Monthly Program Status Report – PROJECT

Reporting Period:	**December 2016**
Contracting Agency:	Food and Drug Administration (FDA)
FDA Project Manager:	Shaila Shaheed, Shaila.Shaheed@fda.hhs.gov, Thomas Permutt, thomas.permutt@fda.hhs.gov,
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FDA COTR:	Shaila Shaheed, Shaila.Shaheed@fda.hhs.gov,
Contract / Order:	HHSF223201310230C
Contractor PI:	Daniel Scharfstein, dscharf@jhu.edu, 410-955-2420
Project Team:	Aidan McDermott (Computer Programmer)
Description of Activity:	A recent FDA-sponsored National Research Council Report recommended that "examining sensitivity to the assumptions about the missing data mechanism should be a mandatory component of reporting." While the Report outlines a framework for conducting sensitivity analysis, there are two major problems with existing methods: (1) they have not been implemented in software packages and (2) they do not adequately address non-monotone missing data patterns (i.e., patients provide data irregularly). The objective of this project is to address these gaps by: 1) creating unified and coherent methods for global sensitivity analysis of clinical trials with monotone and non-monotone missing data, 2) developing free, open source and reproducible software in SAS and R to implement the methods, and 3) demonstrating the methods and software using real clinical trial data.

Project Health Check							
Health ▸	**Budget**		**Schedule**		**Resources**	**Deliverables**	
Notes ▸	Within Budget		On Schedule		Adequate	On Target	

Budget Tracking – (TOTAL CONTRACT CEILING)

POP	Ceiling Remaining	Cumulative Funding	Year Funding (Year 1)	Spent to Date	Year Funding Remaining	Month Invoice	Funding Covers
Base	$1,094,565	$1,094,565	$1,094,565	$1,055,905.45 ($45,315.66 committed)	$38,659.55	$978,225.48	Salary, fringe, other expenses, and indirect costs

Activity Summary and Highlights

We worked on revising the *Biometrics* manuscript and revising the software package.

Key Accomplishments	
Current Reporting Period	***Planned for Next Period***
• Work on revisions to *Biometrics* paper • Updated SAMON to accommodate missing values coded as NA • Updated SAMON to output confidence levels other than 95%	• Update SAMON to handle negative and non-integer values • Revisions to *Biometrics* paper • Submit *Clinical Trials* manuscript • Complete write-up of case studies

Issues and Risks

Category	Priority	Status	Opened	Issue	Description
Contract (FDA)	1	Closed	9/30/13	Intellectual Property	Revision to contract regarding intellectual property language.
Dissemination (FDA)	2	Closed	2/15/14	Website	FDA Personnel cannot connect to www.missingdatamatters.org from their office computers.
Software (JHU)	1	Closed	3/15/14	Coverage of Confidence Intervals	Simulations indicate that standard procedures for constructing confidence intervals are not providing adequate coverage with typical sample sizes.
Computing (JHU)	1	Closed	4/21/14	Periods of slow performance of computing cluster	A new computing cluster was installed at Johns Hopkins. We are experiencing periods of slow performance on the cluster.
Personnel (JHU)	1	Closed	5/21/14	Re-Distribution of Effort	Starting April 1, Aidan McDermott has reduced his percent effort by 20%. Chenguang Wang joined the project starting July 15.
Invoicing (FDA)	1	Closed	6/6/14	Payment of Invoices	Invoices have not been paid.
Computing (FDA)	1	Closed	6/6/14	Software on FDA Cluster	Investigate the steps needed to run software on FDA cluster
Personnel (JHU)	1	Closed	1/13/15	New Effort	Yi Lu joined the project to work on confidence intervals.
Software (JHU)	1	Closed	6/15/16	Coverage of Confidence Intervals	Simulations indicate that standard procedures for constructing confidence intervals are not providing adequate coverage with typical sample sizes.
Funding	1	Closed	9/15/16	No Cost Extension	There will approximately $125,000 of unspent by the end of the project period.

Other Activities

Attachments and References

Deliverable	**Due Date**
Allow SAMON to handle negative and non-integer values	New Release on 3/1/2017
Allow SAMON to handle missing values coded as NA	
Change the syntax in SAMON so the dropout model parameters are denoted by H instead of P and the outcome model parameters are denoted by F instead of Q.	
Change SAMON to output confidence intervals of levels other than 95%	
Allow SAMON to handle more flexible exponential tilting functions	
Revise *Biometrics* manuscript to address reviewer comments.	12/31/16
Submit SAMON case study manuscript to *Clinical Trials* or *Statistics in Medicine*.	1/31/17
Submit manuscript that describes the partial imputation procedure for handling missing data prior to drop-out.	3/31/17

Yellow items are completed.