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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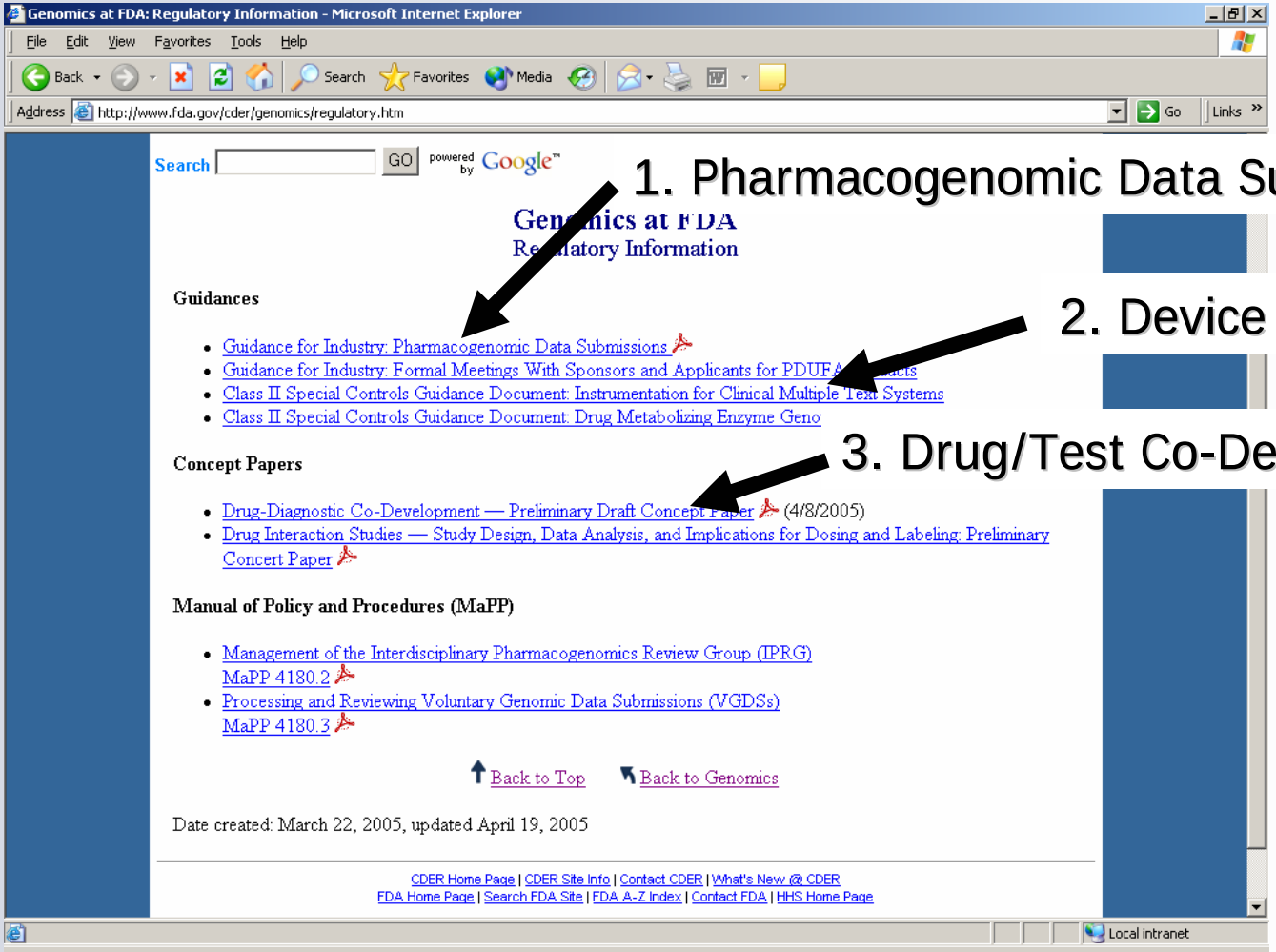
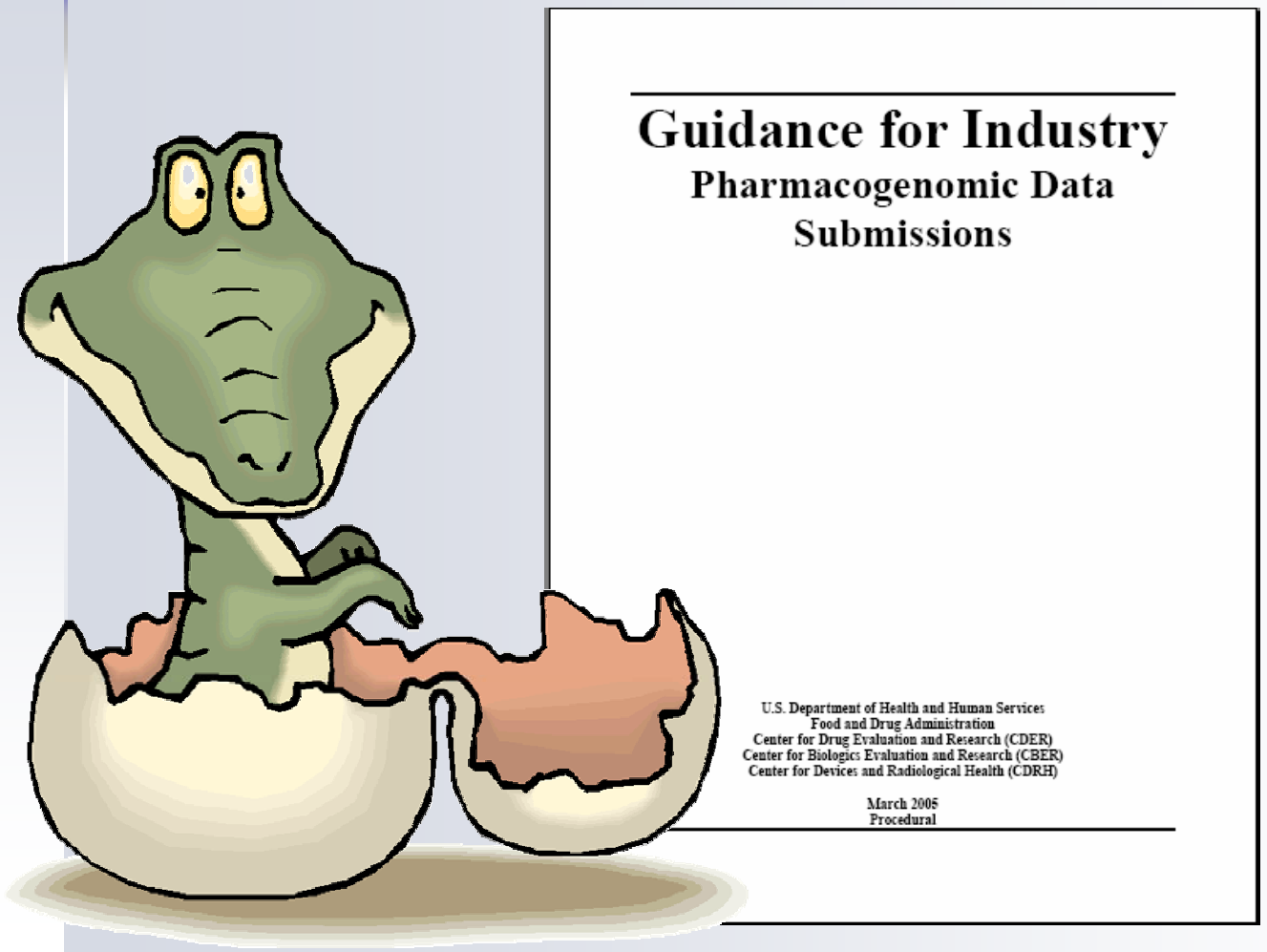
Incorporating Pharmacogenomics into Drug Development: The Role of Regulators

- 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)



Guidance for Industry: Pharmacogenomic Data Submissions



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?

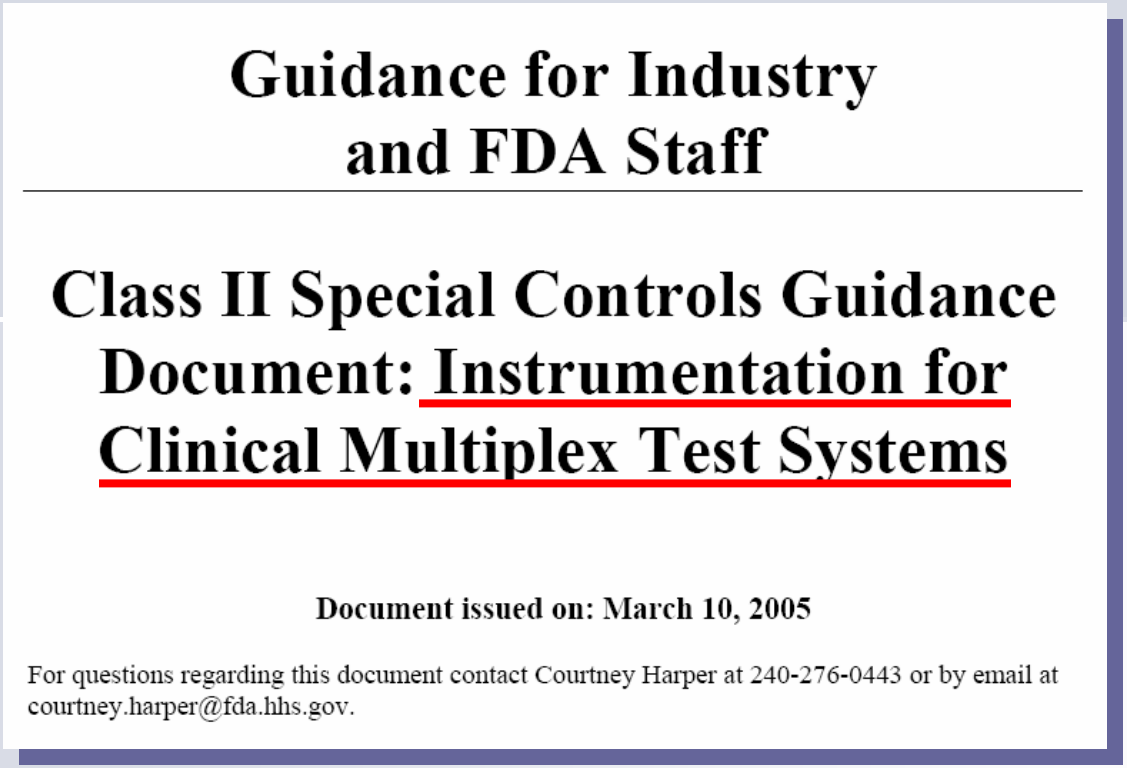
- Does not provide information on how to validate genomic biomarkers
- Does not provide information on how to use genomic biomarker during drug or device development process (scientific vs. regulatory guidance)
- Does not expand into other "-omics' areas such as proteomics or metabolomics
- Does not 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



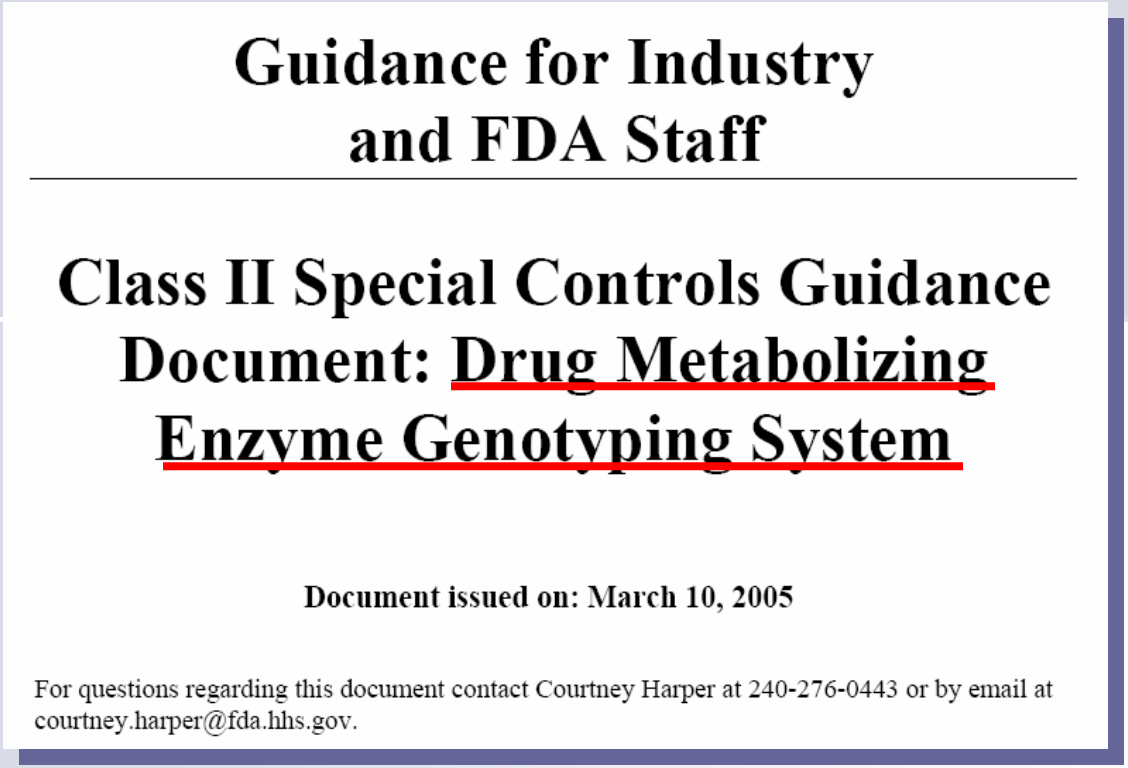
Guidance for Industry and FDA Staff

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 [...].

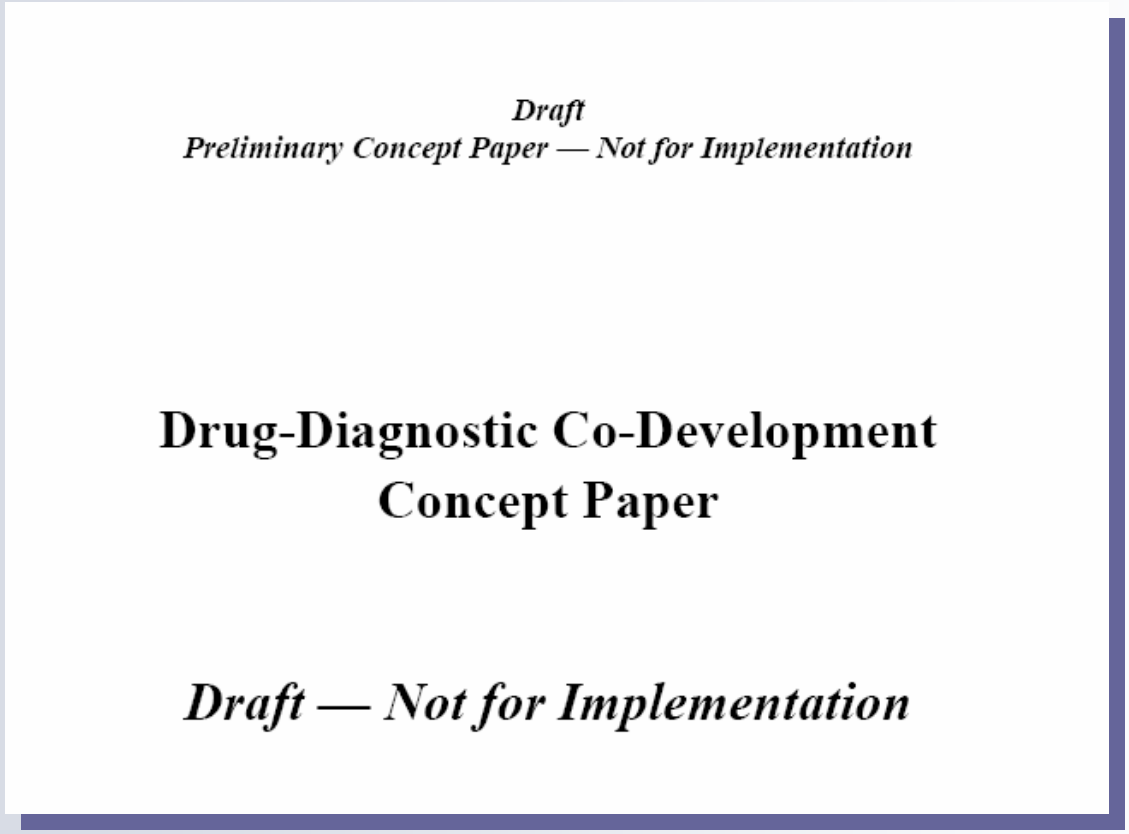
New Tools for Personalized Medicine

"FDA Clears Test for Patient DNA to Screen for Drug Effectiveness"

Wall Street Journal, January 11, 2005

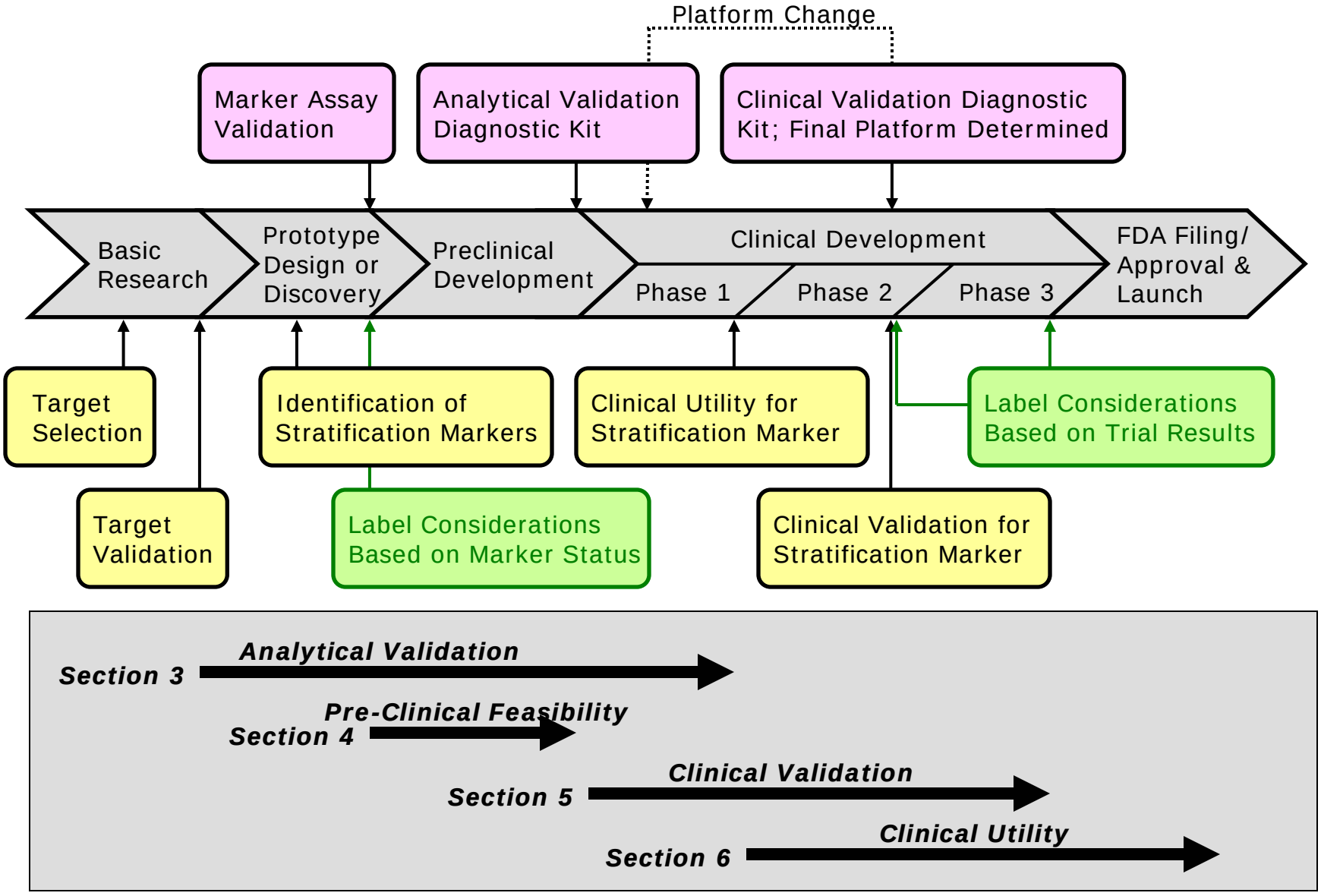
- **Chip measures alleles of CYP2C19 and CYP2D6**
- **Tool to reduce over- and under-dosing**
- **Estimated 20% reduction in adverse events**

Putting it All Together: Drug/Test Co-Development

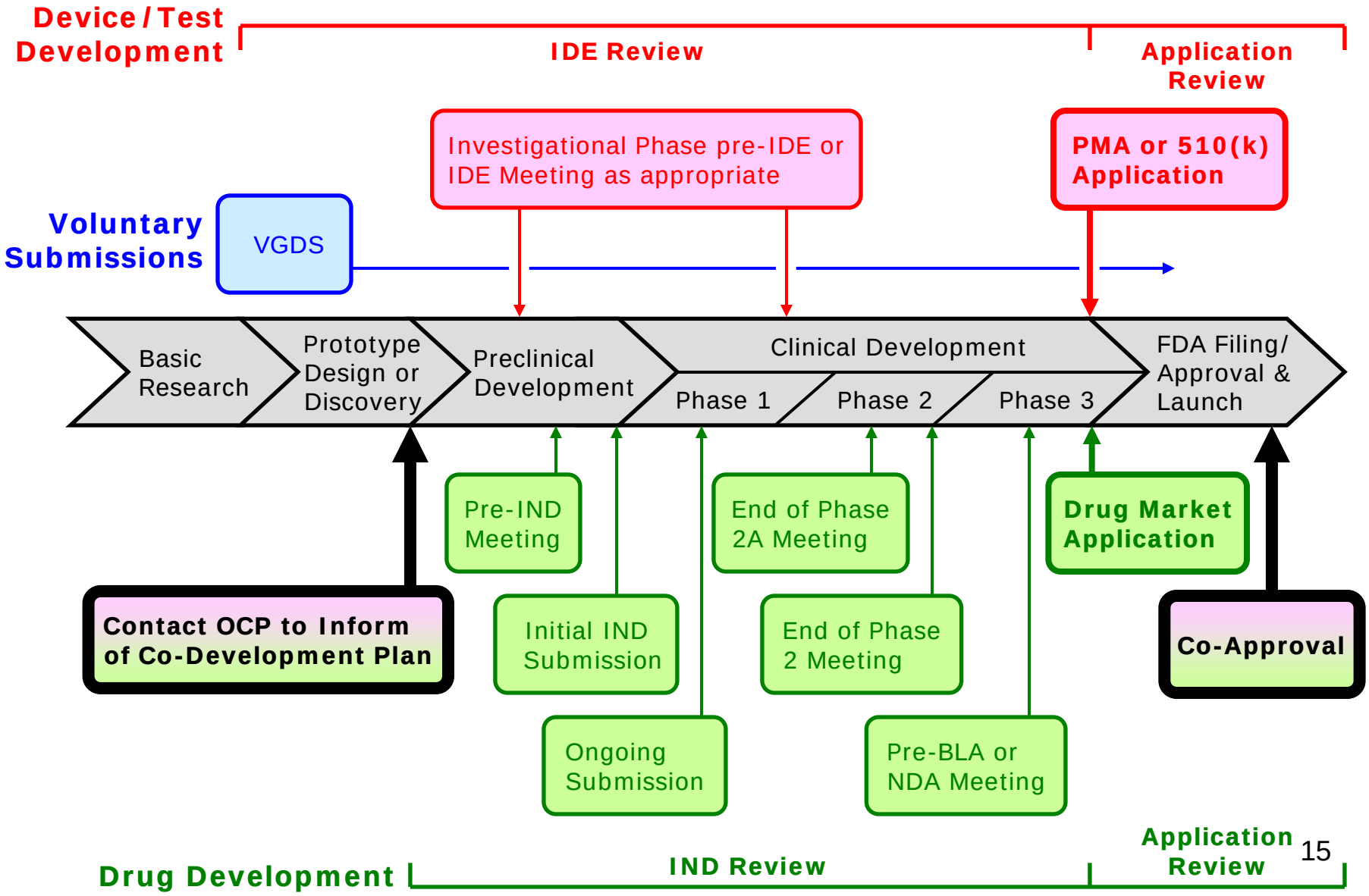


April 8, 2005

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

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www.fda.gov/cder/genomics

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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?