FINAL AGENDA

The MicroArray Quality Control (MAQC) Project:

An FDA-led Effort Toward Personalized Medicine

The 8th MAQC Project Meeting

Development and Validation of Predictive Models

Monday-Wednesday
March 24–26, 2008
9:00 am – 6:00 pm Eastern Daylight Time

US FDA
Advisors and Consultants Staff Conference Room
Room 1066
5630 Fishers Lane
Rockville, MD 20857, USA

Meeting Objectives:

1. Present Data Analysis Protocols (DAPs) and analysis results;
2. Select MAQC's "best" model for each of the 13 endpoints from the six data sets;
3. Finalize a plan for generating additional gene expression and genotyping data;
4. Decide on manuscript topics, team leaders, and timeline.

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

Participants should consider information exchanged during the MAQC meeting as confidential.

Monday, March 24, 2008 (Day One)

8:00 am	Registration & Continental Breakfast	
Session I-A: MAQC-II Overview and Working Group Updates Chair: Federico Goodsaid (CDER/FDA)		
9:00 am	Welcoming Remarks	Robert O'Neill (CDER/FDA)
9:20 am	Overview of MAQC-II and Meeting Agenda	Leming Shi (NCTR/FDA)
9:45 am	Clinical Working Group	Wendell Jones (Expression Analysis)
9:55 am	Toxicogenomics Working Group	Richard Judson (EPA)
10:05 am	Titration Working Group (and ERCC Update)	Marc Salit (NIST)
10:20 am	Regulatory Biostatistics Working Group (RBWG)	Greg Campbell (CDRH/FDA)
10:30 am	Genome-Wide Association Working Group (GWAWG)	Federico Goodsaid (CDER/FDA)
10:40 am	JMAC: Japan MicroArray Consortium	Kazuhisa Fukushima (Japan)
11:00 am	Coffee Break & Poster View	
Session I-B: Validation (Blinded) Data Sets Chair: **Lajos Pusztai** (MD Anderson Cancer Center)		
11:30 am	Existing Validation Sets: Hamner (Mouse Lung Tumor) Iconix (Rat Liver Carcinogen) NIEHS (Rat Necrosis) BR (Breast Cancer) MM (Multiple Myeloma) NB (Neuoblastoma)	Lajos Pusztai Pierre Bushel (NIEHS/NIH) Lajos Pusztai (MDACC) Yiming Zhou (UAMS) Benedikt Brors (DKFZ)
12:00 pm	Generating Additional Gene Expression and Genotyping Data	Leming Shi
12:05 pm	Contributions Are Needed from MAQC-II Participants	Manufacturers, Service Providers, and All
12:30 pm	Lunch & Poster View	
Session I-C: Data Analysis Protocols (DAPs) and Analysis Results (1) Chair: **Greg Campbell** (CDRH/FDA)		
2:00 pm	1. CAS (Chinese Academy of Sciences, China)	Tieliu Shi
2:20 pm	2. CDRH (Center for Devices and Radiological Health, FDA)	Samir Lababidi
2:40 pm	3. CIPF (Centro de Investigacion Principe Felipe, Spain)	Ignacio Medina
3:00 pm	4. Cornell (Weill Medical College of Cornell University)	Fabien Campagne
3:20 pm	5. DKFZ (German Cancer Research Center, Germany)	Benedikt Brors
3:40 pm	6. EPA (U.S. Environmental Protection Agency)	Zhen Li and Fathi Elloumi
4:00 pm	Coffee Break & Poster View	
Session I-D: Data Analysis Protocols (DAPs) and Analysis Results (2) Chair: **Wendell Jones** (Expression Analysis)		
4:30 pm	7. GeneGo	Andrej Bugrim
4:50 pm	8. FBK (Fondazione Bruno Kessler, Italy)	Cesare Furlanello
5:10 pm	9. NCTR (National Center for Toxicological Research, FDA)	Huixiao Hong
5:30 pm	10. NIEHS (National Institute of Environmental Health Sciences)	Jianying Li and Jeff Chou
5:50 pm	Discussion	All
6:00 pm	Adjourn Day One	

Tuesday, March 25, 2008 (Day Two)

8:00 am	Continental Breakfast	
Session II-A: Data Analysis Protocols (DAPs) and Analysis Results (3) Chair: **Lakshmi Vishnuvajjala** (CDRH/FDA)		
9:00 am	11. NWU (Northwestern University)	Simon Lin
9:20 am	12. Princeton (Princeton University)	Jianqing Fan
9:40 am	13. SAI (Systems Analytics Inc.)	John Zhang
10:00 am	14. SAS (SAS Institute Inc.)	Russ Wolfinger
10:20 am	15. SIB (Swiss Institute of Bioinformatics, Switzerland)	Vlad Popovici
10:40 am	16. Spheromics (Umeå University, Sweden)	Max Bylesjö
11:00 am	Coffee Break & Poster View	
Session II-B: Data Analysis Protocols (DAPs) and Analysis Results (4) Chair: **Tim Davison** (Asuragen)		
11:30 am	17. SuperArray (SuperArray Bioscience Corporation)	Guozhen Liu
11:50 am	18. Tsinghua (Tsinghua University, China)	Shicai Fan
12:10 pm	19. USM (University of Southern Mississippi)	Youping Deng
12:30 pm	Lunch & Poster View	
Session II-C: Data Analysis Protocols (DAPs) and Analysis Results (5) Chair: **Kenneth Hess** (MD Anderson Cancer Center)		
2:00 pm	20. JHSPH (Johns Hopkins Bloomberg School of Public Health)	Rafael Irizarry
2:20 pm	21. UML (University of Massachusetts Lowell)	Dalila Megherbi
	New data analysis teams:	
2:40 pm	22. GT (Georgia Institute of Technology – Emory University)	May Wang
2:55 pm	23. Cornell2 (Cornell University)	Wei Wang
3:10 pm	24. SDSU (South Dakota State University)	Xijin Ge
3:25 pm	25. KU (University of Kansas)	Luke Huan
	The following teams are unable to attend the meeting:	*Team Leader*
	1. Almac (Almac Diagnostics, UK)	*Juergen von Frese*
	2. CBC (CapitalBio Corporation, China)	*Liang Zhang*
	3. Ligand (Ligand Pharmaceuticals)	*Wen Luo*
	4. NIEHS2 (National Institute of Environmental Health Sciences)	*Jennifer Fostel*
	5. Roche (Roche Palo Alto LLC)	*Mark Fielden*
	6. UCLA (Cedars-Sinai Medical Center of UCLA)	*Xutao Deng*
	7. UIUC (University of Illinois at Urbana-Champaign)	*Sheng Zhong*
	8. ZJU (Zhejiang University, China)	*Xiaohui Fan*
3:40 pm	Discussion	All
4:00 pm	Coffee Break & Poster View	
Session II-D: Selection of MAQC's "Best" Models and Distribution of Validation Data Sets Co-Chairs: **Bob Wagner** (CDRH/FDA) and **Wendell Jones** (Expression Analysis)		
4:30 pm	Selecting MAQC's "Best" Model for Each Data Set (Endpoint)	All
5:45 pm	Logistics on Distributing Validation Data Sets	Leming Shi (NCTR/FDA)
5:50 pm	Template for Reporting Prediction Results	Wendell Jones (EA)
6:00 pm	Adjourn Day Two	

Wednesday, March 26, 2008 (Day Three)

8:00 am	Continental Breakfast	
Session III-A: Manuscript Preparation (1) Chair: **Jim Fuscoe** (NCTR/FDA)		
9:00 am	1. The "Main" Manuscript	Leming Shi (NCTR/FDA)
	2. Cross-Site Prediction Reproducibility (Breast Cancer)	Fraser Symmans (MDACC)
	3. Cross-Platform Transferability of Models (NIEHS Data)	Huixiao Hong (NCTR/FDA)
	4. Cross-Tissue Prediction (NIEHS Data)	Jeff Chou (NIEHS)
	5. Array Data Quality and Model Prediction Performance	Wendell Jones (EA)
	6. Normalization Methods and Model Prediction Performance	Rafael Irizarry (JHSPH)
	7. Batch Effect Removal and Model Prediction Performance	John Zhang (SAI)
	8. Cross-Batch/Platform Prediction	Andrej Bugrim (GeneGo)
	9. RBWG "Statistical Methodologies"	Greg Campbell (CDRH/FDA)
	10. Titration Manuscript(s)	Marc Salit (NIST)
	11. Genome-Wide Association	Huixiao Hong (NCTR/FDA)
	12. One-color *vs*. Two-color: Neuroblastoma (Agilent Platform)	Russ Wolfinger (SAS) Benedikt Brors (DKFZ)
	13. Multiple Myeloma: Gene Expression and Genotyping	Yiming Zhou (UAMS)
	14. Uncertainties in the Multiple-Biomarker Classifier Problem	Weijie Chen (CDRH/FDA)
	15. What Has Been Learned/Improved (TGxDAT Experience)?	Roger Perkins (NCTR/FDA)
	16. Multi-Path Learning Integrates Pathways into Microarray Analysis	Andrej Bugrim (GeneGo)
	… Additional Manuscript Proposals Are Welcome	Volunteers
11:00 am	Coffee Break & Poster View	
Session III-B: Manuscript Preparation (2) Chair: **Leming Shi** (NCTR/FDA)		
11:30 am	Discussion	All
12:20 am	Timeline VO: April 28 (Detailed Manuscript Outline) V1: July 14 (Full Manuscript) V2: Aug. 4 (Revised) V3: Aug. 18 (Revised, Ready for Institutional Clearance) V4: Sept. 1 (Revised, Almost Ready for Peer Review) VS: Sept. 8, 2008 (Submission for Peer Review)	Leming Shi (NCTR/FDA)
12:30 pm	Lunch & Poster View	
Session III-C: Genome-Wide Association Working Group (GWAWG) Chair: **Federico Goodsaid** (CDER/FDA)		
1:30 pm	GWA Data Sets	Nick Xiao (SAIC/NCI)
1:50 pm	GWA Data Analysis Plans	Huixiao Hong (NCTR/FDA)
2:20 pm	WTCCC Data Analysis Team	Silvia Vega (Rosetta) Li Zhang (CDER/FDA)
3:00 pm	Genome-Wide CNV Association and Batch Effects in the WTCCC Data Sets	Christophe Lambert (Golden Helix)
3:30 pm	JMP Genomics and GWA Data Analysis	Russ Wolfinger (SAS)
Concurrent Session: MAQC-II Titration Working Group Meeting (Mini Conference Room 1106) *Chair: **Marc Salit** (NIST)*		
1:30 pm ~ 3:30 pm	*Walt Liggett, Jean Lozach, Anne Bergstrom Lucas, Ron Peterson, Rich Shippy, Martin Schumacher, Leming Shi, Jean and Danielle Thierry-Mieg, Russ Wolfinger, ...*	
4:00 pm	Discussion	All
4:50 pm	Summary of the Meeting	Leming Shi (NCTR/FDA)
5:00 pm	Adjourn the Meeting	

Registration

The MAQC meeting is open to everyone and there is no registration fee. However, if you plan to attend the meeting, please contact Leming Shi (Leming.Shi@fda.hhs.gov, +1-870-543-7387) as soon as possible so that a seat will be reserved for you.

Meeting Venue

US Food and Drug Administration
Advisors and Consultants Staff Conference Room
Room 1066
5630 Fishers Lane
Rockville, MD 20857, USA

Poster Presentations

All meeting participants are encouraged to present their data analysis results or other information related to microarrays in posters to enhance the interactions among meeting participants.

Transportation

The local airports are:

Ronald Reagan Washington National Airport (DCA)
Washington Dulles International (IAD)
Baltimore/Washington International Thurgood Marshall (BWI)

The FDA conference room is close to the Metro Twinbrook station of the "red line" (http://www.wmata.com/metrorail/systemmap.cfm).

Hotel

The following hotels are within walking distance to the FDA conference room and to the Metro Twinbrook station of the "red line" (http://www.wmata.com/metrorail/systemmap.cfm):

Hilton Washington DC/Rockville Executive Meeting Center
1750 Rockville Pike
Rockville, MD 20852
301-468-1100
http://www.rockvillehotel.com/

Ramada Inn Rockville
1775 Rockville Pike
Rockville, MD 20852
301-881-2300
http://www.ramadarockville.com/

Summary of MAQC-II Data Sets

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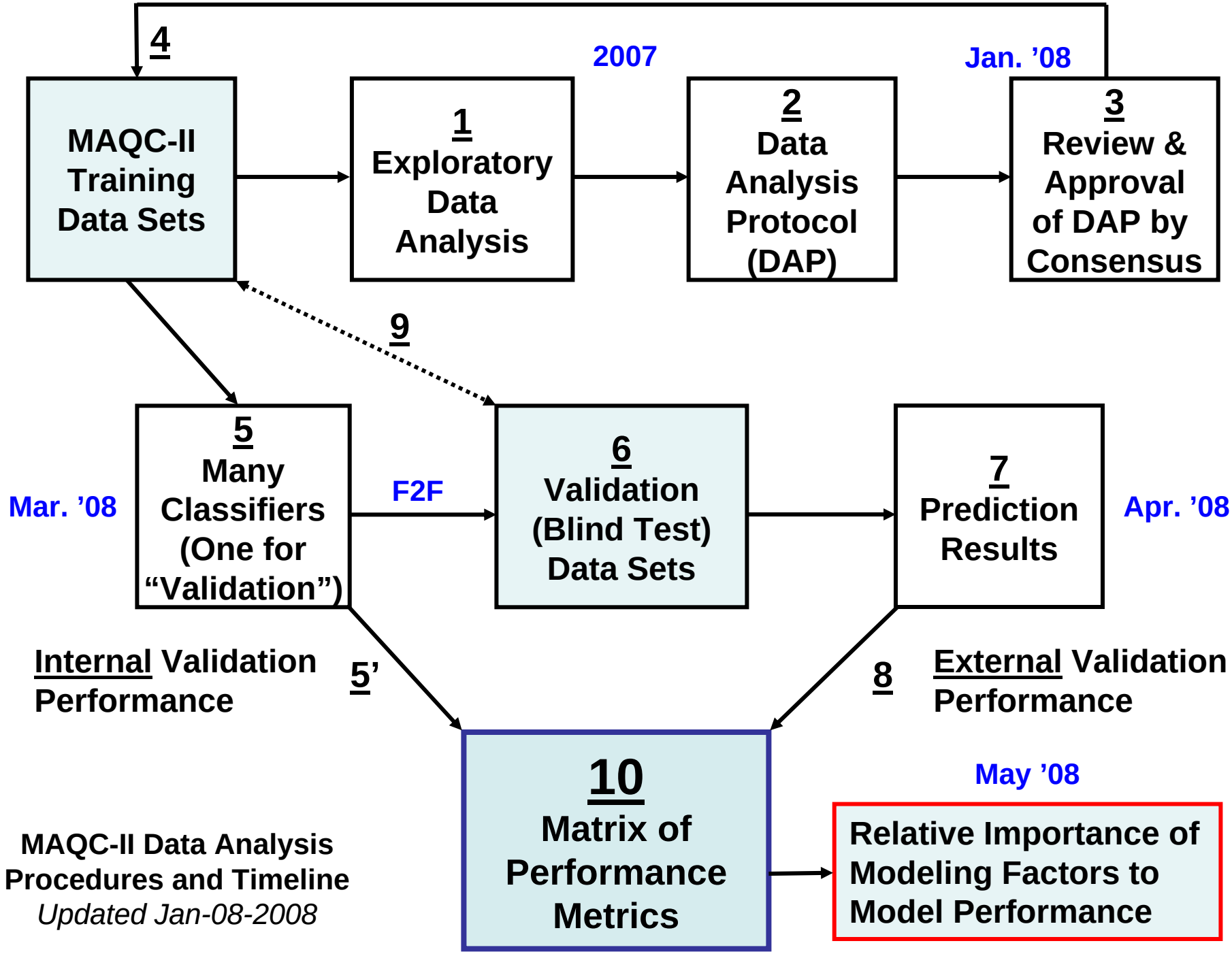
Table 1 A: MAQC-II Data Analysis Teams Are Required to Predict the 13 Endpoints from Six Data Sets

No.	Date Set Code	Endpoint Code	Endpoint Description	Excel Column Header*	Excel Column*	Number of Samples	Positives	Negatives	P/N Ratio
1	Hamner	A	Lung Tumor	**Class_LT_NLT**	**C**	70	26	44	0.59
2	Iconix	B	Liver Carcinogen	**Class**	**B**	216	73	143	0.51
3	NIEHS	C	Overall Necrosis Score	**Class**	**C**	214	79	135	0.58
4	BR	D	Treatment Response	**pCR**	**O**	130	33	97	0.34
5		E	Estrogen Receptor Status	**erpos**	**H**	130	80	50	1.6
6	MM	F	Overall Survival Milestone Outcome	**OS_MO**	**AB**	**340**	**51**	**289**	**0.18**
7		G	Event-free Survival Milestone Outcome	**EFS_MO**	**AA**	**340**	**84**	**256**	**0.33**
8		H	Clinical Parameter S1	**CPS1**	**S**	340	194	146	1.33
9		I	Clinical Parameter R1	**CPR1**	**T**	340	200	140	1.43
10	NB	J	Overall Survival Milestone Outcome	**OS_MO**	**AM**	**238**	**22**	**216**	**0.10**
11		K	Event-free Survival Milestone Outcome	**EFS_MO**	**AL**	**239**	**49**	**190**	**0.26**
12		L	Newly Established Parameter S	**NEP_S**	**AN**	246	145	101	1.44
13		M	Newly Established Parameter R	**NEP_R**	**AO**	246	145	101	1.44

*See Excel files listed in Table 1B. Endpoints (OS and EFS related) described in red have been updated based on the outcome of a "milestone" survey time; note that these endpoints are unbalanced.


4
2007
Jan. '08
MAQC-II Training Data Sets
1 Exploratory Data Analysis
2 Data Analysis Protocol (DAP)
3 Review & Approval of DAP by Consensus
9
Mar. '08
5 Many Classifiers (One for "Validation")
F2F
6 Validation (Blind Test) Data Sets
7 Prediction Results
Apr. '08
Internal Validation Performance
5'
8
External Validation Performance
10 Matrix of Performance Metrics
May '08
Relative Importance of Modeling Factors to Model Performance
MAQC-II Data Analysis Procedures and Timeline
Updated Jan-08-2008