AGENDA

The MicroArray Quality Control (MAQC) Project:
An FDA-Led Effort Toward Predictive and Personalized Medicine

The 11th MAQC Project Meeting

SEQC – The Sequencing Quality Control Project (MAQC-III)

Monday, March 9, 2009
6:00 pm – 9:00 pm CDT

&

Tuesday, March 10, 2009
8:00 am – 3:00 pm CDT

Doubletree Hotel, Salon B
424 West Markham Street
Little Rock, AR 72201, USA
+1-501-372-4371
www.doubletreelr.com

Leming.Shi@fda.hhs.gov
Tel: +1-870-543-7387 (O)
+1-501-258-3615 (C)

http://edkb.fda.gov/MAQC/
http://www.nature.com/nbt/focus/maqc/

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

Monday, March 9, 2009 (Day One)

5:00 pm	Registration, Salon B	
6:00 pm	Working dinner starts ($10/person, cash only)	
Session A: Analysis Results of SEQC "In-house" Sequence Data Sets		
6:10 pm	Welcoming remarks by William Slikker, Jr.	Director, NCTR/FDA
6:15 pm	Overview of SEQC progress	NCTR/FDA
6:20 pm	Danielle and Jean Thierry-Mieg	NCBI
7:00 pm	Eric Olson	Geospiza
7:30 pm	Christopher Mason	Yale University
8:00 pm	Jun Li	University of Michigan
8:15 pm	Mark Alter	Columbia University
8:30 pm	Tobias Guennel	Virginia Commonwealth University
8:45 pm	Discussion	
??	Adjourn	
Tuesday, March 10, 2009 (Day Two) **Session B**: Additional Analysis Results of SEQC "In-house" Sequence Data Sets		
7:30 am	Continental breakfast, Salon B	
8:00 am	Peter Grant	Genomatix Software
8:20 am	Guy Kol	GenomeQuest
8:40 am	Joaquin Dopazo	Centro de Investigación Príncipe Felipe (CIPF)
9:00 am	John Thompson: DGE and RNA-Seq protocols	Helicos BioSciences
9:20 am	Additional presenters welcome	
10:00 am	Coffee break	
Session C: Study Objectives, Resources, Contributions, Organization, and Timeline		
10:30 am	Self-introduction: "Why am I here today?"	All participants (30 seconds/person)
11:00 am	Federico Goodsaid	CDER/FDA
11:30 am	Proposals and suggestions	All
12:00 pm	Lunch ($10/person, cash only)	
1:00 pm	Discussion	
3:00 pm	Adjourn	

Every one is welcome to attend the following two seminars scheduled at the National Center for Toxicological Research, U.S. Food and Drug Administration, 3900 NCTR Road, Jefferson, AR 72079. The NCTR campus is about 35 miles south of Little Rock.

Monday, March 9, 2009, 10 AM

Accelerating diagnostic biomarker discovery through translational bioinformatics

Rong Chen, Ph.D. (Stanford Center for Biomedical Informatics Research)

Diagnostic biomarkers are molecular signatures that can be used to identify the presence or absence of a particular disease state. In the past decade, increasingly voluminous genetic, genomic, and phenotypical data have been deposited into public repositories, such as NCBI Gene Expression Omnibus (GEO). We have developed a series of bioinformatics tools to integrate and reason over many genome-scale measurements and experimental modalities to identify different types of diagnostic biomarkers, and deliver them to clinicians and biologists. As an example, we will show you how we integrated gene expression data from GEO to identify three non-invasive protein biomarkers for solid-organ transplant rejection.

Wednesday, March 11, 2009, 10 AM

Gene expression data: The key to better understanding adverse events? Are canonical toxicity profiles a predictive possibility?

James Flynn, Ph.D. (NextBio)

Clinical attrition due to drug toxicities and adverse events plague scientists from medicinal chemists to clinicians. With hundreds of drugs, toxins, and herbs reported to cause liver injury, the occurrence of severe hepatotoxicity too frequently leads to drug failure. Can expression profiles better delineate physiological perturbations assigned to compound classes? In this seminar, the NextBio data search and discovery platform will be used to explore rich, publically available data sets from CMAP2.0, Iconix and others for canonical toxicity profiles of drugs used in the treatment of Metabolic Syndrome X. A focus will be on fatty acid metabolism pathways and mitochondrial effects.

대한 독성 유전 · 단백체 학회
2009년도 국제 학술대회 및 정기총회

5th International Conference on Toxicogenomics (ICT) &
2nd Toxicogenomics Integrated Environmental Science (TIES)

보건 · 위해성 첨단 미래 기술 및 국제 독성 유전체 학회 첫걸음

Towards Improvement of Toxicogenomics and Initiatives for International Federations on Toxicogenomics (IFT)

2009 ICT

The Joint Symposium of 5th ICT & 2nd TIES

September 20 (Sun)~23 (Wed), 2009
Renaissance Seoul Hotel, Korea

후 원 : 환경부, 국립환경과학원, 한국 과학기술 연구원, 한국과학기술정보연구원, 한국 과학 기술 단체 총연합회, 한국 과학 재단, 한국 환경기술 진흥원 독성유전체 통합형과제사업, 인하대학교 의과대학 의약물 독성연구소

2009년 특별회원사 : 플래티늄 회원사=(주)지노첵, 골드회원사=(주)이바이오젠

2009년 후원사 : (주)인실리코젠, 박영주 콜렉션

2009년 광고 및 부스 회원사 : 한국화학시험연구원, 유현하이텍, (주)지앤시바이오, (주)대한과학, 보스톤사이언티픽코리아(주), 씨앤지 기획, (주)일신바이오베이스, (주)LG화학, (주)마크로젠, (주)메드빌, 신일제약(주), (주)서린바이오사이언스, 엘에스케이, (주)내츄럴엔도텍, 넥스타테크놀로지(주), (주)인실리코젠, 한국로슈진단, (주)대명사이언스, 바이오포유, 비엠에스, (주)이즈텍, 고운건설(주)

Congratulations!!

Impact Factor of Our Official Journal "Molecular and Cellular Toxicology" (ISSN 1738-642X) is 0. 759 (2008)

대한 독성 유전·단백체학회

The Korean Society of **Toxicogenomics** and **Toxicoproteomics**

http://www.tox.or.kr

[Speaker's Presentation Materials]

Plenary Lecture I

The MicroArray Quality Control (MAQC) Project: Enabling Personalized Medicine with Genomics and Bioinformatics

Dr. Leming Shi

NCTR, FDA, USA

[Speaker's Presentation Materials]

The MicroArray Quality Control (MAQC) Project: Enabling Personalized Medicine with Genomics and Bioinformatics

Leming Shi

National Center for Toxicological Research, U.S. Food and Drug Administration, 3900 NCTR Road, Jefferson, AR 72079, U.S.A.

The MicroArray Quality Control (MAQC) project, initiated and being led by the U.S. Food and Drug Administration (FDA), was originally designed to address concerns about microarray reliability as well as data analysis issues (http://edkb.fda.gov/MAQC/). The MAQC-I evaluated technical performance of various microarray platforms and advantages and limitations of competing data analysis methods in identifying differentially expressed genes (http://www.nature.com/nbt/focus/maqc/). The MAQC-II has been working toward consensus on "best practices" of developing and validating microarray-based predictive models for clinical and preclinical applications. The recently initiated MAQC-III (or SEQC) is evaluating technical performance and addressing bioinformatics challenges of next-generation sequencing technologies in the analysis of DNA and RNA samples. Experiences gained from these community-wide efforts are critical for the MAQC-IV (or PADRE) to predict patient-specific adverse drug reactions and efficacy via bioinformatics and genomics. Outcomes of the MAQC project are providing a solid scientific foundation to refine FDA guidance on the submission and review of pharmacogenomic data. The MAQC efforts, with enthusiastic participation from academia, industry, and the government, are facilitating the appropriate generation, analysis, and application of microarray and next-generation sequencing data in the discovery, development, and review of FDA-regulated products.

Keyword: Genomics, bioinformatics, predictive model, personalized medicine, microarray quality control, next-generation sequencing, drug efficacy, adverse drug reaction

[Speaker's Presentation Materials]

The MicroArray Quality Control (MAQC) Project:
Enabling Personalized Medicine with
Genomics and Bioinformatics

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National Center for Toxicological Research
U.S. Food and Drug Administration
Jefferson, Arkansas, U.S.A

MAQC

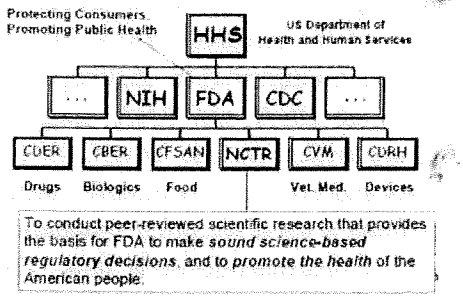
Seoul, Korea
September 21, 2009

IC [illegible] Views expressed in this presentation are those of the presenter and not necessarily those of the U.S. FDA FDA

Outline

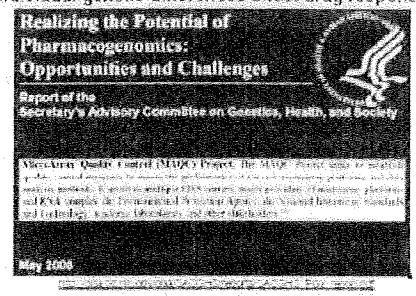
- FDA, PGx, and Personalized Medicine
- MicroArray Quality Control (MAQC) Project
  - MAQC I: DEG – Differentially Expressed Genes
  - MAQC II: Classifiers, GWA, and CNV
  - MAQC III: SEQC – SEquencing Quality Control
  - MAQC IV: PADRE – Predicting ADR and Efficacy via a patient-specific drug-protein interactome

HHS, FDA, and NCTR

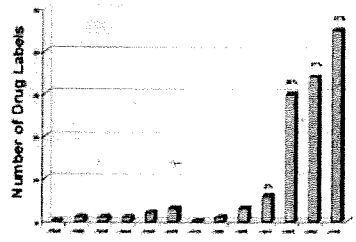


To conduct peer-reviewed scientific research that provides the basis for FDA to make *sound science-based regulatory decisions*, and to *promote the health* of the American people.

Pharmacogenomics (PGx) is the study of how individual genetic differences affect drug response



Labels of Approved Drugs with Pharmacogenomic Information

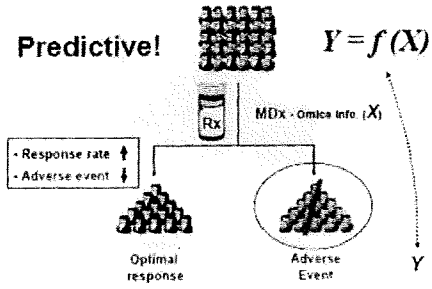


Pharmacogenomic biomarkers of susceptibility to adverse drug reactions (ADRs)

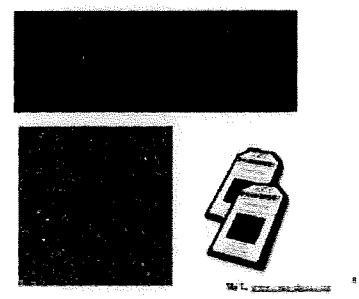
Aviganl MI
Personalized Medicine,
6(1): 67-76 (2009)

[Speaker's Presentation Materials]

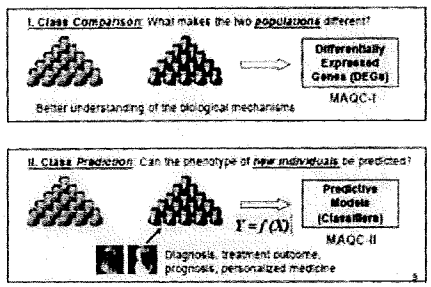
FDA and Personalized Medicine



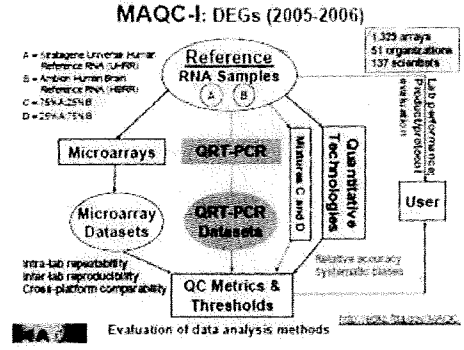
DNA Microarrays for Biomarker Discovery



Two Types of Microarray Applications



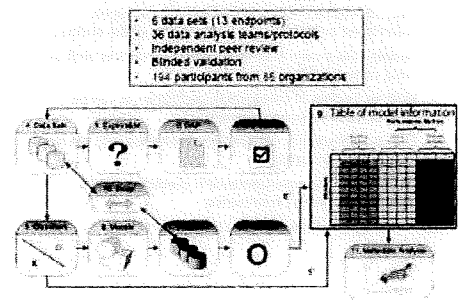
MAQC-I: DEGs (2005-2006)



MAQC-I Summary

1. Microarray challenges: data quality and data analysis
2. Reference RNA materials: laboratory performance (protocols, equipments, reagents, and technicians)
3. Reference data sets: capabilities and limitations of data analysis methods
4. **Microarray results (DEGs): reproducible and reliable**

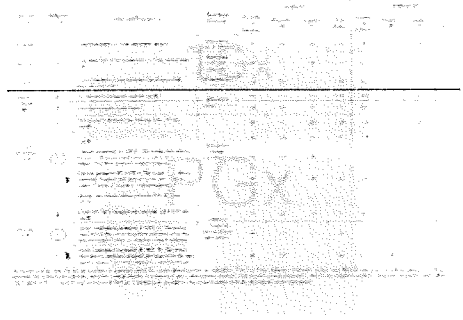
MAQC-II: Classifiers (2007-2009)



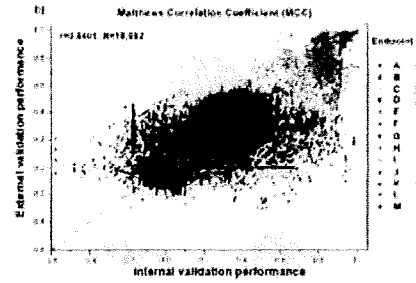
[Speaker's Presentation Materials]

MAQC-II Data Sets

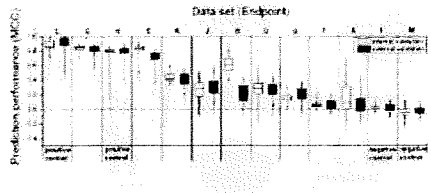
Over 1,000 arrays
36 organizations
154 scientists



Internal validation performance versus external validation performance



Prediction performance is data set dependent



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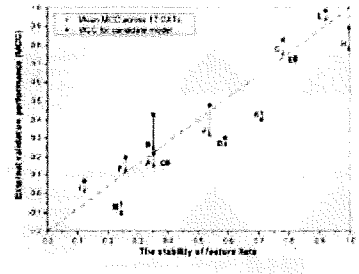
The Stability of feature lists is positively correlated with endpoint predictability



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MAQC-II Summary

1. The achievable prediction performance is largely determined by the intrinsic predictability of the endpoint.
2. Simple data analysis methods often perform as well as more complicated approaches.
3. Multiple models of comparable performance can be developed for a given endpoint.
4. The level of stability of gene lists correlates with the level endpoint predictability.
5. Internal validation performance is predictive of the external validation performance.
6. Following good modeling practices is critical.

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Outline

MAQC-III: SEQC – SEquencing Quality Control

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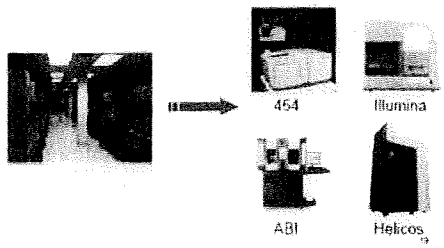
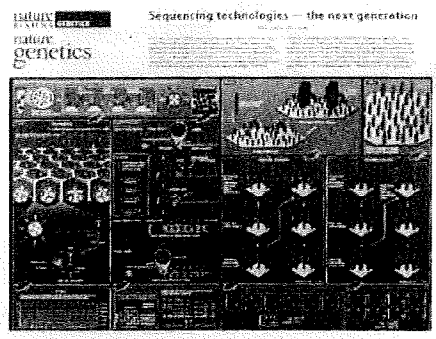
[Speaker's Presentation Materials]

Next-Generation Sequencing (NGS): *"Genome Center in a Mail Room"*

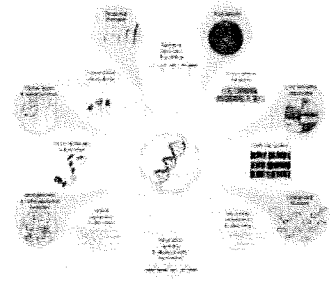


Major Players in Next-Generation Sequencing (NGS)

Vendor: Product	Million reads/run	Read length (bp)
• Helicos: HeliScope	600	~30
• Illumina: Genome Analyzer II	150	35-70
• Life Tech/ABI: SOLiD3	200	35-50
• Roche/454: GS FLX Titanium	1	~400



Many Applications of Next-Generation Sequencing



Kahvejian A, *Nature Biotechnology* 2008

RNA-Seq: a revolutionary tool for transcriptomics PERSPECTIVES

"Although RNA-Seq is still in the early stages of use, it has clear advantages over previously developed transcriptomic methods. ... As the cost of sequencing continues to fall, RNA-Seq is expected to **replace microarrays for many applications** that involve determining the structure and dynamics of the transcriptome."

Nature Biotechnology's Call for Action

Editorial, *Nature Biotechnology*, October 2008

"... a related endeavor that would help better benchmark the different next-generation sequencing technologies would be to carry out an initiative similar to the MicroArray Quality Control [MAQC] consortium where different platforms would be compared against one another as well as against DNA microarrays or quantitative PCR."

[Speaker's Presentation Materials]

SEQC (MAQC-III) Objectives (2009-2011)

1. Assess technical performance of NGS platforms by generating benchmark data sets with reference samples
2. Evaluate advantages and limitations of various bioinformatics strategies for data analysis
3. Compare data from NGS to those from other technologies such as microarrays and qPCR
4. Prepare the FDA for the next wave of submission of genomic data from NGS
5. Facilitate further development of NGS
6. Provide a learning opportunity for the community

NGS: Next-generation sequencing

Initial Focus of SEQC Data Analysis:
Quantitation of (differential) gene expression

NGS Performance:
1. Intra-site repeatability
2. Inter-site reproducibility
3. Cross-platform comparability

NGS *vs.* microarray

Performance at the level of:
1. Sequence
2. Absolute expression
3. Relative expression
4. Differentially expressed genes
5. Predictive models
6. *"New biology"?*

"Truth":
1. ERCC controls
2. Tissue titration mixtures
3. qPCR (and microarrays)
4. Clinical outcome

Note: NGS has many other powerful applications, but they will be addressed after gene expression quantitation.

Huge Amounts of Sequence Data Have Been Generated by Four Vendors Using MAQC Reference RNA Samples (A and B) ("In-House" Data Sets)

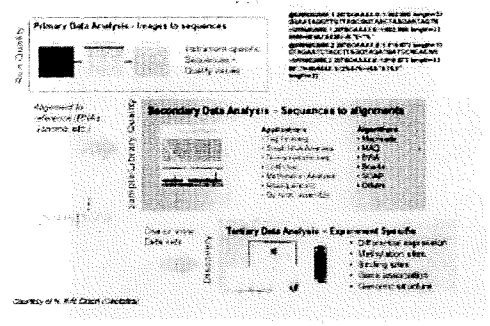
- Helicos
- Illumina
- LifeTech/ABI
- Roche/454

230 GB
4 billion reads

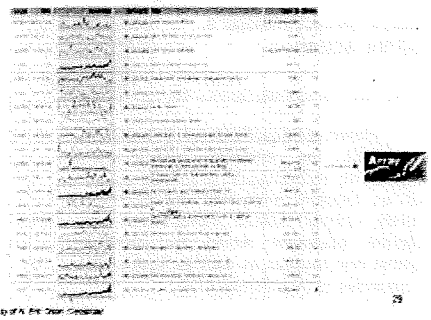
1. Develop and test bioinformatics pipelines
2. Better understand RNA sequence data and their analysis
3. Help better design the "official" SEQC study
4. Reconstruction (expansion) of the human transcriptome

>50 people from >40 organizations are analyzing the data.

NGS Data Analysis Flow



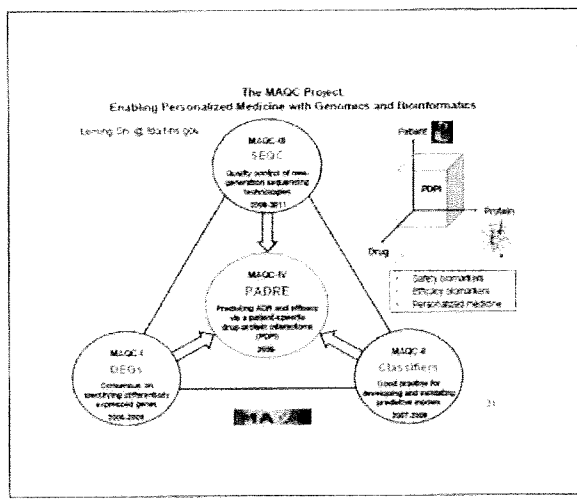
Alignment Results



Outline

MAQC-IV: PADRE – Predicting ADR and Efficacy via a patient-specific drug-protein interactome

[Speaker's Presentation Materials]



NIST to Make External RNA Control Consortium Spike-ins Available for Array ... - BioArray News

07.10.2009
By Justin Petrone

The US National Institute of Standards and Technology plans to make standard reference RNA controls available to microarray users by early next year, BioArray News has learned.

Developed by the External RNA Controls Consortium, an ad hoc group of participants from industry, the government, and academia, the spike-in RNA controls will be designed to enable researchers to measure the performance of their assays, according to Marc Salit, the chairman of the ERCC and a research chemist at NIST.

Salit told BioArray News this week that the ERCC has agreed upon a library of 96 controls composed of synthetic mammalian RNA that NIST will sell to array users at cost. As part of the controls development process, array platform manufacturers agreed to add probes to their arrays that will detect the control RNA without interfering with existing content.

"People really want to have confidence in their measurements," Salit said. "These controls are designed to give people that confidence."

Gaithersburg, Md.-based NIST has developed a plasmid DNA library that will be used to create the RNA controls using in vitro transcription. ERCC members Affymetrix, Atactic Technologies, **invitrogen**, and the Stanford Genome Technology Center aided NIST in the construction of the

library. Ultimately, NIST will make its library available to users like core labs or commercial vendors that will use it to manufacture RNA controls.

Salit said that the ERCC is now going through the process of certifying the sequences of the plasmid inserts in the library as standard reference material. He said that certification of the library of 96 controls, including about 95,000 bases, should be completed by the end of this year, allowing NIST to make the reference RNAs available in 2010.

ERCC members Ambion and Commonwealth Biotechnologies are developing traceable RNA controls from the library, Salit added. "We are working with Ambion and CBI to make sure that these controls will be commercially available," he said. "This way, they can assert traceability to the reference material.

"We will work with any manufacturers that are interested in making derivatives of that," Salit said. "We are trying to enable the world to have traceable reference material to facilitate gene expression measurements in regular applications."

'A Long Process'

Established in 2003, the ERCC has delayed the targeted release date for its controls several times. After agreeing on a test plan for developing the spike-in controls in 2005, the ERCC embarked on testing 176 proposed controls with the aim of narrowing in on a set of 96 that could work reliably across all array platforms. The controls were tested at Illumina, Affy, Agilent Technologies, and the National Institute of Allergy and Infectious Diseases. The target date for making them available was pushed back from mid-2006 to the end of 2007 and then to mid-2008 (see BAN 7/17/2007).

Salit said that part of the reason for that delay is that the certification process for the library has taken longer than expected. For instance, the ERCC had to work with the International Standards Organization to amend its definition of certified reference material to include sequences.

"We had to develop a new approach to certification of a reference material in order to certify sequence; this hasn't been done before," said Salit. "We worked to have the ISO definition of certified reference material changed to accommodate this need. Our new work here was in developing a way to express confidence in the base calls, when aggregating sequence data from many alternate measurements."

The ERCC test sites have also done an extended dynamic range study on the controls, and the ERCC has also done "authoritative sequencing" on the spike-ins. "NIST will issue this as standard reference material," Salit said. "That means the controls are backed up with multiple measurement methods and sufficient experimental measurements to allow us to estimate any uncertainty."

After gathering data from multiple labs with multiple sequencing instruments, Salit said that the ERCC is integrating all those data and classifying each base. Based on these evaluations, each base in NIST's library will have an estimate of confidence, ranging from "high confidence" to "ambiguous." Salit said he expects the "overwhelming majority" of the bases in the library to fall into the first category. He added that the ERCC is doing another round of second-generation sequencing to include more data in certification process.

"We are expecting to have reference material on the street in 2010," Salit said. "It's been a long process and we've learned a lot along the way."

BMRG バイオメディカル研究部門・バイオメジャー研究グループ
Bio-Measurement Research Group, Biomedical Research Institute

関口 勇地

第五回バイオアナリシス標準化連絡会

第一回産総研連絡会
第二回産総研連絡会
第三回産総研連絡会
第四回産総研連絡会
第五回産総研連絡会

以下の日程で、第5回バイオアナリシス標準化連絡会を開催いたします。産業技術総合研究所関係者の参加は自由です。ご興味をお持ちの方はお気軽にご参加ください。

日時：2010年1月25日（月） 15:00-17:00

場所：産総研つくば中央第六 6-9棟 228（第一会議室）

講師：Marc Salit博士
National Institute of Standards and Technology (NIST), USA
Chemical Science and Technology Laboratory
Multiplexed Biomolecular Science Group, Leader

演題：NIST SRM 2374: A certified reference material designed to support confidence in gene expression measurements

要旨
NIST has hosted the External RNA Control Consortium, an industry-initiated ad-hoc standards development effort, to develop materials that can be used to assess the technical performance of gene expression assays. This effort has led to the development of a new reference material, "NIST SRM 2374: DNA Sequence Library for External RNA Controls." SRM 2374 is a library of 96 plasmids, each packaged individually, which will be certified for the sequence of the unique inserts. Each plasmid is designed for simple in vitro transcription of RNA from the insert, either directly from a linearized plasmid, or from PCR product amplified from the plasmid. The inserts range in length from approximately 250 nucleotides to 2500 nucleotides, and in GC content from approximately 35% to approximately 50%. The average length is approximately 1000 nucleotides.
I will present the latest data from the ERCC testing of these materials, which includes performance assessment results for 4 different microarray platforms at 3 different test sites. Performance is assessed in this model experiment in both signal- and ratio-space, using a multiple-pool design. Discussion will be presented of a possible use scenario that is based on periodic "validation" with routine control-chart monitoring.
I will also discuss in detail the SRM certification process, for which we established a new approach to certifying qualitative properties; and plans for commercial dissemination of traceable RNA CRMs.

バイオアナリシス標準化連絡会設立趣意
計測標準研究部門・生物機能工学研究部門

バイオ・メディカル分野の発展に伴い、バイオアナリシス（生体由来物質の計量等）の標準化に関する要望が今後ますます高まっていくことが予想される。バイオアナリシスの標準化において、標準プロトコルの整備、国家標準物質の頒布等産総研の果たすべき役割は大きい。メートル条約のもと、バイオ計測の国際標準化の一翼を担う国際度量衡委員会物質量諮問員会バイオアナリシスワーキンググループ（CIPM/CCQM/BAWG）においても、バイオアナリシス分野の標準化や標準物質に関する議論がされているところである。しかしながら、バイオ・メディカル分野は広範であることから、バイオアナリシス標準化の要望に対応するためには産総研内の関連ユニットの協力が不可欠である。BAWGでの課題をはじめとした様々なバイオアナリシスの標準化に関する情報を産総研内の関連ユニットにおいて共有し、国内状況を踏まえた上で適宜対応していく必要がある。
こうした背景から、本連絡会を設立し、BAWG等の国際ならびに国内の動向についての情報交換を行う場を提供することにより、バイオアナリシス分野の円滑な標準化推進に資することを目指す。なお、本連絡会は、計測標準研究部門および生物機能工学研究部門を事務局とした自主的な機関とし、当面産総研内について参加はオープンとする。なお、本連絡会として研究テーマ提案や予算獲得等を目指すものではない。

活動目的
1) バイオアナリシス分野の標準化に関する情報（BAWG等の活動）を産総研内で共有する。
2) 必要に応じてBAWG等で行われるパイロットスタディへの参加者を募集・推薦する。
3) 必要に応じてCCQMやBAWGの活動への提案・提言について意見をまとめる。
4) 計測標準の枠組みの考え方を理解し、その普及を行う。
5) バイオ標準あるいはバイオ計測の標準化に関して意見交換を行う。
6) 国内あるいはCCQM以外の国際的な標準化に関連する活動についての情報を共有する。
7) その他上記に関連する情報共有、意見交換を行う。

活動内容
CCQM関連活動の報告（NMIJ）、標準化活動についての報告(各参加者)、意見交換等で2-3ヶ月に1回、2時間程度の会合を持つ。

独立行政法人医薬品医療機器総合機構　平成２１年度計画

独立行政法人通則法（平成１１年法律第１０３号）第３０条第１項の規定に基づき、平成２１年３月３１日付けをもって認可された独立行政法人医薬品医療機器総合機構中期計画を達成するため、同法第３１条第１項の定めるところにより、次のとおり、平成２１年度計画を定める。

平成２１年　３月３１日
平成２１年１１月　５日

独立行政法人医薬品医療機器総合機構
理事長　近　藤　達　也

・特定フィブリノゲン製剤及び特定血液凝固第Ⅸ因子製剤によるＣ型肝炎感染被害者に対する給付業務等の実施に当たっては、個人情報に特に配慮し、適切に業務を行う。

２　審査等業務及び安全対策業務

（１）先端的な医薬品・医療機器に対するアクセスの迅速化

【新医薬品】

ア　的確かつ迅速な審査の実施

・新医薬品の審査期間をはじめとする審査迅速化のための工程表については、毎年度その進捗状況について評価・検証等を行うとともに必要な追加方策を講じる。

・新医薬品及び生物系医薬品に関する審査チームについて、審査チームの増加が必要な分野及び今後必要となる分野の選定のための検討を行うとともに、適切な増員・配置により審査チームの増強を実施し、審査の迅速化を図る。

・プロジェクトマネジメント制度を展開し、申請品[illegible]況の適切な把握等により進行管理の充実を図[illegible]て示す方式（機構事前見解提示

・審査等業務進行管理委員会等で[illegible]談の実施を確保する。また、対面助言か[illegible]課題解決のた[illegible]場合を６０％について達成する。

カ　新技術の評価等の推進

・バイオ・ゲノム・再生医療といった先端技術を応用した医薬品の治験相談、承認審査について、高度な知見を有する外部専門家を活用する。

・先端技術を応用した製品に係る国の評価指針の作成に協力するとともに、評価の際に考慮すべき事項（point-to-consider）の作成対象を選定する。

・臨床試験実施前の細胞・組織利用医薬品及び遺伝子治療用医薬品に関する事前審査について、資料整備相談等の利用等を促し、迅速な実施を図る。また、遺伝子組換え生物等の使用等の規制による生物の多様性の確保に関する法律（以下「カルタヘナ法」という。）に関する事前審査について、行政側期間の目標（第１種使用の承認については６ケ月、第２種使用の確認については３ケ月とし、それぞれ５０％（中央値））を達成するため、申請の手引きを作成し、意見等を求める。

・「バイオ品質分野」の相談に努めるとともに、新たに「PGx/ゲノム・バイオマーカーに関する対面助言」の相談区分を設ける。

さらに、治験相談とは別にベンチャー企業のための相談事業を実施する。

・「先端医療開発特区（以下「スーパー特区」という。）」に採択された案件について、厚生労働省が実施する薬事相談に協力する。

Current PMDA projects to promote Global Drug Development including Japan

Yoshiaki Uyama, Ph.D
PMDA

22nd Annual EuroMeeting
March 8-10, 2010
Monaco

www.diahome.org

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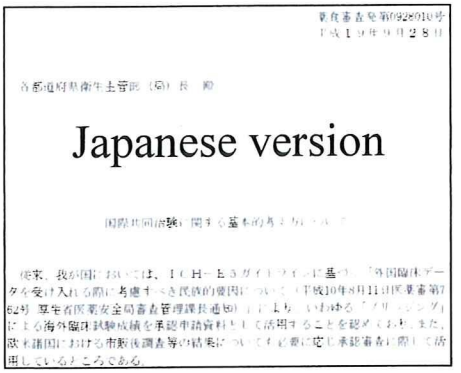
Outline

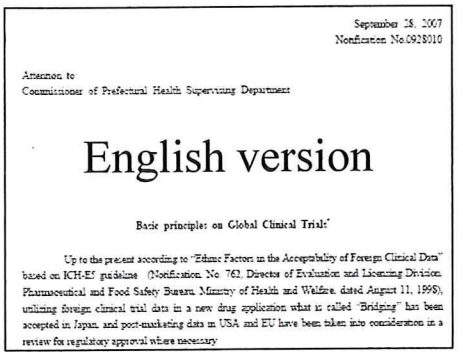
- Situation & Challenges of Global Clinical Trials including Japan
- Progress of New Consultation Process
  - Prior Assessment Consultation
  - PGx/Biomarekr Qualification Meeting

Situation & Challenges of Global Clinical Trials including Japan

Guidance (2007)
Basic Principles on Global Clinical Trials



Japanese version



English version

Basic principles on Global Clinical Trials

Up to the present according to "Ethnic Factors in the Acceptability of Foreign Clinical Data" based on ICH-E5 guideline (Notification No. 762, Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health and Welfare, dated August 11, 1998), utilizing foreign clinical trial data in a new drug application what is called "Bridging" has been accepted in Japan, and post-marketing data in USA and EU have been taken into consideration in a review for regulatory approval where necessary.

—Key Message—

- Encourage Japan's participation in global drug development
- Promote to conduct global clinical trials more appropriately in consideration with ethnic factors

Japanese : http://www.pmda.go.jp/operations/notice/2007/file/0928010.pdf
English : http://www.pmda.go.jp/operations/notice/2007/file/0928010-e.pdf

Guidance (2007)
Basic Principles on Global Clinical Trials

- Impacts
  - Markedly increase numbers and % of clinical trial notification (CTN) of Global Clinical Trials including Japan
  - Promote sample size considerations in scientific arena

e.g. ➢ Kawai, N et al, An Approach to Rationalize Partitioning Sample Size Into Individual Regions in a Multiregional Trial, *Drug Info. J.* 42, 139-147 (2008)

➢ Quan, H et al, Sample size considerations for Japanese patients in a multi-regional trial based on MHLW guidance. *Pharmaceut. Statist.* Published Online: Jun 4 2009 4:09AM 10.1002/pst.380 (2009).