Data Integrity in the Regulated Laboratory

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Topics

- The Stakes for Your Laboratory
- Fat Fingers and Falsification
- Human Controls
- Significant Risk Items
- Detecting Integrity Risks (Process)
- System Configuration and Intended Use
- Testing into Compliance
- Success in Data Integrity

The Stakes

1st – Your Test Results
2nd – Your Decisions
3rd – Your Customers
4th – Your Reputation
5th – Your Profits
6th – Your Business

How much are you willing to pay for a result you do not trust?

"Fat Fingers"

- Unintended data errors (e.g. data transposition)
- Example: pH of 7.48 *observed* but 7.84 *recorded*
- Once recorded, nearly impossible to detect
- Impossible to eliminate when humans involved
- Best case error rate: 0.5% (simple mechanical)

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Falsification

- Intentional action by an individual or group (collusion)
- Done to improve appearance of records or achieve results beyond resources. For example:
  - Back dating test results, destroying original worksheets
  - Using another's account (speed review/release)
  - Creating test results (and audit trails)
- Audit trail review
  - Can detect individual actions—if reviewed(!)
  - In extreme cases, it is falsified – misleads inspector

How much are you willing to pay for a result you do not trust?

People

- 50%+ of data integrity controls are *human* controls
- Must be trained for data integrity
- The following undermine integrity:
  - Leadership: "just get it done by….."
  - Shared accounts or passwords (or Sticky notes)
  - Conflicts of interest in job roles (Do, Approve, Admin)
  - Everyone has "Supervisor" rights

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Significant Risk Items-1

Business Processes and Oversight

- Manual Data Recording
- Improper Sample and Data processing
- Inadequate investigation of anomalous data
- Failure to track and trend recurring patterns in data
- Superficial data reviews
- Vendor/Collaborator management (Q Agreement)

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Significant Risk Items-2

Systems-Related

- Instrument/Software Configuration and Control
- Clock Management
- Interfaces (validation, push or pull)
- Access Management (roles, conflicts of interest)

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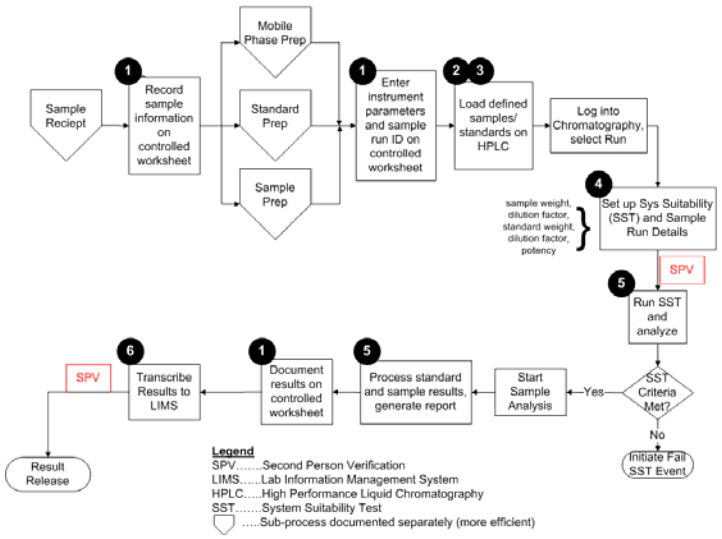
Detecting Integrity Risks

HPLC Generic Flowchart



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Detecting Integrity Risks

Risk #	Identified Risk	Business Impact	Risk Likelihood	Probability of Detection	Risk	Comments
1	Incorrect data recorded and executed on worksheet.	High	Medium	Medium	High	Might create invalid data if failure occurs. If error is large, will cause shift in result. Mitigate with real time SPV of raw data entry
2	Wrong method template selected	High	Low	High	Low	Should be detected in SPV, as template record is linked to test run.
3	Samples or standards not loaded on in correct order on HPLC	High	Low	High	Low	Usually detected in SPV. Sometimes immediately detectable—cause method acceptability criteria to fail.
4	Incorrect SST or sample run setup	High	Low	High	Low	Should be detected in SPV. Might generate invalid data before detected.
5	Manual integration is improper, making failing results appear as passing	High	Low	High	Low	Detectable in SPV.
6	Incorrect information written on worksheet and inputted into LIMS	High	Medium	High	Medium	Detectable in SPV. Small data set to review. If released, could cause incorrect batch decisions.

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System Configuration

Critical to data integrity !

- Configuration must match intended use
- Directly impacts raw data (therefore test results)
- Requires IT, Lab, Quality skills for proper setup
- Must be access controlled (or mitigated)
- Critical component of the validated state

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Testing Into Compliance

- A form of hiding data, largely confined to labs
- Undocumented test performed with the intent to view an outcome *before* making a decision to report
- Violates 211.194(a)

a) Laboratory records shall include **complete data** derived from **all tests** necessary…

- Aided by interfaces that require user to push files forward (e.g. instrument to LIMS)

Test Run accountability

- Can be unintentional—attempting to use "good science"

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Success in Data Integrity

Laboratory

- Trains personnel to create and preserve data integrity
- Knows the data needed to provide a complete test record
- Reviews raw data, critical audit trails/metadata
- Retains raw data, critical audit trails/metadata for defined period

Quality Unit

- Trains personnel to inspect records for data integrity
- Assures that quality system can detect aberrant data before release
- Inspects data regularly to verify quality system is followed
- Reviews quality system for performance and execution

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Speaker Contact & Thanks

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Parting Thought

You might have Data Integrity issues if you hear …

- "It is mostly about a few companies making up test results."
- "We have no problem: we've never dismissed anyone for falsifying data. "
- "It is mostly an IT problem."
- "We know how to make this product. It is the lab's fault."
- "Review every manual integration in chromatography? That's crazy talk!"
- "It is just a fad that will blow over in a few years."

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