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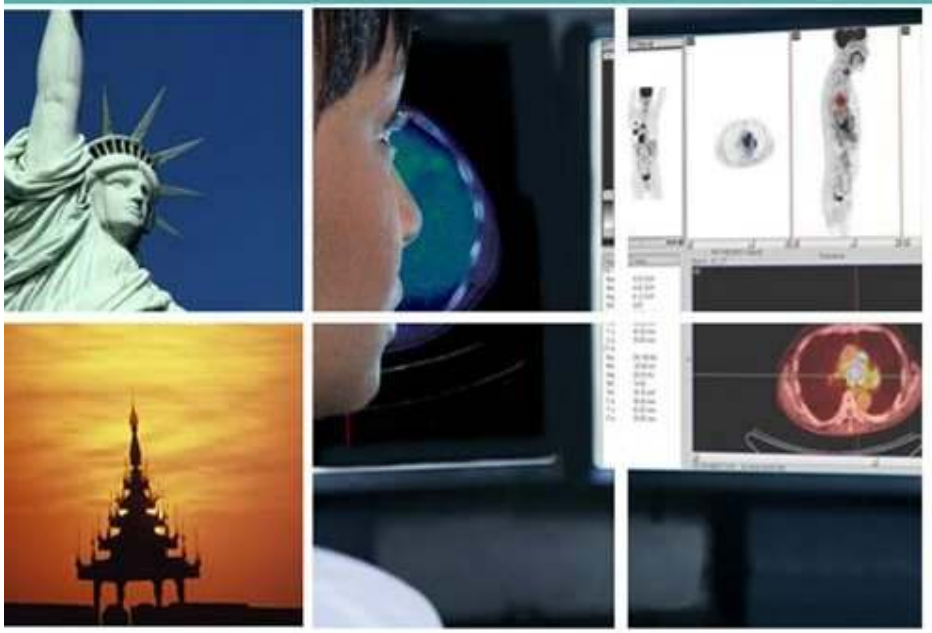
Mapping Life Pixel by Pixel ™ Medical Imaging



RSNA/SNM/FDA

April 13, 2010 - April 14, 2010

Two Topic Imaging Workshop:

"Standards for Imaging Endpoints in Clinical Trials"

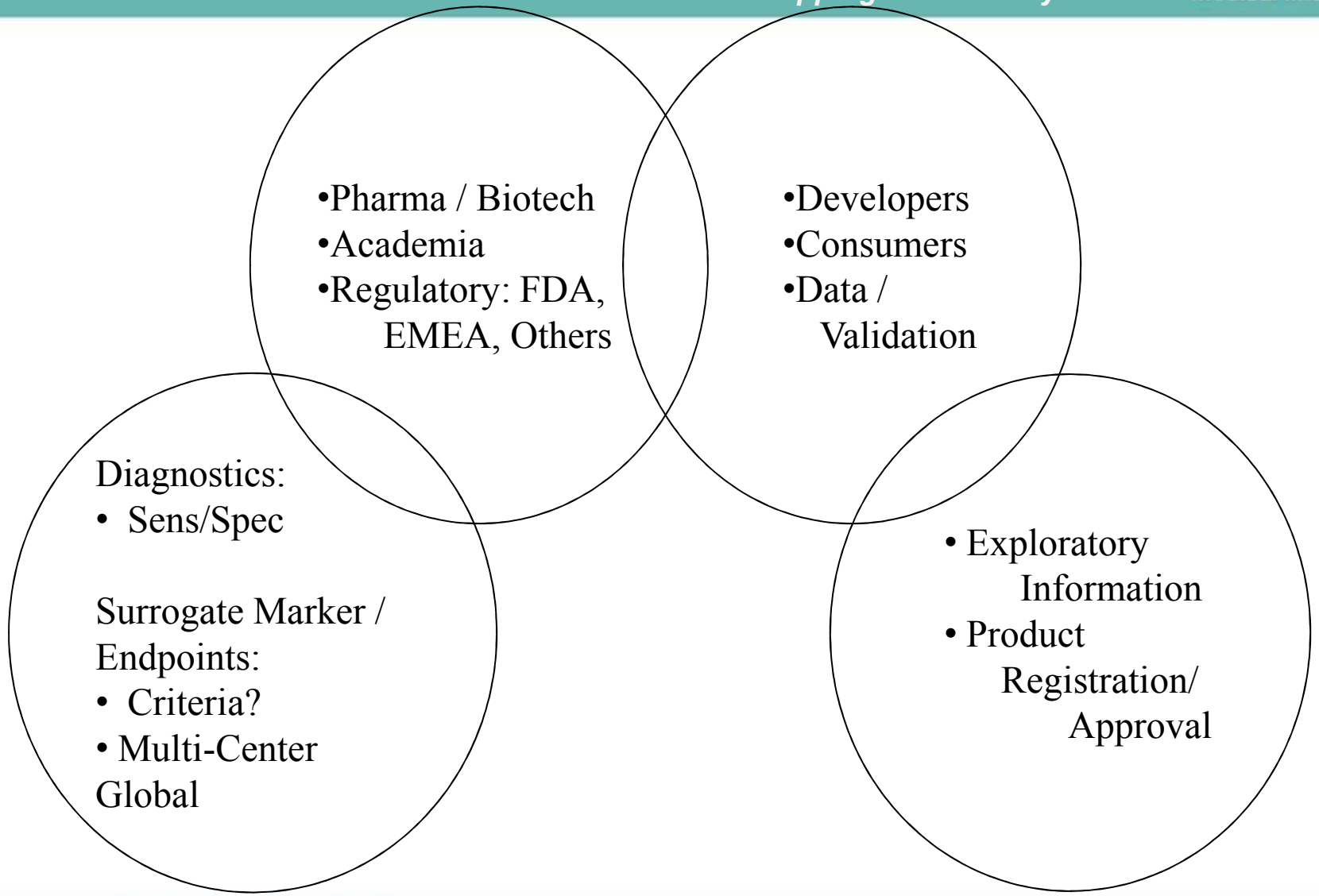
Management of Image Data Workflow

Ted Gastineau

President

ICON Medical Imaging

User Driven


•Pharma / Biotech
•Academia
•Regulatory: FDA, EMEA, Others
•Developers
•Consumers
•Data / Validation
Diagnostics:
• Sens/Spec
Surrogate Marker / Endpoints:
• Criteria?
• Multi-Center Global
• Exploratory Information
• Product Registration/ Approval

Our Role = Data Integrity

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- Deliver: Solutions and Service
- **Reduce variability**
- **Reduce bias**
- **Comply with Good Clinical Practice**

- **Education: Who cares?**

FDA Guidance

- 1990 First Commercial Imaging Core Labs
- 1996 Clinton-Kessler Initiative
- 1997 "Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products."
- 1997 "FDA Approval of New Cancer Treatment Uses for Marketed Drug and Biological Products."
- 2004-2008 Critical Path

FDA Guidance

- 1997 – 2004 "Guidance For Industry: Developing Imaging Drug and Biological Products,
  Part 1: Conducting Clinical Safety Assessments,
  Part 2: Clinical Indications;
  Part 3: Design, Analysis and Interpretation of Clinical Studies"
- 2005-2007 "Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics."
- 2008 "DIA/PHARMA/FDA Charter Working Group"
- 2009 "Guidance for Industry: New Contrast Imaging Indication Considerations for Devices and Approved Drug and Biological Products."

Image data flow: complete audit trail

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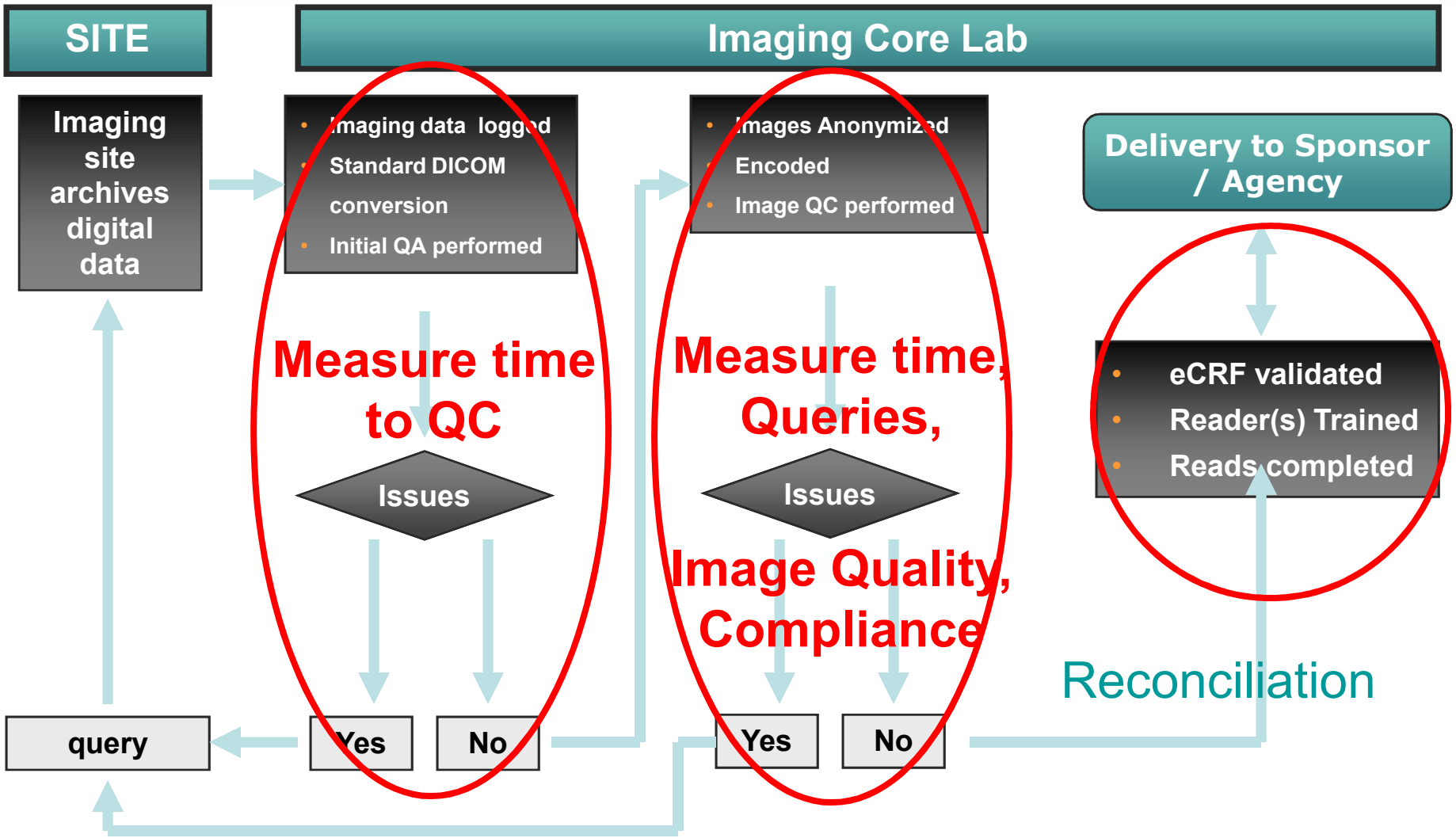

True Integration

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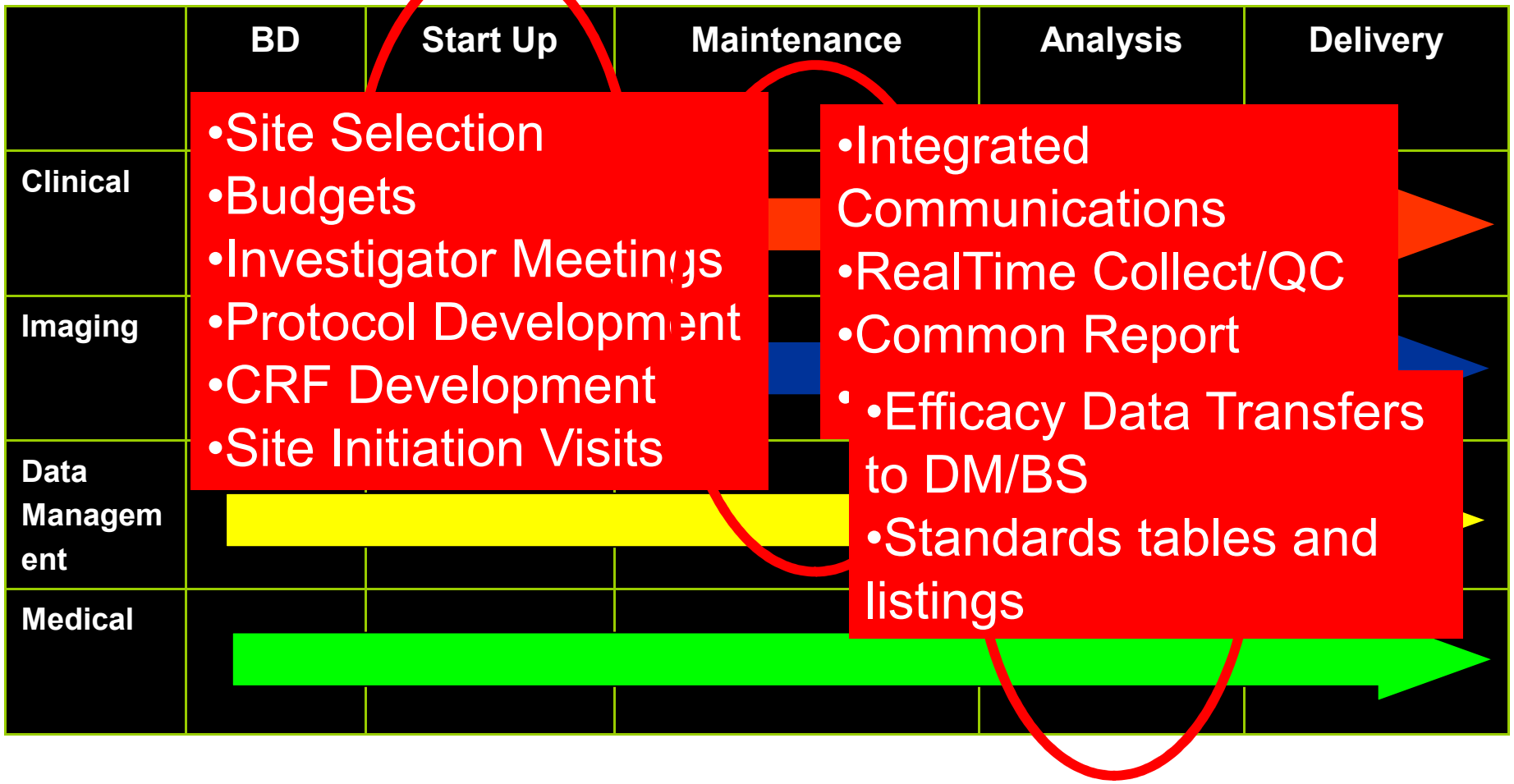

Study Documents

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- Imaging Manual
  - Instruction Manual for sites
    - Protocol Review
    - Image Acquisition
    - Archival / Shipping
    - Team Contact Listing
- Procedure Manual
  - Study Specific Document
    - IMI / Sponsor Responsibilities
    - Data Handling
    - QC / Query process
    - Quantification / Read Design
- Staffing Plan
  - IMI Team
  - Roles / Responsibilities
- Communication / Escalation Plan
- Database Set up
  - Data Plan
  - Study Timelines
  - Study Specific QC forms
  - Study Specific Query Process

Study Documents

- Charter / Methodology
  - Guideline for
    - Trial Objectives
    - How images will be acquired, transported, managed, blinded, and reviewed
    - Guidelines for execution of Review(s)
    - Matched with Protocol and Stat Plan
- Systems Requirement Specification (SRS)
- Data Delivery Specification (DDS)
  - Outlines data listing fields sponsor requires
  - Outlines delivery schedule / frequency

Start-up Activities

- Site feasibility support
- Imaging site technical evaluation surveys
  - Establish communication with imaging personnel
  - Determine “Standard of Care” imaging
  - Archival process at the site
  - Establish image data delivery requirements
  - Transmission
  - Referral centers
  - Collection of sample image data / phantoms

Site Training

- Review protocol requirements with assigned study coordinator / technologist/ radiologist/ physicist to determine:
  - Data flow
  - Personnel/equipment required
  - Archive capabilities & digital records retention policy
  - Do standard operations encompass imaging requirements or do methods need to change to accommodate study?

Image Data Submission Options

- Digital image data:
  - Electronic Networks– end-to-end digital solution – electronic DTF
  - Secure FTP
  - Web-Based – electronic DTF
  - DICOM Server push
  - DVD or CD via courier – paper DTF
- Image data on film:
  - Via courier – paper DTF
- De-Identification:
  - Remains a site dependent issue
  - “Private Tags” often contain data
  - Privacy (HIPPA etc) addressed through “portal” or at core lab
  - Need enough data to assure source verification
  - Study Specific SOP required

Study Maintenance

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- On-going “real time” collection of imaging data
- Quality Control of image data
  - notification of QC results to sites (1-5 days)
  - Image Data Queries followed to resolution
- “RealTime” reads as needed: completed in 24-48hrs
  - Enrollment
  - Confirmation (Reduce Censoring)
  - Quality Control
- Study Reports
  - 24/7 access to images / Work-flow status
  - Weekly / Monthly Study & Site Status Reports (MCC group)
  - Study Specific Communication & Escalation Plan

Data Reconciliation

- Clean transfers from clinical CRF
  - Site/Subject identifiers
  - Scan Date
  - Modality
  - Anatomy
- Queries generated based on discrepancies
  - Mismatches (i.e., date, modality)
  - Missing data
- Reconciled datasets moved to Reader's queues

Standardization: Industry/Entity

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Design	Implementation	Management	Analysis	Delivery
Acquisition •Standardized •Practical •Sensitive Documents •Manuals •Charters •80-20 Rule	•Site Evaluation •Radiology Budgets •Site Technical Support •Performance Metrics	•Real Time Transmission •Continual Review •Common Format: DICOM •De-identification •QA/QC •Create Audit Trail •Common Reporting •Performance Metrics	•Standardized •Objective •Reproducible •Archived •Audit Trail	•Databased •Permanent •Open