Considerations for a Corporate

Data Integrity

Program

(What's So Funny 'Bout) Part 11 and Data Integrity

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Connecting a World of Pharmaceutical Knowledge

Acknowledgements

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Agenda

data integrity lifecycle

eight steps to take

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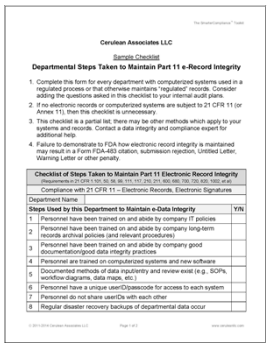
Helpful Reference Materials



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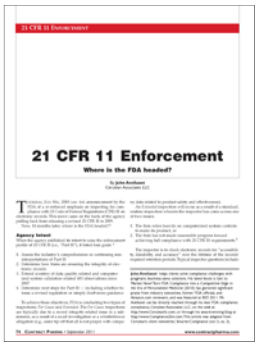
Sample Checklist

Departmental Steps Taken to Maintain Part 11 e-Record Integrity

1. Complete this form for every department with computerized systems used in a regulated process or that otherwise maintains "regulated" records. Consider adding the questions asked in this checklist to your internal audit plans.
2. If no electronic records or computerized systems are subject to 21 CFR 11 (or Annex 11), then this checklist is unnecessary.
3. This checklist is a partial list; there may be other methods which apply to your systems and records. Contact a data integrity and compliance expert for additional help.
4. Failure to demonstrate to FDA how electronic record integrity is maintained may result in a Form FDA-483 citation, submission rejection, Untitled Letter, Warning Letter or other penalty.

Checklist of Steps Taken to Maintain Part 11 Electronic Record Integrity (Requirements in 21 CFR 11.10(), 10, 30, 50, 70, 90, 111, 117, 210, 211, 600, 680, 700, 720, 820, 1000, et al)		
Compliance with 21 CFR 11 – Electronic Records, Electronic Signatures		
Department Name		
Steps Used by this Department to Maintain e-Data Integrity		**Y/N**
1	Personnel have been trained on and abide by company IT policies	
2	Personnel have been trained on and abide by company long-term records archival policies (and relevant procedures)	
3	Personnel have been trained on and abide by company good documentation/good data integrity practices	
4	Personnel are trained on computerized systems and new software	
5	Documented methods of data input/entry and review exist (e.g., SOPs, workflow diagrams, data maps, etc.)	
6	Personnel have a unique user/ID/passcode for access to each system	
7	Personnel do not share user/IDs with each other	
8	Regular disaster recovery backups of departmental data occur	



21 CFR 11 Enforcement

Where is the FDA headed?

Electronic Archiving – a 100 Year Experiment

Abstract

1 Introduction

available for download (until June 20th) at www.ceruleanllc.com/ISPE

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Postmarket Adverse Event Data

From § 314.80(i) Recordkeeping

"The applicant shall maintain for a period of 10 years records of all adverse drug experiences known to the applicant, including raw data and any correspondence relating to adverse drug experiences.**"**

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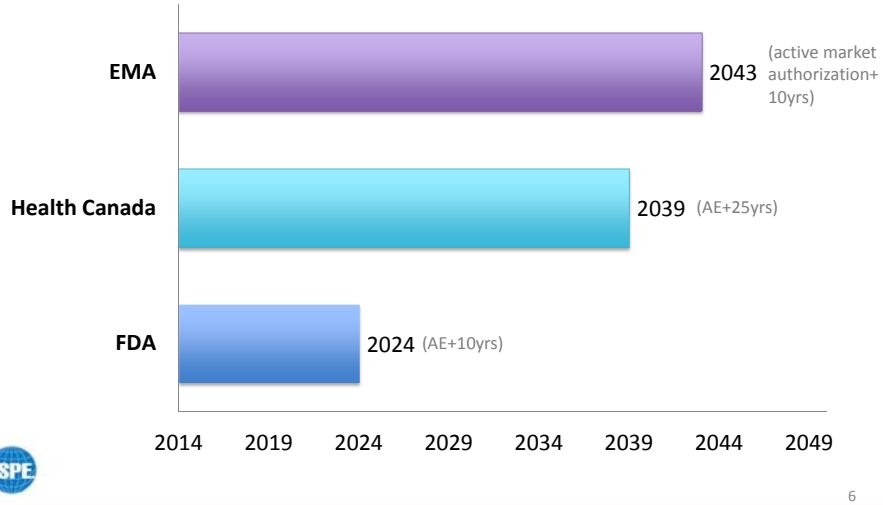

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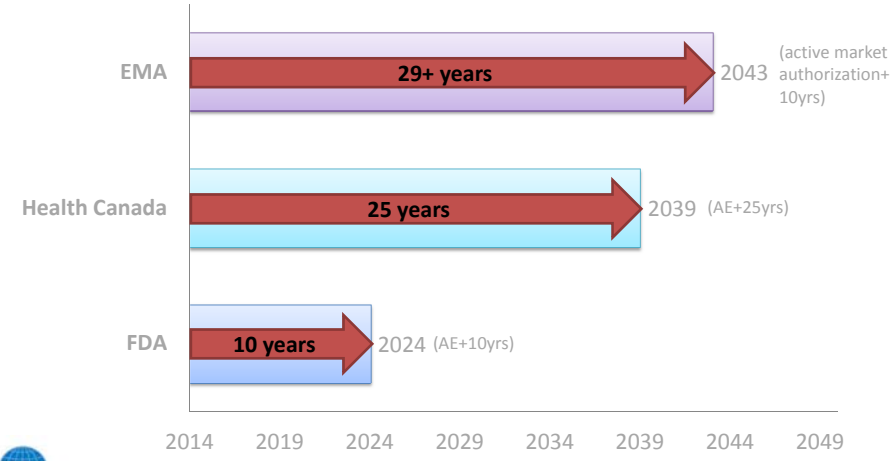
ALCOA+ controls across data lifespan

(attributable, legible, contemporaneous, original, accurate, complete, consistent, enduring, available)



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Translation:

Data integrity controls cover the **life of the data**
not the life of any one system

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Data Integrity Lifecycle

Creation → Processing Manipulation → Semi-Active Storage (or transmittal) → Long-Term Archival

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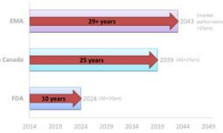
Data Integrity Lifecycle



Creation → Processing Manipulation → Semi-Active Storage (or transmittal) → Long-Term Archival

What are your ALCOA+ controls for 10, 25, 29+ Years?

Ex: what are your data chain-of-custody controls across vendors, sites, etc. for 10, 25, 29+ years?

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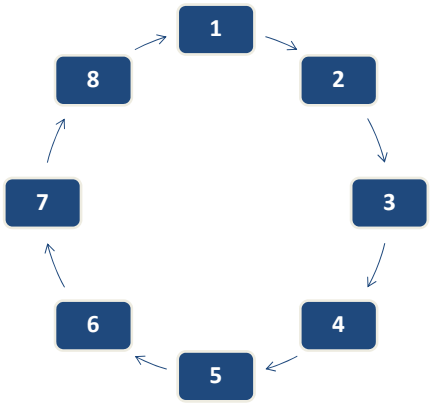
Eight Step Process



assemble a core team
educate the team
develop overall strategy
data map to define controls
verify vendor compliance
prioritize and implement
monitor, measure and audit
re-evaluate and revise

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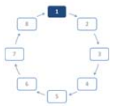
Assemble a Core Team



- quality
- IT
- records management
- legal (or corporate compliance)
- functional representatives (mfg., clinical, etc.)

and maybe…
- regulatory affairs
- validation
- vendor management
- audit

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Example: Senior Management

- Show them recent, sample enforcement actions that have humiliated other firms
- Explain how data integrity simply asks

  "Can the agency trust our data?"
- Discuss how a data lifecycle-focus can help limit the scope and cost (and avoid Part 11 mistakes of the past)
- Review the costs of poor data integrity
  - 3rd most common reason for a delayed or rejected submission
  - untrustworthy product release records lead to public recall
  - 5th most common warning letter – and attendant loss of revenue

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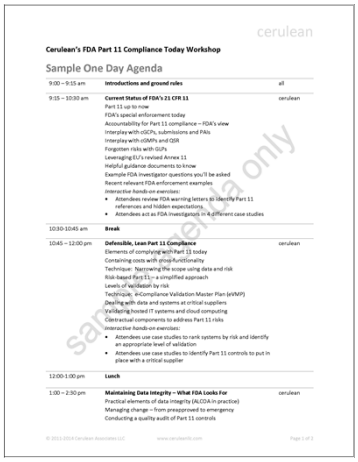
Educate the Team

- In-person workshops
- Webinars
- Consider combining with a data integrity gap analysis
  - discuss results in workshop (or use workshop to lay the groundwork for expected audit results)
  - make sure gap analysis covers all four data lifecycle stages!



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Ceruleen's FDA Part 11 Compliance Today Workshop

Sample One Day Agenda

9:00 – 9:15 am	**Introductions and ground rules**	all
9:15 – 10:30 am	**Current Status of FDA's 21 CFR 11**	cerulean
	Part 11 up to now FDA's special enforcement today Accountability for Part 11 compliance – FDA's view Interplay with cGCPs, submissions and PAIs Interplay with cGMPs and QSR Forgotten risks with GUPs Leveraging EU's revised Annex 11 Helpful guidance documents to know Example FDA investigator questions you'll be asked Recent relevant FDA enforcement examples *Interactive hands-on exercises:* • Attendees review FDA warning letters to identify Part 11 references and hidden expectations • Attendees act as FDA investigators in 4 different case studies	
10:30-10:45 am	**Break**	
10:45 – 12:00 pm	**Defensible, Lean Part 11 Compliance**	cerulean
	Elements of complying with Part 11 today Containing costs with group functionality Technique: Narrowing the scope using data and risk Risk-based Part 11 – a simplified approach Levels of validation by risk Technique: #Compliance Validation Master Plan (#VMP) Dealing with data and systems at critical suppliers Validating hosted IT systems and cloud computing Contractual components to address Part 11 risks *Interactive hands-on exercises:* • Attendees use case studies to rank systems by risk and identify an appropriate level of validation • Attendees use case studies to identify Part 11 controls to put in place with a critical supplier	
12:00-1:00 pm	**Lunch**	
1:00 – 2:30 pm	**Maintaining Data Integrity – What FDA Looks For**	cerulean
	Practical elements of data integrity (ALCOA in practice) Managing change – from preapproved to emergency Conducting a quality audit of Part 11 controls	

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Develop Overall Strategy

- Overall principles
- Roadmap
- Roadmap deliverables
- Progress to date
- Leveraged resources
- Team roles
- Financials
- Metrics for success

Data Integrity Strategy Contents

Topics	Pages
Vision & Strategy	3-11
Roadmap	12-30
2014 Forecast Spend	31-33
Appendices: Charter, Resources, Metrics, Teams, Wireframes	34-45

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Example: Leverage Your RRS

Record Category	Record Type / Description (Examples)	Minimum Retention Period	Retention Review Date	Regulatory Reference

Other considerations:
- data "owner" or steward
- process or equipment that produces the data
- if data is created/held on your behalf by a vendor

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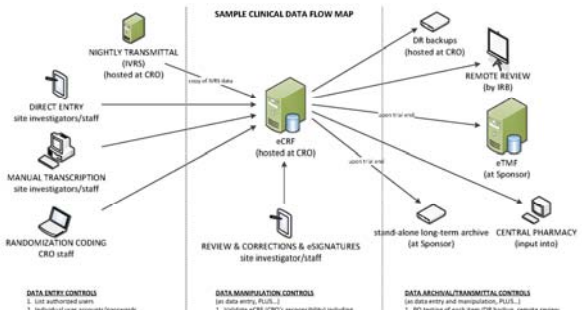
Data Map to Define Controls



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Example: Data Archival

sticky-shed syndrome
(moisture or oxide shedding)

disc-rot
(chemical degradation)

software-rot
(dormant v. active)

rodents
(physical damage)

bit-rot
(data degradation)

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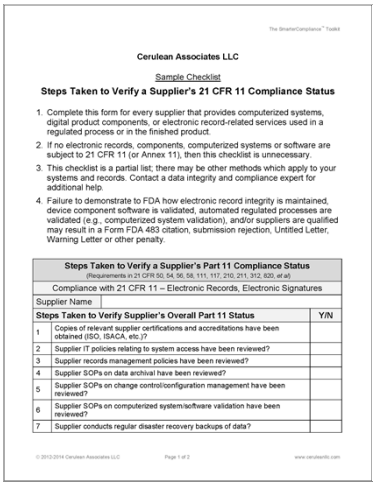
Verify Vendor Compliance

- conduct audits
- look for undocumented data "review" points, etc.
- incorporate controls into contracts and quality/technical agreements
- ALWAYS verify what will happen to your data at vendor after transfer to your possession



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Sample Checklist

Steps Taken to Verify a Supplier's 21 CFR 11 Compliance Status

1. Complete this form for every supplier that provides computerized systems, digital product components, or electronic record-related services used in a regulated process or in the finished product.
2. If no electronic records, components, computerized systems or software are subject to 21 CFR 11 (or Annex 11), then this checklist is unnecessary.
3. This checklist is a partial list; there may be other methods which apply to your systems and records. Contact a data integrity and compliance expert for additional help.
4. Failure to demonstrate to FDA how electronic record integrity is maintained, device component software is validated, automated regulated processes are validated (e.g., computerized system validation), and/or suppliers are qualified may result in a Form FDA 483 citation, submission rejection, Untitled Letter, Warning Letter or other penalty.

Steps Taken to Verify a Supplier's Part 11 Compliance Status (Requirements in 21 CFR 50, 54, 56, 58, 111, 117, 210, 211, 312, 820, et al)		
Compliance with 21 CFR 11 – Electronic Records, Electronic Signatures		
Supplier Name		
Steps Taken to Verify Supplier's Overall Part 11 Status		**Y/N**
1	Copies of relevant supplier certifications and accreditations have been obtained (ISO, ISACA, etc.)?	
2	Supplier IT policies relating to system access have been reviewed?	
3	Supplier records management policies have been reviewed?	
4	Supplier SOPs on data archival have been reviewed?	
5	Supplier SOPs on change control/configuration management have been reviewed?	
6	Supplier SOPs on computerized system/software validation have been reviewed?	
7	Supplier conducts regular disaster recovery backups of data?	

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Prioritize and Implement

- Use risk assessment techniques to prioritize
- Consider using risk to define control depths
- Track progress on a site-by-site basis

Data Integrity Strategy Contents

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Monitor, Measure & Audit

- verify departmental compliance with policies (annually)
- verify vendor compliance rates
- conduct periodic fire drills of DR backups and long-term archives
- combine with internal quality audits
- rigorous sampling (*c=0*)
- review NARA sampling standard (36 CFR § 1234.30) for e-media

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Example: Calibrate Benefits

32% reduction in product liability litigation **costs**

save up to **$438,000** per year

lower **validation** costs by **30%**

Sources:
The Information Management Journal, March/April 2013
Norton Rose Fulbright LLP's *Litigation Trends Survey*, October 2011
Biopharmaceuticals: Biochemistry and Biotechnology, Gary Walsh, 2003

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Re-Evaluate and Revise

- Quality Systems Management Review (QSMR)
- Annual Product Review (APR)
- End of a clinical trial (or end of each phase)
- After an independent data integrity audit

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Key Point Review

- Integrity risks are persistent thru data lifecycle
- ALCOA+ runs from data creation to disposition
- Core team must be cross-functional
- Educate the team – do not assume knowledge
- Use the simplified 8-step process to start
- Mix automated, procedural, vendor controls
- Leverage your corporate RRS to narrow scope
- Continuously audit and revise to improve

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Kick-Start Your Data Integrity

1. Download the helpful reference material at www.ceruleanllc.com/ISPE (until June 20th)
   - Checklist: *Departmental Steps Taken to Maintain Data Integrity*
   - Article: *21 CFR 11 Enforcement – Where is the FDA Headed?*
   - Article: *Electronic Archiving – a 100 Year Experiment*
2. Identify four functional leaders in your organization who work in the data lifespan and invite them to your core team
3. Review the key points covered in this presentation with your core team
4. Talk through the helpful reference material with your team
5. Verify your organization has a (relatively) recent RRS

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About Your Presenter

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John Avellanet gives practical, compliance solutions to simplify and streamline compliance for clients around the world. Winner of the 2009 & 2011 Best of Business Services award by the Small Business Commerce Association, Mr. Avellanet has earned international acclaim for his business-savvy, pragmatic FDA compliance and data integrity advice.

His latest book, **Get to Market Now! Turn FDA Compliance into a Competitive Edge**, was featured at BIO 2011 and has garnered multiple five-star reviews from industry publications, blogs, Amazon.com readers, and former FDA officials.

He has a breadth of experience designing, implementing, and being accountable for quality systems and compliance programs for FDA, DEA, ICH, BIS, GHTF, and ISO. For more than 15 years, John was directly accountable for regulatory compliance, records management, and information technology, most recently as a *C*-level executive for a *Fortune 50* combination device subsidiary.

In 2006, Mr. Avellanet founded his independent lean compliance consulting and training firm, **Cerulean Associates LLC**.

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About Your Presenter

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Recent Resume Highlights

- Lead author of 2 certification courses for US RAPS
- IRO for Dr. Comfort Corporate Integrity Agreement
- Member, ISPE GAMP Data Integrity Working Group
- 2010 and 2011 Top 10 FDA Compliance Blog
- 2010 Top 50 Pharma/Biotech Blog
- 2009 and 2011 US Best of Business Services Award
- 2008-2012 Guest Lecturer at NIH
- 2006 Lifetime Achievement Award – Who's Who of Biopharma & Device Executives

FDA Lean Compliance Services

- Streamline **SOPs** and policies
- Simplify **Part 11** and **data integrity** compliance
- Perform **audits** for compliance and cost-effectiveness
- Develop **FDA recordkeeping** policies
- Conduct private **training** and corporate workshops
- Serve as consent decree **IRO** and litigation support

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