

Food and Drug Administration – Electronic Submission Process

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Member, CDER Electronic Submissions Working Group

NIH Cancer Imaging Informatics Workshop

Bethesda Marriott Hotel

September 25-27, 2002

Electronic Submission Processes: CBER & CDER

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Acknowledgements

- George Mills, CBER
- Michael Fauntleroy, CBER
- Randy Levin, CDER

Disclaimer

Views expressed in this presentation are those of the speaker and not, necessarily, of the Food and Drug Administration

Outline: Electronic Submissions

- Regulatory Environment
- Center Views
 - CBER
 - CDER
- Development of Standards
 - CDISC
 - FDA Data Council
 - Patient Profile Viewer (PPV)
 - HL7
- Images

Regulatory Environment

- Regulations
- Guidance
- Guidance vs. Regulation
- Center-Views

Regulations

- Predicate Regulations
 - Each Center
 - Based on submission type (NDAs, BLAs, ANDAs, INDs, Supplements)
- 21 CFR 11
 - All Centers
 - Basically a “good practice” document
 - Electronic capture/handling **and** submission
 - Impact on cost? “Voluntary” program.
 - Docket reflects what is acceptable

Regulations: 21 CFR 11

- *Electronic Records; Electronic Signatures*
- http://www.fda.gov/ora/compliance_ref/part11

Regulations: Enforcement

- *Enforcement Policy: Electronic Records; Electronic Signatures -- Compliance Policy Guide; Guidance for FDA Personnel*
- Compliance Policy Guides Manual. Section 160.850
- Federal Register / Vol. 64, No. 146 / Friday, July 30, 1999
- [Docket No. 99D-1458]

Regulations: Guidance

Electronic Record - Electronic Signatures 21 CFR Part 11 Guidance Documents Dockets Established - Topics for Guidance Development		
Subject	- Docket Number - Dockets Management Branch	
Archiving	00D-1539	Please note: The information you seek at a docket may be located or updated on other page(s) within the docket.
Audit Trails	00D-1541	
Electronic Copies for FDA	00D-1540	
Glossary	00D-1543	
Time Stamps	00D-1542	
Validation	00D-1538	

Guidance

- Represents “best current advice”
- Recognized that there will be changes
- Provides grounds for discussion / negotiation
- May be taken too literally

Guidance: Boilerplate

- “...represents the Agency's current thinking on regulatory submissions in electronic format.”
- “It does ... not operate to bind FDA or the public.”
- “An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.”

Regulatory Environment

Regulation

Guidance

FDA/BIMO Guidance: “Computerized Systems”

- Bioresearch Monitoring (BIMO) Program
- *Computerized Systems Used In Clinical Trials*

http://www.fda.gov/ora/compliance_ref/bimo/ffinalcct.htm

Center-Views: CDER/CBER

- Docket process -- the side of 21 CFR 11
- Consistency?
 - Different regulations
 - Different priorities
 - Different business practices
 - Clients
 - Resources
 - Scale
 - Sign-off
- New “General Considerations” guidance

Center-Views: CDER/CBER

- “In some cases, the guidance for one center differs from that for the other center because of differences in procedures and in the computer infrastructures in the centers.”
- “We will work to minimize these differences wherever possible.”

CDER/CBER

General Strategy for Developmental Efforts

- A different Center may take the lead in developing a specific application
- Others Centers consult / observe
- Applies to both infrastructure development and work with regulated industry
- CDER/CBER working together on eCTD document room concept

CBER/CDER Guidance

- *Guidance for Industry: Providing Regulatory Submissions in Electronic Format - General Considerations - 1/28/1999*
- *Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format -- Prescription Drug Advertising and Promotional Labeling - 1/31/2001*

<http://www.fda.gov/cder/guidance/index.htm>

CBER/CDER:

General Considerations

- Paper: PDF
- Data: SAS Transport, Version 5.0
- Organization: specified files (names, placement)
- Media: CD ROM or Magnetic Tape

CBER: Guidance

- *REVISED Guidance for Industry: Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format - Biologics Marketing Applications [Biologics License Application (BLA), Product License Application (PLA) / Establishment License Application (ELA) and New Drug Application (NDA)] 11/12/99*

<http://www.fda.gov/cber/esub/esubguid.htm>

CBER: Guidance

Guidance for Industry: Providing Regulatory Submissions to CBER in Electronic Format - Investigational New Drug Applications (INDs) - 3/26/2002

CBER: Process -- Application

- “The absence of a complete electronic database in an acceptable format to permit CBER review and statistical analyses may be considered to be inadequate, thereby resulting in a **RTF** decision.”
- “Following this guidance document should help ensure that your electronic submission meets the requirements set forth in the regulations and can be easily archived, loaded on network drives, and reviewed within specified time frames using CBER desktop standards.”
- All electronic -- OK.

CBER: Process -- CRFs

- “Prior to the submission of CRFs captured using remote data entry, a sponsor should discuss their submission with the effected review division and consult the Guidance for Industry: Computerized Systems used in Clinical Trials, May 10, 1999, available at [http:// www. fda. gov/ cber/ guidelines. htm.](http://www.fda.gov/cber/guidelines.htm)”

CBER: Future Directions

- Electronic Sig -- 3 options (Adobe, Verisign & Entrust)
- Secure e-mail: beta-testing with 7 partners -
- 2 finished
- With docket announcement, aiming to make option to sponsors in October (all paper or all electronic -- no mixed submissions)
- Paves way for total integration of IND/NDA receipt, administration and review of electronic documents

CBER: Contact

Michael B. Fauntleroy

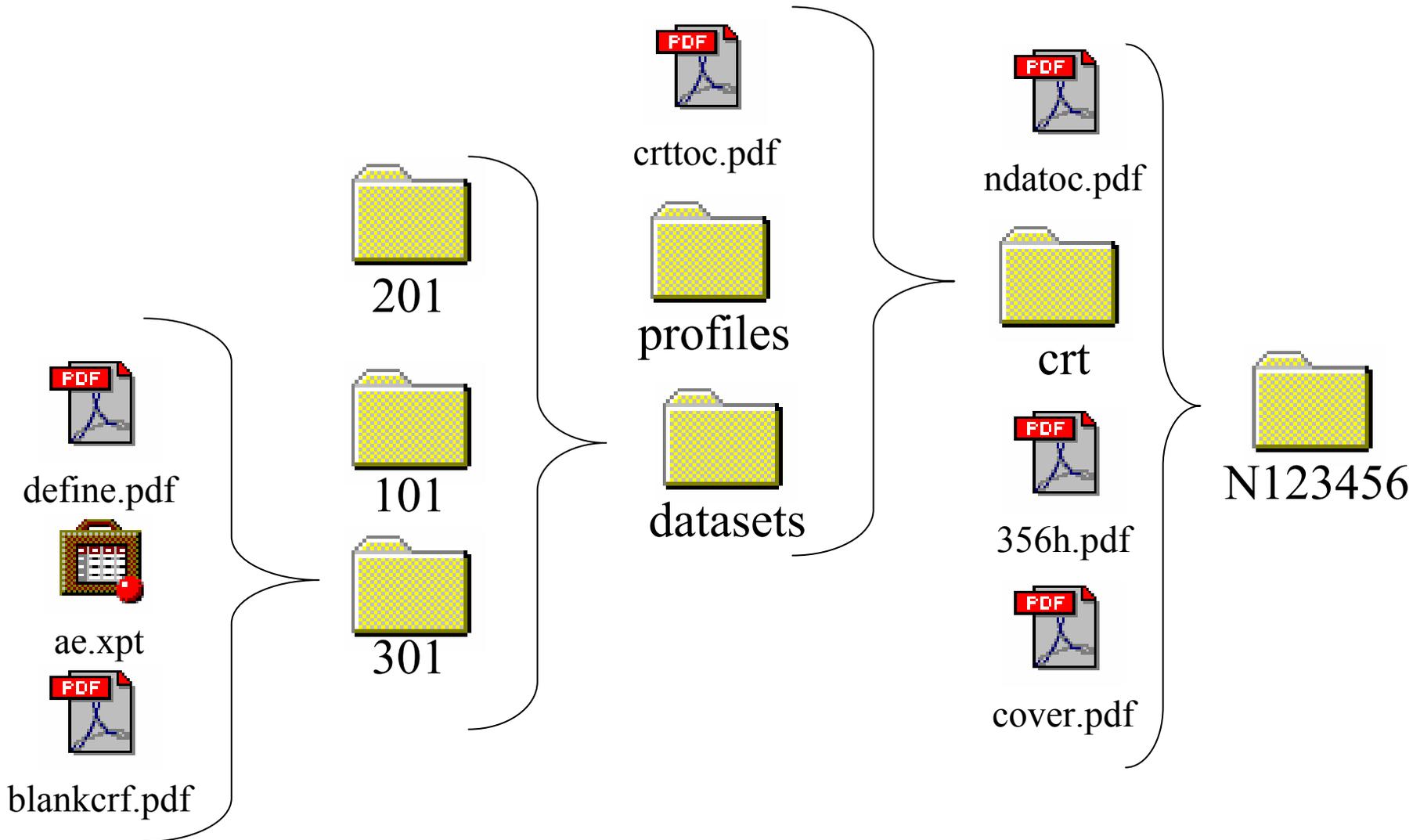
301- 827- 5132

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CDER: Guidance

- <http://www.fda.gov/cder/regulatory/ersr/default.htm>
- *Providing Regulatory Submissions in Electronic Format – NDAs, January 1999*

NDA: Organization of the Files



NDA Data: Organizing Dataset Files

- CRTs
 - One domain = one dataset xpt file
- Analysis datasets
 - One analysis dataset = one dataset xpt file
- Data views
 - Data listings
 - One domain = one dataset xpt file or PDF file
 - Profiles
 - One subject = one profile PDF file

NDA Data: Domains

- Demographics
- Inclusion criteria
- Exclusion criteria
- Concomitant medication
- Medical history
- Drug exposure
- Disposition
- Efficacy results
- PK
- Microbiology
- Adverse events
- labs (chemistry, hematology, urinalysis)
- ECG
- Vital signs
- Physical exam

CDER: Process

- Consult with review division
- MAPP 7600.6 -- *Requesting and Accepting Non-Archivable Electronic Records for New Drug Applications*, 11/12/99
- Paper copies of certain documents submitted with electronic for review (may consult with division)

CDER: Future Directions

- IND, eCTD and XML
- Data and Information Standards
 - CDISC, HL7, Data Council
 - Patient Profile Viewer (PPV)

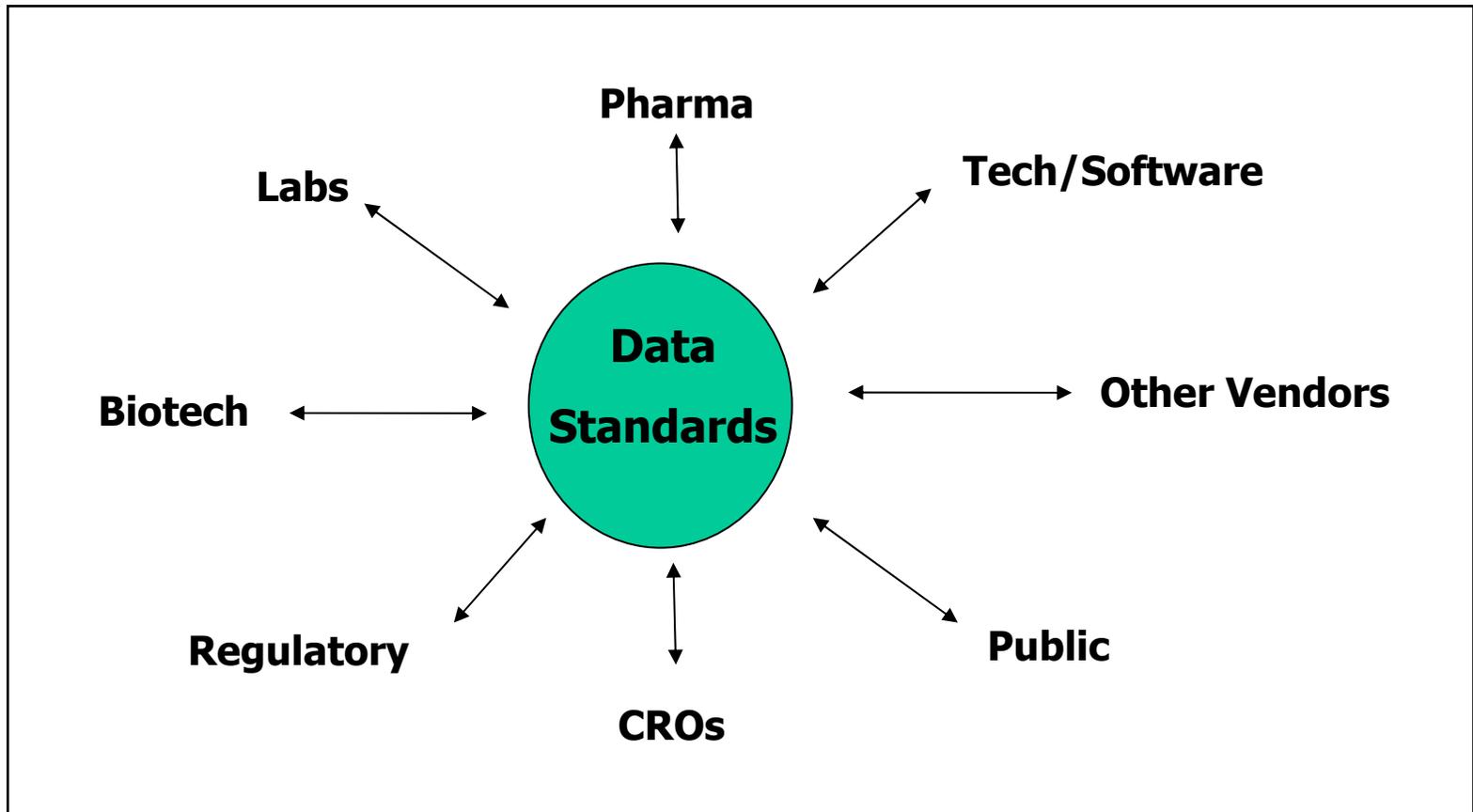
CDER: Future Directions -- IND

- ...plan on upgrading the electronic IND filing and review process to include the use of XML-based technology.
- ...working toward accepting the electronic common technical document using XML for marketing applications and will build on this to accept XML-based electronic INDs
- ...hope to have XML specifications for electronic INDs available in 2003.

CDER: Future Directions -- Data Standards

- New data standards guidance
- Clinical Data Interchange Consortium (CDISC) and Health Level 7 (HL7)
- FDA Data Council -- attention from HHS
- Review Tools
- Data Warehouse

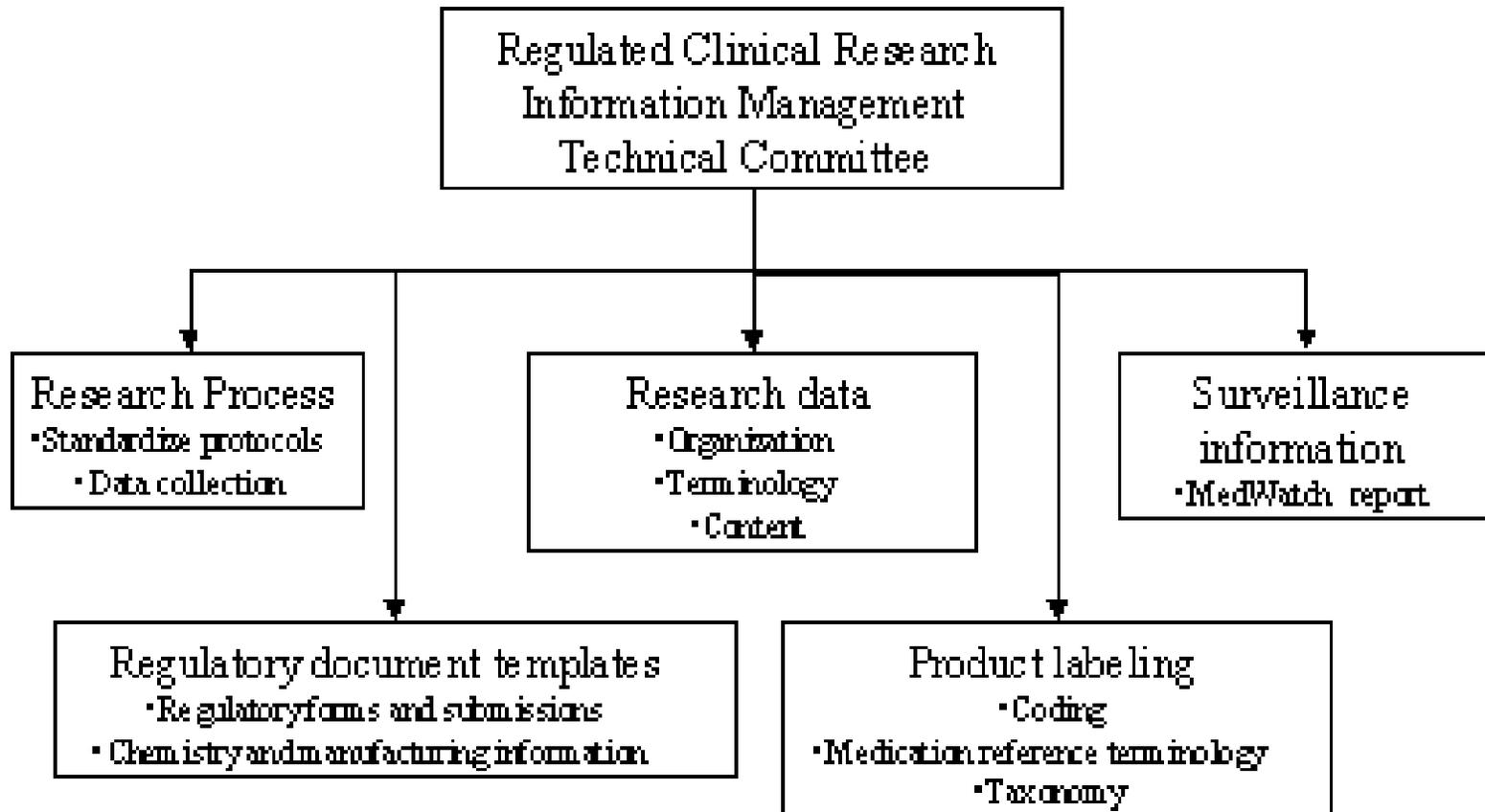
Data Standards: A Shared Vision



Data Standards: Health Level 7 (HL7)

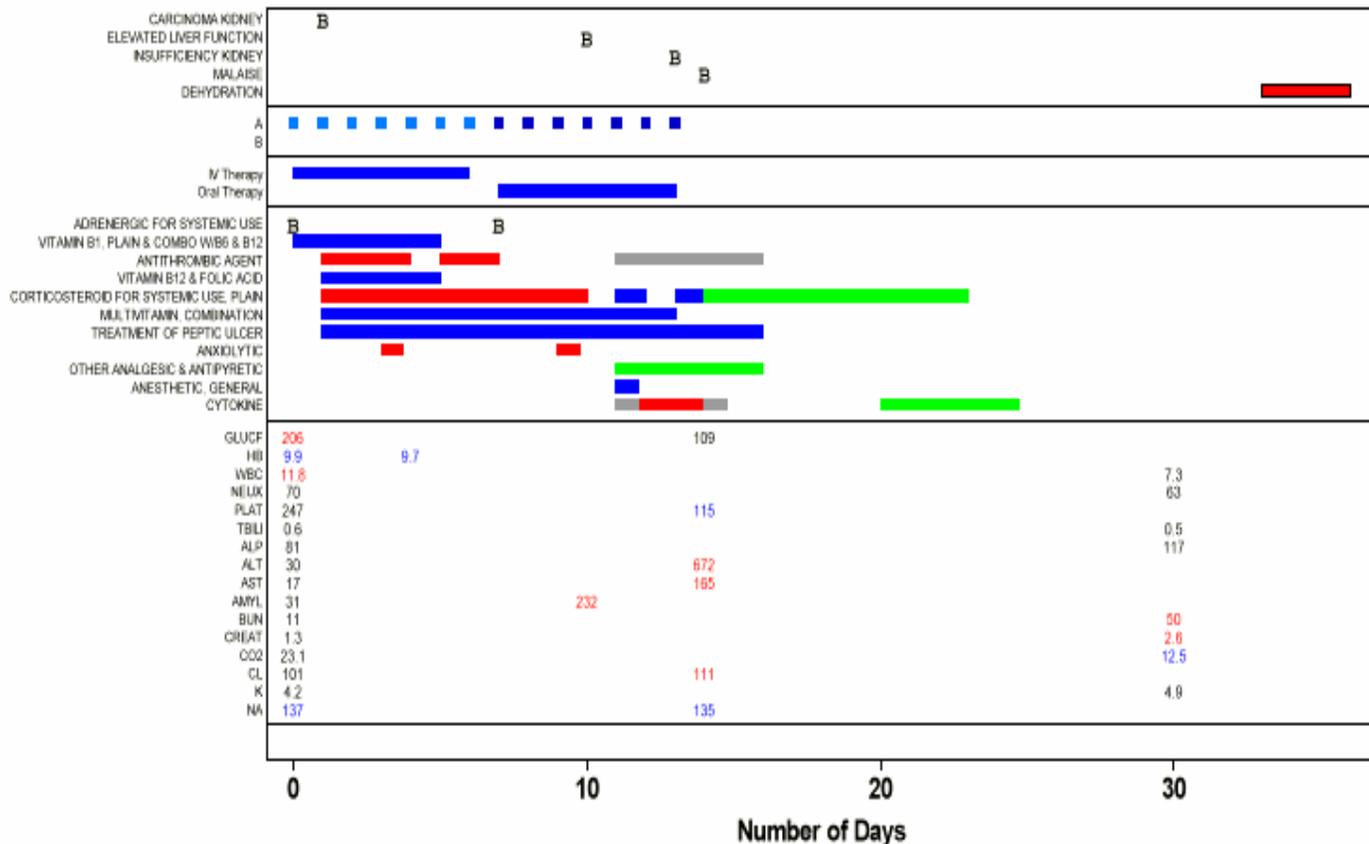
- Open, consensus standard -- ANSI-accreditation
- Connection to Designated Standards Maintenance Organization (DSMO) maintains standards for US Health Insurance Portability and Accountability Act of 1996 (HIPAA)
- HL7 has a close association with American Medical Informatics Association (AMIA)
- Formal agreement with CDISC
- Randy Levin (CDER) and CDISC representative co-chair *Regulated Clinical Research Information Management Technical Committee*.

Information Standards: HL7



Future Directions: Data Standards and Review Tools

Patient time-line summary graph for Clinical Trial data
 AEs, medications, lab results linked on a common timeline



Patient Profile Viewer (PPV): Federal Register Notice

Federal Register / Vol. 66, No. 237 / Monday,
December 10, 2001

[Docket No. 01N- 0496]

Patient Profile Viewer; Notice of Pilot Project

AGENCY: Food and Drug Administration,
HHS.

Patient Profile Viewer: Federal Register Notice

- ...pilot project involving the testing of the Patient Profile Viewer (PPV)
- ...computer software that allows a reviewer to display data collected from case report tabulations (CRTs) submitted in electronic format
- ...working with PPD Informatics ... under a Cooperative Research and Development Agreement (CRADA)

Patient Profile Viewer: Federal Register Notice

...in an effort to improve review efficiency,
develop standards for submission of data,
and eliminate the need for the submission
of patient profiles by applicants of new
drug applications (NDAs)

CDER: Contact

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* Brand new Office

CDER/CBER: Electronic Images

- Primarily CBER initiative, CBER hardware
- 4 vendors (no standards established?)
- Database and images
- Experience
 - CBER -- surrogate radiographic indicator as primary
 - CDER -- oncology, tumor response
- Not on docket [i.e., not Electronic Document Room (EDR) submission]
- Contact 3 - 6 months prior to submission

Electronic Images: Contact

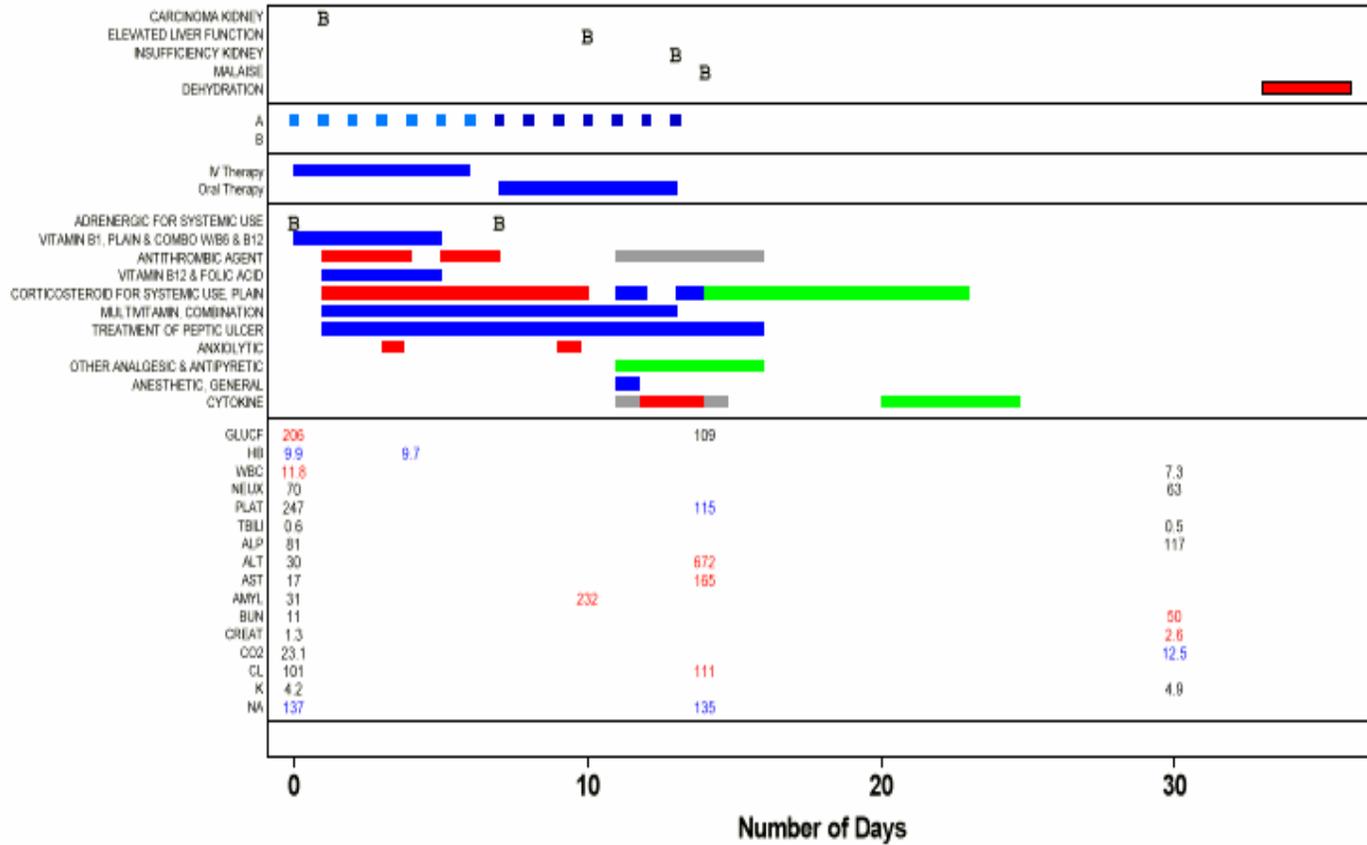
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YOUR PICTURES HERE

THANK YOU

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