Animal Study Considerations

FDA Small Business
Regulatory Education for Industry (REdI)
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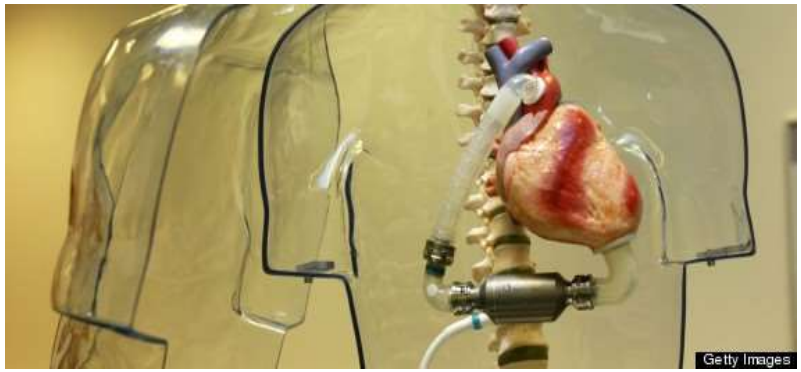
Everybody Dreams of Gold



Overview

- **Why Conduct a GLP Study?**
- **The Six Steps for a GLP Study**
- **Two Tips to Save Time, Money, & Resources**

U.S. FOOD & DRUG ADMINISTRATION

$90,000 ⇨$1,000,000

Cost of a GLP Study

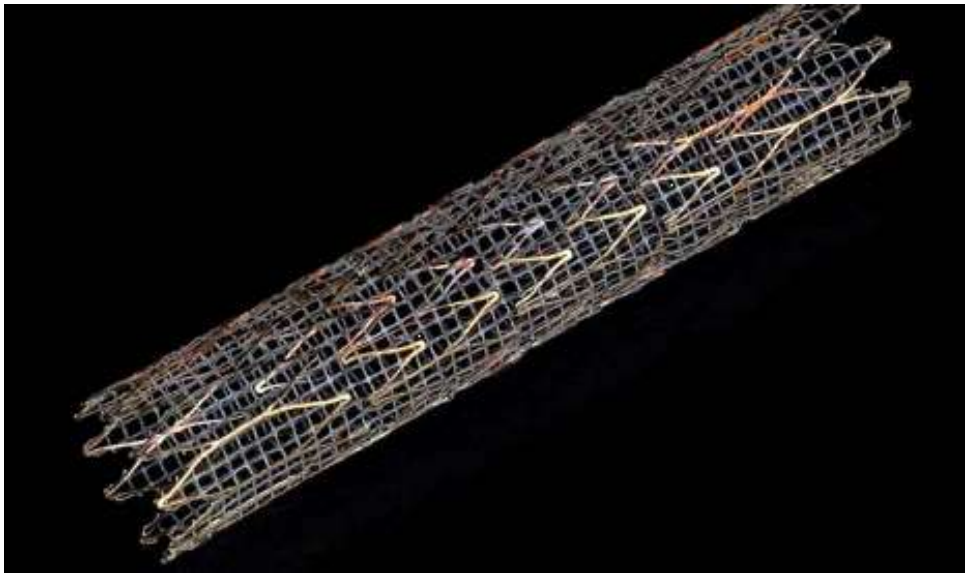
Why Conduct a GLP Study?

- ✓ **Assures that study results are valid and accurate**
  - Requires a detailed signed/dated protocol
  - Test facility appoints a study director
  - Quality assurance ensures the study is conducted in accordance with the protocol and test facility SOPs
- ✓ **Is not an exploratory or pilot study – you should know what to expect**

Complete a GLP Study: 6 Steps

1. Finalize and Lock Device Design
2. Identify Questions of Safety
3. Write the GLP Study Protocol
4. Select the Test Facility
5. Collect and Analyze the Data
6. Write the Final Study Report

Step 1: Finalize/Lock Device Design



Step 2: Identify Questions of Safety

- ✓ **Identify Safety Objectives (Risk Assessment)**

- ✓ **Will data collection require single/multiple sampling time points?**

Step 3: Write the GLP Protocol

Consider the following elements:

- **Proposed IFU Statement**
  - What type(s) of data are needed?
- **Simulate Clinical Use**
  - Clinically Meaningful Study Time Points
  - Selection of the Animal Model
- **Safety Study Objectives**
  - Define Acceptability Criteria
  - Preferably Quantitative Not Qualitative

Step 3: Write the GLP Protocol

Proposed Acceptability Criteria

Safety	1. **XXX device must not be inferior in comparison to control device with respect to procedural complications.** **Inferior is defined as ≥ 5% failure rate when compared to control failure rate.** **Failure in this case is defined as clinical harm.**
	2. XXX device must not have more bleeding events than the control device. **A bleeding event is defined by a fall in hematocrit (HCT) of ≥ 20%.** **Study success is defined as the number of bleeding events with the test device is ≤ the number of bleeding events with the control device.**

Step 3: Write the GLP Protocol

Proposed Acceptability Criteria

Safety	**1. XXX device must not be inferior in comparison to control device with respect to procedural complications.** **Inferior is defined as ≥ 5% failure rate when compared to control failure rate. Acceptable if control failure rate is defined and considered clinically acceptable.** **Failure in this case is defined as clinical harm. Unacceptable as too subjective.**
	2. XXX device must not have more bleeding events than the control device. **A bleeding event is defined by a fall in hematocrit (HCT) of ≥ 20%. Acceptable if considered a clinically acceptable definition.** **Study success is defined as the number of bleeding events with the test device is ≤ the number of bleeding events with the control device.**

Step 4: Test Facility Selection

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This is what matters:

- ✓ **How many similar procedures has the surgeon performed? Volume matters.**
- ✓ **Facility experience – facilities with high success rate tend to have:**
  - Experienced support staff to watch for trouble
  - Experienced support staff that can manage pain
  - The facility's infection rate: should be < 1%.

Step 4: Test Facility Selection

Staffing: Experience and Numbers

- ✓ **Technician number varies with model complexity**
  - **Emergency/critical care background**
- ✓ **Shifts**
  - **Should overlap**
  - **Consider telemonitoring**
- ✓ **Contact Information**

Step 4: Test Facility Selection

Cardiac Xenotransplantation: Telemonitoring and Telemetry

Baboon Recipient Monitored Via Telemetry

Telemetry Data from the Baboon

Step 5: Collect and Analyze the Data

- ✓ **How is the data collected and saved?**
  - What type(s) of case report forms are needed?
  - Are individual animal medical records maintained in a standard, recognized format?
- ✓ **Do key personnel know that they must write reports?**
- ✓ **Does the pathologist have access to the medical records?**

Step 6: Write the Final Study Report

- ✓ **Information specified in 21 CFR § 58.185.**
- ✓ **A Quality Assurance Unit (QAU) statement describing:**
  - Dates the study was monitored
  - Dates findings were reported
- ✓ **Reports from key personnel:**
  - In-life Veterinarian Report
  - Pathology Report

A Poll Question

Which of the Six Steps is most challenging for you?

1. Finalize and Lock Device Design
2. Identify Questions of Safety
3. Write the GLP Study Protocol
4. Test Facility Selection
5. Collect and Analyze the Data
6. Write the Final Study Report

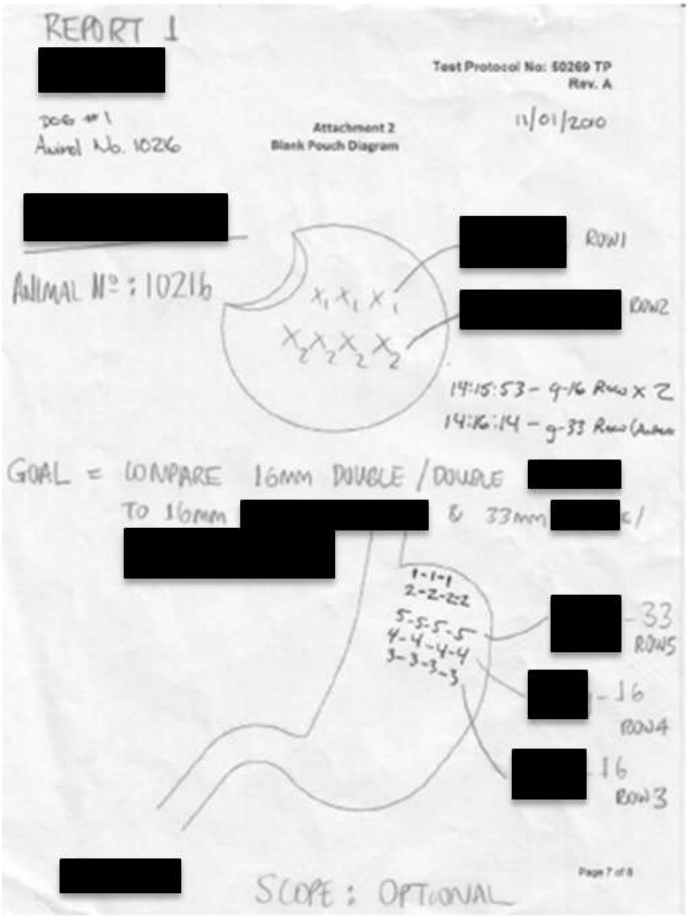
2 Tips to Save Time, Money, Resources

1. **Use the Pre-Submission Process Wisely**

2. **Spend Money Wisely**
   - **Conduct a Comprehensive Risk Assessment**
   - **Conduct Exploratory Animal Studies**
   - **Think "outside-the-box"**
   - **Get what you pay for**

Tip 1: Pre-Submission Process

- ✓ Seriously consider your IFU statement
- ✓ Include a meaningful draft preclinical study outline
- ✓ Ask focused questions
- ✓ Limit Supplements



Tip 2: Spend Money Wisely
Comprehensive Risk Assessment

- ✓ **Guide study design**
- ✓ **Consider device-related and procedural-related risks**
- ✓ **Make sure an experienced clinician is involved**

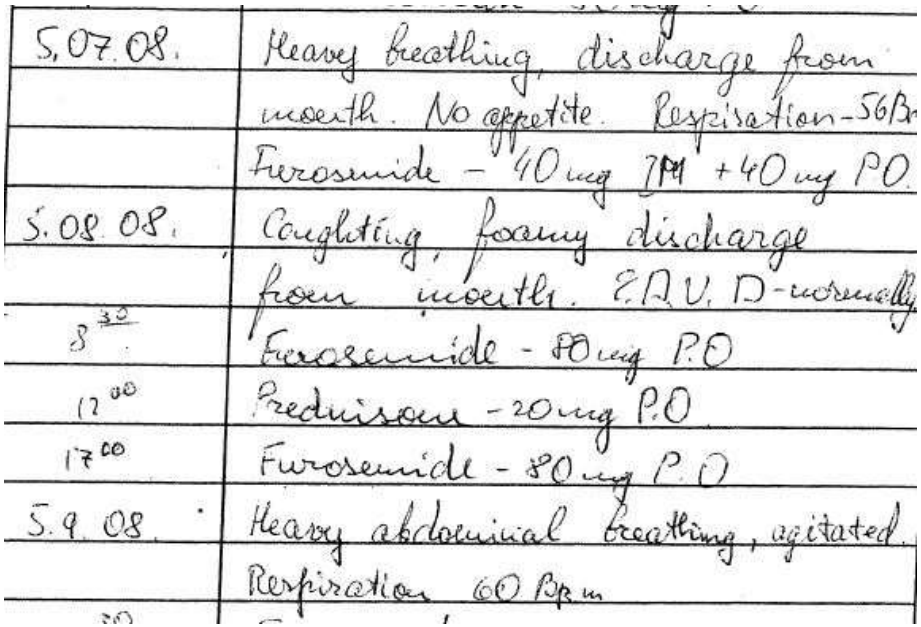
Tip 2: Spend Money Wisely
Conduct Exploratory Studies

- ✓ **Investigate "advantages/disadvantages" of animal models**
- ✓ **Refine implant approach and/or overall study procedures**
- ✓ **Provide an estimate of "variability" of intra- and inter-animal responses**
- ✓ **Verify final device design before GLP studies**

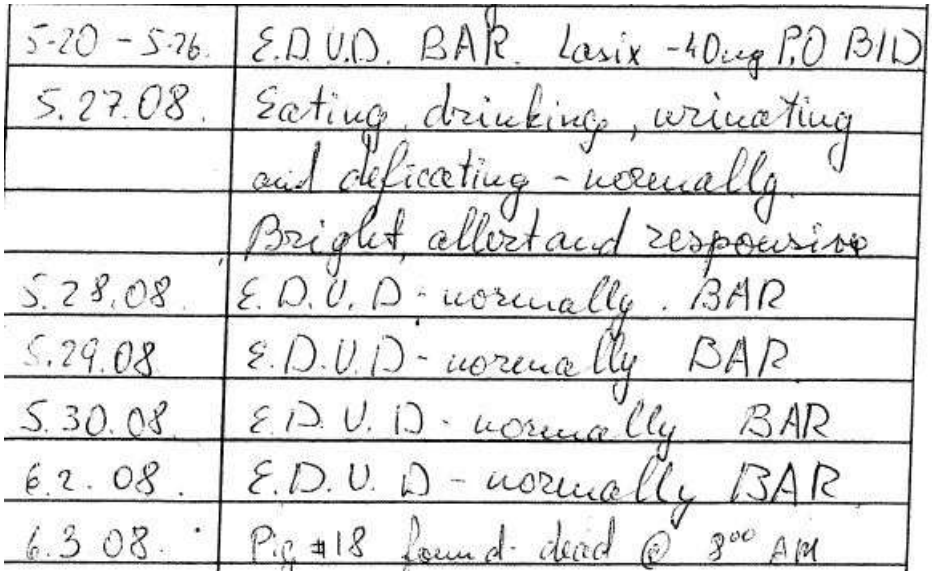
Tip 2: Spend Money Wisely
Think "Outside-the-Box"

- ✓ **Collaborate with the biocompatibility team**
- ✓ **Be cost-effective**
- ✓ **Provide your own equipment and/or expertise**

Tip 2: Spend Money Wisely
Did You Pay for This?

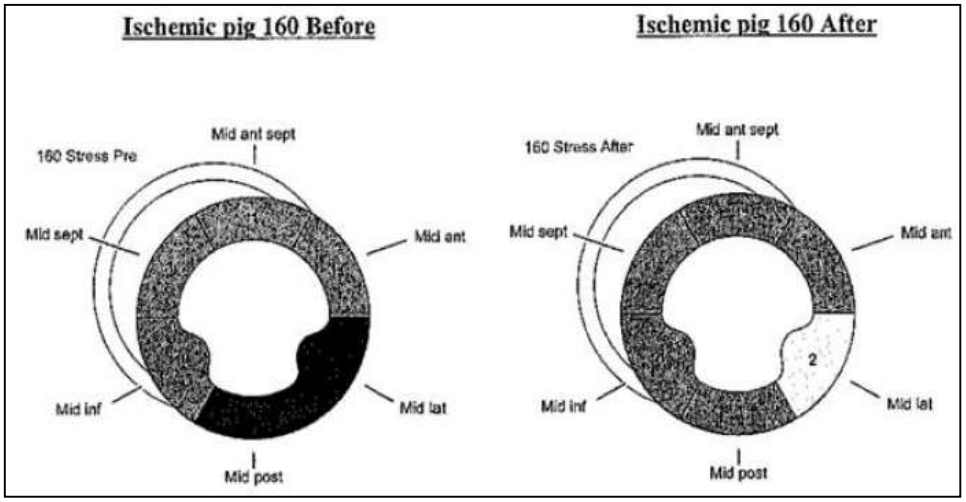


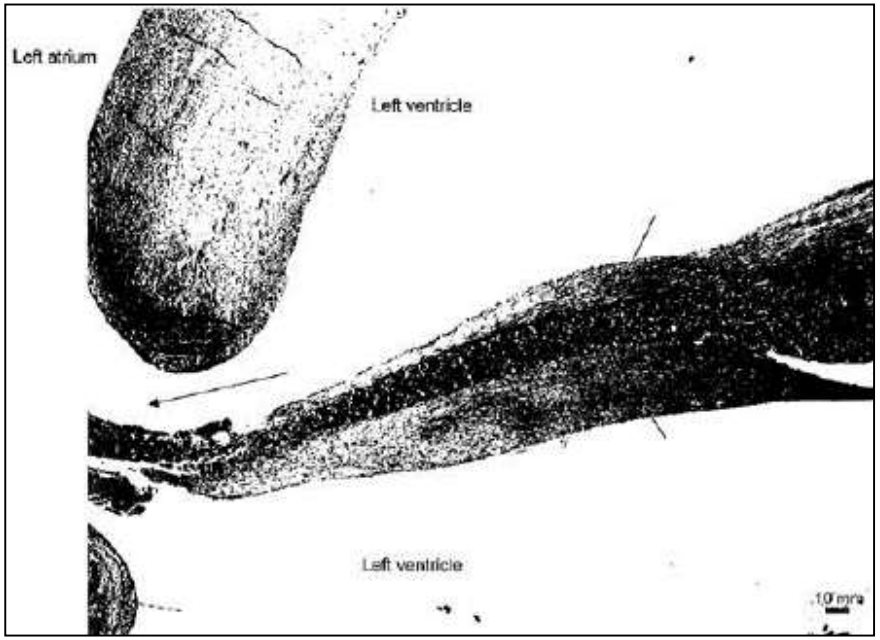
5.07.08.	Heavy breathing, discharge from
	mouth. No appetite. Respiration-56Br
	Furosemide - 40 mg 7PM + 40 mg PO
5.08.08.	Coughing, foamy discharge
	from mouth. E.D.U.D-normally
8[30]	Furosemide - 80 mg P.O
12[00]	Prednisone - 20 mg P.O
17[00]	Furosemide - 80 mg P.O
5.9.08.	Heavy abdominal breathing, agitated.
	Respiration 60 Brpm



5-20 - 5-26.	E.D.U.D. BAR. Lasix - 40 mg P.O BID
5.27.08.	Eating, drinking, urinating
	and defecating - normally.
	Bright, alert and responsive
5.28.08.	E.D.U.D - normally. BAR
5.29.08.	E.D.U.D - normally BAR
5.30.08.	E.D.U.D - normally BAR
6.2.08.	E.D.U.D - normally BAR
6.3.08.	Pt #18 found dead @ 3[00] AM

Tip 2: Spend Money Wisely
Did You Pay for This?





Summary

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Questions

Please complete the session survey:

surveymonkey.com/r/DEV-D1S02

Call to Action

Hallmarks of a successful GLP study include:

- Well-planned; simulates clinical use of the device per the IFU
- Safety objectives address known risks, including performance and handling of the device
- Well-documented, excellent post-procedure monitoring
- Pathology report with all high quality gross and microphotographs
- Copies of all raw data are appended to the final report


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