Maintaining Calibration Programs
– Compliance Perspective
(483s, Warning Letters, & Consent
Decrees)

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Pennsylvania Convention Center
Philadelphia, PA USA
Wm. Andy Ferrell - Bio

• Bachelors and Masters degrees from East Carolina University
• Engineer with big pharma companies from 1989 to 1996
• Speaking on topics such as:
  – Smart Asset Management
  – Emerging Trends in Calibration Compliance
  – Predictive Maintenance and Calibration Programs: Improving Operations
• Founded PCI in 1996
• PCI is 110 person firm. Headquartered in RTP, NC with 5 field offices and national consulting & technical service coverage
• PCI’s Technical Services: delivering calibration, maintenance, and repair services for both manufacturing and laboratory equipment
• PCI’s Consulting Services: building calibration & maintenance programs including developing business workflows and policies, implementing software systems, FDA remediation plan development & execution. We development world class maintenance & calibration programs
Introductions: Who are you?

- Name
- Your role
- Company
- Industry
- Regulatory Concern
- What are you seeking to get from this workshop
What we will cover

- What is a Calibration Program?
- Basic Calibration Requirements
- The FDA
- Regulations and Guidances
- What Happened?
  - 483s, Warning Letters, & Consent Decrees
  - Calibration Observations
  - Maintenance Observations
- Q&A
A comparison of a measurement standard (Calibration Standard) of known accuracy with another instrument of unknown accuracy to detect, correlate, report, or eliminate by adjustment any variation in the accuracy of the item being compared.
Why Calibrate?

Every day, industries throughout the world perform a huge number of measurements.

The results of these measurements are used to make decisions that could affect people’s lives both personally and in the workplace.
Without Calibrations

- All of us would pay more at the Gas station.
- Food would be weighed incorrectly.
- No more watching your favorite television shows or listening to your favorite songs on the radio, because due to calibration errors, the frequency would be off enough that TV and radios would be useless.
Without Calibrations

- Ingredients in your prescription drugs could cost more or even more important cause illness or death.
- Because of incorrect calibrations, criminals could be either not convicted or released on bad evidence.
In pharmaceutical manufacturing and other life science businesses, companies take measurements throughout the various stages of the product life cycle to ensure product integrity.

The certification and calibration of instrumentation, combined with a robust calibration management system, helps achieve product integrity throughout all production processes.
Calibration Program Basics

- Calibration Policy and support Procedures (SOP)
- Calibration Records
- Qualified Personnel, Training, & Ongoing Training
- Calibration Labeling
- Calibration Intervals
- Calibration Logistics / Scheduling
- Define Out of Tolerance conditions or Non Conformance
- Process for Investigation of Non Conformances
- Adequacy of Calibration Standards
- Traceability (and Reverse Traceability)
- Analysis of Calibration Data
- Continuous Improvement (Auditing)
Basic Calibration Software Requirements

✓ Ability to capture unique instrument equipment identification, description and classification for each instrument in a calibration program

✓ Ability to capture the calibration test points for each instrument

✓ Ability to schedule calibration services for assigned specified intervals

✓ Ability to handle multiple test ranges

✓ Ability to record calibration data
User Requirements (URS)

✓ Ability to run a matrix report showing, for a specific time period and by various selection criteria:

• Total # of scheduled calibrations
• Total # of active and total # of inactive instruments at the beginning of time period
• Total # of scheduled calibrations [redundant, 1st above]  
• Total # of active and total # of inactive units as they were at the end of time period
• Net change in total # of scheduled calibrations
Performance Metrics
Make strategic objectives clear, in order to focus and bring together the total organization

Tie the core business processes to the objectives

Focus on critical success factors for each of the processes, recognizing there will be variables

Track performance trends and highlight progress and potential problems

Identify possible solutions to the problems
Performance Metrics

What Gets Measured Gets Done.

What Gets Measured, Improves!!!
Performance Metrics: Example

% Calibrations performed: Laboratory Instruments

Calibrations Scheduled

% calibrations performed

Performance Metrics: Example
Calibration Program Checks and Balances

- Both internal corporate compliance and third-party regulatory bodies conduct Audits throughout the pharmaceutical industry to ensure that manufacturers are following their own procedures and to see how they react to issues and deviations to their processes.

- A robust calibration system is vital to ensure that when similar audit points are challenged, it can be demonstrated that systems, processes, and procedures are in place to address potential noncompliance issues.
The FDA
The FDA

What are the CFRs?

- Code of Federal Regulations. Often referred to as Titles.
- There are 50 Titles or CFRs.
Why The FDA?
A bottle of Bayer's 'Heroin'. Between 1890 and 1910 heroin was sold as a non-addictive substitute for morphine. It was also used to treat children suffering with a strong cough.
Metcalf's Coca Wine was one of a huge variety of wines with cocaine on the market. Everybody used to say that it would make you happy and it would also work as a medicinal treatment.
Mariani wine (1875) was the most famous Coca wine of its time. **Pope Leo XIII** used to carry one bottle with him all the time. He awarded Angelo Mariani (the producer) with a Vatican gold medal.
Produced by the Maltine Manufacturing Company of New York. It was suggested that you should take a full glass with or after every meal. Children should only take half a glass.
Opium for Asthma

At 40% alcohol plus 3 grams of opium per tablet. It didn't cure you... but you didn't care!
Cocaine Tablets (1900)

All stage actors, singers, teachers and preachers had to have them for a maximum performance. Great to 'smooth' the voice.
The FDA

CFR 21
The Code of Federal Regulations (CFR) is the codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government.

It is divided into 50 titles that represent broad areas subject to Federal regulation. Each volume of the CFR is updated once each calendar year and is issued on a quarterly basis.
The Code of Federal Regulations

- CFRs are divided into 50 Titles
- Title 21 - Food and Drugs
Some of the 50 CFRs

• Title 1: General Provisions
• Title 2: Grants and Agreements
• **Title 3: The President**
• Title 6: Homeland Security
• Title 10: Energy
• Title 11: Federal Elections
• **Title 12: Banks and Banking**
Some of the 50 CFRs

- **Title 21: Food and Drugs** (administered by the FDA)
- Title 22: Foreign Relations
- Title 23: Highways
- Title 24: Housing and Urban Development
- Title 25: Indians
- **Title 26: Internal Revenue**
- Title 27: Alcohol, Tobacco Products and Firearms
- Title 28: Judicial Administration
- **Title 29: Labor**
Some of the 50 CFRs

- Title 35: Reserved (formerly Panama Canal)
- Title 36: Parks, Forests, and Public Property
- Title 37: Patents, Trademarks, and Copyrights
- Title 38: Pensions, Bonuses, and Veterans' Relief
- Title 39: Postal Service

- Title 45: Public Welfare

- Title 49: Transportation
- **Title 50: Wildlife and Fisheries**
What are cGMPs

• **Current Good Manufacturing Practices**
• A set of federal regulations - Laws
• Jointly developed with industry
• Applies to drug products and drug components
The FDA and cGMPs

History of the FDA & cGMPs

- **1906**: Food & Drug Act passed
- **1931**: FDA became the enforcer
- **1938**: FD & C Act passed
- **1962**: Proof of efficacy required
- **1963**: GMPs first devised
- **1976**: cGMPs proposed
FDA Departments

– Office of Regulatory Affairs
– Center for Biologics and Research (CBER)
– Center for Drug Evaluation and Research (CDER)
– Center for Devices and Radiological Health (CDRH)
– Center for Food Safety and Applied Nutrition
– Center for Veterinary Medicine
– Enforcement Policy Directory
– Office of Combination Products (OCP)
The FDA

FDA Organizational Chart

FDA Commissioner

- OCP
- CDER
- CDRH
- CBER
Regulations & Guidances
Regulations & Guidances

Regulations are Law.

- Example: the FDA has GMPs (Good Manufacturing Practices) or CFR 21.

  *CFR 21 is Code of Federal Regulations for Food and Drugs.*

- Regulations are usually vague.
21 CFR Part 58: GLP for Nonclinical Laboratory Studies

- Subpart D: Equipment
  - Sec. 58.63: Maintenance and Calibration of Equipment
    (a) Equipment shall be adequately *inspected, cleaned, and maintained*. Equipment used for the generation, measurement, or assessment of data shall be adequately *tested, calibrated, and/or standardized*. 
21 CFR Part 58: GLP for Nonclinical Laboratory Studies

- Subpart D: Equipment
- Sec. 58.63: Maintenance and Calibration of Equipment

(b) The written standard operating procedures required under Sec. 58.81 (b) (11) shall set forth in sufficient detail the methods, materials, and schedules to be used in the routine inspection, cleaning, and shall specify, when appropriate, remedial action to be taken in the event of failure or malfunction of equipment. The written standard operating procedure shall designate the person responsible for the performance of each operation.
Subpart D - Equipment Sec. 68 Automatic, mechanical, and electronic equipment

(a) Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product. If such equipment is so used, it shall be **routinely calibrated, inspected, or checked according to a written program designed to assure proper performance**. Written records of those calibration checks and inspections shall be maintained. [43 FR 45077, Sept. 29, 1978, as amended at 60 FR 4091, Jan. 20, 1995]
(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.
Guidances are not Law. Usually published by industry organizations.

- Much more specific than Regulations.
- Following Guidances does not provide 100% certainty of zero observations or violations.
Regulation & Guidance

Guidance Documents - Benchmarking

- ISPE GAMP Calibration Management (second edition)
- ISPE GAMP Validation of Lab Computerized Systems
- NCSLI RP-6 Calibration Control Systems
- ISO 17025 General Requirements for Calibration Labs
- ISO 98 Guide for Measurement Uncertainties
If we follow all the Guidelines, we are guaranteed to be in compliance with the Regulations.

True?

No, False

All Guidelines are fallible.
Jean Piaget was a scientist who in the early 1900's studied the tendency to focus attention on only one characteristic of shape. In particular, he studied the human inability to distinguish identical volumes in different sized containers.

Piaget studied the inability of small children to understand that cylinders with different aspect ratios could have the same volume. Small children have difficulty conceiving the shift in volume from one dimension (say the width of a glass) to another dimension (say the height of a glass). They have difficulty visualizing that there is no more liquid in a tall, slender glass than in the shorter, wider glass. He showed that for certain individuals, this tendency could extend into adulthood.
This is illustrated in the following Figure:

- Shinny Glass
- Wide Fat Glass
The Visual Measure

The tendency is to believe that even though the two glasses have the same volume, the tall, slender glass has more volume because the height of the liquid is greater.

This fact explains why studies show that mixed drinks at bars that use short, wide glasses are typically stronger then the same drink at bars that use tall, slender glasses. The height of a 1.5 oz. shot of alcohol in the short, wide glass is not as high as the same 1.5 oz. shot in the tall, slender glass. When bartenders pour a shot in a short, wide glass they have the tendency to think that since the liquid level is not very high they have mis-poured, and so add a little more alcohol to the drink.

The moral of this study is always get your mixed drink from bars that use short, wide glasses.
The Beer Gauge

This misconception of *relative* volume is what leads us to think that the relatively small top portion of a pint glass could not contain such a large percentage of the total volume. In fact, if beer is poured into a pint glass to about 1/2 inch from the top, *13% of the beer is GONE*.

A pour to about 1 inch from the top of the glass leaves out *25% of the beer*. This is illustrated below, where the "Beer Gauge" is used to indicate the amount of beer missing from the pint glass.
The Beer Gauge

13% of Beer Missing

25% of Beer Missing
Your Bonus

The PCI Logo'd BEER GAUGE!

Use Responsibly
FDA Citations
483s, Warning Letters & Consent Decrees

Disclaimer: All data is from FDA.gov. Data has been estimated based on information reported from FDA. There is no guarantee that this data is all-inclusive, as many reports and results are not listed on the website, and many calibration and maintenance related observations can overlap.
Definitions

483s: A Factory Inspection Form that lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance.

Warning Letters: A letter that notifies regulated industry about violations that FDA has documented during its inspections or investigations.

Consent Decrees: A final, binding judicial decree or judgment memorializing a voluntary agreement between parties to a suit in return for withdrawal of a criminal charge or an end to a civil litigation.
## Frequency of Observations

<table>
<thead>
<tr>
<th>Center Name</th>
<th>FY 2011 # of 483s issued</th>
<th>FY 2012 # of 483s issued</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foods</td>
<td>3827</td>
<td>3057</td>
</tr>
<tr>
<td>Devices</td>
<td>1035</td>
<td>1090</td>
</tr>
<tr>
<td>Drugs</td>
<td>758</td>
<td>787</td>
</tr>
<tr>
<td>Incidental text</td>
<td>422</td>
<td>421</td>
</tr>
<tr>
<td>Bioresearch monitoring</td>
<td>297</td>
<td>283</td>
</tr>
<tr>
<td>Veterinary medicine</td>
<td>289</td>
<td>243</td>
</tr>
<tr>
<td>Biologics</td>
<td>258</td>
<td>237</td>
</tr>
<tr>
<td>Human tissue for transplantation</td>
<td>146</td>
<td>138</td>
</tr>
<tr>
<td>Parts 1240 and 1250</td>
<td>109</td>
<td>110</td>
</tr>
<tr>
<td>Special requirements</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>Radiological health</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>Sum Product Area 483s from System*</td>
<td>7187</td>
<td>6406</td>
</tr>
<tr>
<td>Actual Total in system 483s**</td>
<td>6547</td>
<td>5797</td>
</tr>
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</table>

Source: [http://www.fda.gov/iceci/EnforcementActions/ucm250720.htm](http://www.fda.gov/iceci/EnforcementActions/ucm250720.htm)
### Number of 483’s issued

**Inspections ending between 10/1/2011 and 9/30/2012**

<table>
<thead>
<tr>
<th>Center Name</th>
<th>FY 2012 483’s issued</th>
<th>Calibration Related 483’s</th>
</tr>
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<tbody>
<tr>
<td>Foods</td>
<td>3057</td>
<td></td>
</tr>
<tr>
<td>Devices</td>
<td>1090</td>
<td>7%</td>
</tr>
<tr>
<td>Drugs</td>
<td>787</td>
<td>18%</td>
</tr>
<tr>
<td>Incidental text</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Bioresearch monitoring</td>
<td>283</td>
<td></td>
</tr>
<tr>
<td>Veterinary medicine</td>
<td>243</td>
<td></td>
</tr>
<tr>
<td>Biologics</td>
<td>237</td>
<td>16%</td>
</tr>
</tbody>
</table>
Frequency of Observations

Calibration Related 483's

- Biologics
- Devices
- Drugs
Frequency of Observations

Cleaning and Maintenance Related 483's

2006 2007 2008 2009 2010 2011 2012

- Biologics
- Devices
- Drugs
<table>
<thead>
<tr>
<th>Cite ID</th>
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<th>Long Description</th>
<th>Frqncy</th>
</tr>
</thead>
<tbody>
<tr>
<td>15030</td>
<td>21 CFR 606.60(b)</td>
<td>Equipment calibration frequency</td>
<td>Equipment used in the [collection][processing][compatibility testing][storage and distribution] of blood and blood components is not observed, standardized and calibrated with at least the frequency required.</td>
<td>15</td>
</tr>
<tr>
<td>94</td>
<td>21 CFR 606.100(b)(15)</td>
<td>Schedules and procedures for equipment &amp; calibration</td>
<td>The standard operating procedure fails to include a written description of schedules and procedures for equipment maintenance and calibration.</td>
<td>10</td>
</tr>
<tr>
<td>4425</td>
<td>21 CFR 606.60(a)</td>
<td>Equipment observed, standardized, calibrated</td>
<td>Due to inadvertent temperature exposure Source Plasma was required to be relabeled as &quot;Source Plasma Salvaged,&quot; however, the original label was not covered with [a complete new label containing the appropriate information] [a partial label (with the appropriate new information) covering the incorrect information regarding storage temperature.</td>
<td>10</td>
</tr>
<tr>
<td>9044</td>
<td>21 CFR 600.10(b)</td>
<td>Personnel capabilities</td>
<td>Equipment used in the [collection] [processing] [compatibility testing] [storage and distribution] of blood and blood components is not [observed] [standardized] [calibrated] on a regularly scheduled basis as prescribed in the SOP Manual.</td>
<td>4</td>
</tr>
</tbody>
</table>
## 2012 Calibration Common Observations – Devices

<table>
<thead>
<tr>
<th>Cite ID</th>
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<th>Long Description</th>
<th>Frqncy</th>
</tr>
</thead>
<tbody>
<tr>
<td>3233</td>
<td>21 CFR 820.72(a)</td>
<td>Calibration, Inspection, etc. Procedures Lack of or Inadequate</td>
<td>Procedures to ensure equipment is routinely [calibrated] [inspected] [checked] [maintained] have not been [adequately] established.</td>
<td>52</td>
</tr>
<tr>
<td>3235</td>
<td>21 CFR 820.72(a)</td>
<td>Equipment control activity documentation</td>
<td>Equipment [calibrations] [inspections] [checks][maintenance activities] have not been documented.</td>
<td>13</td>
</tr>
<tr>
<td>3236</td>
<td>21 CFR 820.72(b)</td>
<td>Calibration procedures - content</td>
<td>Calibration procedures do not include [specific directions and limits for accuracy and precision] [provisions for remedial action].</td>
<td>3</td>
</tr>
<tr>
<td>3239</td>
<td>21 CFR 820.72(b)</td>
<td>Remedial action - documentation</td>
<td>Evaluations of out-of-calibration equipment and remedial actions taken were not documented.</td>
<td>3</td>
</tr>
<tr>
<td>Cite Id</td>
<td>Ref No</td>
<td>Short Desc</td>
<td>Long Description</td>
<td>Frqncy</td>
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<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>127421 CFR</td>
<td>211.68(a)</td>
<td>Calibration/Inspection/Checking not done</td>
<td>Routine [calibration] [inspection] [checking] of  [automatic] [mechanical] [electronic] equipment is not performed according to a written program designed to assure proper performance.</td>
<td>69</td>
</tr>
<tr>
<td>435221 CFR</td>
<td>211.160(b)(4)</td>
<td>Calibration - at intervals, written program, remedial action</td>
<td>The calibration of [instruments] [apparatus] [gauges] [recording devices] is not done at suitable intervals [in accordance with an established written program] [with provisions for remedial action in the event accuracy and/or precision limits are not met].</td>
<td>42</td>
</tr>
<tr>
<td>361321 CFR</td>
<td>211.160(b)(4)</td>
<td>Establishment of calibration procedures</td>
<td>Procedures describing the calibration of instruments, apparatus, gauges and recording devices are [not written or followed] [deficiently written or followed].</td>
<td>14</td>
</tr>
<tr>
<td>126121 CFR</td>
<td>211.68(a)</td>
<td>Written calibration / inspection records not kept</td>
<td>Records of the [calibration checks] [inspections] of automatic, mechanical or electronic equipment, including computers or related systems are not maintained.</td>
<td>9</td>
</tr>
<tr>
<td>203421 CFR</td>
<td>211.194(d)</td>
<td>Laboratory equipment calibration records</td>
<td>Laboratory records do not include complete records of the periodic calibration of laboratory [instruments] [apparatus] [gauges] [recording devices].</td>
<td>7</td>
</tr>
<tr>
<td>Cite ID</td>
<td>Ref No</td>
<td>Short Desc</td>
<td>Long Desc</td>
<td>Frqncy</td>
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<td>---------</td>
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<td>------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>9421 CFR 606.100(b)(15)</td>
<td>Schedules and procedures for equipment &amp; calibration</td>
<td>The standard operating procedure fails to include a written description of schedules and procedures for equipment maintenance and calibration.</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>5721 CFR 606.60(a)</td>
<td>Maintain and clean equipment</td>
<td>Failure to [maintain] [locate] equipment used in the [collection] [processing] [compatibility testing] [storage] [distribution] of blood and blood products [in a clean and orderly manner] [so as to facilitate cleaning and maintenance].</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>9077 21 CFR 600.12(a)</td>
<td>Maintenance - completeness</td>
<td>The [manufacturing] [distribution] records [are not legible and indelible] [do not detail the various steps of manufacture of the product].</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>16521 CFR 606.170(a)</td>
<td>Adverse reaction - Maintenance of Reports</td>
<td>Failure to maintain reports of complaints of adverse reactions regarding each unit of blood or blood product arising as a result of [blood collection] [transfusion].</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
## 2012 Maintenance Common Observations – Devices

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<thead>
<tr>
<th>Cite ID</th>
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</tr>
</thead>
<tbody>
<tr>
<td>3226</td>
<td>21 CFR 820.70(g)(1)</td>
<td>Maintenance schedule, Lack of or inadequate schedule</td>
<td>Schedules for the adjustment, cleaning, and other maintenance of equipment have not been [adequately] established.</td>
<td>21</td>
</tr>
<tr>
<td>3235</td>
<td>21 CFR 820.72(a)</td>
<td>Equipment control activity documentation</td>
<td>Equipment [calibrations] [inspections] [checks][maintenance activities] have not been documented.</td>
<td>13</td>
</tr>
<tr>
<td>14721</td>
<td>21 CFR 820.70(g)(2)</td>
<td>Periodic equipment inspections</td>
<td>Periodic inspections of equipment [were not] conducted to ensure adherence to applicable maintenance schedules [were not documented].</td>
<td>5</td>
</tr>
<tr>
<td>3113</td>
<td>21 CFR 820.70(g)</td>
<td>Equipment design and installation</td>
<td>Equipment used in the manufacturing process has not been appropriately [designed] [constructed] [placed] [installed] to facilitate maintenance, adjustment, cleaning, and use.</td>
<td>2</td>
</tr>
</tbody>
</table>
### 2012 Maintenance Common Observations – Drugs

<table>
<thead>
<tr>
<th>Cite ID</th>
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<th>Long Desc</th>
<th>Frqncy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1215</td>
<td>21 CFR 211.67(b)</td>
<td>Written procedures not established/followed</td>
<td>Written procedures are not [established] [followed] for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.</td>
<td>73</td>
</tr>
<tr>
<td>1213</td>
<td>21 CFR 211.67(a)</td>
<td>Cleaning / Sanitizing / Maintenance</td>
<td>Equipment and utensils are not [cleaned] [maintained] [sanitized] at appropriate intervals to prevent [malfunctions] [contamination] that would alter the safety, identity, strength, quality or purity of the drug product.</td>
<td>65</td>
</tr>
<tr>
<td>1177</td>
<td>21 CFR 211.63</td>
<td>Equipment Design, Size and Location</td>
<td>Equipment used in the manufacture, processing, packing or holding of drug products is not [of appropriate design] [of adequate size] [suitably located] to facilitate operations for its [intended use] [cleaning and maintenance].</td>
<td>54</td>
</tr>
</tbody>
</table>

Continued.....
<table>
<thead>
<tr>
<th>Cite ID</th>
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<th>Short Desc</th>
<th>Long Description</th>
<th>Frqncy</th>
</tr>
</thead>
<tbody>
<tr>
<td>430321</td>
<td>CFR 211.67 b)</td>
<td>Written procedures fail to include</td>
<td>Written procedures for cleaning and maintenance fail to include [assignment of responsibility] [maintenance and cleaning schedules] [description in sufficient detail of methods, equipment and materials used] [description in sufficient detail of the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance] [instructions for removal or obliteration of previous batch identification] [instructions for protection of clean equipment from contamination prior to use] [parameters relevant to the operation].</td>
<td>36</td>
</tr>
<tr>
<td>197521</td>
<td>CFR 211.182</td>
<td>Written records kept in individual logs</td>
<td>Written records of major equipment [cleaning] [maintenance] [use] are not included in individual equipment logs.</td>
<td>28</td>
</tr>
<tr>
<td>122721</td>
<td>CFR 211.67(c)</td>
<td>Cleaning/maintenance records not kept</td>
<td>Records are not kept for the [maintenance] [cleaning] [sanitizing] [inspection] of equipment.</td>
<td>19</td>
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</table>
The FDA is issuing a record number of 483s over the past 3 years with more enforcement officers and activity under current administration.

- Give example of 483 or Warning Letter you experienced.
- What was the issue and how did you resolve it?
Calibration
Observations
10. Failure to establish and maintain adequate procedures to ensure that equipment is **routinely calibrated**, inspected, checked, and maintained, as required by 21 CFR 820.72(a).

For example: Your firm continues to use the *(b)(4)* patient simulator, S/N *(b)(4)*, as part of final acceptance testing activities for the ANX 3.0 Autonomic Nervous System Monitor, when the testing equipment manufacturer disclaims in their operating and service manual the use of this product as a certification test instrument for medical devices. Also, a review of the Ansar Master Equipment List revealed that the *(b)(4)* patient simulator required an annual calibration that had not been done.
3. Your firm has failed to calibrate instruments and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met [21 C.F.R. § 211.160(b)(4)].

Two examples of violations of § 211.160(b)(4) are as follows:

a. Your firm does not have an established written program to calibrate/qualify the Perkin Elmer Clarus gas chromatograph (GC) at suitable intervals.

b. Your firm did not calibrate and qualify the Jasco high performance liquid chromatography (HPLC) instrumentation adequately, in that there is no periodic qualification or evaluation of the pump, oven, injector, or detector. The “Use and Calibration of HPLC” procedure does not include criteria to define adequate calibration of the instrument.

Your response indicates that a use, maintenance, and qualification procedure for the GC will be separated from the procedure for the “Determination of (b)(4) and (b)(4) by Gas Chromatography” by March 2012. Additionally, your response indicates that the HPLC procedure will be revised to include operational performance and acceptance criteria by March 2012.
7. Failure to adequately validate computer software for its intended use according to an established protocol, as required by 21 CFR 820.70(i).

For example, upon request for the protocol used during the validation of your firm’s software-controlled audiometer device calibration system, your firm stated that it did not have a pre-established protocol for conducting the validation.

We reviewed your firm’s response and conclude that it is not adequate. Your firm did not submit supporting documentation indicating that it will create a requirement that protocols be used during future software validations. Your firm’s response did not address why no protocol was used during the validation of the audiometer testing equipment software. Your firm’s response also did not include evidence to indicate that a corrective action was implemented or that a systemic corrective action was considered (including reviewing all software validations to ensure that the validations were conducted as required).
8. Failure to maintain adequate calibration procedures that include specific directions and limits for accuracy and precision, as required by 21 CFR 820.72(b).

For example, your firm’s calibration procedure, (b)(4) does not contain specification limits for accuracy and precision. Also, the testing records, (b)(4) do not contain specification limits or a record of the results of calibration testing. Lastly, your firm’s process engineer, (b)(4), however, this specification is not established in your firm’s calibration procedure.

We reviewed your firm’s response and conclude that it is not adequate. Your firm did not submit evidence or supporting documentation to correct the issue of not documenting calibration specifications. Your firm did not provide documentation to indicate that it revised the testing procedure to include specification limits for finished product and that it will begin to maintain records of all calibration results that include specification limits. Your firm’s response did not include evidence to indicate that a corrective action was implemented or that a systemic corrective action was considered.
Failure investigations were not always extended to determine the underlying cause of the problem in order to determine an appropriate implementation of corrective actions. For example:

i) CAPA 15082 was generated to investigate (b)(4) assay value assignment performed using the incorrect calibration reference. Investigation into the causes disclosed that at the time the (b)(4) Calibrator value assignment process was converted from the (b)(4) to the (b)(4) series, the (b)(4) instrument calibration procedures had not been implemented. Corrective actions included update of procedures to ensure proper escalation of failures and document the calibration of records. However, this CAPA was not extended to evaluate the lack and/or inadequacy of established controls and procedures that allowed the transfer of value assignment process to an instrument for which no calibration procedures had been implemented for that specific value. Furthermore, no investigation was conducted to determine the decision of using the previous S-Cal values as the (b)(4) Calibrator instead of the (b)(4) reference (b)(4) as established by procedures and the lack of a planned deviation request in order to depart from the established manufacturing process.
7. Failure to establish and maintain adequate procedures to ensure that all inspection, measuring, and test equipment, including mechanical, automated, or electronic inspection and test equipment, is suitable for its intended purposes and is capable of producing valid results, as required by 21 CFR 820.72(a). For example, your firm was unable to confirm, during the course of the inspection, with documented evidence, that the following equipment was calibrated and routinely maintained:

According to the (b)(4), the equipment required weekly and monthly maintenance. In addition, the catalog indicates that the (b)(4) Your firm has no documentation that preventive maintenance was conducted.

According to the (b)(4) for the (b)(4), the equipment requires weekly, monthly, and annual maintenance and annual calibration of the (b)(4). Your firm has no documentation that preventive maintenance was conducted.
2. Your firm has **failed to calibrate instruments** and recording devices at suitable intervals in accordance with an **established written program** containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met [21 C.F.R. § 211.160(b)(4)]. For example:

a. Several laboratory instruments (i.e., incubator #277, incubator #612, FT-IR spectrophotometer #597, ICP spectrometer #532, atomic absorption spectrophotometer #481, oven #112, and vacuum oven #113) used to analyze various drug components and drug products **were either out of calibration, had not received proper maintenance according to your schedule, or a combination of both**. Five of the seven instruments had no calibration records prior to the start of the inspection.

In your response, your firm states that all annual calibrations and scheduled maintenance will be current and documented, and that your analysts will be trained to comply with SOP 600-G-0050. However, your response only refers to those instruments listed above and does not include a review of all analytical instrumentation to ensure calibration and scheduled maintenance was performed. In addition, your response does not assess the validity of prior analytical test results using instruments that were not calibrated or lacked proper maintenance.
2. Your quality control laboratory has not followed written procedures for testing and laboratory controls designed to assure that the drug products you tested have the identity, strength, quality, and purity they purport or are represented to possess [21 C.F.R. § 211.160(a)(b)(3)(4)].

For example,

b. The calibration program, under SOP-CAL-0000, requires that each instrument must have a written calibration procedure. The inspection found that there is no procedure approved for the calibration of the Fluorimeter used to test your raw material.

We are concerned that the failure to follow established procedures is a repeat violation, also cited during the 2007 inspection.
1. Failure to establish and maintain adequate procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a). For example, the underlying cause of the following non-conformities was not investigated and corrective actions were not identified:

2. Failure to establish and maintain adequate procedures to ensure that all inspection, measuring, and test equipment, including mechanical, automated, or electronic inspection and test equipment, is suitable for its intended purposes and is capable of producing valid results, as required by 21 CFR 820.72(a). For example, your firm was unable to confirm, during the course of the inspection, with documented evidence, that the following equipment was calibrated and routinely maintained:

According to the (b)(4), the equipment required weekly and monthly maintenance. In addition, the catalog indicates that the (b)(4) Your firm has no documentation that preventive maintenance was conducted.
3. Your firm failed to assure that equipment used in the manufacture, processing, packing, or holding of a drug product is of appropriate design for its intended use [21 C.F.R. § 211.63]. For example:

The calibration of thermocouples (TCs) used during the validation of your terminal steam sterilizers is not performed before or after the autoclave cycles. Your response failed to provide data to support that the TCs used during the validation runs are within acceptable calibration range. The calibration of these TCs provides assurance of an accurate reading of the temperature in the sterilizer. Please provide your sterilization cycle summary for all the terminal sterilizers and cycles used by your facility, with the appropriate parameters and conclusion of the data generated.
4. **Failure to calibrate, in accordance with written procedures** and an established schedule, weighing equipment critical for ensuring the quality of APIs.

For example, your firm failed to properly calibrate the *(b)(4)* scale *(b)(4)* within the range of its intended use. Although the *(b)(4)* scale was calibrated to 500mg (0.5g) and underwent daily verifications to 100mg (0.1g), the scale was used numerous times to determine laboratory sample weights as small as 10mg (0.01g).

In your response, your firm provided certification calibration records from your calibration services contractor to address actual use ranges of the balances. **Your response, however, is inadequate because you do not include any information regarding a calibration program to ensure future calibration of balances on a routine basis.**
Employees are not given training in the particular operations they perform as part of their function.

Specifically, there is no documentation of training or instructing laboratory personnel to restrict their usage of balances and scales to "use ranges" as opposed to calibrated ranges and/or manufacturer-suggested ranges.
A similar shimming event occurs on your production line for the knife/cutter, which is used to create a perforation between bags. In this case, shims are measured prior to insertion with an uncalibrated caliper and no record of the event is logged.

According to your Sr. Production Maintenance Mechanic, "Have to maintain perimeter seal, so important not to over-shim. Over-shimming can cause seam issues".
Certain inspection, measuring, and test equipment is not suitable for its intended purposes. Specifically, The Purpose of your firm's most recent revision of Standard Operating Procedure titled Manufacturing Process inspection System (Revision 15, effective 6130/2010), is to "Describe the procedure to perform quality inspections during the manufacturing process." Additionally, at least one Measurement Instruction Sheet is associated with each product lot manufactured by your firm. The MIS sheet details each dimensional measurement that must be checked by your employees to determine whether or not design specifications are met. SOP (b)(4) delineates how your employees are to complete MIS sheets in order to perform in-process acceptance activities for products manufactured by your firm. MIS sheets call for the use of a caliper, micrometer, and/or height gage to routinely perform dimensional measurements for many products manufactured by your firm, including the Continuum hip cup.

Your firm performs in-process acceptance activities after each of these phases. The Continuum hip cup dimensions measured using a caliper, micrometer, or height gage during such in-process activities are as follows: (b)(4)

According to your firm’s management, the calibration specifications and resolution limits for your calipers, micrometers, and height gage are as follows: (b)(4)

As shown above, the measurement precision of your firm’s calipers, micrometers, and height gages is limited by the respective calibration specification. The precision limitations of your measurement instruments do not allow your firm to definitively ensure that design specifications are being fulfilled in 11 of 11 Device History Records reviewed.
After machining the final Continuum hip cup post-diffusion bonding, your firm uses a height gage to verify that the overall cup height is at least \((b)(4)\). According to your firm’s management, your height gages read out to 1/10,000 of an inch (i.e. four decimal places). Suppose the measurement reads 0.8360 inches, and so it is deemed to be within your design specification. However, due to the precision limit of your firm’s height gage, the actual overall cup height may in fact be 0.8350 inches.

**In this situation your firm would incorrectly allow the final Continuum hip cup to “pass” this particular check, as opposed to deeming the part to be a nonconformance per SOP \((b)(4)\).**
The “Sterilization/Depyrogenation Cycle Validation for Various Glass Carboys in Hot Air Oven (b)(4)” document the time REDACTED and temperature (b)(4) of the depyrogenation of glassware.

However, there is no record to document that the device that measures time is calibrated to a reference standard.
On 06/24/10 a request was made for the last performance qualification for the Walk-In Stability Chamber (25/60), calibration of the two front RH and TC (on the left and right inside of the chamber door) with traceability to NIST and NIST certificates. Also requested were all alarm excursions, any unplanned maintenance conducted on the chamber, and the last vendor maintenance conducted back to 01/01/09. On 06/30/10, I was provided a printout of alarms from 08/01/07 to present.

I looked at the RH alarms and there were no alarms from 07/09 to present, only RH excursions from 08/01/07 to 06/10/09. Next QCU said calibrations for the four probes were available for my review. I was provided the four probe calibrations with no certificates of calibration traceable to NIST standards. The request was again made on 06/30/10 for review on 07/02/10.
Maintenance Observations
4. Failure to establish adequate procedures for corrective and preventive action as required by 21 CFR 820.100(a). Specifically, the corrective actions taken in response to CAR 0179 were not effectively implemented. For example, validation was not conducted according to established procedures (as noted in #3 above).

Also, (b)(4) Maintenance Procedure, QUAL-3057, created as part of the corrective action, references a form (QUAL-4045 “(b)(4)” ) which was not being used. Instead, an uncontrolled document “(b)(4)” was being used.
3. Failure to have an adequate **maintenance procedure** to prevent contamination or carry-over of a material that would alter the quality of the API.

For example, the inspection revealed that between August 2010 and August 2011, **at least ten (10) maintenance requests were submitted** as a result of oil leaks detected during manufacturing. This trend of contamination of API with hydraulic oil **indicates an inadequate equipment maintenance program**.

Your response acknowledges continued repairs to equipment for leaking hydraulic oil and states that you repaired the equipment each time a leak was detected. However, your response is inadequate because it fails to explain why your firm continually authorized the use of manufacturing equipment known to be defective. In addition, your response did not provide a prevention strategy to minimize the possibility of future contamination.

In response to this letter you should **provide an evaluation of your entire preventive maintenance program**. Your response should also include an evaluation of all major pieces of manufacturing equipment to determine if they are suitable for the manufacture of drugs. Note that if a piece of equipment requires constant repairs, the maintenance program may not be enough to offset its inadequacy.
5. Failure to establish and maintain schedules for the adjustment, cleaning, and other maintenance of equipment to ensure that manufacturing specifications are met, as required by 21 CFR 820.70(g)(1).

For example, there is no documented schedule for the adjustment, cleaning, and other maintenance of the firm's (b)(4) machine which contains (b)(4)

We reviewed your response and conclude that it is not adequate because your Equipment Maintenance, Repair and Replacement procedure does not provide a required interval for calibrations or checking the film guide and film feed switch. There are examples of conflicting or not clearly defined maintenance requirements such as: the firm’s SOP states that major replacement or upgrade in the machinery calls for recalibration of the part involved, but the major parts are not defined. The SOP also states that the “Air Filter on Compressor needs to be checked every six months, change as necessary,” but it is required to be changed every 6 months on the Maintenance checklist. Additionally, the Maintenance and Repair Record Log does not account for preventive maintenance and calibrations.
7. Failure to establish and maintain adequate schedules for the adjustment, cleaning, and other maintenance of equipment, as required by 21 CFR 820.70(g)(1).

For example, there are **no established maintenance procedures** and **records** for the ultrasonic bath and drying oven in the cleaning and packaging clean room which are used for the final cleaning of implants prior to packaging. The procedures regarding the ultrasonic cleaners and drying oven in, PRD-SOP-17 Operations of Ultrasonic Cleaners and incomplete draft of, PRD-SOP-XX Operation and Maintenance of Drying Oven (Cleanroom), do not define how maintenance will be performed and documented.

We have reviewed your response and have concluded that it is inadequate. According to your firm’s response, the issue of a lack of maintenance procedures for several processes and some equipment has been noted during an internal audit of the facility. At the time of the inspection, the documentation of maintenance procedures for the specific equipment mentioned in the observation had not been completed. Maintenance procedures for all other equipment are currently being written. Your firm’s response is not adequate because you failed to submit documentation that includes evidence of implementation of correction and proposed corrective action. Your firm’s response also does not include a discussion of the cause of the nonconformity.
Failure to establish and maintain adequate schedules for the adjustment, cleaning, and other maintenance of equipment to ensure that manufacturing specifications are met, as required by 21 CFR 820.70(g)(1). For example, the procedure (b)(4) these maintenance requirements are not always documented (b)(4).

The adequacy of your firm’s response cannot be determined at this time. Maintenance Procedure PR 25 and associated forms were revised to identify that all maintenance activities will be documented at time of completion, including signatures and dates of individuals who conducted them. Review of maintenance schedules and records was incorporated into the Internal Audit Schedule. Training was completed on April 30, 2012. A review of all maintenance schedules against the equipment manufacturers’ recommended maintenance guidelines will be performed by October 31, 2012. Maintenance activity logs will be created by October 31, 2012, for each piece of critical equipment to document required activities and their performance. However, no documentation or evidence of implementation of the corrective actions or systemic corrective actions was provided.
3. Failure to have an **adequate maintenance procedure** to prevent contamination or carry-over of a material that would alter the quality of the API.

For example, the inspection revealed that between August 2010 and August 2011, at least ten (10) maintenance requests were submitted as a result of oil leaks detected during manufacturing. This trend of contamination of API with hydraulic oil indicates an inadequate equipment maintenance program.

Your response acknowledges continued repairs to equipment for leaking hydraulic oil and states that you repaired the equipment each time a leak was detected. However, your response is inadequate because it fails to explain why your firm continually authorized the use of manufacturing equipment known to be defective. In addition, your response did not provide a prevention strategy to minimize the possibility of future contamination.
5. Equipment used for compounding of PET drugs is not inspected for suitability immediately before use to ensure proper maintenance has been completed according to appropriate, written procedures [(b)(4)] titled "Synthesizer Unit Maintenance").

Your firm did not provide any supporting information to demonstrate that the **daily, weekly, and monthly maintenance steps have been performed** on the Synthesizer Units 3 and 4 as per written procedure.
5. **Failure to establish and maintain adequate schedules** for adjustment, cleaning, and other maintenance of equipment to ensure that manufacturing specifications are met, as required by 21 CFR 820.70(g)(1). For example:

Although your current Preventive Maintenance Schedule for Equipment and Systems procedure (#432, Rev. 19, Effective April 3, 2011) *identifies a grace period* for (b)(4) preventive maintenance (PM) activities, it does not identify any grace period for (b)(4) activities. The Cleanroom Maintenance Procedure in effect at the initiation of the inspection (#823 Rev. 3) requires a (b)(4) PM for the Medical Manufacturing area (b)(4) inspections were due on May 25, 2011, June 8, 2011, and August 4, 2011, but were not done until May 31, 2011 (6 days beyond due date), June 19, 2011, (11 days beyond due date), and August 8, 2011, (4 days beyond due date), respectively.

The adequacy of your response dated September 15, 2011, cannot be determined at this time because your firm did not submit documentation of training on SOP 423 Preventive Maintenance Schedule for Equipment and Systems, Rev. 20. Your firm performed a root cause analysis, product safety impact analysis for the late PMs which found no impact, and resulted in the following corrective actions: a revised SOP 423 to allow a grace period for (b)(4) inspections; monitoring compliance with these procedures through their internal audit program; and employee retraining on the updated SOPs.
5. Schedules for the adjustment, cleaning, and other maintenance of equipment were not adequately established, per 21 CFR 820.70(g)(1).

For example, your Preventative Maintenance Program procedure, PMP-WI001, requires maintenance records to be maintained for five years; however, your firm was only able to produce records for two years, and those records were incomplete. Furthermore, maintenance activities were not performed in accordance with your Preventative Maintenance Control Plan, PMP-CP-001.

Your response indicates that the preventative maintenance program procedure and preventative maintenance control plan, along with corresponding forms, will be reviewed and revised as necessary. This response cannot be considered as adequate as no revised procedures were provided. Furthermore, your response refers to the corrective actions specified for the management review of the quality system. As stated above, we do not consider that response to be satisfactory.
Maintenance logs for the HPLC unit and dissolution apparatus were requested (b)(4) on 06/22/10.

QC Team leader informed me that maintenance logs are all electronic in (b)(4) but no one in the lab had access. *Records not retrievable.*

Maintenance logs for HPLC unit (b)(4) and both dissolution apparatuses were again requested on 06/24/10.

On 06/24/10, management said that if maintenance was performed on the dissolution apparatuses that it would be written in the Usage logs in the lab.

All Usage Logs were requested from 2007 - 2010 for HPLC unit (b)(4) and dissolution apparatuses (b)(4) on 06/24/10.

Usage logs from 2007 - 2009 were not received as of 06/28/10.
No Quality review was conducted concerning impact on batches that were manufactured during equipment failures. **No maintenance records were completed describing what was done to fix (b) (4) equipment.**

Equipment failures were not trended by Quality to determine the scope of the manufacturing equipment failures and the overall impact on the manufacturing process and products produced. No deviation reports were generated, reviewed and approved by the firm's Quality Control Unit regarding the following manufacturing incidents:
A. For packaging Lot (b)(4) Mylanta Maximum Strength Original Flavor Liquid, consisting of manufacturing batch #s (b)(4) multiple manufacturing deviations occurred as follows: During packaging of (b)(4), the capper machine crashed, and the operator's purged (b)(4) gallons of in-process product. The cooling loop failed and an additional (b)(4) gallons of in-process materials was destroyed. Leaky bottles were also observed by operators.

B. For Packaging Lot (b)(4) Mylanta Supreme RS Cherry Flavor Liquid manufacturing batch #s (b)(4), multiple manufacturing deviations occurred as follows: The line was down for issues with the labeler, no records were available describing the labeler malfunctions, and (b)(4) gallons of in-process materials were purged. In addition, due to a malfunctioning bottle cleaner there were bottles slipping.

C. For Packaging Lot (b)(4) Mylanta Regular Strength Original Flavor Liquid, manufacturing batch (b)(4), multiple manufacturing deviations occurred: The gasket blew off the elbow, the tank was shut down, and in-process materials were drained from the feed line.
Routine Inspection of mechanical and electronic equipment is not performed according to a written program designed to assure proper performance. Specifically,

A. There is no Preventive Maintenance program for the following equipment in (b)(4)
   A. Dissolution Apparatuses (b)(4)
   B. (b)(4) for Rapid Resolution
   C. Autotitrator
   D. Spectrometer

B. There is no preventative maintenance requirements written in (b)(4) for (b)(4).

C. There is no written procedure approved by Quality Control Unit/Quality Assurance describing the firm’s electronic (b)(4) program. For example: (b)(4) SOP for Preventative Maintenance, Quality Notifications, Inventory Control, etc.
D. No written procedure is approved by QA describing Preventative Maintenance tasks and their frequency for completion concerning monthly tasks for the walk-in (b)(4) RH stability chamber. (b)(4) for (b)(4), reads in part:

***RESPONSIBILITY*** The Facilities Group is responsible for maintaining and repairing the Chamber *** The Facilities Group will coordinate all repair work and perform calibrations per the (b)(4) schedule***.

Review of the last (b)(4) of (b)(4) printout for monthly tasks completed were identified in (b)(4) as “confirmed”. According the (b)(4) he gets a work order with the tasks to complete and after he confirms the work order is complete in (b)(4) he throws the work order away. Hence, there is no way in (b)(4) to identify what tasks were actually performed.
E. No written procedure describing the frequency and explicit maintenance checks to be conducted by the manufacturer of the (b)(4) RH stability chamber on a (b)(4) basis.

F. No double signature that verifies preventive and unplanned maintenance entered into (b)(4) is completed and correctly performed. Rather, double signatures indicate that tasks completed were entered into the electronic (b)(4) system versus verification that maintenance was conducted. For example, the (b)(4) RH stability chamber was alarming and out of specification for temperature from 02/06 – 08/10 and again on 2/11/10. A fuse was replaced on 02/08 and 11/10. This emergency entry (b)(4) was written as a (b)(4) and not entered into (b)(4) until 2/18/10 versus on 02/08/10 and 02/11/10 when the problems with the compressor/fuses were observed.
Points to Ponder

• Preventive maintenance on an optimal schedule will decrease downtime, increase production, lower total cost of ownership of equipment and lower costs of production.

• Equipment performance is one of the greatest sources of variation in quality, especially in mature processes. Defined and controlled processes for maintenance are an important part of securing quality and compliance. (As a result, structure to control these processes are increasingly being expected by regulatory agencies.)
Points to Ponder

• Given the above two statements, maintenance enhancements often offer the next best area for productivity gains for a mature organization aiming to compete on value, quality and compliance.

• Producing results from a maintenance organization that meet these high-minded statements then becomes the next challenge. Fortunately, this is an area in which PCI is committed to helping our customers excel. PCI embraces the new best-in-class maintenance management solutions, provides the tools to facilitate improvements and our experienced consultants are a valuable resource to help ensure the success of your new maintenance initiatives.
Final Thoughts...

- 483’s happen everyday
- Staff training/awareness
- Treat deviations as learning tools
Maintaining Calibration Programs – Compliance Perspective

Q & A
THANK YOU

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