

Monthly Program Status Report – PROJECT

Reporting Period:	October 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	\$1,088,680.46 (\$128,516.74 committed)	\$5,884.54	\$935,179.59	Salary, fringe, other expenses, and indirect costs

Activity Summary and Highlights
Our <i>Biometrics</i> submission received an excellent review (acceptable for publication subject to minor revisions). We worked on revising the manuscript. We posted new R and SAS versions of SAMON that incorporate a feature that handles non-monotone missing data prior to drop-out. Deliverables of the no-cost extension are on schedule.

Key Accomplishments	
Current Reporting Period	Planned for Next Period
<ul style="list-style-type: none"> • Work on revisions to <i>Biometrics</i> paper • Posted new R and SAS versions of SAMON 	<ul style="list-style-type: none"> • Revisions to <i>Biometrics</i> paper • Submit <i>Clinical Trials</i> 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 <i>Biometrics</i> manuscript to address reviewer comments.	12/31/16
Submit SAMON case study manuscript to <i>Clinical Trials</i> or <i>Statistics in Medicine</i> .	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.