FINAL AGENDA

Toward Consensus on "Best Practices" for the Generation, Analysis, and Application of Microarray Data in the Discovery, Development, and Review of FDA-regulated Products

The 7th Meeting
MicroArray Quality Control (MAQC) Project

Development and Validation of Predictive Models

Thursday-Friday
May 24-25, 2007
9:00 am – 6:00 pm EDT

SAS Institute Inc.
Building V
100 SAS Campus Drive
Cary, NC 27513, USA
http://www.sas.com/; http://www.jmp.com/

http://edkb.fda.gov/MAQC/

- MAQC contact: Leming.Shi@fda.hhs.gov, Tel : +1-870-543-7387
- Participants are expected to be familiar with the "MAQC-II Research Plan". Contact Leming.Shi@fda.hhs.gov if you do not have it.
- Participants should consider information exchanged during the MAQC meeting as confidential.

Thursday, May 24, 2007 (Day One)

Session I-A: MAQC-II Overview and Working Group Updates Chair: **Russ Wolfinger** (SAS)		
9:00 am	Welcoming Remarks	John Sall Co-founder of SAS
9:05 am	Overview of MAQC-II and Meeting Agenda	Leming Shi (NCTR)
9:20 am	Clinical Working Group	Wendell Jones (EA)
9:35 am	Toxicogenomics Working Group	Federico Goodsaid (CDER)
9:50 am	Titration Working Group	Rich Shippy (Affymetrix)
10:05 am	Regulatory Biostatistics Working Group (RBWG)	Greg Campbell (CDRH)
10:20 am	Performance Metrics to be used by MAQC-II for Evaluating Predictive Classifiers/Models	Lakshmi Vishnuvajjala (CDRH)
10:30 am	Discussion	All
10:40 am	Coffee break	
Session I-B: Analysis Results from the Titration and Clinical Working Groups Chair: **Jim Fuscoe** (NCTR/FDA)		
11:00 am	Analysis Results from the Titration Working Group: What are we learning from the MAQC titration study?	Marc Salit (NIST)
11:45 am	Analysis Results from the Clinical Working Group: Array QC: breast cancer and neuroblastoma (8 mins) Hold-out set for UAMS multiple myeloma data (2 mins) Gene-by-gene array quality analysis (5 mins) Summary of classifiers: breast cancer data (5 mins for each presenter) Discussion (10 mins)	 Wendell Jones (EA) Wendell Jones (EA) Jim Willey (Univ. Toledo) Roger Perkins (NCTR) Weiwei Shi (GeneGo) Russ Wolfinger (SAS) John Zhang (SAI)
12:30 pm	Lunch	
Session I-C: Analysis Results from the Toxicogenomics Working Group – A Pilot Exercise for MAQC-II Data Analysis Chair: **Greg Campbell** (CDRH/FDA)		
2:00 pm	Coordination of Data Analysis Effort – The Hamner Data Set	Weida Tong (NCTR)
2:20 pm	Summary of Classifiers – NIEHS/NIH	Pierre Bushel (NIEHS)
2:30 pm	Summary of Classifiers – Swiss Institute of Bioinformatics	Mauro Delorenzi (SIB)
2:40 pm	Summary of Classifiers – University of Southern Missouri	Youping Deng (USM)
2:50 pm	Summary of Classifiers – NCTR/FDA	Roger Perkins (NCTR)
3:00 pm	Summary of Classifiers – Chinese Academy of Sciences	Tieliu Shi (CAS)
3:10 pm	Summary of Classifiers – SAS Institute Inc.	Russ Wolfinger (SAS)
3:20 pm	Summary of Classifiers – Systems Analytics Inc.	John Zhang (SAI)
3:30 pm	RBWG Review of Statistical Analysis Plans (SAPs)	Tim Davison (Asuragen)
3:40 pm	Coffee break	
Session I-D: Availability of Tissue/RNA Samples and Generation of New Data Co-Chairs: **Fraser Symmans** (MD Anderson Cancer Center) and **Federico Goodsaid** (CDER/FDA)		
4:00 pm	Breast Cancer: Institut Bordet Eppendorf	Desmedt Christine (Bordet) Peter Herzer (Eppendorf)
4:25 pm	Multiple Myeloma: University of Arkansas for Medical Sciences Millennium Pharmaceuticals Inc.	Wendell Jones (EA) George Mulligan (MPI)
4:45 pm	Neuroblastoma: University of Cologne	André Oberthür (Cologne)
5:00 pm	Toxicogenomics: The Hamner Institutes for Health Sciences	Rusty Thomas (Hamner)
5:10 pm	Cross-laboratory and cross-platform reproducibility of model prediction results	Fraser Symmans (MDACC)/ Christos Hatzis (Nuvera)

5:25 pm	Microarray Platforms Affymetrix Agilent Eppendorf Illumina NimbleGen PhalanxBiotech TeleChem ArrayIt Alternative Platforms Applied Biosystems Gene Express Panomics SuperArray	Confirmation of support from representatives of platform providers
5:40 pm	Prioritizing Studies for the Generation of New Data	All
5:55 pm	Summary of Day One	Leming Shi (NCTR)
6:00 pm	Adjourn Day One	
6:15 pm	Bus Tour of SAS Campus	
6:45 pm	Dinner at Prestonwood Country Club, Salon B & C 300 Prestonwood Parkway, Cary, NC 27513 Tel: 919-467-2566, http://www.prestonwoodcc.com/	All participants are invited. Kindly sponsored by JMP.

Friday, May 25, 2007 (Day Two)

Session II-A: FDA Regulatory Perspectives on Genomics Co-Chairs: **Uwe Scherf** (CDRH/FDA) and **Rick Jensen** (Virginia Bioinformatics Institute)		
9:00 am	MammaPrint: The FDA Review and Approval Process	Reena Philip (CDRH)
9:25 am	Companion Guidance to the FDA Pharmacogenomics Guidance	Federico Goodsaid (CDER)
9:45 am	Uncertainties in the Multiple-Biomarker Classifier Problem	Bob Wagner (CDRH)
10:20 am	Discussion	All
10:40 am	Coffee break	
Session II-B: Genome-Wide Association Working Group (GWAWG) Co-Chairs: **Federico Goodsaid** (CDER/FDA) and **Leming Shi** (NCTR/FDA)		
11:00 am	Genome-Wide Association Studies: New Paradigm or the Same Old Genes?	Teri Manolio (NHGRI)
11:45 am	Genome-Wide Association Studies and FDA's Voluntary eXploratory Data Submission (VXDS)	Federico Goodsaid (CDER)
12:00 pm	Proposal and Discussion: Genome-Wide Association Working Group (GWAWG) under MAQC-II	Federico Goodsaid (CDER) Nick Xiao (SAIC/NCI)
12:30 pm	Lunch	
Session II-C: Data Analysis Strategies Chair: **Tim Davison** (Asuragen)		
2:00 pm	General Principles on the Development and Validation of Predictive Models based on Microarray Data	Kenneth Hess (MDACC)
2:20 pm	Logistic Considerations in Data Distribution and Data Analysis	Weida Tong (NCTR)
2:40 pm	Experimental Design for Data Analysis Combinations	Russ Wolfinger (SAS)
3:00 pm	Percellome: "Per Cell" Normalization Method for mRNA Measurement by Quantitative PCR and Microarrays	Jun Kanno (National Institute of Health Sciences)
3:20 pm	Discussion	All
3:40 pm	Coffee break	
Session II-D: Data Analysis Teams Chair: **Wendell Jones** (Expression Analysis)		
4:00 pm	Date Set (Disease) Specific Teams: Breast cancer Neuroblastoma Multiple myeloma Hamner mouse-lung-tumor Iconix-EPA liver carcinogenicity	Data Analysis Coordinators: Xutao Deng (UCLA/CSHS) Russ Wolfinger (SAS) Roger Perkins (NCTR) Weida Tong (NCTR) Richard Judson (EPA)

	Titration Data Some Preliminary Proposals: Effect of array data quality on model prediction performance Cross-laboratory and cross-platform reproducibility of model prediction results Batch effect on model prediction performance RBWG "statistical methodologies"	Marc Salit/Russ Wolfinger Wendell Jones (EA) Fraser Symmans (MDACC)/ Christos Hatzis (Nuvera) John Zhang (SAI) Lakshmi Vishnuvajjala/ Gene Pennello (CDRH)
4:50 pm	Open Presentation/Discussion (limited to 5~7 mins per presenter): Anne Bergstrom Lucas (Agilent) Xutao Deng (CSHS) Guozhen Liu (SuperArray) Jean & Danielle Thierry-Mieg (NCBI) Bill Worzel (Genetics Squared) Others	
5:55 pm	Summary of the Meeting	Leming Shi (NCTR)
6:00 pm	Adjourn the Meeting	

Reaffirmation of MAQC-II Goals

We would like to remind all MAQC-II members that the main goal of MAQC-II is to understand better the algorithms leading to classifiers for the analysis of microarray data. The important goal of validation for single classifier sets generated through internal validation drives the initial schedule of this MAQC-II collaboration. However, each analysis group is expected to include a report on the exploratory performance in the test dataset for the other classifier candidates from the internal validation stage. This will enable a comparison of the gap between predicted performance from internal validation and actual performance in the test dataset, even though these classifiers did not undergo formal validation. The Clinical and Toxicogenomics Working Groups will be responsible for collating the results of this exploratory work.

Disclaimer

Participation in the MAQC project is completely voluntary. No fund whatsoever is available from the MAQC to any participant. Participants agree to cover all their own costs as a result of voluntary involvement in the MAQC project. The US Food and Drug Administration (FDA) has solicited DNA microarray gene expression data sets as well as proposals to analyze these data sets in order to evaluate the impact of different analysis protocols on the selection of genes and their associated predictive models for biomarker pattern development (*Federal Register*, 71(77), 20707-8, April 21, 2006; available at http://www.fda.gov/nctr/science/centers/toxicoinformatics/maqc/docs/FederalRegister_MAQC_FollowUp.pdf). The MAQC project is being coordinated by the FDA, but there are no regulatory rights conveyed to anyone by the participation of FDA personnel in this project. Although FDA personnel are involved in the MAQC project, the views expressed in the MAQC-II Research Plan, at face-to-face meeting or other circumstances are not FDA guidance and do not necessarily represent FDA policy.

Transportation

The local airport is "RDU" (Raleigh/Durham International Airport).

Attendees driving themselves to the SAS Campus will need to stop at the front security gate upon arrival and identify themselves as a participant in the MAQC Meeting in Building V. Parking will be reserved for the attendees in the lot at Building V.

SAS will have a bus to take people to and from lunch on Thursday and Friday on the SAS campus. If the weather is nice, many people may decide to walk since the Café is a very short (not even a block) distance from Building V. After lunch, the bus will take people back to Building V for the afternoon sessions. On Thursday (6:15 pm), SAS will offer people the option of taking a brief (15 minutes) tour of the SAS campus.

Hotel

A list of SAS-recommended hotels: http://support.sas.com/training/fyi/ca.html.

Thursday Dinner

All MAQC meeting participants are invited to a dinner kindly sponsored by JMP at:
Prestonwood Country Club, Salon B & C, 300 Prestonwood Parkway, Cary, NC 27513.
Tel: 919-467-2566, http://www.prestonwoodcc.com/

Dress Code: "Gentlemen are expected to wear a collared shirt at all times and denim blue jeans are not allowed throughout the club's facilities."

U.S. Federal Government Employees: The U.S. FDA's Ethics and Integrity Staff has determined that "all participants are allowed to accept the free meal because this is considered to be a G-1 WAG [Widely Attended Gathering] event".

There will be a SAS bus that can take you directly from the SAS campus over to Prestonwood (~6 miles) for dinner if you do not want to drive yourselves. After the dinner, the bus can bring you back to the SAS parking lot. You may also be taken back to your hotels directly if you wish.

Participation by Phone

If you cannot physically attend the meeting, you may want to dial-in to the meeting using the following access information through the entire MAQC meeting:

USA Toll Free Number:	1-866-802-6141
International Callers:	+1-210-453-1165
Passcode:	8698206#

We may be able to allow a few participants to join via WebEx. In fairness to the expected large audience in the SAS conference room, callers are asked to minimize the number and length of their questions/comments because the audio quality may be less than satisfactory. We reserve the right to disconnect the conference call if the audience in the SAS conference room decides that there is too much disruption by the calls. Thanks in advance for your understanding. If you plan to attend by phone/WebEx, please e-mail leming.shi@fda.hhs.gov.

SAS/JMP Contact

Robin Hughes, JMP Marketing, 919-531-5806 (O), Robin.Hughes@jmp.com

FDA/NCTR Contacts

Leming Shi, 870-543-7387 (O), 501-258-3615 (C), Leming.Shi@fda.hhs.gov
Weida Tong, 870-543-7142 (O), 501-412-1749 (C), Weida.Tong@fda.hhs.gov

List of Confirmed Participants (As of May 18, 2007)

No.	Name	Organization	No.	Name	Organization
1	Wenjun Bao	SAS Institute	56	Charles Ma	Phalanx Biotech Group
2	William T. Barry	Duke University	57	Sergei Makarov	Attagene
3	Anne Bergstrom Lucas	Agilent	58	Teri Manolio	NIH/NHGRI
4	Vincent Bertholet	Eppendorf Array Technology	59	George J. Mulligan	Millennium Pharmaceuticals
5	Norman Birchfield	EPA	60	Padraic Neville	SAS Institute
6	Guy Bowman	InforSense, LLC	61	Paul E. Nisson	SuperArray
7	Anne Bullard	SAS Institute	62	André Oberthuer	University of Cologne
8	Pierre Bushel	NIH/NIEHS	63	Oluwole Odujinrin	Customized Therapeutics LLC
9	Gregory Campbell	FDA/CDRH	64	Grier P. Page	University of Alabama
10	Jennifer G. Catalano	FDA/CBER	65	Richard S. Paules	NIH/NIEHS
11	Damien Chaussabel	Baylor Institute for Immunology Research	66	Gene A. Pennello	FDA/CDRH
12	Desmedt Christine	Institut Jules Bordet	67	Edward J Perkins	US Army Engineer Research and Development Center
13	Tzu-Ming Chu	SAS Institute	68	Roger Perkins	FDA/NCTR (Z-Tech)
14	Shannon Conners	SAS Institute	69	Ron Peterson	Novartis
15	Michael B. Datto	Duke University Medical Center	70	Reena Philip	FDA/CDRH
16	Timothy S. Davison	Asuragen	71	Laura H. Reid	Expression Analysis
17	Francoise de Longueville	Eppendorf Array Technology	72	Todd Richmond	NimbleGen Systems, Inc.
18	Mauro Delorenzi	Swiss Institute of Experimental Cancer Research	73	Marc Salit	NIST
19	Adam Dempsey	XceedMolecular	74	John Sall	SAS Institute
20	Xutao Deng	UCLA/Cedars-Sinai	75	Uwe Scherf	FDA/CDRH
21	Youping Deng	University of Southern Mississippi	76	Banalata Sen	EPA
22	David J. Dix	EPA	77	Robert A. Setterquist	Ambion
23	Pan Du	Northwestern University	78	Imran Shah	EPA
24	Stephen W Edwards	EPA	79	Joe Shambaugh	Genedata (USA) Inc.
25	Meg G Ehm	GlaxoSmithKline	80	Leming Shi	FDA/NCTR
26	Patton Fast	InforSense, LLC	81	Tieliu Shi	Chinese Academy of Sciences
27	Kazuhisa Fukushima	Yokogawa Electric Corp.	82	Weiwei Shi	GeneGo Inc.
28	Federico M. Goodsaid	FDA/CDER	83	Richard Shippy	Affymetrix
29	Xu Guo	Affymetrix	84	Dave D. Smith	Luminex
30	Paul K. Haje	TeleChem ArrayIt	85	W. Fraser Symmans	MD Anderson Cancer Center
31	Christos Hatzis	Nuvera Biosciences, Inc.	86	Tsetska Takova	NimbleGen Systems, Inc.
32	Yudong He	Rosetta Inpharmatics (Merck)	87	Pei-Yi Tan	SAS Institute
33	Kenneth Hess	MD Anderson Cancer Center	88	Danielle Thierry-Mieg	NIH/NCBI
34	Susan Hester	EPA	89	Jean Thierry-Mieg	NIH/NCBI
35	Lingkang Huang	NIH/NIEHS	90	Venkata Thodima	University of Southern Mississippi
36	Robin Hughes	SAS Institute	91	Russell S. Thomas	Hamner Institutes for Health Sciences
37	Melody Humbles	Tecan	92	Guy Tillinghast	Riverside Regional Medical Center
38	Ansar Jawaid	AstraZeneca	93	Bernadette Toner	GenomeWeb
39	Brandon D. Jeffy	Iconix	94	Weida Tong	FDA/NCTR
40	Roderick V. Jensen	Virginia Bioinformatics Institute	95	Silvia Vega	Rosetta Biosoftware
41	Charles D. Johnson	Asuragen	96	Lakshmi Vishnuvajjala	FDA/CDRH
42	Wendell D. Jones	Expression Analysis	97	Juergen von Frese	Almac Diagnostics
43	Richard Judson	EPA	98	Robert F Wagner	FDA/CDRH
44	Jun Kanno	National Institute of Health Sciences	99	Stephen J. Walker	Wake Forest University
45	Channa Keshava	EPA	100	William Ward	EPA
46	Nagalakshmi Keshava	EPA	101	Jeffrey F Waring	Abbott
47	Samir Lababidi	FDA/CDRH	102	Liling L Warren	GlaxoSmithKline
48	Ben Larman	tecnoparco.org	103	James C. Willey	University of Toledo
49	Dai J Li	FDA/CDRH	104	Russell D Wolfinger	SAS Institute
50	Lei Li	Baylor University Medical Center	105	Bill Worzel	Genetics Squared
51	Wayne Liao	Phalanx Biotech Group	106	Shujian Wu	Bristol-Myers Squibb
52	Simon Lin	Northwestern University	107	Nianqing Xiao	NCI (SAIC)
53	Guozhen (Gordon) Liu	SuperArray	108	George Yuan	Affymetrix
54	Edward K. Lobenhofer	Cogenics, a Division of Clinical Data	109	John Zhang	Systems Analytics
55	Jun Luo	Systems Analytics			