QUality, Integration, Best practices,
Innovation, and Technology

Good Documentation Practices

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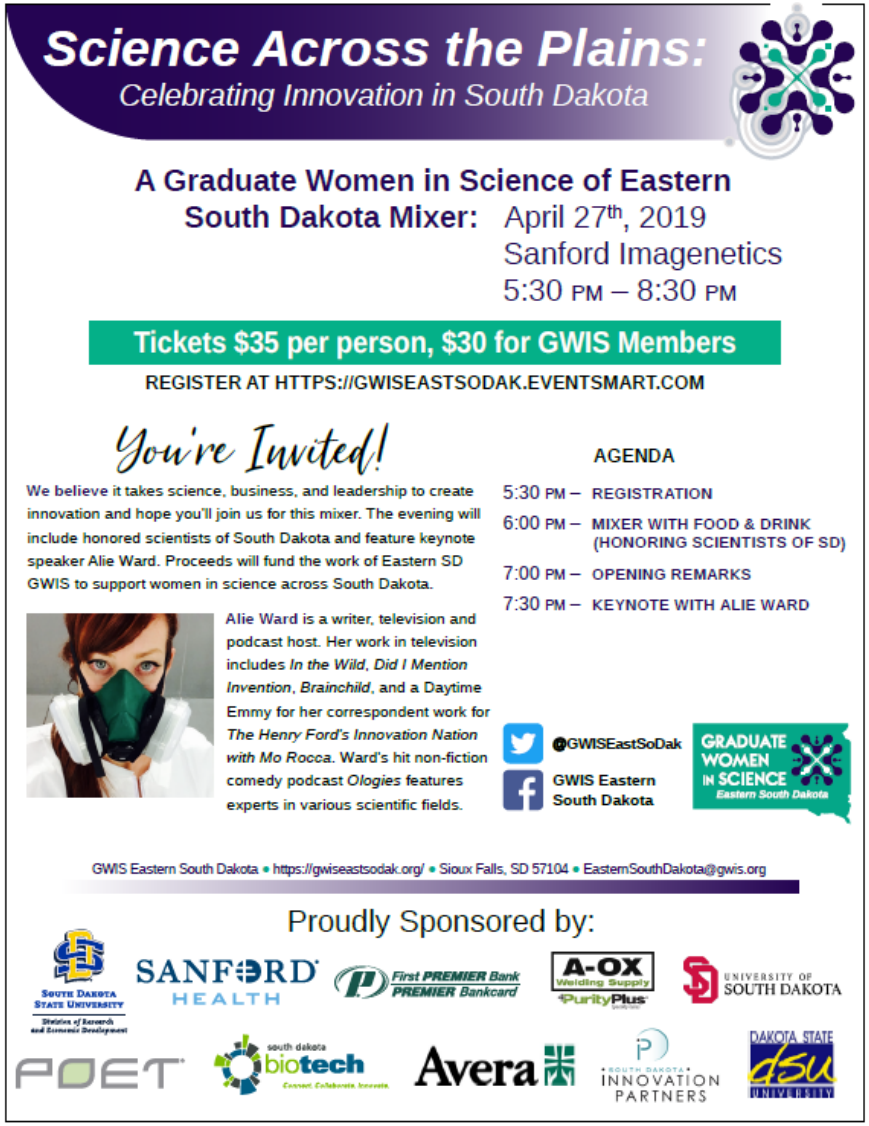
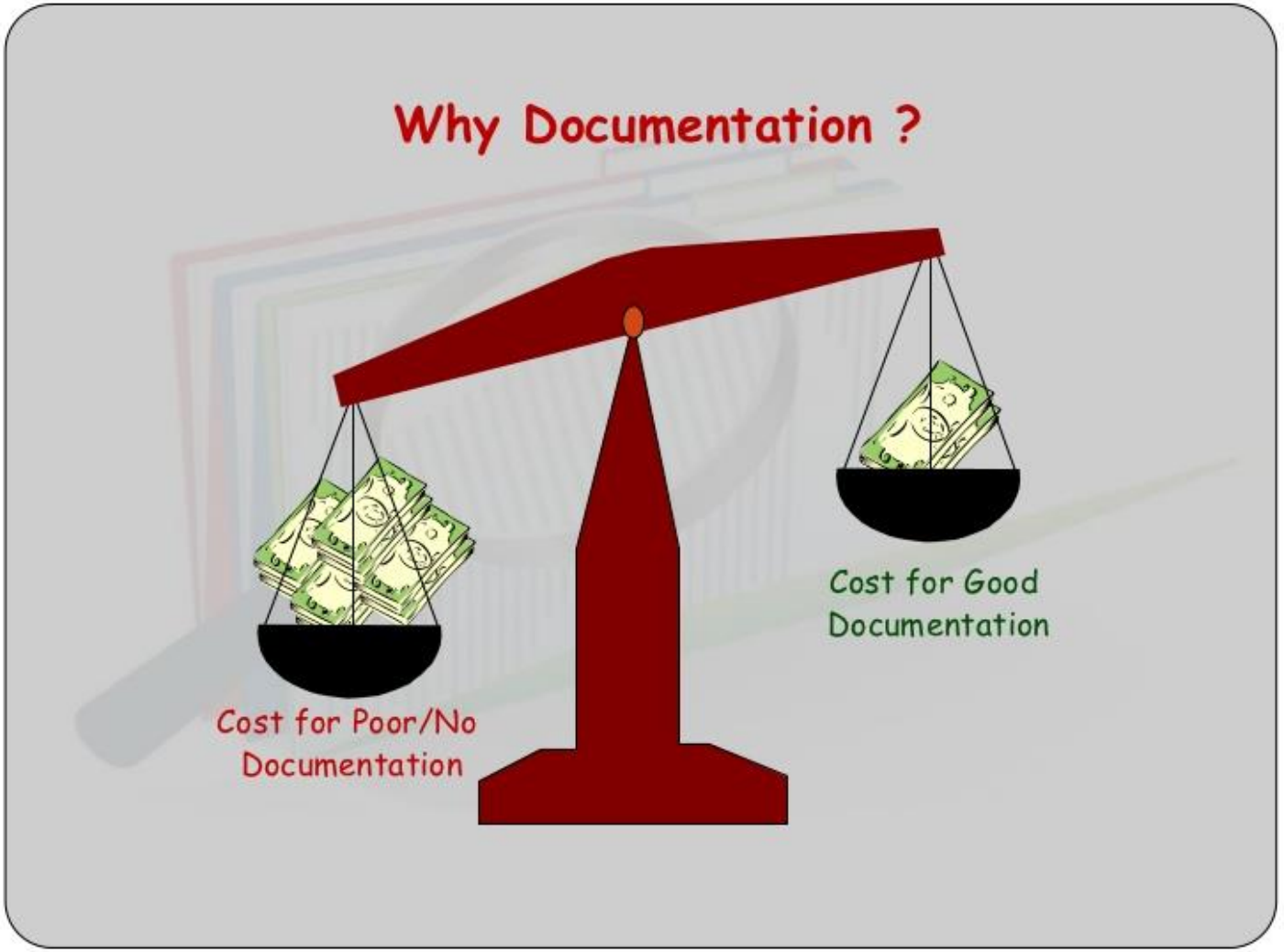
Announcements

- Slides from March Meeting.
- Topics for future QUIBITs?
  - GMP Facility Design Considerations.
  - ISO 17025





What does this figure mean?
Do you agree?

GDP in Regulations and Standards

- FDA
  - GLP
  - GMP
- USDA
  - Animal Biologics
- ISO 13485: Medical Devices

FDA GLP

- **21CFR§58.130 Conduct of a nonclinical laboratory study.**
  - **All data generated** during the conduct of a nonclinical laboratory study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink.
  - All data entries shall be dated on the date of entry and signed or initialed by the person entering the data.
  - Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change.
  - In automated data collection systems, the individual responsible for direct data input shall be identified at the time of data input.
  - Any change in automated data entries shall be made so as not to obscure the original entry, shall indicate the reason for change, shall be dated, and the responsible individual shall be identified.

FDA GMP

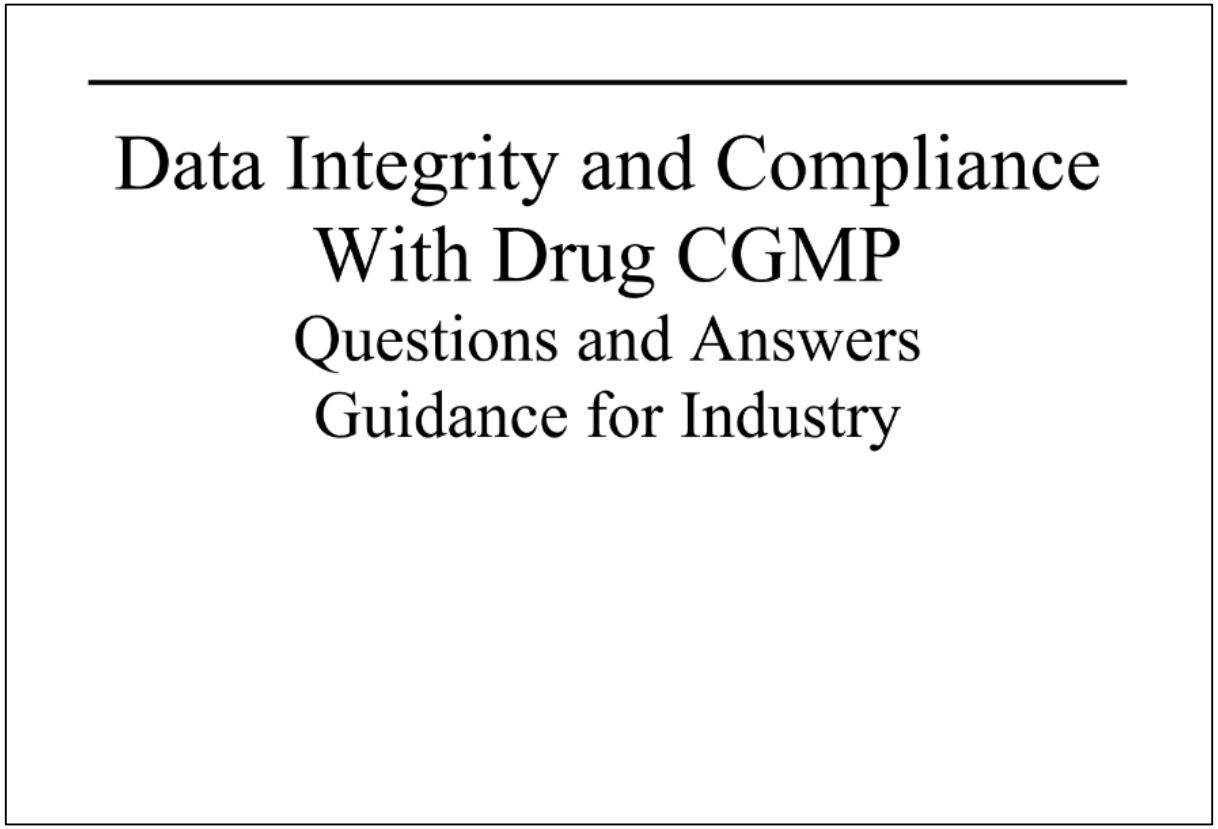
USDA Animal Biologics

- **9CFR§116.1**
- (1) Records shall be made concurrently with the performance of successive steps in the development and preparation of biological products, including new products under development. Such records shall include the date and where critical, the time that each essential step was taken, the identity and quantity of ingredients added or removed at each step, and any gain or loss of product from the beginning to the end of product preparation.
- (2) Records shall be legible and indelible; shall be as detailed as necessary for a clear understanding of each step by one experienced in the preparation of biological products; and shall be verified by initials or signature of the person immediately responsible for the action taken.

ISO 13485: 2016 Medical Devices

- 4.2.5
  - “Records shall remain legible, readily identifiable and retrievable. Changes to a record shall remain identifiable.”

Guidance Document to help answer questions about regulations



What is "data integrity"?

- *Data integrity* refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate **(ALCOA).**

FDA's Questions

- When considering how to meet many of the GDP regulatory and standard requirements, it may be useful to ask the following questions:
  - Are controls in place to ensure that data is complete?
  - Are activities documented at the time of performance?
  - Are activities attributable to a specific individual?
  - Can only authorized individuals make changes to records?
  - Is there a record of changes to data?
  - Are records reviewed for accuracy, completeness, and compliance with established standards?
  - Are data maintained securely from data creation through disposition after the record's retention period?

Question for the group

- Does your current program include a Documentation/Data Integrity SOP?

ALCOA +

ALCOA +

- Attributable
- Legible
- Contemporaneous
- Original
- Accurate
- +
  - Complete
  - Consistent
  - Enduring
  - Available
- Traceable

PART 58 -- GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES
Subpart G--Protocol for and Conduct of a Nonclinical Laboratory Study

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER A--GENERALPART 58 -- GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES Subpart G--Protocol for and Conduct of a Nonclinical Laboratory Study

Sec. 58.130 Conduct of a nonclinical laboratory study.

(a) The nonclinical laboratory study shall be conducted in accordance with the protocol.
(b) The test systems shall be monitored in conformity with the protocol.
(c) Specimens shall be identified by test system, study, nature, and date of collection. This information shall be located on the specimen container or shall accompany the specimen in a manner that precludes error in the recording and storage of data.
(d) Records of gross findings for a specimen from postmortem observations should be available to a pathologist when examining that specimen histopathologically.
(e) All data generated during the conduct of a nonclinical laboratory study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the date of entry and signed or initialed by the person entering the data. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change. In automated data collection systems, the individual responsible for direct data input shall be identified at the time of data input. Any change in automated data entries shall be made so as not to obscure the original entry, shall indicate the reason for change, shall be dated, and the responsible individual shall be identified.
[43 FR 60013, Dec. 22, 1978, as amended at 52 FR 33781, Sept. 4, 1987; 67 FR 9585, Mar. 4, 2002]

III. QUESTIONS AND ANSWERS

1. Please clarify the following terms as they relate to CGMP records:

a. What is "data integrity"?

For the purposes of this guidance, *data integrity* refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).[5]

Data integrity is critical throughout the CGMP data life cycle, including in the creation, modification, processing, maintenance, archival, retrieval, transmission, and disposition of data after the record's retention period ends.[6] System design and controls should enable easy detection of errors, omissions, and aberrant results throughout the data's life cycle.

FDA: ucm495891

ALCOA +

- Attributable ← Who did what?
- Legible ← Must be readable
- Contemporaneous ← Written when performed
- Original ← Not photocopied
- Accurate ← Actual data. Avoid guesses etc….
- +
  - Complete ← No blanks or missing details
  - Consistent ← Same practices (e.g., date format)
  - Enduring ← Designed to last throughout retention period (no acid based tape)
  - Available ← Can be readily retrieved
- Traceable ← Can you match your documents to events?

FDA Warning Letter Snippets

At your Chikalthana site, our investigators observed poor documentation practices during in-process testing. Specifically, an operator performed the in-process tablet **(b)(4)** testing for the **(b)(4)** mg tablet batch #**(b)(4)** without the batch record or a manufacturing form to document the results contemporaneously. The FDA investigator was informed that the pre-test and post-test weight values are documented in the batch record located in a separate manufacturing room rather than in the same room where the actual weights are measured. Moreover, your operator stated that he records the two weights with **(b)(4)** significant figures into the batch record from memory. Your investigation into this issue is inadequate because it did not consider other in-process tests or whether the operator(s) have been involved in the same poor documentation practices for others batches. Your response does not indicate whether this poor documentation practice is an isolated case or is a matter of widespread behavior in this facility.

FDA Warning Letter Snippets

Your employees did not complete batch production and control records immediately after activities were performed. When QA reviewers noticed missing entries in the batch records, they made a list of all the missing items on separate, uncontrolled pieces of paper that were provided to the production manager. Data were later entered into CGMP documents after operations had already ended as though they had been entered at the time of the operation.

For example, on November 17, 2014, we saw eight production records for (b)(4) and (b)(4) that had blank entries for weights of material used for production, checked-by signatures, accessories used, in-house batch numbers, quantity added, and product labeling for material dried specimens. The yield report sheet and batch summary sheet were also incomplete.

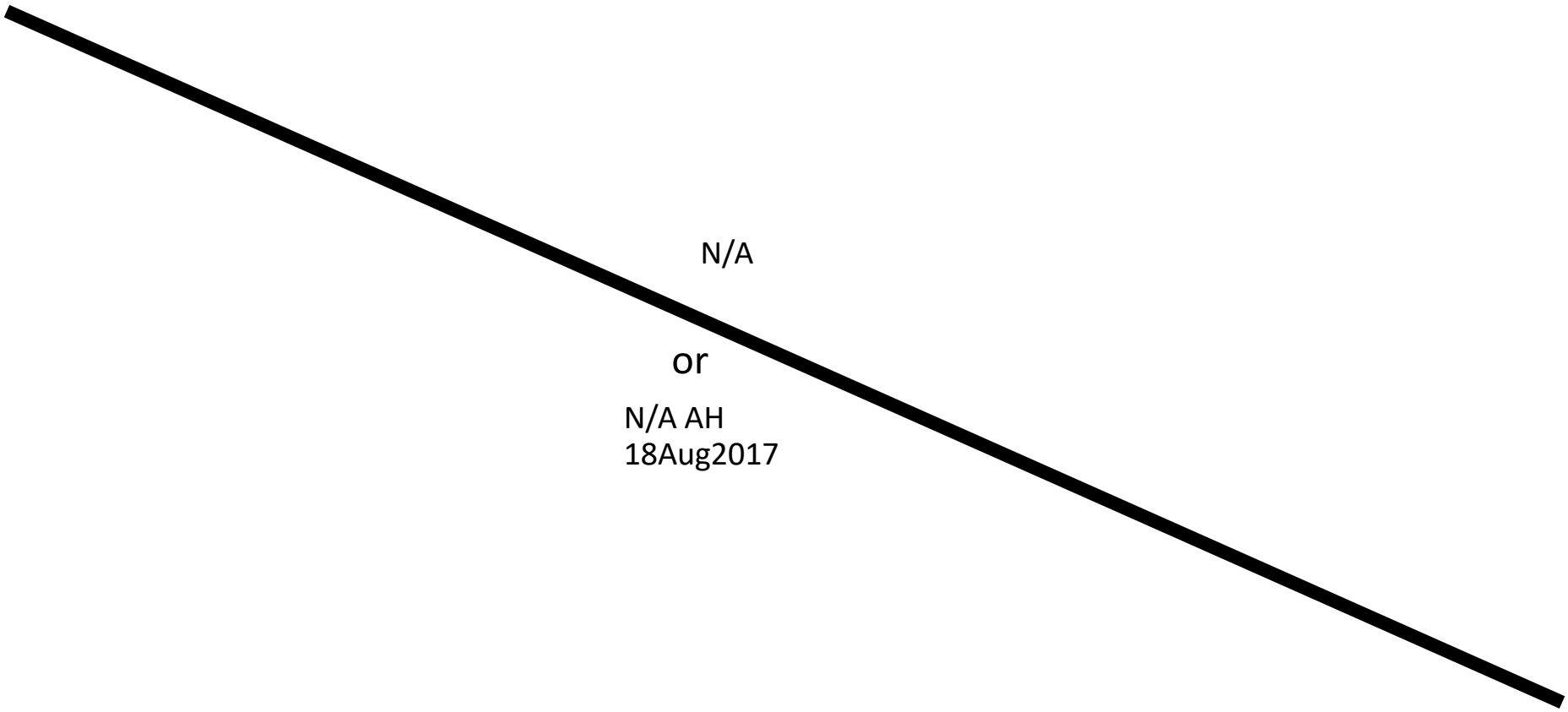
SLIDR

- When errors occur, they must be corrected and corrected properly.
- Use the following:
  - Single Line
  - Initials
  - Date
  - Reason
- Footnotes can be used as well.

"24Aug2017" Wrong date listed. AFH 24Aug2017.

Samples were tested on ~~23Aug2017~~ using HPLC

Blank Spaces



Additional Notes

- For decimals, add a 0.
  - E.g., 0.3mm not .3mm.
- For time use standard format in workplace.
  - E.g., 1352hrs, 1:52pm.
- Use standardized date:
  - 7/6/17, 6/7/17, 20170706, 06Jul2017.
- Ink color may be specified.
- Pencils are prohibited.
- White-out is prohibited.
- Ditto marks prohibited: “ ” or lining down.

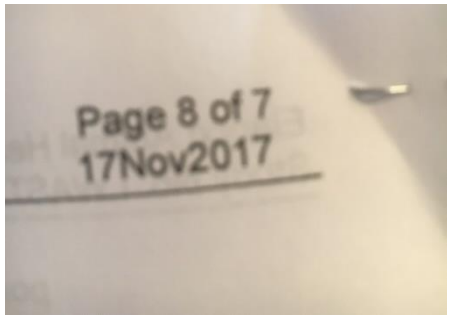
Additional Notes

- Copy must have “Copy” stamp. 

- Pagination must be in place.
- Data must be controlled.
  - Should you allow data to leave the premises?
  - How will you (and how fast can you) retrieve it during an audit?
- Don’t double document if you can.
- Ink used shouldn’t smear. 
- Avoid slang.
  - “Assay was jacked up.”
- Sticky notes…..prohibited.

Example…

- How many errors can you find?



TRAINING ONLY

Name of Media: DMEM	Lot Number: ASL 32093	Expiry Date: 06/09/17
Supplier: Invitrogen	Cat. No.: 31966	Date Received: 10 Jan 2017
Condition upon Receipt: NA	Incubator ID:	

Growth Promotion Tests: Incubation Time-3 days

Test Solution: *Staphylococcus aureus* ATCC 6538 Prepared by/date:		Lot Number: SA 3306 AH49C
Supplier: Fisher	Cat. No.: 49376	Expiry Date: 09-06-2017
Date/Time/Tech Inoculated & Incubated: Aaron Harmon		**Expected Result: < 100 cfu**
Date/Time/Tech Read & Reported:		Results (cfu): ~~105~~ 99 AH 8-21-17

Test Solution: *Pseudomonas aeuriginosa* ATCC 9027 Prepared by/date:		Lot Number: [redacted]
Supplier:	Cat. No.:	Expiry Date:
Date/Time/Tech Inoculated & Incubated: NA		**Expected Result: < 100 cfu**
Date/Time/Tech Read & Reported:		Results (cfu):

Test Solution: *Bacillus subtilis* ATCC 6633 Prepared by/date:		Lot Number:
Supplier: BD	Cat. No.: BD 7301	Expiry Date: NA AH 21 Aug 2017
Date/Time/Tech Inoculated & Incubated: 21 Aug 2017 / 6:34 / Aaron Harmon		**Expected Result: < 100 cfu**
Date/Time/Tech Read & Reported:		Results (cfu): 28

Things to Ponder?

- What if your initials are NA?
- What if you need to write in cold wet areas?
- What if your pen runs out of ink halfway through writing a word?
- What if you are generating data at midnight?
- What if you are working in an anaerobe chamber/glove box?
- What if your data is eaten by an animal?
- What if you spill soda on your document?
- What is the value of your data?