FDA activities in Newborn Screening and Genetics

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Disclaimer

The information presented is descriptive and general. These comments are mine and will not serve to bind the agency.

No confidential information is presented.

Introduction

- FDA's interest in newborn screening, genomics, and inborn errors of metabolism.
  - Top Down
  - Bottom Up
  - Middle Out

Topics

- Critical Path Initiative
- CDRH/OIVD
  - Genomics Working Group
- CDER
  - Treatments (drugs and biologics) for inborn errors of metabolism under a single division (DGP).

Critical Path Initiative

- “The Critical Path Initiative is FDA's effort to stimulate and facilitate a national effort to modernize the scientific process through which a potential human drug, biological product, or medical device is transformed from a discovery or "proof of concept" into a medical product.” (*underscore mine*)
  - http://www.fda.gov/oc/initiatives/criticalpath/initiative.html, March 2006

Critical Path and Genomics

- Genomics is one of multiple components of the Critical Path.
  - Hierarchical and interdisciplinary involvement
    - Interdisciplinary Pharmacogenomics Working Group
  - Guidance for Industry: Pharmacogenomic Data Submissions
  - Class II Special Controls Guidance Documents
    - Instrumentation for Clinical Multiplex Test Systems
    - Drug Metabolizing Enzyme Genotyping System

Critical Path and Genomics

- Anticipation
- Preparation
  - Training
  - Process development
  - Internal/external guidance development
- Involvement

Genomics Publications

- Huang, S-M, Goodsaid, F, Rahman, A, Frueh, F, and Lesko LJ Application of Pharmacogenomics in Clinical Pharmacology Toxicology Mechanisms and Methods, 2006;16:89-99.
- Andersson T, Flockhart DA, Goldstein DB, Huang SM, Kroetz DL, Milos PM, Ratain MJ, Thummel K.Drug-metabolizing enzymes: evidence for clinical utility of pharmacogenomic tests. Clin Pharmacol Ther. 2005 Dec;78(6):559-81.
- Baker SC, Bauer SR, Beyer RP, et. al. The External RNA Controls Consortium: a progress report.Nat Methods. 2005 Oct;2(10):731-4.
- Frueh FW, Goodsaid F, Rudman A, Huang S-M, Lesko LJ The Need for Education in Pharmacogenomics: a regulatory perspective. Pharmacogenomics Journal. 2005;5(4):218-20.
- Harper CC, Philip R, Robinowitz M, Gutman SI.FDA perspectives on pharmacogenetic testing. *Expert Rev Mol Diagn*. 2005 Sep;5(5):643-8.

Genomics Publications

- Thompson, K.L., Rosenzweig, B.A., Pine, P.S., Retief, J., Turpaz, Y., Afshari, C.A., Hamadeh, H.K., Damore, M.A., Boedigheimer, M., Blomme, E., Ciurlionis, R., Waring, J.F., Fuscoe, J.C., Paules, R., Tucker, C.J., Fare, T., Coffe, E.M., He, Y., Collins, P.J., Jarnagin, K., Fujimoto, S., Ganter, B., Kiser, G., Kaysser-Kranich,T., Sina, J. and Sistare, F.D. Use of a mixed tissue RNA design for performance assessments on multiple microarray formats. Nucleic Acids Research, 33(22):e187, 2005.
- Shi L, Tong W, Fang H, Scherf U, Han J, Puri RK, Frueh FW, Goodsaid FM, Guo L, Su Z, Han T, Fuscoe JC, Xu ZA, Patterson TA, Hong H, Xie Q, Perkins RG, Chen JJ, Casciano DA. Cross-platform comparability of microarray technology: intra-platform consistency and appropriate data analysis procedures are essential. BMC Bioinformatics. 2005 Jul 15;6 Suppl 2:S12.
- Shi L, Tong W, Su Z, Han T, Han J, Puri RK, Fang H, Frueh FW, Goodsaid FM, Guo L, Branham WS, Chen JJ, Xu ZA, Harris SC, Hong H, Xie Q, Perkins RG, Fuscoe JC.
  Microarray scanner calibration curves: characteristics and implications. BMC Bioinformatics. 2005 Jul 15;6 Suppl 2:S11
- Xie, H, Frueh, FW Pharmacogenomics steps toward personalized medicine Future Medicine. 2005;2(4):325-337.

CDRH/OIVD

- Devices:
  - Intended for use in:
    - diagnosis of disease or other conditions
    - cure, mitigation, treatment, or prevention of disease, OR
  - Intended to affect:
    - structure or any function of the body, and
    - does not achieve any of it's primary intended purposes through chemical action within or on the body, and
    - which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

Adapted from 21 CFR 201(h)

CDRH/OIVD

- In vitro diagnostic devices generally include* clinical laboratory tests of biological tissues (for example: blood, urine, spinal fluid) such as:

cardiac markers (troponin)
inborn errors of metabolism (PKU)
genetic tests
infectious disease markers (CMV)
inherited blood disorders (SS, SC)

(eg: chemistry, hematology, microbiology, etc)

*This refers to voluntary submissions to the agency. It ignores the issue of homebrew tests and analyte specific reagents, which will not be discussed today.

CDRH/OIVD

- Newborn screening In Vitro Diagnostic Devices
  - Traditional biochemical tests undergo pre-market review in the Division of Chemistry-Toxicology Device
  - Review team size depends on the nature and complexity of the submission
- OIVD: primary compliance activity resides in-house

Genomics
Working Group

Voluntary

NBS/Genomics

- Genomics working group
  - Variety of participants by job description
  - Variety of participants by training
  - Common interest in genetics and genomics
  - Individual interests
    - Newborn Screening
    - Pharmacogenetics
    - Pharmacogenomics

Genomics Working Group

- Journal Club Functions
  - Instructing each other
    - Biochemistry
    - Medicine
    - Genetics
    - Mathematics/Statistics
    - etc

Genomics Working Group

- Attendance at professional meetings (staying current and relevant)
- Relationships with professional organizations
- Relationships across HHS sectors

Genomics Working Group

- Outside presenters
  - Academic (university, NIH, etc.)
  - Industry (open to presentations regarding topics throughout the pipeline; TPLC)

Division of Gastroenterology Products

- Drugs and Biological products to treat (example only):
  - Inflammatory Bowel Disease
  - Nausea
  - **Inborn Errors of Metabolism**

DGP/IEM

- Treatments for many/most inborn errors will be review under one “roof”.

- Examples:
  - Myozyme (Pompe, GSD-II)
  - Fabrazyme (an LSD)
  - Cerezyme (Gaucher Type 1)
  - Naglazyme (MPS-VI)
  - Buphenyl (UCD w/ ↑NH3)
  - Orfadin (Tyrosinemia type I)

Summary

- Newborn screening, Genetics/Genomics, and Inborn Errors of Metabolism are on the map at FDA.