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1D: Pathology Informatics, Ancillary Systems, Special and Emerging Data Sources and Device Integration

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Clinical Informatics
Board Review Course

Clinical Informatics Subspecialty Delineation of Practice (CIS DoP)

Domain 1: Fundamental Knowledge and Skills (no Tasks are associated with this Domain which is focused on fundamental knowledge and skills)

Clinical Informatics

K001. The discipline of informatics (e.g., definitions, history, careers, professional organizations)
K002. Fundamental informatics concepts, models, and theories
K003. Core clinical informatics literature (e.g., foundational literature, principle journals, critical analysis of literature, use of evidence to inform practice)
K004. Descriptive and inferential statistics
K005. Health Information Technology (HIT) principles and science
K006. Computer programming fundamentals and computational thinking
K007. Basic systems and network architectures
K008. Basic database structure, data retrieval and analytics techniques and tools
K009. Development and use of interoperability/exchange standards (e.g., Fast Health Interoperability Resources [FHIR], Digital Imaging and Communications in Medicine [DICOM])
K010. Development and use of transaction standards (e.g., American National Standards Institute X12)
K011. Development and use of messaging standards (e.g., Health Level Seven [HL7] v2)
K012. Development and use of ancillary data standards (e.g., imaging and Laboratory Information System[LIS])
K013. Development and use of data model standards
K014. Vocabularies, terminologies, and nomenclatures (e.g., Logical Observation Identifiers Names and Codes [LOINC], Systematized Nomenclature of Medicine --Clinical Terms [SNOMED-CT], RxNorm, International Classification Of Diseases[ICD], Current Procedural Terminology [CPT])
K015. Data taxonomies and ontologies
K016. Security, privacy, and confidentiality requirements and practices
K017. Legal and regulatory issues related to clinical data and information sharing
K018. Technical and non-technical approaches and barriers to interoperability
K019. Ethics and professionalism

The Health System

K020. Primary domains of health, organizational structures, cultures, and processes (e.g., health care delivery, public health, personal health, population health, education of health professionals, clinical research)
K021. Determinants of individual and population health
K022. Forces shaping health care delivery and considerations regarding health care access
K023. Health economics and financing
K024. Policy and regulatory frameworks related to the healthcare system
K025. The flow of data, information, and knowledge within the health system

Domain 2: Improving Care Delivery and Outcomes

K026. Decision science (e.g., Bayes theorem, decision analysis, probability theory, utility and preference assessment, test characteristics)
K027. Clinical decision support standards and processes for development, implementation, evaluation, and maintenance
K028. Five Rights of clinical decision support (i.e., information, person, intervention formats, channel, and point/time in workflow)
K029. Legal, regulatory, and ethical issues regarding clinical decision support
K030. Methods of workflow analysis
K031. Principles of workflow re-engineering
K032. Quality improvement principles and practices (e.g., Six Sigma, Lean, Plan-Do-Study-Act [PDSA] cycle, root cause analysis)
K033. User-centered design principles (e.g., iterative design process)
K034. Usability testing
K035. Definitions of measures (e.g., quality performance, regulatory, pay for performance, public health surveillance)
K036. Measure development and evaluation processes and criteria
K037. Key performance indicators (KPIs)
K038. Claims analytics and benchmarks
K039. Predictive analytic techniques, indications, and limitations
K040. Clinical and financial benchmarking sources (e.g., Gartner, Healthcare Information and Management Systems Society [HIMSS] Analytics, Centers for Medicare and Medicaid Services [CMS], Leapfrog)
K041. Quality standards and measures promulgated by quality organizations (e.g., National Quality Forum [NQF], Centers for Medicare and Medicaid Services [CMS], National Committee for Quality Assurance [NCQA])
K042. Facility accreditation quality and safety standards (e.g., The Joint Commission, Clinical Laboratory Improvement Amendments [CLIA])
K043. Clinical quality standards (e.g., Physician Quality Reporting System [PQRS], Agency for Healthcare Research and Quality [AHRQ], National Surgical Quality Improvement Program [NSQIP], Quality Reporting Document Architecture [QRDA], Health Quality Measure Format [HQMF], Council on Quality and Leadership [CQL], Fast Health Interoperability Resources [FHIR] Clinical Reasoning)
K044. Reporting requirements
K045. Methods to measure and report organizational performance
K046. Adoption metrics (e.g., Electronic Medical Records Adoption Model [EMRAM], Adoption Model for Analytics Maturity [AMAM])
K047. Social determinants of health
K048. Use of patient-generated data
K049. Prediction models
K050. Risk stratification and adjustment
K051. Concepts and tools for care coordination
K052. Care delivery and payment models

Domain 3: Enterprise Information Systems

K053. Health information technology landscape (e.g., innovation strategies, emerging technologies)
K054. Institutional governance of clinical information systems
K055. Information system maintenance requirements
K056. Information needs analysis and information system selection
K057. Information system implementation procedures
K058. Information system evaluation techniques and methods
K059. Information system and integration testing techniques and methodologies
K060. Enterprise architecture (databases, storage, application, interface engine)
K061. Methods of communication between various software components
K062. Network communications infrastructure and protocols between information systems (e.g., Transmission Control Protocol/Internet Protocol [TCP/IP], switches, routers)
K063. Types of settings (e.g., labs, ambulatory, radiology, home) where various systems are used
K064. Clinical system functional requirements
K065. Models and theories of human-computer (machine) interaction (HCI)
K066. HCI evaluation, usability engineering and testing, study design and methods
K067. HCI design standards and design principles
K068. Functionalities of clinical information systems (e.g., Electronic Health Records [EHR], Laboratory Information System [LIS], Picture Archiving and Communication System [PACS], Radiology Information System [RIS] vendor-neutral archive, pharmacy, revenue cycle)
K069. Consumer-facing health informatics applications (e.g., patient portals, mobile health apps and devices, disease management, patient education, behavior modification)
K070. User types and roles, institutional policy and access control
K071. Clinical communication channels and best practices for use (e.g., secure messaging, closed loop communication)
K072. Security threat assessment methods and mitigation strategies
K073. Security standards and safeguards
K074. Clinical impact of scheduled and unscheduled system downtimes
K075. Information system failure modes and downtime mitigation strategies (e.g., replicated data centers, log shipping)
K076. Approaches to knowledge repositories and their implementation and maintenance
K077. Data storage options and their implications
K078. Clinical registries
K079. Health information exchanges
K080. Patient matching strategies
K081. Master patient index
K082. Data reconciliation
K083. Regulated medical devices (e.g., pumps, telemetry monitors) that may be integrated into information systems
K084. Non-regulated medical devices (e.g., consumer devices)
K085. Telehealth workflows and resources (e.g., software, hardware, staff)

Domain 4: Data Governance and Data Analytics

K086. Stewardship of data
K087. Regulations, organizations, and best practice related to data access and sharing agreements, data use, privacy, security, and portability
K088. Metadata and data dictionaries
K089. Data life cycle
K090. Transactional and reporting/research databases
K091. Techniques for the storage of disparate data types
K092. Techniques to extract, transform, and load data
K093. Data associated with workflow processes and clinical context
K094. Data management and validation techniques
K095. Standards related to storage and retrieval from specialized and emerging data sources
K096. Types and uses of specialized and emerging data sources (e.g., imaging, bioinformatics, internet of things (IoT), patient-generated, social determinants)
K097. Issues related to integrating emerging data sources into business and clinical decision making
K098. Information architecture
K099. Query tools and techniques
K100. Flat files, relational and non-relational/NoSQL database structures, distributed file systems
K101. Definitions and appropriate use of descriptive, diagnostic, predictive, and prescriptive analytics
K102. Analytic tools and techniques (e.g., Boolean, Bayesian, statistical/mathematical modeling)
K103. Advanced modeling and algorithms
K104. Artificial intelligence
K105. Machine learning (e.g., neural networks, support vector machines, Bayesian network)
K106. Data visualization (e.g., graphical, geospatial, 3D modeling, dashboards, heat maps)
K107. Natural language processing
K108. Precision medicine (customized treatment plans based on patient-specific data)
K109. Knowledge management and archiving science
K110. Methods for knowledge persistence and sharing
K111. Methods and standards for data sharing across systems (e.g., health information exchanges, public health reporting)

Domain 5: Leadership and Professionalism

K112. Environmental scanning and assessment methods and techniques
K113. Consensus building, collaboration, and conflict management
K114. Business plan development for informatics projects and activities (e.g., return on investment, business case analysis, pro forma projections)
K115. Basic revenue cycle
K116. Basic managerial/cost accounting principles and concepts
K117. Capital and operating budgeting
K118. Strategy formulation and evaluation
K119. Approaches to establishing Health Information Technology (HIT) mission and objectives
K120. Communication strategies, including one-on-one, presentation to groups, and asynchronous communication
K121. Effective communication programs to support and sustain systems implementation
K122. Writing effectively for various audiences and goals
K123. Negotiation strategies, methods, and techniques
K124. Conflict management strategies, methods, and techniques
K125. Change management principles, models, and methods
K126. Assessment of organizational culture and behavior change theories
K127. Theory and methods for promoting the adoption and effective use of clinical information systems
K128. Motivational strategies, methods, and techniques
K129. Basic principles and practices of project management
K130. Project management tools and techniques
K131. Leadership principles, models, and methods
K132. Intergenerational communication techniques
K133. Coaching, mentoring, championing and cheerleading methods
K134. Adult learning theories, methods, and techniques
K135. Teaching modalities for individuals and groups
K136. Methods to assess the effectiveness of training and competency development
K137. Principles, models, and methods for building and managing effective interdisciplinary teams
K138. Team productivity and effectiveness (e.g., articulating team goals, defining rules of operation, clarifying individual roles, team management, identifying and addressing challenges)
K139. Group management processes (e.g., nominal group, consensus mapping, Delphi method)

Knowledge Statements from the DoP

Pathology Informatics and…

Information System Selection and Implementation
(ancillary systems ONLY)

- K056. Information needs analysis and information system selection
- K057. Information system implementation procedures

Integrating data and devices

- K083. Regulated medical devices (e.g., pumps, telemetry monitors) that may be integrated into information systems

Precision Medicine

- K108. Precision medicine (customized treatment plans based on patient-specific data)

Specialized and Emerging Data Sources

- K095. Standards related to storage and retrieval from specialized and emerging data sources
- K096. Types and uses of specialized and emerging data sources (e.g., imaging, bioinformatics, internet of things (IoT))
  - Patient-generated data and social determinants covered elsewhere
- K097. Issues related to integrating emerging data sources into business and clinical decision making

Pathology Informatics

Abbreviations and Terminology

EHR	Electronic Health Record
LIS	Laboratory Information System*
Lab	Any laboratory performing clinical testing on a patient. Includes: • Anatomic Pathology (Surgical pathology, cytology, autopsy), Clinical Laboratories, Specialized laboratories, Reference laboratories
RIS	Radiology Information System
System	Refers to any separate or integrated system which performs a limited set of functions in the healthcare organization (e.g., LIS, RIS, Pharmacy system but **also** middleware, devices, instruments scanners, etc.)

*Another, less frequently used, abbreviation is **LIMS** (laboratory information management system). LIMS usually, but not always, refers to an information system used in a research (not clinical) laboratory.

Pathology Informatics and Ancillary Systems

- Relationship of EHRs with ancillary systems (e.g., LIS, RIS)
  - Architectures between EHRs and Ancillary Systems
  - Support Models for ancillary systems
  - Laboratory Regulations and Standards that impact EHRs
- The Laboratory as an Automation Driver
  - Devices, device/data integration and validation
  - Interfaces and automation lines
  - Barcodes and Radiofrequency Identification Tags (RFID)
- Basics of digital imaging (radiology and pathology)
  - Telepathology
  - Teleradiology
- Precision Medicine and Genomics
  - Impact on clinical informatics
  - Next-generation sequencing and bioinformatics
  - Genomic data privacy
- Big data and computational pathology

Why Pathology Informatics?

- Classic example of an ancillary system to EHR
  - Similar architectures with radiology and pharmacy systems
- Contributes huge amount of discrete data to EHRs
  - Data management, validation, integration and reconciliation is core to the pathology specialty
- Numerous integrated and interfaced devices, many of which are regulated
  - Will also discuss other regulated devices such as pumps and telemetry devices
- Workflows highly automated (barcodes, robotics)
- Precision medicine diagnostics are performed in laboratories
- Laboratories are highly regulated by federal law
- Pathology programs require clinical informatics training for residents
  - Publicly available teaching toolkits
- **Three pathologists help develop the Clinical Informatics board exam questions**

Information System Architectures

- **Integrated system** (LIS, RIS, Rx)
  - System or module is an integrated module/component of the EHR
  - System shares tables with the EHR (e.g., patient tables)
- **Interfaced system** (LIS, RIS, Rx)
  - Separate from the EHR
  - Communications usually occur through HL7 interfaces
  - With reference to the EHR:

Internal system	System and EHR are both owned and managed by the same health care entity
External system	System is owned and managed by a different health care entity than the EHR (i.e., reference lab)

Integrated Systems

Advantages

- May be less expensive at contract signature (short-term)
- No EHR interfaces to maintain
- Same hardware platform (usually)
- May allow for unique EHR functionality that is hard to do with standard HL7 interfaces

Disadvantages

- Will not work when EHR is down
- Functionality may be limited
  - Workarounds, safety issues
  - Microbiology, Blood bank
  - Less ability to interface with middleware, instruments
- May be more expensive long-term (e.g., FTEs, 3rd party modules)
- Incorrect assumptions that EHR displays are the same as the system-displays
- May not work in the absence of an EHR
- May not work with multiple EHRs (e.g., different EHR for inpatient vs. outpatients)

Interfaced (Separate) Systems

Advantages

- Works in absence of EHR
- Works with multiple EHRs
- Functionality may be more tailored for laboratory
  - Fewer errors
  - Better turnaround time
- May be less expensive long-term

Disadvantages

- May be more expensive at contract signature (short-term)
- HL7 interfaces to EHRs must be implemented and maintained
- Separate system hardware has to be purchased and managed
- Some functionality may not be available with standard HL7 interfaces
- Still may not be able to support more highly specialized areas (e.g., HLA, Genomics, Cytogenetics)

K056. Information needs analysis and information system selection

K057. Information system implementation procedures

(ancillary systems only)

Ancillary System Evaluation and Selection

- See lectures on EHR system evaluation, selection and implementation
- Use all skills in project management, change management, workflow re-engineering and leadership
- System-specific recommendations for evaluation
  - Radiology Systems: https://www.ajronline.org/doi/full/10.2214/AJR.12.10326
  - LIS toolkit: https://www.pathologyinformatics.org/toolkit.php
- **Data migration** may be required
  - Will be discussed later in this lecture

Support Models for Systems

- **Central Organizational Management**
  - Central IT staff for the health care entity manage the LIS as well as the EHR
  - Common model with integrated systems

- **Departmental Management**
  - e.g., Laboratory manages the LIS
    - Hardware, software and networks
  - Common model with interfaced systems

- **Hybrid Management**
  - IT staff that manage the EHR also manage some, but not all, components of the LIS or RIS
    - Hardware and/or networks
  - Department manages the rest of the system (laboratory manages LIS, radiology manages RIS, etc.)

Pathologists, Radiologists and Clinical Informatics

- A CMIO is to an EHR…
  - What a Director of Pathology Informatics is to an LIS
  - What a Director of Radiology informatics is to a RIS
- Radiologists and pathologists specializing in Clinical Informatics
  - Provide medical oversight for the RIS or LIS
  - Provide medical oversight for laboratory or radiology components of an EHR
  - Good resource for specialty specific IT regulations, practice and implementations

Pathologists as Clinical Informaticists

- Pathologists have a long history of clinical informatics practice
  - First publications of laboratory informatics in the 1940s
  - Laboratories were the first areas in hospitals to adopt computer systems
- American Board of Pathology co-sponsored application for the Clinical Informatics Exam with the American Board of Preventive Medicine
- As of December 2019:
  - 2% of all physicians are pathologists (Federation of State Medical Boards)
  - 6.89% (141 of 2044) of all board-certified clinical informaticists are pathologists – steadily increasing from 6% over the last 3 years.

Laboratory Regulations and EHRs

- **CLIA** (cont.) – 42 CFR § 493.1291(a)
  - The laboratory must … **ensure test results and other patient-specific data are accurately and reliably sent from the point of data entry (whether interfaced or entered manually) to final report destination**, in a timely manner.
  - Includes:
    - Calculated results
    - Results to interfaced systems (including EHRs)
    - Results from outside laboratories, satellites and point of care locations

- Laboratories must be accredited by a **CLIA-deemed agency** every two years
  - Examples: CAP, AABB, ASHI, COLA, TJC
  - Must require compliance with all CLIA requirements
  - May have additional standards exceeding CLIA
  - Some of these impact EHRs
    - CAP GEN.48500 Phase II
    - "There is a procedure to verify that patient results are accurately transmitted from the point of data entry (interfaced instruments and manual input) to patient reports (whether paper or electronic)."

Laboratory Accreditation and EHRs

- **CLIA** (cont.) – 42 CFR § 493.1291(c) and (d)
- The test report must indicate the following:
  - For positive patient identification, either the patient's name and identification number, or an unique patient identifier and identification number.
  - **The name and address of the laboratory location where the test was performed.**
  - The test report date.
  - The test performed.
  - Specimen source, when appropriate.
  - The test result and, if applicable, the **units of measurement** or interpretation, or both.
  - Any information regarding the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability.
- **Pertinent "reference intervals" or "normal" values**, as determined by the laboratory performing the tests, **must** be available to the authorized person who ordered the tests and, if applicable, the individual responsible for using the test results.

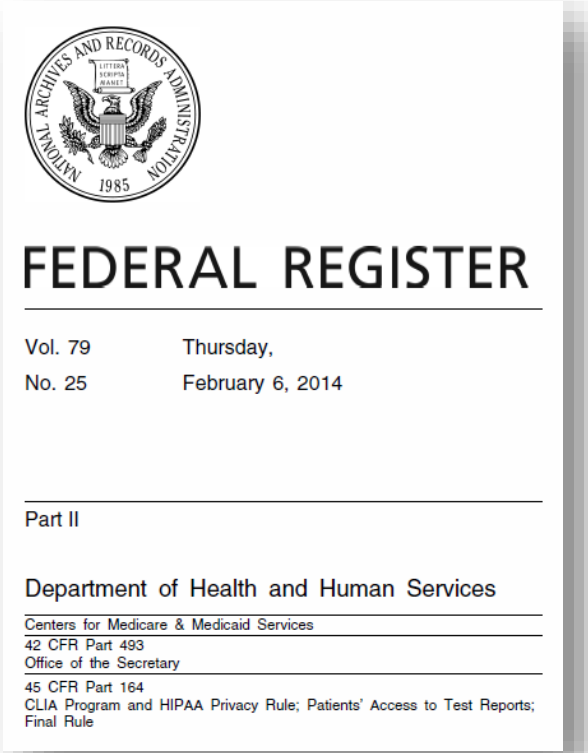
- Perrotta et al 2016
- Studied 16 lab tests at 45 institutions (1059 lab results)

Data Element	% of lab results
Result accurately transmitted to EHR	99.3%
All CLIA required result elements transmitted to EHR: - CPOE < 50% of orders - CPOE >= 50% of orders	69.6% - 28.6% (median) - 93.8% (median)
Most common CLIA elements missing from EHR: - Date/time of test result or report - Name/address of performing laboratory	 - 12.8% - 12.6%
Results were appropriately formatted in EHR	90.9%

Patient Access to Laboratory Results

Before the Patient Access Rule and 21st Century Cures Act:

- Covered entity required to provide patient with “designated record set” EXCEPT for laboratory results:
  - did **NOT** apply to PHI maintained by a covered entity subject to CLIA (**Laboratory**) or exempt from CLIA (**CLIA-exempt laboratory**)
- **ONC reported outcry from patients about lack of access to their own laboratory data**
- Outcry from others who perceived CLIA as imposing barriers to health information exchange



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FEDERAL REGISTER

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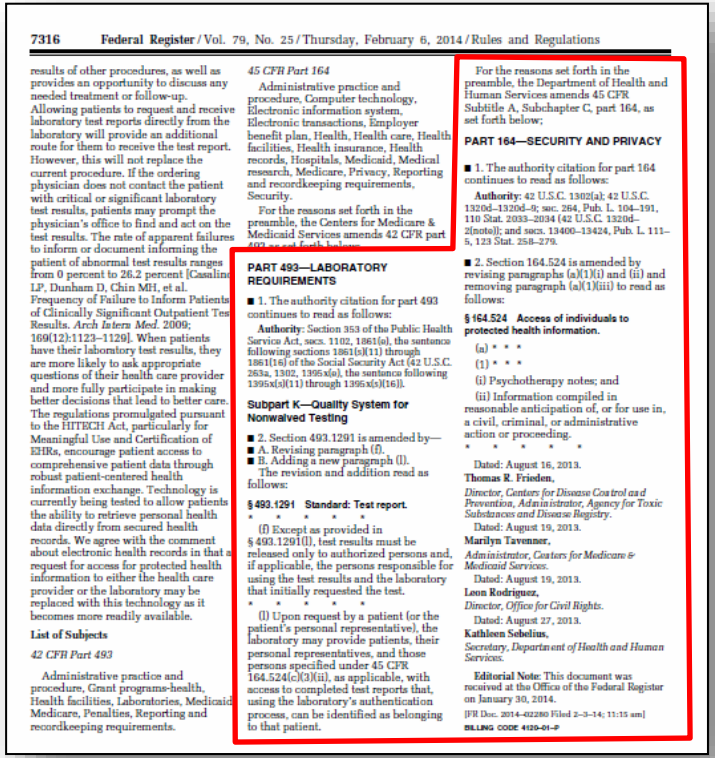
No. 25 February 6, 2014

Part II

Department of Health and Human Services

Centers for Medicare & Medicaid Services
42 CFR Part 493
Office of the Secretary
45 CFR Part 164
CLIA Program and HIPAA Privacy Rule; Patients' Access to Test Reports; Final Rule

Patient Access Rule and 21st Century Cures Act



7316 Federal Register / Vol. 79, No. 25 / Thursday, February 6, 2014 / Rules and Regulations

results of other procedures, as well as provides an opportunity to discuss any needed treatment or follow-up. Allowing patients to request and receive laboratory test reports directly from the laboratory will provide an additional route for them to receive the test report. However, this will not replace the current procedure. If the ordering physician does not contact the patient with critical or significant laboratory test results, patients may prompt the physician's office to find and act on the test results. The rate of apparent failures to inform or document informing the patient of abnormal test results ranges from 0 percent to 26.2 percent [Casalino LP, Dunham D, Chin MH, et al. Frequency of Failure to Inform Patients of Clinically Significant Outpatient Test Results. *Arch Intern Med*. 2009; 169(12):1123–1129]. When patients have their laboratory test results, they are more likely to ask appropriate questions of their health care provider and more fully participate in making better decisions that lead to better care. The regulations promulgated pursuant to the HITECH Act, particularly for Meaningful Use and Certification of EHRs, encourage patient access to comprehensive patient data through robust patient-centered health information exchange. Technology is currently being tested to allow patients the ability to retrieve personal health data directly from secured health records. We agree with the comment about electronic health records in that a request for access for protected health information to either the health care provider or the laboratory may be replaced with this technology as it becomes more readily available.

List of Subjects

42 CFR Part 493

Administrative practice and procedure, Grant programs-health, Health facilities, Laboratories, Medicaid, Medicare, Penalties, Reporting and recordkeeping requirements.

45 CFR Part 164

Administrative practice and procedure, Computer technology, Electronic information system, Electronic transactions, Employer benefit plan, Health, Health care, Health facilities, Health insurance, Health records, Hospitals, Medicaid, Medical research, Medicare, Privacy, Reporting and recordkeeping requirements, Security.

For the reasons set forth in the preamble, the Centers for Medicare & Medicaid Services amends 42 CFR part 493 as set forth below:

PART 493—LABORATORY REQUIREMENTS

■ 1. The authority citation for part 493 continues to read as follows:

Authority: Section 353 of the Public Health Service Act, secs. 1102, 1861(e), the sentence following sections 1861(s)(11) through 1861(1)(6) of the Social Security Act (42 U.S.C. 263a, 1302, 1395x(e), the sentence following 1395x(s)(11) through 1395x(s)(16)).

Subpart K—Quality System for Nonwaived Testing

■ 2. Section 493.1291 is amended by—
■ A. Revising paragraph (f).
■ B. Adding a new paragraph (l).
The revision and addition read as follows:

§ 493.1291 Standard: Test report.

* * * * *

(f) Except as provided in § 493.1291(l), test results must be released only to authorized persons and, if applicable, the persons responsible for using the test results and the laboratory that initially requested the test.

* * * * *

(l) Upon request by a patient (or the patient's personal representative), the laboratory may provide patients, their personal representatives, and those persons specified under 45 CFR 164.524(c)(3)(ii), as applicable, with access to completed test reports that, using the laboratory's authentication process, can be identified as belonging to that patient.

For the reasons set forth in the preamble, the Department of Health and Human Services amends 45 CFR Subtitle A, Subchapter C, part 164, as set forth below;

PART 164—SECURITY AND PRIVACY

■ 1. The authority citation for part 164 continues to read as follows:

Authority: 42 U.S.C. 1302(a); 42 U.S.C. 1320d–1320d–9; sec. 264, Pub. L. 104–191, 110 Stat. 2033–2034 (42 U.S.C. 1320d–2(note)); and secs. 13400–13424, Pub. L. 111–5, 123 Stat. 258–279.

■ 2. Section 164.524 is amended by revising paragraphs (a)(1)(i) and (ii) and removing paragraph (a)(1)(iii) to read as follows:

§ 164.524 Access of individuals to protected health information.

(a) * * *

(1) * * *

(i) Psychotherapy notes; and

(ii) Information compiled in reasonable anticipation of, or for use in, a civil, criminal, or administrative action or proceeding.

* * * * *

Dated: August 16, 2013.

Thomas R. Frieden,

Director, Centers for Disease Control and Prevention, Administrator, Agency for Toxic Substances and Disease Registry.

Dated: August 19, 2013.

Marilyn Tavenner,

Administrator, Centers for Medicare & Medicaid Services.

Dated: August 19, 2013.

Leon Rodriguez,

Director, Office for Civil Rights.

Dated: August 27, 2013.

Kathleen Sebelius,

Secretary, Department of Health and Human Services.

Editorial Note: This document was received at the Office of the Federal Register on January 30, 2014.

[FR Doc. 2014-02280 Filed 2–3–14; 11:15 am]

BILLING CODE 4120–01–P

- **Patient Access Rule**
  - SUPERSEDES all state laws on release of laboratory results to patients
  - Applies to ALL CLIA laboratories and CLIA-exempt laboratories who…
    - Perform even just ONE HIPAA financial transaction
- **21st Century Cures Act**
  - Covered elsewhere
  - Laboratory and pathology data included in the information for immediate release

Laboratory Regulations and EHRs

- **Transfusion (blood bank) systems** are regulated by the FDA
  - High risk (Class III) medical device
  - Blood bank systems make determinations on what products or organs get transfused and/or transplanted
  - Guidance on software validation
    - Has good recommendations for validation of health software in general

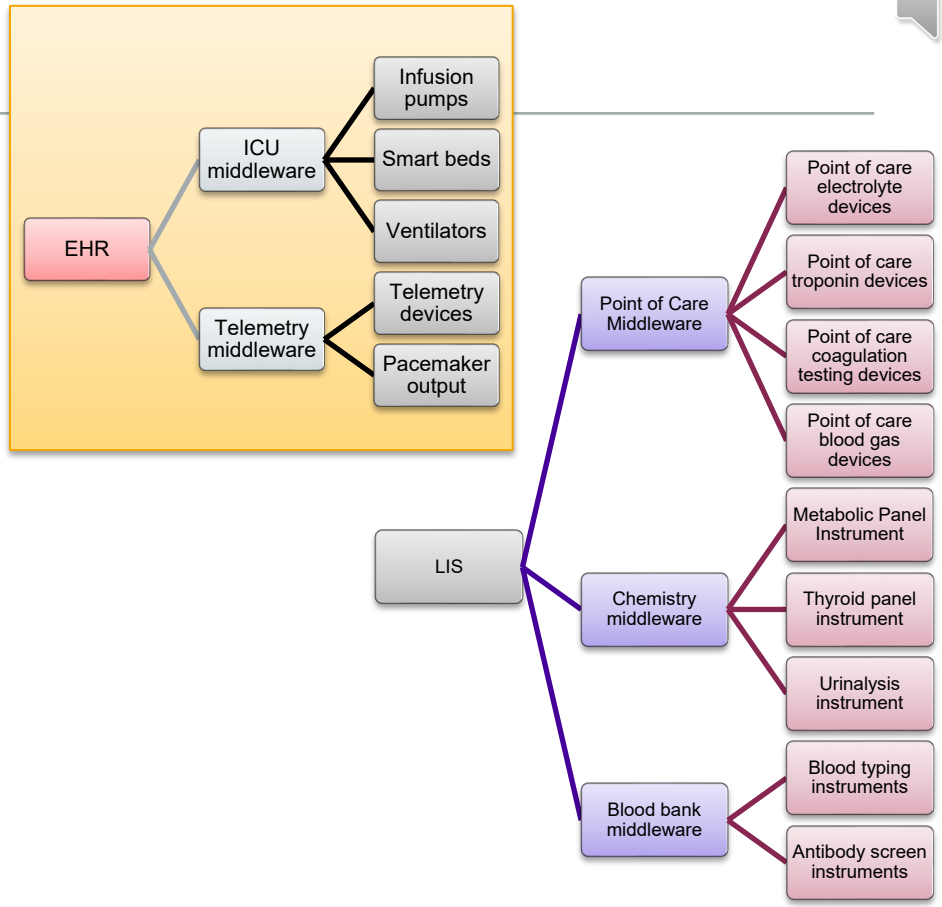
FDA Guidance for Industry: Blood Establishment Computer System Validation in the User's Facility

Ancillary Systems and EHRs

- Challenges for departments
  - Department personnel may not have access to the EHR
    - Additional barriers if the lab or department is outside the covered entity for the EHR
  - Systems may have many EHR interfaces (e.g., Reference Labs)
  - EHR manipulations of system data ***after*** result is posted
  - Departmental manipulations of data with unseen impact to EHR displays
- EHR users and administrators
  - EHRs may have results from multiple laboratories, radiology departments, etc.
  - If allowed to make changes to EHR display of result data then…
    - Risk of non-compliance, confusion and potential for patient harm
  - Don't have access to ancillary systems to compare views
    - May not know when ancillary data is inaccurately displayed
    - Fail to prevent common errors
    - **Integrated systems are NOT immune to these errors.**

Middleware

- Software that “sits in the middle” between two different systems
- Often on its own server
  - Needs test environment / server
- Often performs functions not available on the device or system
  - Trends
  - Calculations and transformations
  - Critical value functions
  - Documentation (e.g., for RBAV = “read back and verify”)
  - Notifications

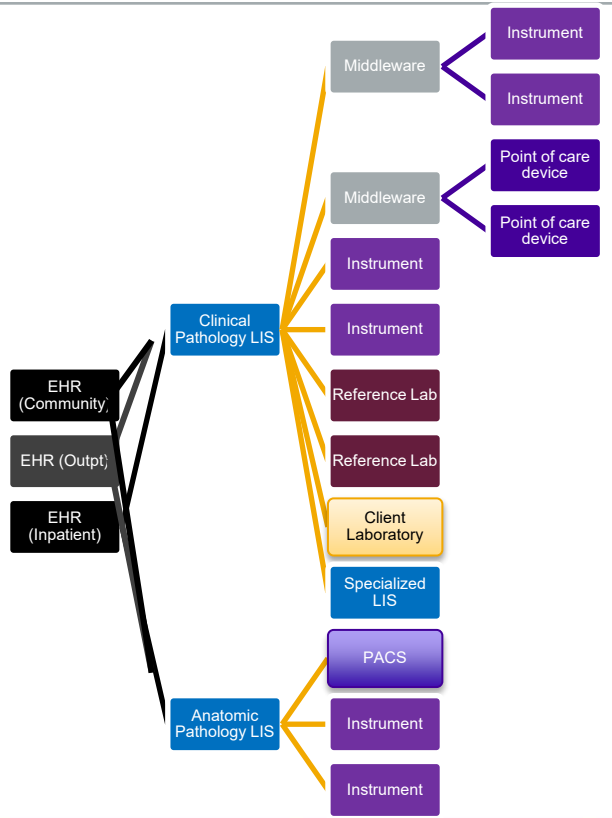


Ancillary System Interfaces

- Even when your ancillary system is integrated (vs. interfaced) to the EHR, there are a number of other systems which may be interfaced to it
  - Not uncommon for a laboratory to have well over 300 integrated devices connected to the LIS, for radiology to have several hundred connected devices to the RIS
- **System interfaces**
  - Used to communicate information between two databases
  - >90% of laboratory interfaces are HL7 interfaces
    - Real-time for clinical patient care activities
    - Nightly for billing, data warehousing
  - Few custom and “flat-file” interfaces
    - Certain instrument interfaces

Ancillary System Interfaces

- Ancillary systems and EHRs communicate via interfaces with…
  - One or more EHRs (internal/external)
  - One or more outside ancillary systems
    - External services (e.g., reference laboratories; send orders out)
    - Outreach clients (LIS receives orders in)
  - One to multiple middleware servers
    - Automation line servers
    - Point of Care device management
    - Blood typing instrument management
    - Autoverification management
  - Instruments and devices
  - Fax Servers
  - Print servers
  - Billing systems
  - Interface engines



Interfaced Systems and Devices

Bidirectional interfaces

- Information flows in both directions
- Can be complicated to set up
- **Symmetrical**
  - Type of information exchanged in both directions is the **same**
  - Example: ADT messages
- **Asymmetrical**
  - Information flows in both directions, but type of information is **different**
  - Example: Orders in one direction; Results in another

Unidirectional interfaces

- Information flows in **one direction only**
  - Billing systems, data warehouses, print servers, fax servers, mobile device messaging systems
- Can be less work to implement, except...
  - May have to test against many downstream devices in different locations
  - Often drive workflow → visual triggers
    - Printed labels, documents, billing queues
    - Movement of specimens down a robotic line
- When broken → no workflow triggers
  - Absence of triggers → delayed detection of problem

Device Informatics Terms to Know

Automation Line

- Laboratories
  - Robotically operated specimen track which moves specimens from point of entry to the instrument that will perform the test
  - Scans specimen label barcode
  - Uses accession # from barcode to query LIS for pending orders
  - Sends the sample to the appropriate instrument for testing
- Pharmacies
  - Often referred to as robots
  - Package medications for delivery robotically

Autoverification

- Definition:
  - Results that meet certain criteria may be automatically verified (signed and released) by the middleware instead of a person
- Autoverification facilitates doing 10x as many laboratory tests with the same number of employees
  - When it isn't working, volume may quickly outpace staff's ability to keep up

AUTO10-A: Autoverification of Clinical Laboratory Test Results; Approved Guideline. Volume 26; Number 32. January 2012. Clinical and laboratory Standards Institute.

K083. Regulated medical devices (e.g., pumps, telemetry monitors) that may be integrated into information systems

Regulated Medical Devices

- In the United States, a **regulated medical device** is
  - **Subject to FDA regulation and may require FDA pre-market approval or clearance**
  - An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
    - recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
    - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, **or**
    - intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and
  - which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).

- Examples
  - Heart monitors
  - Infusion pumps
  - Ventilators
  - Pacemakers
  - Telemetry devices
  - Laboratory instruments
  - Radiology scanners
  - Smart beds
  - Anesthesia machines
  - Etc.

https://www.fda.gov/industry/regulated-products/medical-device-overview
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/unique-device-identification-direct-marking-devices

Classes of Regulated Devices (Risk-based)

Class	Risk to patient and/or user	% devices	Description	FDA clearance or pre-market approval required?	Exempt from GMP requirements?	Examples
Class I	Low to moderate	47%	• General controls required only	• If exempt, none. • If not exempt, 510(k) clearance required	Some	• Enema kits • Manual stethoscopes • Bandages • Bed pans
Class II	Moderate to high	43%	• General and Special controls required	• If exempt, none. • If not exempt, 510(k) clearance required	No	• Powered wheelchairs • WSI scanners • Pregnancy test kits
Class III	High	10%	• Sustain or support life or… • Have unreasonable risk of illness or injury • General and Special controls required	• If substantial equivalence to another FDA-approved device, 510(k) clearance required • If not substantially equivalent, then Premarket Approval (PMA) required	No	• Implanted devices • Ventilators • Anesthesia machines

Many nuances to these classifications!

GMP: Good Manufacturing Practices (a.k.a. Quality System (QS) regulation)
https://www.fda.gov/medical-devices/classify-your-medical-device/class-i-ii-exemptions

510(k) clearance
- 2+ months for FDA decision

Premarket Approval (PMA)
- 3+ years for FDA decision

Regulated Medical Devices - SaMD

- **SaMD: Software as a Medical Device**
  - Definition from International Medical Device Regulators Forum (IMDRF)
  - Software intended to be used for one or more medical purposes that perform these purposes without being part of a medical device
- Medical software may be classified as SaMD if…
  - Software is performing more functions than is necessary as part of its hardware
  - Software used with device was developed by a third party (not the device manufacturer)

- https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd

Regulated Medical Devices – Important Facts

- Any changes to an FDA approved device may **invalidate** its approval
- Includes the addition of any software or functions outside the scope of the FDA approval
  - Alerts and alarms
  - Prioritization of data
  - Calculations and transformations of data
  - Installation of anti-malware or encryption software
  - https://www.fda.gov/media/88572/download
- Ensure changes will not invalidate FDA approval if FDA approval is desired or necessary for use

Regulated Medical Devices – Important Facts

- Naming conventions for devices
  - Unique identification of each device is critical
    - Especially when device ID used in data transfer
    - https://www.ismp.org/resources/ehr-smart-pump-interoperability-resulted-electronic-documentation-different-flow-rates
      - Each device MUST have unique identification
      - Device ID must be accurate on each device, especially if using RFID or bar codes in the process for identification - require a double check that these are accurate

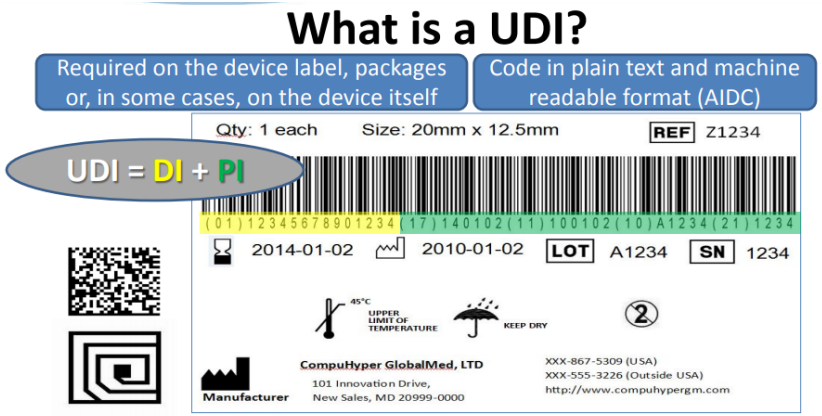
Unique Device Identifier (UDI)

- Purpose
  - To facilitate rapid and accurate identification of a (FDA-approved) device
  - Enable access to information concerning the device
  - To provide standard and clear way to identify the device in EHRs, information systems, claims data sources and registries
- https://www.fda.gov/media/96818/download
- Not currently a requirement for manufacturers, but soon may be

- EHR device integration issues with UDI https://pubmed.ncbi.nlm.nih.gov/24322986/
- FDA Amendments of 2007 + FDA Safety and Innovation Act of 2012 ➔ **UDI final rule** 9/24/2013
- However…
  - Many information systems don't have a place to put the UDI
  - Healthcare organizations developing their own device names instead

Unique Device Identifier (UDI)

- Construction
  - UDI = Device Identifier (DI) + Production Identifier (PI)
- Labeling requirements
  - **Agency** issuing a UDI must be FDA-accredited, conform to ISO standards for UDI
  - **Labeler** must work with at least 1 accredited issuing agency and use the issuing agency rules to build their UDI



Device Identifier (DI)	Production Identifier (PI)

• Mandatory fixed portion of UDI (see yellow in image above)
• Identifies
  • labeler (manufacturer)
  • Specific version of model or device
  • Never changes once assigned
• Entered into Global UDI database (GUDID)
	• Conditional, variable portion of UDI (see green in image above)
	• Not required for Class I devices
	• May include:
	  • Lot, batch, serial number
	  • Expiration date, manufacture date
	• NOT submitted or stored in the GUDID

Regulated Medical Devices – Important Facts

- Alerts and alarms
  - May fire at the device, in the information system or both (choose wisely)
  - Beware of **alarm fatigue**
    - Important alerts (signal) are ignored because the overall number of alerts is high (noise)
    - Especially in highly wired environments (e.g., ICUs, radiology departments, laboratories)
  - Be sure to consider overall environment (# devices, # alarms, can they be heard? Are staff present to respond?)

- Some studies have shown that over 50% (sometimes over 90%) of alerts and alarms are unnecessary (non-interventional)

https://commons.wikimedia.org/wiki/File:Kapiolani_Neonatal_ICU.jpg

Regulated Medical Devices – Important Facts

- Security and privacy are imperative
  - Mobile devices are easily lost or stolen – can the device be remote wiped? Tracked via RFID or beacon?
  - Devices can be hacked or infected with malware to cause them to malfunction
    - Consider implantable devices
- Source of information loss as well as new threats
  - Loss or theft of devices with PHI may require security breach notification
- Does the device comply with HIPAA final security rule requirements?
  - Just because it is FDA-approved does not mean it is compliant with HIPAA

Device Communication

- HL7 real-time transfer
- Custom flat-file transfer with manual or semi-automated upload-download
- **ASTM protocol**: American Society for Testing and Materials
  - International standards organization
  - Creates standards surrounding testing instruments of all kinds, including healthcare and medical
    - Surgical, Laboratory
  - Also a real-time transfer mechanism
  - Decreasingly common among laboratory instruments
  - Created ASTM protocol for data transfer from laboratory instruments to computer systems
    - ASTM standard E1381 deprecated and replaced with CLSI standard LIS01 for low-level protocol transfer
    - ASTM standard E1394 deprecated and replaced with CLSI standard LIS02 for standard protocol transfer

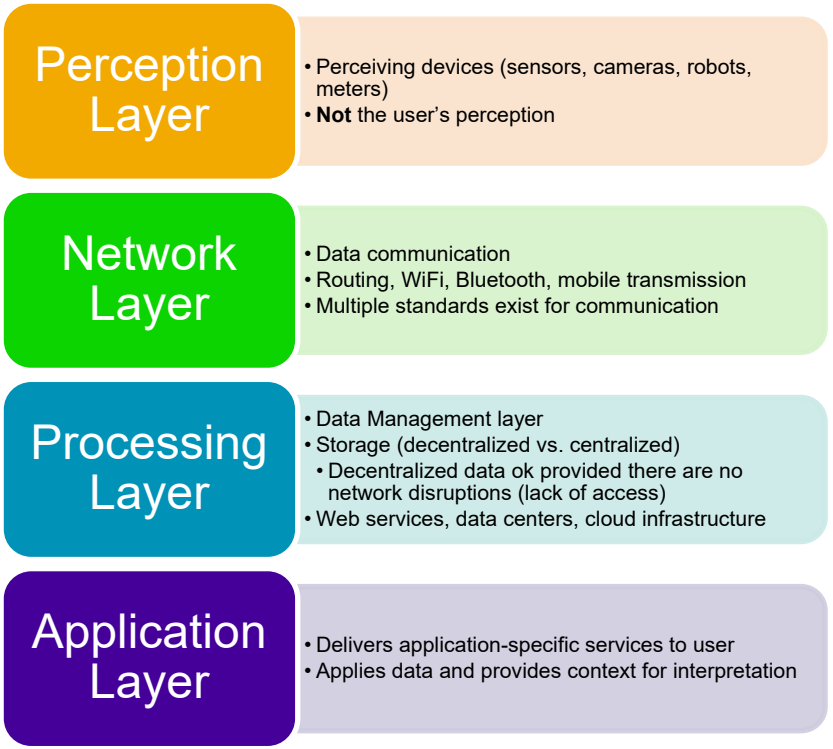
Internet of Things (IoT)

(Specialized and emerging data sources)

K096. Types and uses
K095. Standards related to storage and retrieval
K097. Issues related to integrating into business and clinical decision making

Definitions

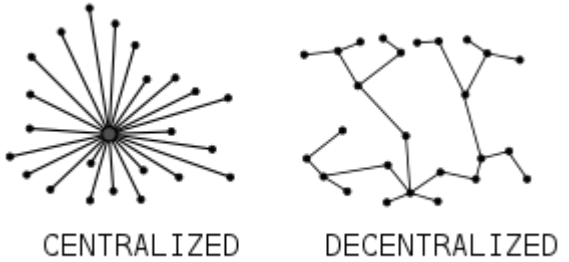
- **Internet of Things (IoT)**
  - System of digital devices (things) to the internet
  - Can collect, store, send and receive data over a network
  - No requirement for human-to-human or human-to-computer interaction
- **Healthcare IoT**: data being handled is health data
  - Internet of Medical Things (IoMT)
  - May includes patient-wearables (covered elsewhere), mobile phones, computing devices, laboratory instruments, radiology scanners, implantable devices, pumps, monitors, etc.
- Abosata 2021, Ye 2020



Internet of Things (IoT)

- Expected to expand to 75 billion devices by 2025 [Abosata 2021]
- Taxonomy of IoT in healthcare [Aghdam 2021]
- Each “thing” has metadata
  - Object identification
  - Location
  - Processes
  - Services
  - [Abu-Elkheir 2013]

- Requires good data management practices
  - Online → Summarize data
  - Offline →
    - Storage
      - Constant access/updates vs. archival (read-only)
      - Decentralized vs. centralized
    - Logging
    - Auditing



Privacy and Security Issues

- Security and privacy are major obstacles to adoption
  - Societal concerns about inappropriate collection and distribution of data
  - May expose healthcare organization to cyber threats via exploited vulnerabilities
    - Bad news:
      - Estimated 70% of most frequently used IoT are vulnerable to several types of threats
      - Need to apply security services; may be challenging with patient- or staff-owned devices
      - No available secure and dynamic access control model for IoT devices
      - Device identification is variable
    - Good news:
      - Many IoT devices are constrained by power and memory

- Ye 2020, Abosata 2021, Aftab 2021

IoT Healthcare Standards

Svanström 2016

ISO/IEEE 11073-20601:2016	Health informatics - Personal health device communication - Part 20601: Application profile - Optimized exchange protocol
ISO/IEEE 11073-10404:2010	Health informatics - Personal health device communication - Part 10404: Device specialization – Pulse Oximeter
Networking standards	There are many! [Aghdam 2021, https://telnyx.com/resources/wireless-iot-network-standards] Bluetooth, WiFi, mobile communication platforms [GS1 IoT] 
Open Data (OData) Protocol	OASIS standard that defines best practice for developing HTTP-based and RESTful APIs (https://www.odata.org/getting-started/basic-tutorial/)

Issues Integrating into Decision-making

- Issues with integrating **IoT** into business and clinical decision-making
  - Device data
    - May not be compatible with target health system (interoperability issues)
    - May be overwhelming
  - Data ownership, rights to distribute or delete
  - There are MANY standards for IoT – which to choose?
  - Reimbursement considerations
  - Provides rich set of resources to collect data on and monitor patients, healthcare workers, movements, etc.
  - FHIR helpful with data transfer

https://pubmed.ncbi.nlm.nih.gov/33170132/

Imaging

(Specialized and emerging data sources)

K096. Types and uses
K095. Standards related to storage and retrieval
K097. Issues related to integrating into business and clinical decision making

Basics of Digital Imaging

- **Pixel**
  - Smallest component of an image
  - Print vs. digital
- **Image Size**
  - Overall size of the image in its final form (digital or printed)
  - Width by height
  - Contains no information on image resolution
  - Important to know if need to decide on resolution

- **Image resolution**
  - A.k.a **pixel density**
  - Commonly referenced as **Dots per inch (DPI)**
    - The number of pixels per inch of screen
    - The number of printed pixels per inch of print medium
    - Average computer screen DPI are 96 to 120
    - Average minimum printed DPI = 300 (can vary significantly)
  - Computer screens reference pixels in width x height
    - Does not indicate resolution because no information on screen size

Basics of Digital Imaging

- Image resolution (continued)
  - Gross images → low resolution OK
  - Microscopic images → high resolution desired
  - NOTE: Balance resolution against the final image size desired
    - Small image size → low resolution
    - Large image size → high resolution
  - Goal: Avoid **pixelation**
    - Images which have a low resolution-to-size ratio and therefore enable the human eye to see the individual pixels in the image

- To compress or not to compress…
  - **Image Compression**
    - Reducing the amount of memory that an image occupies by various mathematical algorithms
    - Reduced size means it is faster to load and view
    - May be lossy or lossless

Image Compression

Lossy compression

- Some original data is permanently lost after compression
- Must balance amount of compression against loss of image quality
- Substantial data reduction possible without obvious loss of image quality
- 50% compression → 90% reduction in file size

Lossless compression

- Memory (file size) is reduced but…
- All original image data can be recovered when uncompressed

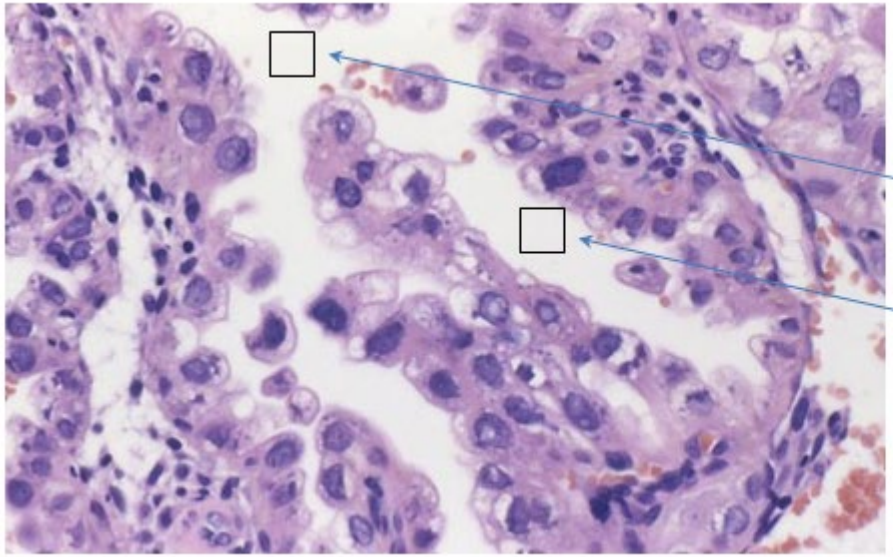
File Types and Default Compression

File Type	File Description	File Extension	Uses Lossy Algorithms	Uses Lossless Algorithms	Uses no compression
Image	Bitmap image	BMP		X	
	Graphics Interchange Format	GIF		X	
	Joint Photographic Experts Group	JPG, JPEG	X		
	Joint Photographic Experts Group	JPEG 2000	X	X	
	Portable Document Format	PDF	*	X	
	Portable Network Graphics	PNG		X	
	Raw image signal	RAW			X
	Tagged Image File Format	TIF, TIFF	*	X	
Video	Moving Picture Experts Group	MPEG (MP4)	X		
Audio	Free Lossless Audio Codec	FLAC		X	
	Moving Picture Experts Group Audio	MPEG (MP3)	X		
	Waveform Audio File Format	WAV			X

* This file type can use lossy algorithms, but lossless algorithms are the default.

Image Compression

- How compression works (the really over-simplified model…)



Same 3 bytes of color data over a larger area of pixels – saved as 1 pixel of data

The decision to use lossy vs. lossless may depend on the media type

PACS

- **Picture Archiving and Communication System (PACS)** Seeram 2019
- Computers and servers that are dedicated to the storage, retrieval, distribution and presentation of digital images
- Most radiology departments have a PACS
  - 2000 → 8.5% of radiology depts have PACS
  - 2008 → 76%
- Pathology departments much less likely to have a PACS despite wide image use

- Tieche et al 2010

Vendor-Neutral Archive (VNA)

- Theoretical definition
  - Single image repository that is able to house/federate all desired images regardless of their source, data type or vendor system that created them
- Purpose
  - One-stop-shop for all image archiving and dissemination
    - Radiology, Cardiology, Endoscopy, Pathology, etc.
  - Provides viewer support (directly or via 3rd party such as EHR)
- In reality…
  - No VNA works with all images, but some can get close
- Shoemaker 2011

Telepathology vs. Teleradiology

Telepathology

- **Diagnosis** which results in a **report** is rendered from a digital microscopic image ONLY
  - No examination of original glass slides prior to report
- Differs from **teleradiology** because…
  - images cannot be acquired directly from the specimen/patient
  - Telepathologist may be on-site
  - Telepathology has CLIA implications

Teleradiology

- Most radiology images acquired digitally
- Teleradiology means that the images are transmitted off-site electronically for review and interpretation
- Most teleradiology within US governed by state law

Teleradiology | American College of Radiology | American College of Radiology (acr.org)

Leung ST, Kaplan KJ. Medicolegal aspects of telepathology. *Hum Pathol.* 2009;40(8):1137-1142. [Abstract]

Whole Slide Imaging (WSI) Systems

- Specialized image acquisition devices
- Very high resolution capability
  - Single uncompressed image of entire slide at 40x = around 50 GB
- Like other lab tests, use of WSI devices can occur through
  - CLIA validation pathway (Pantanowitz et al 2013)
  - FDA pre-market approval of WSI device
- FDA
  - Whole slide imaging devices downgraded from Class III to Class II
  - Require premarket approval when intended to be used for primary diagnosis
  - Final guidance for PMA submissions issued in April 2016
  - First FDA approved Whole Slide Image device in April 2017
  - FDA Final Guidance 2016
  - Press Release

Additional Telepathology Definitions

- Whole slide images are typically used for telepathology diagnosis
  - Compared to radiology images, these images are huge (250 MB to 1 GB per slide is common)
- **Static Telepathology**
  - Entire image is captured then transmitted
  - Transmission can be *in toto* or in pieces (tiling)
- **Dynamic Telepathology**
  - Live video feed
  - With or without remote control of scanner
- **Hybrid telepathology** systems do both

DICOM

- **Digital Imaging and Communications in Medicine** (http://dicom.nema.org/)
  - International standard for medical images and related information (ISO 12052)
  - First developed by Radiology and Cardiology
  - DICOM compliance helps ensure that radiology and other images produced at one facility can be read at a different facility (interoperable imaging)
  - Working Group 26 is Pathology
  - Supplements 122, 145, 222 are for Whole Slide Imaging
- DICOM helps structure **metadata**
  - Information contained within the image (diagnosis, features) is UNSTRUCTURED
  - Image analysis: Science of extracting meaningful features from images
    - Big Data science

http://dicom.nema.org/dicom/Conf-2005/Day-1_Seminar/B11_Simon_BasicDICOMConcepts_v1.pdf

Issues Integrating into Decision-making

- Issues with integrating **imaging** into business and clinical decision-making
- DICOM-compliant images have fewer issues because of structured metadata
  - Image itself however is still unstructured
  - May need manual coding of features for better data retrieval across populations
- Non-DICOM-compliant images
  - A lot of pathology images fall into this category as do patient photos
  - Images may lack adequate metadata (e.g., may only use a file name for identification)
    - Some may be located in a file server where deletions can occur in error
- Putting images in a robust image management system (e.g., PACS) helps assign attributes and totals to images to assist with decision making, data retrieval and research
  - Can also be important for medicolegal cases (e.g., images before, during and after events)

K108. Precision Medicine

(customized treatment plans based on patient-specific data)

Precision (vs. Personalized) Medicine

- **Precision Medicine**
  - Tailoring of medical treatment to individual (primarily genetic) characteristics of the patient
  - To classify subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment
  - Concentrate preventative or therapeutic options on those who will benefit
  - Spares expense and side effects for those who will not benefit
  - **Relies on data, analytics and information**
- **Personalized Medicine**
  - Approach to patients that considers genetic make-up but with attention to the patient's preferences, beliefs, attitudes, knowledge and social context
  - **Relies on personal interaction**
- Precision Medicine: From Science to Value (nih.gov)

Omics Definitions

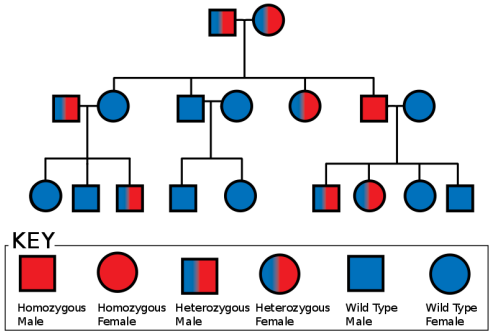
Term	Definition	References
Genomics	Applying techniques of molecular biology to genetic mapping and sequencing of targeted areas or complete genomes of selected organisms, organizing results in database and with applications of the data	1
Transcriptomics	Analysis of the transcriptome by generating genome-wide mRNA profiles, allowing description of gene expression	2
Epigenomics	Study of inherited changes in gene expression caused by non-sequence related portions of genome (e.g., methylation)	3
Proteomics	Analysis of expression, localization, function and interaction of proteins expressed by genetic material of an organism (related: lipidomics, glycomics)	4
Phenomics	Systematic study of phenotypes on a genome-wide scale	5
Metabolomics	Identifying and determining the specific metabolites in biological samples under normal vs. altered conditions promoted by disease, drug treatment, dietary intervention, or environmental modulation	6
Metagenomics	Variable definitions • Study of genetic material recovered directly from environmental samples • a.k.a. environmental genomics, ecogenomics or community genomics • **In medicine, study of non-human genetic material recovered from patient samples for diagnosis and therapy**	7, 8
Pharmacogenomics	Study of using DNA and amino acid sequence data to inform drug development and testing as well as **drug therapy in an individual patient** • Genetic variants that impact how a medication is metabolized (toxicity vs. no intended effect vs. expected non-toxic effect) • Unique in that these variants don't express themselves until the patient is challenged with an outside stimulus (medication, anesthetic, etc.)	9

Information Systems and Omics - Opportunities

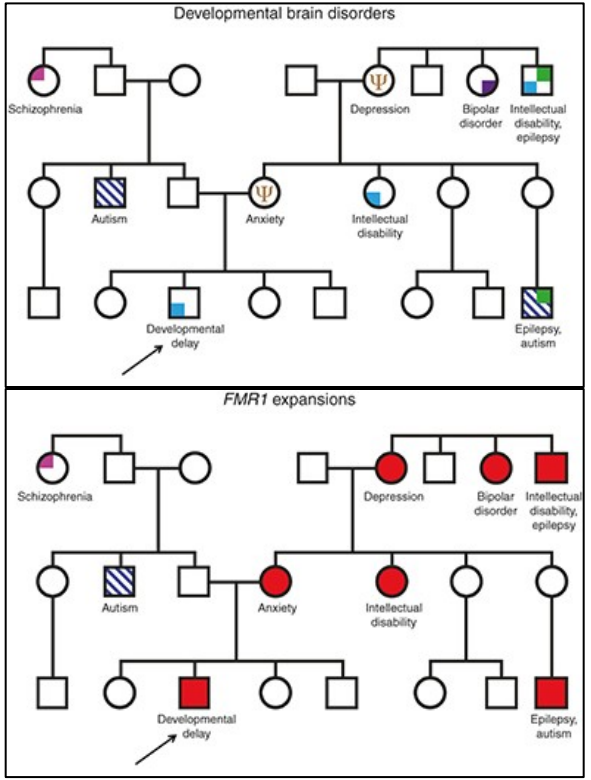
- Omics data can be used to
  - Predict current risk
  - Predict future risk
  - Assist with diagnosis, prognosis and therapy
  - Enable robust specimen identification at the genome level
  - Correlate biomedical images with other omics data (e.g., tumor sequencing results)
- Discrete data enables better rule-writing
  - Drug-genome alerts
  - Transfusion-genome alerts
  - Suggested therapies based on genetic profile, cancer proteome
  - Suggested testing based on phenotypic profile and/or family history

Information Systems and Omics - Challenges

- Some systems support **pedigree** entries
  - *Not everyone knows how to read them*
- Some systems can store genetic variant information, but display and interpretation still a work in progress

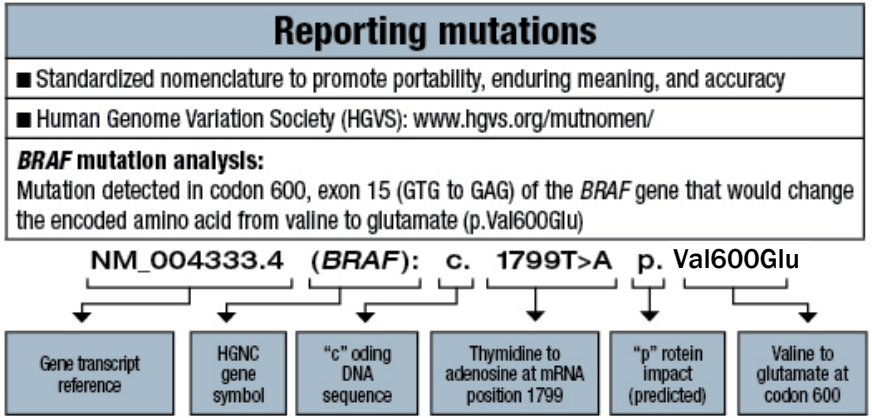


https://commons.wikimedia.org/wiki/File:Autosomal_Recessive_Pedigree_Chart.svg



https://www.nature.com/articles/gim201592/figures/1

Information Systems and Omics - Challenges

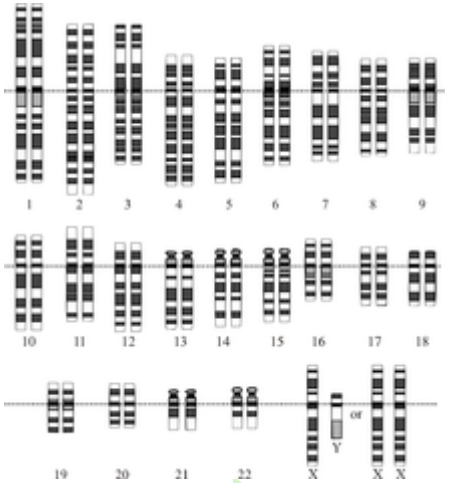


- **Large amount of data**
  - Each variant has many data points
  - There are many variants per test
    - Hundreds of variants in targeted panels
    - Millions of variants in whole genomes

- **No international consensus on how to represent data** in an information system
  - International standards for nomenclature can be complex (HGVS, ISCN) or non-existent
  - Common vs. formal terms (*BRAF* V600E)
- **Omics data must not be used in a vacuum**: Ackerman et al 2016
  - Report interpretation and clinical context are critical
  - Variants may have variable penetrance, effects from other variants, environment, etc.

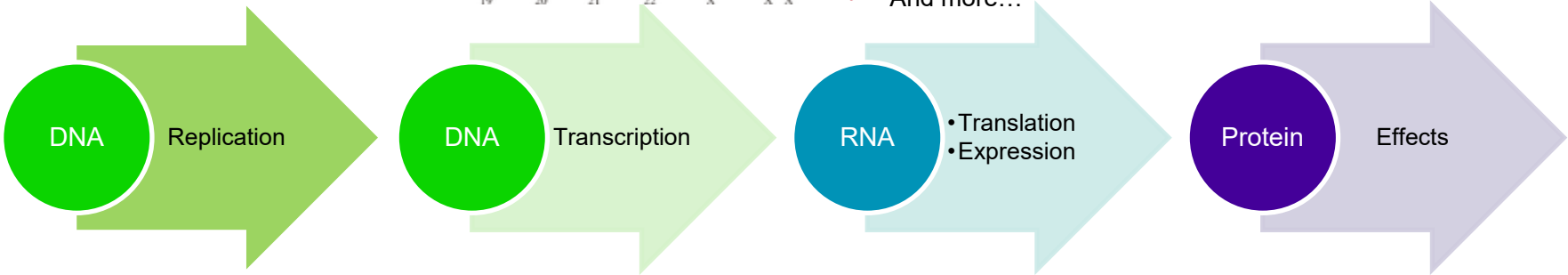
Human Genome

- 3 billion base-pairs (**genome**)
- 22 diploid autosomes + 1 set sex chromosomes (XX or XY)
- ~ 20,000 protein coding genes = **exome**



Other genetic effects…

- Variants on the cis (same) or trans (different) chromosome
- Methylation (transcriptional silencing, genetic imprinting)
- Alternative splicing, promoter effects, enhancer effects
- Euchromatin vs. heterochromatin structure
- Variants influencing the function of other variants in the same gene (e.g., poly-T in intron 8 of *CFTR*) or different genes (TCF7L2 in CF-related diabetes)
- Translocations (fusions), inversions, copy number variants, etc.
- And more…



Next-Generation Sequencing

- NGS
- Better term: **massively parallel sequencing**
- DNA is sequenced in short overlapping fragments then aligned to the reference and variants detected

- Integrated Genomics Viewer
  https://www.broadinstitute.org/software/igv/download

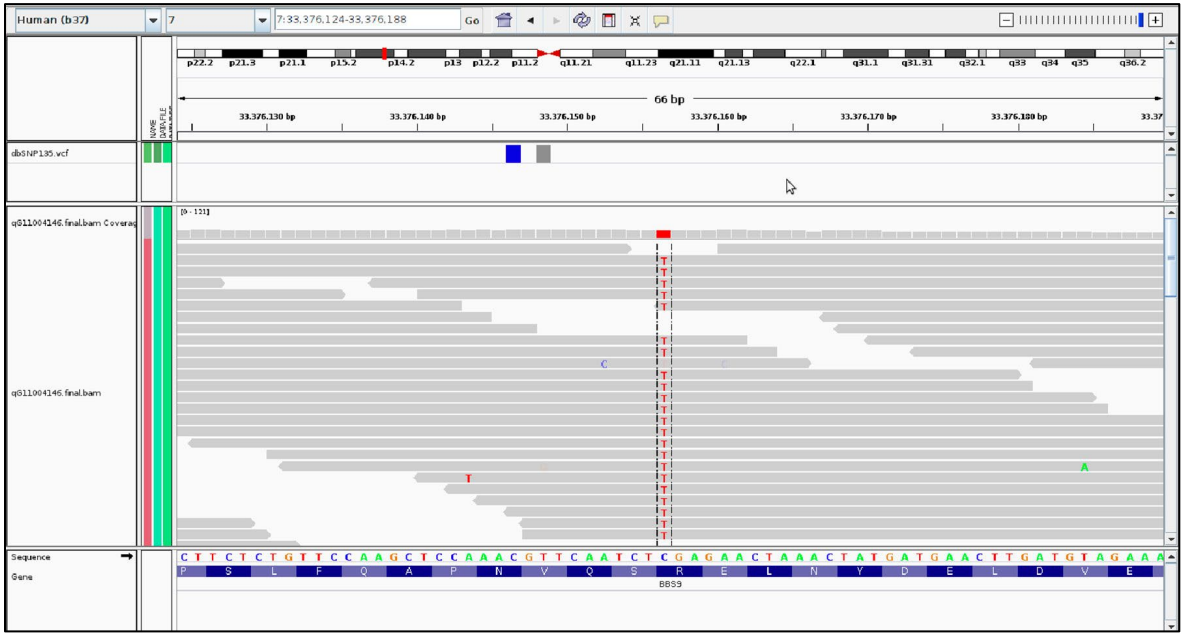
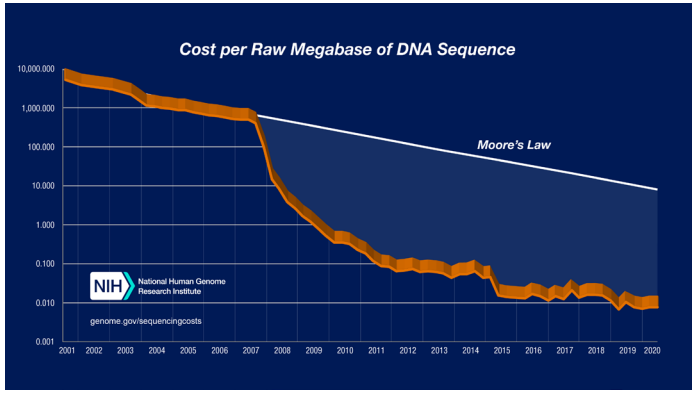
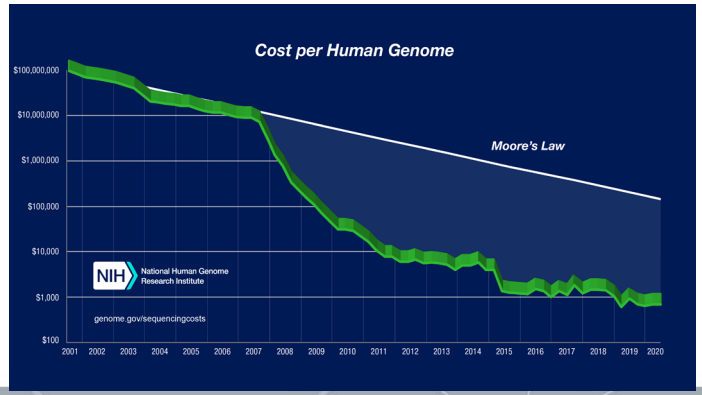


Image above from: http://www.analesdepediatria.org/es/sindrome-bardet-biedl-aplicacion-diagnostica-secuenciacion/articulo/S1695403313003822/

Clinical Informatics for Genomics

- **Next-generation sequencing**
  - High-throughput genetic analysis
    - Targeted panel → exome → genome
  - Raw signal is translated to interpretable results using computational algorithms (**bioinformatics pipelines**)
    - no electropheresis gel or electropherogram to look at
  - Cost per base sequenced has surpassed Moore's Law (observation that the number of transistors in a dense integrated circuit (IC) doubles about every two years for *the same cost*)





https://www.genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data

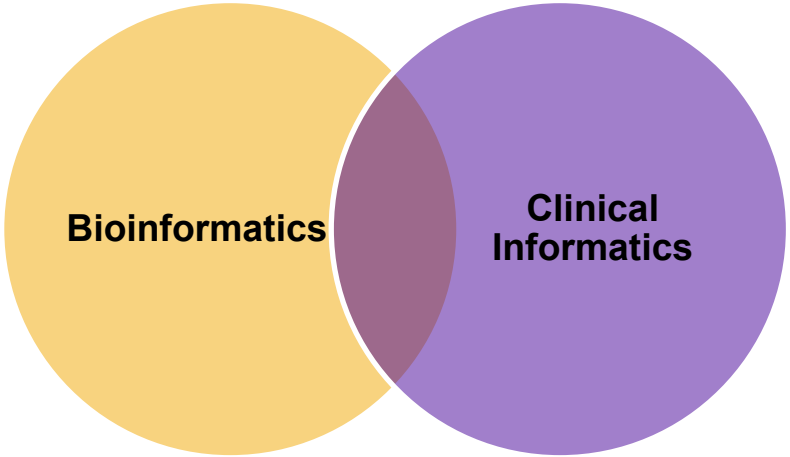
Bioinformatics and Big Data

(Specialized and emerging data sources)

K096. Types and uses
K095. Standards related to storage and retrieval
K097. Issues related to integrating into business and clinical decision making

Definitions

- **Next generation sequencing uses BOTH bioinformatics and clinical informatics**



- **Bioinformatics**
  - Many definitions → deriving knowledge from computer analysis of biological data (Institut Pasteur)
- **Clinical Informatics**
  - The application of informatics and information technology to deliver healthcare services

The American Medical Informatics Association (AMIA) – www.amia.org

May 2017

SPECIAL ARTICLE

Guidelines for Validation of Next-Generation Sequencing–Based Oncology Panels

A Joint Consensus Recommendation of the Association for Molecular Pathology and College of American Pathologists

Lawrence J. Jennings,*† Maria E. Arcila,*† Christopher Corless,*‡ Suzanne Kamel-Reid,*¶‖ Ira M. Lubin,*·** John Pfeifer,*†† Robyn L. Temple-Smolkin,‡‡ Karl V. Voelkerding,*§§¶¶ and Marina N. Nikiforova*‖‖

Sample

Pre-Sequencing

Sequencing

Bioinformatics Analysis

Variant Interpretation

Reporting

Jan 2017

SPECIAL ARTICLE

Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer

A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists

Marilyn M. Li,*† Michael Datto,*‡ Eric J. Duncavage,*§ Shashikant Kulkarni,*¶ Neal I. Lindeman,*‖ Somak Roy,*·** Apostolia M. Tsimberidou,*†† Cindy L. Vnencak-Jones,*‡‡ Daynna J. Wolff,*§§ Anas Younes,*¶¶ and Marina N. Nikiforova*·**

Jan 2018

The Journal of Molecular Diagnostics, Vol. 20, No. 1, January 2018

ELSEVIER

the Journal of Molecular Diagnostics

jmd.amjpathol.org

SPECIAL ARTICLE

Standards and Guidelines for Validating Next-Generation Sequencing Bioinformatics Pipelines

A Joint Recommendation of the Association for Molecular Pathology and the College of American Pathologists

Somak Roy,*† Christopher Coldren,*† Arivarasan Karunamurthy,*† Nefize S. Kip,*§¶ Eric W. Klee,*‖ Stephen E. Lincoln,*·** Annette Leon,*†† Mrudula Pullambhatla,‡‡ Robyn L. Temple-Smolkin,‡‡ Karl V. Voelkerding,*§§ Chen Wang,*‖ and Alexis B. Carter*¶¶

May 2015

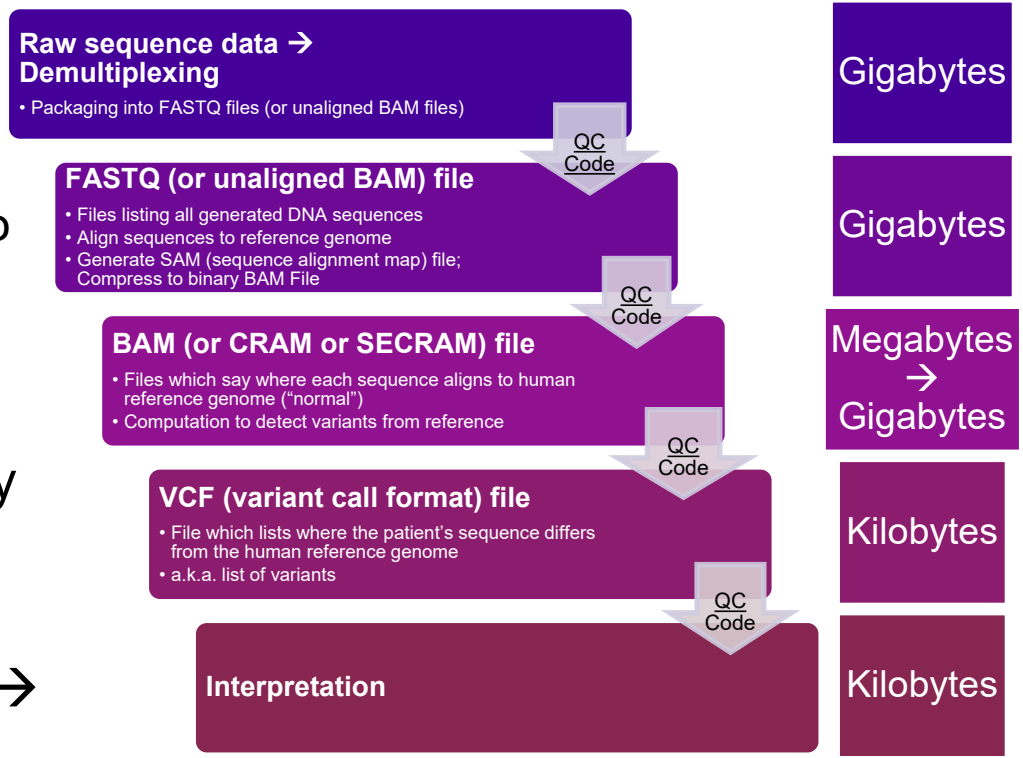
© American College of Medical Genetics and Genomics ACMG STANDARDS AND GUIDELINES | Genetics inMedicine

Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology

Sue Richards, PhD[1], Nazneen Aziz, PhD[2,16], Sherri Bale, PhD[3], David Bick, MD[4], Soma Das, PhD[5], Julie Gastier-Foster, PhD[6,7,8], Wayne W. Grody, MD, PhD[9,10,11], Madhuri Hegde, PhD[12], Elaine Lyon, PhD[13], Elaine Spector, PhD[14], Karl Voelkerding, MD[13] and Heidi L. Rehm, PhD[15]; on behalf of the ACMG Laboratory Quality Assurance Committee

Bioinformatics

- Bioinformatics pipeline
  - Multiple sets of one or more computational algorithms performed in series/parallel to analyze biological data
  - **Not** limited to NGS data
- Critical to collect and check quality metrics along the way
- **Require intensive computational firepower**
- Genomics pipeline process →



NGS Bioinformatics Standards

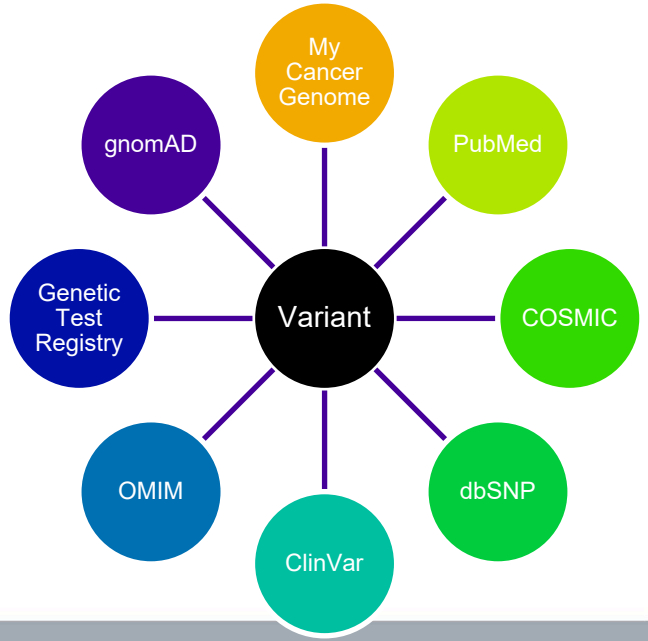
Standard	Other versions	Description	Reference
FASTQ	uBAM (unaligned BAM); FASTA	• Simple text file format for **nucleic acid sequence** • FASTQ includes quality scores for each base; FASTA does not	Cook 2010 FASTQ Format Specification
SAM	BAM, CRAM, SECRAM	• Sequence alignment map (SAM) • BAM is a binary compressed SAM • Describes where the human sequence **aligns to (is located on) the human reference genome**	SAM / BAM Format Specification
VCF	gVCF, GVF	• Variant call format (VCF) file • List of changes (**variants**) present in the sample which are **not** in the human reference genome	VCF Format Specification

NGS Bioinformatics Standards - more

Standard	Examples	Description	Reference
GRC	GRCh37 (hg19) GRCh38 (hg38)	Genome Reference Consortium • Defines “normal” human reference • GRCh37 (hg19) - 2009 • GRCh38 (hg38) - 2013	https://www.ncbi.nlm.nih.gov/grc
HGVS	*BRAF* c.1799T>A *BRAF* p.Val600Glu	• Human Genome Variation Society • Provides **nomenclature for variants**	https://www.hgvs.org/
ISCN	46,XX,t(8;21) 1p31.1	• International System for Human **Cytogenomic Nomenclature**	https://iscn.karger.com/
HGNC	*ATRX* *CFTR*	• HUGO Gene Nomenclature Committee • International standard for gene symbols (gene abbreviations)	https://www.genenames.org/

Annotation and Interpretation of NGS Data

- Only about 20% of variants have known significance
- Other 80% have to be researched



- Online genomic references to help determine significance of variants are
  - Are constantly being updated by multiple (often anonymous) sources
  - Data may be unstructured
  - Data **often** uncurated

This is **Big Data**

Big Data

- Characterized by **four** Vs:

Volume	Large amounts of data

Berman JJ. *Principles of Big Data: Preparing, Sharing, and Analyzing Complex Information.* Amsterdam: Morgan Kaufmann; 2013.

NIST Special Publication 1500-1: NIST Big Data Interoperability Framework: Volume 1, Definitions, 2015.

Big Data

- Characterized by **four** Vs:

Volume	Large amounts of data
Variety	Many different types of data
Velocity	Constantly accumulating new data
Variability	Change in data over time

Berman JJ. *Principles of Big Data: Preparing, Sharing, and Analyzing Complex Information.* Amsterdam: Morgan Kaufmann; 2013.

NIST Special Publication 1500-1: NIST Big Data Interoperability Framework: Volume 1, Definitions, 2015.

Big Data

Not all "big" data is big data

- NGS test results
  - Pipeline source data have volume but usually **lack** velocity, variety and variability, however…
  - Interpreters use big data resources to assist with interpretation
    - Constantly being updated by multiple (often anonymous) sources
    - Data may be unstructured
    - Data **often** uncurated
    - Examples: PubMed, COSMIC, ClinVar, ClinGen, OMIM, dbSNP, Ensembl, GnomAD, etc.

Big Data

- Other (less commonly thought of) examples of big data:
  - **Laboratory Information System (LIS)**
  - **Electronic Health Record (EHR)**
  - Why?

Volume	Large amounts of data
Variety	Many different types of data
Velocity	Constantly accumulating new data
Variability	Change in data over time

Big vs. Small Data

	Small Data Resource	Big Data Resource
Design	Answer **specific** questions or serve specific purpose	Provide answers to **protean** questions on variable topics, current and future, and to serve many different and flexible purposes
Location	Within **one** institution, server, computer or file	In **many** places
Structure	**Highly structured**; limited data types	**Unstructured data of many types** (e.g., free text, sound, images, video)
Preparation	**Few** prepare the data (usually the end-user)	**Many** prepare the data (usually **not** the end-user)
Longevity	**Short** (discarded when project is completed)	**Long** (data is kept in perpetuity)

Berman JJ. *Principles of Big Data: Preparing, Sharing, and Analyzing Complex Information.* Amsterdam: Morgan Kaufmann; 2013.

Big vs. Small Data (cont.)

	Small Data Resource	Big Data Resource
Measurements	**One** set of standard units of measure for data; easy to verify data quality	**Many** different sets of units of measure; difficult to verify quality of data
Reproducibility	**Easy** to repeat a project with new data to verify quality of results	**Hard (to impossible)** to repeat a project with new data to verify quality of results
Stakes	**Small** costs; easy to recover from project failure	**Expensive**; failure can lead to bankruptcy
Introspection	**Highly organized** data (rows and columns)	**Loosely or unorganized** data (may be inscrutable)
Analysis	Analysis can occur **all together** and all at the **same time**	Analysis occurs in **incremental steps** (unless performed on grid/parallel/super computing resources)

Berman JJ. *Principles of Big Data: Preparing, Sharing, and Analyzing Complex Information.* Amsterdam: Morgan Kaufmann; 2013.

Small Data

Structured data

Tools

Knowledge

ACTIONABLE

BIG Data

Unstructured BIG data

Tools

Structured data

Knowledge

Computational Pathology

- General Definition
  - Using computation for the interpretation of multiparameter data to improve health care
- More full definition
  - An approach to diagnosis
  - Incorporates multiple sources of raw data
  - Extracts biologically and clinically relevant information from these data to generate diagnostic inferences and predictions
  - Presents clinically actionable knowledge to end-users
- Louis et al 2014, Louis et al 2016

Issues Integrating into Decision-making

- Issues integrating **bioinformatics** data into business and clinical decision-making
  - Most bioinformatic data is embedded in free-text reports
  - Discrete data may be dissociated from context (interpretation) and from other related results
  - Subject matter nomenclature and concepts not broadly known or understood in medicine
  - Better access to this data could result in better understanding of patient population, health needs and risks
- Issues integrating **big data** into business and clinical decision-making
  - Even though health information systems are big data by default…
  - Information systems are not equipped with appropriate data science tools for analysis
  - Analysis of big data a rapidly growing field (Data Science)
  - Better access to this data could result in better prediction of future trends for staffing, resource needs, quality of care issues, disparities so that outcomes can be improved

Genomic Privacy Law

Privacy and Genetic Information

Federal Law	Effective Date
HIPAA Final Security Rule	Apr 21, 2003
Health Information Technology for Economic and Clinical Health Act (HITECH)	Feb 17, 2009
Genetic Information Non-discrimination Act (GINA)	May 21, 2009
HIPAA Omnibus Rule	Sep 23, 2013

GINA

- Genetic Information Nondiscrimination Act of 2008 (GINA)
- Generally prohibits group health plans and health insurance issuers from
  - discriminating based on genetic information
  - requesting or requiring genetic testing
  - collecting of genetic information
- Required Dept Health and Human Services to re-write HIPAA to include genetic information as PHI

- Defined "genetic information"
  - **Genetic services**: genetic tests, genetic counseling, or genetic education
  - **Genetic tests**: analysis of human DNA, RNA, chromosomes, proteins, or metabolites, if the analysis detects genotypes, mutations, or chromosomal changes
    - Does **not** include an analysis of proteins or metabolites directly related to a manifested disease, disorder, or pathological condition
- Genetic information must still meet the definition of being individually identifiable, i.e., classified as "any other uniquely identifying number, characteristic or code"

HIPAA Omnibus Rule

- In effect September 23, 2013
- Requires “Genetic Information” (as defined by GINA) to be treated as PHI under HIPAA
  - Genetic information must first be individually identifiable
  - Huge implications for research on genetic material
  - Caution is advised when deidentifying genetic information
    - Simply removing the name, DOB, etc. may not be enough
    - **Genetic reidentification** can occur with limited DNA
    - Hansson et al 2016
- Forensic DNA matching
  - **CODIS system:** requires 20 small loci
  - About 0.0000004% of genome
- Other references
  - NIH Genomic Data Sharing Policy

Pathology Informatics – Bar Codes and RFID

Bar Codes

- Code used to represent alphanumeric characters, like an accession number or encounter number
- Can be “read” by a barcode reader (scanner) and decoded into the original data
- Advantages
  - Reduces manual typing errors
  - Improves speed of data entry
- Strong recommendations supported by guidelines: ensure that the human-readable version of the encoded data is *always* printed next to the barcode

- Linear Bar Codes

Code 39	
Code 128A	
Code 128B	
Code 128C	

Linear (1D) Bar Codes

- Disadvantages
  - Very space intensive for the amount of data encoded
  - Damage and misprints can result in **substitution errors** (data decoded is not what was intended for printing) at an alarmingly high rate (1 in 88,000 barcodes on armbands)
  - Without intentional data structures and parsing software, there is no way to know what information the barcode contains
    - Is it an MRN, Financial number or Master Patient Index?

Snyder ML, Carter A, Jenkins K, Fantz CR. Patient misidentifications caused by errors in standard bar code technology. *Clin Chem.* 2010;56(10):1554-1560.

2D Bar Codes

- Encoded data represented in two dimensions
- Two major types
  - Stacked 1D
    - e.g., PDF417
  - Matrix
    - QR code
    - DataMatrix
    - Aztec

- "The AMIA Clinical Informatics Board Review Course"

PDF417 

DataMatrix 

QR code 

2D Bar Codes

- Encoded data represented in two dimensions
- Two major types
  - Stacked 1D
    - e.g., PDF417
  - Matrix
    - QR code
    - DataMatrix
    - Aztec

- "The AMIA Clinical Informatics Board Review Course"

PDF417 

DataMatrix 

QR code 

The AMIA Clinical Informatics Board Review Course

TEC-IT.COM

Bar Codes

Type of Error	Estimated Unrecognized Character Error Rate
Manual Entry	1 in 300
1D barcode	1 in 88,000* to 37 million
2D/matrix barcode	1 in sextillions (10^{21})

Snyder ML, Carter A, Jenkins K, Fantz CR. Patient misidentifications caused by errors in standard bar code technology. *Clin Chem.* 2010;56(10):1554-1560.

Linear (1D) vs. 2D Bar Codes

	1D Barcode	2D Barcode
Data density – amount of data it can contain	Usually only 1 identifier	Multiple identifiers
Can encode redundancy of data	No	Yes
Damage/Printer Error Correction and Detection Algorithms	No	Yes
Number of data integrity checks	0 (most 1D barcodes) OR 1 (Code 128 only)	>1
Ease of installation	Easy	Harder

Bar Code Standards

Asset	Current Barcode Standard	Required barcode symbology	Comments/Reference
Clinical Laboratory Labels	CLSI AUTO02-A2	Code 128 A Code 128 B Code 128 C	• Code 128 has **required** check digit • All other linear barcodes have NO check digit • Barcode **content** not specified • Code 39 (*optional* check digit) *deprecated years ago...* • CLSI AUTO12-A regards human-readable component only • Standard for 2D barcodes (AUTO14) is in progress
Blood products (medical products of human origin)	ISBT 128	Code 128 or 2D	• Specifications for symbology, **encoded content, printers, and scanning software** (increases safety) • accepted by FDA for medical products of human origin (FDA Blood Labeling) • AABB requires all blood labeled on or after May 1, 2008 to be labeled with ISBT128 (Codabar no longer allowed)

Bar Code Standards

Asset	Current Barcode Standard	Required barcode symbology	Comments/Reference
Anatomic Pathology Specimens	No standard available for barcode	None	• CAP Uniform Labeling of Blocks and Slides standard applies to human-readable component only • Standard for 2D barcodes (AUTO14) is in progress
Medications	GS1-128 (formerly UCC/EAN-128) or HIBCC	Code 128	• Barcode symbology must be linear • Must contain National Drug Code at a minimum • Syntax should be compliant with HIBCC or UCC/EAN
Patient armbands	None	None	• **Critical barcode** • **No standards**

Drug Bar Code Requirements

- Regulated and mandated by the FDA
- Only certain entities must place barcodes (hospitals are exempted)
- Drug bar codes must contain, at a minimum, the appropriate National Drug Code (NDC) number in a **linear** bar code that meets European Article Number/Uniform Code Council (EAN.UCC) or Health Industry Business Communications Council (HIBCC) standards.
- Additionally, the bar code must:
  - (i) Be surrounded by sufficient blank space (**quiet zone**) so that the bar code can be scanned correctly; and
  - (ii) Remain intact under normal conditions of use.
- **References**
  - 21 CFR part 201 (https://www.gpo.gov/fdsys/pkg/FR-2004-02-26/pdf/04-4249.pdf)
  - Additional guidance here: https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM267392.pdf
  - HIBCC standard

RFID

- Radio Frequency Identification
  - Uses radio waves to broadcast data from an electronic tag mounted on an object to a scanner/reader
  - Some can be read from several meters away and beyond the line of sight of the reader
  - Bulk reading is possible
  - U.S. Passports and many other items now have RFIDs
- Two types (and a hybrid)
  - **Passive RFID**
    - does not use a battery
  - **Active RFID**
    - has an on-board battery
    - always broadcasts or beacons its signal
  - **Battery-assisted passive (BAP) RFID**
    - small battery on board
    - activated when in the presence of a RFID reader

Bar Codes vs. RFID

	Barcodes	RFID tags
Item must be in scanner's line of sight	Yes	Not always
Bulk scanning possible	No	Yes
Prone to damage	Yes	No
Can be used to locate a missing specimen?	No	Yes
Discarded items can be scanned in error?	No	Yes
Easy to make HIPAA compliant	Yes	No
Cost	Cheap	Expensive
Interference problem with multiple items next to each other?	No	Yes (items closer than 1 cm will interfere with the signal)

Question

Two-dimensional (2D) barcodes are superior to linear (one-dimensional or 1D) barcodes because:

A. Barcode readers know what data is encoded in a 2D barcode automatically but they don't with 1D barcodes.

B. 2D barcodes never require special software in the laboratory information system to read them (unlike 1D barcodes).

C. 2D barcodes can contain multiple data elements where 1D barcodes can usually only just contain one data element.

D. 2D barcodes are easier to setup and install than 1D barcodes.

Answer

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C. 2D barcodes can contain multiple data elements where 1D barcodes can usually only just contain one data element.

D. 2D barcodes are easier to setup and install than 1D barcodes.

Because of their significantly greater data density, two-dimensional barcodes may contain multiple data elements where one-dimensional barcodes, in most cases in healthcare, only contain one data element such as an accession number for a laboratory specimen or medical record number on a patient's armband. Similar to one-dimensional barcodes, two-dimensional barcodes by themselves do not indicate what type of data is encoded. Because two-dimensional barcodes have significantly higher data density, descriptors can be included in the encoded content, but these descriptors still require software to interpret them. Both one-dimensional and two-dimensional barcodes may require special software in order to read them, particularly if they encode more than one data element. Outside of ISBT 128 barcodes, linear barcodes rarely contain more than one data element, whereas it is more common to find multiple data elements encoded in two-dimensional barcodes. Therefore, the need for additional software to interpret multi-element data can make set up of two-dimensional barcodes more difficult than non-ISBT 128 linear barcodes.

Key Readings

- Pantanowitz L, Balis UGJ, Tuthill JM, eds. *Pathology Informatics: Theory & Practice.* 1st ed. Chicago, IL: ASCP Press; 2012.
- Sinard JH. Pathology LIS: Relationship to Institutional Systems. *Practical Pathology Informatics: Demystifying Informatics for the Practicing Anatomic Pathologist.* New York: Springer; 2006:173-206.
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- Williams S, Henricks WH, Becich MJ, Toscano M, Carter AB. Telepathology for patient care: what am I getting myself into? *Adv Anat Pathol.* 2010;17(2):130-149. [Abstract]
- Snyder ML, Carter A, Jenkins K, Fantz CR. Patient misidentifications caused by errors in standard bar code technology. *Clin Chem.* 2010;56(10):1554-1560. [Abstract]
- Clinical Laboratory Improvement Amendments (CLIA) of 1988, Laboratory Requirements, 42 CFR § 493, http://www.gpo.gov/fdsys/pkg/CFR-2012-title42-vol5/pdf/CFR-2012-title42-vol5-part493.pdf
- Guidance for Industry: Blood Establishment Computer System Validation in a User's Facility. Food and Drug Administration (FDA). April 2013. https://www.fda.gov/media/72533/download Last accessed: August 20, 2020.

Key Readings

- Liao F. The Data Life Cycle. AMIA Health Informatics Course. Accessed August 20, 2021.

Supplemental Material

Patient Access Rule (supplemental material)

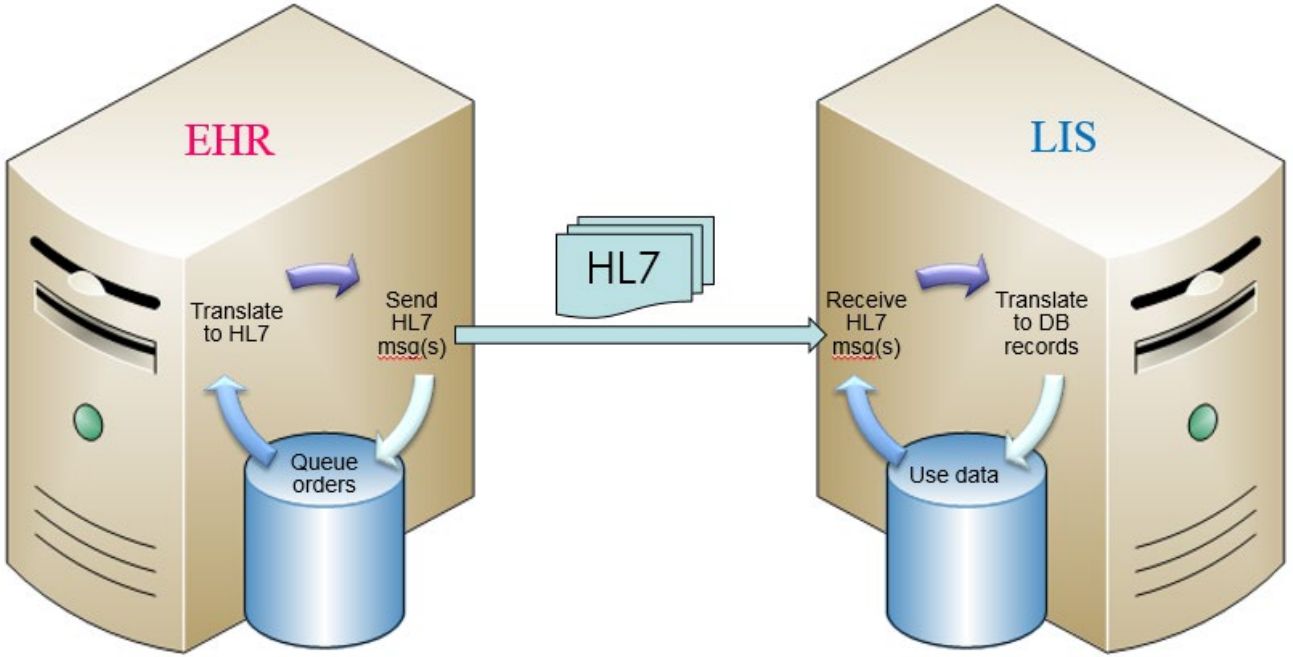
- Patients can request laboratory results from “designated record set” directly from the laboratory
- Laboratories must comply with request
  - Same rules as for other health care entities
- Labs may refer the patient to medical records to comply with the rule IF…
  - Medical records has all the requested data AND
  - Medical Records complies with HIPAA for release of information
- Laboratories do not have to interpret results for the patient
- Patient does not need ordering provider’s permission
- Reports must be compliant with CLIA requirements

Laboratory Informatics Guidelines and Standards

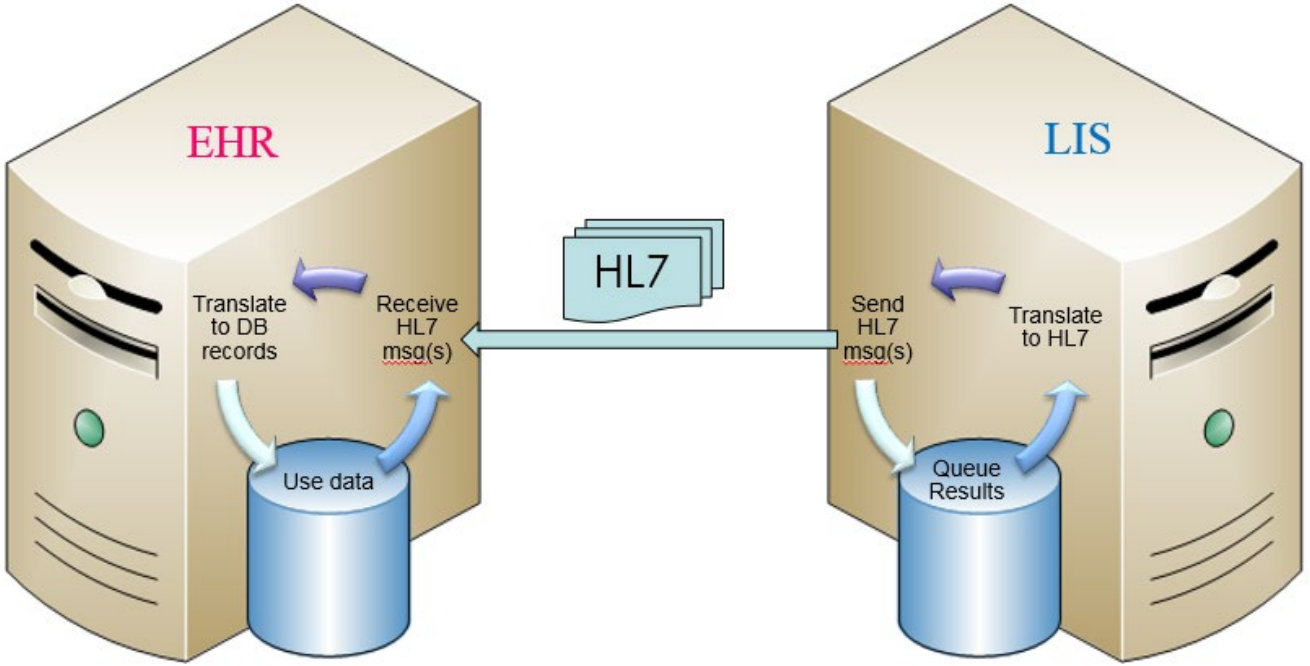
- **Clinical and Laboratory Standards Institute**
  - www.clsi.org
  - International standards development organization for laboratories
  - Consensus-driven (reflect equal representation from government, industry, and health care professions)
  - **Standards ≠ Regulations**

- AUTO01-A: Laboratory Automation: Specimen Container/Specimen Carrier; Approved Standard
- AUTO02-A2: Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition
- AUTO03-A2: Laboratory Automation: Communications With Automated Clinical Laboratory Systems, Instruments, Devices, and Information Systems; Approved Standard—Second Edition
- AUTO04-A: Laboratory Automation: Systems Operational Requirements, Characteristics, and Information Elements; Approved Standard
- AUTO05-A: Laboratory Automation: Electromechanical Interfaces; Approved Standard
- AUTO07-A: Laboratory Automation: Data Content for Specimen Identification; Approved Standard
- AUTO08-A: Managing and Validating Laboratory Information Systems; Approved Guideline
- AUTO09-A: Remote Access to Clinical Laboratory Diagnostic Devices via the Internet; Approved Standard
- AUTO10-A: Autoverification of Clinical Laboratory Test Results; Approved Guideline
- AUTO11-A2: Information Technology Security of In Vitro Diagnostic Instruments and Software Systems; Approved Standard—Second Edition
- AUTO12-A: Specimen Labels: Content and Location, Fonts, and Label Orientation; Approved Standard
- AUTO13-A2 (replaces GP19-A2): Laboratory Instruments and Data Management Systems: Design of Software User Interfaces and End-User Software Systems Validation, Operation, and Monitoring; Approved Guideline—Second Edition
- LIS01-A2: Specification for Low-Level Protocol to Transfer Messages Between Clinical Laboratory Instruments and Computer Systems; Approved Standard—Second Edition
- LIS02-A2: Specification for Transferring Information Between Clinical Laboratory Instruments and Information Systems; Approved Standard—Second Edition
- LIS03-A: Standard Guide for Selection of a Clinical Laboratory Information Management System
- LIS04-A: Standard Guide for Documentation of Clinical Laboratory Computer Systems
- LIS05-A: Standard Specification for Transferring Clinical Observations Between Independent Computer Systems
- LIS06-A: Standard Practice for Reporting Reliability of Clinical Laboratory Information Systems; Approved Standard
- LIS07-A: Standard Specification for Use of Bar Codes on Specimen Tubes in the Clinical Laboratory
- LIS08-A: Standard Guide for Functional Requirements of Clinical Laboratory Information Management Systems

HL7 Orders Interface



HL7 Results Interface



Integration of Devices

- http://medicalconnectivity.com/2017/09/05/update-integrationinterfacing-of-medical-devices-to-an-electronic-health-record/
- https://hitinfrastructure.com/news/lessons-learned-from-ehr-integration-of-medical-devices
- https://ehrintelligence.com/news/integrating-medical-devices-into-the-emr-data-repository

Determine clinical utility

- For new as well as existing devices
- Do a clinical walkthrough where the use of the device and in what context is clear
- Ensure all user stakeholder groups are represented
- Devices and their integration are expensive, so you want to get this right the first time

Examine the device

- Determine current or needed firmware version of each device
- Need to purchase or already purchased?
- Does it perform the desired functions? - match to clinical walkthrough
- Type of connection
  - Wired
    - Analog (RS232)
    - Ethernet (TCP/IP)
  - Wireless
  - Bluetooth
- Determine how many current devices will need to be replaced and with what in order to integrate
  - May cost more up front, but will often cost less in the long run

Integration of Devices

- http://medicalconnectivity.com/2017/09/05/update-integrationinterfacing-of-medical-devices-to-an-electronic-health-record/
- https://hitinfrastructure.com/news/lessons-learned-from-ehr-integration-of-medical-devices
- https://ehrintelligence.com/news/integrating-medical-devices-into-the-emr-data-repository

Examine information system

- Can the information system interface to the device (or middleware) in the manner required?

Middleware required?

- Usually needed when
  - Data needs to be transformed prior to being sent to system
    - ASTM → TCP/IP
    - Calculations and conversions
  - Additional functions need to be performed on data prior to sending to system
    - Manual review of abnormal or unusual values
    - Aggregating data from different instruments for comparison and interpretation

Integration of Devices

- http://medicalconnectivity.com/2017/09/05/update-integrationinterfacing-of-medical-devices-to-an-electronic-health-record/
- https://hitinfrastructure.com/news/lessons-learned-from-ehr-integration-of-medical-devices
- https://ehrintelligence.com/news/integrating-medical-devices-into-the-emr-data-repository

If middleware is required…

- Can you get a test system (server) for middleware?
  - Necessary for testing and upgrades
  - Test middleware is routed to your test EHR
  - Devices are connected to the test middleware (and test EHR) for testing before implementation and before taking any upgrade into production
- Does it have a device directory? Enables identifying the instrument that produced the data and its location

Alerts and alarms

- Determine what, if any alerts, are available in the information system
  - Current issue
  - Warn of future predicted issue (e.g., hypoglycemia in a diabetic)
- Determine what alerts are needed in the device and how they will function
  - Signal-to-noise ratio is critical, especially if alarms are intended for timely intervention
  - Beware of **alarm fatigue**, especially in highly wired areas with many devices (ICUs, laboratories) - middleware may help
- No data
- Data with errors or unexpected values

Integration of Devices

- http://medicalconnectivity.com/2017/09/05/update-integrationinterfacing-of-medical-devices-to-an-electronic-health-record/
- https://hitinfrastructure.com/news/lessons-learned-from-ehr-integration-of-medical-devices
- https://ehrintelligence.com/news/integrating-medical-devices-into-the-emr-data-repository

Information system → device

- Types - need a specific list…be judicious and only transfer what you need; the more data you transfer, the more risk if the device is lost or stolen
  - Consider units of measure and whether conversion is required (degF vs. degC, units of time, units, etc.)
  - Does the device follow common standards (e.g., ISMP)
  - Patient information
  - Orders or requests
  - Other
- Manner in which the data is expected to be transferred
  - Bar code driven - specify triggers
  - Flat-file (push) - specify triggers
  - Real-time (HL7 or ASTM; usually automated)

Device → information system

- Data to be transferred - need a specific list…be judicious; only transfer the data that is needed for care (some devices have 200 parameters, of which you only need 30…or 5)
  - Reduce noise, improve signal
  - user ID
  - Patient IDs
    - If no patient IDs, then how will data be associated with the patient?
  - Result data
  - UDI
  - Comments or other information
- Manner in which the data is expected to be transferred
  - Flat-file (push)
  - Real-time (HL7 or ASTM) - (usually automated)

Integration of Devices

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Security

- Is the operating system and software protected against vulnerabilities (i.e., not outdated or subject to malware?)
- Does the vendor perform routine vulnerability checks of its systems?
- Can this device be accessed remotely via the web? What security measures are in place?
- Can the device export data to sites that are not sanctioned by the healthcare organization (web, cloud database, personal devices such as phones, etc.)

Testing

- Devices should be connected to test systems (middleware, EHR, LIS, RIS, etc.)
- Test devices in different physical locations (e.g., ICU vs. OR), especially if environment is expected to be different between locations
- Two phases
  - **Unit testing**
    - Verification that device is working as expected
  - **Integration testing**
    - Verifying that information is transferring from the device to middleware to information system as expected and with appropriate clinical context (usability)
- **Post-go-live verification**
  - Check some of the devices being used in production immediately after go-live to ensure that they are working as expected

Integration of Devices

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Documentation

- Document all aspects of the system (device, middleware, information system)
  - Make, model, firmware version, software version and all configurations
  - Data map:
    - List of discrete data elements in the device and where they map to in the middleware and/or information system
  - Connection descriptions (cabling, ports, networking, etc)
  - Data conversion calculations (can be checked anytime for accuracy)
  - Alert configurations
  - Information that may be important for troubleshooting

Documentation

- Backup and disaster recovery of data
- Instructions for device replacement as needed (configuration, testing, etc.)
- Be sure that calculations and data conversions can be easily checked when troubleshooting
- Troubleshooting guide