Pharmacogenomic Data Submissions: Strategy and Implementation

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FDA's Mission and Drug Development

- FDA's mission is to protect and advance public health …
- … by helping to speed innovations that make medicines and foods more effective, safer and more affordable.
- This mission is reflected in the **Critical Path** Initiative
  - lists opportunities on the "critical path" to new medical products

Stagnation → Innovation

The Critical Path white paper lists opportunities on the "critical path" to new medical products:

Opportunity: "The emerging techniques of pharmacogenomics and proteomics show great promise for contributing biomarkers to target responders, monitor clinical response, and serve as biomarkers of drug effectiveness. *However*, much development work and standardization of the biological, statistical, and bioinformatics methods must occur before these techniques can be easily and widely used. Specific, targeted efforts could yield early results."

NCI and FDA Announce Joint Program to Streamline Cancer Drug Development

- FDA Commissioner Mark McClellan, M.D., Ph.D., and NCI Director Andrew von Eschenbach, M.D., said today that they will establish a multi-part Interagency Agreement to enhance the efficiency of clinical research and the scientific evaluation of new cancer medications. Areas of collaboration include:

- "Developing markers of clinical benefit (biomarkers) for evaluating new cancer medicines. The two agencies will work to develop a standard approach for evaluating biomarkers that demonstrate a drug's clinical effectiveness and that can potentially serve in clinical trials … "

Processing of Genomic Data Submissions from Industry to FDA

VOLUNTARY or REQUIRED
Genomic Data Submission

FDA

Receiving
Tracking
Archiving

Meeting between sponsor or review division and IPRG

IPRG

Ext. Advisory Committee As Needed

VGDS Review

Report back to sponsor or review division

Conferences, Workshops with Industry

Data, Knowledge

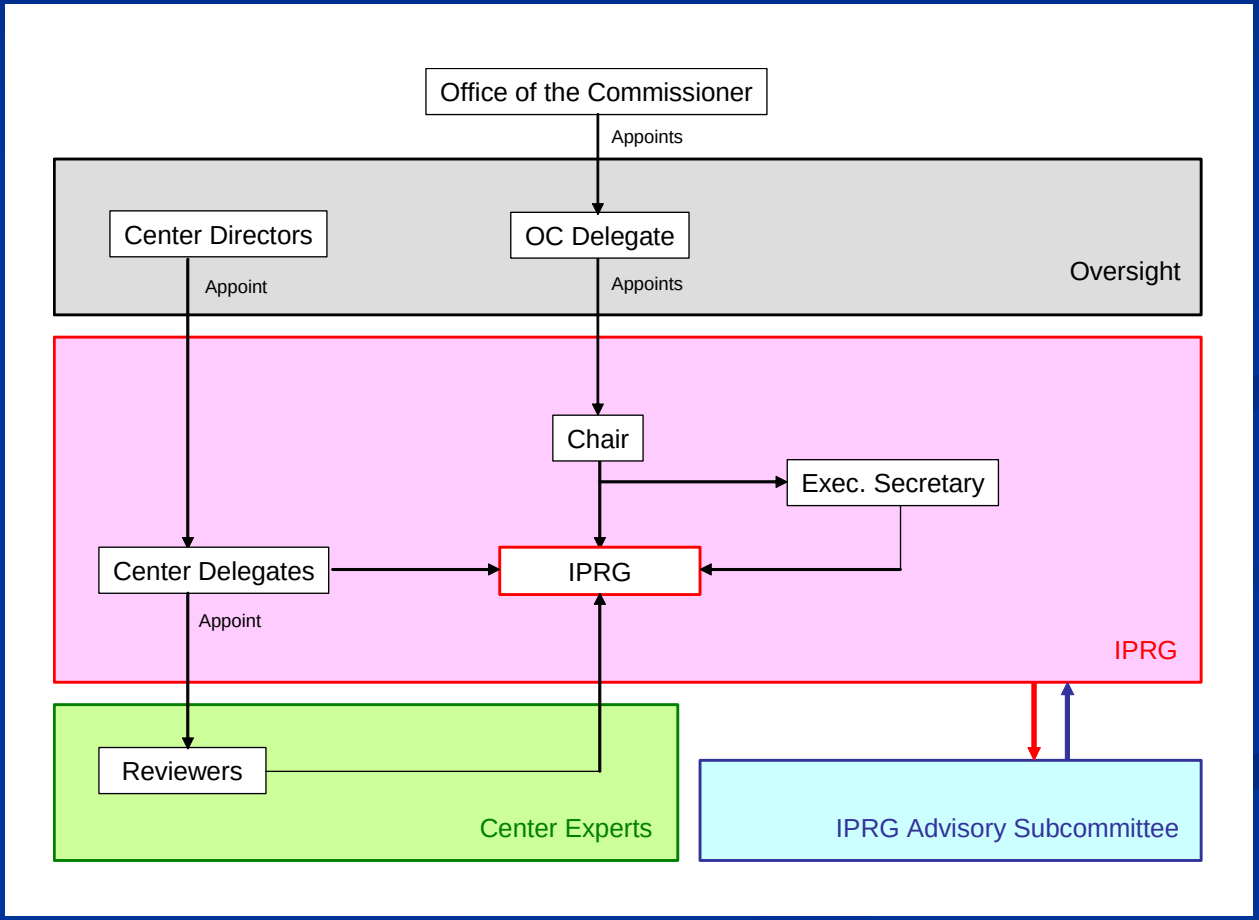
Education

Critical Path to New Medical Products: PGx Opportunity

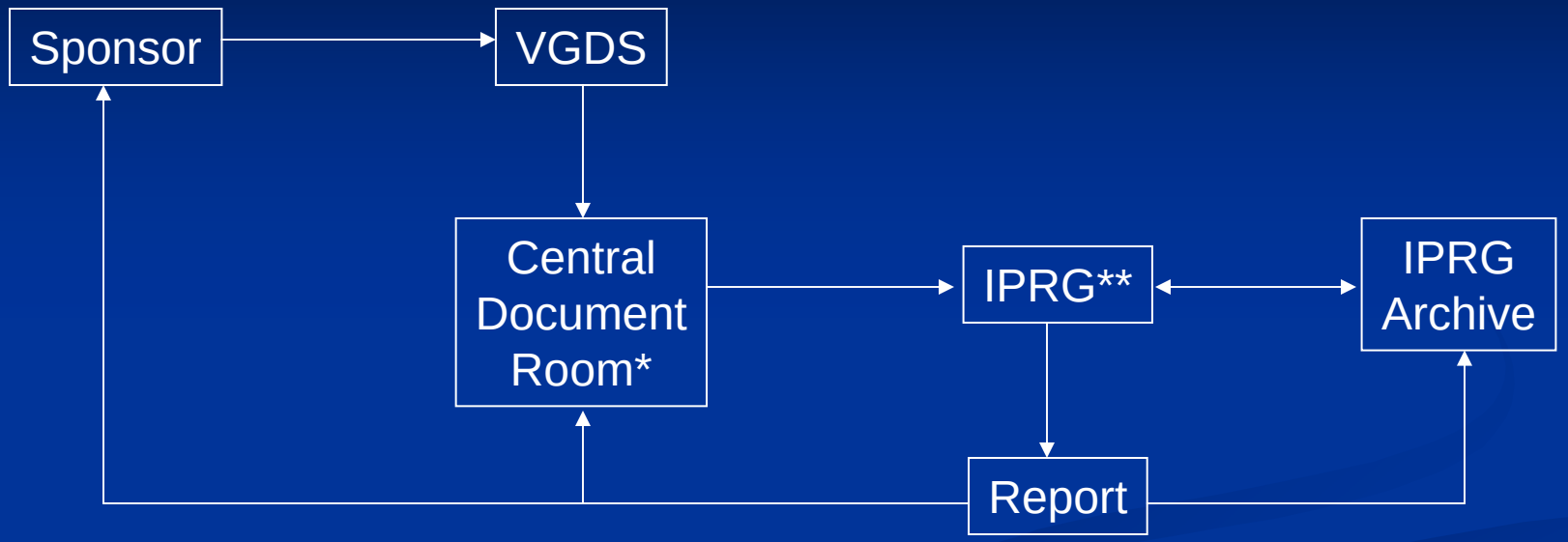
IPRG / PGWG Activities

- Genomic Data Submissions
  - Voluntary Genomic Data Submissions (VGDS)
  - Required submissions (IND, NDA, BLA)
- Policy development (U.S. & global)
- Education (internal, external)
- Research
  - CRADA on Biomarker Validation
  - Clinical trials protocols
  - Analysis of all labeling containing PGx
- IT
  - Database development
  - Software development

IPRG – Organization



PROCEDURE FOR RECEIPT AND PROCESSING OF VGDSs



* Central Document Room is responsible for:

Receive and process voluntary submissions
Establish a pre-IND application if a submission is a stand alone VGDS
Code submission
Enter data into the corporate database for tracking

** VGDS Project Manager is responsible for:

Data entry in the corporate database /Archive
Delivery of VGDS to IPRG
Enter report into DFS
Provide admin support to group

VGDS Submissions

- Received 23 VGDS requests to date and have scheduled or held 12 already.
- Includes two Joint FDA-EMEA VGDS's with an additional two joint meeting requests being planned.
- Includes multiple VGDS's on different drugs and follow-up VGDS submissions of the initial study.

VGS Submission Types

- **Therapeutic Areas:**
  - Cancer (multiple types)
  - Alzheimer's Disease
  - Hypertension
  - Hypoglycemia
  - Depression
  - Obesity
  - Rheumatoid Arthritis
- **Scientific and PGx areas:**
  - Biomarkers
  - Genotyping Devices
  - Microarrays
  - Analysis Software
  - Databases
  - Metabolic Pathways
  - Biostatistics
  - Enrichment design

Steps Towards Harmonization: VGDS Goes Global

- May 17, 2005: first joint FDA/IPRG – EMEA/PGWP – sponsor meeting
- Videoconference
- Preparation:
  - Interaction before meeting included in depth scientific evaluation of sponsor questions
  - This pre-meeting dialogue between FDA and EMEA resulted in a better product
  - Sponsor provided excellent presentation for interactive discussion via videoconference: presenters were present at EMEA (London, UK) and FDA (Rockville, MD)

Steps Towards Harmonization: VGDS Goes Global, cont'd

- Meeting minutes are jointly prepared by FDA and EMEA and are shared with sponsor
- What we learned, next steps:
  - FDA and EMEA evaluated, with only minor differences, the submission similarly, no dispute over science
  - Both agencies adjusted their usual format to accommodate the requirements necessary for a joint event
- Positive experience: next meeting planned for Q4 2005
- MOU and "Best Practices"
- First step to "harmonizing"?

Pharmacogenomic Guidance Development

- Multiplex Tests for Heritable DNA Markers, Mutations and Expression Patterns (Draft)
  - www.fda.gov/cdrh/oivd/guidance/1210.html
- Guidance for Industry: cGMP for Combination Products
  - www.fda.gov/oc/combination/oclove1dft.html
- Guidance for Industry: Pharmacogenomic Data Submissions
  - http://www.fda.gov/cder/genomics/regulatory.htm
- Pharmacogenomic Drug Device Co-development Concept Paper (guidance in development)
  - www.fda.gov/cder/genomics/whatsNew.htm

Scientific and Public Input into PGx

- Pharmacogenomics Workshop #1, First FDA/PWG/PhRMA/DruSafe Workshop, May 2002
- Draft Guidance on Genomic Data Submissions , November 2003
  - Docket 2003D-0497
- FDA/DIA Pharmacogenomics Workshop #2: Draft GDS guidance, Nov. 2003 (in collaboration with PWG/PhRMA/BIO)
- FDA/DIA Pharmacogenomic Workshop on CoDevelopent of Drugs, Biologicals and Device Products, July 2004 (in collaboration with PWG/PhRMA/BIO/Advamed/MDMA)
  - Docket 2004N-0279
- FDA/DIA Pharmacogenomics Workshop #3, Optimizing the Benefit/Risk of Drug Development and Therapy, May 2005 (in collaboration with PWG/PhRMA/BIO)
- FDA/PWG/PhRMA/BIO/DIA Application and Validation of Genomic Biomarkers for Use in Drug Development and Regulatory Submissions, October 2005 (in collaboration with PWG/PhRMA/BIO)

DIA

Co-sponsored by DIA, FDA, PhRMA, BIO, & PWG

HYATT REGENCY BETHESDA • ONE BETHESDA METRO CENTER • BETHESDA, MD, USA

BETHESDA, MD OCTOBER 6–7, 2005

APPLICATION AND VALIDATION OF GENOMIC BIOMARKERS FOR USE IN DRUG DEVELOPMENT AND REGULATORY SUBMISSIONS

Co-sponsors

DIA
Drug Information Association

FDA
US Food and Drug Administration

PhRMA
Pharmaceutical Research and Manufacturers of America

PWG
Pharmacogenetics Working Group

BIO
Biotechnology Industry Organization

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OVERVIEW

Evaluation of genomic biomarkers can contribute to a transformation of the drug development process. This transformation requires a clear and efficient path by which biomarkers can be identified and validated. Recent workshops on pharmacogenomics and drug/test co-development, as well as with the release of the "Guidance for Industry: Pharmacogenomic Data Submissions" and the planned "Drug/Test Co-development" guidance, underline the importance of the elucidation, characterization and use of genomic biomarkers.

In this workshop, scientists from the pharmaceutical and diagnostic industries as well as from regulatory agencies and academic institutions will propose and discuss mechanisms by which a scientific consensus may be reached on the identification and validation of genomic biomarkers. It is the goal of the workshop to define a "submission package" that describes what type of data should be submitted to the FDA for a successful qualification of a novel genomic biomarker of safety or efficacy.

TARGET AUDIENCE

The target audience for this meeting will be research nurses, scientists from industrial, academic and government laboratories associated with the identification and validation of biomarkers. This meeting will be particularly useful for scientists responsible for clinical pharmacology and for the selection of populations for clinical evaluation.

ONLINE REGISTRATION WILL BE AVAILABLE SOON! www.diahome.org *Monitor the website for the most current details.*

DIA, 800 Enterprise Road, Suite 200, Horsham, PA 19044-3595, USA tel: +1-215-442-6100 fax: +1-215-442-6199 email: dia@diahome.org

FDA/PhRMA/BIO/PWG/DIA WORKSHOP

APPLICATION AND VALIDATION OF GENOMIC BIOMARKERS FOR USE IN DRUG DEVELOPMENT AND REGULATORY SUBMISSIONS

KEYNOTE ADDRESSES:

- **IMPORTANCE OF GENOMIC BIOMARKER VALIDATION IN THE CONTEXT OF PHARMACOGENOMIC INITIATIVES AT THE FDA**
  Janet Woodcock, MD
  Deputy Commissioner for Operations and Chief Operating Officer, FDA

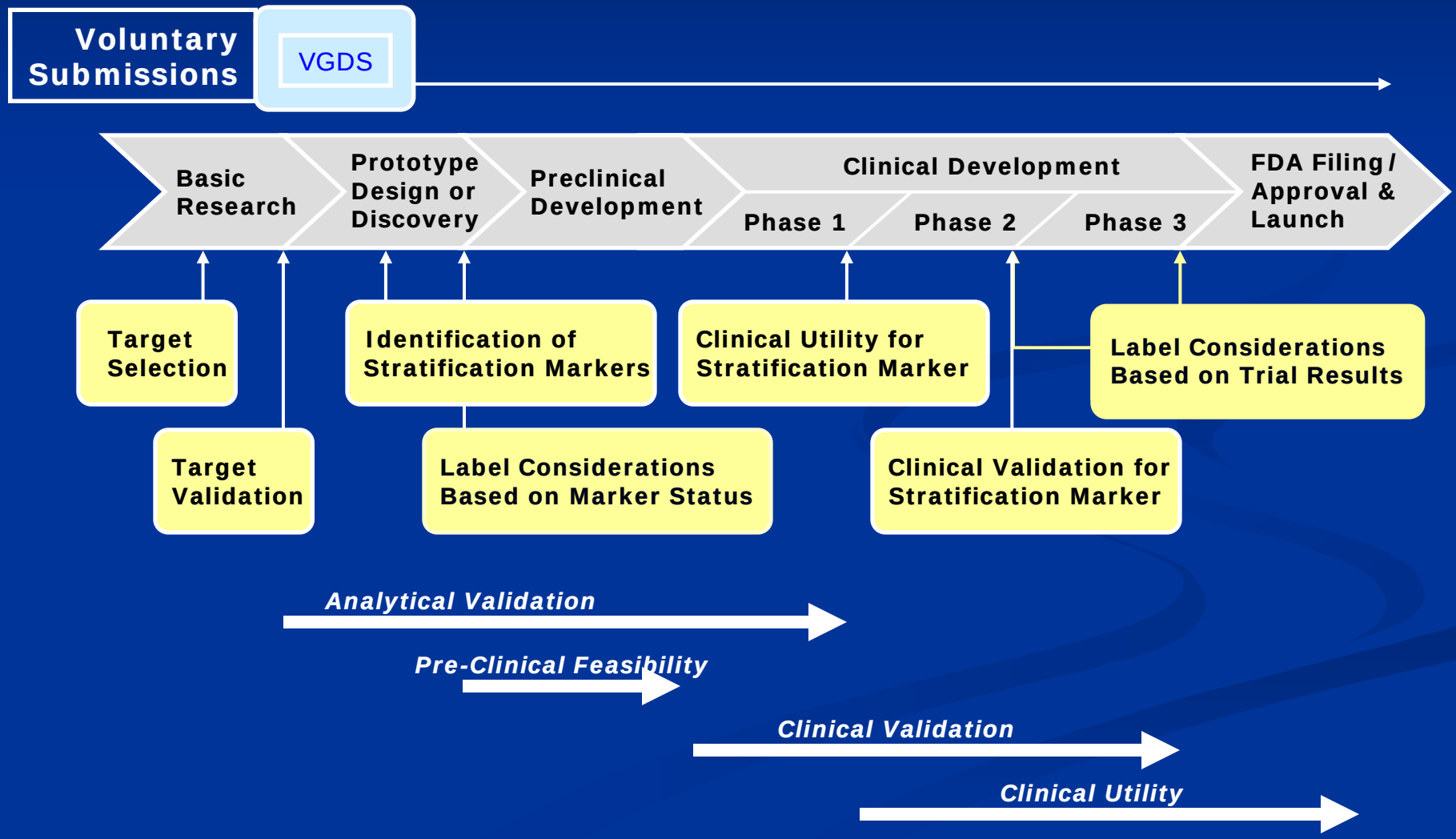
- **CURRENT AND ANTICIPATED USE OF GENOMIC BIOMARKERS IN DRUG DEVELOPMENT**
  Professor Klaus Lindpaintner, MD, MPH
  Roche Distinguished Scientist and Vice President, Research Head, Roche Genetics &Roche Center for Medical Genomics,

- **USE OF GENOMIC BIOMARKERS IN A REGULATORY ENVIRONMENT**
  Robert J. Temple, MD
  Director, Office of Medical Policy, CDER, FDA

SCIENTIFIC AND REGULATORY TOPICS DISCUSSED:

- SAFETY BIOMARKERS
- EFFICACY BIOMARKERS
- UPDATE ON THE HL-7 TOXICOGENOMICS
- ELECTRONIC SUBMISSION WORKGROUP
- STANDARDS FOR SAFETY AND EFFICACY BIOMARKERS BREAKOUT
- VALIDATION OF SAFETY AND EFFICACY BIOMARKERS BREAKOUT
- INTRODUCING GENOMIC BIOMARKERS INTO DRUG DEVELOPMENT TO IMPROVE SAFETY AND EFFICACY
- ESTABLISHING A REGULATORY FRAMEWORK FOR BIOMARKERS, FUTURE TRENDS
- DEVELOPING AND VALIDATING GENOMIC BIOMARKERS
- HOW TO INCORPORATE AND USE GENOMIC BIOMARKERS FOR REGULATORY DECISION MAKING
- DATABASE DEVELOPMENT FOR SAFETY AND EFFICACY

Use of Biomarkers in Drug Development – and the *Strategic* Use of VGDS



Consortia Proposal

- Biomarker consortia
  - Can expedite aggregation of data
  - Spread costs/risks
  - Adapt competitive mindset
    - Data sharing/IP
- Involvement of regulators important
  - BM selection for qualification
  - Protocol review
  - Can still maintain independence in data review and policy formation
- Several consortia under discussion/ forming

Courtesy of Chris Webster (Millennium /PhRMA)

Concluding Remarks

- VGDS and PGx programs at FDA have been successful and FDA has been the regulatory lead in numerous PGx areas including guidance development, analysis of PGx data, international collaboration (e.g., FDA-EMEA joint briefings, WHO CIOMS), and PGx workshops.
- VGDS submissions have provided FDA with significant PGx data and information in numerous therapeutic, scientific and technical areas which would otherwise be unavailable.
- PGx research needs to be seen in the context of biomarker development and validation as well as disease management to expedite the approval of new drugs and indications.
- Need to provide data in a manner that FDA and industry can readily analyze and which expedites review.
- FDA does not develop drugs or PGx tests, but it can encourage them to be developed.
- SACGHS could help as a group by recommending the formation of a task force to develop national standards for PGx assays.

www.fda.gov/cder/genomics