Basic Good Laboratory Practice

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Goals

• Outline the concept of Good Laboratory Practice (GLP)
• Provide some specific guidelines applicable to day to day work in the laboratory
• Get you to think about your work with a GLP perspective
Good Laboratory Practice

• FDA has a specific set of regulations governing GLP for studies of interest to them
• This presentation is about GLP in the broader sense of things that improve quality in the laboratory, although many of the concepts apply to FDA GLP
• Under FDA GLP, many occurrences herein of “should” become “must”
Concept

In general, a GLP quality program is designed to ensure that:

• Experiments are conducted according to a well-defined protocol, by qualified personnel, using equipment and methods suitable to the task

• Sufficient, verified documentation exists to reconstruct every aspect of the study performed
Why?

• Have you ever:
  – Realized too late that the samples from your experiment were not collected properly?
  – Found out that analysis methods or equipment in your laboratory provide unreliable results, after you have submitted a paper including those results?
  – Been unable to figure out what exactly was done, when, and by whom at a critical phase of a study?
Can we all agree?

Even if you never do a GLP study for FDA, these kinds of problems are best avoided!

It is a waste of animals, time, and money to conduct experiments that may produce unreliable and possibly invalid results.
What does it mean?

In general, the GLP program should ensure that:

• Experiments are conducted according to a well-defined protocol, by qualified personnel, using equipment, reagents, and methods suitable to the task

• Sufficient, verified documentation exists to reconstruct every aspect of the study performed
Well-defined protocol....

- Unique study number
- Should be available before experiment starts
- Supplemented by Standard Operating and Study-Specific Procedures (SOPs and SSPs)
- All method details included or referenced
- Amendments documented
- Deviations documented
- Test article characterization and handling
- Approval by study director and management
Qualified personnel....

- Importance of the Study Director (SD)
- Organizational chart
- Job descriptions
- Documentation of qualifications and training
- Training program for personnel
- Document that applicable SOPs have been read and that the study protocol has been read/reviewed by study personnel
Suitable equipment and reagents....

- Equipment specification and qualification
- Maintenance procedures and records
- Calibration procedures and records
- Computer systems should be validated

- Reagents should be made, stored and labeled correctly; expired reagents must be discarded
Suitable methods....

• Validated assays – make sure they reproducibly measure what they are supposed to
• SOPs should be reviewed annually to ensure they are current, and also approved by management
• SOPs – usually confidential but may be inspected on site by clients and auditors
• SSPs – study specific procedures, or confidential to a particular client
Verified documentation....

- All entries should be signed/initialed and dated
- Should be dated on day of entry
- All raw data should be archived
- Management should approve all equipment, protocols, procedures as meeting required standards
Reconstruct the study....

- Secure, controlled archives
- Protocol, amendments, deviations
- Procedure documentation (forms)
- Facility documentation
- Equipment documentation
- Raw data
- Document control
- Sample labeling, collection records, chain of custody documentation
- Audits – of the protocol, critical phases, and reports
Example from an FDA audit

Study plan: Receive 50 serum samples and perform a prolactin assay

Audit trail: sample receipt records > freezer logbooks > freezer temperature records > assay validation (precision, LOD, LOQ) > assay reagent receipt & storage > assay QC > pipette calibration and use records > assay data rejection criteria > assay database import records > verification of report data against raw data

Findings: freezer chart malfunctions, out of calibration pipettes in lab, failure to record pipette numbers on assay records
In practice

• Let’s start to develop some GLP habits…
• All personnel have a role to play!
Practical Tips – Recording Data

• Data must be recorded
  – In ink
  – Signed/initialed
  – Dated (unambiguously!) on the date recorded
  – Legible

• Dates:
  – 01/08/2008 – is that Aug 1 or Jan 8?
  – Use 08-Jan-08 or another unambiguous form
Practical Tips – Correcting Data

• When corrections are made to data
  – Original entry should not be obscured
  – A reason for the change should be given
  – The correction should be dated and initialed

<table>
<thead>
<tr>
<th>Animal ID</th>
<th>Body Weight</th>
</tr>
</thead>
<tbody>
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<td>128</td>
<td>50.5</td>
</tr>
<tr>
<td>129</td>
<td>49.4</td>
</tr>
</tbody>
</table>

None  □
None  □
None  □
None  □
None  □  scaled on
None  □
None  □  Hair lost

Date: 08 - Jan - 2008
Recorded by: [Signature]

0 weight recorded incorrectly by [Signature] 8/Jan/08
Practical Tips – Forms

• Forms are a very useful way to record necessary information such as documentation of when and by whom procedures are performed

• Provides a place for all necessary information to help ensure it is all recorded

• If well-designed can make it faster and easier to record the information
# Example

**Experiment #:** AL06045

<table>
<thead>
<tr>
<th>Animal ID</th>
<th>Body Weight</th>
<th>Clinical Signs</th>
</tr>
</thead>
<tbody>
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<td>45.1</td>
<td>None □</td>
</tr>
<tr>
<td>124</td>
<td>50.3</td>
<td>None □</td>
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<tr>
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<td>50.2</td>
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<tr>
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<td>None □</td>
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<tr>
<td>127</td>
<td>48.3</td>
<td>None □</td>
</tr>
<tr>
<td>128</td>
<td>50.5</td>
<td>None □</td>
</tr>
<tr>
<td>129</td>
<td>49.4</td>
<td>None □ Scales on back</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None □ Hair loss on rump</td>
</tr>
</tbody>
</table>

**Date:** 08 - JAN - 2008

**Recorded by:** [Signature]

*CHECK WEIGHT RECEIVED: 47 JAN 2008*
Practical Tips - Specimens

• All specimens should be labeled:
  – Unique label (often an accession #)
  – Unique study number
  – Animal/patient number
  – Date(/time) collected
  – Type of specimen
Practical Tips - Reagents

• All prepared reagents should be labeled:
  – What is the reagent
  – Date of preparation
  – Expiration date
  – Identity of the preparer

• Purchased reagents
  – Date received
  – Date opened

Discard Expired Reagents!
Practical Tips – Chain of Custody

• It is really important to keep chain of custody documentation
  – Test article
  – Samples
  – Critical reagents

• Record
  – Who received it, when, from whom
  – When and where placed in storage
  – Transfer to whom (signature!), when
Practical Tips – Equipment

• At the very least, equipment should have a maintenance and calibration log
• There should be an SOP for each piece of equipment describing periodic maintenance requirements
• Document that equipment functions correctly – e.g. freezer/refrigerator temperature logs, pipette calibration, microCT calibration checks, etc.
Next Steps

- Perform a gap analysis to identify what needs to be done to implement GLP

*What you can do right away:*

- Practice GLP habits in your record keeping
- Document your qualifications and training
- Write SOPs for everything that you do
- Distribute SOPs and document who reads them
- Setup equipment logbooks