STRATEGIC INITIATIVE IN BIOSTATISTICS

Department of Statistics
University of Missouri-Columbia

Proposed March 10, 2005

1. BRIEF DESCRIPTION

a. Title

A Strategic Initiative in Biostatistics.

b. Abstract

This initiative has two main objectives. They are (1) to organize and establish a biostatistics research and support center, and (2) to develop and support biostatistics graduate programs. Nationally and internationally over the last decade, the use and demand of Statistics, especially biostatistics, has seen exponential growth. Biostatistics has its own significant body of intellectual knowledge. But biostatistics also is related to, and has a critical impact on, the success of other existing research programs at the University of Missouri - Columbia and on research programs MU is working and planning to develop. The requisite critical mass of biostatistics expertise on the MU campus does not exist. We propose strategic faculty hires to address this deficiency.

c. Brief statement of mission

The mission of this initiative is to develop a world-class biostatistics research and support center that will make pathbreaking contributions to the field, provide substantive biostatistical collaboration with MU faculty in the social and life sciences, contribute to improving the health of all Missourians, and to develop graduate programs in biostatistics that support these activities and provide Missourians the opportunity to train in biostatistics within the State of Missouri.

d. Vision

Given the growth of biostatistics and the need for it to be a critical component of many other research programs, there is an urgent need to enhance biostatistical expertise at MU. With the development of this initiative, MU will enjoy international recognition for its biostatistics research and training programs. It also will be recognized as having world-class

biostatistical collaborations in many other fields, including fields in life sciences such as in the public health sciences and bioinformatics.

e. Brief description

This initiative has two main objectives. They are (1) to organize or establish a biostatistics research and support center, and (2) to provide faculty to develop and support biostatistics graduate programs.

f. Brief history/background of initiative at MU

In 2001, an interdisciplinary campus-wide task force commissioned by then Vice Chancellor Winship on the status of Biostatistics and Epidemiology on the University of Missouri-Columbia campus conducted an extensive research and wrote a report, which was endorsed by then Provost Brady Deaton. This report strongly recommends substantial development in biostatistics. The time has come.

g. Other documentation describing the initiative

This initiative is synergistic to the *Social Science Mission Enhancement Statistics Initiative* which was awarded, but had funding severely curtailed because of system-wide budget constraints. It also provides foundational support to meeting the goals put forth in the report prepared in the Fall of 2004 and the Winter of 2005 by the *Chancellor's Committee on the Feasibility of a Masters Degree Program in Public Health*. This report will be presented to Chancellor Deaton imminently.

2. LIST OF ACTIVE PARTICIPANTS

a. Department

This initiative will be developed within the Statistics Department. However, active participants have serious commitments and collaborations in the College of Food, Agriculture and Natural Resources and with faculty in the health sciences. With more of a critical mass of biostatistics expertise, these collaborations will expand.

b. Specific faculty members who have high involvement in project

This initiative is supported by two active senior faculty, two tenure-track assistant professors and one non-regular consulting faculty.

Nancy Flournoy has a distinguished career with over 100 peer reviewed publication in applied and theoretical biostatistics. Her expertise is in adaptive designs for clinical trials. She is a Fellow of the Institute of Mathematical Statistics, the American Statistical Association, the International Statistics Institute, the World Academy of Art and Science and the American Association for the Advancement of Science.

Jianguo (Tony) Sun a well-funded rising star in biostatistics. He is up for promotion to full professor this year and he is expanding his leadership roles in the department and nationally. His expertise is in survival analysis, in particular, he develops new methodology for interval censored data analysis.

Jing Qiu joined the Statistics Department in 2004 as an assistant professor from Cornell University. Her expertise is in bioinformatics, in particular, in gene expression data analysis methodologies and statistical genetics. Her salary support is shared by CAFNR and A&S.

Christie Spinka joined the Statistics Department in 2004 as an assistant professor from Texas A&M. Her expertise is in statistical genetics, in particular, in genetic epidemiology, association, population genetics and molecular phylogeny. Her salary support is shared by CAFNR and A&S.

Leonard Hearne had a private consulting practice before coming to Columbia in 2002. Now he is a resident instruction assistant professor in the Statistics Department with funding shared by the Life Science Center and A&S. He has taken a leadership role at MU in the analysis of microarray data. He developed a statistics course on the subject for non-statistics graduate students, postdoctoral fellows and laboratory technicians that was offered in Fall 2004 for the first time.

With additional biostatistics faculty, external experts in biostatistics will see more than Nancy Flournoy and Jianguo (Tony) Sun as individuals at MU. They will see a vibrant active research group. External experts in the life sciences, including the public health sciences, will see the results of their collaborations in the quality and significance of their collaborators

work.

c. Others

Lori Thombs, Director of the Social Science Statistics Center (SSSC) - a Mission Enhancement activity - will contribute to and benefit by the Biostatistics Initiative, as will *Doug Steinley*, Assistant Professor of Psychology, who spends part time in SSSC. SSSC has a growing presence on campus, but does not have sufficient manpower to provide needed statistical consultation to all the social sciences and all the life sciences as well. Maintaining momentum at this time is critical to the SSSC being seen as a vital active partner in research and graduate education at MU. This initiative will provide a strategic thrust to realizing the SSSC mission of statistical consulting for faculty and students in the social sciences.
Scott Holan, assistant professor in statistics, is funded jointly by CAFNR and A&S. He is finding biotechnical applications for his time series expertise through the *Statistics Consulting Outpost* located in the Life Sciences Center.
Mark Ellerseick, Experimental Station Statistician, will have a synergistic relationship with faculty supported by this initiative, as will any statistics faculty hired in the School of Medicine.

Those faculty who are currently involved in Bioinformatics program development and in Public Health program development will find their efforts supported and enhanced by this initiative. Indeed, support for this initiative is a critical component needed to advance Bioinformatics and the Public Health Sciences. Funding Biostatistics now is a strategic approach to providing a strong foundation for enhancing these other important initiatives.

3. BRIEF DESCRIPTION OF CURRENT CONTRIBUTIONS RELATED TO THE BIOSTATISTICS INITIATIVE

a. Grants

(Tony) Jianguo Sun, Associate Professor, is currently holding a four years NIH grant for $400,000 direct cost. It is the largest single person grant in the Department of Statistics. Before this, he had a five years NIH grant for $325,000 direct cost.

Nancy Flournoy, Professor and Chair, leads the statistics component of a grant proposal, Charles W. Caldwell PI, on MU transdisciplinary research on energetics and cancer. This

grant has been submitted to NIH National Cancer Institute with a total of $2,196,871.29 requested.

Leonard B. Hearne was awarded funding for Current Use Pesticides: Assessing Exposure and Spermatotoxicity by the U.S. EPA. The grant runs from 01-01-2005 - 10-31-2007 and the award total is $672,821.00. He was funded for 10% time as a Co-PI with Shanna Swan. It is not clear what his role will be with her relocating to Rochester. *Leonard Hearne* has two grants pending with Eric Antoniou PI. One is on Molecular mechanisms of bovine follicular selection submitted to the COOP State Research, Education and Extension Service for $106,688 and another on Functional genomics of ovarian follicle slection submitted to NIH National Institute of Child Health for $73,500. His third pending grant award with Toshihiko Ezashi PI is on NIH Controlling differentiation of human embryonic development for $367,500. His forth pending grant with Khalid Meksem of Southern Illinois Univesity PI is on Investigating Disease Resistance Signaling Networks in Response to Cyst Nematode Parasitism in Soybean for $1,566,010.

Many of our graduate students do their dissertation work in biostatistics, but others leave MU every year because they can't get their degree in *biostatistics*. Therefore, the active faculty in this strategic initiative now are working on a NIH training grant in biostatistics. The prospects for successful funding would be greatly enhanced if we already had established graduate programs in biostatistics. However, even if unsuccessful, this application will provide visibility and lay the groundwork for future funding, which is much more likely with the support of this initiative than without it.

b. Notable scholarly publications in biostatistics from MU initiative participants

Publications **from last two years** by the faculty members listed in 2 (b) are listed below.

Stylianou, M, Proschan, M. **Flournoy, N**. (2003). Estimating the probability of toxicity at the target dose following an up-and-down design, Statistics in Medicine 22 535-543.

Rabie, H., **Flournoy, N**. (2004). Optimal designs for contingent response models. MoDa 7 Advances in Model-Oriented Design and Analysis 133-142. A.D. Bucchianico, H. Lauter and H.P. Wynn, editors. Heidelberg: Physica-Verlag.

Paul, RK, Rosenberger, WF, **Flournoy, N** (2004). Quantile estimation following non-parametric phase I clinical trials with ordinal response. Statistics in Medicine 23 2483-2495.

Gezmu, M, **Flournoy, N**. (2005). Group up-and-down designs for phase I clinical trials. Journal of Statistical Planning and Inference, in press.

Duty, P., **Flournoy, N** (2005). Practical considerations for constructing confidence intervals for nonlinear functions. Joint Statistical Meetings 2004 Proceedings. In press.

Ivanova, A, **Flournoy, N** (2005). Up-and-down designs in toxicity studies. Statistical Methods for Dose-finding Studies. Chevret, S. (ed). John Wiley & Sons, Ltd. In press.

Rabie, H. and **Flournoy, N** (2005). Limiting optimal designs for the contingent response model. Proceedings of the 5h St. Petersburg Workshop on Simulation. St. Petersburg, Russia. In press.

Qiu, J. and Hwang J.T.G. (2004), "Sharp Simultaneous Intervals for the Means of Selected Populations with Application to Microarray Data Analysis", submitted.

Cui, X., Hwang J.T.G., **Qiu, J**., Blades, N.J. and Churchill, G.A. (2005), "Improved Statistical Tests for Differential Gene Expression by Shrinking Variance Components Estimates", Biostatistics 6, 59-75.

Spinka C, Carroll RJ, and Chatterjee N (submitted). Analysis of Case-Control Studies of Genetic and Environmental Factors with Missing Genetic Information and Haplotype-Phase Ambiguity.

Fan R, **Spinka C**, Jin L, Jung JS (2005). Pedigree linkage disequilibrium mapping of quantitative trait loci. European Journal Human Genetics 13: 216-231.

Sanders LM, Henderson CE, Hong MY, Barhoumi R, Burghardt RC, Wang N, **Spinka CM**, Carroll RJ, Turner ND, Chapkin RS, and Lupton JR (2004). An increase in reactive

oxygen species by dietary fish oil coupled with the attenuation of antioxidant defenses by dietary pectin enhances rat colonocyte apoptosis. Journal of Nutrition 134: 3233-3238.

Spinka C, Holan S, and Spinka H (2004). Estimating relative luminosity for RHIC spin physics. Nuclear Instruments and Methods A 530: 536-540.

Sun, J., Park, D-H., Sun, L. and Zhao, X (2005) Semiparametric Regression Analysis of Longitudinal Data with Informative Observation Times. Journal of the American Statistical Association, accepted.

Zhang, Z., Sun, L., Zhao, X. and **Sun, J**. (2005) Regression Analysis of Interval-censored Failure Time Data with Linear Transformation Models. The Canadian Journal of Statistics, accepted.

Sun, J and Sun, L. (2005) Semiparametric Linear Transformation Models for Current Status Data. The Canadian Journal of Statistics, accepted.

Zhang, Z., **Sun, J** and Sun, L. (2005) Statistical Analysis of Current Status Data with Informative Observation Times. Statistics in Medicine, accepted.

Sun, J, Zhao, Q. and Zhao, X. (2005) Generalized Log Rank Tests for Interval-Censored Failure Time Data. Scandinavian Journal of Statistics, Vol. 32, 49-57.

Fang, H., Li, G. and **Sun, J** (2005) Maximum Likelihood Estimation in a Semiparametric Logistic/Proportional-Hazards Mixture Model. Scandinavian Journal of Statistics, Vol. 32, 59-75.

Zhao, X., Lim, H. and **Sun, J** (2005) Estimating Equation Approach for Regression Analysis of Failure Time Data in the Presence of Interval-Censoring. Journal of Statistical Planning and Inference, Vol. 129, 145-157.

Sun, L., Kim, Y. and **Sun, J**. (2004) Regression Analysis of Doubly Censored Failure Time Data Using the Additive Hazards Model. Biometrics, Vol. 60, No. 3, 637-643.

Zhou, X., Sun, L. and **Sun, J**. (2004) A Uniform Semiparametric Approach for Longitudinal Data Analysis. Far East Journal of Theoretical Statistics, Vol. 13, 233-256.

Sun, J., Lim, H. J. and Zhao, X. (2004) An Independence Test for Doubly Censored Failure Time Data. Biometrical Journal, Vol. 46, 503-511.

Yang, J., **Sun, J**. and Hammer, D. (2004) Distribution Normality of pH and H^+ Activities in Soil. Environmental Chemistry Letters, 2, 159-162.

Zhao, Q. and **Sun, J**. (2004) Generalized Log-rank Test for Mixed Interval-censored Failure Time Data. Statistics in Medicine, Vol. 23, No. 10, 1621-1629.

Sun, J., Sun, L. and **Flournoy**, N. (2004) Additive Hazards Model for Competing Risks Analysis of the Case-cohort Design. Communication in Statistics: Theory and Methods, Vol. 33, No. 2, 351-366.

Sun, J., Kim, Y. and Schmitt, C. J. (2003). Longitudinal Analysis of Bioaccumulative Contaminants in Freshwater Fishes. Environmental and Ecological Statistics, Vol. 10, 419-428.

Sun, J., Liao, Q. and Chiu, J-R. (2003). Simple and Direct Nonparametric Estimation of a Survival Function in the Presence of Reporting Lags. Journal of Nonparametric Statistics, 395-401.

Sun, J. and Fang, H. B. (2003). A Nonparametric Test for Panel Count Data. Biometrika, Vol. 90, 199-208.

Hu, X. J., **Sun, J**. and Wei, LJ. (2003). Regression Parameter Estimation from Panel Counts. Scandinavian Journal of Statistics, Vol. 30, 25-43.

Lim, H. J. and **Sun, J**. (2003). Nonparametric Tests for Interval-Censored Failure Time Data. Biometrical Journal, Vol. 45, 263-276.

In addition, **Nancy Flournoy** is co-editor of a complete volume of the *Journal of Statistical Inference and Planning*, currently in press, on *Adaptive Designs in Clinical Trials*.

c. Other departmental resources

Statistical software support experts in the Department of Statistics, *Ray Bacon* and *Margie Gurwit*, will we available to assist faculty and projects supported by this initiative.

The Statistics Department holds a weekly Biostatistics Working Seminar led by **Dr. Tony Sun**. He has kept this seminar, which is extremely popular among Statistics graduate students, going every semester for last six years. It is open to all faculty and students who are interested in biostatistics.

Active faculty in biostatistics are supported by state-of-the-art high-end computer equipment that is funded by research grants and by A&S.

4. RESOURCES TO DESIRED ADVANCE BIOSTATISTICS WITH PRIORITY VALUE

We request four faculty positions in biostatistics, two at the Assistant Professor level and two at the Associate Professor level. These faculty will provide a strategic boost to biostatistical expertise at MU. The Associate Professors will jump-start the impact of this initiative and are critical to having biostatistical support for developing bioinformatics, clinical research and the public health sciences.

A total of **$523,000** is requested for
Two Associate Professors: $100,000 plus benefits = $128,000 each.
Two Assistant Professors: $75,000 plus benefits = $96,000 each.
Start-up and recruitment funds for first hire: $75,000

Hiring will be done in phases, so salary savings from the first year can be used to provide start-up funds for later hires. Making just one hire in the first year after funds are made available, funds also will be available for initial administrative support. This support will be used to begin to develop graduate programs in biostatistics, to obtain training grants, and

initiate one if funded, and to support biostatistical operations.

Space and office furniture will be needed to house these faculty. The Statistics Department is crunching to the maximum to accommodate replacement positions filled this year.

5. CONTRIBUTIONS OF THE STRATEGIC BIOSTATISTICS INITIATIVE TO MU AND UM GOALS

a. Objectives from strategic plans addressed by initiative

This initiative has two main objectives and they are to establish and provide a biostatistics graduate program and to organize or establish a biostatistics research and support center. The importance of biostatistics and the need of a graduate program and a research and support center for MU have been well documented by the report given in 2001 by the task force commissioned by then Vice Chancellor Winship on the status of Biostatistics and Epidemiology on the University of Missouri-Columbia campus. The report was endorsed by then Provost Brady Deaton and strongly recommended development in this direction.

The use and demand of general Statistics have seen exponential growing during the last 10 years. One way to see this is through the exploding job market for Statistics graduates, which is similar to that for computer science graduates 10 years earlier. In terms of applications and job opportunities in Statistics, more than half are on biostatistics. Most of statistics research funding is in biostatistics and some statistics training grants are also available from the federal government to meet the demand. There is no graduate program in Missouri and thus we cannot provide Missourians the opportunity that we can and they deserve. Without the development of our own program right now, we will lose the opportunity to others and may well never get an opportunity to do so in the future.

Biostatistics not only has its own field and importance, but also is related to and has essential impact on the success of other research programs that exist or MU is planning to develop. For the existing programs such as those in life science, it is well-known that the majority of research funding is from NIH, and to improve the impact of their funding, NIH wants to see the participation of biostatisticians. For programs that are under development, such as bioinformatics and public health, biostatistics is a key component and they will not be successful without biostatistics component and support. In other words, a strong biostatistics research and support initiative will greatly enhance the possibility of success or

the opportunity of the full development of these programs in MU. It should be noted that current existing consulting services and manpower in biostatistics in MU is far less than what is needed even for existing programs.

b. Outcomes and measure of success

The success of this initiative, if funded and implemented, will be the establishment of a world-class graduate program on biostatistics and the establishment of a biostatistics research and support center with a good number of NIH funded projects in MU.

c. Potential Impact

The implementation of this initiative has four main potential impacts on MU, the State of Missouri and the Nation. One is that it will provide all Missourians an opportunity to join a graduate program in biostatistics in Missouri; it will attract and keep the best people here in MU and Missouri. The second impact is that a strong biostatistics program will help the whole field of statistics, and biostatistics itself, to grow much stronger in terms of attracting the best faculty and students and obtaining research and training fundings. The third impact is that the strong biostatistics research and support resource will greatly help other research programs in MU and UM to get fundings and to succeed. Lastly a whole and strong biostatistics program will definitely bring the nation's and world's attention to MU and enhance the status of MU and UM.