klompas	Active			
	P01 CD000260-02	09/30/05 - 09/29/08	20%	
	7 U01 GM076672-02	02/01/07 - 01/31/08	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	35%	new AHRQ one
			65%	
	Pending			
	ESP VAERS	XX/XX/XX - XX/XX/XX	20%	
Platt	Active			
	5 U18 HS10391-07	09/29/06 - 09/30/07	19%	
	1 U01 GM76672-01	02/01/07 - 01/31/08	15%	
	5 P01 CD000260-02	09/30/05 - 09/29/08	20%	
	200200200732	09/20/03 - 09/19/12	5%	
	U01 CI000344-01	02/01/06 - 09/19/11	12%	
	HHSF22320051001	09/23/05 - 09/22/10	15%	
	SCDPH5225 5 337HAR0000	04/01/07 - 08/31/07	2.08%	
	MTA53	01/01/07 - 12/31/09	1.66%	
	1 R01 PH0000032-01	09/30/06 - 09/29/08	2.08%	
	1 R01 AI066304-01A1	08/01/06 - 07/31/10	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	3%	new AHRQ one
			99.82%	
	Pending			
	None			

9/6/07

OTHER SUPPORT
Ross LAZARUS, M.B.B.S., M.Med., M.P.H.
(Brigham and Women's Hospital)

ACTIVE – Brigham Administered Grants

2 U01 HL065899-05 (Weiss) 08/01/05 – 06/30/10 0.60 calendar
NIH/ NHLBI \$1,452,435

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. Overlap: None.

P01CD000260 (Platt) 01/01/06 – 12/31/08 1.2 calendar
Centers for Excellence in Public Health Informatics (ESP) \$932,178

Using Electronic Medical Records to Support Core Public Health Needs

This work will build directly on this group's accomplishments in developing the CDC National Bioterrorism Syndromic Surveillance Demonstration Project. ESP will serve three major functions: 1) Completely transparent reporting of conditions where all required information can be extracted from EMRs, 2) Initiation of reporting that triggers an automated query to clinicians if non-extractable information, and 3) Automatic responses to electronic queries by health authorities regarding demographic and treatment status of individuals with positive laboratory tests. Overlap: None

1 R01 HG003646-01A1 (Lazarus) 12/01/05 – 11/30/10 3.96 calendar
NIH \$2,266,379

A Genetic Association Research Statistical Framework (BISTI)

The specific aims of this project include software support for importing experimental data and genomic annotation; methods for statistical power calculations and for selecting maximally informative subsets of markers during experimental design; methods for visualizing and summarizing experimental results; established and recently developed methods supporting statistical inference on single markers, multiple markers and on the epistatic and gene by environment interactions characteristic of these diseases and needed for emerging fields of study such as pharmacogenetics. Overlap: None.

1 P01 HL083069 (Weiss) 12/01/06 – 11/30/11 2.4 calendar
NIH \$1,515,000

Common Genetic Determinants of Asthma and COPD (PPG Core 3 - Bioinformatics)

The goal of this core is to develop novel bioinformatics tools to be used by Projects 1-4 of the grant, the analysis of human and mouse microarray datasets, and the maintenance of the PPG website, which will be modeled from a former Channing Laboratory PGA website. In addition, this core will provide a wide variety of statistical tools for genetic association analysis, as well as up-to-date information on genetic association studies, mouse genetics, and the functional genomics work of Projects 1-4. Overlap: None.

1 R01 HL066289 (Weiss) 4/1/07-3/31/11 0.60 Calendar
NIH/NHLBI \$2,940,680

The Genetic Epidemiology of Asthma in Costa Rica

The goal of this competing continuation grant is to use linkage disequilibrium mapping to test the hypothesis that a gene(s) on chromosome 12q24 influences asthma and airway responsiveness in Costa Ricans, and that a gene(s) on chr. 20p12 influences total serum IgE in male Costa Ricans. This goal will be accomplished by a) genotyping SNPs in these regions to perform fine-mapping family-based association studies to identify candidate genes for asthma and/or its intermediate phenotypes, and b) testing for association between SNPs and haplotypes in selected candidate genes and asthma and/or its intermediate phenotypes in families of children with asthma.

ACTIVE (Continued) – Brigham Administered GrantsR01 HL086601-01 (Raby)
NIH/NHLBI

12/01/06-11/30/10

0.36 Calendar

Genetics and Gene Expression Profiling in Asthma

The goal of this project is to integrate gene expression microarray data with family-based genetic association studies to identify genetic variants that influence the severity of asthma through regulation of gene expression. Overlap: None

1 R18 HS017045-01 (~~Platt~~) (Lazarus)
AHRQ~~07/01/07-06/30/09~~
~~\$247,144~~

2.40 calendar

Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)

This project seeks to perform systems analysis, design and application programming for enhancements to existing ESP software to enable the creation and management of diagnosis and therapeutic exposure registries.

PENDING – Brigham Administered Grants (Lazarus)1 R01 HL092197-01 (Tantisira)
NIH/NHLBI04/01/08 – 03/31/13
\$412,054

0.30 Calendar

Integrative Pharmacogenomics of Leukotriene Inhibition in Asthma

This project seeks to identify genetic markers most closely associated with the genetic expression signature resulting from administration of medications that block the leukotriene pathway in asthma. By demonstrating that these markers also correlate with the clinical response in asthma, the markers may eventually be used to help predict therapeutic response to anti-leukotriene medications in asthma. Since asthma remains the leading cause of childhood hospitalizations and school absences in the United States, optimizing pharmacologic therapy has the potential to substantially decrease the morbidity and financial burden related to this disease.

9/4/07

OTHER SUPPORT
Ross LAZARUS, M.B.B.S., M.Med., M.P.H.
(Brigham and Women's Hospital)

ACTIVE – Brigham Administered Grants

2 U01 HL065899-05 (Weiss) 08/01/05 – 06/30/10 0.60 calendar
NIH/ NHLBI \$1,452,435

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. Overlap: None.

P01CD000260 (Platt) 01/01/06 – 12/31/08 1.2 calendar
Centers for Excellence in Public Health Informatics (ESP) \$932,178

Using Electronic Medical Records to Support Core Public Health Needs

This work will build directly on this group's accomplishments in developing the CDC National Bioterrorism Syndromic Surveillance Demonstration Project. ESP will serve three major functions: 1) Completely transparent reporting of conditions where all required information can be extracted from EMRs, 2) Initiation of reporting that triggers an automated query to clinicians if non-extractable information, and 3) Automatic responses to electronic queries by health authorities regarding demographic and treatment status of individuals with positive laboratory tests. Overlap: None

1 R01 HG003646-01A1 (Lazarus) 12/01/05 – 11/30/10 3.96 calendar
NIH \$2,266,379

A Genetic Association Research Statistical Framework (BISTI)

The specific aims of this project include software support for importing experimental data and genomic annotation; methods for statistical power calculations and for selecting maximally informative subsets of markers during experimental design; methods for visualizing and summarizing experimental results; established and recently developed methods supporting statistical inference on single markers, multiple markers and on the epistatic and gene by environment interactions characteristic of these diseases and needed for emerging fields of study such as pharmacogenetics. Overlap: None.

1 P01 HL083069 (Weiss) 12/01/06 – 11/30/11 2.4 calendar
NIH \$1,515,000

Common Genetic Determinants of Asthma and COPD (PPG Core 3 - Bioinformatics)

The goal of this core is to develop novel bioinformatics tools to be used by Projects 1-4 of the grant, the analysis of human and mouse microarray datasets, and the maintenance of the PPG website, which will be modeled from a former Channing Laboratory PGA website. In addition, this core will provide a wide variety of statistical tools for genetic association analysis, as well as up-to-date information on genetic association studies, mouse genetics, and the functional genomics work of Projects 1-4. Overlap: None.

1 R01 HL066289 (Weiss) 4/1/07-3/31/11 0.60 Calendar
NIH/NHLBI \$2,940,680

The Genetic Epidemiology of Asthma in Costa Rica

The goal of this competing continuation grant is to use linkage disequilibrium mapping to test the hypothesis that a gene(s) on chromosome 12q24 influences asthma and airway responsiveness in Costa Ricans, and that a gene(s) on chr. 20p12 influences total serum IgE in male Costa Ricans. This goal will be accomplished by a) genotyping SNPs in these regions to perform fine-mapping family-based association studies to identify candidate genes for asthma and/or its intermediate phenotypes, and b) testing for association between SNPs and haplotypes in selected candidate genes and asthma and/or its intermediate phenotypes in families of children with asthma.

ACTIVE (Continued) – Brigham Administered Grants

R01 HL086601-01 (Raby) 12/01/06-11/30/10 0.36 Calendar
NIH/NHLBI

Genetics and Gene Expression Profiling in Asthma

The goal of this project is to integrate gene expression microarray data with family-based genetic association studies to identify genetic variants that influence the severity of asthma through regulation of gene expression. Overlap: None

TBA (Platt) 07/01/07- 06/30/09 2.40 calendar
ESPH (b)(4)

Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)

This project seeks to perform systems analysis, design and application programming for enhancements to existing ESP software to enable the creation and management of diagnosis and therapeutic exposure registries.

PENDING – Brigham Administered Grants (Lazarus)

1 R01 HL092197-01 (Tantisira) 04/01/08 – 03/31/13 0.30 Calendar
NIH/NHLBI \$412,054

Integrative Pharmacogenomics of Leukotriene Inhibition in Asthma

This project seeks to identify genetic markers most closely associated with the genetic expression signature resulting from administration of medications that block the leukotriene pathway in asthma. By demonstrating that these markers also correlate with the clinical response in asthma, the markers may eventually be used to help predict therapeutic response to anti-leukotriene medications in asthma. Since asthma remains the leading cause of childhood hospitalizations and school absences in the United States, optimizing pharmacologic therapy has the potential to substantially decrease the morbidity and financial burden related to this disease.

(b)(6) Ph.D.
Other Support

ACTIVE

Prime: Lovelace Clinic Foundation (Mapel)

LCF030207

HPHC PI (Brown)

(b)(4)

3/1/07-2/28/08

1.2 calendar (10%)

(b)(4)

Pneumonia and Upper Respiratory Tract Infections Among COPD Patients Using Fluticasone/Salmeterol in Combination Versus Other Steroids and Bronchodilators Alone

The primary goal of this project is to examine whether COPD patients prescribed Advair have a higher risk for pneumonia as compared to patients who are treated with other ICS and/or bronchodilators alone.

Role: Primary Investigator

Prime: Harvard Pilgrim Health Care (Platt)

2U18HS10391

HPHC PI (Platt)

AHRQ

9/29/2006-9/30/2007

2.4 calendar (20%)

\$259,964.00 (Core, yr 4; Dataset yr4 – HPHC Direct Costs)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 2)

The Centers for Education and Research in Therapeutics (CERT) is an initiative funded by the Agency for Healthcare Research and Quality to conduct research and provide education that optimizes use of drugs, devices, and biological products. Ten sites in the HMO Research Network are collaborating as a CERT.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

200-2002-00732

HPHC PI (Platt)

AHIP

10/1/06-9/30/07

2.4 calendar (20%)

\$105,994.00 (HPHC Direct Costs)

Using Electronic Health Data to Assess Influenza Vaccine Safety

This project represents a CDC and FDA jointly funded study to evaluate the development of a system for active surveillance of influenza vaccines. The study builds on the prior work of the Vaccine safety datalink (VSD) and is intended to lay the groundwork for an active surveillance program involving large, diverse populations that could be implemented to monitor an influenza pandemic. The two main projects goals are to a.) improve the nation's ability to use electronic health data for rapid assessment of adverse reactions to influenza vaccine, including pandemic influenza vaccine; and b.) expand the size of the population for which electronic health data can be used for influenza vaccine, including pandemic influenza vaccine, safety assessment

Role: Co-Investigator

Prime: Group Health Cooperative (Larsen)

HHSN268200425216C

HPHC PI (Platt)

NHLBI

9/30/04-9/29/07

1.8 calendar (15%)

\$173,718.00 (HPHC Direct Costs)

The HMO Coordinated Clinical Studies Network

The Coordinated Clinical Studies Network (CCSN) is an unparalleled research facility for clinical and health services research that builds on the current capacity of the HMO Research Network (HMORN). The CCSN supports the full range of research that HMORN members regularly conduct, which includes cancer, infectious and chronic disease surveillance, health services and health economics research, behavioral, mental health and substance abuse studies, genomic research, complementary and alternative medicine, dental research, pharmacoepidemiological and pharmaco-economic investigations as well as analyses of systems change and organizational behavior. The project's deliverables are to build and sustain a research infrastructure, establish HMORN CCSN web site to coordinate all Network communications, establish External & Internal Advisory Committees for the CCSN, build budget templates and pre-negotiated project budgets for network based research, and create a document repository for IRB and other reviews.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

HHSF223200510012C C.O.A. #3

HPHC PI (Platt)

FDA

5/1/06-12/31/07

1.2 calendar (10%)

\$114,776.00 (HPHC Direct Costs)

ADHD Drugs and Cardiovascular Outcomes –Full Study

This project is a retrospective cohort study of the use of medications for ADHD and the risk of serious arrhythmias. The study drugs include all medications with a label indication for treatment of ADHD. These include the amphetamine-related psychostimulants, other stimulants (pemoline), and SNRIs (atomoxetine).

Prime: CRN – Group Health Cooperative

U19CA079689

HPHC PI (Fletcher)

NCI

5/1/07 – 4/30/12

.84 calendar (7%)

\$263,090.00 (HPHC Direct Costs, yr 1)

Cancer Research Network Across Health Care Systems – Infrastructure

The CRN has successfully developed a productive collaborative cancer research consortium. We plan to improve the research capacity of the CRN and use it to conduct a broad array of cancer research studies that relate to NCI research priorities or questions of importance to CRN investigators and our academic collaborators.

PENDING

Prime: Harvard Pilgrim Health Care (Lazarus)

XXXXXXX

HPHC PI (Lazarus)

AHRQ

Funding Period: TBD

HPHC Direct Costs: TBD

1.2 Year 1, 1.08 in Year 2 (9.5%)

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Prime: Kaiser Permanente Northern California (Herrinton)

XXXXXXX

HPHC PI (Brown)

NIA

10/1/07-9/30/11

1.6 calendar (13%)

\$115,636.00 (HPHC Direct Costs, yr 1)

Age Disparities in Use of Biologics for Rheumatoid Arthritis

The proposed community-based study will investigate each of these factors, comparing RA patients ≥65 years with younger patients. *The study is directed toward rheumatologists, health planners, and policy makers. It will assess whether elders have adequate and appropriate access to biologic agents, thereby allowing refinement of drug coverage policies to improve their use among elders.* This question is of critical importance as there are an increasing number of new biologic therapies on the horizon for a wide range of inflammatory diseases, and the number of Medicare enrollees continues to grow.

Prime: Harvard Pilgrim Health Care (Platt)

XXXXXXX

HPHC PI (Brown)

AHRQ

10/01/07-9/30/11

3.6 calendar (30%)

\$263,090.00 (HPHC Direct Costs, yr 1)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 3)

The overall vision of the HMO Research Network CERT is to advance population health through acquisition and widespread dissemination of knowledge about best therapeutics practices. We accomplish this by taking advantage of the research and dissemination opportunities afforded by health plans' defined populations, their large provider groups, and their unique data sources. In the aggregate these health plans cover a substantial majority of the U.S. population. This leads to this CERT's theme, "Improving therapeutics' use, safety, and effectiveness, through research, dissemination, and education using health plans' defined populations, providers, delivery systems, and data."

Aim 1. To enhance the collective ability of the HMO Research Network and other health plans' collective to advance therapeutics knowledge by leveraging unique data sources within a very large, generalizable population.

Aim 2. To develop and implement new multi-faceted methods for disseminating and promoting best therapeutic practices.

OVERLAP:

None at present.

Should all of the pending grant proposals be funded, Dr. Brown's level of effort for the period of the overlap (May 1 – September 30) on some of his projects will be adjusted to ensure that his level of effort does not exceed 100%.

OTHER FINANCIAL SUPPORT

(b)(6)

ACTIVE

K24 HL 068041 (Gillman) 9/30/01 – 6/30/11 0.48 calendar
NIH \$164,963

Patient-oriented research in early life origins of CVD

The research focus of this midcareer patient-oriented investigator award is a study of maternal diet, placental hormones, and offspring blood pressure. The award also serves as a mechanism to strengthen the PI's mentorship capabilities.

K24 HD 047667 (Lieu) 7/01/04 – 6/30/09 0.60 calendar
NICHD \$128,633

Enhancing Prevention for Children in Diverse Populations

This mid-career investigator award in patient-oriented research supports Dr. Lieu's time for mentoring beginning investigators and will add new activities to an ongoing study on racial/ethnic disparities in medication use by children with persistent asthma.

R01 HL 075504 (Gillman) 8/01/04 – 4/30/08 0.24 calendar
NIH \$480,665

Maternal Fatty Acids, Child Obesity and Asthma Immunity

In this expansion of Project Viva, a prospective longitudinal cohort study of pregnant women and children, our goal is to examine associations of maternal gestational fatty acid intake, fatty acid levels in offspring blood, fetal growth, and postnatal weight status with markers of allergy and inflammation at the age of 3 years.

R21 LM 008707 (Kleinman) 6/01/05 – 5/31/08 2.88 calendar
NIH/NLM \$116,250

Methods for evaluating bioterrorism surveillance tools

In this application, we propose developing tools to compare statistical methods for detection of bioterrorist attack. We will explore: 1) weighted ROC curves; 2) generalized multidimensional ROC surfaces; and 3) cost-based evaluation incorporating investigation and false positive costs as well as the value of mortality and morbidity incurred and averted by each method.

R01 HD 050966 (Gillman) 8/01/05 – 7/31/10 0.48 calendar
NIH \$428,764

Improving primary care to prevent childhood obesity

The overall goal of this research is to assess an innovative, sustainable primary care practice change intervention to prevent obesity among young children. To achieve this goal, we will conduct a cluster-randomized controlled trial in 10 pediatric practices of a large multi-site group practice in eastern Massachusetts. The trial will include 400 children age 2-5 years at elevated risk of obesity based on their and their parents' body mass indexes. The primary aim is to assess the extent to which the intervention, compared with the usual care control condition, reduces change in body mass index over a 6-month intervention and 2-year follow-up period.

P01 CD 000260 (Platt) 9/30/05 – 9/29/08 1.20 calendar
CDC \$101,648

Public Health Information Center of Excellence: Enhancing Public Health Through Electronic Medical and Personal Health Records

The center will link Electronic Medical Records (EMRs), Personally Controlled Health Records (PCHRs), and electronic public health reporting and communication systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities to build on existing infrastructure to enhance communications to improve public health practices.

ACTIVE (cont.)

U01 GM 076672 (Platt) 2/01/06 – 1/31/11 1.80 calendar
NIGMS \$3,001,609

Modeling Health Systems Infectious Disease Data

This project will develop models for early detection and monitoring of infectious disease outbreaks. These models will be applied at different geographical scales, from individual wards of a single hospital to a whole country, as well as for different data specificity from very general symptoms to microbial disease strains and antimicrobial resistance profiles.

R01 HD 034568 (Gillman) 8/01/06 – 6/30/10 0.96 calendar
NIH \$770,607

Pre- and peri-natal predictors of childhood obesity

The aim of this prospective longitudinal cohort study of pregnant women and their children is to examine the roles of prenatal dietary and hormonal factors, infant feeding, and postnatal growth in the development of obesity and related disorders at 7 years of age in Project Viva.

R01 AI 066304 (Finkelstein) 8/01/06 – 7/31/10 0.24 calendar
NIH \$494,303

Post-PCV pneumococcal population genetics and resistance

This study will 1) measure trends in carriage of *Streptococcus pneumoniae* in a multi-community sample of young children following introduction of pneumococcal conjugate vaccine, including changes in prevalence, serotypes carried, and serotype-specific antibiotic resistance; 2) Test competing hypotheses to account for in pneumococcal population structure following PCV7 introduction; and, 3) Determine if previously documented risk factors for carriage of *S. pneumoniae* (overall) and penicillin non-susceptible *S. pneumoniae* continue to predict carriage in the post-PCV7 era.

R01 PH 000032 (Kulldorff) 9/30/06 – 9/29/08 1.20 calendar
NIH \$496,499

Data evaluation for early disease outbreak detection

This project evaluates and compares the efficacy of different health services data sources for early disease outbreak detection, including telephone inquiries, ambulatory care visits, emergency department visits, laboratory test requests and results, radiology tests, hospitalizations, drug prescriptions and drug dispensing.

R21 DK 073739 (Rich-Edwards) 9/30/06 – 8/31/08 0.60 calendar
NIH \$150,000

Lactation and diabetes risk factors in women

This study will examine the associations of lactation duration with levels of insulin resistance at 3 years postpartum.

R01 HL 064925 (Gillman) 5/15/07 – 3/31/11 0.60 calendar
NIH \$487,869

Maternal vitamin D, adiposity in early life, and risk of childhood asthma

The overall goal of this proposal is to examine associations of maternal and child nutritional status with development of asthma-related outcomes by the age of 7 years.

ACTIVE (cont.)

R18 HS 017201 (Simon) 9/01/07 – 6/30/10 0.60 calendar
AHRQ \$225,000

Improving Laboratory Monitoring in Community Practices: A Randomized Trial

Medication errors occur frequently among patients in the ambulatory setting and cause many preventable adverse drug events; thus, they constitute an important target for patient safety and quality improvement. We propose a community-based randomized controlled trial of clinical-decision support to improve laboratory monitoring of medication use and a results management program to improve the timely follow-up of abnormal laboratory tests. This practical clinical trial will evaluate the effectiveness of promoting clinicians' use of commercially available healthcare information technology to improve medication safety in the ambulatory care setting.

PENDING

(Lazarus) 7/01/07 – 6/30/09 0.24 calendar
AHRQ \$500,000

ESP: VAERS

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). We will use electronic medical records available from all ambulatory care encounters in a large multi-specialty practice to achieve this goal.

R01 (Oken) 12/01/07 – 11/30/11 0.60 calendar
NIH \$303,562

Effects of prenatal diet and mercury exposure on child behavior and development

The goals of this project are to study associations of maternal fish intake and blood levels of mercury, n-3 fatty acids, and selenium during pregnancy with child cognition and behavior at age 7 years.

R01 (McCray) 2/01/08 – 1/31/11 0.60 calendar
NIH \$8,105 (Subcontract)

Personalized Autism Information Resources (PAIR)

This project tests the hypothesis that targeted, customized, and literacy-aware health information delivered in a just-in-time fashion leads to: 1) improved control of autism spectrum disorders by affected families, and 2) enhanced communication between the affected families and the health care team.

G13 (Kleinman) 4/01/08 – 3/31/11 1.70 calendar
NIH \$50,000

SAS/R dictionary for health researchers

The product of this project will be a dictionary that will contain instructions for doing tasks common to statistical analysis of public health data in the two most important statistical software packages. Currently users of these packages find it difficult to transfer their knowledge from one system to another, limiting their analyses and making them less productive. Since much medical advancement depends on statistical analysis, the book will enable quicker and more accurate advancement by making statistical analysis more productive and more accurate.

PENDING

(Oken) 1/01/08 – 12/31/10 0.60 calendar
ADA \$173,868

Promoting health behaviors to avoid excessive gestational weight gain

The goal of the proposed project is to pilot test a practice-based intervention to improve weight-related behaviors and to reduce the prevalence of excessive gestational weight gain among overweight and obese women receiving their prenatal care at Harvard Vanguard Medical Associates (HVMA), a diverse multi-specialty group practice in eastern Massachusetts.

OVERLAP

Should additional grants be funded during the award period of currently active grants, I will reduce effort on one or more to ensure that my total effort does not exceed 12.00 calendar person months.

Other Support for 17045				
Personnel	Award Number	Dates of Award	Percentage	
Lazarus	Active			
	2 U01 HL065899-05	08/01/05 - 06/30/10	5.0%	
	P01 CD000260	01/01/06 - 12/31/08	10.0%	
	1 U54 LM008748	09/15/04 - 07/31/07	24.0%	
	1 R01 HG003646-01A1	12/01/05 - 11/30/10	33.0%	
	1 P01 HL083069	12/01/06 - 11/30/11	20.0%	
	1 R01 HL066289	04/01/07 - 03/31/11	5.0%	
	R01 HL086601-01	12/01/06 - 11/30/10	3.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	20.0%	new AHRQ one
			120.0%	
	Pending			
	1 R01 HL092197-01	04/01/08 - 03/31/13	2.5%	
	TBA (Platt)	XX/XX/XX - XX/XX/XX	20.0%	
Brown	Active			
	LCF030207	03/01/07 - 02/28/08	10.0%	
	2 U18 HS10391	09/29/06 - 09/30/07	20.0%	
	200-2002-00732	10/01/06 - 09/30/07	20.0%	
	HHSN268200425216C	09/30/04 - 09/29/07	15.0%	
	HHSF223200510012C C.O.A. #3	05/01/06 - 12/31/07	10.0%	
	U19CA079689	05/01/07 - 04/30/12	7.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	10.0%	new AHRQ one
			92.0%	
	Pending			
	HPHC PI (Lazarus)	TBD	9.5%	
	HPHC PI (Brown)	07/01/07 - 06/30/11	13.0%	
	HPHC PI (Brown)	09/30/07 - 09/29/11	30.0%	
	HPHC PI (Fletcher)	05/01/07 - 04/30/12	7.0%	
Kleinman	Active			
	K24 HL 068041	09/30/01 - 06/30/11	4.0%	
	K24 HD 047667	07/01/04 - 06/30/09	5.0%	
	R01 HL 075504	08/01/04 - 04/30/08	2.0%	
	R21 LM 008707	08/01/05 - 05/31/08	2.4%	
	R01 HD 050966	08/01/05 - 07/31/10	4.0%	
	P01 CD 000260	09/30/05 - 09/29/08	10.0%	
	U01 GM 076672	02/01/06 - 01/31/11	15.0%	
	R01 HD034568	08/01/06 - 06/30/10	8.0%	
	R01 A1 066304	08/01/06 - 07/31/10	2.0%	
	R01 PH 000032	09/30/06 - 09/29/08	10.0%	
	R21 DK 073739	09/30/06 - 08/31/08	5.0%	
	R01 HL064925	05/15/07 - 03/31/11	5.0%	
	R18 HS 017201	09/01/07 - 06/30/10	5.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	2.0%	new AHRQ one
			79.4%	
	Pending			
	R18 (Simon)	07/01/07 - 06/30/10	5.0%	
	R01 (Oken)	12/01/07 - 11/30/11	5.0%	
	R01 (McCray)	02/01/08 - 01/31/11	5.0%	
	G13 (Kleinman)	04/01/08 - 03/31/11	14.2%	
	(Oken)	01/01/08 - 12/31/10	5.0%	
Klompas	Active			
	P01 CD000260-02	09/30/05 - 09/29/08	20.0%	
	7 U01 GM076672-02	02/01/07 - 01/31/08	10.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	35.0%	new AHRQ one
			65.0%	
	Pending			
	ESP VAERS	XX/XX/XX - XX/XX/XX	20.0%	
Platt	Active			
	5 U18 HS10391-07	09/29/06 - 09/30/07	19.0%	
	1 U01 GM76672-01	02/01/07 - 01/31/08	15.0%	
	5 P01 CD000260-02	09/30/05 - 09/29/08	20.0%	
	200200200732	09/20/03 - 09/19/12	5.0%	
	U01 CI000344-01	02/01/06 - 09/19/11	12.0%	
	HHSF22320051001	09/23/05 - 09/22/10	15.0%	
	SCDPH5225 5 337HAR0000	04/01/07 - 08/31/07	2.1%	
	MTA53	01/01/07 - 12/31/09	1.7%	
	1 R01 PH0000032-01	09/30/06 - 09/29/08	2.1%	
	1 R01 AI066304-01A1	08/01/06 - 07/31/10	5.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	3.0%	new AHRQ one
			99.8%	
	Pending			
	None			

(b)(6)

Other Support

ACTIVE

Prime: Harvard Pilgrim Health Care (Simon)

XXXXXXXXXX

HPHC PI (Simon)

State of Oregon Atty. Gen. Trust Fund

11/7/2005-12/31/2007

0.6 calendar (5%)

HPHC Total Costs: \$399,990

"Reducing Unnecessary Use of Heavily Marketed Medicines: A Randomized Controlled Trial of Computerized Prescribing Alerts and Clinician Education"

We are undertaking a group-randomized controlled trial to reduce the use of potentially unnecessary medications for which equally efficacious, less expensive alternatives exist. All fourteen sites at Harvard Vanguard Medical Associates encompassing 550 physicians are participating in the study.

PENDING

Prime: Harvard Pilgrim Health Care (Lazarus)

XXXXXXXXXX

HPHC PI (Lazarus)

AHRQ

Funding Period: TBD

0.6 Year 1, 0.6 in Year 2 (0.5%)

HPHC Direct Costs: TBD

Electronic Support for Public Health – Vaccine Adverse Events Reporting System (ESP VAERS)

Routine Vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

8/30

Updated

(b)(5)

Other Support for 17045				
Personnel	Award Number	Dates of Award	Percentage	
Lazarus	Active			
	2 U01 HL085899-05	08/01/05 - 06/30/10	5.0%	
	P01 CD000260	01/01/06 - 12/31/08	10.0%	
	1 U54 LM008748	09/15/04 - 07/31/07	24.0%	
	1 R01 HG003646-01A1	12/01/05 - 11/30/10	33.0%	
	1 P01 HL083068	12/01/08 - 11/30/11	20.0%	
	1 R01 HL066289	04/01/07 - 03/31/11	5.0%	
	R01 HL086601-01	12/01/06 - 11/30/10	3.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	20.0%	new AHRQ one
			120.0%	
	Pending			
	1 R01 HL092197-01	04/01/08 - 03/31/13	2.5%	
	TBA (Platt)	XX/XX/XX - XX/XX/XX	20.0%	
Brown	Active			
	LCF030207	03/01/07 - 02/28/08	10.0%	
	2 U18 HS10391	09/29/06 - 09/30/07	20.0%	
	200-2002-00732	10/01/06 - 09/30/07	20.0%	
	HHSN268200425216C	09/30/04 - 09/29/07	15.0%	
	HHSF223200510012C C.O.A. #3	05/01/06 - 12/31/07	10.0%	
	U19CA079689	05/01/07 - 04/30/12	7.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	10.0%	new AHRQ one
			92.0%	
	Pending			
	HPHC PI (Lazarus)	TBD	9.5%	
	HPHC PI (Brown)	07/01/07 - 06/30/11	13.0%	
	HPHC PI (Brown)	09/30/07 - 09/29/11	30.0%	
	HPHC PI (Fletcher)	05/01/07 - 04/30/12	7.0%	
Kleinman	Active			
	K24 HL 068041	09/30/01 - 06/30/11	4.0%	
	K24 HD 047867	07/01/04 - 06/30/09	5.0%	
	R01 HL 075504	08/01/04 - 04/30/08	2.0%	
	R21 LM 008707	08/01/05 - 05/31/08	2.4%	
	R01 HD 050986	08/01/05 - 07/31/10	4.0%	
	P01 CD 000260	09/30/05 - 09/29/08	10.0%	
	U01 GM 076672	02/01/06 - 01/31/11	15.0%	
	R01 HD034568	08/01/06 - 06/30/10	8.0%	
	R01 A1 068304	08/01/06 - 07/31/10	2.0%	
	R01 PH 000032	09/30/06 - 09/29/08	10.0%	
	R21 DK 073739	09/30/06 - 08/31/08	5.0%	
	R01 HL064925	05/15/07 - 03/31/11	5.0%	
	R18 HS 017201	09/01/07 - 06/30/10	5.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	2.0%	new AHRQ one
			79.4%	
	Pending			
	R18 (Simon)	07/01/07 - 06/30/10	5.0%	
	R01 (Oken)	12/01/07 - 11/30/11	5.0%	
	R01 (McCray)	02/01/08 - 01/31/11	5.0%	
	G13 (Kleinman)	04/01/08 - 03/31/11	14.2%	
	(Oken)	01/01/08 - 12/31/10	5.0%	
Klompas	Active			
	P01 CD000260-02	09/30/05 - 09/29/08	20.0%	
	7 U01 GM076672-02	02/01/07 - 01/31/08	10.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	35.0%	new AHRQ one
			65.0%	
	Pending			
	ESP VAERS	XX/XX/XX - XX/XX/XX	20.0%	
Platt	Active			
	5 U18 HS10391-07	09/29/06 - 09/30/07	19.0%	
	1 U01 GM76672-01	02/01/07 - 01/31/08	15.0%	
	5 P01 CD000260-02	09/30/05 - 09/29/08	20.0%	
	200200200732	09/20/03 - 09/19/12	5.0%	
	U01 CI000344-01	02/01/06 - 09/19/11	12.0%	
	HHSF22320051001	09/23/05 - 09/22/10	15.0%	
	SCDPH5225 5 337HAR0000	04/01/07 - 08/31/07	2.1%	
	MTA53	01/01/07 - 12/31/09	1.7%	
	1 R01 PH0000032-01	09/30/06 - 09/29/08	2.1%	
	1 R01 AI066304-01A1	08/01/06 - 07/31/10	5.0%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	3.0%	new AHRQ one
			99.8%	
	Pending			
	None			

8/30

original

Other Support for 17045				
Personnel	Award Number	Dates of Award	Percentage	
Lazarus	Active			
	2 U01 HL065899-05	08/01/05 - 06/30/10	5%	
	P01 CD000260	01/01/06 - 12/31/08	10%	
	1 U54 LM008748	09/15/04 - 07/31/07	24%	
	1 R01 HG003648-01A1	12/01/05 - 11/30/10	33%	
	1 P01 HL083089	12/01/06 - 11/30/11	20%	
	1 R01 HL066289	04/01/07 - 03/31/11	5%	
	R01 HL086601-01	12/01/06 - 11/30/10	3%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	20%	new AHRQ one
			120%	
	Pending			
	1 R01 HL092197-01	04/01/08 - 03/31/13	2.50%	
	TBA (Platt)	XX/XX/XX - XX/XX/XX	20%	
Brown	Active			
	LCF030207	03/01/07 - 02/28/08	10%	
	2 U18 HS10391	09/29/06 - 09/30/07	20%	
	200-2002-00732	10/01/06 - 09/30/07	20%	
	HHSN268200425216C	09/30/04 - 09/29/07	15%	
	HHSF223200510012C C.O.A. #3	05/01/06 - 12/31/07	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	10%	new AHRQ one
			85%	
	Pending			
	HPHC PI (Lazarus)	TBD	9.50%	
	HPHC PI (Brown)	07/01/07 - 06/30/11	13%	
	HPHC PI (Brown)	09/30/07 - 09/29/11	30%	
	HPHC PI (Fletcher)	05/01/07 - 04/30/12	7%	
Kleinman	Active			
	K24 HL 068041	09/30/01 - 06/30/11	4%	
	K24 HD 047867	07/01/04 - 06/30/09	5%	
	R01 HL 075504	08/01/04 - 04/30/08	2%	
	R21 LM 008707	06/01/05 - 05/31/08	24%	
	R01 HD 050966	08/01/05 - 07/31/10	4%	
	P01 CD 000260	09/30/05 - 09/29/08	10%	
	U01 GM 076672	02/01/06 - 01/31/11	15%	
	R01 HD034588	08/01/06 - 06/30/10	8%	
	R01 A1 066304	08/01/06 - 07/31/10	2%	
	R01 PH 000032	09/30/06 - 09/29/08	10%	
	R21 DK 073739	09/30/06 - 08/31/08	5%	
	R01 HL064925	05/15/07 - 03/31/11	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	2%	new AHRQ one
			96%	
	Pending			
	R18 (Simon)	07/01/07 - 06/30/10	5%	
	R01 (Oken)	12/01/07 - 11/30/11	5%	
	R01 (McCray)	02/01/08 - 01/31/11	5%	
	G13 (Kleinman)	04/01/08 - 03/31/11	14.16%	
	(Oken)	01/01/08 - 12/31/10	5%	
Klompas	Active			
	P01 CD000260-02	09/30/05 - 09/29/08	20%	
	7 U01 GM076672-02	02/01/07 - 01/31/08	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	35%	new AHRQ one
			65%	
	Pending			
	ESP VAERS	XX/XX/XX - XX/XX/XX	20%	
Platt	Active			
	5 U18 HS10391-07	09/29/06 - 09/30/07	19%	
	1 U01 GM76672-01	02/01/07 - 01/31/08	15%	
	5 P01 CD000260-02	09/30/05 - 09/29/08	20%	
	200200200732	09/20/03 - 09/19/12	5%	
	U01 CI000344-01	02/01/06 - 09/19/11	12%	
	HHSF22320051001	09/23/05 - 09/22/10	15%	
	SCDPH5225 5 337HAR0000	04/01/07 - 08/31/07	2.08%	
	MTA53	01/01/07 - 12/31/09	1.66%	
	1 R01 PH0000032-01	09/30/06 - 09/29/08	2.08%	
	1 R01 AI066304-01A1	08/01/06 - 07/31/10	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	3%	new AHRQ one
			99.82%	
	Pending			
	None			

(b)(6)
Other Support

ACTIVE

Prime: Lovelace Clinic Foundation (Mapel)

LCF030207

HPHC PI (Brown)

(b)(4)

3/1/07-2/28/08

1.2 calendar (10%)

(b)(4)

Pneumonia and Upper Respiratory Tract Infections Among COPD Patients Using Fluticasone/Salmeterol in Combination Versus Other Steroids and Bronchodilators Alone

The primary goal of this project is to examine whether COPD patients prescribed Advair have a higher risk for pneumonia as compared to patients who are treated with other ICS and/or bronchodilators alone.

Role: Primary Investigator

Prime: Harvard Pilgrim Health Care (Platt)

2U18HS10391

HPHC PI (Platt)

AHRQ

9/29/2006-9/30/2007

2.4 calendar (20%)

\$259,964.00 (Core, yr 4; Dataset yr4 – HPHC Direct Costs)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 2)

The Centers for Education and Research in Therapeutics (CERT) is an initiative funded by the Agency for Healthcare Research and Quality to conduct research and provide education that optimizes use of drugs, devices, and biological products. Ten sites in the HMO Research Network are collaborating as a CERT.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

200-2002-00732

HPHC PI (Platt)

AHIP

10/1/06-9/30/07

2.4 calendar (20%)

\$105,994.00 (HPHC Direct Costs)

Using Electronic Health Data to Assess Influenza Vaccine Safety

This project represents a CDC and FDA jointly funded study to evaluate the development of a system for active surveillance of influenza vaccines. The study builds on the prior work of the Vaccine safety datalink (VSD) and is intended to lay the groundwork for an active surveillance program involving large, diverse populations that could be implemented to monitor an influenza pandemic. The two main projects goals are to a.) improve the nation's ability to use electronic health data for rapid assessment of adverse reactions to influenza vaccine, including pandemic influenza vaccine; and b.) expand the size of the population for which electronic health data can be used for influenza vaccine, including pandemic influenza vaccine, safety assessment

Role: Co-Investigator

Prime: Group Health Cooperative (Larsen)

HHSN268200425216C

HPHC PI (Platt)

NHLBI

9/30/04-9/29/07

1.8 calendar (15%)

\$173,718.00 (HPHC Direct Costs)

The HMO Coordinated Clinical Studies Network

The Coordinated Clinical Studies Network (CCSN) is an unparalleled research facility for clinical and health services research that builds on the current capacity of the HMO Research Network (HMORN). The CCSN supports the full range of research that HMORN members regularly conduct, which includes cancer, infectious and chronic disease surveillance, health services and health economics research, behavioral, mental health and substance abuse studies, genomic research, complementary and alternative medicine, dental research, pharmacoepidemiological and pharmaco-economic investigations as well as analyses of systems change and organizational behavior. The project's deliverables are to build and sustain a research infrastructure, establish HMORN CCSN web site to coordinate all Network communications, establish External & Internal Advisory Committees for the CCSN, build budget templates and pre-negotiated project budgets for network based research, and create a document repository for IRB and other reviews.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

HHSF223200510012C C.O.A. #3

HPHC PI (Platt)

FDA

5/1/06-12/31/07

1.2 calendar (10%)

\$114,776.00 (HPHC Direct Costs)

ADHD Drugs and Cardiovascular Outcomes –Full Study

This project is a retrospective cohort study of the use of medications for ADHD and the risk of serious arrhythmias. The study drugs include all medications with a label indication for treatment of ADHD. These include the amphetamine-related psychostimulants, other stimulants (pemoline), and SNRIs (atomoxetine).

Prime: CRN – Group Health Cooperative

U19CA079689

HPHC PI (Fletcher)

NCI

5/1/07 – 4/30/12

.84 calendar (7%)

\$263,090.00 (HPHC Direct Costs, yr 1)

Cancer Research Network Across Health Care Systems – Infrastructure

The CRN has successfully developed a productive collaborative cancer research consortium. We plan to improve the research capacity of the CRN and use it to conduct a broad array of cancer research studies that relate to NCI research priorities or questions of importance to CRN investigators and our academic collaborators.

PENDING**Prime: Harvard Pilgrim Health Care (Lazarus)**

XXXXXXXX

HPHC PI (Lazarus)

AHRQ

Funding Period: TBD

HPHC Direct Costs: TBD

1.2 Year 1, 1.08 in Year 2 (9.5%)

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Prime: Kaiser Permanente Northern California (Herrinton)

XXXXXXXX

HPHC PI (Brown)

NIA

10/1/07-9/30/11

1.6 calendar (13%)

\$115,636.00 (HPHC Direct Costs, yr 1)

Age Disparities in Use of Biologics for Rheumatoid Arthritis

The proposed community-based study will investigate each of these factors, comparing RA patients ≥ 65 years with younger patients. *The study is directed toward rheumatologists, health planners, and policy makers. It will assess whether elders have adequate and appropriate access to biologic agents, thereby allowing refinement of drug coverage policies to improve their use among elders.* This question is of critical importance as there are an increasing number of new biologic therapies on the horizon for a wide range of inflammatory diseases, and the number of Medicare enrollees continues to grow.

Prime: Harvard Pilgrim Health Care (Platt)

XXXXXXXX

HPHC PI (Brown)

AHRQ

10/01/07-9/30/11

3.6 calendar (30%)

\$263,090.00 (HPHC Direct Costs, yr 1)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 3)

The overall vision of the HMO Research Network CERT is to advance population health through acquisition and widespread dissemination of knowledge about best therapeutics practices. We accomplish this by taking advantage of the research and dissemination opportunities afforded by health plans' defined populations, their large provider groups, and their unique data sources. In the aggregate these health plans cover a substantial majority of the U.S. population. This leads to this CERT's theme, "Improving therapeutics' use, safety, and effectiveness, through research, dissemination, and education using health plans' defined populations, providers, delivery systems, and data."

Aim 1. To enhance the collective ability of the HMO Research Network and other health plans' collective to advance therapeutics knowledge by leveraging unique data sources within a very large, generalizable population.

Aim 2. To develop and implement new multi-faceted methods for disseminating and promoting best therapeutic practices.

OVERLAP:

None at present.

Should all of the pending grant proposals be funded, Dr. Brown's level of effort for the period of the overlap (May 1 – September 30) on some of his projects will be adjusted to ensure that his level of effort does not exceed 100%.

OTHER FINANCIAL SUPPORT

(b)(6)

ACTIVE

K24 HL 068041 (Gillman) 9/30/01 – 6/30/11 0.48 calendar
NIH \$164,963

Patient-oriented research in early life origins of CVD

The research focus of this midcareer patient-oriented investigator award is a study of maternal diet, placental hormones, and offspring blood pressure. The award also serves as a mechanism to strengthen the PI's mentorship capabilities.

K24 HD 047667 (Lieu) 7/01/04 – 6/30/09 0.60 calendar
NICHD \$128,633

Enhancing Prevention for Children in Diverse Populations

This mid-career investigator award in patient-oriented research supports Dr. Lieu's time for mentoring beginning investigators and will add new activities to an ongoing study on racial/ethnic disparities in medication use by children with persistent asthma.

R01 HL 075504 (Gillman) 8/01/04 – 4/30/08 0.24 calendar
NIH \$480,665

Maternal Fatty Acids, Child Obesity and Asthma Immunity

In this expansion of Project Viva, a prospective longitudinal cohort study of pregnant women and children, our goal is to examine associations of maternal gestational fatty acid intake, fatty acid levels in offspring blood, fetal growth, and postnatal weight status with markers of allergy and inflammation at the age of 3 years.

R21 LM 008707 (Kleinman) 6/01/05 – 5/31/08 2.88 calendar
NIH/NLM \$116,250

Methods for evaluating bioterrorism surveillance tools

In this application, we propose developing tools to compare statistical methods for detection of bioterrorist attack. We will explore: 1) weighted ROC curves; 2) generalized multidimensional ROC surfaces; and 3) cost-based evaluation incorporating investigation and false positive costs as well as the value of mortality and morbidity incurred and averted by each method.

R01 HD 050966 (Gillman) 8/01/05 – 7/31/10 0.48 calendar
NIH \$428,764

Improving primary care to prevent childhood obesity

The overall goal of this research is to assess an innovative, sustainable primary care practice change intervention to prevent obesity among young children. To achieve this goal, we will conduct a cluster-randomized controlled trial in 10 pediatric practices of a large multi-site group practice in eastern Massachusetts. The trial will include 400 children age 2-5 years at elevated risk of obesity based on their and their parents' body mass indexes. The primary aim is to assess the extent to which the intervention, compared with the usual care control condition, reduces change in body mass index over a 6-month intervention and 2-year follow-up period.

P01 CD 000260 (Platt) 9/30/05 – 9/29/08 1.20 calendar
CDC \$101,648

Public Health Information Center of Excellence: Enhancing Public Health Through Electronic Medical and Personal Health Records

The center will link Electronic Medical Records (EMRs), Personally Controlled Health Records (PCHRs), and electronic public health reporting and communication systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities to build on existing infrastructure to enhance communications to improve public health practices.

ACTIVE (cont.)

U01 GM 076672 (Platt) 2/01/06 – 1/31/11 1.80 calendar
NIGMS \$3,001,609

Modeling Health Systems Infectious Disease Data

This project will develop models for early detection and monitoring of infectious disease outbreaks. These models will be applied at different geographical scales, from individual wards of a single hospital to a whole country, as well as for different data specificity from very general symptoms to microbial disease strains and antimicrobial resistance profiles.

R01 HD 034568 (Gillman) 8/01/06 – 6/30/10 0.96 calendar
NIH \$770,607

Pre- and peri-natal predictors of childhood obesity

The aim of this prospective longitudinal cohort study of pregnant women and their children is to examine the roles of prenatal dietary and hormonal factors, infant feeding, and postnatal growth in the development of obesity and related disorders at 7 years of age in Project Viva.

R01 AI 066304 (Finkelstein) 8/01/06 – 7/31/10 0.24 calendar
NIH \$494,303

Post-PCV pneumococcal population genetics and resistance

This study will 1) measure trends in carriage of *Streptococcus pneumoniae* in a multi-community sample of young children following introduction of pneumococcal conjugate vaccine, including changes in prevalence, serotypes carried, and serotype-specific antibiotic resistance; 2) Test competing hypotheses to account for in pneumococcal population structure following PCV7 introduction; and, 3) Determine if previously documented risk factors for carriage of *S. pneumoniae* (overall) and penicillin non-susceptible *S. pneumoniae* continue to predict carriage in the post-PCV7 era.

R01 PH 000032 (Kulldorff) 9/30/06 – 9/29/08 1.20 calendar
NIH \$496,499

Data evaluation for early disease outbreak detection

This project evaluates and compares the efficacy of different health services data sources for early disease outbreak detection, including telephone inquiries, ambulatory care visits, emergency department visits, laboratory test requests and results, radiology tests, hospitalizations, drug prescriptions and drug dispensing.

R21 DK 073739 (Rich-Edwards) 9/30/06 – 8/31/08 0.60 calendar
NIH \$150,000

Lactation and diabetes risk factors in women

This study will examine the associations of lactation duration with levels of insulin resistance at 3 years postpartum.

R01 HL 064925 (Gillman) 5/15/07 – 3/31/11 0.60 calendar
NIH \$487,869

Maternal vitamin D, adiposity in early life, and risk of childhood asthma

The overall goal of this proposal is to examine associations of maternal and child nutritional status with development of asthma-related outcomes by the age of 7 years.

ACTIVE (cont.)

R18 HS 017201 (Simon) 9/01/07 – 6/30/10 0.60 calendar
 AHRQ \$225,000

Improving Laboratory Monitoring in Community Practices: A Randomized Trial

Medication errors occur frequently among patients in the ambulatory setting and cause many preventable adverse drug events; thus, they constitute an important target for patient safety and quality improvement. We propose a community-based randomized controlled trial of clinical-decision support to improve laboratory monitoring of medication use and a results management program to improve the timely follow-up of abnormal laboratory tests. This practical clinical trial will evaluate the effectiveness of promoting clinicians' use of commercially available healthcare information technology to improve medication safety in the ambulatory care setting.

PENDING

(Lazarus) 7/01/07 – 6/30/09 0.24 calendar
 AHRQ \$500,000

ESP: VAERS

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). We will use electronic medical records available from all ambulatory care encounters in a large multi-specialty practice to achieve this goal.

R01 (Oken) 12/01/07 – 11/30/11 0.60 calendar
 NIH \$303,562

Effects of prenatal diet and mercury exposure on child behavior and development

The goals of this project are to study associations of maternal fish intake and blood levels of mercury, n-3 fatty acids, and selenium during pregnancy with child cognition and behavior at age 7 years.

R01 (McCray) 2/01/08 – 1/31/11 0.60 calendar
 NIH \$8,105 (Subcontract)

Personalized Autism Information Resources (PAIR)

This project tests the hypothesis that targeted, customized, and literacy-aware health information delivered in a just-in-time fashion leads to: 1) improved control of autism spectrum disorders by affected families, and 2) enhanced communication between the affected families and the health care team.

G13 (Kleinman) 4/01/08 – 3/31/11 1.70 calendar
 NIH \$50,000

SAS/R dictionary for health researchers

The product of this project will be a dictionary that will contain instructions for doing tasks common to statistical analysis of public health data in the two most important statistical software packages. Currently users of these packages find it difficult to transfer their knowledge from one system to another, limiting their analyses and making them less productive. Since much medical advancement depends on statistical analysis, the book will enable quicker and more accurate advancement by making statistical analysis more productive and more accurate.

PENDING

(Oken)

1/01/08 – 12/31/10 0.60 calendar

ADA

\$173,868

Promoting health behaviors to avoid excessive gestational weight gain

The goal of the proposed project is to pilot test a practice-based intervention to improve weight-related behaviors and to reduce the prevalence of excessive gestational weight gain among overweight and obese women receiving their prenatal care at Harvard Vanguard Medical Associates (HVMA), a diverse multi-specialty group practice in eastern Massachusetts.

OVERLAP

Should additional grants be funded during the award period of currently active grants, I will reduce effort on one or more to ensure that my total effort does not exceed 12.00 calendar person months.

OTHER SUPPORT**Ross LAZARUS, M.B.B.S., M.Med., M.P.H.**

(Brigham and Women's Hospital)

ACTIVE – Brigham Administered Grants

2 U01 HL065899-05 (Weiss) 08/01/05 – 06/30/10 0.60 calendar
NIH/ NHLBI \$1,452,435

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. Overlap: None.

P01CD000260 (Platt) 01/01/06 – 12/31/08 1.2 calendar
Centers for Excellence in Public Health Informatics (ESP) \$932,178

Using Electronic Medical Records to Support Core Public Health Needs

This work will build directly on this group's accomplishments in developing the CDC National Bioterrorism Syndromic Surveillance Demonstration Project. ESP will serve three major functions: 1) Completely transparent reporting of conditions where all required information can be extracted from EMRs, 2) Initiation of reporting that triggers an automated query to clinicians if non-extractable information, and 3) Automatic responses to electronic queries by health authorities regarding demographic and treatment status of individuals with positive laboratory tests. Overlap: None

1 U54 LM008748 (Kohane) 09/15/04 – 07/31/07 2.88 calendar
NIH/NHLBI \$186,000

Genetics and Pharmacogenetics of Common Complex Disease

This work will perform as part of the Informatics for Integrating Biology and the Bedside (I²B²) project and will lead to the development and implementation of methods and tools to improve genetic epidemiological and pharmacogenetic research in complex disease.

Overlap: None.

1 R01 HG003646-01A1 (Lazarus) 12/01/05 – 11/30/10 3.96 calendar
NIH \$2,266,379

A Genetic Association Research Statistical Framework (BISTI)

The specific aims of this project include software support for importing experimental data and genomic annotation; methods for statistical power calculations and for selecting maximally informative subsets of markers during experimental design; methods for visualizing and summarizing experimental results; established and recently developed methods supporting statistical inference on single markers, multiple markers and on the epistatic and gene by environment interactions characteristic of these diseases and needed for emerging fields of study such as pharmacogenetics. Overlap: None.

1 P01 HL083069 (Weiss) 12/01/06 – 11/30/11 2.4 calendar
NIH \$1,515,000

Common Genetic Determinants of Asthma and COPD (PPG Core 3 - Bioinformatics)

The goal of this core is to develop novel bioinformatics tools to be used by Projects 1-4 of the grant, the analysis of human and mouse microarray datasets, and the maintenance of the PPG website, which will be modeled from a former Channing Laboratory PGA website. In addition, this core will provide a wide variety of statistical tools for genetic association analysis, as well as up-to-date information on genetic association studies, mouse genetics, and the functional genomics work of Projects 1-4. Overlap: None.

ACTIVE (Continued) – Brigham Administered Grants

1 R01 HL066289 (Weiss) 4/1/07-3/31/11 0.60 Calendar
NIH/NHLBI \$2,940,680

The Genetic Epidemiology of Asthma in Costa Rica

The goal of this competing continuation grant is to use linkage disequilibrium mapping to test the hypothesis that a gene(s) on chromosome 12q24 influences asthma and airway responsiveness in Costa Ricans, and that a gene(s) on chr. 20p12 influences total serum IgE in male Costa Ricans. This goal will be accomplished by a) genotyping SNPs in these regions to perform fine-mapping family-based association studies to identify candidate genes for asthma and/or its intermediate phenotypes, and b) testing for association between SNPs and haplotypes in selected candidate genes and asthma and/or its intermediate phenotypes in families of children with asthma.

R01 HL086601-01 (Raby) 12/01/06-11/30/10 0.36 Calendar
NIH/NHLBI

Genetics and Gene Expression Profiling in Asthma

The goal of this project is to integrate gene expression microarray data with family-based genetic association studies to identify genetic variants that influence the severity of asthma through regulation of gene expression. Overlap: None

PENDING – Brigham Administered Grants (Lazarus)

1 R01 HL092197-01 (Tantisira) 04/01/08 – 03/31/13 0.30 Calendar
NIH/NHLBI \$412,054

Integrative Pharmacogenomics of Leukotriene Inhibition in Asthma

This project seeks to identify genetic markers most closely associated with the genetic expression signature resulting from administration of medications that block the leukotriene pathway in asthma. By demonstrating that these markers also correlate with the clinical response in asthma, the markers may eventually be used to help predict therapeutic response to anti-leukotriene medications in asthma. Since asthma remains the leading cause of childhood hospitalizations and school absences in the United States, optimizing pharmacologic therapy has the potential to substantially decrease the morbidity and financial burden related to this disease.

TBA (Platt) xx/xx/xx- xx/xx/xx 2.40 calendar
AHRQ \$XXX, XXX

Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)

This project seeks to perform systems analysis, design and application programming for enhancements to existing ESP software to enable the creation and management of diagnosis and therapeutic exposure registries.

Note: If any of the pending grants change status to active, Dr. Lazarus will adjust his active support to accommodate the new effort.

(b)(6)

Other Support

ACTIVE

Prime: Lovelace Clinic Foundation (Mapel)

LCF030207

HPHC PI (Brown)

(b)(4)

3/1/07-2/28/08

(b)(4)

1.2 calendar (10%)

Pneumonia and Upper Respiratory Tract Infections Among COPD Patients Using Fluticasone/Salmeterol in Combination Versus Other Steroids and Bronchodilators Alone

The primary goal of this project is to examine whether COPD patients prescribed Advair have a higher risk for pneumonia as compared to patients who are treated with other ICS and/or bronchodilators alone.

Role: Primary Investigator

Prime: Harvard Pilgrim Health Care (Platt)

2U18HS10391

HPHC PI (Platt)

AHRQ

9/29/2006-9/30/2007

2.4 calendar (20%)

\$259,964.00 (Core, yr 4; Dataset yr4 – HPHC Direct Costs)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 2)

The Centers for Education and Research in Therapeutics (CERT) is an initiative funded by the Agency for Healthcare Research and Quality to conduct research and provide education that optimizes use of drugs, devices, and biological products. Ten sites in the HMO Research Network are collaborating as a CERT.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

200-2002-00732

HPHC PI (Platt)

AHIP

10/1/06-9/30/07

2.4 calendar (20%)

\$105,994.00 (HPHC Direct Costs)

Using Electronic Health Data to Assess Influenza Vaccine Safety

This project represents a CDC and FDA jointly funded study to evaluate the development of a system for active surveillance of influenza vaccines. The study builds on the prior work of the Vaccine safety datalink (VSD) and is intended to lay the groundwork for an active surveillance program involving large, diverse populations that could be implemented to monitor an influenza pandemic. The two main projects goals are to a.) improve the nation's ability to use electronic health data for rapid assessment of adverse reactions to influenza vaccine, including pandemic influenza vaccine; and b.) expand the size of the population for which electronic health data can be used for influenza vaccine, including pandemic influenza vaccine, safety assessment

Role: Co-Investigator

Prime: Group Health Cooperative (Larsen)

HHSN268200425216C

HPHC PI (Platt)

NHLBI

9/30/04-9/29/07

1.8 calendar (15%)

\$173,718.00 (HPHC Direct Costs)

The HMO Coordinated Clinical Studies Network

The Coordinated Clinical Studies Network (CCSN) is an unparalleled research facility for clinical and health services research that builds on the current capacity of the HMO Research Network (HMORN). The CCSN supports the full range of research that HMORN members regularly conduct, which includes cancer, infectious and chronic disease surveillance, health services and health economics research, behavioral, mental health and substance abuse studies, genomic research, complementary and alternative medicine, dental research, pharmacoepidemiological and pharmacoeconomic investigations as well as analyses of systems change and organizational behavior. The project's deliverables are to build and sustain a research infrastructure, establish HMORN CCSN web site to coordinate all Network communications, establish External & Internal Advisory Committees for the CCSN, build budget templates and pre-negotiated project budgets for network based research, and create a document repository for IRB and other reviews.

Role: Co-Investigator

Prime: Harvard Pilgrim Health Care (Platt)

HHSF223200510012C C.O.A. #3

HPHC PI (Platt)

FDA

5/1/06-12/31/07

1.2 calendar (10%)

\$114,776.00 (HPHC Direct Costs)

ADHD Drugs and Cardiovascular Outcomes –Full Study

This project is a retrospective cohort study of the use of medications for ADHD and the risk of serious arrhythmias. The study drugs include all medications with a label indication for treatment of ADHD. These include the amphetamine-related psychostimulants, other stimulants (pemoline), and SNRIs (atomoxetine).

PENDING

Prime: Harvard Pilgrim Health Care (Lazarus)

XXXXXXXX

HPHC PI (Lazarus)

AHRQ

Funding Period: TBD

1.2 Year 1, 1.08 in Year 2 (9.5%)

HPHC Direct Costs: TBD

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Prime: Kaiser Permanente Northern California (Herrinton)

XXXXXXXX

HPHC PI (Brown)

NIA

7/1/07-6/30/11

1.6 calendar (13%)

\$115,636.00 (HPHC Direct Costs, yr 1)

Age Disparities in Use of Biologics for Rheumatoid Arthritis

The proposed community-based study will investigate each of these factors, comparing RA patients ≥ 65 years with younger patients. *The study is directed toward rheumatologists, health planners, and policy makers. It will assess whether elders have adequate and appropriate access to biologic agents, thereby allowing refinement of drug coverage policies to improve their use among elders.* This question is of critical importance as there are an increasing number of new biologic therapies on the horizon for a wide range of inflammatory diseases, and the number of Medicare enrollees continues to grow.

Prime: Harvard Pilgrim Health Care (Platt)

XXXXXXXX

HPHC PI (Brown)

AHRQ

9/30/07-9/29/11

3.6 calendar (30%)

\$263,090.00 (HPHC Direct Costs, yr 1)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 3)

The overall vision of the HMO Research Network CERT is to advance population health through acquisition and widespread dissemination of knowledge about best therapeutics practices. We accomplish this by taking advantage of the research and dissemination opportunities afforded by health plans' defined populations, their large provider groups, and their unique data sources. In the aggregate these health plans cover a substantial majority of the U.S. population. This leads to this CERT's theme, "Improving therapeutics' use, safety, and effectiveness, through research, dissemination, and education using health plans' defined populations, providers, delivery systems, and data."

Aim 1. To enhance the collective ability of the HMO Research Network and other health plans' collective to advance therapeutics knowledge by leveraging unique data sources within a very large, generalizable population.

Aim 2. To develop and implement new multi-faceted methods for disseminating and promoting best therapeutic practices.

Prime: CRN – Group Health Cooperative

XXXXXXXX

HPHC PI (Fletcher)

NCI

5/1/07 – 4/30/12

.84 calendar (7%)

\$263,090.00 (HPHC Direct Costs, yr 1)

Cancer Research Network Across Health Care Systems – Infrastructure

The CRN has successfully developed a productive collaborative cancer research consortium. We plan to improve the research capacity of the CRN and use it to conduct a broad array of cancer research studies that relate to NCI research priorities or questions of importance to CRN investigators and our academic collaborators.

OVERLAP:

None at present.

Should all of the pending grant proposals be funded, Dr. Brown's level of effort for the period of the overlap (May 1 – September 30) on some of his projects will be adjusted to ensure that his level of effort does not exceed 100%.

(b)(6)

OTHER FINANCIAL SUPPORT**ACTIVE**

K24 HL 068041 (Gillman) 9/30/01 – 6/30/11 0.48 calendar
NIH \$164,963

Patient-oriented research in early life origins of CVD

The research focus of this midcareer patient-oriented investigator award is a study of maternal diet, placental hormones, and offspring blood pressure. The award also serves as a mechanism to strengthen the PI's mentorship capabilities.

K24 HD 047667 (Lieu) 7/01/04 – 6/30/09 0.60 calendar
NICHD \$128,633

Enhancing Prevention for Children in Diverse Populations

This mid-career investigator award in patient-oriented research supports Dr. Lieu's time for mentoring beginning investigators and will add new activities to an ongoing study on racial/ethnic disparities in medication use by children with persistent asthma.

R01 HL 075504 (Gillman) 8/01/04 – 4/30/08 0.24 calendar
NIH \$480,665

Maternal Fatty Acids, Child Obesity and Asthma Immunity

In this expansion of Project Viva, a prospective longitudinal cohort study of pregnant women and children, our goal is to examine associations of maternal gestational fatty acid intake, fatty acid levels in offspring blood, fetal growth, and postnatal weight status with markers of allergy and inflammation at the age of 3 years.

R21 LM 008707 (Kleinman) 6/01/05 – 5/31/08 2.88 calendar
NIH/NLM \$116,250

Methods for evaluating bioterrorism surveillance tools

In this application, we propose developing tools to compare statistical methods for detection of bioterrorist attack. We will explore: 1) weighted ROC curves; 2) generalized multidimensional ROC surfaces; and 3) cost-based evaluation incorporating investigation and false positive costs as well as the value of mortality and morbidity incurred and averted by each method.

R01 HD 050966 (Gillman) 8/01/05 – 7/31/10 0.48 calendar
NIH \$428,764

Improving primary care to prevent childhood obesity

The overall goal of this research is to assess an innovative, sustainable primary care practice change intervention to prevent obesity among young children. To achieve this goal, we will conduct a cluster-randomized controlled trial in 10 pediatric practices of a large multi-site group practice in eastern Massachusetts. The trial will include 400 children age 2-5 years at elevated risk of obesity based on their and their parents' body mass indexes. The primary aim is to assess the extent to which the intervention, compared with the usual care control condition, reduces change in body mass index over a 6-month intervention and 2-year follow-up period.

P01 CD 000260 (Platt) 9/30/05 – 9/29/08 1.20 calendar
CDC \$101,648

Public Health Information Center of Excellence: Enhancing Public Health Through Electronic Medical and Personal Health Records

The center will link Electronic Medical Records (EMRs), Personally Controlled Health Records (PCHRs), and electronic public health reporting and communication systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities to build on existing infrastructure to enhance communications to improve public health practices.

ACTIVE (cont.)

U01 GM 076672 (Platt) 2/01/06 – 1/31/11 1.80 calendar
NIGMS \$3,001,609

Modeling Health Systems Infectious Disease Data

This project will develop models for early detection and monitoring of infectious disease outbreaks. These models will be applied at different geographical scales, from individual wards of a single hospital to a whole country, as well as for different data specificity from very general symptoms to microbial disease strains and antimicrobial resistance profiles.

R01 HD 034568 (Gillman) 8/01/06 – 6/30/10 0.96 calendar
NIH \$770,607

Pre- and peri-natal predictors of childhood obesity

The aim of this prospective longitudinal cohort study of pregnant women and their children is to examine the roles of prenatal dietary and hormonal factors, infant feeding, and postnatal growth in the development of obesity and related disorders at 7 years of age in Project Viva.

R01 AI 066304 (Finkelstein) 8/01/06 – 7/31/10 0.24 calendar
NIH \$494,303

Post-PCV pneumococcal population genetics and resistance

This study will 1) measure trends in carriage of *Streptococcus pneumoniae* in a multi-community sample of young children following introduction of pneumococcal conjugate vaccine, including changes in prevalence, serotypes carried, and serotype-specific antibiotic resistance; 2) Test competing hypotheses to account for in pneumococcal population structure following PCV7 introduction; and, 3) Determine if previously documented risk factors for carriage of *S. pneumoniae* (overall) and penicillin non-susceptible *S. pneumoniae* continue to predict carriage in the post-PCV7 era.

R01 PH 000032 (Kulldorff) 9/30/06 – 9/29/08 1.20 calendar
NIH \$496,499

Data evaluation for early disease outbreak detection

This project evaluates and compares the efficacy of different health services data sources for early disease outbreak detection, including telephone inquiries, ambulatory care visits, emergency department visits, laboratory test requests and results, radiology tests, hospitalizations, drug prescriptions and drug dispensing.

R21 DK 073739 (Rich-Edwards) 9/30/06 – 8/31/08 0.60 calendar
NIH \$150,000

Lactation and diabetes risk factors in women

This study will examine the associations of lactation duration with levels of insulin resistance at 3 years postpartum.

R01 HL 064925 (Gillman) 5/15/07 – 3/31/11 0.60 calendar
NIH \$487,869

Maternal vitamin D, adiposity in early life, and risk of childhood asthma

The overall goal of this proposal is to examine associations of maternal and child nutritional status with development of asthma-related outcomes by the age of 7 years.

PENDING

(Lazarus) x/xx/xx – x/xx/xx 0.24 calendar
 AHRQ \$XXX,XXX
 ESP: VAERS

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). We will use electronic medical records available from all ambulatory care encounters in a large multi-specialty practice to achieve this goal.

R18 (Simon) 7/01/07 – 6/30/10 0.60 calendar
 NIH \$225,000

Improving Laboratory Monitoring in Community Practices: A Randomized Trial

Medication errors occur frequently among patients in the ambulatory setting and cause many preventable adverse drug events; thus, they constitute an important target for patient safety and quality improvement. We propose a community-based randomized controlled trial of clinical-decision support to improve laboratory monitoring of medication use and a results management program to improve the timely follow-up of abnormal laboratory tests. This practical clinical trial will evaluate the effectiveness of promoting clinicians' use of commercially available healthcare information technology to improve medication safety in the ambulatory care setting.

R01 (Oken) 12/01/07 – 11/30/11 0.60 calendar
 NIH \$303,562

Effects of prenatal diet and mercury exposure on child behavior and development

The goals of this project are to study associations of maternal fish intake and blood levels of mercury, n-3 fatty acids, and selenium during pregnancy with child cognition and behavior at age 7 years.

R01 (McCray) 2/01/08 – 1/31/11 0.60 calendar
 NIH \$8,105 (Subcontract)

Personalized Autism Information Resources (PAIR)

This project tests the hypothesis that targeted, customized, and literacy-aware health information delivered in a just-in-time fashion leads to: 1) improved control of autism spectrum disorders by affected families, and 2) enhanced communication between the affected families and the health care team.

G13 (Kleinman) 4/01/08 – 3/31/11 1.70 calendar
 NIH \$50,000

SAS/R dictionary for health researchers

The product of this project will be a dictionary that will contain instructions for doing tasks common to statistical analysis of public health data in the two most important statistical software packages. Currently users of these packages find it difficult to transfer their knowledge from one system to another, limiting their analyses and making them less productive. Since much medical advancement depends on statistical analysis, the book will enable quicker and more accurate advancement by making statistical analysis more productive and more accurate.

PENDING

(Oken) 1/01/08 – 12/31/10 0.60 calendar
ADA \$173,868

Promoting health behaviors to avoid excessive gestational weight gain

The goal of the proposed project is to pilot test a practice-based intervention to improve weight-related behaviors and to reduce the prevalence of excessive gestational weight gain among overweight and obese women receiving their prenatal care at Harvard Vanguard Medical Associates (HVMA), a diverse multi-specialty group practice in eastern Massachusetts.

OVERLAP

Should additional grants be funded during the award period of currently active grants, I will reduce effort on one or more to ensure that my total effort does not exceed 12.00 calendar person months.

(b)(6)

OTHER FINANCIAL SUPPORT

ACTIVE SUPPORT

P01 CD000260-02 (Platt) 9/30/2005-9/29/2008
PHI Center \$1,551,712
2.4 Person-months

Enhancing Public Health Through Electronic Medical and Personal Health Records

This Center of Excellence in Public Health Informatics will be a partnership of three entities that have expertise in design and use of Electronic Medical Records, Personally Controlled Health Records, and electronic public health reporting and communication systems. The center will link these disparate systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities

Role: Co-Investigator, *Electronic Support for Public Health (ESP) Project*

1 U01 GM076672-02 (Platt) 2/1/2007-1/31/2008
NIGMS \$563,099
1.2 Person-months

Modeling Health Systems Infectious Disease Data

This project will develop models for early detection and monitoring of infectious disease outbreaks. These models will be applied at different geographical scales, from individual wards of a single hospital to a whole country, as well as for different data specificity from very general symptoms to microbial disease strains and antimicrobial resistance profiles.

Role: Co - Investigator

PENDING SUPPORT

XXXXXXXXXXXX (Lazarus) xx/xx/xxxx
ESP VAERS \$xxx,xxx
4.20 Person-months

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP: VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Role: Co-Investigator

PLATT, R.
ACTIVE

5U18HS10391-07 (Platt) 9/29/2006-9/30/2007 2.28 calendar
 AHRQ 147,929

The HMO Research Network Centers for Education and Research on Therapeutics (CERT2)

The major goals of study will continue the CERTs' focus on studies of therapeutics use, safety, and effectiveness, using health plans defined populations and data in eight new initiatives

1U01 GM76672-01 (Platt) 2/1/2007-1/31/2008 1.80 calendar
 NIH 384,867

Modeling Health System Infectious Disease Data

The major goal of this study will be the development of models for the early detection of infectious disease outbreaks and for monitoring an outbreak after it has been detected

5P01CD000260-02 9/30/2005-09/29/2008 2.40 calendar
 CDC 173,229

Enhancing public health through electronic medical and personal health records

This Center of Excellence in Public health Informatics will be a partnership of three entities that have expertise in design and use of Electronic Medical Records, Personally Controlled Health Records, and electronic public health reporting and communication systems.

200200200732 (Platt) 9/20/2003-9/19/2012 0.60 calendar
 CDC 815,703

Vaccine Safety Surveillance and Assessment (VSD2)

The major goal of this project is to study ongoing and emerging topics on the potential association of vaccines with adverse outcomes

U01 CI000344-01 (Platt) 2/1/2006-9/19/2011 1.44 calendar
 CDC 253,444

Prevention Epicenter Program

Continuation of the work to develop population based methods for identifying and preventing health care associated infections (nosocomial infections). This work is being conducted by a consortium of the three largest HMOs and two large integrated delivery systems.

HHSF22320051001 (Platt) 9/23/05 - 9/22/2010 1.8 calendar
 FDA 562,000

HMORN CERT Epidemiologic Studies of Adverse Effects of Marketed Drugs

This study will provide data and resources that can be used to rapidly evaluate safety and utilization patterns of marketed prescription drugs and provide a mechanism for collaborative pharmacoepidemiologic research to protect the public's health.

SCDPH5225 5 337HAR0000 (Platt) 04/01/2007-8/31/2007 0.25 calendar
 Mass Department of Public Health (b)(4)
 MDPH Multi-Site Surveillance: Pandemic Influenza

This study will integrate the data, signal detection, and reporting capabilities of separate existing real-time systems for identifying unusual clusters of illness. This combined reporting and analysis is expected to allow greater power to detect clusters of bioterrorism and other acute health events, and also to improve the efficiency of reporting to the Department of Public Health.

Principal Investigator/Program Director (Last, First, Middle): LAZARUS, Ross

MTA53 (Platt)

01/01/07-12/31/2009

0.20 calendar

(b)(4)

(b)(4)

Risk of Guillain-Barré following meningococcal conjugate (MCV4) vaccination

This project is a multi-site retrospective cohort study of the relationship between immunization with tetravalent meningococcal conjugate vaccine (MCV4) and Guillain-Barré syndrome (GBS) in adolescents over the 42-month period of March 1, 2005 to August 31, 2008.

1R01 PH0000032-01 (Kulldorff)

09/30/06-09/29/2008

0.25 calendar

CDC

987,749

Data Evaluation for Early disease Outbreak Detection

This project evaluates and compares the efficacy of different health services data sources for early disease outbreak detection, including telephone inquiries, ambulatory care visits, emergency department visits, laboratory test requests and results, radiology tests, hospitalizations, drug prescriptions and drug dispensing.

1R01AI066304-01A1(Finkelstein)

8/1/2006-7/31/2010

0.60 calendar

NIH NIAID

494,303

Post-PCV pneumococcal population genetics and resistance

This research project builds directly on previous work by this investigator group who have collected and analyzed pneumococcal isolates from healthy children in 16 distinct communities from 2001 to 2004. We now continue to assess changes in patterns of colonization and serotype-specific antimicrobial resistance; to enhance our understanding of the biological processes which underlie apparent shifts in community carriage and resistance; and to re-assess risk factors for colonization and transmission of *S. pneumoniae* in the decades following universal PCV7 immunization.

PENDING

XXXXXXXXX (Lazarus)

Funding Period: TBD

(.36 Years 1 & 2)

AHRQ

HPHC Direct Costs: TBD

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP: VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Overlap

None

Email for 17 45

- ① When do you anticipate receiving IRB approval;
- ② Fringe Rates used for Harvard Pilgrim Health Care and HVMA^(Subaward 1) need to be verified. I only have them for Subaward 2 - Channing Laboratory, Brigham and Women's Hospital.
- ③ Base Salaries needed for all Other Personnel.
- ④ Office Supplies, Travel, Consultant Services, Equipment, + ADP/Computer Services all need to be itemized for the budgets.
- ⑤ Need ^{documentation} ~~justification~~ of Modified Total Direct Cost Indirect Rate of 75%.
F&A rate agreement shows (b)(4)
- ⑥ Need history of Other Research Support for Senior/Key Personnel ~~for~~ in calendar months and/or percentage. This proposed award needs to be included ~~at~~ plus any pending awards ~~to~~ slated to start within the next 30 days.

17045

① IRB pending - p⁹⁰

Ross Lazarus PI

Jeffrey Brown

Francis Campion

Kenneth Kleinman

Richard Platt

Michael Klompas

Why only 16%?
on budget

2000 of A

budget just
for subaward 2

~~Big stick only~~
Subaward 1

② Fringe Rates used for Primary & ~~both~~ subawards / need to be verified

③ Base Salaries for Other Personnel - Both Primary & Subawards

④ Office Supplies }
Travel } Need to be broken down -
Consultant Services } itemized

Name of Subaward

HVMA - spelled out Harvard Vanguard P¹⁰
Medical Associates

⑤ Equipment }
Travel } Itemized for subaward
Supplies }
~~Consultants~~ }
ADP/Computer Services }

⑦ Other Support

(b)(4)

Revised Other Support for 17045 dated 9/5/07				
Personnel	Award Number	Dates of Award	Percentage	
Lazarus	Active			
	2 U01 HL065899-05	08/01/05 - 08/30/10	5%	
	P01 CD000260	01/01/06 - 12/31/08	10%	
	1 R01 HG003646-01A1	12/01/05 - 11/30/10	33%	
	1 P01 HL083089	12/01/06 - 11/30/11	20%	
	1 R01 HL066289	04/01/07 - 03/31/11	5%	
	R01 HL086601-01	12/01/06 - 11/30/10	3%	
	TBA (b)(6)	07/01/07 - 06/30/09	20%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	20%	new AHRQ one
			116%	
	Pending			
	1 R01 HL092197-01	04/01/08 - 03/31/13	2.50%	
Brown	Active			
	LCF030207	03/01/07 - 02/28/08	10%	
	2 U18 HS10391	09/29/06 - 09/30/07	20%	
	200-2002-00732	10/01/06 - 09/30/07	20%	
	HHSN268200425216C	09/30/04 - 09/29/07	15%	
	HHSF223200510012C C.O.A. #3	05/01/06 - 12/31/07	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	10%	new AHRQ one
			85%	
	Pending			
	HPHC PI (Lazarus)	TBD	9.50%	
	HPHC PI (b)(6)	07/01/07 - 06/30/11	13%	
	HPHC PI (b)(6)	09/30/07 - 09/29/11	30%	
	HPHC PI (b)(6)	05/01/07 - 04/30/12	7%	
Kleinman	Active			
	K24 HL 068041	09/30/01 - 06/30/11	4%	
	K24 HD 047687	07/01/04 - 06/30/09	5%	
	R01 HL 075504	08/01/04 - 04/30/08	2%	
	R21 LM 008707	06/01/05 - 05/31/08	24%	
	R01 HD 050968	08/01/05 - 07/31/10	4%	
	P01 CD 000260	09/30/05 - 09/29/08	10%	
	U01 GM 076672	02/01/06 - 01/31/11	15%	
	R01 HD034568	08/01/06 - 06/30/10	8%	
	R01 A1 068304	08/01/06 - 07/31/10	2%	
	R01 PH 000032	09/30/06 - 09/29/08	10%	
	R21 DK 073739	09/30/06 - 08/31/08	5%	
	R01 HL084925	05/15/07 - 03/31/11	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	2%	new AHRQ one
			96%	
	Pending			
	R18 (b)(6)	07/01/07 - 06/30/10	5%	
	R01 (b)(6)	12/01/07 - 11/30/11	5%	
	R01 (b)(6)	02/01/08 - 01/31/11	5%	
	G13 (b)(6)	04/01/08 - 03/31/11	14.16%	
	(b)(6)	01/01/08 - 12/31/10	5%	
Klompas	Active			
	P01 CD000260-02	09/30/05 - 09/29/08	20%	
	7 U01 GM076672-02	02/01/07 - 01/31/08	10%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	35%	new AHRQ one
			65%	
	Pending			
	ESP VAERS	XX/XX/XX - XX/XX/XX	20%	
Platt	Active			
	5 U18 HS10391-07	09/29/06 - 09/30/07	19%	
	1 U01 GM76872-01	02/01/07 - 01/31/08	15%	
	5 P01 CD000260-02	09/30/05 - 09/29/08	20%	
	200200200732	09/20/03 - 09/19/12	5%	
	U01 CI000344-01	02/01/08 - 09/19/11	12%	
	HHSF22320051001	09/23/05 - 09/22/10	15%	
	SCDPH5225 5 337HAR0000	04/01/07 - 08/31/07	2.08%	
	MTA53	01/01/07 - 12/31/09	1.68%	
	1 R01 PH0000032-01	09/30/06 - 09/29/08	2.06%	
	1 R01 AI066304-01A1	08/01/06 - 07/31/10	5%	
	1 R18 HS017045-01	09/15/07 - 09/14/09	3%	new AHRQ one
			99.82%	
	Pending			
	None			

ANNUAL FSR RECONCILIATION

Information to be used in conjunction with GMS administrative review

Grant Number: R18 HS17045-01 Budget Period End Date: 9/29/08
 Grantee: Harvard Pilgrim Healthcare FSR Receipt Date: 12/16/08
 PI: Lezaros, Ross
 Grant Specialist: Carol Harris

Enter total \$ from prior NOAs awarded figures (this figure should match the total authorization from the previous FSR) or, if 0 year, enter 0

A

Previously awarded

0.00

Enter \$ awarded from original NOA of this budget period (plus supplements) or, if 01 year, the original NOA awarded figure

B

This Award

499,809.00

Does this figure match the FSR? y

(A + B)

Total Awarded to Date

499,809.00

Enter \$ unobligated on the FSR

D

Unobligated Balance

152,780.98

Divide Unobligated Balance (D) by \$ This Award (B)

D / B

% Unobligated

30.56%

☒ Receipt of this FSR and the information which it presents has been entered into the FSR database. The results of my preliminary reconciliation are as follows:

- ☒ No issues concerns noted.
- ☐ For expanded authorities grants, grantee was informed on _____ that the remarks section of the FSR made no mention of the intent to carryover the unobligated balance.
- ☐ Grantee was informed on _____ that a revised FSR must be submitted to correct the authorized federal funds amount.
- ☐ Grantee was informed on _____ that a revised FSR must be submitted updating the recipient share of net outlays in order to meet the matching requirements of the term of award.
- ☐ The grantee was informed on _____ that the application indicated that program income would be earned and a revised FSR using the SF 269 Long Form must be submitted to address program income.
- ☐ The grantee was informed on _____ that the federal share of net outlays may not exceed the total federal funds authorized and a revised FSR must be submitted.
- ☐ The FSR indicated an indirect expense when no indirect expenses are allowable, or the indirect expenses exceed the cap of those allowable for this award. The grantee was informed on _____ that a revised FSR must be submitted.

The above issues have been resolved.

FSR Coordinator: _____

Date 12/16/08

☒ The following possible concerns should be addressed by the grants management specialist assigned to this award:

- ☐ The grant is not covered by expanded authorities, however the remarks section of this FSR indicates that the grantee intends to carryover the unobligated balance.
- ☐ Verify that the previously reported amounts indicated on this FSR match the prior year FSR. Corrective measures may need to be taken.
- ☒ The percent unobligated balance is over 25%. An explanation must be submitted if it has not already been received. OK
- ☒ The GMS specialist should check the unobligated balance against the estimated unobligated balance submitted in the current non-competing application. If the balance is significantly higher than estimated, clarification from the grantee must be submitted. OK

The above issues have been resolved.

Specialist: Carol Harris

Date 4/16/2009

NOTE: Any revised FSRs received by the Specialist should be given to the FSR Coordinator to ensure that the FSR database remains current and correct. All versions of the FSR and any correspondence between AHRQ and the grantee regarding this FSR are attached

ENTERED

12/16/08 FSR Database SPC

**FINANCIAL STATUS REPORT
(Long Form)**

(Follow instructions on the back)

1. Federal Agency and Organizational Element to Which Report is Submitted AHRQ		2. Federal Grant or Other Identifying Number Assigned By Federal Agency 1 R18 HS017045		OMB Approval No. 0348-0039	Page of 1 pages
3. Recipient Organization (Name and complete address, including ZIP code) Harvard Pilgrim Health Care, Inc., 93 Worcester Street, Wellesley, MA 02481					
4. Employer Identification Number 1042452600A1		5. Recipient Account Number or Identifying Number AH000306		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual					
8. Funding/Grant Period (See instructions) From: (Month, Day, Year) 09/30/2007		To: (Month, Day, Year) 09/30/2009		9. Period Covered by this Report From: (Month, Day, Year) 09/30/2007 To: (Month, Day, Year) 09/30/2008	
10. Transactions:		I Previously Reported		II This Period	
		III Cumulative			
a. Total outlays		\$0.00		\$190,541.60	
b. Refunds, rebates, etc.					
c. Program income used in accordance with the deduction alternative					
d. Net outlays (Line a, less the sum of lines b and c)		\$0.00		\$190,541.60	
e. Recipient's share of net outlays, consisting of:					
f. Third party (in-kind) contributions					
g. Other Federal awards authorized to be used to match this award					
h. Program income used in accordance with the matching or cost sharing alternative					
i. All other recipient outlays not shown on lines e, f or g					
j. Total recipient share of net outlays (Sum of lines e, f, g and h)					
k. Federal share of net outlays (line d less line j)				\$190,541.60	
l. Total unliquidated obligations				\$156,486.42	
m. Recipient's share of unliquidated obligations				\$0.00	
n. Federal share of unliquidated obligations				\$156,486.42	
o. Total Federal share (sum of lines k and m)				\$347,028.02	
p. Total Federal funds authorized for this funding period				\$499,809.00	
q. Unobligated balance of Federal funds (Line o minus line n)				\$152,780.98	
Program Income, consisting of:					
r. Disbursed program income shown on lines c and/or g above					
s. Disbursed program income using the addition alternative					
t. Undisbursed program income					
u. Total program income realized (Sum of lines r, s and t)					
11. Indirect Expense		a. Type of Rate (Place "X" in appropriate box) <input type="checkbox"/> Provisional <input checked="" type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed b. Rate (b)(4) c. Base d. Total Amount \$58,452.32 e. Federal Share \$58,452.32			
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. We request carry-forward in the amount of \$152,780.98 from Year 1 to Year 2					
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.					
Typed or Printed Name and Title John Eldh, Grants Accountant				Telephone (Area code, number and extension) (817) 509-3315	
Signature of Authorized Certifying Official <i>Barbara W. Richard</i>				Date Report Submitted 12/12/08	

Previous Edition Usable

269-104

Standard Form 269 (Rev. 7-87)

NSN 7540-01-012-4285

200-498 P.O. 139 (Face)

Prescribed by OMB Circulars A-102 and A-110

ENTERED

*-12/16/08 FSR Database
see Annual FSR Reconciliation sheet - SAC*



Harvard Pilgrim Health Care

12 December 2008

Carol Harris
AHRQ
OPART/GM
540 Gaither Road
Rockville, MD 20850

Re: Interim FSR for 1R18HS017045-01, "Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ESP:VAERS)"; Lazarus (HPHC PI)

Dear Carol,

Enclosed, please find the interim financial status report for the above-referenced project, covering expenditures during the first budget period (09.30.2007-09.29.2008). We are requesting carry forward of \$152,780.98 into the current budget period.

Feel free to call me at 617.509.9933 or e-mail me at nicholas_mulherin@hphc.org if you have any questions.

Best regards,

Nick Mulherin
Grants Manager

Enclosure [1]

Harvard Pilgrim Health Care
Office of Sponsored Programs
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Telephone (617) 509-9843 • Fax (617) 509-9859

Cochran, Sherry (AHRQ/OPART/GM)

From: GFSR@ahrq.hhs.gov
Sent: Saturday, November 29, 2008 3:30 PM
To: Research_Admin@hphc.org
Cc: ross.lazarus@channing.harvard.edu
Subject: Reminder of Financial Status Report (FSR) Requirement: R18 HS17045-01

Business Official:

The above referenced grant budget period ended on 09/29/2008. In accordance with 45 CFR 74.52 and terms and conditions of the award, the grantee is required to submit an annual Financial Status Report (SF269) within 90 days of the end of the budget period.

This is a reminder that the SF269 is due for this grant on 12/28/2008.

Forms are available on-line. The preferred form is SF269 (the "long" form): http://grants.nih.gov/grants/fsr_sf269_long.pdf; however, SF269A (the "short" form) may be filed if the grantee has no program income to report: http://grants.nih.gov/grants/fsr_sf269a_short.pdf.

A hard copy of the annual FSR must be submitted to the attention of the grants management specialist named on the Notice of Grant Award. AHRQ is NOT currently able to accept FSRs electronically via the NIH Commons. Please note that for grants including restricted funds the grantee should state the status of the restricted funds in the "Remarks" section of the FSR (total restricted, total spent in accordance with the restriction, total unexpended restricted funds). Also, for grants under expanded authorities, the "Remarks" section must indicate whether or not non-restricted unobligated funds are being carried forward under expanded authorities (EA) to the next budget period (restricted funds may not be carried forward under EA).

Cc: Ross Lazarus

12/2/2008

Cochran, Sherry (AHRQ/OPART/GM)

From: GFSR@ahrq.hhs.gov
Sent: Thursday, October 30, 2008 4:15 PM
To: Research_Admin@hphc.org
Cc: ross.lazarus@channing.harvard.edu
Subject: Reminder of Financial Status Report (FSR) Requirement: R18 HS17045-01

Business Official:

The above referenced grant budget period ended on 09/29/2008. In accordance with 45 CFR 74.52 and terms and conditions of the award, the grantee is required to submit an annual Financial Status Report (SF269) within 90 days of the end of the budget period.

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A hard copy of the annual FSR must be submitted to the attention of the grants management specialist named on the Notice of Grant Award. AHRQ is NOT currently able to accept FSRs electronically via the NIH Commons. Please note that for grants including restricted funds the grantee should state the status of the restricted funds in the "Remarks" section of the FSR (total restricted, total spent in accordance with the restriction, total unexpended restricted funds). Also, for grants under expanded authorities, the "Remarks" section must indicate whether or not non-restricted unobligated funds are being carried forward under expanded authorities (EA) to the next budget period (restricted funds may not be carried forward under EA).

Cc: Ross Lazarus

11/10/2008

Cochran, Sherry (AHRQ/OPART/GM)

From: GFSR@ahrq.hhs.gov
Sent: Tuesday, September 30, 2008 3:05 PM
To: Research_Admin@hphc.org
Cc: ross.lazarus@channing.harvard.edu
Subject: Reminder of Financial Status Report (FSR) Requirement: R18 HS17045-01

Business Official:

The above referenced grant budget period ended on 09/29/2008. In accordance with 45 CFR 74.52 and terms and conditions of the award, the grantee is required to submit an annual Financial Status Report (SF269) within 90 days of the end of the budget period.

This is a reminder that the SF269 is due for this grant on 12/28/2008.

Forms are available on-line. The preferred form is SF269 (the "long" form): http://grants.nih.gov/grants/fsr_sf269_long.pdf; however, SF269A (the "short" form) may be filed if the grantee has no program income to report: http://grants.nih.gov/grants/fsr_sf269a_short.pdf.

A hard copy of the annual FSR must be submitted to the attention of the grants management specialist named on the Notice of Grant Award. AHRQ is NOT currently able to accept FSRs electronically via the NIH Commons. Please note that for grants including restricted funds the grantee should state the status of the restricted funds in the "Remarks" section of the FSR (total restricted, total spent in accordance with the restriction, total unexpended restricted funds). Also, for grants under expanded authorities, the "Remarks" section must indicate whether or not non-restricted unobligated funds are being carried forward under expanded authorities (EA) to the next budget period (restricted funds may not be carried forward under EA).

Cc: Ross Lazarus

10/29/2008

AWARD BACKER

GRANT NUMBER:

5 R18 H5017045-02

FILE CONTENTS:

	File Tab Number	File Tab Section Label	Document Examples
T-5 GRANT (1-flip folders)	Front Cover	Financial Status Report(s)	FSR(s)
	1	Application/Appendix/Pre-Award Materials	Application, Appendix, Green sheet, GMS Worksheet, Communication with grantee, IRB, Other Support, NGA, Post-Award Actions
	2	Funding Documents	Funding Memo, PO/OEREP correspondence regarding funding
	Back Cover	Miscellaneous	General Questions, Distribution Copies for NGA's
T-1 GRANT (3-flip folders)	Front Cover	Financial Status Report(s)	FSR(s)
	1	Application/Appendix	Application, Appendix, Green sheet, Excel Spreadsheets, GMS Worksheet, NGA, Post-Award Actions
	2	Pre-Award Material	Communication with applicant, IRB, Other Support
	3	Summary Statement & Related Documents	Summary Statement and Documentation
	4	Funding Documents	Funding Memo, Paylist, Portfolio Memo, PO/OEREP correspondence regarding funding
	5	Institutional Information	F&A, EIN establishment, ORI, FWA
	Back Cover	Miscellaneous	General Questions, FOA, Distribution Copies for NGA's

9/30/09 1st NCE

OFFICIAL FILE

Agency for Healthcare Research and Quality

NOTICE OF AWARD

RESEARCH
Department of Health and Human Services
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

Issue Date: 09/30/2009



Grant Number: 5R18HS017045-02 REVISED

Principal Investigator:
ROSS LAZARUS, MBBS

Project Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES

BARBARA RICHARD
Director, Office of Sponsored Programs
Harvard Pilgrim Health Care
133 Brookline Ave
6th Floor
Boston, MA 02215

Award e-mailed to: research_admin@harvardpilgrim.org

Budget Period: 09/30/2008 – 09/29/2010

Project Period: 09/30/2007 – 09/29/2010

Dear Business Official:

The Agency for Healthcare Research and Quality hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to HARVARD PILGRIM HEALTH CARE in support of the above referenced project. This award is pursuant to the authority of 42 USC 299a 42 CFR 67, PL 101-239 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.

All investigators and directors of research projects supported by grants from the Agency for Healthcare Research and Quality are expected to make their research results promptly and widely available to the health professions, public administrators, and the scientific community. All published reports, both formal and informal, should acknowledge grant support with the following footnote: "This project was supported by grant number R18HS017045 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality." When a manuscript resulting from this grant is accepted for publication, the principal investigator must promptly notify the project officer of its acceptance and the date it is scheduled to be published.

Award recipients are also responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. For additional information, please visit <http://www.iedison.gov>.

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

Sincerely,

A handwritten signature in blue ink that reads "Michelle Burr".

Michelle Burr
Grants Management Officer
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

Additional information follows

SECTION I – AWARD DATA – 5R18HS017045-02 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	(b)(4);
Fringe Benefits	(b)(6)
Personnel Costs (Subtotal)	
Supplies	\$401
Travel Costs	\$2,090
Consortium/Contractual Cost	(b)(4)
Federal Direct Costs	(b)(4)
Federal F&A Costs	
Approved Budget	\$499,405
Federal Share	\$499,405
TOTAL FEDERAL AWARD AMOUNT	\$499,405
AMOUNT OF THIS ACTION (FEDERAL SHARE)	\$0

Fiscal Information:

CFDA Number: 93.226
EIN: 1042452600A1
Document Number: RHS017045A
Fiscal Year: 2008

IC	CAN	2008
HS	K72PS53	\$499,405

AHRQ Administrative Data:

PCC: CP3 / OC: 4145

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R18HS017045-02 REVISED

For payment and HHS Office of Inspector General Hotline information, see the AHRQ Home Page at <http://www.ahrq.gov/fund/awdrsrc.htm>.

SECTION III – TERMS AND CONDITIONS – 5R18HS017045-02 REVISED

This award is based on the application submitted to, and as approved by, AHRQ on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following: (see AHRQ Home Page at <http://www.ahrq.gov> for certain references cited below)

- The grant program legislation and program regulation cited in this Notice of Grant Award.
- The restrictions on the expenditure of federal funds in appropriations acts to the extent those restrictions are pertinent to the award.
- 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- The HHS Grants Policy Statement, including addenda, in effect as of the beginning of the budget period. NOTE: For budget periods beginning before October 1, 2006, the PHS Grants Policy Statement (last revised 4/94) remains applicable in accordance with the original award for that budget period.
- Standard terms and conditions can be found at <http://www.ahrq.gov/fund/awdrsrc.htm>.
- Additional terms and conditions:

AHRQ POLICY REGARDING PRE-AWARD COSTS

The following applies to all AHRQ awards except for NRSA Fellowship Awards (F31 or F32) and AHRQ Dissertation (R36) awards, which do not allow pre-award costs:

Unless otherwise indicated by term of award, the grantee may, at its own risk, incur obligations and expenditures to cover project-related costs prior to the effective date of an award provided the following criteria are met:

1. The costs incurred are considered reasonable, allocable, and necessary to the conduct of the project.
2. The costs are allowable under the potential award.
3. When required for specific expenditures or activities, AHRQ prior approval was obtained.

For new and competing continuation awards, the costs must be incurred within 90 days prior to the effective date of the award, otherwise AHRQ prior approval is required.

In allowing the applicant/grantee this flexibility, AHRQ expects the applicant/grantee to be fully aware that such borrowing against future year support must not impair its ability to accomplish the project objectives within the approved timeframe or in any way adversely affect the conduct of the project. Additionally, the incurrence of costs prior to the award of a grant imposes no obligation on the Federal Government to either make the award or increase the amount of the approved budget.

Treatment of Program Income:
Additional Costs

SECTION IV – AHRQ Special Terms and Condition – 5R18HS017045-02 REVISED

In accordance with the grantee's correspondence dated August 26, 2009, this revised award extends the budget and project period through September 29, 2010, without additional funds. The grantee institution is responsible for ensuring that all necessary human subject reviews are performed as required during this extended period.

Although the end date of this project has been extended, 45 CFR 74.52 requires the submission of an annual progress report and an annual Financial Status Report (FSR) (SF269). Therefore, an interim progress report reflecting progress through September 29, 2009 and an interim FSR reflecting budget expenditures through September 29, 2009 must be submitted to the Grants Management Specialist named on this Notice of Award no later than 90 days from this date.

THE FOLLOWING TERMS OF AWARD FROM THE PREVIOUS NOTICE OF AWARD ISSUED ON 9/17/2008 ALSO APPLY TO THIS AWARD:

This grant is included under expanded authorities.

This award is subject to the requirements of Section 106 (g) of the Trafficking Victims Protection Act of 2000, as amended (22 U.S.C. 7104). For the full text of the award term, go to <http://www.ahrq.gov/fund/trafficking.htm>.

As proposed in the application, the Principal Investigator, Dr. Ross Lazarus, will devote 20% effort to this grant. Any reduction in this level of effort requires the prior written approval of AHRQ.

The grantee is required to participate in an annual patient safety and health IT conference sponsored or supported by AHRQ. The date and location of the conference will be communicated to the grantee after grant award. The Principal Investigator and at least one program staff member from the project are required to attend the annual conference.

Awardees are required to fully cooperate with AHRQ contractors in promoting the Agency's patient safety and health IT initiative activities.

AHRQ strongly encourages grantees to submit quarterly reports on project status, lessons learned, and challenges encountered. This will support AHRQ's mission and enable AHRQ to tailor its interactions with grantees to be most supportive of the individual projects in the Health IT portfolio. These reports will be submitted electronically to the AHRQ National Resource Center for Health IT, the AHRQ coordination center for the HIT program.

This award represents the final year of the competitive segment for this grant. AHRQ policy requires submission of the following final reports within 90 days after the grant's final budget period expires:

FINAL FINANCIAL STATUS REPORT

The final Financial Status Report submitted to this office must agree with the final expenditures reported on the PMS 272 to the Payment Management System. Use Standard Form 269. It is available online at: http://grants1.nih.gov/grants/fsr_sf269_long.pdf

FINAL INVENTION STATEMENT AND CERTIFICATION

This statement shall include all inventions which were conceived or put into practice during the entire project period. Use Form HHS 568. It is available online at: <http://grants.nih.gov/grants/hhs568.pdf>

FINAL PROGRESS REPORT

The Final Progress Report is needed to describe the results of the research funded by the Agency. It will be made available to the public, and, therefore, should not include any copyrighted, private, or proprietary information.

The Final Progress Report is subject to a 20 page limit (minimum of 4 pages). Reports exceeding 20 pages will not be accepted. The report format should include the following seven (7) labeled elements:

1. TITLE PAGE (Title, Principal Investigator and Team Members, Organization, Inclusive Dates of the Project, Federal Project Officer, Acknowledgment of Agency Support, and Grant Number)
2. STRUCTURED ABSTRACT (200 words maximum). Include five headings: Purpose, Scope, Methods, Results, and Key Words
3. PURPOSE (Objectives of the study)
4. SCOPE (Background, Context, Settings, Participants, Incidence, Prevalence)
5. METHODS (Study Design, Data Sources/Collection, Interventions, Measures, Limitations)
6. RESULTS (Principal Findings, Outcomes, Discussion, Conclusions, Significance, Implications)
7. LIST OF PUBLICATIONS and PRODUCTS (Bibliography of Outputs from the study. Follow the AHRQ Citation Style Format at: <http://www.ahrq.gov/fund/refstyle.htm>)

The AHRQ Grant Final Report Template is available online at <http://www.ahrq.gov/fund/reptemp.htm>

Please note that AHRQ's Policy on the Inclusion of Priority Populations in Research (<http://grants.nih.gov/grants/guide/notice-files/NOT-HS-03-010.html>), indicates that AHRQ will monitor the implementation of the policy during the development, review, award, and conduct of research. To facilitate this monitoring, grantees whose projects were funded based on a competing application submitted on or after the October 1, 2003, application receipt date are required to include in the final report a report of progress related to the inclusion of AHRQ priority populations. Additional details can be found on the AHRQ Grant Final Report Template.

If this project includes a Minority Supplement, the Final Progress Report must include, within the 20-page limit, a distinctly identified Final Progress Report for the Minority Supplement project.

For further details on the requirements of the Final Progress Report, contact your project officer.

If you have copies of publications (not previously submitted) that resulted from the grant project, submit these under separate cover directly to the project officer of your grant; do not include them as part of the Final Progress Report.

SUBMISSION REQUIREMENTS

The Final Progress Report should be submitted as electronic file attachments to e mail at: grantfpr@ahrq.gov. Acceptable formats are Word, WordPerfect, or ASCII format. PDF files are not acceptable.

The Final Financial Status Report and the Final Invention Statement should be submitted to:

Agency for Healthcare Research and Quality
Grants Management/OPART
540 Gaither Road
Rockville, MD 20850

FAILURE TO COMPLY

Failure to submit the required reports in a timely manner may result in the imposition of a special award provision or the withholding of funding of other eligible projects or activities involving the grantee organization or the principal investigator.

None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of executive level I of the Federal Executive pay scale (currently at a level of \$191,300).

The grantee institution has been identified as a non-profit organization and as such is subject to OMB Circular A-122 ?Cost Principles for Non-Profit Organizations? (http://www.whitehouse.gov/omb/circulars/a122/a122_2004.html). If the grantee believes this designation is incorrect, contact the grants management specialist named on the Notice of Award immediately. NOTE: A subawardee or contractor under this grant is subject to the cost principles applicable to its type of organization.

Recipients of Federal funds are subject to annual audit requirements as specified in OMB Circular A-133 (<http://www.whitehouse.gov/omb/circulars/a133/a133.html>). Grantees should refer to the above Circular for the current annual Federal fund expenditure threshold level which requires audit. Note that for-profit organizations and foreign entities have the option of conducting a Single Audit (using OMB Circular A-133) or a program-specific audit as provided in 45 CFR 74.26 (http://a257.g.akamaitech.net/7/257/2422/05dec20031700/edocket.access.gpo.gov/cfr_2003/octqtr/pdf/45cfr74.26.pdf).

No individual may be committed to more than 100% professional time and effort. In the event that an individual's commitment exceeds 100%, the grantee must make adjustments to reduce effort. For AHRQ-sponsored projects, significant reductions in effort (i.e., in excess of 25% of the originally proposed level of effort) for the Principal Investigator and key personnel named on this Notice of Award must receive prior written approval from AHRQ.

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 submitted via e-mail or may be mailed to:

AHRQ
OPART / Grants Management
540 Gaither Road
Rockville, MD 20850

Grants Management Specialist: CAROL HARRIS
Email: carol.harris@ahrq.hhs.gov **Phone:** (301) 427-1448 **Fax:** (301) 427-1462

Program Official: STEVE BERNSTEIN
Email: sbernste@ahrq.gov **Phone:** (301) 427-1581 **Fax:** (301) 427-1595

SPREADSHEET SUMMARY

GRANT NUMBER: 5R18HS017045-02 REVISED

INSTITUTION: HARVARD PILGRIM HEALTH CARE

<i>Budget</i>	<i>Year 2</i>
Salaries and Wages	(b)(4);
Fringe Benefits	(b)(6)
Personnel Costs (Subtotal)	
Supplies	\$401
Travel Costs	\$2,090
Consortium/Contractual Cost	(b)(4)
TOTAL FEDERAL DC	
TOTAL FEDERAL F&A	
TOTAL COST	\$499,405

<i>Facilities and Administrative Costs</i>	<i>Year 2</i>
F&A Cost Rate 1	(b)(4)
F&A Cost Base 1	
F&A Costs 1	

REVISED AWARD CHECKLIST

GRANT NUMBER: 5 R18 HSO17045-02
 GRANTEE INSTITUTION: Harvard Pilgrim Hlth Care
 PI: Barbara Richard
 PO: Manjeth Edgular
 GMS: BAA for CH

REASON FOR REVISION	
Finalize provisional award	<input checked="" type="checkbox"/>
Remove/modify restrictive term(s)	
Administrative supplement	
Add funds (adjustment) (Prior year funds? Y N)	
No-cost extension (1 st <input checked="" type="checkbox"/> 2 nd <input type="checkbox"/>) <u>12 mos</u>	<u>9/29/10</u>
Carry over funds from _____ year	
Partial pay funds from _____ year	
Other (see remarks):	

ITEMS 1 – 7 TO BE COMPLETED BY GMS, NOT BY 1ST LEVEL REVIEWER

- Required business official endorsement in place? ☒
- Required FSR in file and reviewed? n/a
- For Extension, Partial Payment, or Carryover, FSR and FCO-E report (PMS) reconciled? ☒
- PO recommendation obtained via: memo _____ e-mail _____ N/A ☒
- Terms, as applicable:

Explanation of revision ☒; **"Terms of Original Award" stmt** ☒;
 [Make sure the following terms, as appropriate, appear under the terms of original award;
 check below if they have been added because they were missing]:

- | | |
|--|-----------------------------|
| EA or not EA <input checked="" type="checkbox"/> | Salary cap _____; |
| Trafficking Victims _____; | |
| Cost principles _____; | Audit requirements _____; |
| T5 applic requirements _____; | FSR requirements _____; |
| Other support _____; | Human Subjects _____; |
| Inquiries _____; | Terms of cooperation _____; |
| "Final Year" reports _____; | E-NGA establishment _____; |
| SF424 R&R transition _____; | Other _____; |
- Is e-mail NGA de-activated? Y ☐ N ☒ N/A (not e-mail enabled)
 - Addresses (PI, Grantee, etc.) confirmed/updated in IMPAC II? ☒ Y ☐ N
 - Is this a retro-active NCE? Y ☐ N ☒; If Yes, GMS is to remove record from Grants Closeout Module (GCM) just prior to forwarding award to GMO for release. Date removed: _____

REMARKS: See email exchange of CH Re: NCE
Carol received NCE 8/26/09, I followed up to verify authorized
bus. official 9/13/09

CON'T? _____

PREPARED BY: BAA DATE: 9/13/09

1ST LEVEL REVIEWER: M. Burn DATE: 9/30/09

*Moved to NCE
to file. award
still to
after NCE
form*

INQUIRY: Document Data w/ FCO Segments Extended DATE: 09/03/2009 TIME: 11:15:40 AM

*** SEARCH PARAMETERS *****

GRANT AWARD: RHS017045A

*ACCT** *PIN* *****DUNS***** *****Organization Name*****

4715G 4715 1042452600A1 071721088 HARVARD PILGRIM HEALTH CARE, INC

HHS-REG: 01 STATE: MA PMT: ACH STOP: N MAN-REV: N 272: File GROUP: F21 USER: VNK5LHJ

AGY* *****GRANT DOC*****

RS DS

AUTHORIZED **DISBURSED*** **CHG-ADV*** *RPT DISB*

RI CT

***CANCELED AUTH** **CANCELED DISB** **CANCELED CHG**

FS

DOC FUTURE AUTH* **DOC SNAP DISB **DOC SNAP CHRG**

A O

FCO AUTHORIZED **FCO DISBURSED** **FCO CHG-ADV*** *SUB ACCT*

N 2

FCO FUTURE AUTH* **FCO SNAP DISB **FCO SNAP CHRG**

O

K RHS017045A 999,214.00 558,397.14 558,397.14 06/30/2009

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1042452600A1 .00 .00

N 2

2007-K72PS53-4145 499,809.00 558,397.14 509,419.39

O

09/30/07 09/29/08 499,809.00 499,809.00

O

2008-K72PS53-4145 499,405.00 58,588.14 58,588.14

O

09/30/08 09/29/09 .00 58,588.14 9,610.39

DOC AUTHORIZED** **DOC DISBURSED** **DOC CHG-ADV

DOC CANCEL AUTH* **DOC CANCEL DISB **DOC CANCEL CHG**

DOC FUTURE AUTH* **DOC SNAP DISB **DOC SNAP CHRG**

FCO AUTHORIZED **FCO DISBURSED** **FCO CHG-ADV***

FCO FUTURE AUTH* **FCO SNAP DISB **FCO SNAP CHRG**

TOTAL: 999,214.00 558,397.14 558,397.14

.00 .00

558,397.14 509,419.39

999,214.00 558,397.14

558,397.14 558,397.14

558,397.14 509,419.39

HITS: 1

OPEN & CLOSED:

HITS: 1

OPEN:

84,343,111.58

CLOSED:

39,990,040.25

44,353,071.33

Hits: 2

509,419.39

***** Inquiry Results Complete *****

***** You may now make another selection from the Menu *****

Alvarado, Barbara (AHRQ/IOD)

From: Alvarado, Barbara (AHRQ/IOD)
Sent: Tuesday, September 22, 2009 3:59 PM
To: 'Nicholas_Mulherin@harvardpilgrim.org'
Subject: RE: FW: 5R18HS0127045-02 No Cost Extension Request

This request has been processed and is awaiting GMO approval, however with the end of the fiscal year upon us we are working diligently to get all NCE processed and approved as quickly as possible. Your patience and understanding is greatly appreciated, you should receive the NOA by next week.

Respectfully,

Barbara Alvarado
 Grants Management
 Agency for Healthcare Research and Quality (AHRQ)
 Office of Performance, Accountability, Resources, and Technology (OPART)
 540 Gaither Road, Suite 4210
 Rockville, MD 20850
 Phone: 301-427-1459
 Fax: 301-427-1462

FILE COPY

From: Nicholas_Mulherin@harvardpilgrim.org [mailto:Nicholas_Mulherin@harvardpilgrim.org]
Sent: Tuesday, September 22, 2009 3:51 PM
To: Alvarado, Barbara (AHRQ/IOD)
Subject: Re: FW: 5R18HS0127045-02 No Cost Extension Request

Dear Ms. Alvarado,

I was wondering if you could let me know when HPHC could expect the NOA for the NCE for this project. Anything you can let me know would be great.

thank you,
 Nick

Nicholas Mulherin/CORP/HPHC wrote on 09/03/2009 10:22:34 AM:

> Good morning. Yes - Barbara Richard is the authorized institutional
 > official. Please feel free to let me know if you need anything else.
 >
 > thanks,
 > Nick
 >
 > "Alvarado, Barbara (AHRQ/IOD)" <Barbara.Alvarado@AHRQ.hhs.gov> wrote
 > on 09/03/2009 10:18:06 AM:
 >
 > > Mr. Mulherin,
 > >
 > > Thank you for your email to Ms. Harris advising us of your intension
 > > to extend Grant Number 5 R18 HS 017045-02 for 12 months (September
 > > 29, 2010). This notification or request must be endorsed by an
 > > authorized institutional official (are you authorized) or is Ross
 > > Lazarus or Barbara Richard's an authorized institutional official?
 > >
 > > Respectfully,
 > >
 > > Barbara Alvarado
 > > Grants Management
 > > Agency for Healthcare Research and Quality (AHRQ)

9/22/2009

> > Office of Performance, Accountability, Resources, and Technology (OPART)
 > > 540 Gaither Road, Suite 4210
 > > Rockville, MD 20850
 > > Phone: 301-427-1459
 > > Fax: 301-427-1462

> > From: Burr, Michelle (AHRQ)
 > > Sent: Wednesday, August 26, 2009 3:27 PM
 > > To: Alvarado, Barbara (AHRQ/IOD)
 > > Subject: FW: 5R18HS0127045-02 No Cost Extension Request

> > Hello, Barbara. Please process the attached no cost extension under
 > > expanded authorities. Please use the information in the attached
 > > letter as well as the information in the attached e-mail exchange
 > > between Carol and the grantee confirming that the extension is being
 > > done under expanded authorities. Maintain all of this documentation
 > > in the file and note it on the green sheet.

> > Thanks!
 > > Michelle

> > From: Harris, Carol A. (AHRQ)
 > > Sent: Wednesday, August 26, 2009 3:12 PM
 > > To: Burr, Michelle (AHRQ)
 > > Subject: FW: 5R18HS0127045-02 No Cost Extension Request
 > > Actually, the notification is attached. Sorry about that!

> > Carol A. Harris
 > > Agency for Healthcare Research and Quality
 > > Office of Performance, Accountability, Resources, and Technology (OPART)
 > > Grants Management
 > > 540 Gaither Road
 > > Room 4208
 > > Rockville, MD 20850
 > > Phone: 301-427-1448
 > > Fax: 301-427-1462

> > From: Nicholas_Mulherin@harvardpilgrim.org [mailto:
 > > Nicholas_Mulherin@harvardpilgrim.org]
 > > Sent: Wednesday, August 26, 2009 2:23 PM
 > > To: Harris, Carol A. (AHRQ)
 > > Cc: Julie_Dunn@harvardpilgrim.org
 > > Subject: 5R18HS0127045-02 No Cost Extension Request

> > Dear Ms. Harris,

> > Attached, please find a copy of Harvard Pilgrim's formal request for
 > > a one-year no cost extension on 5R18HS0127045-02, "Electronic
 > > Support for Public Health - Vaccine Adverse Event Reporting System
 > > (ESP:VAERS)." Please let me know if you need any additional information.

> > thank you,
 > > Nick Mulherin

> > Nick Mulherin

9/22/2009

> > Grants Manager, Sponsore programs
> > Harvard Pilgrim Health Care
> > 133 Brookline Avenue, 5th Floor
> > Boston, MA 02215
> > Ph. 617.509.9933, Fx. 617.509.9859
> > nicholas_mulherin@hphc.org
> >
> >
> > -----
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> > prohibited. If you received this email in error, please notify the
> > sender by reply and delete the message without saving, copying or
> > disclosing it. Thank you. [attachment "5R18HS017045-02 No Cost
> > Extension Request.pdf" deleted by Nicholas Mulherin/CORP/HPHC]
> > ----- Message from "Harris, Carol A. (AHRQ)" <Carol.Harris@ahrq.hhs.
> > gov> on Wed, 26 Aug 2009 15:11:26 -0400 -----
> >
> > To:
> >
> > "Burr, Michelle (AHRQ)" <Michelle.Burr@ahrq.hhs.gov>
> >
> > Subject:
> >
> > FW: 5R18HS0127045-02 No Cost Extension Request
> >
> > Below is a no cost extension under expanded authorities that needs
> > processing.
> >
> > Thanks!
> >
> > Carol A. Harris
> > Agency for Healthcare Research and Quality
> > Office of Performance, Accountability, Resources, and Technology (OPART)
> > Grants Management
> > 540 Gaither Road
> > Room 4208
> > Rockville, MD 20850
> > Phone: 301-427-1448
> > Fax: 301-427-1462
> >
> >
> > From: Harris, Carol A. (AHRQ)
> > Sent: Wednesday, August 26, 2009 3:11 PM
> > To: 'Nicholas_Mulherin@harvardpilgrim.org'
> > Cc: Julie_Dunn@harvardpilgrim.org
> > Subject: RE: 5R18HS0127045-02 No Cost Extension Request
> >
> > Thank you, Nick! You are correct that AHRQ grantees are not able to
> > process no cost extensions through the Commons, and a formal
> > "notification" to AHRQ is the appropriate route to take. A revised
> > Notice of Award will be issued to extend the budget period.
> >
> > Have a great day!
> >
> > Carol A. Harris
> > Agency for Healthcare Research and Quality
> > Office of Performance, Accountability, Resources, and Technology (OPART)
> > Grants Management
> > 540 Gaither Road
> > Room 4208

9/22/2009

> > Rockville, MD 20850
> > Phone: 301-427-1448
> > Fax: 301-427-1462
> >
> >
> > From: Nicholas_Mulherin@harvardpilgrim.org [mailto:
> > Nicholas_Mulherin@harvardpilgrim.org]
> > Sent: Wednesday, August 26, 2009 2:31 PM
> > To: Harris, Carol A. (AHRQ)
> > Cc: Julie_Dunn@harvardpilgrim.org
> > Subject: RE: 5R18HS0127045-02 No Cost Extension Request
> >
> >
> > Yes, that is correct. I checked the eRA Commons, but there was no
> > link available for setting up the NCE (as there would be for an NIH
> > award), so I figured a formal letter would be the best way to proceed.
> >
> > thanks,
> > Nick
> >
> > "Harris, Carol A. (AHRQ)" <Carol.Harris@ahrq.hhs.gov> wrote on
> > 08/26/2009 02:27:32 PM:
> >
> > > Are you requesting the no cost extension under the auspices of
> > > expanded authorities?
> > >
> > > Carol A. Harris
> > > Agency for Healthcare Research and Quality
> > > Office of Performance, Accountability, Resources, and Technology (OPART)
> > > Grants Management
> > > 540 Gaither Road
> > > Room 4208
> > > Rockville, MD 20850
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> > > Sent: Wednesday, August 26, 2009 2:23 PM
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> > >
> > > Dear Ms. Harris,
> > >
> > > Attached, please find a copy of Harvard Pilgrim's formal request for
> > > a one-year no cost extension on 5R18HS0127045-02, "Electronic
> > > Support for Public Health - Vaccine Adverse Event Reporting System
> > > (ESP:VAERS)." Please let me know if you need any additional information.
> > >
> > > thank you,
> > > Nick Mulherin
> > >
> > >
> > > - -
> > > Nick Mulherin
> > > Grants Manager, Sponsored Programs
> > > Harvard Pilgrim Health Care
> > > 133 Brookline Avenue, 5th Floor
> > > Boston, MA 02215
> > > Ph. 617.509.9933, Fx. 617.509.9859

9/22/2009

> > > nicholas_mulherin@hphc. .g

> > >

> > >

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9/22/2009

Alvarado, Barbara (AHRQ/IOD)

From: Nicholas_Mulherin@harvardpilgrim.org
Sent: Thursday, September 03, 2009 10:23 AM
To: Alvarado, Barbara (AHRQ/IOD)
Subject: Re: FW: 5R18HS0127045-02 No Cost Extension Request

Good morning. Yes — Barbara Richard is the authorized institutional official. Please feel free to let me know if you need anything else.

thanks,
 Nick

"Alvarado, Barbara (AHRQ/IOD)" <Barbara.Alvarado@AHRQ.hhs.gov> wrote on 09/03/2009 10:18:06 AM:

> Mr. Mulherin,
 >
 > Thank you for your email to Ms. Harris advising us of your intension
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 >
 > Respectfully,
 >
 > Barbara Alvarado
 > Grants Management
 > Agency for Healthcare Research and Quality (AHRQ)
 > Office of Performance, Accountability, Resources, and Technology (OPART)
 > 540 Gaither Road, Suite 4210
 > Rockville, MD 20850
 > Phone: 301-427-1459
 > Fax: 301-427-1462
 >

> From: Burr, Michelle (AHRQ)
 > Sent: Wednesday, August 26, 2009 3:27 PM
 > To: Alvarado, Barbara (AHRQ/IOD)
 > Subject: FW: 5R18HS0127045-02 No Cost Extension Request
 >
 >

> Hello, Barbara. Please process the attached no cost extension under
 > expanded authorities. Please use the information in the attached
 > letter as well as the information in the attached e-mail exchange
 > between Carol and the grantee confirming that the extension is being
 > done under expanded authorities. Maintain all of this documentation
 > in the file and note it on the green sheet.
 >

> Thanks!
 > Michelle
 >
 >
 >

> From: Harris, Carol A. (AHRQ)
 > Sent: Wednesday, August 26, 2009 3:12 PM
 > To: Burr, Michelle (AHRQ)
 > Subject: FW: 5R18HS0127045-02 No Cost Extension Request
 > Actually, the notification is attached. Sorry about that!

9/3/2009

>
> Carol A. Harris
> Agency for Healthcare Research and Quality
> Office of Performance, Accountability, Resources, and Technology (OPART)
> Grants Management
> 540 Gaither Road
> Room 4208
> Rockville, MD 20850
> Phone: 301-427-1448
> Fax: 301-427-1462
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> From: Nicholas_Mulherin@harvardpilgrim.org [mailto:
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> Sent: Wednesday, August 26, 2009 2:23 PM
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> - -
> Nick Mulherin
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> Harvard Pilgrim Health Care
> 133 Brookline Avenue, 5th Floor
> Boston, MA 02215
> Ph. 617.509.9933, Fx. 617.509.9859
> nicholas_mulherin@hphc.org
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> Subject:
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9/3/2009

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> Carol A. Harris
> Agency for Healthcare Research and Quality
> Office of Performance, Accountability, Resources, and Technology (OPART)
> Grants Management
> 540 Gaither Road
> Room 4208
> Rockville, MD 20850
> Phone: 301-427-1448
> Fax: 301-427-1462

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> From: Harris, Carol A. (AHRQ)
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> To: 'Nicholas_Mulherin@harvardpilgrim.org'
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> > Carol A. Harris
> > Agency for Healthcare Research and Quality
> > Office of Performance, Accountability, Resources, and Technology (OPART)

*date used
released
request*

> > Grants Management
> > 540 Gaither Road
> > Room 4208
> > Rockville, MD 20850
> > Phone: 301-427-1448
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> >
> > thank you,
> > Nick Mulherin
> >
> >
> >
> > Nick Mulherin
> > Grants Manager, Sponsored Programs
> > Harvard Pilgrim Health Care
> > 133 Brookline Avenue, 5th Floor
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> > Ph. 617.509.9933, Fx. 617.509.9859
> > nicholas_mulherin@hphc.org
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Alvarado, Barbara (AHRQ/IOD)

From: Alvarado, Barbara (AHRQ/IOD)
Sent: Thursday, September 03, 2009 10:18 AM
To: 'nicholas_mulherin@hphc.org'
Subject: FW: 5R18HS0127045-02 No Cost Extension Request
Attachments: 5R18HS017045-02 No Cost Extension Request.pdf; FW: 5R18HS0127045-02 No Cost Extension Request

Mr. Mulherin,

Thank you for your email to Ms. Harris advising us of your intension to extend Grant Number 5 R18 HS 017045-02 for 12 months (September 29, 2010). This notification or request must be endorsed by an **authorized institutional official** (are you authorized) or is Ross Lazarus or Barbara Richard's an authorized institutional official?

Respectfully,

Barbara Alvarado
 Grants Management
 Agency for Healthcare Research and Quality (AHRQ)
 Office of Performance, Accountability, Resources, and Technology (OPART)
 540 Gaither Road, Suite 4210
 Rockville, MD 20850
 Phone: 301-427-1459
 Fax: 301-427-1462

From: Burr, Michelle (AHRQ)
Sent: Wednesday, August 26, 2009 3:27 PM
To: Alvarado, Barbara (AHRQ/IOD)
Subject: FW: 5R18HS0127045-02 No Cost Extension Request

Hello, Barbara. Please process the attached no cost extension under expanded authorities. Please use the information in the attached letter as well as the information in the attached e-mail exchange between Carol and the grantee confirming that the extension is being done under expanded authorities. Maintain all of this documentation in the file and note it on the green sheet.

Thanks!
 Michelle

From: Harris, Carol A. (AHRQ)
Sent: Wednesday, August 26, 2009 3:12 PM
To: Burr, Michelle (AHRQ)
Subject: FW: 5R18HS0127045-02 No Cost Extension Request

Actually, the notification is attached. Sorry about that!

Carol A. Harris
Agency for Healthcare Research and Quality
Office of Performance, Accountability, Resources, and Technology (OPART)
Grants Management

9/3/2009

540 Gaither Road
Room 4208
Rockville, MD 20850
Phone: 301-427-1448
Fax: 301-427-1462

From: Nicholas_Mulherin@harvardpilgrim.org [mailto:Nicholas_Mulherin@harvardpilgrim.org]
Sent: Wednesday, August 26, 2009 2:23 PM
To: Harris, Carol A. (AHRQ)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: 5R18HS0127045-02 No Cost Extension Request

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thank you,
Nick Mulherin

--
Nick Mulherin
Grants Manager, Sponsored Programs
Harvard Pilgrim Health Care
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Ph. 617.509.9933, Fx. 617.509.9859
nicholas_mulherin@hphc.org

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9/3/2009

Alvarado, Barbara (AHRQ/IOD)

From: Burr, Michelle (AHRQ)
Sent: Wednesday, August 26, 2009 3:27 PM
To: Alvarado, Barbara (AHRQ/IOD)
Subject: FW: 5R18HS0127045-02 No Cost Extension Request
Attachments: 5R18HS017045-02 No Cost Extension Request.pdf; FW: 5R18HS0127045-02 No Cost Extension Request

Hello, Barbara. Please process the attached no cost extension under expanded authorities. Please use the information in the attached letter as well as the information in the attached e-mail exchange between Carol and the grantee confirming that the extension is being done under expanded authorities. Maintain all of this documentation in the file and note it on the green sheet.

Thanks!
Michelle

From: Harris, Carol A. (AHRQ)
Sent: Wednesday, August 26, 2009 3:12 PM
To: Burr, Michelle (AHRQ)
Subject: FW: 5R18HS0127045-02 No Cost Extension Request

Actually, the notification is attached. Sorry about that!

Carol A. Harris
Agency for Healthcare Research and Quality
Office of Performance, Accountability, Resources, and Technology (OPART)
Grants Management
540 Gaither Road
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thank you,
Nick Mulherin

8/26/2009

--
Nick Mulherin
Grants Manager, Sponsored Programs
Harvard Pilgrim Health Care
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Boston, MA 02215
Ph. 617.509.9933, Fx. 617.509.9859
nicholas_mulherin@hphc.org

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8/26/2009



Harvard Medical
School



Harvard Pilgrim
Health Care

Department of Population Medicine

August 26, 2009

Carol Harris
Grants Management Specialist
AHRQ/OPART/GM
540 Gaither Road
Rockville, MD 20850

RE: 5 R18 HS017045 , Electronic Support for Public Health - Vaccine Adverse Event
Reporting System (ESP:VAERS)

Dear Ms. Harris:

We seek approval for a one-year no cost extension for the above-referenced project.

Unanticipated technical issues resulted in substantial IT & programming delays, which have been previously reported quarterly to AHRQ. However, the majority of these issues have been resolved, and ESP:VAERS is currently on its way towards being implemented and tested in collaboration with Atrius Health, the same multi-site, multi-specialty medical practice with over 600,000 patients where ESP is already deployed. We anticipate that ESP:VAERS will lead to better measurement of the safety profile of vaccines, and improve available measures of the quality and safety of existing and future vaccination programs in health care.

If you have any questions regarding this request, please contact Nick Mulherin, Grants Manager, at 617.509.9933 or nicholas_mulherin@hphc.org.

Sincerely,

Ross Lazarus
ESP:VAERS Principal Investigator

Barbara Richard
Director, Office of Sponsored Programs

Alvarado, Barbara (AHRQ/IOD)

From: Harris, Carol A. (AHRQ)
Sent: Wednesday, August 26, 2009 3:11 PM
To: Burr, Michelle (AHRQ)
Subject: FW: 5R18HS0127045-02 No Cost Extension Request

Below is a no cost extension under expanded authorities that needs processing.

Thanks!

Carol A. Harris
Agency for Healthcare Research and Quality
Office of Performance, Accountability, Resources, and Technology (OPART)
Grants Management
540 Gaither Road
Room 4208
Rockville, MD 20850
Phone: 301-427-1448
Fax: 301-427-1462

From: Harris, Carol A. (AHRQ)
Sent: Wednesday, August 26, 2009 3:11 PM
To: 'Nicholas_Mulherin@harvardpilgrim.org'
Cc: Julie_Dunn@harvardpilgrim.org
Subject: RE: 5R18HS0127045-02 No Cost Extension Request

Thank you, Nick! You are correct that AHRQ grantees are not able to process no cost extensions through the Commons, and a formal "notification" to AHRQ is the appropriate route to take. A revised Notice of Award will be issued to extend the budget period.

Have a great day!

Carol A. Harris
Agency for Healthcare Research and Quality
Office of Performance, Accountability, Resources, and Technology (OPART)
Grants Management
540 Gaither Road
Room 4208
Rockville, MD 20850
Phone: 301-427-1448
Fax: 301-427-1462

From: Nicholas_Mulherin@harvardpilgrim.org [mailto:Nicholas_Mulherin@harvardpilgrim.org]
Sent: Wednesday, August 26, 2009 2:31 PM
To: Harris, Carol A. (AHRQ)
Cc: Julie_Dunn@harvardpilgrim.org
Subject: RE: 5R18HS0127045-02 No Cost Extension Request

Yes, that is correct. I checked the eRA Commons, but there was no link available for setting up the NCE (as there would be for an NIH award), so I figured a formal letter would be the best way to proceed.

8/26/2009

thanks,
Nick

"Harris, Carol A. (AHRQ)" <Carol.Harris@ahrq.hhs.gov> wrote on 08/26/2009 02:27:32 PM:

> Are you requesting the no cost extension under the auspices of
> expanded authorities?

> Carol A. Harris

> Agency for Healthcare Research and Quality
> Office of Performance, Accountability, Resources, and Technology (OPART)
> Grants Management
> 540 Gaither Road
> Room 4208
> Rockville, MD 20850
> Phone: 301-427-1448
> Fax: 301-427-1462

> From: Nicholas_Mulherin@harvardpilgrim.org [mailto:
> Nicholas_Mulherin@harvardpilgrim.org]
> Sent: Wednesday, August 26, 2009 2:23 PM
> To: Harris, Carol A. (AHRQ)
> Cc: Julie_Dunn@harvardpilgrim.org
> Subject: 5R18HS0127045-02 No Cost Extension Request

> Dear Ms. Harris,

> Attached, please find a copy of Harvard Pilgrim's formal request for
> a one-year no cost extension on 5R18HS0127045-02, "Electronic
> Support for Public Health - Vaccine Adverse Event Reporting System
> (ESP:VAERS)." Please let me know if you need any additional information.

> thank you,
> Nick Mulherin

> Nick Mulherin
> Grants Manager, Sponsored Programs
> Harvard Pilgrim Health Care
> 133 Brookline Avenue, 5th Floor
> Boston, MA 02215
> Ph. 617.509.9933, Fx. 617.509.9859
> nicholas_mulherin@hphc.org

> -----
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> hereby notified that any review, disclosure, reproduction,
> distribution or other use of this communication is strictly
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> disclosing it. Thank you.

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8/26/2009

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First Level Review of Competing and Noncompeting Applications

Reviewer, check yes if OK; check NO if not; if not applicable, check N/A
After 1st level review and correction of identified issues, GMS should forward file to GMO for release

Grant # : <u>5 R18 HS 17045-02</u>			Yes	No	Corrected	NA
Organization in letter and address matches (NGA face page)			✓			
Award includes categorical budget			✓			
Awarded level no more than committed level/appropriate level			✓			
If UC1, federal share is no more than non-federal share						✓
EIN matches either application face page (competings) or previous NGA (non-competings)			✓			
Document number appropriate			✓			
CAN # verified			✓			
If grantee is for-profit, program income is deductive alternative						✓
PO and GMS listed on NGA			✓			
Terms include:	<input checked="" type="checkbox"/> Correct Cost Principles <input checked="" type="checkbox"/> A-133 Audit <input checked="" type="checkbox"/> EA or <input type="checkbox"/> not EA	<input checked="" type="checkbox"/> Program-specific Salary Cap <input checked="" type="checkbox"/> Other Support <input checked="" type="checkbox"/> Trafficking	Terms of Cooperation <input type="checkbox"/> T-5 and <input type="checkbox"/> FSR OR <input checked="" type="checkbox"/> Close Out Term			
File Contents Include:						
GMS worksheet signed by FM			✓			
Specialist checklist completed, signed and dated			✓			
Funding memo/PO review and approval documentation			✓			
Signed/dated face page			✓			
IRB within 12 months of budget period start date <input checked="" type="checkbox"/> OR appropriate exemption # designated			✓			
Evidence of cost analysis of budget and budget justification			✓			
Skip year FSR annotated, initialed and dated						✓
Resolution of excessive unobligated balance issues						✓
Issues from prior year resolved and any revision necessary done			✓			

Detail any problems identified, and return to GMS for resolution

Reviewer: _____

Date: 9/12/08

AHRQ NON-COMPETING GRANT/COOPERATIVE AGREEMENT AWARD CHECKLIST

GRANT NUMBER: 5R18 HS017045-02 GRANTEE INST'N: Harvard Pilgrim Healthcare, Inc. PI: Ross Lazarus PO: Marybeth Farguhar GMS: Carol Harris BACK-UP GMS, if applicable: N/A		Any budget limits or other special requirements by requirements imposed by original RFA/PA? RFA-07-002 Project period may not exceed 2 years; Total costs are limited to \$1 million, with no more than \$500K in budget period. PI & one other person must attend AHRQ-sponsored meetings.																					
A. FUNDING 1. Continuing supplemental commitment (____ admin; ____ MIN.) requested? 2. Funding memo addressing parent and, if applicable, supplement in file? 3. Co-funding anticipated? If Yes: Source: ____ Co-funding commitment document in file (MOU or IAA or NIH worksheet). 4. Complete application (i.e. checklist <input checked="" type="checkbox"/> ; signatures <input checked="" type="checkbox"/> ; appendices <input type="checkbox"/>)? 5. Program income anticipated? If Yes, use program income term on NOA. 6. Inventions? If yes, copy of the face page given to AHRQ GM invention coordinator on ____		<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 33%;">Y</th> <th style="width: 33%;">N</th> <th style="width: 33%;">N/A</th> </tr> <tr> <td>1. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>2. <input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>3. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>4. <input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> </tr> <tr> <td>5. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>6. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Y	N	N/A	1. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	3. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	4. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	5. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	6. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
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B. ORGANIZATIONAL INFORMATION 1. Indicate date GMS checked following sources: • NEAR Listing 9/05/2008 (source: National External Audit Review Center) (http://odoerdb2.od.nih.gov/gmac/topics/highrisk_main.html) • GSA Debarment List (check Grantee org., PI & key personnel) 9/05/2008 (http://www.epls.gov/) • ORI Scientific Misconduct List (check PI and key personnel) 9/05/2008 (http://ori.dhhs.gov/misconduct/documents/Alert_04-08.pdf) • GM delinquent final report list (check PI) 9/05/2008 (5/23/2008 list) [If PI is on list, do not issue this award before delinquent report is received unless you consult with GMO] IF THE GRANTEE AND/OR AN INVESTIGATOR WAS FOUND ON ANY OF THE LISTINGS UNDER #1, HOW RESOLVED: A Jeffrey D. Brown and Jeffrey Todd Brown appeared on the GPLS. According to the bio-sketch found in the 01 year file, the Jeffrey Brown working on this grant is Jeffrey Stuart Brown; therefore, Dr. Jeffrey Stuart Brown is cleared to receive salary support from this grant.																							
2. For-profit grantee? If Yes, use "Deductive Alternative" for Program Income.		<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>2. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>			2. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																
2. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																					
C. COLLABORATIVE INFORMATION 1. Any new consortium(s) added to project? If Yes, name of consortium(s) ____ NOTE: Either a 'Statement of Intent to Establish a Consortium' for each new consortium OR a statement from the authorized institutional official of the parent grant that the consortium participant(s) are prepared to establish the necessary inter-organizational agreement(s) consistent with HHS policy needs to be in the file. 2. Any new consultants? If Yes, letter of involvement on file? 3. Any new foreign involvement? If Yes, date State Dept. clearance received: ____		<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>1. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>2. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>3. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>			1. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	3. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>										
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3. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																					
D. HUMAN SUBJECTS 1. Human Subjects involved? If Yes, complete as appropriate: Grantee's Assurance #: FWA00000100 Exemption #: ____ or IRB approval date: 10/18/2007 2. Is this a change from involvement in previous year? 3. Human Subject involvement at any other site(s)? All sites have Assurance? HS NOTES: Brigham & Women's Hospital's assurance number is FWA00000484, and Harvard Vanguard Medical Associates' assurance number is FWA00001459		<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>1. <input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>2. <input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>3. <input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>			1. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	2. <input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	3. <input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>										
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GRANT NUMBER: **5R18 HS017045-02**

E. FINANCIAL INFORMATION

1. Cost analysis completed (budget justification, etc. adequate)?
[Use "Remarks" section to explain additional information requested from Grantee.
Show any adjustments on budget page and/or explain in "Remarks."]
2. Any TBN positions from previous year still TBN? If so, follow-up with grantee as to why and document in "Remarks" section.
3. Other support acceptable for all key personnel?
4. Any career development awards or joint appointments requiring budget adjustment? If so, who?
5. Identifiable CMS Data required? If yes, ensure costs are not included in award.
6. Grantee anticipates unobligated balance of **\$75,000-\$125,000** TCs as of the end of the previous budget period. If > 25% of previous budget period's TCs, explanation provided by Grantee and accepted by PO?
7. Disposition of Prior Year Funds:
 - a. Appropriate FSR (____ year) reviewed & in file? **Not due yet**
 - b. For expanded authorities grants, is the unobligated balance 25% or more of total costs awarded in last fiscal year's award (refer to FSR reconciliation form)?
If Yes, has grantee provided and AHRQ accepted explanation of balance?
 - c. For non-Expanded Authorities grants, \$____ balance used as:
____ offset to current award, or ____ carry over to ____ year award, or ____ held in reserve pending demonstration of need (address in "Remarks").
8. Any annualized salaries over Executive Level I salary cap budgeted? If so, who? ____
Grantee may retain and rebudget funds *provided* excess salary funds were not built into this year's committed level, otherwise budget, and possibly future year committed levels, must be adjusted.
9. PMS print out (AUTH TC) in file; GMS has verified that authorized level of funding through previous budget period is correct.
10. IMPAC II Award Worksheet Report signed by FM and in file?

F. AWARD

1. Follow-up completed on any restrictions on previous year's award?
NOTES: **IRB restriction removed on NOA dated 12/07/2007**
2. Awarded at committed level? If No, explain in "Remarks" section.
3. TERMS OF AWARD (TOA) in **bold** are required on all/most NOAs. **Order of terms:** selected terms should normally be grouped and ordered according to ranking (i.e. 1s first, 2s second, etc.). Mark terms to be included.

1.	EA or not EA	<input checked="" type="checkbox"/>	5.	FSR Requirements	<input type="checkbox"/>
1.	Trafficking Victims	<input checked="" type="checkbox"/>	5.	T5 Application Requirements	<input type="checkbox"/>
2.	Co-funding	<input type="checkbox"/>	5.	"Final Year" reports	<input checked="" type="checkbox"/>
2.	Unallowable Costs	<input type="checkbox"/>	6.	Terms of Cooperation	<input type="checkbox"/>
2.	Partial Pay / Carryover	<input type="checkbox"/>	7.	Program Income	<input type="checkbox"/>
3.	Award Level	<input type="checkbox"/>	7.	Inventions	<input type="checkbox"/>
3.	Provisional Award	<input type="checkbox"/>	7.	Salary Cap for Fiscal Year	<input checked="" type="checkbox"/>
3.	Human Subjects No follow up required	<input checked="" type="checkbox"/>	7.	Cost Principles	<input checked="" type="checkbox"/>
3.	Restriction on funds awarded	<input type="checkbox"/>	7.	Audit Requirements	<input checked="" type="checkbox"/>
4.	Program-Specific	<input checked="" type="checkbox"/>	7.	Other Support	<input checked="" type="checkbox"/>
4.	Progress Reports (more than annually)	<input type="checkbox"/>	7.	E-NOA Establishment	<input type="checkbox"/>

Other Reasons: ☐

4. NOA E-mail notification disabled? For: terms ☐; spreadsheets ☐;
N/A bec. Grantee is not e-mail enabled ☐ (use E-NOA TOA)
5. Addresses (PI, Grantee, etc.) confirmed/updated in IMPAC II?

-GMS Signature on next page-

PAGE 2 of 3

	Y	N	N/A
1.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
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G. REMARKS

1. On 9/05/2008, the GMS sent an email to the Business Official to request the following:
 - a. Unobligated balance amount from the 01 year.
 - b. When will the TBN Programmer at Harvard Pilgrim Health Care be named?
 - c. Please explain why the efforts for Lazarus, (b)(6) and Katica do not match the budget justification.
 - d. Please explain why Brigham and Women's Health's originally requested 8.0 calendar months for the Programmer, (b)(6) but the 02 year states that (b)(6) is now the Project Manager, and her effort has dropped down to .30 calendar months. Also, (b)(6) is now listed as the Programmer at 6.70 calendar months, and the originally requested secretarial person, at .30 calendar months, has disappeared.
 - e. When will the TBN Programmer for Harvard Vanguard Medical Associates be named?
2. On 9/09/2008, the Business Official responded to the GMS' email of 9/05/2008 with the following responses (summarized):
 - a. Unobligated balance amount of \$75-\$125K due to internal and subcontract administrative delays. This is at or below 25%, since they are unsure of exact unobligated balance amount, the GMS did not contact the PO for approval.
 - b. TBN Programmer has been identified as (b)(6) MPH.
 - c. A revised budget justification was provided to match the actual budget for BWH.
 - d. It appears as though the budget lines on the original application were off by one line, making it look as though the levels of effort had been adjusted in the 02 year. It was determined that the clerical position was not needed. Mr (b)(6) replaces (b)(6)
 - e. TBN Programmer at HVMA has been identified as (b)(6)
3. On 9/10/2008, the GMS printed the NOA, and gave to GMO for review.

PREPARED BY: Candace HarrisDATE: 9/10/2008Con't? N

Principal Investigator/Program Director LAZARUS, ROSS	Degree MBBS	Grant No 5-R18-HS-017045-02	IRG ZHS1	CFDA 93 226	Appl ID 7499529
Grantee Organization HARVARD PILGRIM HEALTH CARE, INC	Entlty No 1042452600A1	Total Project Period from: 09/30/07 thru: 09/29/09			

GM checklist status: Not started

Award Worksheet Report

Title/Tr.area Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES)	For Budget Period from: 09/30/08 thru: 09/29/09
FY FUNDS: 2008 PROG CLASS: CP3 CAN: K72PS53 (SINGLE-CAN) CNCL: 200800 CNCL Action: MISCONDUCT IN SCIENCE: RFA NO: HS07-002 IPF NO: 444701 KIND OF ORG: Other health, human resrces, environment/community OWNERSHIP: serv org Private, Nonprofit independent CARRYOVER AUTHORITY: FEDERAL DEMONSTRATIONS:	DOCUMENT NO: RHS017045A PS: 169 CNCL Priority: EXP DATE: 04/30/09 AIDS RELATED: N GENDER: 1A MINORITY: 1A CHILD: 1A EXCEPTION TRACKING: IC HUMAN SUBJECT: 30 VERT ANIMAL: 10 PHASE III CODE: N PROGRAM INCOME: Additional Costs APPL RECEIVED DATE: 06/26/08 SNAP AWARD: FOREIGN INVOLVEMENT: CLINICAL TRIAL CODE: No Clinical Trial
	EXPEDITED REVIEW: N INST. ASSURANCE FILED? Y IRB CERTIFICATION FILED? Y ASSURANCE NO. FWA00000100 DATE 10/18/07 SPEC SUPLMNT INDICATOR: NGA RELEASE DATE CURR. ISSUE DATE: 09/17/08 ESNAP?: N

Budget

Direct

Year 2

Salaries and Wages	(b)(4);
Fringe Benefits	(b)(6)
Personnel Costs (Subtotal)	
Consultant Services	\$0
Equipment	\$0
Supplies	\$401
Travel Costs	\$2,090
Patient Care (Inpatient)	\$0
Patient Care (Outpatient)	\$0
Alterations and Renovations	\$0
Other Costs	\$0
Consortium/Contractual Cost	(b)(4)
	\$429,927
Direct Costs	(b)(4)
Indirect Costs	
Total Approved	\$499,405
Fee	\$0
Non-Federal	\$0
Unob. bal. Prior Budget	\$0
Increase/Decrease Amount	+\$0
Award Amount	\$499,405

F&A

Year 2

FA Cost Base 1	(b)(4)
FA Cost Rate 1	
FA costs 1	

GM Comments

Authorized Officials

Principal Investigator/Program Director LAZARUS, ROSS	Degree MBBS	Grant No 5-R18-HS-017045-02	IRG ZHS1	CFDA 93 226	Appl ID 7499529
Grantee Organization HARVARD PILGRIM HEALTH CARE, INC	Entity No 1042452600A1	Total Project Period from: 09/30/07 thru: 09/29/09			

Program Official: Marybeth Farquhar
e-Signature By:
e-Signature Date:

Specialist Name: Carol Harris
e-Signature By: Carol Harris
e-Signature Date: 09/05/2008

GM Officer: Joan Metcalfe
e-Signature By:
e-Signature Date:

X

Signature (Optional)

Date

X

Carol Harris 9/10/08
Signature (Optional)

Date

X

Signature (Optional)

Date

Janet Jordan
9/10/08

Principal Investigator/Program Director LAZARUS, ROSS	Degree MBBS	Grant No 5-R18-HS-017045-02	IRG ZHS1	CFDA 93 226	Appl ID 7499529
Grantee Organization HARVARD PILGRIM HEALTH CARE, INC.	Entity No 1042452600A1	Total Project Period from: 09/30/07 thru: 09/29/09			

Signature Notes

- a. Grants Management Officer Sign Note:
- b. Specialist Sign Note:
- c. Program Official Sign Note:

Harris, Carol A. (AHRQ)

From: Julie_Dunn@harvardpilgrim.org
Sent: Tuesday, September 09, 2008 1:09 PM
To: Harris, Carol A. (AHRQ)
Cc: (b)(6) Nicholas_Mulherin@hphc.org; ross.lazarus@channing.harvard.edu
Subject: Re: Additional information needed for grant #5R18 HS017045-02, PI: Ross Lazarus
Importance: High
Attachments: 1R18HS014045_Lazarus_ESP_VAERS_Yr2response_9.08.pdf

Hello Ms. Harris,

On behalf of Dr. Lazarus, please accept the attached responses to the questions posed below, along with supporting documentation, as needed. Please confirm receipt of this e-mail at your convenience.

The signed original will also be sent via overnight FedEx to your attention. Please let me know if you have any questions or require any additional information.

Thank-you,

Julie

Julie D. Dunn, MPH
 Project Manager
 Therapeutics Research &
 Infectious Disease Epidemiology (TIDE)
 Department of Ambulatory Care and Prevention
 Harvard Medical School / Harvard Pilgrim Healthcare
 133 Brookline Ave, 6th Floor
 Boston, MA 02215
 Phone: (617) 509-9880 / Fax: (617) 859-8112
<http://www.dacp.org/tide/>

Harris, Carol A. (AHRQ) wrote:

> Dear Ms. Richard,
 >
 >
 >
 > Thank you for the non-competing continuation application for grant #5R18
 > HS017045-02, PI: Ross Lazarus. Upon my initial review of the
 > application, I've found that the following items are needed before I can
 > issue the 02 year award for this grant:
 >
 >
 > 1. Does Harvard Pilgrim Healthcare expect any unobligated balance
 > amount from the 01 year, and if so, how much? Although the
 > application does not request the amount if it is below 25% of the
 > total costs awarded, it is required for AHRQ's determination of
 > the budget for the future year of this grant.
 > 2. When will the TBN Programmer position at Harvard Pilgrim
 > Healthcare be named?
 > 3. Brigham and Women's Hospital's (BWH's) budget justification does
 > not match the salary budget page for the efforts of Lazarus,
 > (b)(6) Please clarify.

9/10/2008

> 4. On the original application, BWH requested an effort of 8.0
 > calendar months for the Programmer position, which was named as
 > (b)(6) but now the application states that Ms.
 > Senter-Sylvia is the Project Manager with a decreased effort of
 > .30 calendar months, and a new person, (b)(6) is listed as
 > the Programmer at 6.70 calendar months. Please explain. Also,
 > the clerical person in the 02 year has disappeared.
 > 5. When will the TBN Programmer position at Harvard Vanguard Medical
 > Associates be named?

> A response, *_endorsed by the authorized institutional official_*, no
 > later than Wednesday, September 10, 2008, is requested.

> Thank you!

> *Carol A. Harris*

> *Agency for Healthcare Research and Quality*

> *Office of Performance, Accountability, Resources, and Technology (OPART)*

> *Grants Management*

> *540 Gaither Road*

> *Room 4337*

> *Rockville, MD 20850*

> *Phone: 301-427-1448*

> *Fax: 301-427-1462*

Ross Lazarus MBBS MPH, Director of Bioinformatics
 Channing Laboratory, 181 Longwood Ave., Boston MA 02115, USA.

 The information contained in this email message and any attachments may be privileged and/or confidential. It is for intended addressee(s) only. If you are not the intended recipient, you are hereby notified that any review, disclosure, reproduction, distribution or other use of this communication is strictly prohibited. If you received this email in error, please notify the sender by reply and delete the message without saving, copying or disclosing it. Thank you.

9/10/2008



Department of Ambulatory Care and Prevention

September 8, 2008

Carol A. Harris
Agency for Healthcare Research and Quality (AHRQ)
Office of Performance, Accountability, Resources & Technology (OPART)
Grants Management
540 Gaither Road
Room 4337
Rockville, MD 20850

RE: 5R18 HS017045-02 / Response to ESP:VAERS Year 2 Continuation inquiry

Dear Ms. Harris:

Per your e-mail request dated 9/05/2008, please find responses & supporting documents to address the outstanding questions, below.

1. Does Harvard Pilgrim Healthcare expect any unobligated balance amount from the 01 year, and if so, how much? Although the application does not request the amount if it is below 25% of the total costs awarded, it is required for AHRQ's determination of the budget for the future year of this grant.

Yes, it is expected that HPHC will request carry forward of unobligated balance from Year1. Due to some internal & subcontract administrative delays, we anticipate that this balance will be approximately \$75,000-125,000.

2. When will the TBN Programmer position at Harvard Pilgrim Healthcare be named?
The individual serving as the programmer / research analyst for this project has been identified as Taliser Avery, MPH.

3. Brigham and Women's Hospital's (BWH's) budget justification does not match the salary budget page for the efforts of Lazarus, (b)(6) Please clarify.
Please refer to the attached revised BWH budget justification, which now correctly illustrates the figures found on the salary budget page, which are correct.

Attachment to 9/9/08 email from Julie Dunn

4. On the original application, BWH requested an effort of 8.0 calendar months for the Programmer position, which was named as (b)(6) but now the application states that Ms. (b)(6) is the Project Manager with a decreased effort of .30 calendar months, and a new person, (b)(6) is listed as the Programmer at 6.70 calendar months. Please explain. Also, the clerical person in the 02 year has disappeared.

According to our original submission document, Ms. (b)(6) was listed as Information Technology Manager (Project Manager) with an effort of .30. Her effort & position remain the same during Year 2. It was determined that the clerical position was not needed during the upcoming Year2.

The programmer in the original submission was (b)(6) Ms. (b)(6) has since left BWH and her efforts on this project have been replaced by Mr. (b)(6) another programmer at BWH.

5. When will the TBN Programmer position at Harvard Vanguard Medical Associates be named? The HVMA programmer for this study has been identified as (b)(6) also serves as a lead programmer for the ESP project, so is very familiar with system infrastructure.

Please contact me with any additional questions regarding this submission.

Sincerely,


Barbara Richard
Director, Office of Sponsored Programs

Attachment to 9/9/08 email from Julie Dunn



September 8, 2008

Carol A. Harris
Agency for Healthcare Research and Quality (AHRQ)
Office of Performance, Accountability, Resources & Technology (OPART)
Grants Management
540 Gaither Road
Room 4337
Rockville, MD 20850

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Please contact me with any additional questions regarding this submission.

Sincerely,



Barbara Richard
Director, Office of Sponsored Programs

BWH Year 2 :BUDGET JUSTIFICATION – Continuation Page (REVISED)
Electronic Support for Public Health-Vaccine Adverse Reporting System

Brigham and Women's Hospital (Subcontract Site)

Personnel

Fringe benefits are calculated at (b)(4) for professionals and (b)(4) for non-professionals.

Professional Personnel

Ross Lazarus, MBBS, MPH (Principal Investigator 2.40 months effort). Dr. Lazarus leads day-to-day activities including implementation of algorithms for syndromic surveillance, website enhancements and maintenance, and procedures for monitoring and will direct all new developments.

Non-Professional Personnel

(b)(6) (Project Manager, 0.30 months effort). (b)(6) ensures data base integrity, and works with Dr. Lazarus to perform the communication and data transfer functions. She supervises all staff working on this project, in addition to managing the project milestones and expenditure under the direction of Dr. Lazarus.

(b)(6) (Programmer/Analyst, 6.70 months effort). (b)(6) leads all work on the distributed console enhancements and will design and implement all Data Center side web services application and web site code.

(b)(6) (Project Coordinator, 0.30 months effort). (b)(6) assists Dr. Lazarus and the Study Team with preparation of annual reviews and manuscript preparation. He prepares progress reports and facilitates communication between the sites involved in the project.

Supplies

1. Amount of \$1,031 has been requested to cover the cost of consumable office supplies.

Total Supplies: \$1,031**Travel**

Dr. Lazarus will travel once a year to a scientific meeting. The cost of travel per trip is \$2,570.

Total Travel: \$ 2,570**Other Expenses**

SUN/PC costs are increased 4.0% each year.

Channing Laboratory Computer Facility

The Channing Laboratory computer facility provides access to two components: UNIX based system for data storage and analysis and system support for desktop network of PCs. Charges for each component is based on FTE effort on each grant. Channing Laboratory computing infrastructure will be used for all development and testing, and Channing web server and web services infrastructure will provide the primary site for software and documentation distribution. All current research grants at the Channing pay a fixed annual contribution per FTE to the computing budget. The fee has been a component of every NIH grant submitted from the Channing over the past 5 years, and has always been accepted by NIH reviewers to date. The Channing Laboratory computer facility provides access to Linux and Solaris based servers for centralized authentication, email,

security, audit, automated backup and recovery, web servers, data storage and analysis. The Channing computer system includes a grid of more than 20 Sun servers and blades (including two 4 CPU and one 8 core main servers) and a 12TB SAN, three Oracle (2 production and 1 development) Sunfire v440 and Sun Enterprise 450 servers, and a 32 CPU Linux cluster, together with duplicated failover Sun server redirectors and multiple redundant backend web servers. Each individual study contributes to the overall costs of the UNIX based data storage and analysis component. Current annual costs for system administration, data storage and processing including software licenses (such as the EMC Legato backup suite, Veritas Foundation Suite, SAS and SPlus statistical packages), security auditing and administration, automated backup systems, software programming and hardware maintenance, and planned replacement of obsolete hardware are more than \$600,000 for approximately 300 users in 35 projects in areas of chronic disease epidemiology, respiratory epidemiology, pharmacoepidemiology, and statistics. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load in year 2 of the project will be (b)(4)

PC Desktop System Support

The Channing computer system operates a network of desktop computers for investigators to use in their daily work activities. Services supported include word processing, graphical presentations, and spreadsheets. The costs of maintaining the network include software licenses, service contracts on desktops and printers and personnel to maintain the hardware as well as replacement of obsolete equipment. Annual costs are \$300,000 serving 230 users within the Channing Laboratory at 181 Longwood Avenue. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load in year 2 of the project will be (b)(4)

Total funds requested for computing: (b)(4)

Harris, Carol A. (AHRQ)

From: Harris, Carol A. (AHRQ)
Sent: Friday, September 05, 2008 3:51 PM
To: 'research_admin@hphc.org'
Cc: 'ross.lazarus@channing.harvard.edu'; Farquhar, Marybeth (AHRQ); Harris, Carol A. (AHRQ)
Subject: Additional information needed for grant #5R18 HS017045-02, PI: Ross Lazarus

Dear Ms. Richard,

Thank you for the non-competing continuation application for grant #5R18 HS017045-02, PI: Ross Lazarus. Upon my initial review of the application, I've found that the following items are needed before I can issue the 02 year award for this grant:

1. Does Harvard Pilgrim Healthcare expect any unobligated balance amount from the 01 year, and if so, how much? Although the application does not request the amount if it is below 25% of the total costs awarded, it is required for AHRQ's determination of the budget for the future year of this grant.
2. When will the TBN Programmer position at Harvard Pilgrim Healthcare be named?
3. Brigham and Women's Hospital's (BWH's) budget justification does not match the salary budget page for the efforts of Lazarus, (b)(6). Please clarify.
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5. When will the TBN Programmer position at Harvard Vanguard Medical Associates be named?

A response, endorsed by the authorized institutional official, no later than Wednesday, September 10, 2008, is requested.

Thank you!

Carol A. Harris
Agency for Healthcare Research and Quality
Office of Performance, Accountability, Resources, and Technology (OPART)
Grants Management
540 Gaither Road
Room 4337
Rockville, MD 20850
Phone: 301-427-1448
Fax: 301-427-1462

9/5/2008

INQUIRY: Authorization Transactions Extended

DATE: 09/10/2008 TIME: 05:27:08 PM

*** SEARCH PARAMETERS *****

GRANT AWARD: RHS017045A

*ACCT** *PIN* ****EIN***** *****DUNS***** *****Organization Name*****

4715G 4715 1042452600A1

HARVARD PILGRIM HEALTH CARE, INC

HHS-REG: 01 STATE: MA PMT: ACH STOP: N MAN-REV: N 272: File GROUP: F21 USER: VNK5LHJ

DOC:RHS017045A OP DIV:K AUTH TC's Follow --

T/C RM *****FCO***** *****INC-AUTH***** POST DT TIME START DT END DT ISSU

050 15 2007-K72PS53-4145

.00 12/05/07 11:48 09/30/07 09/29/08 12/0

050 13 2007-K72PS53-4145

499,809.00 09/20/07 10:45 09/30/07 09/29/08 09/2

NET TC:

499,809.00

Hits: 2

***** Inquiry Results Complete *****

You may now make another selection from the Menu

Name	(b)(6)	
Classification	Individual	
Exclusion Type	Reciprocal	
Description	none	
Address(es) --		
Verify Street 1	<input type="text"/>	
Verify Street 2	<input type="text"/>	
Address	St. Charles, MN, 55972	
DUNS	none	
<input type="button" value="Verify"/>		
CT Action(s) --		
Action Date	05-Oct-2000	
Termination Date	Indef.	
CT Code	R	
Agency	OPM	
Agency POC	OPM Contacts	
EPLS Create Date	20-Dec-2000	
EPLS Modify Date		
Action Date	20-Jun-2000	
Termination Date	Indef.	
CT Code	Z1	
Agency	HHS	
Agency POC	HHS Contacts	
EPLS Create Date	20-Jul-2000	
EPLS Modify Date		

Name	(b)(6)	
Classification	Individual	
Exclusion Type	Reciprocal	
Description	none	
Address(es) --		
Verify Street 1	<input type="text"/>	
Verify Street 2	<input type="text"/>	
Address	Trabuco Canyon, CA, 92679	
DUNS	none	
<input type="button" value="Verify"/>		
CT Action(s) --		
Action Date	19-Nov-2001	
Termination Date	Indef.	
CT Code	R	
Agency	OPM	
Agency POC	OPM Contacts	
EPLS Create Date	29-Aug-2002	
EPLS Modify Date		
Action Date	20-Sep-2001	
Termination Date	Indef.	
CT Code	Z1	
Agency	HHS	
Agency POC	HHS Contacts	
EPLS Create Date	06-Feb-2002	
EPLS Modify Date		

* The (b)(6) on this grant is (b)(6)

(b)(6) according to his biosketch in the 01 year file

Rate Agreements

Agreement Text for: N2055808.TXT

Agreement Date: 01/02/2008

NPrfMA Harvard Pilgrim Health Care Inc 1042452600A1 01 02 08 0558

NONPROFIT RATE AGREEMENT

EIN 1042452600A1

DATE January 2 2008

ORGANIZATION

Harvard Pilgrim Health Care Inc

FILING REF The preceding
Agreement was dated

November 26 2007 93 Worcester S

Wellesley

MA 02481

The rates approved in this agreement are for use on grants contracts and other agreements with the Federal Government subject to the conditions in Section III

RATE TYPES	FIXED	FINAL	PROV	PROVISIONAL	PRED	PREDETERMINED
------------	-------	-------	------	-------------	------	---------------

TYPE	EFFECTIVE PERIOD	RATE	LOCATIONS	APPLICABLE TO
	FROM TO			

PRED 01 01 07 12 31 07

PRED 01 01 07 12 31 07

PRED 01 01 08 12 31 09

PRED 01 01 08 12 31 09

PROV 01 01 10 UNTIL AMENDED

(b)(4)

On Site

Research A

Off Site

Research A

On Site

Research B

Off Site

Research B

Use same rates and
for fiscal year ending December 31 2009

A Base Total direct costs excluding capital expenditures buildings individual items of equipment alterations and renovations and subawards

B Base Total direct costs excluding capital expenditures building individual items of equipment alterations and renovations and that portion of each subaward in excess of 25 000

ORGANIZATION

Harvard Pilgrim Health Care Inc

AGREEMENT DATE January 2 2008

TREATMENT OF PAID ABSENCES

Vacation holiday sick leave pay and other paid absences are included in salaries and wages and are claimed on grants contracts and other agreements as part of the normal cost for salaries and wages Separate claims for the costs of these paid absences are not made

Treatment of Fringe benefits Fringe benefits applicable to direct salaries and wages are treated as direct costs except incentive compensation which is treated as an indirect cost

Equipment means an article of nonexpendable tangible personal property having a useful life of more than one year and an acquisition cost of 1 000 or more per unit

ORGANIZATION

Harvard Pilgrim Health Care Inc

AGREEMENT DATE January 2 2008

A LIMITATIONS

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant contract or other agreement only to the extent that funds are available Acceptance of the rates is subject to the following conditions

1 Only costs incurred by the organization were included in its indirect cost pool as finally accepted such costs are legal obligations of the organization and are allowable under the governing cost principles 2 The same costs that have been treated as indirect costs are not claimed as direct costs 3 Similar types of costs have been accorded consistent accounting treatment and 4 The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government In such situations the rates would be subject to renegotiation at the discretion of the Federal Government

B ACCOUNTING CHANGES

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency Such changes include but are not limited to changes in the charging of a particular type of cost from indirect to direct Failure to obtain approval may result in cost disallowances

C FIXED RATES

If a fixed rate is in this Agreement it is based on an estimate of the costs for the period covered by the rate When the actual costs for this period are determined an adjustment will be made to a rate of a future year s to compensate for the difference between the costs used to establish the fixed rate and actual costs

D USE BY OTHER FEDERAL AGENCIES

The rates in this Agreement were approved in accordance with the authority in Office of Management and Budget Circular A 122 Circular and should be applied to grants contracts and other agreements covered by this Circular subject to any limitations in A above The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement

E OTHER

If any Federal contract grant or other agreement is reimbursing indirect costs by a means other than the approved rate s in this Agreement the organization should 1 credit such costs to the affected programs and 2 apply the approved rate s to the appropriate base to identify the proper amount of indirect costs allocable to these programs

BY THE ORGANIZATION
Harvard Pilgrim Health Care Inc

ON BEHALF OF THE FEDERAL G
DEPARTMENT OF HEALTH AND H

ORGANIZATION

AGENCY

SIGNATURE

SIGNATURE

NAME

Robert I Aaronson
NAME

TITLE

DIRECTOR DIVISION OF COST ALLO
TITLE

DATE

January 2 2008
DATE 0558

HHS REPRESENTATIVE Michael St
Telephone
212 264 2069

Rate Agreements

Agreement Text for: H2051707b.TXT

Agreement Date: 11/14/2007 (7b)

HsptMA Brigham And Women s Hospital 1042312909A1 11 14 07 0517

HOSPITAL RATE AGREEMENT

EIN 1042312909A1

DATE November 14 2007

HOSPITAL
Brigham And Women s Hospital
Office of Research Administration
75 Francis Street
Boston

FILING REF The preceding
Agreement was dated
September 24 2007

MA 02115

The rates approved in this agreement are for use on grants contracts and other
agreements with the Federal Government subject to the conditions in Section III

RATE TYPES	FIXED	FINAL	PROV	PROVISIONAL	PRED	PREDETERMINED
------------	-------	-------	------	-------------	------	---------------

TYPE	EFFECTIVE PERIOD FROM TO	RATE	LOCATIONS	APPLICABLE TO
------	-----------------------------	------	-----------	---------------

PRED	10 01 06 09 30 08	(b)(4)	On Site	Research
------	-------------------	--------	---------	----------

PRED	10 01 06 09 30 08	(b)(4)	Off Site	Research
------	-------------------	--------	----------	----------

PROV	10 01 08 UNTIL AMENDED	(b)(4)		
------	------------------------	--------	--	--

Use same rates and
for fiscal year ending September 30 2008

Base Total direct costs less items of equipment major subcontracts alterations
and renovations animal charges hospitalization and other fees related to patient
care

HOSPITAL
Brigham And Women s Hospital
Office of Research Administration

AGREEMENT DATE November 14 2007

RATE TYPES	FIXED	FINAL	PROV	PROVISIONAL	PRED	PREDETERMINED
------------	-------	-------	------	-------------	------	---------------

TYPE	EFFECTIVE PERIOD FROM TO	RATE	LOCATIONS	APPLICABLE TO
------	-----------------------------	------	-----------	---------------

FIXED	10 01 07 09 30 08	(b)(4)	All	Professional
-------	-------------------	--------	-----	--------------

FIXED	10 01 07 09 30 08	(b)(4)	All	Non Professional
-------	-------------------	--------	-----	------------------

FIXED	10 01 07 09 30 08	(b)(4)	All	Intern Residents Fel
-------	-------------------	--------	-----	----------------------

PROV	10 01 08 UNTIL AMENDED	(b)(4)		
------	------------------------	--------	--	--

Use same rates and
for fiscal year ending September 30 2008

Salaries and wages

DESCRIPTION OF FRINGE BENEFITS

HOSPITAL

Brigham And Women s Hospital
Office of Research Administration

AGREEMENT DATE November 14 2007

TREATMENT OF FRINGE BENEFITS

The fringe benefits are charged using the rate \$ listed in the Fringe Benefits Section of this Agreement The fringe benefits included in the rate \$ are listed below

TREATMENT OF PAID ABSENCES

Vacation holiday sick leave pay and other paid absences are included in salaries and wages and are claimed on grants contracts and other agreements as part of the normal cost for salaries and wages Separate claims for the costs of these paid absences are not made

1 The fringe benefit rates include the following

FICA Pension Disability Group Life Insurance Time Accrual Training
Costs Uniforms Workers Compensation Unemployment FITICORP MBTA
Subsidy Employee Allowances Activities Awards FSA Admin Parking
Subsidy Cafeteria Subsidy Tuition Benefit Amortized Past Service
Exp ESL Sick Lv Pension Human Resources Health Ins and
Dental Vision Info Malpractice Insurance Home Office Fringe

- 2 Off Site Definition For all activities performed in facilities not owned by the organization and to which rent is directly allocated to the project s the off site rate will apply
- 3 The following rates shall be used for research contracts performed at Brigham and Women s Hospital

TYPE	FROM	TO	RATE	LOCATION	BASE
Fixed	10 1 06	9 30 08	(b)(4)	On Site	Same as in Sec I
Prov	10 1 08	Until Amended		On Site	Same as in Sec I

- 4 Effective October 1 2004 equipment means an article of nonexpendable tangible personal property having a useful life of more than one year and an acquisition cost of 5 000 or more per unit

This Rate Agreement updates Fringe Benefit Rates only

HOSPITAL
Brigham And Women s Hospital
Office of Research Administration

AGREEMENT DATE November 14 2007

A LIMITATIONS

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costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year's to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D USE BY OTHER FEDERAL AGENCIES

The rates in this Agreement were approved in accordance with the cost principles promulgated by the Department of Health and Human Services and should be applied to the grants, contracts, and other agreements covered by these regulations, subject to any limitations in A above. The hospital may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E OTHER

If any Federal contract, grant, or other agreement is reimbursing indirect costs by a means other than the approved rates in this Agreement, the organization should: 1. credit such costs to the affected programs; and 2. apply the approved rates to the appropriate base to identify the proper amount of indirect costs allocable to these programs.

BY THE HOSPITAL
Brigham And Women's Hospital
Office of Research Administration

HOSPITAL

ON BEHALF OF THE FEDERAL GOVERNMENT
DEPARTMENT OF HEALTH AND HUMAN SERVICES

AGENCY

SIGNATURE

NAME

TITLE

DATE

SIGNATURE

Robert I. Aaronson
NAME

DIRECTOR, DIVISION OF COST ALLOCATION
TITLE

November 14, 2007
DATE 0517

HHS REPRESENTATIVE: Joseph Guadagno
Telephone: 202 264 2069

DOMESTIC INSTITUTIONS/COMPONENTS

[NEW SEARCH](#)

CONTAINING 'Brigham' (4)

Find institution/component in table below and click corresponding 'Detail' link to view assurance.

Assurances/Components Found					
Assurance	Institution/Component	Type	City	State or Country	
FWA00000484	Brigham & Women's Hosp	F	Boston	MASSACHUSETTS	Detail
FWA00001266	Brigham Young U	F	Provo	UTAH	Detail
FWA00005741	Brigham Young U Public Schools Assoc	F	Provo	UTAH	Detail
FWA00001121	Dana-Farber/Brigham and Women's Cancer Center at Faulkner Hospital	C	Boston	MASSACHUSETTS	Detail

* Where Type: 'F' = FWAs, 'M' = MPAs, 'C' = Components, 'I' = CPAs

If you have questions about human subject research, click ohrp@osophs.dhhs.gov

If you have questions/suggestions about this web page, click

[WEBMASTER](#)

Updated August 5, 2004

Principal Investigator: **LAZARUS, Ross**

Electronic Support for Public Health – vaccine Adverse Event Reporting System
(ESP:VAERS)

Grant Number: 1 R18 HS017045-02

Non-Competing Grant Progress Report

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Department of Health and Human Services
Public Health Services

Review Group

Type

Activity

Grant Number

R18

HS017045-02

Grant Progress Report

Total Project Period

From: 9/30/2007

Through: 9/29/2009

Requested Budget Period

From: 9/30/2008

Through: 9/29/2009

1. TITLE OF PROJECT

Electronic Support for Public Health - Vaccine Adverse Event Reporting System

2a. PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR

(Name and address, street, city, state, zip code)

Ross Lazarus

Harvard Pilgrim Health Care

133 Brookline Avenue, 6th Floor

Boston, MA 02215

2b. E-MAIL ADDRESS

ross.lazarus@channing.harvard.edu

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

Department of Ambulatory Care & Prevention

2d. MAJOR SUBDIVISION

2e. Tel: 617-525-2730

Fax: 617-525-0958

3a. APPLICANT ORGANIZATION

(Name and address, street, city, state, zip code)

Harvard Pilgrim Health Care

93 Worcester Street

Wellesley, MA 02481

3b. Tel: 617-509-9950

Fax: 617-509-9859

3c. DUNS: 07-172-1088

4. ENTITY IDENTIFICATION NUMBER

1042452600A1

6. HUMAN SUBJECTS ☐ No ☒ Yes6a. Research
Exempt☒ No ☐ YesIf Exempt ("Yes" in
6a):

Exemption No.

If Not Exempt ("No" in
6a):

IRB approval date

10/18/2007

5. NAME, TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL

Barbara W. Richard Director, Office of Sponsored
Programs, Harvard Pilgrim Health Care, 133 Brookline
Ave., 6th Floor Boston, MA 02215

Tel: 617-509-9950

Fax: 617-509-9859

E-MAIL: Research_Admin@HPHC.org

6b. Federal Wide Assurance No. FWA00000100

6c. NIH-Defined Phase III

Clinical Trial ☒ No ☐ Yes7. VERTEBRATE ANIMALS ☒ No ☐ Yes

7a. If "Yes," IACUC approval Date

7b. Animal Welfare Assurance No.

10. PROJECT/PERFORMANCE SITE(S)

Organizational Name: applicant organization

DUNS:

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT \$429,927

8b. TOTAL \$499,404

Street 1:

Street 2:

9. INVENTIONS AND PATENTS ☒ No ☐ Yes

If "Yes,"

☐ Previously Reported☐ Not Previously Reported

City:

County:

State:

Province:

Country:

Zip/Postal Code:

Congressional Districts:

11. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 13)

Barbara W. Richard Director, Office of Sponsored Programs (Research_Admin@HPHC.org)

TEL: 617-509-9950

FAX: 617-509-9859

E-MAIL:

12. Corrections to Page 1 Face Page

13. 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

11. (In ink)

DATE

Barbara W. Richard

6/25/08

HPHC Budget

Project #1: ESP		Principal Investigator/Program Director (Last, First, Middle): LAZARUS, Ross					
DETAILED BUDGET FOR NEXT BUDGET PERIOD DIRECT COSTS ONLY		FROM 09/30/08	THROUGH 09/29/09	GRANT NUMBER 1R18HS017075-02			
PERSONNEL (Applicant organization only)		Months Devoted to Project DOLLAR AMOUNT REQUESTED (omit cents)					
NAME	ROLE ON PROJECT	Cal Mnth	Acad Mnth	Summer Mnth	SALARY REQUESTED	FRINGE BENEFITS	TOTALS
LAZARUS, Ross**	Principal Investigator	(b)(4); (b)(6)					
Platt, Richard	Co-Investigator						
(b)(6)							
CONSULTANT COSTS							
** Lazarus supported via (b)(4)							
EQUIPMENT (Itemize)							
* Note. \$1,740 of consultant fees was rebudgeted to travel.							
\$ 490 of consultant fee rebudgeted to travel.							
\$ 196 " " supplies.							
SUPPLIES (Itemize by category)							
Consumable office supplies		401.					
* Budget reviewed - no comments*							
TRAVEL							
AHRQ meetings & conferences		(200) 401. (205)					
PATIENT CARE COSTS							
INPATIENT							
OUTPATIENT							
ALTERATIONS AND RENOVATIONS (Itemize by category)							
OTHER EXPENSES (Itemize by category)							
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		(b)(4)					
CONSORTIUM/CONTRACTUAL COSTS							
DIRECT COSTS							
FINANCE AND ADMINISTRATION COSTS							
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		(432,675) \$ 429,927 (429,715)					

Program Director/Principal Investigator (Last, First, Middle): LAZARUS, Ross

BUDGET JUSTIFICATION

GRANT NUMBER
1 R18 HS017045-02

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

No significant changes to report.

CURRENT BUDGET PERIOD

FROM
9/30/2007

THROUGH
9/29/2008

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

Department of Health and Human Services
Public Health Service

Grant Progress Report

Review Group 0 Type 0 Activity 0 Grant Number 1 R18 HS017045-02

Total Project Period

From: 09/30/07

Through: 09/29/09

Requested Budget Period

From: 09/30/08

Through: 09/29/09

1. TITLE OF PROJECT

ELECTRONIC SUPPORT FOR PUBLIC HEALTH-VACCINE ADVERSE EVENT REPORTING SYSTEM

2a. PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR

(Name and address, street, city, state, zip code)

Ross Lazarus

Channing Laboratory

181 Longwood Avenue

Boston, MA 02115

2b. E-MAIL ADDRESS

ross.lazarus@channing.harvard.edu

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

Department of Medicine

2d. MAJOR SUBDIVISION

Channing Laboratory

2a. Tel: 617.525.2730 Fax: 617-525-0958

3b. Tel: 617-954-9660 Fax: 617-954-9680

3c. DUNS 030-811-269

3a. APPLICANT ORGANIZATION

(Name and address, street, city, state, zip code)

Brigham and Women's Hospital

75 Francis Street

Boston, Massachusetts 02115

4. ENTITY IDENTIFICATION NUMBER

1042312909A1

6. HUMAN SUBJECTS

☒ No ☒ Yes6a. Research
Exempt☐ No ☒ YesIf Exempt ("Yes" in
6a):

Exemption No. 6a

If Not Exempt ("No" in
6a):

IRB approval date

5. NAME, TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL

Deanna Citerne

Associate Director, Pre-Award Services

75 Francis Street

Boston, Massachusetts 02115

Tel: 617.954.9660 FAX 617.954.9680

E-MAIL: bwhgc@partners.org

6b. Federal Wide Assurance No.

6c. NIH-Defined Phase III

Clinical Trial

☒ No ☐ Yes

7. VERTEBRATE ANIMALS

☒ No ☐ Yes

7a. If "Yes," IACUC approval Date

7b. Animal Welfare Assurance No.

10. PROJECT / PERFORMANCE SITES

Brigham and Women's Hospital

Organizational Name: Brigham and Women's Hospital

DUNS: 030-811-269

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT \$ 136,717 8b. TOTAL \$ 239,255

9. INVENTIONS AND PATENTS ☒ No ☐ Yes

If "Yes,"

☐

Previously Reported

☐

Not Previously Reported

Street 1: 75 Francis Street

Street 2:

City: Boston

County:

State: MA

Province:

Country: USA

Zip/Postal Code: 02115

Congressional District: 8th

11. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 13)

Leigh Curley, Pre Award Team Lead

TEL: 617.954.9660

FAX: 617.954.9680

E-MAIL:

bwhgc@partners.org

12. Corrections to Page 1 Face Page

13. 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
(1. (In ink)

DATE



6/19/08

1 R18 HS017045-02

Program Director/Principal Investigator (Last, first, middle):

LAZARUS, Ross

BWH
Budget

DETAILED BUDGET FOR NEXT BUDGET PERIOD — DIRECT COSTS ONLY		FROM 09/30/08	THROUGH 09/29/09	GRANT NUMBER 1 R18 HS017045-02
PERSONNEL (Applicant organization only)		Months Devoted to Project		
NAME	ROLE ON PROJECT	Cal. Months	Acad. Months	Summer Months
LAZARUS, Ross	Principal Investigator	(b)(4); (b)(6)	(b)(4); (b)(6)	(b)(4); (b)(6)
(b)(6)	Project Manager	(b)(4); (b)(6)	(b)(4); (b)(6)	(b)(4); (b)(6)
	Programmer	(b)(4); (b)(6)	(b)(4); (b)(6)	(b)(4); (b)(6)
	Project Coordinator	(b)(4); (b)(6)	(b)(4); (b)(6)	(b)(4); (b)(6)
SUBTOTAL		(b)(4); (b)(6)	(b)(4); (b)(6)	(b)(4); (b)(6)
CONSULTANT COSTS		DOLLAR AMOUNT REQUESTED (omit cents)		
* note: (b)(4) from HPHC consultant fees was allocated to BWH.		0		
EQUIPMENT (Itemize)		0		
SUPPLIES (Itemize by category)		0		
Consumable Office Supplies		1,031	(15,000)	0
* Budget reviewed - no increases *				
TRAVEL			(1,000)	1,031
PI, one trip per year, \$2,570 per trip				
PATIENT CARE COSTS			(2,500)	2,570
INPATIENT				0
OUTPATIENT				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				0
OTHER EXPENSES (Itemize by category)			(16,744)	0
Project share of Channing SUN systems costs		5,265		
Project share of Channing PC costs		1,680		
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		(b)(4)	(b)(4)	6,945
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		
		FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		(124,712)	\$ 239,255	(123)

Program Director/Principal Investigator (Last, First, Middle): LAZARUS, Ross

BUDGET JUSTIFICATION

GRANT NUMBER
1 R18 HS017045-02

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

Please see the continuation page for the detailed budget justification.

CURRENT BUDGET PERIOD

FROM
09/30/2007

THROUGH
09/29/2008

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

None

BWH Year 2 :BUDGET JUSTIFICATION – Continuation Page (REVISED)
Electronic Support for Public Health-Vaccine Adverse Reporting System

Brigham and Women's Hospital (Subcontract Site)

Personnel

Fringe benefits are calculated at (b)(4) for professionals and (b)(4) for non-professionals.

Professional Personnel

Ross Lazarus, MBBS, MPH (Principal Investigator 2.40 months effort). Dr. Lazarus leads day-to-day activities including implementation of algorithms for syndromic surveillance, website enhancements and maintenance, and procedures for monitoring and will direct all new developments.

Non-Professional Personnel

(b)(6) Project Manager, 0.30 months effort). (b)(6) ensures data base integrity, and works with Dr. Lazarus to perform the communication and data transfer functions. She supervises all staff working on this project, in addition to managing the project milestones and expenditure under the direction of Dr. Lazarus.

(b)(6) (Programmer/Analyst, 6.70 months effort). (b)(6) leads all work on the distributed console enhancements and will design and implement all Data Center side web services application and web site code.

(b)(6) (Project Coordinator, 0.30 months effort). (b)(6) assists Dr. Lazarus and the Study Team with preparation of annual reviews and manuscript preparation. He prepares progress reports and facilitates communication between the sites involved in the project.

Supplies

1. Amount of \$1,031 has been requested to cover the cost of consumable office supplies.

Total Supplies: \$1,031

Travel

Dr. Lazarus will travel once a year to a scientific meeting. The cost of travel per trip is \$2,570.

Total Travel: \$ 2,570

Other Expenses

SUN/PC costs are increased 4.0% each year.

Channing Laboratory Computer Facility

The Channing Laboratory computer facility provides access to two components: UNIX based system for data storage and analysis and system support for desktop network of PCs. Charges for each component is based on FTE effort on each grant. Channing Laboratory computing infrastructure will be used for all development and testing, and Channing web server and web services infrastructure will provide the primary site for software and documentation distribution. All current research grants at the Channing pay a fixed annual contribution per FTE to the computing budget. The fee has been a component of every NIH grant submitted from the Channing over the past 5 years, and has always been accepted by NIH reviewers to date. The Channing Laboratory computer facility provides access to Linux and Solaris based servers for centralized authentication, email,

security, audit, automated backup and recovery, web servers, data storage and analysis. The Channing computer system includes a grid of more than 20 Sun servers and blades (including two 4 CPU and one 8 core main servers) and a 12TB SAN, three Oracle (2 production and 1 development) Sunfire v440 and Sun Enterprise 450 servers, and a 32 CPU Linux cluster, together with duplicated failover Sun server redirectors and multiple redundant backend web servers. Each individual study contributes to the overall costs of the UNIX based data storage and analysis component. Current annual costs for system administration, data storage and processing including software licenses (such as the EMC Legato backup suite, Veritas Foundation Suite, SAS and SPlus statistical packages), security auditing and administration, automated backup systems, software programming and hardware maintenance, and planned replacement of obsolete hardware are more than \$600,000 for approximately 300 users in 35 projects in areas of chronic disease epidemiology, respiratory epidemiology, pharmacoepidemiology, and statistics. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load in year 2 of the project will be (b)(4)

PC Desktop System Support

The Channing computer system operates a network of desktop computers for investigators to use in their daily work activities. Services supported include word processing, graphical presentations, and spreadsheets. The costs of maintaining the network include software licenses, service contracts on desktops and printers and personnel to maintain the hardware as well as replacement of obsolete equipment. Annual costs are \$300,000 serving 230 users within the Channing Laboratory at 181 Longwood Avenue. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load in year 2 of the project will be (b)(4)

Total funds requested for computing: (b)(4)

BUDGET JUSTIFICATION – Continuation Page**Using Electronic Medical Records to Support Core Public Health Needs**

Brigham and Women's Hospital (Subcontract Site)

Personnel

Fringe benefits are calculated at (b)(4) for professionals and (b)(4) for non-professionals.

Professional Personnel

Richard Platt, MD, MSc (Principal Investigator (Primary), Percentage effort on HPHC Primary Budget). Dr. Platt provides overall oversight for this project, participates in the Bioterrorism Working Group, and is principal liaison with Drs. (b)(6) the Massachusetts Department of Public Health (MDPH) Special Activities Epidemiologist, and with other personnel responsible for bioterrorism response activities in this cooperative agreement. Dr. (b)(6) salary is listed on the HPHC budget.

Ross Lazarus, MBBS, MPH (Principal Investigator (Subcontract) 1.44 months effort). Dr. Lazarus leads day-to-day activities including implementation of algorithms for syndromic surveillance, website enhancements and maintenance, and procedures for monitoring and will direct all new developments.

Non-Professional Personnel

(b)(6) (Project Manager, 1.00 months effort). (b)(6) ensures data base integrity, and works with Dr. Lazarus to perform the communication and data transfer functions. She supervises all staff working on this project, in addition to managing the project milestones and expenditure under the direction of Dr. Lazarus.

(b)(6) (Programmer/Analyst, 1.06 months effort). (b)(6) leads all work on the distributed console enhancements and will design and implement all Data Center side web services application and web site code.

(b)(6) (Project Coordinator, 2.40 months effort). (b)(6) assists Dr. Lazarus and the Study Team with preparation of annual reviews and manuscript preparation. He prepares progress reports and facilitates communication between the sites involved in the project.

Supplies

1. Amount of \$571 has been requested to cover the cost of consumable office supplies.

Total Supplies: \$571**Other Expenses**

SUN/PC costs are increased 4.0% each year.

Channing Laboratory Computer Facility

The Channing Laboratory computer facility provides access to two components: UNIX based system for data storage and analysis and system support for desktop network of PCs. Charges for each component is based on FTE effort on each grant. Channing Laboratory computing infrastructure will be used for all development and testing, and Channing web server and web services infrastructure will provide the primary site for software and documentation distribution. All current research grants at the Channing pay a fixed annual contribution per FTE to the computing budget. The fee has been a component of every NIH grant submitted from the Channing over the past 5 years, and has always been accepted by NIH reviewers to date. The Channing Laboratory

computer facility provides access to Linux and Solaris based servers for centralized authentication, email, security, audit, automated backup and recovery, web servers, data storage and analysis. The Channing computer system includes a grid of more than 20 Sun servers and blades (including two 4 CPU and one 8 core main servers) and a 12TB SAN, three Oracle (2 production and 1 development) Sunfire v440 and Sun Enterprise 450 servers, and a 32 CPU Linux cluster, together with duplicated failover Sun server redirectors and multiple redundant backend web servers. Each individual study contributes to the overall costs of the UNIX based data storage and analysis component. Current annual costs for system administration, data storage and processing including software licenses (such as the EMC Legato backup suite, Veritas Foundation Suite, SAS and SPlus statistical packages), security auditing and administration, automated backup systems, software programming and hardware maintenance, and planned replacement of obsolete hardware are more than \$600,000 for approximately 300 users in 35 projects in areas of chronic disease epidemiology, respiratory epidemiology, pharmacoepidemiology, and statistics. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load is (b)(4) (in the coming year, the project has only 10 months; therefore, the total cost will be (b)(4))

PC Desktop System Support

The Channing computer system operates a network of desktop computers for investigators to use in their daily work activities. Services supported include word processing, graphical presentations, and spreadsheets. The costs of maintaining the network include software licenses, service contracts on desktops and printers and personnel to maintain the hardware as well as replacement of obsolete equipment. Annual costs are \$300,000 serving 230 users within the Channing Laboratory at 181 Longwood Avenue. Each study is charged on a per FTE basis at a rate of (b)(4) per FTE and total costs may vary annually depending on the personnel load.

The total personnel load is (b)(4) (in the coming year, the project has only 10 months; therefore, the total cost will be (b)(4))

Total funds requested for computing: (b)(4)

Program Director/Principal Investigator (Last, first, middle):

LAZARUS, Ross

GRANT NUMBER

1 R18 HS017045-02

CHECKLIST - BWH

1. PROGRAM INCOME (See instructions.)

All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. 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 following policies, assurances and/or certifications listed in the application instructions when applicable. Descriptions of individual assurances/certifications are provided in Part III of the PHS 398, and listed in part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after the Progress Report (Form Page 5.)

3. FACILITIES AND ADMINISTRATIVE (F & A) COSTS

Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS Agency Cost Advisory Office.

F&A costs will **not** be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

☒ DHHS Agreement dated: 08/27/07

☐ No Facilities and Administrative Costs Requested.

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

CALCULATION*

Entire proposed budget period:

Amount of base \$ (b)(4) x Rate applied (b)(4) = F & A costs (b)(4)

Add to total direct costs from Form Page 2 and enter new total on Face Page, Item 8b.

*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)

Department of Health and Human Services
Public Health Services

Review Group	Type 1	Activity R18	Grant Number HS017045-02
Total Project Period			
From: 9/30/2007		Through: 9/29/2009	
Requested Budget Period			
From: 9/30/2008		Through: 9/29/2009	

Grant Progress Report

1. TITLE OF PROJECT

Electronic Support for Public Health - Vaccine Adverse Event Reporting System

2a. PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR

(Name and address, street, city, state, zip code)

Francis X. Campion, MD, FACP

Harvard Vanguard Medical Associates
133 Brookline Avenue, Office of Clinical
Research
Boston, MA 02215

2b. E-MAIL ADDRESS

Francis_Campion@vmed.org

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

Internal Medicine

2d. MAJOR SUBDIVISION

Kenmore

2e. Tel: 617-421-5907

Fax: 617-629-6090

3a. APPLICANT ORGANIZATION

(Name and address, street, city, state, zip code)

Harvard Vanguard Medical Associates, Inc.
275 Grove Street, Suite 3-300
Newton, MA 02466

3b. Tel: 617-421-2532

Fax: 617-421-6021

3c. DUNS: 837855790

4. ENTITY IDENTIFICATION NUMBER

043397450

6. HUMAN SUBJECTS ☐ No ☒ Yes

6a. Research Exempt

☒ No ☐ Yes

If Exempt ("Yes" in
6a):
Exemption No.

If Not Exempt ("No" in
6a):
IRB approval date
10/18/2007

5. NAME, TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL

Richard Marshall, MD - Director of Research;
Harvard Vanguard Medical Associates 133 Brookline
Avenue, Office of Clinical Research Boston, MA 02215

Tel: 617-859-5480

Fax: 617-421-6021

E-MAIL: richard_marshall@vmed.org

6b. Federal Wide Assurance No. FWA00001459

6c. NIH-Defined Phase III

Clinical Trial ☒ No ☐ Yes

7. VERTEBRATE ANIMALS ☒ No ☐ Yes

7a. If "Yes," IACUC approval Date

7b. Animal Welfare Assurance No.

10. PROJECT/PERFORMANCE SITE(S)

Organizational Name: Harvard Pilgrim Healthcare

DUNS: 07-172-1088

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT \$54,570

8b. TOTAL \$ 89,631

Street 1: 133 Brookline Ave, 6th Floor

Street 2:

9. INVENTIONS AND PATENTS ☒ No ☐ Yes

If "Yes," ☐ Previously Reported
☐ Not Previously Reported

City: Boston

County:

State: MA

Province:

Country: USA

Zip/Postal Code: 02215

Congressional Districts: 9

11. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 13)

Richard Marshall, MD - Director of Research (richard_marshall@vmed.org)

TEL: 617-859-5480

FAX: 617-421-6021

E-MAIL:

12. Corrections to Page 1 Face Page

13. 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
11. (In ink)

R Marshall MD

DATE

6/24/08

Program Director/Principal Investigator (Last, First, Middle): LAZARUS, Ross

BUDGET JUSTIFICATION

GRANT NUMBER
1 R18 HS017045-02

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

No significant changes to report.

CURRENT BUDGET PERIOD

FROM
9/30/2007

THROUGH
9/29/2008

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

Principal Investigator/Program Director (Last, first, middle): LAZARUS, Ross

CHECKLIST - HVMA

TYPE OF APPLICATION (Check all that apply.)

- ☐ NEW application. (This application is being submitted to the PHS for the first time.)
- ☐ REVISION of application number: _____
(This application replaces a prior unfunded version of a new, competing continuation/renewal, or supplemental/revision application.)
- ☐ COMPETING CONTINUATION of grant number: _____
(This application is to extend a funded grant beyond its current project period.)
- ☐ SUPPLEMENT to grant number: _____
(This application is for additional funds to supplement a currently funded grant.)
- ☐ CHANGE of principal investigator/program director.
Name of former principal investigator/program director: _____
- ☐ CHANGE of Grantee Institution. Name of former institution: _____
- ☐ FOREIGN application ☐ Domestic Grant with foreign involvement Country(ies) involved: _____

INVENTIONS AND PATENTS
(Competing continuation/renewal appl. only)

- ☐ No ☐ Previously reported
☐ Yes. If "Yes," ☐ 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 requested. 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 following policies, assurances and/or certifications when applicable. Descriptions of individual assurances/certifications are provided in Part III. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

-Human Subjects; -Research Using Human Pluripotent Stem Cells;
-Research on Transplantation of Human Fetal Tissue; -Women and
Minority Inclusion Policy; -Inclusion of Children Policy; -
Vertebrate Animals;

-Debarment and Suspension; -Drug- Free Workplace
(applicable to new [Type 1] or revised [Type 1] applications
only); - Lobbying; -Non-Delinquency on Federal Debt; -
Research Misconduct; -Civil Rights (Form HHS441 or HHS
690); -Handicapped Individuals (Form HHS 641 or HHS
690); -Sex Discrimination (Form HHS 639-A or HHS 690); -
Age discrimination (Form HHS 680 or HHS 690); -
Recombinant DNA and Human Gene Transfer Research; -
Financial Conflict of Interest -Smoke Free workplace; -
Prohibited Research; -Select Agent Research; -PI
Assurance

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

- ☐ DHHS Agreement dated: _____ ☐ No Facilities and Administration Costs Requested
- ☐ DHHS Agreement being negotiated with _____ 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: \$	X Rate Applied	%=F&A costs
b. 02 year	Amount of base: \$ (b)(4)	X Rate Applied (b)(4)	%=F&A costs (b)(4) ✓
c. 03 year	Amount of base: \$	X Rate Applied	%=F&A costs \$0
d. 04 year	Amount of base: \$	X Rate Applied	%=F&A costs \$0
e. 05 year	Amount of base: \$	X Rate Applied	%=F&A costs \$0
TOTAL F&A Costs			(b)(4) ✓

*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.):

HVMA uses the approved HPHC off-site indirect rate of 27.6% for this award

OTHER SUPPORT**Ross LAZARUS, M.B.B.S., M.Med., M.P.H.**

(Brigham and Women's Hospital)

ACTIVE – Brigham Administered Grants2 U01 HL065899-05 (Weiss)
NIH/ NHLBI08/01/05 – 06/30/10
\$1,452,435

0.60 CM

590

The Pharmacogenetics of Asthma Treatment

The major goal of this project is to determine the genetic basis for differences observed in patient responses to various asthma treatments. Overlap: None.

1 P01 HK000016-04 (Platt)

01/01/06 – 12/31/08
\$932,178

1290 1.44 CM

Centers for Excellence in Public Health Informatics (ESP)

Enhancing Public Health through Electronic Medical & Personal Health Records/ Informatics Core

This work will build directly on this group's accomplishments in developing the CDC National Bioterrorism Syndromic Surveillance Demonstration Project. ESP will serve three major functions: 1) Completely transparent reporting of conditions where all required information can be extracted from EMRs, 2) Initiation of reporting that triggers an automated query to clinicians if non-extractable information, and 3) Automatic responses to electronic queries by health authorities regarding demographic and treatment status of individuals with positive laboratory tests. Overlap: None

1 R01 HG003646-01A1 (Lazarus)
NIH12/01/05 – 11/30/08
\$2,266,379

390 4.68 CM

A Genetic Association Research Statistical Framework (BISTI)

The specific aims of this project include software support for importing experimental data and genomic annotation; methods for statistical power calculations and for selecting maximally informative subsets of markers during experimental design; methods for visualizing and summarizing experimental results; established and recently developed methods supporting statistical inference on single markers, multiple markers and on the epistatic and gene by environment interactions characteristic of these diseases and needed for emerging fields of study such as pharmacogenetics. Overlap: None.

1 P01 HL083069 (Weiss)
NIH03/23/07 – 01/31/12
\$1,515,000

1581.82 CM

Common Genetic Determinants of Asthma and COPD (PPG Core 3 - Bioinformatics)

The goal of this core is to develop novel bioinformatics tools to be used by Projects 1-4 of the grant, the analysis of human and mouse microarray datasets, and the maintenance of the PPG website, which will be modeled from a former Channing Laboratory PGA website. In addition, this core will provide a wide variety of statistical tools for genetic association analysis, as well as up-to-date information on genetic association studies, mouse genetics, and the functional genomics work of Projects 1-4. Overlap: None.

1 R01 HL066289 (Weiss)
NIH/NHLBI4/1/07-3/31/11
\$2,940,680

12 0.10 CM

The Genetic Epidemiology of Asthma in Costa Rica

The goal of this competing continuation grant is to use linkage disequilibrium mapping to test the hypothesis that a gene(s) on chromosome 12q24 influences asthma and airway responsiveness in Costa Ricans, and that a gene(s) on chr. 20p12 influences total serum IgE in male Costa Ricans. This goal will be accomplished by a) genotyping SNPs in these regions to perform fine-mapping family-based association studies to identify candidate genes for asthma and/or its intermediate phenotypes, and b) testing for association between SNPs and haplotypes in selected candidate genes and asthma and/or its intermediate phenotypes in families of children with asthma.

ACTIVE (Continued) – Brigham Administered GrantsR01 HL086601-01 (Raby)
NIH/NHLBI

12/01/06-11/30/10

37% 0.36 CM

Genetics and Gene Expression Profiling in Asthma

The goal of this project is to integrate gene expression microarray data with family-based genetic association studies to identify genetic variants that influence the severity of asthma through regulation of gene expression. Overlap: None

1 R18 HS017045-01 (Lazarus)
AHRQ09/30/07- 09/29/09
\$247,144

26% 2.40 CM

Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)

This project seeks to perform systems analysis, design and application programming for enhancements to existing ESP software to enable the creation and management of diagnosis and therapeutic exposure registries.

1 R01 HL093076A (Raby)
NIH07/01/08 – 06/30/12
\$491,542

57% 0.60 CM

Structural Genetic Variation in Asthma

We will perform a family-based genome-wide association study of DNA copy-number variation (CNVs) in 430 families ascertained through the Childhood Asthma Management Program (CAMP) to identify novel CNVs that confer risk for childhood asthma. Identified loci will be tested for replication in three independent asthma cohorts of diverse ancestry. Follow-up SNP-based linkage disequilibrium mapping studies and functional evaluations will be performed for CNVs demonstrating consistent and reproducible association with asthma.

5
12
39
15
3
20
3
100%

(b)(6)

Other Support**ACTIVE****Prime: CRN – Group Health Cooperative****U19CA079689****HPHC PI (Fletcher)****NCI**

5/1/07 – 4/30/12

.84 calendar (7%)

\$263,090.00 (HPHC Direct Costs, yr 1)

Cancer Research Network Across Health Care Systems – Infrastructure

The CRN has successfully developed a productive collaborative cancer research consortium. We plan to improve the research capacity of the CRN and use it to conduct a broad array of cancer research studies that relate to NCI research priorities or questions of importance to CRN investigators and our academic collaborators.

Prime: Harvard Pilgrim Health Care (Platt)**HHS A290200500331 Task Order 5****HPHC PI (Platt)****AHRQ**

9/25/2007 – 12/24/2008

2.88 calendar (24%)

HPHC Direct Costs: \$1,681,835

Developing a Distributed Research Network and Cooperative to Conduct Population-based Studies and Safety Surveillance

To support AHRQ's Effective Health Care program, the DECIDE centers at the HMO Research Network Center for Education and Research on Therapeutics (HMORN CERT) and the University of Pennsylvania will develop a design and specifications for a scalable distributed research network to support a wide array of purposes related to therapeutics, including comparative effectiveness, safety, and utilization, as well as quality of care research. They will implement a prototype, conduct a proof of principle research project on hypertension therapy, and make recommendations for future expansion of the network.

Prime: Harvard Pilgrim Health Care (Platt)

1.8 calendar (15%)

HHS F223200710017C**HPHC PI (Brown)****AHIP**

9/30/2007 – 9/29/2008

HPHC Direct Costs: \$114,464

Using Electronic Health Data for Influenza Vaccine Safety: New Methodologies and Considerations (Flu II)

The primary goal of the proposed activities is to build on and expand the activities undertaken as part of the previous FDA sponsored pandemic flu study (Elective K) and other FDA sponsored flu activities. This additional funding will support a number of new activities, including, collaboration with FDA on implementation and interpretation of sequential methods for active flu safety surveillance, assessment of key methodological considerations in conducting real-time surveillance using administrative claims data, and evaluation of selected outcome measures across data sources.

Prime: Harvard Pilgrim Health Care (Lazarus)**1R18HS017045****HPHC PI (Lazarus)****AHRQ**

10/01/2007 – 9/30/2008

1.08 calendar (9%)

HPHC Direct Costs: \$449,809

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Prime: Harvard Pilgrim Health Care (Platt)

1U18HS016955-1

HPHC PI (Brown)

AHRQ

10/01/07-9/30/11

3.6 calendar (30%)

\$263,090.00 (HPHC Direct Costs, yr 1)

The HMO Research Network Center for Education and Research in Therapeutics (CERT 3)

The overall vision of the HMO Research Network CERT is to advance population health through acquisition and widespread dissemination of knowledge about best therapeutics practices. We accomplish this by taking advantage of the research and dissemination opportunities afforded by health plans' defined populations, their large provider groups, and their unique data sources. In the aggregate these health plans cover a substantial majority of the U.S. population. This leads to this CERT's theme, "Improving therapeutics' use, safety, and effectiveness, through research, dissemination, and education using health plans' defined populations, providers, delivery systems, and data."

Prime: Harvard Pilgrim Health Care (Platt)

HPHC PI (Platt)

11/01/2004 – 10/31/2008

(b)(4)

(b)(4)

(b)(4)

Enhanced Identification of Adverse Drug Events

The primary objective of this study is to develop and test population-based systems for early identifications of adverse drug events and characterization of unsafe prescribing practices. Analyses will use Sequential Probability Ratio Testing (SPRT), the Poisson Gamma Shrinkage Method, and the Tree-Based Scan Statistic to evaluate their performance in detecting suspected and unsuspected adverse drug event associations.

OVERLAP:

None at present.

11
24
15
9
30
3
90%

OTHER FINANCIAL SUPPORT

(b)(6)

ACTIVE SUPPORT

1R18HS017045 (Lazarus)
ESP VAERS

10/1/2007 – 9/30/2008
\$449,809
1.20 Person-months

10%

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP: VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Role: Co-Investigator

OTHER FINANCIAL SUPPORT

(b)(6)

ACTIVE

K24 HL 068041 (Gillman) NIH	9/30/01 – 7/31/11 \$164,904	0.48 calendar 40%
Patient-oriented research in early life origins of CVD The research focus of this midcareer patient-oriented investigator award is a study of maternal diet, placental hormones, and offspring blood pressure. The award also serves as a mechanism to strengthen the PI's mentorship capabilities.		
K24 HD 047667 (Lieu) NICHD	7/01/04 – 6/30/09 \$128,633	0.48 calendar 40%
Enhancing prevention for children in diverse populations This mid-career investigator award in patient-oriented research supports Dr. Lieu's time for mentoring beginning investigators and will add new activities to an ongoing study on racial/ethnic disparities in medication use by children with persistent asthma.		
R01 HL 075504 (Gillman) NIH	8/01/04 – 4/30/09 \$460,889	0.24 calendar 20%
Maternal fatty acids, child obesity and asthma immunity In this expansion of Project Viva, a prospective longitudinal cohort study of pregnant women and children, our goal is to examine associations of maternal gestational fatty acid intake, fatty acid levels in offspring blood, fetal growth, and postnatal weight status with markers of allergy and inflammation at the age of 3 years.		
R01 HD 050966 (Gillman) NIH	8/22/05 – 6/30/10 \$394,738	0.54 calendar 45%
Improving primary care to prevent childhood obesity The overall goal of this research is to assess an innovative, sustainable primary care practice change intervention to prevent obesity among young children. To achieve this goal, we will conduct a cluster-randomized controlled trial in 10 pediatric practices of a large multi-site group practice in eastern Massachusetts. The trial will include 400 children age 2-5 years at elevated risk of obesity based on their and their parents' body mass indexes. The primary aim is to assess the extent to which the intervention, compared with the usual care control condition, reduces change in body mass index over a 6-month intervention and 2-year follow-up period.		
P01 CD 000260 (Platt) CDC	9/30/05 – 9/29/08 \$101,648	1.20 calendar 10%
Public Health Information Center of Excellence: Enhancing public health through electronic medical and personal health records The center will link Electronic Medical Records (EMRs), Personally Controlled Health Records (PCHRs), and electronic public health reporting and communication systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities to build on existing infrastructure to enhance communications to improve public health practices.		
U01 GM 076672 (Platt) NIGMS	2/01/06 – 1/31/11 \$3,001,609	1.20 calendar 10%
Modeling health systems infectious disease data This project will develop models for early detection and monitoring of infectious disease outbreaks. These models will be applied at different geographical scales, from individual wards of a single hospital to a whole country, as well as for different data specificity from very general symptoms to microbial disease strains and antimicrobial resistance profiles.		

ACTIVE (cont.)

R01 HD 034568 (Gillman)

7/01/06 – 6/30/10

0.96 calendar

NIH

\$700,109

Pre- and peri-natal predictors of childhood obesity

The aim of this prospective longitudinal cohort study of pregnant women and their children is to examine the roles of prenatal dietary and hormonal factors, infant feeding, and postnatal growth in the development of obesity and related disorders at 7 years of age in Project Viva.

R01 AI 066304 (Finkelstein)

8/01/06 – 7/31/10

0.24 calendar

NIH

\$494,303

Post-PCV pneumococcal population genetics and resistance

This study will 1) measure trends in carriage of *Streptococcus pneumoniae* in a multi-community sample of young children following introduction of pneumococcal conjugate vaccine, including changes in prevalence, serotypes carried, and serotype-specific antibiotic resistance; 2) Test competing hypotheses to account for in pneumococcal population structure following PCV7 introduction; and, 3) Determine if previously documented risk factors for carriage of *S. pneumoniae* (overall) and penicillin non-susceptible *S. pneumoniae* continue to predict carriage in the post-PCV7 era.

R21 DK 073739 (Rich-Edwards)

9/30/06 – 8/31/08

0.48 calendar

NIH

\$72,597

Lactation and diabetes risk factors in women

This study will examine the associations of lactation duration with levels of insulin resistance at 3 years postpartum.

R01 PH 000032 (Kleinman)

9/30/06 – 9/29/08

1.20 calendar

NIH

\$496,499

Data evaluation for early disease outbreak detection

This project evaluates and compares the efficacy of different health services data sources for early disease outbreak detection, including telephone inquiries, ambulatory care visits, emergency department visits, laboratory test requests and results, radiology tests, hospitalizations, drug prescriptions and drug dispensing.

R01 HL 064925 (Gillman)

5/15/07 – 3/31/11

0.48 calendar

NIH

\$657,580

Maternal vitamin D, adiposity in early life, and risk of childhood asthma

The overall goal of this proposal is to examine associations of maternal and child nutritional status with development of asthma-related outcomes by the age of 7 years.

(Lazarus)

7/01/07 – 6/30/09

0.24 calendar

AHRQ

\$500,000

ESP: VAERS

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). We will use electronic medical records available from all ambulatory care encounters in a large multi-specialty practice to achieve this goal.

ACTIVE (cont.)

R18 HS 017201 (Simon) 9/01/07 – 6/30/10 0.48 calendar
 AHRQ \$225,000

Improving laboratory monitoring in community practices: A randomized trial
 Medication errors occur frequently among patients in the ambulatory setting and cause many preventable adverse drug events; thus, they constitute an important target for patient safety and quality improvement. We propose a community-based randomized controlled trial of clinical-decision support to improve laboratory monitoring of medication use and a results management program to improve the timely follow-up of abnormal laboratory tests. This practical clinical trial will evaluate the effectiveness of promoting clinicians' use of commercially available healthcare information technology to improve medication safety in the ambulatory care setting.

R01 ES 016314 (Oken) 4/01/08 – 2/28/12 0.60 calendar
 NIH \$258,028

Effects of prenatal diet and mercury exposure on child behavior and development
 The goals of this project are to study associations of maternal fish intake and blood levels of mercury, n-3 fatty acids, and selenium during pregnancy with child cognition and behavior at age 7 years.

PENDING

R01 (Gillman) 7/01/08 – 6/30/12 0.60 calendar
 NIH \$250,000

Limiting weight gain in overweight pregnant women: Effects on mother and child
 The overall goal of this proposal is to assess the effects of an intervention to limit excessive gestational weight gain among overweight and obese pregnant women on markers of adiposity and cardio-metabolic risk in mother, fetus, and newborn.

(Taveras) 7/01/08 – 6/30/09 0.36 calendar
 CDC \$50,000

Early child feeding patterns and risk of childhood obesity: Longitudinal analyses of Project Viva
 To examine the longitudinal relationship between parental control of infant feeding, in particular restriction and pressure to eat, with measures of overweight and adiposity at age 3 years; and to examine if maternal prenatal concern about her child's future weight and eating is associated with the use of controlling and restrictive practices in early childhood and with obesity and adiposity at age 3 years.

R01 (Mandl) 10/01/08 – 9/30/11 0.60 calendar
 NIH \$43,554

Informatics-enabled transitions: Capacitating care of complex pediatric patients
 This project advances a powerful model of using a personally controlled health record (PCHR) for process and information integration across ambulatory settings and a health plan. The patient and family-centered technology facilitates the chronic care model and capacitates the medical home to provide high quality care across populations of complex patients during high risk transitions.

PENDING (cont.)

G13 (Kleinman)

12/01/08 – 11/30/10 1.80 calendar

NIH

\$50,000

SAS/R dictionary for health researchers

The product of this project will be a dictionary that will contain instructions for doing tasks common to statistical analysis of public health data in the two most important statistical software packages. Currently users of these packages find it difficult to transfer their knowledge from one system to another, limiting their analyses and making them less productive. Since much medical advancement depends on statistical analysis, the book will enable quicker and more accurate advancement by making statistical analysis more productive and more accurate.

OVERLAP

Should additional grants be funded during the award period of currently active grants, I will reduce effort on one or more to ensure that my total effort does not exceed 12.00 calendar person months.

OTHER FINANCIAL SUPPORT

(b)(6)

ACTIVE SUPPORT

801HK000016-03 (Platt) 9/30/2007 – 9/29/2008
CDC Center of Excellence in PHI Center \$1,467,013
2.4 Person-months

Enhancing Public Health Through Electronic Medical and Personal Health Records

This Center of Excellence in Public Health Informatics will be a partnership of three entities that have expertise in design and use of Electronic Medical Records, Personally Controlled Health Records, and electronic public health reporting and communication systems. The center will link these disparate systems by developing scalable information infrastructures to enable information exchange between individuals, health care providers and public health authorities

Role: Co-Investigator, *Electronic Support for Public Health (ESP) Project*

1R18HS017045 (Lazarus) 10/1/2007 – 9/30/2008
ESP VAERS \$449,809
4.20 Person-months

Electronic Support for Public Health - Vaccine Adverse Events Reporting System (ESP: VAERS)

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS).

Role: Co-Investigator

For New and Renewal Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED
For Non-competing Progress Reports (PHS 2590) – Submit only Active Support for Key Personnel

PHS 398/2590 OTHER SUPPORT

PLATT, RICHARD
ACTIVE

1U01 GM76672-03 (Platt)	2/1/2006 – 1/31/2011	1.80 calendar
NIH	\$552,777	15%
Modeling Health System Infectious Disease Data (MIDAS)		

The major goal of this study will be the development of models for the early detection of infectious disease outbreaks and for monitoring an outbreak after it has been detected.

8P01HK000016-03 (Platt)	9/30/2005 – 9/29/2009	20% 2.40 calendar
CDC	\$1,669,013	
Public Health Informatics Center of Excellence		

This Center of Excellence in Public Health Informatics will be a partnership of three entities that have expertise in design and use of Electronic Medical Records, Personally Controlled Health Records, and electronic public health reporting and communication systems.

200-2002-00732 (Platt)	9/20/2003 – 9/19/2012	4% 0.48 calendar
CDC via AHIP	\$884,345	
Vaccine Safety Surveillance and Assessment (VSD2)		

The major goal of this project is to study ongoing and emerging topics on the potential association of vaccines with adverse outcomes.

5U01 CI000344-03 (Platt)	2/1/2006 – 9/19/2011	15% 1.8 calendar
CDC	\$298,466	
Eastern Massachusetts Prevention Epicenter Program		

Continuation of the work to develop population-based methods for identifying and preventing healthcare-associated infections (nosocomial infections). This work is being conducted by a consortium of the three largest HMOs and two large integrated delivery systems in Massachusetts.

HHSF22320051001 (Platt)	9/23/2005 – 9/22/2010	7% 0.12 calendar
FDA	\$562,000	
HMORN CERT Epidemiologic Studies of Adverse Effects of Marketed Drugs		

This study will provide data and resources that can be used to rapidly evaluate safety and utilization patterns of marketed prescription drugs and provide a mechanism for collaborative pharmacoepidemiologic research to protect the public's health.

HHSA290200500331 (Platt)	08/29/2005 – 08/28/2010	2% 2.40 calendar
AHRQ	\$1,800,000	
The DECIDE Network		

The overall aim of this proposal is to use the health plans' defined populations, providers, delivery systems, and unique data resources to develop information about therapeutic effectiveness within typical clinical settings.

HHSF23200710017C (Platt)

FDA

09/30/2007 – 09/29/2008 17th 0.10 calendar

\$150,000

Using Electronic Health Data for Influenza Vaccine Safety: New Methodologies and Considerations (FLUII)

The goal of this project is to use real-time vaccine safety surveillance to plan for a pandemic.

MTA53 (Platt)

01/01/2007 – 12/31/2009 (b)(4)

(b)(4)

(b)(4)

Risk of Guillain-Barré following meningococcal conjugate (MCV4) vaccination

This project is a multi-site retrospective cohort study of the relationship between immunization with tetravalent meningococcal conjugate vaccine (MCV4) and Guillain-Barré syndrome (GBS) in adolescents over the 42-month period of March 1, 2005 to August 31, 2008.

1R18HS017045 (Lazarus)

9/30/2007 – 9/30/2009 39th .36 calendar

AHRQ

\$499,809

Electronic Support of Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)

Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Approved reports will be securely transferred to the CDC VAERS program as electronic messages in an interoperable health data exchange format (HL7).

HHS NCRR (Nadler)

5/19/2008 – 4/30/09 17th

2.0 calendar

NIH

\$22,148,106

CTSA – Developing Future Leaders of Clinical and Translational Research.

Harvard joins the National Institutes of Health's Clinical and Translational Science Award (CTSA) consortium. Creating a unique network of medical research institutions across the nation, the consortium is working to reduce the time it takes for laboratory discoveries to become treatments for patients and to engage communities in clinical research efforts. It also is fulfilling the critical need to train the next generation of clinical and translational researchers. The consortium is led by the National Center for Research Resources (NCRR), a part of the NIH.

PENDING:

None

OVERLAP:

None

Principal Investigator/Program Director LAZARUS, Ross

PROGRESS REPORT SUMMARY	GRANT NUMBER 1 R18 HS017045-02	
	PERIOD COVERED BY THIS REPORT	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR: Lazarus, Ross, MBBS, MPH	FROM 09/30/2007	THROUGH 09/29/2008
APPLICANT ORGANIZATION Harvard Pilgrim Health Care		
TITLE OF PROJECT (Repeat title shown in Item 1 on first page) Electronic Support for Public Health – Vaccine Adverse Event Reporting System (ESP:VAERS)		
A. Human Subjects (Complete Item 6 on the Face Page) Involvement of Human <input checked="" type="checkbox"/> No Change Since Previous <input type="checkbox"/> Change		
B. Vertebrate Animals (Complete Item 7 on the Face Page) Use of Vertebrate Animals <input checked="" type="checkbox"/> No Change Since Previous <input type="checkbox"/> Change		
C. Select Agent Research <input checked="" type="checkbox"/> No Change Since Previous <input type="checkbox"/> Change		
D. Multiple PI Leadership Plan <input checked="" type="checkbox"/> No Change Since Previous <input type="checkbox"/> Change		
SEE PHS 2590 INSTRUCTIONS.		

WOMEN AND MINORITY INCLUSION: See PHS 398 Instructions. Use Inclusion Enrollment

Vaccination programs are a cornerstone of modern public health. Public and professional confidence in health care quality depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of ESP:VAERS is to improve the quality of health care by improving the quality of physician-initiated adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). ESP:VAERS is on its way towards being implemented and tested in collaboration with Atrius Health, the same multi-site, multi-specialty medical practice with over 600,000 patients where ESP is already deployed. We anticipate that ESP:VAERS will lead to better measurement of the safety profile of vaccines, and improve available measures of the quality and safety of existing and future vaccination programs in health care.

A. Specific Aims – no change

B. Studies and Results

Aim 1: *Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.*

During this first-year, the majority of effort has been focused upon the consultative development, refinement, validation & testing of adverse event (AE) criteria for identifying case histories that might be suggestive of an adverse effect following vaccination. In collaboration with our Atrius Health, Brighton Collaboration and CDC partners, we have identified the specific data elements needed, and developed functioning representations of adverse event (AE) criteria definition and case detection algorithms. In addition to review by the internal CDC Brighton Collaboration liaison, our AE criteria has also received review & comment from the CDC's Clinical Immunization Safety Assessment (CISA) Network. We can identify and generate HL7 messages for cases of fever within arbitrary periods of vaccination, and those messages are currently in validation testing as we extend the complexity of AE algorithms.

The consultation process allowed us to refine the design of our systems and computer code to the agreed specifications. We have a functioning use case specification and can quickly extend this to the range of conditions. Testing and validation are underway, and development and testing of the more complex case detection algorithms is underway.

Aim 2: *Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).*

With help from our CDC partners, we have reviewed and agreed upon an initial HL7 specification describing the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project. Sample test messages have been supplied, and we have PHINMS functioning between Harvard and Constella.

We have established PHINMS communication and have code producing VAERS HL7 reports for fever within 4 days of a vaccination as a test case. In addition, we have ironed out detailed issues having to do with multiple vaccinations received during one office visit, and multiple AE's arising from single or multiple vaccination events. Progress with this aim is underway & currently in test-phase. We expect to begin submission to VAERS within the next 3 months.

Aim 3: *Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.*

As ESP:VAERS is still in the programming/implementation stages we have yet to have an opportunity to perform these performance assessments. Measurement of system impact will be measures via a cluster randomized trial, which is expected to begin during the 2nd to 3rd quarters of Year 2.

Aim 4: *Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.*

The ESP:VAERS case-management website is currently under construction. This activity cannot be completed until the more fundamental code is tested and stable since the detection algorithms will drive the web site. The existing web site at <http://esphealth.org> will serve as the prototype as planned.

C. Significance

Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems, to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Every patient receiving a vaccine will be automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions will be evaluated for values suggestive of an adverse event. When a possible adverse event is detected, it will be recorded, and the appropriate clinician will be notified electronically. Clinicians will be able to preview a pre-populated report, with information from the electronic medical record about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment about whether they wish to send a report. Clinicians will have the option of adding free-text comments to pre-

populated VAERS reports, or to document their decision not to send a report. Approved reports will be securely transferred to VAERS as electronic messages in an interoperable health data exchange format (HL7).

As the majority of ESP:VAERS activity during this quarter has been related to logistical / programming activity in order to prepare for system implementation, there has been no data collection that would inform Key Findings at this time.

The ESP:VAERS project is of great interest to a number of external groups. An ESP:VAERS introductory poster was presented at the CDC's annual Vaccine Safety Datalink (VSD) in April, 2008.

Year 1 Publications & Presentations

- Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. *Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS*. The CDC Vaccine Safety Datalink (VSD) Annual Meeting. Atlanta, GA; April, 2008. ([see appendix](#))

D. Plans

In the coming year, we plan to evaluate the ESP:VAERS system by comparing adverse event findings to those in the Vaccine Safety Datalink project, and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

E. Project-Generated Resources

Once code is tested, finalized & ready to share, we plan to modify the existing ESP resource center (<http://esphealth.org>) , and in particular, the Subversion repository available at <http://esphealth.org/trac/ESP/browser/trunk/ESP> to include the new ESP:VAERS source code and documentation.



Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS



R. Lazarus¹, M. Klompas¹, X. Hou², F.X. Campion¹, J. Dunn¹, R. Platt¹

¹)Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA

²) Channing Laboratory, Boston, MA

Introduction

Vaccination programs form a cornerstone of modern, preventive public health practice since they permit effective control of a wide variety of important, preventable communicable diseases. Public and professional confidence in the safety of vaccination programs is an important element for ensuring that routine vaccination is widely supported and encouraged.

The CDC and FDA Vaccine Adverse Event Reporting System (VAERS) is the national resource for evaluation of adverse event reports. VAERS accepts notifications in both paper and electronic forms, but all of these reports require transcribing demographic and clinical information by hand from the clinical records to the report, whether paper or electronic form. Manual reporting involves substantial opportunity costs, requiring that a busy clinician divert time and effort from providing direct clinical care. As a result, it seems unlikely that manual reporting can ever provide complete and comprehensive data on all clinically relevant adverse events following vaccination. Electronic medical record (EMR) systems are increasingly used in ambulatory care, and offer an important resource for improving public health surveillance and reporting through automation, by decreasing the reporting burden on busy clinicians.

Earlier VSD Project

As part of the VSD study **Elicited Surveillance and Reporting of Vaccine Adverse Events**, an alerting and reporting system for vaccine adverse events was implemented within the EpicCare EMR at Harvard Vanguard Medical Associates.

Features:

- Real-time alerts to clinicians within the EMR
- Clinician input on the potential adverse event while the event is fresh
- Clinician decision on whether to submit the report to VAERS or not

Limitations:

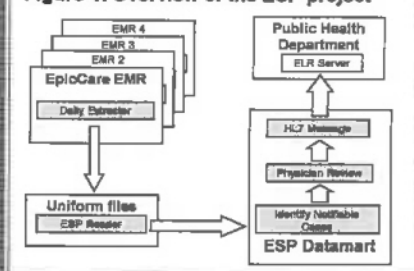
- Inability to implement electronic submission to VAERS (requires manual submission)
- Requirement for Epic support and programming

The ESP project

ESP:VAERS is a collaboration involving researchers from DACP and CDC, funded by the AHRQ, to develop criteria and algorithms to identify important adverse events in ambulatory care EMR data, and to format and securely send electronic VAERS reports directly to the CDC.

ESP:VAERS is an extension of the Electronic Support for Public Health (ESP) project, an automated system using EMR data to detect and securely report cases of notifiable disease to a local public health authority. ESP has been deployed in Massachusetts for more than a year and provides a ready-made platform for automatically converting clinical, laboratory, prescription, and demographic data from almost any EMR system into database tables on a completely independent server, physically located and secured by the same logical and physical security as the EMR data itself. This distributed model for surveillance is far more acceptable to organizations responsible for securing protected health information than allowing their data to leave their direct control for use in more centralized surveillance models. The ESP project is part of the PHI Center of Excellence at Harvard Medical School, which is sponsored by the CDC's National Center for Public Health Informatics (8P01HK00015-03).

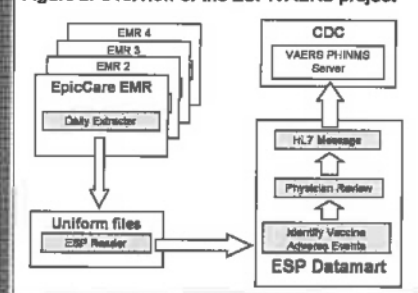
Figure 1: Overview of the ESP project



ESP:VAERS Design

The data flow required for the ESP:VAERS system is already available as part of the ESP system (on the left side of Figures 1 and 2). The system is constructed to automatically collect a regular daily extract of all transactions from the host EMR, and convert them into relational database tables on the independent ESP server, located in the host EMR computing facility.

Figure 2: Overview of the ESP:VAERS project



New elements required to build ESP:VAERS are:

1. Criteria and algorithms for identifying potential adverse events following (eg within 30 days) vaccination
2. A mechanism for feeding potential adverse event information back to the vaccinating clinician where a VAERS report may be required, and a mechanism for the clinician to indicate whether a report should be sent if there is any uncertainty
3. An agreed specification for the electronic report format
4. A secure messaging system for electronic reports to be sent

Progress to date

In collaboration with the CDC and representatives from the Brighton Collaboration, a draft set of specifications for reporting and algorithms along with HL7 criteria have been agreed upon. The informatics team is currently developing and testing software to facilitate messaging and report formatting, which will be securely transmitted directly to VAERS via the CDC PHINMS system.

Conclusions

EMR data will allow for the creation and fully automated transmission of VAERS reports for the most important adverse events following vaccination. When a potential adverse event is detected, input from the clinician will be needed to ensure that only relevant events are reported. However, once the clinician has reviewed the clinical data and made a decision, the VAERS report will be formatted and sent directly to the CDC without any further manual intervention. This new reporting mechanism is expected to reduce average health care practice VAERS manual reporting intervals, which currently range from 16 to 38 days.

By prospectively identifying potential adverse events for clinician review and obviating the manual transcription step currently required to prepare and submit VAERS reports, we believe that the comprehensiveness and reliability of adverse event reporting after vaccination will be substantially improved. As part of the ESP:VAERS project, we will conduct a randomized trial within participating practices to evaluate this hypothesis.

We welcome potential collaborators wishing to evaluate our systems. Like ESP (see <http://esp.health.org>), ESP:VAERS software and documentation will all be made readily available under an approved Open Source license as soon as it is stable and reliable. Please contact Julie Dunn (Julie_Dunn@harvardpilgrim.org) for further information.

Program Director/Principal Investigator (Last, first, middle): LAZARUS, Ross

GRANT NUMBER
1P01HK000016-04

CHECKLIST - HPHC

1. PROGRAM INCOME (See instructions.)

All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. 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 of the PHS 398, and listed in Part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after the Progress Report (Form Page 5).

3. FACILITIES AND ADMINISTRATIVE (F&A) COSTS

Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS Agency Cost Advisory Office.

F&A costs will **not** be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

☒ DHHS Agreement dated: 1/02/08 ☐ No Facilities and Administrative Costs Requested.
☐ No DHHS Agreement, but rate established with _____ Date _____

CALCULATION*

Entire proposed budget period: Amount of base \$ (b)(4) x Rate applied (b)(4) % = F&A costs \$ (b)(4)
Add to total direct costs from Form Page 2 and enter new total on Face Page, Item 8b.

*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.):

SENIOR/KEY PERSONNEL REPORT

GRANT NUMBER

1 R01 HS017045-02

Place this form at the end of the signed original copy of the application. Do not duplicate.

All Key Personnel for the Current Budget Period (do not include Other Significant Contributors)

Name	Degree(s)	SSN (last 4 digits)	Role on Project (e.g. PD/PI, Res. Assoc.)	Months Devoted to Project		
				Cal	Acad	Summer
Ross, Lazarus	MBBS, MPH		Principal Investigator	2.40		
(b)(6)	PhD		Co-Investigator	1.08		
	MD		Co-Investigator	1.20		
	ScD		Co-Investigator	0.60		
	MD, MPH		Co-Investigator	3.60		
	MD, MSc		Co-Investigator	0.36		

KEY
PERSONS



Harvard Pilgrim Health Care

25 September 2007

Ross Lazarus
Director of Bioinformatics
Channing Laboratory, Brigham & Women's Hospital
181 Longwood Avenue
Boston, MA 02215

Dear Dr. Lazarus,

Your study, entitled **Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP: VAERS)** and funded by the **Agency for Healthcare Research and Quality (AHRQ)**, has been approved by the Harvard Pilgrim Health Care Office of Sponsored Programs.

As the HPHC Principal Investigator your responsibilities include:

- being aware of and adhering to HPHC's research policies,
- representing the study within HPHC and serving as the principal contact for the study,
- obtaining all required approvals,
- ensuring the study is conducted as stated in the approved protocol,
- assuring that all personnel involved in the study adhere to Harvard Pilgrim's policies regarding confidentiality, scientific integrity, conflict of interest, use of human subjects, and HIPAA privacy rule compliance.
- assuring that all information provided will be used only for the purpose described in this proposal. Any other uses will require the written approval of the HPHC Office of Office of Sponsored Programs,
- reporting any breaches of Harvard Pilgrim's confidentiality or HIPAA privacy policies (or any other policies) to OSP and Harvard Pilgrim's Privacy Officer..

Please contact the office if you have any questions or need any assistance.

Sincerely,

Dennis Ross-Degnan, Sc.D.
Director of Research

Harvard Pilgrim Health Care
Office of Sponsored Programs
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Telephone (617) 509-9843 • Fax (617) 509-9859



Harvard Pilgrim Health Care

November 13, 2007

HPHC IRB#00000882

Ross Lazarus, MBBS, MPH, Mmed
DACP
133 Brookline Ave
Boston, MA 02215

NOTICE OF HUMAN STUDIES COMMITTEE ACTION

HSC#:	3.10.07
Study:	Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESP:VAERS)
Item:	Response to Review
Risk Assignment:	Minimal-46.110(b)
Type of Review:	Subcommittee
Decision:	Study Approved
Approval Date:	October 18, 2007
Expiration Date:	October 17, 2008
Next Review Due:	September 1, 2008

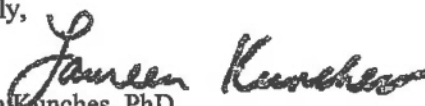
Comments: The subcommittee has reviewed the minor revisions requested by the HSC and approves activation of the study. The conditions for a waiver of authorization and consent have been met and approved for the use and disclosure of PHI from the HealthOne database. A data use agreement is required for use or disclosure of limited datasets.

Please retain this letter with your research records. Research records include all Institutional Review Board submissions and responses which must be kept in the principal investigator's file for a minimum of six (6) years after completion of the study.

Any changes, modifications, or amendments to the study or study procedures require prior written approval from the Human Studies Committee (HSC). Serious adverse events or unanticipated problems involving risks to subjects or others must be reported immediately by telephone to the HSC at 617 509-9587, followed by a written report. The HPHC Human Studies Committee Policies and Procedures and forms are available for reference on the HPHC website (<http://www.harvardpilgrim.org>).

Please remember to use the HSC file number on all documents or correspondence relating to your study.

Sincerely,


Laureen Kunches, PhD
Chair
Human Studies Committee

Harvard Pilgrim Health Care
Office of Sponsored Programs
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Telephone (617) 509-9843 • Fax (617) 509-9859

** human protocol details

Protocol Title: Electronic Support for Public Health: Vaccine Adverse Event Reporting System (ESPL VAERS)
Protocol Number: 2006P000890 Responsible IRB: BWH
PI Name: Ross Lazarus Sponsor Name: Harvard Pilgrim Hlth Care
Approval Date: 05/25/2006 Expiration Date: N/A
Overall Status: Not Human Research
Protocol Administrator: (b)(6) Phone: (b)(6)
Email: (b)(6)@partners.org

** initial review

[View Review Details](#)

dt received	board	review type	meeting date	status date	status	response date	notes
* 5/8/2006	IRB	Not Human Research	6/21/2006	5/25/2006	Approved	N/A	*
5/8/2006	IRB	Not Human Research	6/21/2006	5/9/2006	Pending	N/A	

** study staff

name	position	gets mail
(b)(6)	L-Other	No
	L-Other	Yes

cr#	date received	board	review type	meeting date	status date	status	response date	notes
No records returned for this category								

amend# - (sponsor#)	date received	board	review type	status date	status	response date	notes
1	9/20/2007	IRB	Expedited	9/26/2007	Approved	N/A	

** adverse events

subject ID	date received	board	review type	status date	status	response date	notes
No records returned for this category							

** other events

other event #	date received	board	review type	status date	status	response date	notes
No records returned for this category							



DEPARTMENT OF HEALTH & HUMAN SERVICES

Program Support Center
Financial Management Service
Division of Cost Allocation

26 Federal Plaza-Room 41-122
New York, New York 10278
PHONE: (212)-264-2069
FAX: (212)-264-5478

January 2, 2008

Ms. Marie Montgomery
Senior Vice President/Controller
Harvard Pilgrim Health Care, Inc.
93 Worcester Street
Wellesley, MA 02481-

Dear Ms. Montgomery:

A negotiation agreement is being faxed to you for signature. This agreement reflects an understanding reached between your institution and a member of my staff concerning the rates or amounts that may be used to support your claim for costs on grants and contracts with the Federal Government. The agreement must be signed by a duly authorized representative of your institution and faxed to me; retain a copy for your file. Our fax number is (212) 264-5478. We will reproduce and distribute the agreement to awarding agencies of the Federal Government for their use.

Requirements for adjustments to costs claimed under Federal Grants and Contracts resulting from this negotiation are dependent upon the type of rate contained in the negotiation agreement. Information relating to these requirements is enclosed.

A proposal encompassing all activities of your institution together with the required supporting information must be submitted to my office at the address shown on page 2 for each fiscal year your institution claims costs under grants and contracts awarded by the Federal Government. This proposal is due within six months after the close of your fiscal year. Therefore, a proposal for fiscal year ending December 31, 2008 will be due in my office not later than June 30, 2009. The proposal will be used to establish rates/amounts for the fiscal year subsequent to the last period covered by an approved final, fixed, or predetermined rates(s). Failure to submit a timely proposal will be interpreted as a forfeiture of reimbursement for indirect costs. Therefore, unless a proposal is received by June 30, 2009, future awards made by the Department of Health and Human Services will be for direct costs only and will not provide for the recovery of costs contained in this agreement. In addition, the costs claimed against awards already made may be subject to disallowances.

Ms. Marie Montgomery

- 2 -


January 2, 2008

Your proposal and relevant correspondence should be addressed to:

Department of Health and Human Services
Division of Cost Allocation
26 Federal Plaza, Room 41-122
New York, New York 10278
(212) 264-1823

If you are unable to submit your proposal by the prescribed date, you may request an extension. This request must be submitted prior to the due date of the proposal and must contain a justification for the extension and the date the proposal will be submitted.

Sincerely,


Robert I. Aaronson
Director, Division of
Cost Allocation

PLEASE SIGN AND FAX A COPY OF THE NEGOTIATION AGREEMENT

JAN. 2. 2008 1:30PM

NO. 0296 P. 4/6

ORIGINAL

NONPROFIT RATE AGREEMENT

EIN #: 1042452600A1

DATE: January 2, 2008

ORGANIZATION:
Harvard Pilgrim Health Care, Inc.
93 Worcester Street
Wellesley MA 02481-

FILING REF.: The preceding
Agreement was dated
November 26, 2007

The rates approved in this agreement are for use on grants, contracts and other agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES*

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

TYPE	EFFECTIVE PERIOD		RATE (%)	LOCATIONS	APPLICABLE TO
	FROM	TO			
PRED.	01/01/07	12/31/07	(b)(4)	On-Site	Research (A)
PRED.	01/01/07	12/31/07		Off-Site	Research (A)
PRED.	01/01/08	12/31/09		On-Site	Research (B)
PRED.	01/01/08	12/31/09		Off-Site	Research (B)
PROV.	01/01/10 UNTIL AMENDED		Use same rates and conditions as those cited for fiscal year ending December 31, 2009.		

(A) *Base: Total direct costs excluding capital expenditures (buildings, individual items of equipment; alterations and renovations) and subawards.

(B) *Base: Total direct costs excluding capital expenditures (building, individual items of equipment; alterations and renovations), and that portion of each subaward in excess of \$25,000.

ORGANIZATION:
Harvard Pilgrim Health Care, Inc.

AGREEMENT DATE: January 2, 2008

SECTION II: SPECIAL REMARKS

TREATMENT OF PAID ABSENCES:

Vacation, holiday, sick leave pay and other paid absences are included in salaries and wages and are claimed on grants, contracts and other agreements as part of the normal cost for salaries and wages. Separate claims for the costs of these paid absences are not made.

Treatment of Fringe benefits: Fringe benefits applicable to direct salaries and wages are treated as direct costs, except incentive compensation, which is treated as an indirect cost.

Equipment means an article of nonexpendable tangible personal property having a useful life of more than one year, and an acquisition cost of \$1,000 or more per unit.

ORGANIZATION:
Harvard Pilgrim Health Care, Inc.

AGREEMENT DATE: January 2, 2008

SECTION III: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions:
(1) Only costs incurred by the organization were included in its indirect cost pool as finally accepted; such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) The same costs that have been treated as indirect costs are not claimed as direct costs; (3) Similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from indirect to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the authority in Office of Management and Budget Circular A-122 Circular, and should be applied to grants, contracts and other agreements covered by this Circular, subject to any limitations in A above. The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing indirect costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of indirect costs allocable to these programs.

BY THE ORGANIZATION:

Harvard Pilgrim Health Care, Inc.

(ORGANIZATION)

(SIGNATURE)

Marie Montgomery

(NAME)

SVP, Controller & Treasurer

(TITLE)

January 3, 2008

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

(SIGNATURE)

Robert I. Aaronson

(NAME)

DIRECTOR, DIVISION OF COST ALLOCATION

(TITLE)

January 2, 2008

(DATE) 0558

HHS REPRESENTATIVE: Michael Stanco

Telephone: (212) 264-2069

AUG. 27. 2007 12:20PM

NO. 3762 P. 2



DEPARTMENT OF HEALTH & HUMAN SERVICES

Program Support Center
Financial Management Service
Division of Cost Allocation28 Federal Plaza-Room 41-122
New York, New York 10278
PHONE: (212) 264-2069
FAX: (212) 264-5478

August 27, 2007

Ms. Barbara E. Bierer, M.D.
Senior Vice President, Research
Brigham and Women's Hospital
Office of Research Administration
75 Francis Street
Boston, MA 02115

Dear Dr. Bierer:

A negotiation agreement is being faxed to you for signature. This agreement reflects an understanding reached between your institution and a member of my staff concerning the rates or amounts that may be used to support your claim for costs on grants and contracts with the Federal Government. The agreement must be signed by a duly authorized representative of your institution and faxed to me; retain a copy for your file. Our fax number is (212) 264-5478. We will reproduce and distribute the agreement to awarding agencies of the Federal Government for their use.

Requirements for adjustments to costs claimed under Federal Grants and Contracts resulting from this negotiation are dependent upon the type of rate contained in the negotiation agreement. Information relating to these requirements is enclosed.

In consideration of this agreement, the following was agreed to:

1. The following carry-forward amounts are from the finalization of fringe benefits for fiscal year ended September 30, 2006. The carry-forwards are to be included with your actual fringe benefit rate calculations for the fiscal year specified below:

Fringe Benefit RateFYE 09/30/08

Professional
Non-Professional
Intern, Residents,
and Fellows

(b)(4)

() Denotes Over-Recovery

2. The fringe benefit proposal for fiscal year ending September 30, 2007 is due to be submitted to our office by March 31, 2008.

AUG. 27. 2007 12:20PM

NO. 3762 P. 3

Ms. Barbara E. Bierer, M.D.

-2-

August 27, 2007

A proposal encompassing all activities of your institution together with the required supporting information must be submitted to my office at the address shown below for each fiscal year your institution claims costs under grants and contracts awarded by the Federal Government. This proposal is due within six months after the close of your fiscal year. Therefore, a proposal for fiscal year ending September 30, 2007 will be due in my office not later than March 31, 2008. The proposal will be used to establish rates/amounts for the fiscal year subsequent to the last period covered by an approved final, fixed, or predetermined rate(s). Failure to submit a timely proposal will be interpreted as a forfeiture of reimbursement for indirect costs. Therefore, unless a proposal is received by March 31, 2008, future awards made by the Department of Health and Human Services will be for direct costs only and will not provide for the recovery of costs contained in this agreement. In addition, the costs claimed against awards already made may be subject to disallowances.

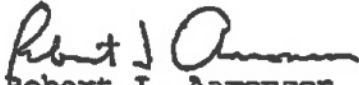
If you are unable to submit your proposal by the prescribed date, you may request an extension. This request must be submitted prior to the due date of the proposal and must contain a justification for the extension and the date the proposal will be submitted.

Your proposal and relevant correspondence should be addressed to:

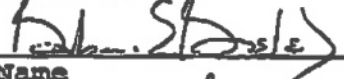
Department of Health and Human Services
Division of Cost Allocation
26 Federal Plaza, Room 41-122
New York, New York 10278
(212) 264-1823

In addition, please acknowledge your concurrence with the comments and conditions cited above by signing this letter in the space provided below and FAX (212-264-5478) it to me with the enclosed negotiation agreement.

Sincerely,


Robert I. Aaronson
Director, Division of
Cost Allocation

Enclosures
Concurrence:


Name
Title
Date 9/14/07

AUG. 27. 2007 12:20PM

NO. 3762 P. 4

HOSPITAL RATE AGREEMENT

ORIGINAL

EIN #: 1042312909A1

DATE: August 27, 2007

HOSPITAL:
Brigham And Women's Hospital
Office of Research Administration
75 Francis Street
Boston

MA 02115-

FILING REF.: The preceding
Agreement was dated
September 25, 2006

The rates approved in this agreement are for use on grants, contracts and other
agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES*RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRBD. (PREDETERMINED)

<u>TYPE</u>	<u>EFFECTIVE PERIOD</u>		<u>RATE (%)</u>	<u>LOCATIONS</u>	<u>APPLICABLE TO</u>
	<u>FROM</u>	<u>TO</u>			
PRED.	10/01/06	09/30/08	(b)(4)	On-Site	Research
PRED.	10/01/06	09/30/08		Off-Site	Research
PROV.	10/01/08	UNTIL AMENDED	Use same rates and conditions as those cited for fiscal year ending September 30, 2008.		

*Base: Total direct costs less items of equipment, major subcontracts, alterations
and renovations, animal charges, hospitalization and other fees related to patient
care.

SEP. 12. 2007 11:49AM

NO. 3853 P. 2

HOSPITAL:Brigham And Women's Hospital
Office of Research Administration

AGREEMENT DATE: August 27, 2007

SECTION I: FRINGE BENEFITS RATES**

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

TYPE	EFFECTIVE PERIOD		RATE(%)	LOCATIONS	APPLICABLE TO
	FROM	TO			
FIXED	10/01/07	09/30/08	(b)(4)	All	Professional
FIXED	10/01/07	09/30/08		All	Non-Professional
FIXED	10/01/07	09/30/08		All	Intern&Residents, Fel
PROV.	10/01/08	UNTIL AMENDED	Use same rates and conditions as those cited for fiscal year ending September 30, 2008.		

**DESCRIPTION OF FRINGE BENEFITS RATE BASE:
Salaries and wages.

AUG. 27. 2007 12:20PM

NO. 3762 P. 6

HOSPITAL:Brigham And Women's Hospital
Office of Research Administration

AGREEMENT DATE: August 27, 2007

SECTION II: SPECIAL REMARKS**TREATMENT OF FRINGE BENEFITS:**

The fringe benefits are charged using the rate(s) listed in the Fringe Benefits Section of this Agreement. The fringe benefits included in the rate(s) are listed below.

TREATMENT OF PAID ABSENCES:

Vacation, holiday, sick leave pay and other paid absences are included in salaries and wages and are claimed on grants, contracts and other agreements as part of the normal cost for salaries and wages. Separate claims for the costs of these paid absences are not made.

1. The fringe benefit rates include the following:

FICA, Pension, Disability, Group Life Insurance, Time Accrual, Training Costs, Uniforms, Workers Compensation, Unemployment, FITICORP, MBTA Subsidy, Employee Allowances/Activities/Awards, FSA Admin., Parking Subsidy, Cafeteria Subsidy, Tuition Benefit, Amortized Past Service Exp., (ESL/Sick Lv./Pension), Human Resources, Health Ins., and Dental/Vision Info., Malpractice Insurance, Home Office Fringe.

2. Off-Site Definition: For all activities performed in facilities not owned by the organization and to which rent is directly allocated to the project(s), the off-site rate will apply.**3. The following rates shall be used for research contracts performed at Brigham and Women's Hospital:**

TYPE	FROM	TO	RATE	LOCATION	BASE
Fixed	10/1/06	9/30/08	(b)(4)	On-Site	Same as in Sec.I
Prov.	10/1/08	Until Amended		On-Site	Same as in Sec.I

4. Effective October 1, 2004, equipment means an article of nonexpendable, tangible personal property having a useful life of more than one year, and an acquisition cost of \$5,000 or more per unit.

This Rate Agreement updates Fringe Benefit Rates only.

AUG. 27. 2007 12:20PM

NO. 3762 P. 7

HOSPITAL:Brigham And Women's Hospital
Office of Research Administration

AGREEMENT DATE: August 27, 2007

SECTION III: GENERAL**A. LIMITATIONS:**

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions:

- (1) Only costs incurred by the organization were included in its indirect cost pool as finally accepted; such costs are legal obligations of the organization and are allowable under the governing cost principles;
- (2) The same costs that have been treated as indirect costs are not claimed as direct costs;
- (3) Similar types of costs have been accorded consistent accounting treatment; and
- (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from indirect to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the cost principles promulgated by the Department of Health and Human Services, and should be applied to the grants, contracts and other agreements covered by these regulations subject to any limitations in A above. The hospital may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing indirect costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of indirect costs allocable to these programs.

BY THE HOSPITAL:Brigham And Women's Hospital
Office of Research Administration

(HOSPITAL)

(SIGNATURE)

(NAME)

(TITLE)

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

(SIGNATURE)

Robert I. Aaronson

(NAME)

DIRECTOR, DIVISION OF COST ALLOCATION

(TITLE)

August 27, 2007

(DATE) 6517

HIS REPRESENTATIVE: Joseph Guarnieri

Telephone: (212) 264-2069

Funding Recommendation Memo (Noncompeting Continuation)

RFA/PA Number: HS07-002

RFA/PA Title: AMBULATORY SAFETY AND QUALITY PROGRAM: ENABLING QUALITY MEASUREMENT TH

Grant Number: R18 HS17045-02

Title: Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ES

Institution: HARVARD PILGRIM HEALTH CARE, INC.

Principal Investigator: LAZARUS, ROSS **New Investigator?** No

Priority Score: **Percentile:**

Reporting Requirement: Quarterly

Project Officer: FARQUHAR, MARYBETH

Center: CP3

Budget Year	AHRQ Total Committed		Project Officer Recommended	
	Direct Costs	Total Costs	Direct Costs	Total Costs
02	\$429,713	\$499,405	\$429,713	\$499,405

Coding Selections	
Core Business:	Creation - Collecting data on and producing measures of the quality, safety, effectiveness, and efficiency of American health care and health care systems
Departmental Coding Theme:	Patient Safety, Quality, and Reducing Medical Errors
Cross Cut Code(s):	Health Information Technology
Field of Science Code:	Medical Sciences

Strategic Goal Area:	Safety/Quality
Portfolio/Program:	Health IT
Outcome Goal:	1.3.36 - Increase the number of ambulatory clinicians using electronic prescribing to over 50%

P.O. Signature:

Margaret Sargus

Date:

8/26/08

Director Signature:

J. Myers

Date:

8/26/08

Identifiable Data
Needed ?:

No

Clinical Trials Registry
?:

No

Data and Safety
Monitoring Plan ?:

Yes

Involvement of Priority
Populations:

Children, Elderly

PO Recommendation:

Recommended

PO Comments:

I recommend this application in the time and amount requested by the grantee.

PHS 398 Abstract:

DESCRIPTION (provided by the applicant): Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Vaccination programs are a cornerstone of modern public health, and are of central importance in preparedness for dealing with potential health emergencies, such as the recurrence of pandemic influenza. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. Our goal is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice will be used. Every patient receiving a vaccine will be automatically identified, and for the next 30 days their health care

diagnostic codes, laboratory tests, and medication prescriptions will be evaluated for values suggestive of an adverse event. When a possible adverse event is detected it will be recorded, and the appropriate clinician will be notified electronically. Clinicians will be able to preview a pre-populated report with information from the electronic medical record about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment about whether they wish to send a report. Clinicians will have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. Approved reports will be securely transferred to VAERS as electronic messages in an interoperable health data exchange format (HL7). We will evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

- Aims of the Project:** The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System. The applicants will apply a comprehensive information management system to the task of improving both the accuracy and timeliness of vaccination adverse reaction reporting.
- Scientific Significance:** Routine vaccination has dramatically decreased the incidence of many serious diseases, and new vaccines are becoming available to improve the quality of health care. Public and professional confidence in vaccination depends on reliable post-marketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified.
- Progress to Date:** During the first year, the majority effort has been focused on the consultative development, refinement, validation and testing of adverse event criteria for identifying case histories that might be suggestive of an adverse effect following vaccination. In collaboration with others, specific data elements were identified and used to develop functioning representations of adverse event criteria definition and case detection algorithms. At present, cases can be identified and an HL7 message for cases with fever within arbitrary periods of vaccination can be generated. These messages are currently in validation testing as the complexity of adverse event algorithms are extended and refined. In addition, the consultation process permitted refinement of the design of

the systems and the computer code which resulted in a use case specification, which may be quickly extended to a range of conditions. Testing and validation are underway, and development and testing of the more complex case detection algorithms is underway. Reviewed an initial HL7 specification that describes the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project. Sample test messages have been supplied, and there is PHINMS functioning between Harvard and Constella. Established PHINMS communication and have code producing VAERS HL7 reports for fever within 4 days of a vaccination as a test case. In addition, the detailed issues having to do with multiple vaccinations received during one office visit, and the multiple adverse events arising from single or multiple vaccination events have been worked through. It is expected that submission to VAERS will begin within the next three months. ESP: VAERS is still in programming/implementation stages, and evaluation is expected to begin during the 2-3 quarters of Year 2. The ESP: VAERS case-management website is currently under construction, and will not be completed until the more fundamental code is tested and stable since the detection algorithms will drive the website.

**Plans for Next
Performance Period:**

In the coming year, the plan is to evaluate the ESP: VAERS system by comparing adverse event findings to those in the Vaccine Safety Datalink project, and in a randomized trial to test the hypothesis that the combination of secure, computer-assisted, clinician approved, adverse event detection and automated electronic reporting will substantially increase the number, completeness, validity and timeliness of physician approved case reports to VAERS compared to the existing spontaneous reporting system.

Comments on Budget:

The proposed budget appears reasonable and necessary to complete the proposed research.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Agency for Healthcare Research and Quality
OPART / Grants Management

FILE COPY

Memorandum

Date: 7/10/08

Subject: Non-Competing Application Transmittal

To: Margbeth Longmire, Project Officer (CDom)From: Carol Harris, Grants Management SpecialistApplication #: 5R18HS017045-02 Principal Investigator: Ross Lazarus

Please review the attached application to see if outside review is necessary. If so, please immediately notify OEREP. If not, please prepare a funding memo citing progress to date and your recommendation for funding for the upcoming year. Thank you.

Due date for Funding Memo

7/31/08

Yes N/A

<input type="checkbox"/>	<input type="checkbox"/>	Cofunding anticipated (\$_____ total costs from _____) <input type="checkbox"/> PO must initiate the paperwork for this year's transfer of funds <input type="checkbox"/> GM staff already have paperwork for this year's transfer of funds
<input type="checkbox"/>	<input type="checkbox"/>	Administrative Supplement funds included in application (approved in previous year for this budget period) (\$_____ total costs)
<input type="checkbox"/>	<input type="checkbox"/>	Large balance of prior year funds available(>25% of current award). Please address this issue in your funding memo. Attach any correspondence from the grantee which you may have regarding the reason grant funds are underutilized. Please comment specifically on this issue as it relates to the progress of the project and the appropriateness of fully funding the upcoming budget period.
<input type="checkbox"/>		Application attached
<input type="checkbox"/>	<input type="checkbox"/>	Appendices attached
<input type="checkbox"/>		Appendices on file with DGM
\$ <u>499,405 TC</u>		Funds requested (This level _____ includes/ _____ excludes the above cofunding (if "excludes," see comments below)


Comments: @ committed level; money was rebudgetted, but all changes are allowable. No concerns upon initial review.

cc: Joan Metcalfe - FYI
OCD Coordinator
OCD
Official File

FINANCIAL STATUS REPORT (Long Form)

(Follow instructions on the back)

interim

1. Federal Agency and Organizational Element to Which Report is Submitted AHRQ		2. Federal Grant or Other Identifying Number Assigned By Federal Agency 1 R18 HS017045		OMB Approval No. 0348-0039	Page of 1 pages
3. Recipient Organization (Name and complete address, including ZIP code) Harvard Pilgrim Health Care, Inc., 93 Worcester Street, Wellesley, MA 02481					
4. Employer Identification Number 1042452600A1		5. Recipient Account Number or Identifying Number AH000306		6. Final Report <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
7. Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual					
8. Funding/Grant Period (See instructions) From: (Month, Day, Year) 09/30/2007		To: (Month, Day, Year) 09/30/2009		9. Period Covered by this Report From: (Month, Day, Year) 09/30/2008	
				To: (Month, Day, Year) 09/30/2009	
10. Transactions:					
		I Previously Reported		II This Period	
		III Cumulative			
a. Total outlays		\$347,028.02		\$263,503.15	
b. Refunds, rebates, etc.					
c. Program income used in accordance with the deduction alternative					
d. Net outlays (Line a, less the sum of lines b and c)		\$347,028.02		\$263,503.15	
				\$610,531.17	
Recipient's share of net outlays, consisting of:					
e. Third party (in-kind) contributions					
f. Other Federal awards authorized to be used to match this award					
g. Program income used in accordance with the matching or cost sharing alternative					
h. All other recipient outlays not shown on lines e, f or g					
i. Total recipient share of net outlays (Sum of lines e, f, g and h)					
j. Federal share of net outlays (line d less line i)				\$610,531.17	
k. Total unliquidated obligations				\$0.00	
l. Recipient's share of unliquidated obligations				\$0.00	
m. Federal share of unliquidated obligations				\$0.00	
n. Total Federal share (sum of lines j and m)				\$610,531.17	
o. Total Federal funds authorized for this funding period				\$999,214.00	
p. Unobligated balance of Federal funds (Line o minus line n)				\$388,682.83	
Program Income, consisting of:					
q. Disbursed program income shown on lines c and/or g above					
r. Disbursed program income using the addition alternative					
s. Undisbursed program income					
t. Total program income realized (Sum of lines q, r and s)					
11. Indirect Expense					
a. Type of Rate (Place "X" in appropriate box)					
<input type="checkbox"/> Provisional <input checked="" type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed					
b. Rate		c. Base		d. Total Amount	
(b)(4)				\$109,844.87	
				e. Federal Share	
				\$109,844.87	
12. Remarks: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation. We request carry forward in the amount of \$388,682.83 into the NCE.					
13. Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.					
Typed or Printed Name and Title John Eldh, Grants Accountant				Telephone (Area code, number and extension) (617) 509-3315	
Signature of Authorized Certifying Official 				Date Report Submitted 11/17/09	



Harvard Pilgrim Health Care

2009 NOV 19 P 3:34

17 November 2009

Carol Harris
AHRQ
OPART/GM
540 Gaither Road
Rockville, MD 20850

Re: Second Interim FSR for 1R18HS017045-01, "Electronic Support for Public Health - Vaccine Adverse Event Reporting System (ESP:VAERS)"; Lazarus (HPHC PI)

Dear Carol,

Enclosed, please find the interim financial status report for the above-referenced project, covering expenditures during the period 09.30.2008 through 09.30.2009. We are requesting carry forward of \$388,682.83 into the no-cost extension year.

Feel free to call me at 617.509.9933 or e-mail me at nicholas_mulherin@hphc.org if you have any questions.

Best regards,

Nick Mulherin
Grants Manager

Enclosure [1]

Harvard Pilgrim Health Care
Office of Sponsored Programs
133 Brookline Avenue, 5th Floor
Boston, MA 02215
Telephone (617) 509-9843 • Fax (617) 509-9859

Lyles, Krista (AHRQ/OMS)

From: julie_lankiewicz@harvardpilgrim.org
Sent: Thursday, December 30, 2010 10:24 AM
To: AHRQ Grant Final Reports; Lavanderos, Angela (AHRQ); Bernstein, Steve (AHRQ)
Cc: ross.lazarus@channing.harvard.edu; Nicholas_Mulherin@hphc.org
Subject: 1R18HS017045 (Lazarus) - ESP:VAERS Final Report Submission
Attachments: Lazarus_1R18HS017045_FinalReport_Submitted.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Hello,

On behalf of Dr. Ross Lazarus, please accept the attached Final Progress Report, Final Financial Status Report (FSR), and Final Invention Statement & Certification Form for AHRQ grant #1R18HS017045: *Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS)*.

Please feel free to contact me with any questions and have a very Happy New Year.

Regards,

Julie

Julie (Dunn) Lankiewicz, MPH
Project Manager
Therapeutics Research &
Infectious Disease Epidemiology (TIDE)
Department of Population Medicine
Harvard Medical School / Harvard Pilgrim Healthcare Institute
133 Brookline Ave, 6th Floor
Boston, MA 02215
Phone: (617) 509-9880 / Fax: (617) 509-4260
www.populationmedicine.org

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Final Progress Report

Electronic Support for Public Health–Vaccine Adverse Event Reporting System
(ESP:VAERS)

Principal Investigator:

Lazarus, Ross, M.B.B.S., M.P.H., M.Med., G.D.Comp.Sci.

Co-Investigator:

Michael Klompas, MD MPH

Organization: Harvard Pilgrim Health Care, Inc.

Project Dates: 12/07 – 09/10, Including No-Cost Extension

Federal Project Officer: Steve Bernstein

Mechanism: RFA: HS07-002: Ambulatory Safety and Quality Program: Enabling
Quality Measurement through Health Information Technology (EQM)

Grant Number: R18 HS 017045

Structured Abstract

Goal: To develop and disseminate HIT evidence and evidence-based tools to improve healthcare decision making through the use of integrated data and knowledge management.

Scope: To create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.

Methods: Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice were used. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions were evaluated for values suggestive of an adverse event.

Results: Restructuring at CDC and consequent delays in terms of decision making have made it challenging despite best efforts to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial and comparison of ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. However, Preliminary data were collected and analyzed and this initiative has been presented at a number of national symposia.

Key Words: electronic health records, vaccinations, adverse event reporting

Purpose

This research project was funded to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS), via the following aims:

Aim 1: Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.

Aim 2: Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).

Aim 3: Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

Aim 4: Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

Scope

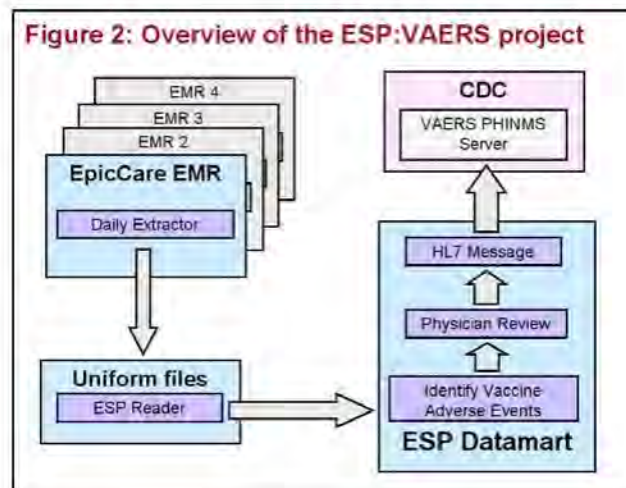
Public and professional confidence in vaccination depends on reliable postmarketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). This project is serving as an extension of the Electronic Support for Public Health (ESP) project, an automated system using electronic health record (EHR) data to detect and securely report cases of certain diseases to a local public health authority. ESP provides a ready-made platform for automatically converting clinical, laboratory, prescription, and demographic data from almost any EHR system into database tables on a completely independent server, physically located and secured by the same logical and physical security as the EHR data itself. The ESP:VAERS project developed criteria and algorithms to identify important adverse events related to vaccinations in ambulatory care EHR data, and made attempts at formatting and securely sending electronic VAERS reports directly to the Centers for Disease Control and Prevention (CDC).

Patient data were available from Epic System's Certification Commission for Health Information Technology-certified EpicCare system at all ambulatory care encounters within Atrius Health, a large multispecialty group practice with over 35 facilities. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions are evaluated for values suggestive of an adverse vaccine event. When a possible adverse event was detected, it was recorded, and the appropriate clinician was to be notified electronically.

Clinicians in-basket messaging was designed to provide a preview a pre-populated report with information from the EHR about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment regarding whether they wish to send a report to VAERS. Clinicians would then have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. The CDC's Public Health Information Network Messaging System (PHIN-MS) software was installed within the facilities so that the approved reports could be securely transferred to VAERS as electronic messages in an interoperable health data exchange format using Health Level 7 (HL7).

Methods & Progress

The goal of **Aim 1**: *Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration, and Aim 2*: *Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS)*, was to construct the below flow of data in order to support the first two Aims:



Existing and functioning ESP components are shown on the left, and Aims 1 and 2 on the right. ESP:VAERS flags every vaccinated patient, and prospectively accumulate that patient's diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions. A main component of **Aim 1** was to *Develop AE criteria to assess these parameters for new or abnormal values that might be suggestive of an adverse effect*. A reporting protocol & corresponding algorithms were developed to detect potential adverse event cases using diagnostic codes, and methods were tested to identify prescriptions or abnormal laboratory values that might be suggestive of an adverse effect. These algorithms were designed to seek both expected and unexpected adverse effects. This reporting protocol was approved by both internal & external partners. We initially prepared a draft document describing the elements, algorithms, interval of interest after vaccination, and actions for broad classes of post-vaccination events, including those to

be reported immediately without delay (such as acute anaphylactic reaction following vaccination), those never to be reported (such as routine check-ups following vaccination) and those to be reported at the discretion and with additional information from the attending physician through a feedback mechanism. The draft was then widely circulated as an initial / working draft for comment by relevant staff in the CDC and among our clinical colleagues at Atrius. In addition to review by the internal CDC Brighton Collaboration liaison, this protocol has also received review & comment via the CDC's Clinical Immunization Safety Assessment (CISA) Network.

The goal of **Aim 2** was the *Development of HL7 messages code for ESP:VAERS to ensure secure transmission to CDC via PHIN-MS*. The HL7 specification describing the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project was implemented. Synthetic and real test data was been generated and transmitted between Harvard and Constella. However, real data transmissions of non-physician approved reports to the CDC was unable to commence, as by the end of this project, the CDC had yet to respond to multiple requests to partner for this activity.

The goal of **Aim 3** was to *Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data*. We had initially planned to evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project—a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. Through a randomized trial, we would also test the hypothesis that the combination of secure, computer-assisted, clinician-approved, adverse event detection, and automated electronic reporting will substantially increase the number, completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system; however, due to restructuring at CDC and consequent delays in terms of decision making, it became impossible to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial, and compare ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. Therefore, the components under this particular Aim were not achieved.

Aim 4 *Distribution of documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems* has been successfully completed. Functioning source code is available to share under an approved open source license. ESP:VAERS source code is available as part of the ESP source code distribution. It is licensed under the LGPL, an open source license compatible with commercial use. We have added the ESP:VAERS code, HL7 and other specifications and documentation to the existing ESP web documentation and distribution resource center <http://esphealth.org>, specifically, the Subversion repository available at : <http://esphealth.org/trac/ESP/wiki/ESPVAERS>.

Results (impact & findings)

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average of 890 possible events, an average of 1.3 events per clinician, per month. These data were presented at the 2009 AMIA conference.

In addition, ESP:VAERS investigators participated on a panel to explore the perspective of clinicians, electronic health record (EHR) vendors, the pharmaceutical industry, and the FDA towards systems that use proactive, automated adverse event reporting. Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of “problem” drugs and vaccines that endanger public health. New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting: reporting is not part of clinicians’ usual workflow, takes time, and is duplicative. Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Inclusion of AHRQ priority populations

The focus of our project was the Atrius Health (formerly HealthOne) provider & patient community. This community serves several AHRQ inclusion populations, specifically low-income and minority populations in primarily urban settings. Atrius currently employs approximately 700 physicians to serve 500,000 patients at more than 18 office sites spread throughout the greater Metropolitan Boston area. The majority of Atrius physicians are primary care internal medicine physicians or pediatricians but the network also includes physicians from every major specialty. The entire adult and pediatric population served by Atrius was included in our adverse event surveillance system (ESP:VAERS). Atrius serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by Atrius is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the Atrius population is under age 18.

List of Publications and Products

ESP:VAERS [source code available as part of the ESP source code distribution]. Licensed under the GNU Lesser General Public License (LGPL), an open source license compatible with commercial use. Freely available under an approved open source license at: <http://esphealth.org>.

Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. *Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS*. The CDC Vaccine Safety Datalink (VSD) Annual Meeting. Atlanta, GA; April, 2008.

Lazarus R, Klompas M *Automated vaccine adverse event detection and reporting from electronic medical records*. CDC Public Health Informatics Network (PHIN) Conference August 27, 2008.

Klompas M, Lazarus R *ESP:VAERS* Presented at the American Medical Informatics Association Annual Symposium; 2009 November 17th.

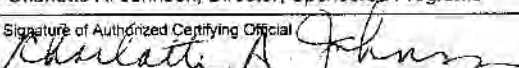
Lazarus R, Klompas M, Kruskal B, Platt R *Temporal patterns of fever following immunization in ambulatory care data identified by ESP:VAERS* Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

Linder J, Klompas M, Cass B, et al. *Spontaneous Electronic Adverse Event Reporting: Perspectives from Clinicians, EHR Vendors, Biopharma, and the FDA*. Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

FINANCIAL STATUS REPORT

(Long Form)

(Follow instructions on the back)

1 Federal Agency and Organizational Element to Which Report is Submitted AHRQ		2 Federal Grant or Other Identifying Number Assigned By Federal Agency 5R18HS017046-02 REVISED		OMB Approval No 0348-0039	Page of 1 of 1 pages
3 Recipient Organization (Name and complete address, including ZIP code) Harvard Pilgrim Health Care, Inc., 93 Worcester Street, Wellesley, MA 02481					
4 Employer Identification Number 104245600A1		5 Recipient Account Number or Identifying Number AH000306/PH000306A		6 Final Report <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
7 Basis <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual					
8 Funding/Grant Period (See instructions) From: (Month, Day, Year) 9/30/2007		To: (Month, Day, Year) 9/29/2010		9 Period Covered by this Report From: (Month, Day, Year) 9/30/2009	
				To: (Month, Day, Year) 9/29/2010	
10 Transactions:		I Previously Reported		II This Period	
				III Cumulative	
a Total outlays		610,531.17		216,985.53	
b Refunds, rebates, etc.				827,516.70	
c Program income used in accordance with the deduction alternative				0.00	
d Net outlays (Line a, less the sum of lines b and c)		610,531.17		216,985.53	
				827,516.70	
Recipient's share of net outlays, consisting of:					
e Third party (in-kind) contributions				0.00	
f Other Federal awards authorized to be used to match this award				0.00	
g Program income used in accordance with the matching or cost sharing alternative				0.00	
h All other recipient outlays not shown on lines e, f or g				0.00	
i Total recipient share of net outlays (Sum of lines e, f, g and h)		0.00		0.00	
				0.00	
j Federal share of net outlays (line d less line i)		610,531.17		216,985.53	
k Total unliquidated obligations				827,516.70	
l Recipient's share of unliquidated obligations				0.00	
m Federal share of unliquidated obligations				0.00	
n Total Federal share (sum of lines j and m)				827,516.70	
o Total Federal funds authorized for this funding period				999,214.00	
p Unobligated balance of Federal funds (Line o minus line n)				171,697.30	
Program Income, consisting of:					
q Disbursed program income shown on lines c and/or g above					
r Disbursed program income using the addition alternative					
s Undisbursed program income					
t Total program income realized (Sum of lines q, r and s)				0.00	
11 Indirect Expense					
a Type of Rate (Place "X" in appropriate box)					
<input checked="" type="checkbox"/> Provisional <input type="checkbox"/> Predetermined <input type="checkbox"/> Final <input type="checkbox"/> Fixed					
b Rate		c Base		d Total Amount	
(b)(4)				120,800.32	
				e Federal Share	
				120,800.32	
12 Remarks. Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation.					
13 Certification: I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.					
Typed or Printed Name and Title Charlotte A. Johnson, Director, Sponsored Programs				Telephone (Area code, number and extension) 617.509.9929	
Signature of Authorized Certifying Official 				Date Report Submitted December 29, 2010	



DEPARTMENT OF HEALTH AND HUMAN SERVICES

**Procedure for Submission of
Final Invention Statement and Certification (For Grant or Award)
Form HHS 568**

A Final Invention Statement and Certification (Form HHS 568) shall be executed and submitted within 90 days following the expiration or termination of a grant or award. The Statement shall include all inventions which were conceived or first actually reduced to practice during the course of work under the grant or award, from the original effective date of support through the date of completion or termination. The Statement shall include any inventions reported previously for the grant or award as part of a non-competing application. This reporting requirement is applicable to grants and awards by Department of Health and Human Services in support of research.

The Final Invention Statement and Certification does not in any way relieve the person responsible for the grant or award, or the institution, of the obligation to assure that all inventions are promptly and fully reported directly to the National Institutes of Health, as required by terms of the grant or award. Information regarding the reporting of inventions, including the reporting form to be followed, may be obtained from the Office of Policy for Extramural Research Administration, Division of Extramural Inventions and Technology Resources, 6705 Rockledge Drive MSC 7980, Bethesda, Maryland 20892-7980, Telephone: (301) 435-1986.

The original of the completed Final Invention Statement and Certification is to be returned to the awarding component that funded the grant or award. The entire grant or award number must appear in the designated box on the form. The period covered by the Final Invention Statement is the project period of the grant or award at a particular grantee institution. If no inventions were involved, insert the word "None" in the first block under item Title of Invention. Each Statement requires the signature of an institution official authorized to sign on behalf of the institution.

The PHS estimates that it will take from 5 to 10 minutes to complete this form. This includes time for reviewing the instructions, gathering needed information, and completing and reviewing the form. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. If you have comments regarding this burden estimate or any other aspects of this collection of information, including suggestions for reducing this burden, send comments to: NIH, Project Clearance Office, 6701 Rockledge Drive MSC 7730, Bethesda, MD 20892-7730, ATTN: PRA (0925-0001). *Do not send this form to these addresses; they are for comments only.*

Department of Health and Human Services
Final Invention Statement and Certification
(For Grant or Award)

DHHS Grant or Award No.

1R18HS017405

- A. We hereby certify that, to the best of our knowledge and belief, all inventions are listed below which were conceived and/or first actually reduced to practice during the course of work under the above-referenced DHHS grant or award for the period


09/30/2007 through 09/30/2010
original effective date date of termination

- B. **Inventions** (Note: If no inventions have been made under the grant or award, insert the word "NONE" under Title below.)

NAME OF INVENTOR	TITLE OF INVENTION	DATE REPORTED TO DHHS
	NONE.	

(Use continuation sheet if necessary)

- C. **Signature** — This block **must** be signed by an official authorized to sign on behalf of the institution.

Title Director, Office of Sponsored Programs		Name and Mailing Address of Institution Harvard Pilgrim Health Care, Inc. 93 Worcester Street Wellesley, MA 02481
Typed Name Charlotte Johnson		
Signature 	Date 12/29/2010	

Privacy Act Statement

The PHS maintains application and grant records as part of a system of records as defined by the Privacy Act: 09-25-0112, Grants and Cooperative Agreements: Research, Research Training, Fellowship, and Construction Applications and Related Awards." The Privacy Act of 1974 (5 USC 522a) allows disclosures for "routine uses" and permissible disclosures.

Some routine uses may be:

1. To the cognizant audit agency for auditing.
2. To a Congressional office from a record of an individual in response to an inquiry from the Congressional office made at the request of that individual.
3. To qualified experts, not within the definition of DHHS employees as prescribed in DHHS regulations (45 CFR 5b.2) for opinions as part of the application review process.
4. To a Federal agency, in response to its request, in connection with the letting of a contract or the issuance of a license, grant, or other benefit by the requesting agency, to the extent that the record is relevant and necessary to the requesting agency's decision on the matter;
5. To organizations in the private sector with whom PHS has contracted for the purpose of collating, analyzing, aggregating, or otherwise refining records in a system. Relevant records will be disclosed to such a contractor, who will be required to maintain Privacy Act safeguards with respect to such records.
6. To the sponsoring organization in connection with the review of an application or performance or administration under the terms and conditions of the award, or in connection with problems that might arise in performance or administration if an award is made.
7. To the Department of Justice, to a court or other tribunal, or to another party before such tribunal, when one of the following is a party to litigation or has any interest in such litigation, and the DHHS determines that the use of such records by the Department of Justice, the tribunal, or the other party is relevant and necessary to the litigation and would help in the effective representation of the governmental party.
 - a. the DHHS, or any component thereof;
 - b. any DHHS employee in his or her official capacity;
 - c. any DHHS employee in his or her individual capacity where the Department of Justice (or the DHHS, where it is authorized to do so) has agreed to represent the employee; or
 - d. the United States or any agency thereof; where the DHHS determines that the litigation is likely to affect the DHHS or any of its components.
8. A record may also be disclosed for a research purpose, when the DHHS:
 - a. has determined that the use or disclosure does not violate legal or policy limitations under which the record was provided, collected, or obtained;
 - b. has determined that the research purpose (1) cannot be reasonably accomplished unless the record is provided in individually identifiable form, and (2) warrants the risk to the privacy of the individual that additional exposure of the record might bring;
 - c. has secured a written statement attesting to the recipient's understanding of, and willingness to abide by, these provisions; and
 - d. has required the recipient to:
 - (1) establish reasonable administrative, technical, and physical safeguards to prevent unauthorized use or disclosure of the record;
 - (2) destroy the information that identifies the individual at the earliest time at which removal or destruction can be accomplished consistent with the purpose of the research project, unless the recipient has presented adequate justification of a research or health nature for retaining such information; and
 - (3) make no further use or disclosure of the record, except (a) in emergency circumstances affecting the health or safety of any individual, (b) for use in another research project, under these same conditions, and with written authorization of the DHHS, (c) for disclosure to a properly identified person for the purpose of an audit related to the research project, if information that would enable research subjects to be identified is removed or destroyed at the earliest opportunity consistent with the purpose of the audit, or (d) when required by law.

The Privacy Act also authorizes discretionary disclosures where determined appropriate by the PHS, including to law enforcement agencies, to the Congress acting within its legislative authority, to the Bureau of the Census, to the National Archives, to the General Accounting Office, pursuant to a court order, or as required to be disclosed by the Freedom of Information Act of 1974(5 USC 552) and the associated DHHS regulations (45 CFR Part 5).

Grant Final Report

Grant ID: R18 HS 017045

**Electronic Support for Public Health–Vaccine Adverse
Event Reporting System (ESP:VAERS)**

Inclusive dates: 12/01/07 - 09/30/10

Principal Investigator:

Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Team members:

Michael Klompas, MD, MPH

Performing Organization:

Harvard Pilgrim Health Care, Inc.

Project Officer:

Steve Bernstein

Submitted to:

The Agency for Healthcare Research and Quality (AHRQ)

U.S. Department of Health and Human Services

540 Gaither Road

Rockville, MD 20850

www.ahrq.gov

Abstract

Purpose: To develop and disseminate HIT evidence and evidence-based tools to improve healthcare decision making through the use of integrated data and knowledge management.

Scope: To create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.

Methods: Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice were used. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions were evaluated for values suggestive of an adverse event.

Results: Restructuring at CDC and consequent delays in terms of decision making have made it challenging despite best efforts to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial and comparison of ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. However, Preliminary data were collected and analyzed and this initiative has been presented at a number of national symposia.

Key Words: electronic health records, vaccinations, adverse event reporting

The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

Final Report

Purpose

This research project was funded to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS), via the following aims:

Aim 1. Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.

Aim 2. Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).

Aim 3. Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

Aim 4. Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

Scope

Public and professional confidence in vaccination depends on reliable postmarketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). This project is serving as an extension of the Electronic Support for Public Health (ESP) project, an automated system using electronic health record (EHR) data to detect and securely report cases of certain diseases to a local public health authority. ESP provides a ready-made platform for automatically converting clinical, laboratory, prescription, and demographic data from almost any EHR system into database tables on a completely independent server, physically located and secured by the same logical and physical security as the EHR data itself. The ESP:VAERS project developed criteria and algorithms to identify important adverse events related to vaccinations in ambulatory care EHR data, and made attempts at formatting and securely sending electronic VAERS reports directly to the Centers for Disease Control and Prevention (CDC).

Patient data were available from Epic System's Certification Commission for Health Information Technology-certified EpicCare system at all ambulatory care encounters within Atrius Health, a large multispecialty group practice with over 35 facilities. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions are evaluated for values

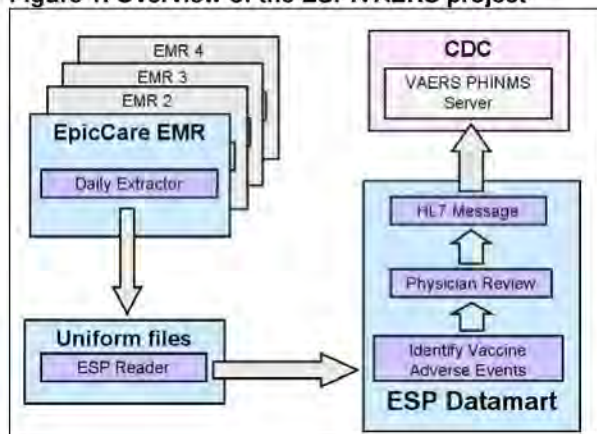
suggestive of an adverse vaccine event. When a possible adverse event was detected, it was recorded, and the appropriate clinician was to be notified electronically.

Clinicians in-basket messaging was designed to provide a preview a pre-populated report with information from the EHR about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment regarding whether they wish to send a report to VAERS. Clinicians would then have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. The CDC's Public Health Information Network Messaging System (PHIN-MS) software was installed within the facilities so that the approved reports could be securely transferred to VAERS as electronic messages in an interoperable health data exchange format using Health Level 7 (HL7).

Methods

The goal of Aim 1: *Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration*, and Aim 2: *Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS)*, was to construct the below flow of data in order to support the first two Aims:

Figure 1. Overview of the ESP:VAERS project



Existing and functioning ESP components are shown on the left, and Aims 1 and 2 on the right. ESP:VAERS flags every vaccinated patient, and prospectively accumulate that patient's diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions. A main component of Aim 1 was to *Develop AE criteria to assess these parameters for new or abnormal values that might be suggestive of an adverse effect*. A reporting protocol & corresponding algorithms were developed to detect potential adverse event cases using diagnostic codes, and methods were tested to identify prescriptions or abnormal laboratory values that might be suggestive of an adverse effect. These algorithms were designed to seek both expected and unexpected adverse effects.

This reporting protocol was approved by both internal & external partners. We initially prepared a draft document describing the elements, algorithms, interval of interest after vaccination, and actions for broad classes of post-vaccination events, including those to be reported immediately without delay (such as acute anaphylactic reaction following vaccination), those never to be reported (such as routine check-ups following vaccination) and those to be reported at the discretion and with additional information from the attending physician through a feedback mechanism. The draft was then widely circulated as an initial / working draft for comment by relevant staff in the CDC and among our clinical colleagues at Atrius. In addition to review by the internal CDC Brighton Collaboration liaison, this protocol has also received review & comment via the CDC's Clinical Immunization Safety Assessment (CISA) Network.

The goal of Aim 2 was the *Development of HL7 messages code for ESP:VAERS to ensure secure transmission to CDC via PHIN-MS*. The HL7 specification describing the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project was implemented. Synthetic and real test data was been generated and transmitted between Harvard and Constella. However, real data transmissions of non-physician approved reports to the CDC was unable to commence, as by the end of this project, the CDC had yet to respond to multiple requests to partner for this activity.

The goal of Aim 3 was to *Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data*.

We had initially planned to evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project—a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. Through a randomized trial, we would also test the hypothesis that the combination of secure, computer-assisted, clinician-approved, adverse event detection, and automated electronic reporting will substantially increase the number, completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system; however, due to restructuring at CDC and consequent delays in terms of decision making, it became impossible to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial, and compare ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. Therefore, the components under this particular Aim were not achieved.

Aim 4 *Distribution of documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems* has been successfully completed. Functioning source code is available to share under an approved open source license. ESP:VAERS source code is available as part of the ESP source code distribution. It is licensed under the LGPL, an open source license compatible with commercial use. We have added the ESP:VAERS code, HL7 and other specifications and documentation to the existing ESP web documentation and distribution resource center <http://esphealth.org>, specifically, the Subversion repository available at: <http://esphealth.org/trac/ESP/wiki/ESPVAERS>.

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average of 890 possible events, an average of 1.3 events per clinician, per month. These data were presented at the 2009 AMIA conference.

In addition, ESP:VAERS investigators participated on a panel to explore the perspective of clinicians, electronic health record (EHR) vendors, the pharmaceutical industry, and the FDA towards systems that use proactive, automated adverse event reporting.

Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of “problem” drugs and vaccines that endanger public health. New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting: reporting is not part of clinicians’ usual workflow, takes time, and is duplicative. Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Inclusion of AHRQ Priority Populations

The focus of our project was the Atrius Health (formerly HealthOne) provider & patient community. This community serves several AHRQ inclusion populations, specifically low-income and minority populations in primarily urban settings.

Atrius currently employs approximately 700 physicians to serve 500,000 patients at more than 18 office sites spread throughout the greater Metropolitan Boston area. The majority of Atrius physicians are primary care internal medicine physicians or pediatricians but the network also includes physicians from every major specialty.

The entire adult and pediatric population served by Atrius was included in our adverse event surveillance system (ESP:VAERS). Atrius serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by Atrius is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the Atrius population is under age 18.

List of Publications and Products

ESP:VAERS [source code available as part of the ESP source code distribution]. Licensed under the GNU Lesser General Public License (LGPL), an open source license compatible with commercial use. Freely available under an approved open source license at: <http://esphealth.org>.

Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS. The CDC Vaccine Safety Datalink (VSD) Annual Meeting. Atlanta, GA; April, 2008.

Lazarus R, Klompas M Automated vaccine adverse event detection and reporting from electronic medical records. CDC Public Health Informatics Network (PHIN) Conference August 27, 2008.

Klompas M, Lazarus R ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 17th.

Lazarus R, Klompas M, Kruskal B, Platt R Temporal patterns of fever following immunization in ambulatory care data identified by ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

Linder J, Klompas M, Cass B, et al. Spontaneous Electronic Adverse Event Reporting: Perspectives from Clinicians, EHR Vendors, Biopharma, and the FDA. Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.