

HHS Efforts and Future Directions in Pharmacogenomics – An Update on FDA Guidances Related to Pharmacogenomics

**Secretary's Advisory Committee on Genetics,
Health, and Society**

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Incorporating Pharmacogenomics into Drug Development: The Role of Regulators

- Pharmacogenomics (PGx) has been identified as a key opportunity in FDA's Critical Path Initiative
- Successful use of PGx requires the knowledge of a genomic biomarker and an appropriate tool to measure it:
 - PGx combines drug therapy with diagnostics
- The regulation of drugs and devices needs to adequately reflect this combination
- FDA encourages the use of PGx in drug development and develops guidances that illustrate the agency's current thinking in this field

Three Kinds of Guidances

(www.fda.gov/cder/genomics/regulatory.htm)

The screenshot shows a Microsoft Internet Explorer browser window displaying the FDA Genomics Regulatory Information page. The page title is "Genomics at FDA: Regulatory Information". The address bar shows the URL: <http://www.fda.gov/cder/genomics/regulatory.htm>. The page content is organized into several sections:

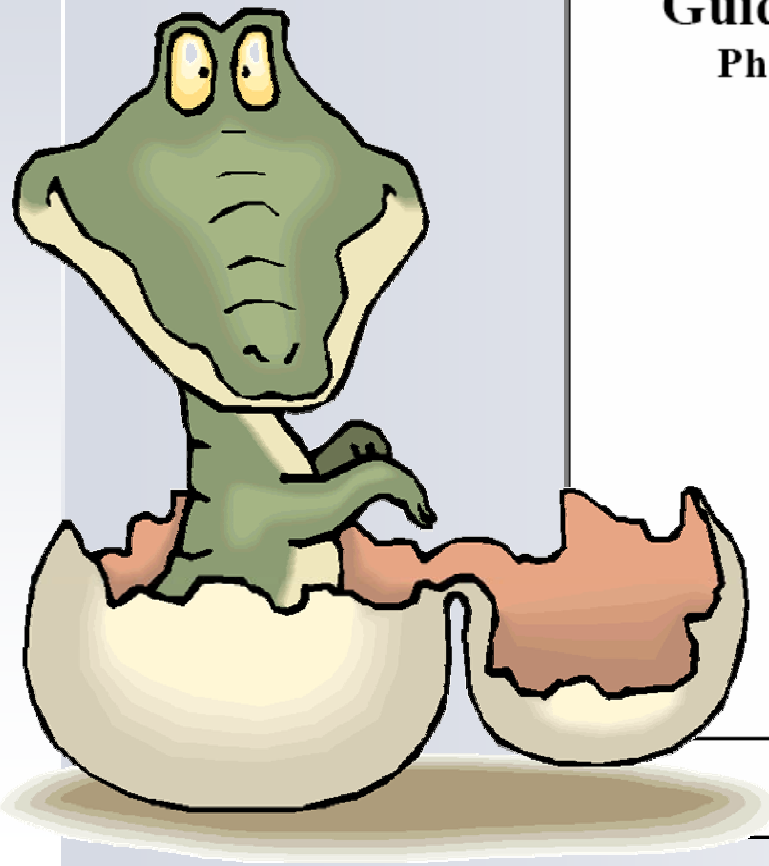
- Guidances**
 - [Guidance for Industry: Pharmacogenomic Data Submissions](#)
 - [Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA](#)
 - [Class II Special Controls Guidance Document: Instrumentation for Clinical Multiple Text Systems](#)
 - [Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Geno](#)
- Concept Papers**
 - [Drug-Diagnostic Co-Development — Preliminary Draft Concept Paper](#) (4/8/2005)
 - [Drug Interaction Studies — Study Design, Data Analysis, and Implications for Dosing and Labeling: Preliminary Concept Paper](#)
- Manual of Policy and Procedures (MaPP)**
 - [Management of the Interdisciplinary Pharmacogenomics Review Group \(IPRG\)](#)
 - [MaPP 4180.2](#)
 - [Processing and Reviewing Voluntary Genomic Data Submissions \(VGDSs\)](#)
 - [MaPP 4180.3](#)

At the bottom of the page, there are links for "Back to Top" and "Back to Genomics", and a date created: "Date created: March 22, 2005, updated April 19, 2005". The footer contains links for "CDER Home Page", "CDER Site Info", "Contact CDER", "What's New @ CDER", "FDA Home Page", "Search FDA Site", "FDA A-Z Index", "Contact FDA", and "HHS Home Page".

Three numbered annotations are overlaid on the page:

- 1. Pharmacogenomic Data Submissions**: An arrow points from this text to the first link in the "Guidances" section: [Guidance for Industry: Pharmacogenomic Data Submissions](#).
- 2. Device Guidances**: An arrow points from this text to the second link in the "Guidances" section: [Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA](#).
- 3. Drug/Test Co-Development**: An arrow points from this text to the first link in the "Concept Papers" section: [Drug-Diagnostic Co-Development — Preliminary Draft Concept Paper](#).

Guidance for Industry: Pharmacogenomic Data Submissions



Guidance for Industry Pharmacogenomic Data Submissions

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

March 2005
Procedural

March 22, 2005

Why this Guidance Is Important

- **FDA Review:** Genomics can help to assess benefit/risk decisions – facilitates review decisions
- **Drug Development:** Guidance empowers FDA to make drug development more efficient (i.e. in IND meetings)
- **Targeted Therapy:** Genomic data submissions are an enabling step for medicines to become more precisely tailored to a patient's unique pathophysiology
- **Communication:** Encouragement of voluntary submissions, which will help to better understand variability in drug-response, foster use of new technologies, ...
- **Outreach:** Stakeholders (i.e. industry, patient advocacy groups, Personalized Medicine Coalition, ...) have expressed great interest and support

What Does the New PG Guidance Do?

- Introduces a classification for genomic biomarkers
- Clarifies what type of genomic data needs to be submitted to the FDA and when
- Introduces a new data submission pathway to share information with the FDA on a voluntary basis
- Encourages the voluntary submission of exploratory genomic data
- Introduces new agency-wide PG review group (IPRG)
- Clarifies how the FDA will review genomic data submissions

What Does the New PG Guidance *Not* Do?

- Does not provide information on how to validate genomic biomarkers
- Does not provide information on how to use genomic biomarker during drug or device development process (scientific vs. regulatory guidance)
- Does not expand into other “-omics’ areas such as proteomics or metabolomics
- Does not equal genomic data with voluntary data
- Does not create new processes for the review of required data submissions

VGDS: A Novel Data Submission Path

- Submission of exploratory PG data submission regardless if subject of an active IND, NDA, or BLA
- Intent to build expertise and foundation for developing scientifically sound regulatory policies
- VGDS creates a forum for scientific discussions with the FDA outside of regular review process:
- Data not used for regulatory decisions

VGDS: A *Successful* Novel Data Submission Path

- First VGDS received in March 2004
- Since, VGDS process has successfully continued: about a dozen submissions received, several more announced
- Evaluation of complex raw data is ongoing – effective dialogue with sponsors has been critical
- First two companies are sending a “follow-up submission” to their first submission
- First joint FDA-EMEA VGDS meeting held in May 2005; Europe and Japan published PG guidances
- Industry interest in voluntary submission process is growing

Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems

Document issued on: March 10, 2005

For questions regarding this document contact Courtney Harper at 240-276-0443 or by email at courtney.harper@fda.hhs.gov.

Instrumentation for clinical multiplex test systems is a device intended to measure and sort multiple signals generated by an assay from a clinical sample. This instrumentation is used with a specific assay to measure multiple similar analytes that establish a single indicator to aid in diagnosis.

Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System

Document issued on: March 10, 2005

For questions regarding this document contact Courtney Harper at 240-276-0443 or by email at courtney.harper@fda.hhs.gov.

A drug metabolizing enzyme genotyping system is a device intended for use in testing DNA to identify the presence or absence of human genotypic markers encoding a drug metabolizing enzyme. This device is used as an aid in determining treatment choice and individualizing treatment dose for therapeutics [...].

New Tools for Personalized Medicine



“FDA Clears Test for Patient DNA to Screen for Drug Effectiveness”

Wall Street Journal, January 11, 2005

- Chip measures alleles of CYP2C19 and CYP2D6
- Tool to reduce over- and under-dosing
- Estimated 20% reduction in adverse events

Putting it All Together: Drug/Test Co-Development

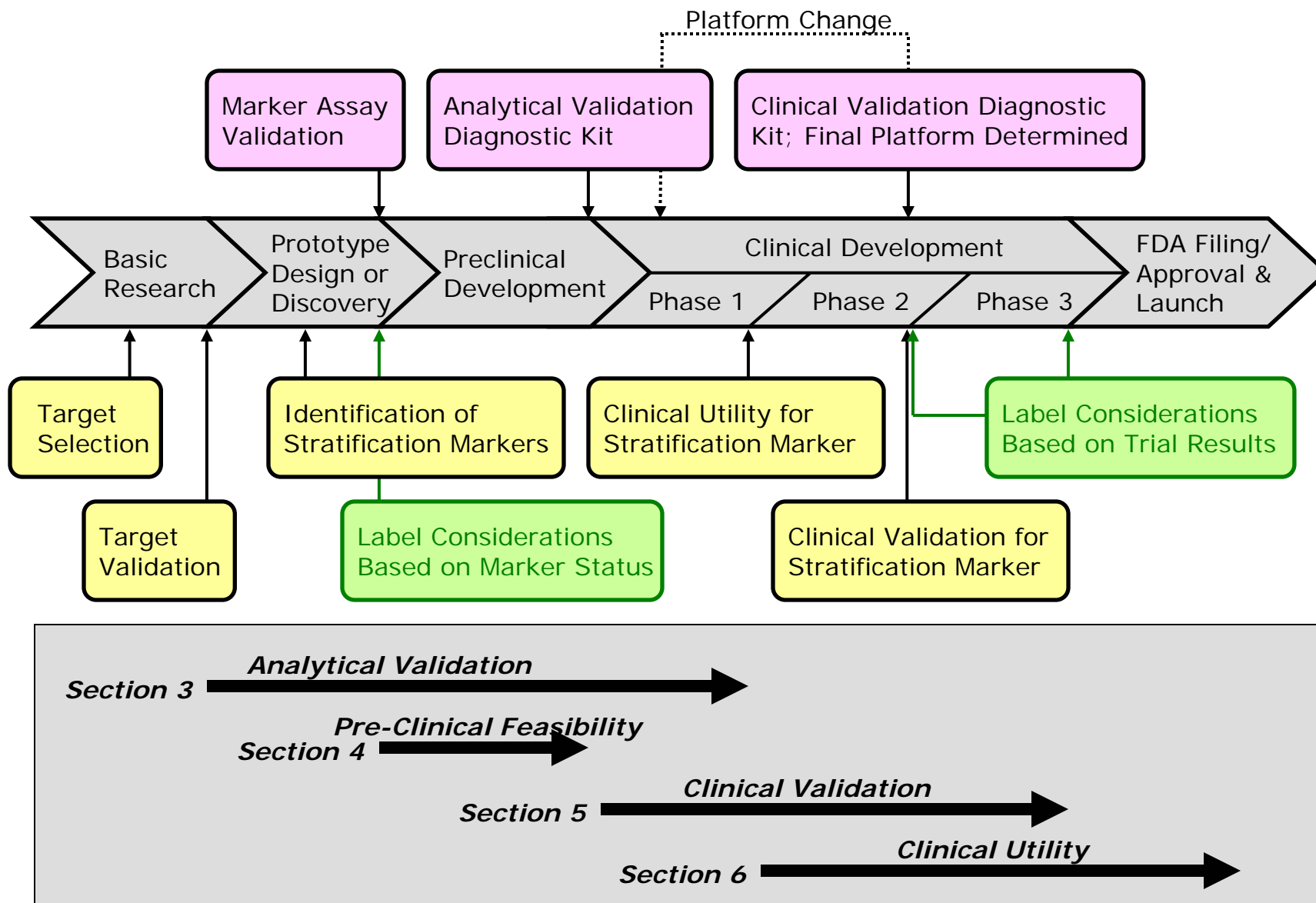
Draft
Preliminary Concept Paper — Not for Implementation

Drug-Diagnostic Co-Development Concept Paper

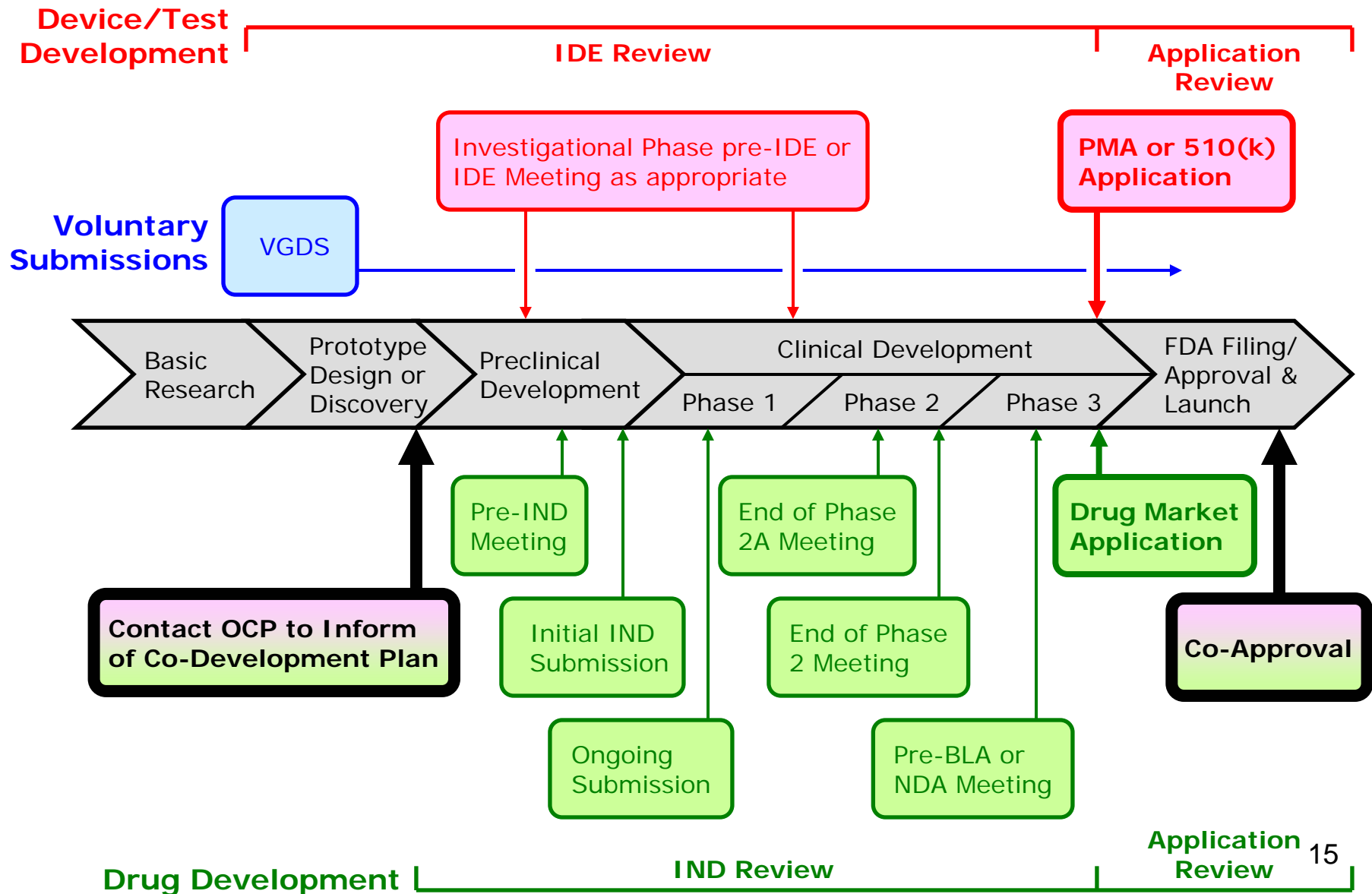
Draft — Not for Implementation

April 8, 2005

Drug-Test Co-Development Process: Key Steps During Development



Drug-Test Co-Development Process: Formal Industry – FDA Interactions



Drug/Test Combination Products: Benefits

- Co-development of drug/test combination products
 - Patient stratification (safety/efficacy)
 - Enrichment in clinical trials (efficacy)
- Product label and/or marketing
 - Should a patient be treated (safety/efficacy)?
 - What is the best dose (efficacy)?
- Can be critical for bringing product to market
- Can save drugs from withdrawal
- Can rescue candidate drugs

Drug/Test Combination Products: Issues

- Strategy (use during drug development only)
- Competitive advantage (i.e. ID responders)
- Timing (development, approval)
- Cost (development, reimbursement)
- Availability of alternative therapy (what if none?)
- Platform (platform change)
- Complexity (point-of-care vs. service laboratories)
- *Clinical usefulness* (i.e. therapeutic area, marketability)

Summary

- FDA encourages the use of PGx and provides a series of tools (i.e. guidance, meeting opportunities) to support the translation of pharmacogenomics into clinical practice
- The combination of drug therapy and use of devices is critical: a guidance to address the strategy and issues of drug/test co-development is being drafted
- PGx Data Submission guidance has been well received and is successfully being implemented
- Regulatory Agencies around the world are interested in pharmacogenomics – FDA is leading the way

Acknowledgements

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www.fda.gov/cder/genomics

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FDA/CDER

Questions to SACGHS

- What does the SACGHS see as future policies that need to be developed by FDA to foster the use of pharmacogenomics in drug development?
- As pharmacogenomics is becoming an integral part of the effort to personalize medicine, what can FDA do to encourage industry to adopt this new paradigm of evidence-based medicine as a business strategy?
- Does the SACGHS have plans or suggestions for a closer interaction between the sister agencies in the department (i.e. FDA, CMS, NIH) as it relates to activities in genomics?