Connecting People, Science and Regulation

Strengthening the Internal Audit Program to Assure Data Integrity, The Industry Perspective

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Agenda

- Importance of a effective Audit Program
- Tell Tale Signs the Audit Program is not effective
- Internal Audit Program & Governance Structures that are effective
- Success Factors
  - Auditor Training
  - Regulatory Intelligence

Why is Data Integrity so Important?

Trustworthy Data is fundamental to Assuring Safety & Efficacy

- **Laboratory records lack complete data derived from all tests necessary to assure compliance with established specifications and standards**
- **Lack of appropriate controls over computer systems to assure that only authorized personnel institute changes in the master production and control records**
- **Lack of thorough investigation of unexplained discrepancy or failure of a batch or any of its components whether the batch is released or not**

Robust

In God we Trust, all others bring data, with Integrity

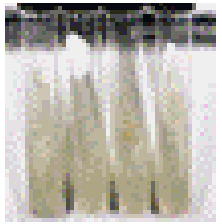
Examples of Data Integrity Issues

Failure to retain complete data, such as:

- **"Trial" sample injection data was not kept as part of batch data**
- **Sample weights, sample preparation and sample dilutions are not retained**
- **Deleted data detected in audit trails**
- **Overwriting data**
- **Ripped up data found in the garbage**
- **Firm deleted all electronic raw data supporting HPLC release testing**
- **Standards were injected and used as sample results**
- **Duplicate logbooks were kept**
- **Complete raw data to support test method validation was not retained**
- **Integration parameters for HPLC analysis were not retained**

Examples of Data Integrity Issues

Not reporting microbiological counts



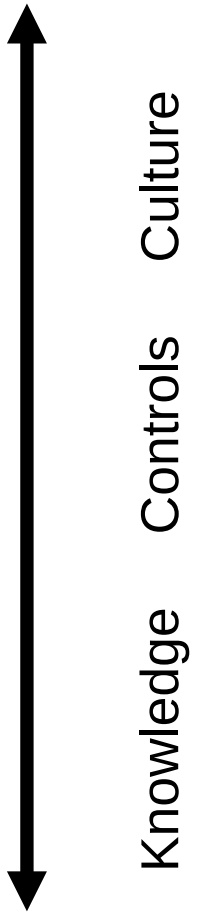
- **Hundreds of environmental monitoring samples were not collected**
- **Some microbiological sample plates/tubes were missing from the incubator**
- **No microbiological testing was conducted; however, microbiological test results were reported on the certificate of analysis (COA)**

Seven Elements of an Effective Compliance Program

- Reporting Concerns
  - Speak Up, Voluntary Disclosure, hotlines
- Enforcement & Discipline
  - Special Investigation/for cause audit

- Oversight - Compliance Committee
- Auditing & Monitoring
- Response & Prevention

- Standards and Procedures
- Education and Training



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Tell Tale Signs of Audit Program not Working

- Health Authority Inspection major findings are a surprise to Management
  - Internal Audit did not detect lack of audit trail
- Management repeatedly fails to open e-mail and read attached audit report
- Executive management rarely ask questions about audit findings
- There is a moratorium on audits because there is backlog of things to fix. Auditor is assigned to fix findings.
- There is no pre-approved annual audit plan
- Audits happen only when Health Authority inspection are scheduled
- There are no metrics to measure performance of the audit program

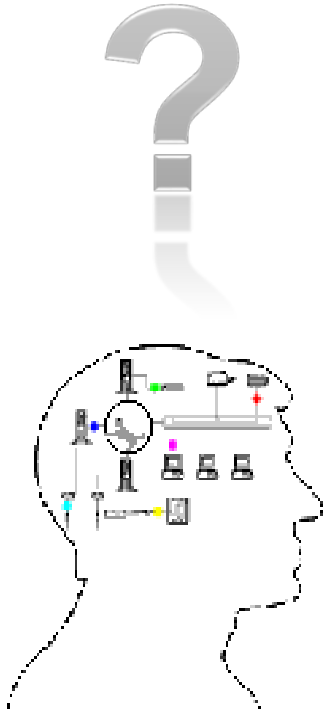
Elements of Effective Audit Programs

- Governance Structure is well defined and Senior Executives are sponsors
  - Examples Compliance Committee, Board of Directors
- Audit program is independent
- Two tiered program
  - Site Level Program focused on execution –SOPs are followed, house keeping, data management, etc
  - Corporate Level focuses on governance systems- ICH Q8, ICH Q(, ICH Q10, effectiveness of site audit system, CAPA system, non-conformance system, data management system
  - Supplier Audit program well defined and coordinated between site and corporate
- Closed loop audit program
  - Program ensures audit findings are tracked to completion and verified
- Regulatory Intelligence integrated into Audit program

Auditor Training

So……

- Are your auditors trained to inflict rigor?
- Are your auditors trained to look for data integrity?
- Do you have auditors who understand computer systems?



What to look for?

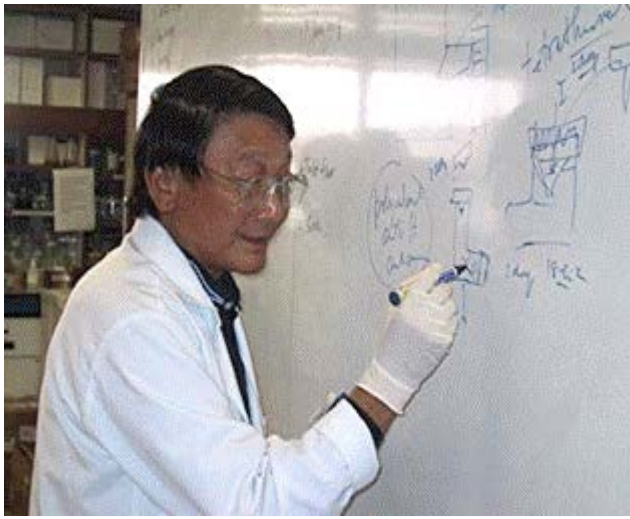
Do the site have procedures and training for…..

- **Document Retention and Destruction**
  - Not just Laboratories; also Manufacturing areas and Warehouses
  - Confidential bins and recycling containers
  - Trash cans
- **Log books**
  - Laboratory; Equipment; Calibration and Maintenance
- **Control over issuance and maintenance of Batch Manufacturing Records and analyst worksheets/logbooks**

What to look for?

Do the site have procedures and training that includes **Good Documentation Practices**…

- Ensure that records are not **incomplete or missing**
- That all original data including analytical and micro worksheets are maintained
- Use of ‘white boards’
- Do not allow use of ‘Post-it Notes’
- Require that all work be completed and documented at time it is performed
- Address how to maintain in-process data
- Training records



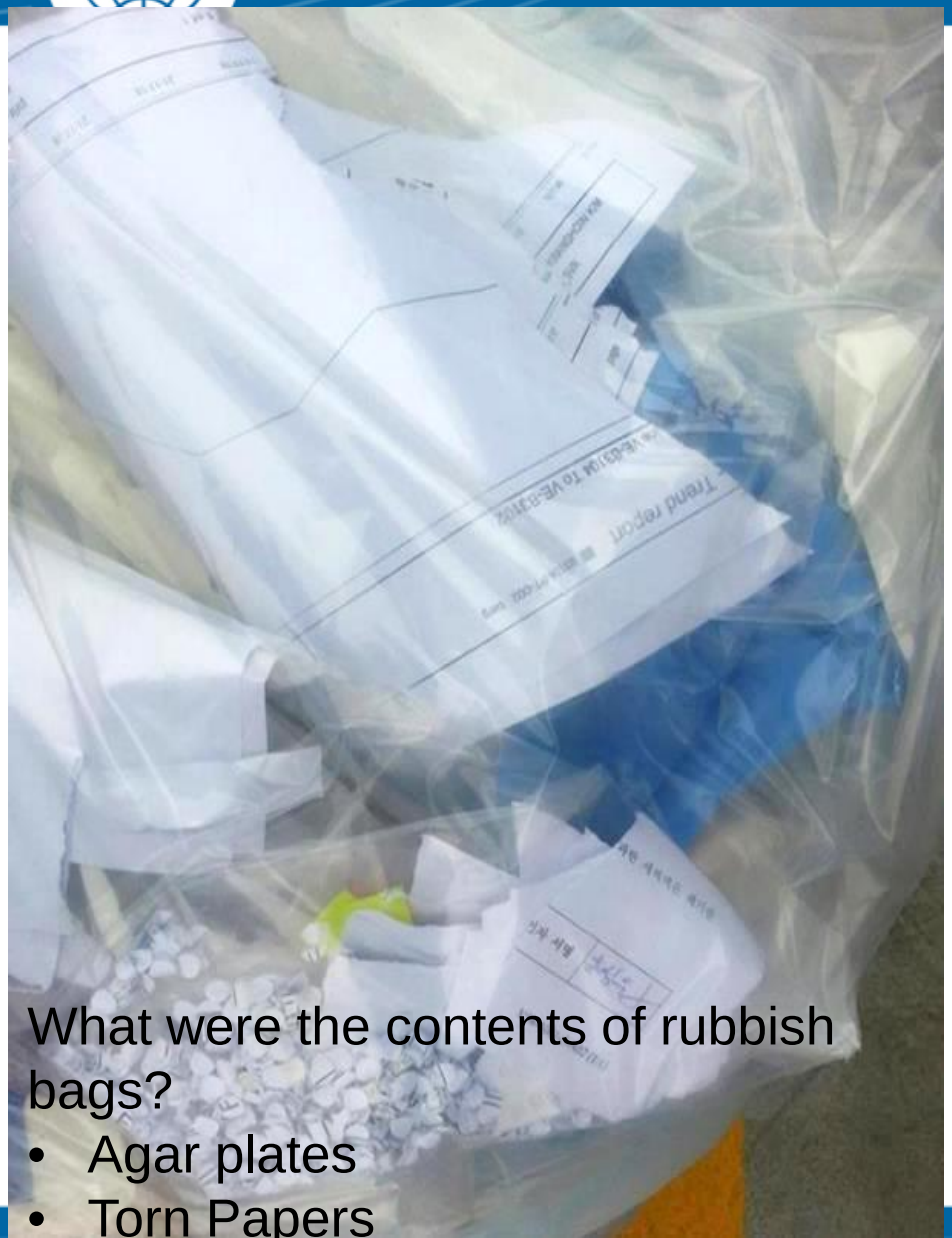
Examples

What to look for?

Warehouse - Inventory Control

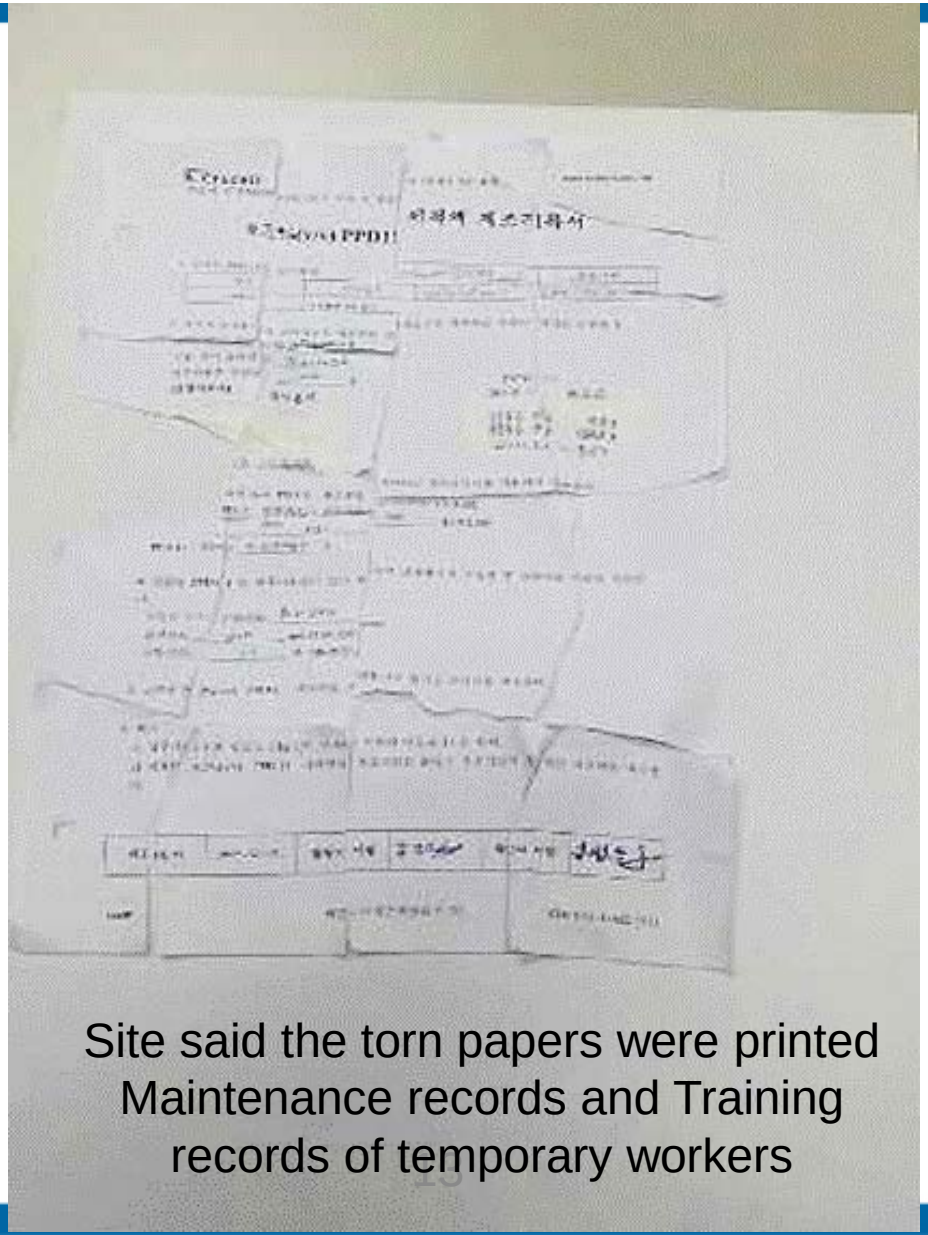
Innocent looking disposal bags found at warehouse entrance?

What to look for?
Look closely



What were the contents of rubbish bags?

- Agar plates
- Torn Papers

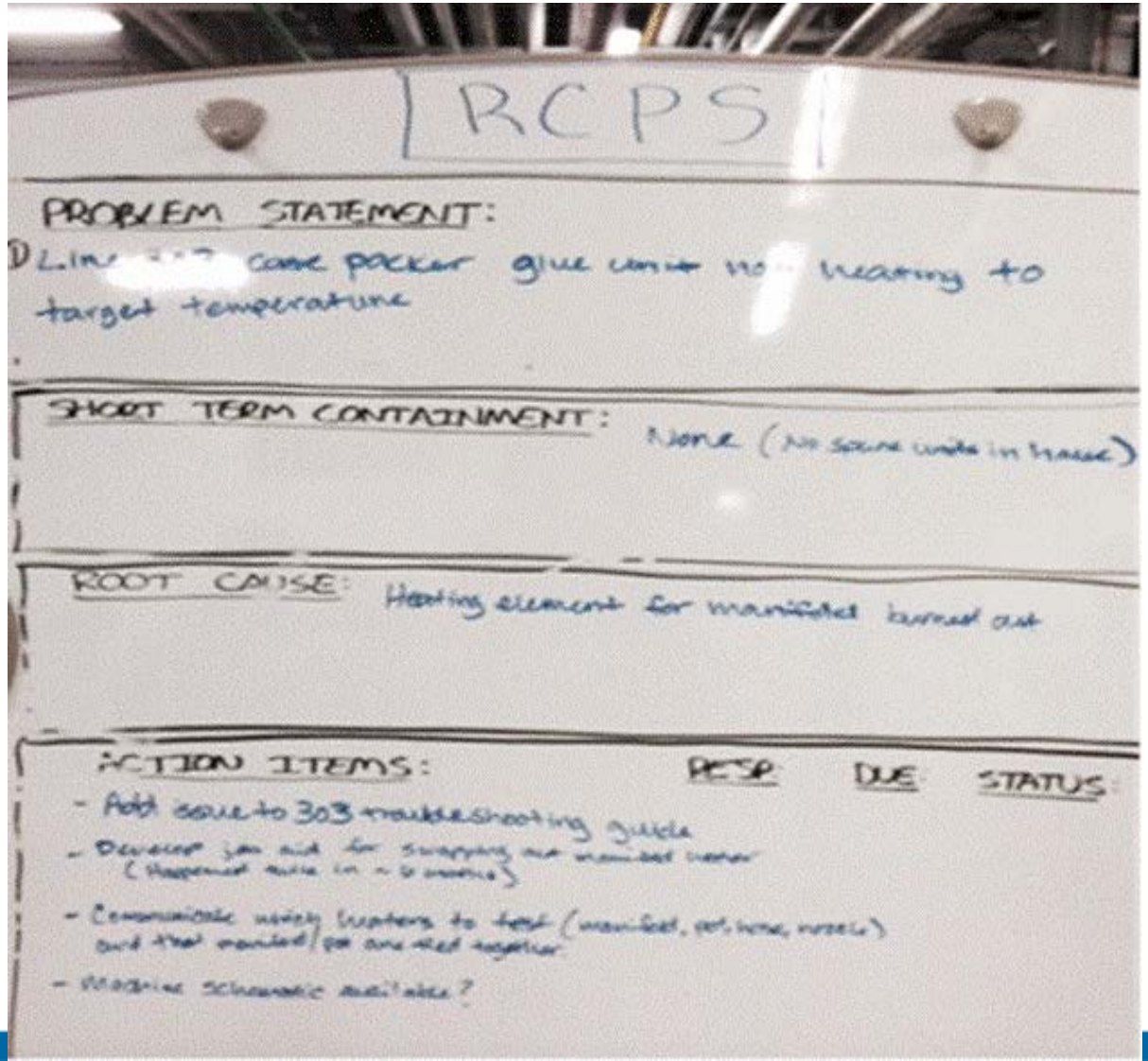


Site said the torn papers were printed Maintenance records and Training records of temporary workers

What to look for?

Check Documentation Control in Manufacturing areas

1a. Check display boards e.g. Root Cause Problem Solving Board



Information recorded on white boards in manufacturing areas is **not documented or available to the Quality Unit**, for example: **Root-Cause Problem Solving (RCPS)** white board in a room. **Action items are not documented**.

What to look for?

1e. Check display boards, SAP, Maintenance, Batch records.

Visual Scheduling Boards (VSBs), including Continuous Improvement boards, may contain information that is **not** controlled, e.g.:

- "XXX Column" stated a 40 cm Protein A column, could **NOT** be used.
- Maintenance documentation indicated the column was **NOT** ready for use.
- What is the SAP status of column?

What to look for?

- The SAP system however indicated the column was **“active”** and **COULD** **be used.**

Mat.No.	Column Description	EMS#	Column Batch #
306166	C524A Packed ColumnProteinA Mabselect 40	10028131	845421

Blocked		: AVAILABLE
Active / Inactive		: Active
Batches Resin		: 7
Batches Since Packing		: 7
Total Regenerations Resin		: 14
Maximum Regenerations		: 180
Max. Contact Time	(Min)	: 26,640
Cumulative Contact Time	(Min)	: 1,806
Date First Storage New Resin		: 18DEC13
Expiry Date Resin		: 31JAN16
Date Last Storage		: 22MAR15
Max Storage	(Days)	: 84
Due Date Storage		: 14JUN15

Integrating Regulatory Intelligence into Auditor Training

- Does your company have a regulatory intelligence program?
  - Warning Letters, new guidance & regulations, Inspectional findings
  - Does the program convert intelligence into actionable and trackable activities?
  - Is the actionable intelligence shared with auditors?
  - Are auditors trained and certified?
    - Internal training
    - External training

Summary

- The key to reducing business and patient risk from data integrity issues is building a strong quality culture.
- Strengthen all seven elements of your compliance program to avoid data integrity issues.
- Increase regulatory intelligence by participating in external training and meetings.