How Post Approval Monitoring and GLP Quality Assurance Audits Compare

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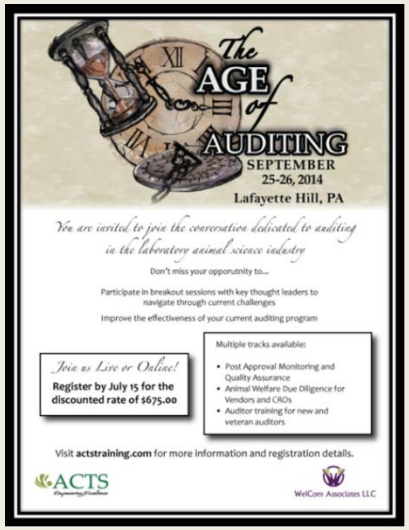

THE AGE OF AUDITING
FEBRUARY 2015

Discussion Topics

- High level discussion of the regulations
  - Animal Welfare
  - Good Laboratory Practice (GLPs)
- Comparison of a Dedicated PAM and QA groups
  - Protocol Review
  - Overall Process
  - Benefits

Why Monitoring/Auditing is Required?

Animal Welfare (AW) Act and Regulations - USDA	Good Laboratory Practices (GLP) Regulations – FDA
SCOPE - All research facilities in the US that use laboratory animals in basic and biomedical research, education and product safety testing – covered species only **Assure Animals are Provided Humane Handling, Care and Treatment**	**SCOPE –** All laboratories conducting non-clinical studies that support or are intended to support applications for research or marketing permits for products regulated by the FDA – all species **Assure Quality and Integrity of Safety Data**
Mandatory animal care committees are vested with oversight responsibility – IACUC **Each Research Facility shall have an Attending Veterinarian (AV)**	**Testing Facility Management (TFM)** **Each study should have a Study Director (SD)** **Assures there is a Quality Assurance Unit (QAU)**

Regulatory Requirements - Roles

AW – Attending Veterinarian		GLP – Study Director
AV has the authority for ensuring adequate veterinary care		Single Point of Control
Each research facility establish and maintain programs of adequate veterinary care • Availability of facilities, personnel and equipment • Methods to prevent, control, diagnose and treat disease and injuries • Daily observations of animals – timely and direct communication with AV • Guidance to PI - handling, anesthesia, analgesia, tranquilization and euthanasia		Approves Study Protocol Data, Observations and Adverse Events of test system are documented Unanticipated study events affecting quality and integrity of study are noted – when and corrective action
Adequate procedural care according to current established veterinary medical procedures		Transfer of all data to archives

Regulatory Requirements - Roles

AW – IACUC	GLP – QA
Every 6 months review program for care and use of animals Every 6 months inspect all research animal facilities	Responsible for monitoring each nonclinical safety study to assure TFM that the facilities, equipment, personnel, methods, practices, records and controls are in conformance with (GLP) regulations
Prepare reports to go to IO Review and investigate concerns involving animal care and use Make recommendations to the IO regarding program, facilities or training	Inspect each study at intervals to ensure study integrity • In-life, process and facility inspections Review study protocols, data and final reports for compliance • GLP regulations & Internal SOPs and Policies
Review and approve or withhold approval of activities related to the care and use of animals - At least Annually continue to review and approve	Submit status reports to TFM

Regulatory Requirements - Roles

IACUC Oversight / PAM	TFM + SD Assures & QA Monitors
• Avoid or minimize pain and distress	• Handling of moribund and dead animals
• PI has considered alternatives	• Test Article and Control Articles
• PI provided written assurance activities are not duplicated in previous experiments	• Maintenance and calibration of equipment • Data handling, storage and retrieval
• Appropriate sedatives, analgesics and anesthesia • Pre- and Post-operative care available	• At start of study animals shall be free of disease • Facility is adequate size and construction
• Euthanasia – when and how • Medical care available and provided as necessary	• **Animals may be treated provided treatment does not interfere with the study**
• Housing, feeding and non-medical care directed by AV	• Housing, feeding, and care of animals
• Personnel are qualified and trained	• Personnel are qualified and trained
Humane Handling, Care and Treatment of Animals	**Quality and Integrity of Data**

Regulatory Requirements - Protocol

AW - IACUC Approves PI Responsible for all Activities		GLP – SD Approves SD Responsible for all Activities
• Species, # of animals		• Species, source, body weight range, age, sex and # of animals
• Rationale for involving animals and appropriateness of species and # of animals		• Description of experimental design, type and frequency of tests or measurements
• Complete description of the proposed use of animal		• Methods to control bias • Statistical Methods
• Description of procedures designed to assure that discomfort and pain to animals will be minimized – use of analgesic, anesthetic and tranquilizing drugs		• Test article ID, dosage, dose volume and frequency of dosing • Dated signature of SD
• Description of Euthanasia Methods		• Records to be Maintained
Humane Handling, Care and Treatment of Animals		**Quality and Integrity of Data**

How We Monitor
PAM & QA

Review Approved Protocols for Compliance

- IACUC/PAM
  - USDA Animal Welfare Act and Regulations
  - The Guide for the Care and Use of Laboratory Animals
  - Public Health Service (PHS) Policy
  - American Veterinary Medical Association Guidelines for the Euthanasia of Animals: 2013 Edition
  - Internal SOPs and Policies

- Study Director/QA
  - **Good Laboratory Practices Regulations - FDA**
  - Compliance Program Guidance Manual
  - Internal SOPs and Policies

How We Monitor
PAM & QA

Observe In-Life Activities

- Observation of animals and procedures
  i.e. Dosing, blood collection, necropsy, euthanasia, surgery, handling and use of controlled substances
- Protocols, Regulations, SOPs, Policies and/or the Guide

Conduct Facility & Process Inspections

- Observation of procedures common to all protocols
  i.e. Analytical process, animal transport, surgery or necropsy
- Tour facility
  i.e. Animal Rooms, HVAC, Surgical Suites, feed/bedding storage and cage wash areas, equipment

Review Notebooks/Data/Records

- Protocol and SOP adherence
- Unexpected events or outcomes are documented
- Appropriate information recorded for recreation of studies
- Training records
- Animal Medical records

Process

PAM	QA
Selection process based on risk • Pain/distress category • perceived USDA scrutiny • Hazardous agents • Novel model/Surgery • Species and # of animals, • Request (i.e. IACUC)	All GLP protocols are selected
Contact Principle Investigator	Contact Study Director
Audit • Protocol • In-life activities • Documentation	Audit • Protocol • In-life activities • Data • Final report
Discussions with support staff Meeting with PI to review observations and Suggestions for Improvement	Discussions with support staff Meeting with SD to review findings
Document Findings & PI provides corrective actions	Document Findings & SD provides corrective actions
Report issued – inform IACUC	Document all inspection & audit dates, when findings were reported to TFM and SD

Benefits of PAM & QA

- Facilitates on-going protocol assessment
- Reduces risk
- Ensures well-being of animals
- Opportunities to refine research procedures
- Measures a program's success
- Illustrates an increased awareness of compliance requirements and inspection readiness
- Simulates regulatory inspections
- Educational opportunities

Positive Outcomes

- **Success** occurs when institutions encourage an educational partnership
- **Trending** –review of audit findings to determine the areas of high risk and areas of improvement
- **Education** – Informing research community of audit trends, best practices, industry standards or changes in regulations or guidelines, company's intent of regulatory interpretation
- **Corrective Action/Preventive Action** (CAPA) – Interactive process research and auditing groups to identify areas of deficiencies and develop a plan for compliance strategies

Consequences

USDA	FDA
Euthanize animals found suffering	
Citations issued	483 issued
Impose civil fines	GLP studies will not be considered in support of an application
Suspend or revoke funding	Authority to disqualify testing facility
Suspend license up to 21 days	

Summary

- Both Programs Ensure and Document
  - Program integrity
  - Compliance with Regulations and Guidelines
  - Adherence to Protocol
- Auditing Skills are Similar and Transferrable
  - The Audit Perspective is Different
    - Animal Welfare or Study Quality and Integrity
    - Different regulations
- How can you integrate Animal Welfare into GLP audits?
- How can you integrate some GLP aspects into Animal Welfare?

Thank you

Questions