Post-Approval Monitoring Program: Pharmaceutical Industry Example

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Merck Frosst Canada, Inc.

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What is an Animal Care and Use Protocol?

- A document submitted by Principal Investigator to the ACC
  - Contains detailed description of the proposed experiment
  - Justifies animal use with the accent on 3Rs
  - Peer-reviewed by scientists, veterinarian and other specialists
  - Reviewed, approved and/or rejected by the ACC
- Approved Protocols are subject to annual review by ACC
  - May be amended/modified subject to approval
  - May be revoked at any time during their lifecycle

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What is Post-approval Monitoring (PAM)?

- A process to ensure program integrity
- Eyes and ears of CCAC (Canadian Council on Animal Care) and our ACC (Animal Care Committee)
- Required by the CCAC by September 2007

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The PAM Team

- Compliance Officer
- Audit Team (Comparative Medicine/researchers)

Role of Compliance Officer

- Coordinate the selection of the approved protocols to be audited by prioritizing the category of protocol and the protocol itself (first protocol)
- Audit 1/3 of the approved ACC protocols (~64) / year
- Training of the auditors
- Coordinate the PAM audit team
- Report to ACC

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The Goals of PAM

- To ensure that our researchers follow the approved protocol (ACC)
- Among other things ensure that :
  - Animal Welfare and well-being are maintained to high standard
  - Researchers are familiar with procedures and endpoints
  - Staff who are performing studies are well trained
  - Safety regulations are adhered to
- Benefits:
  - Increase in self-compliance
  - Continuous refinement of operational procedures
  - Promote best practices in the care and use of animals
- Correct deviations if/when they occur

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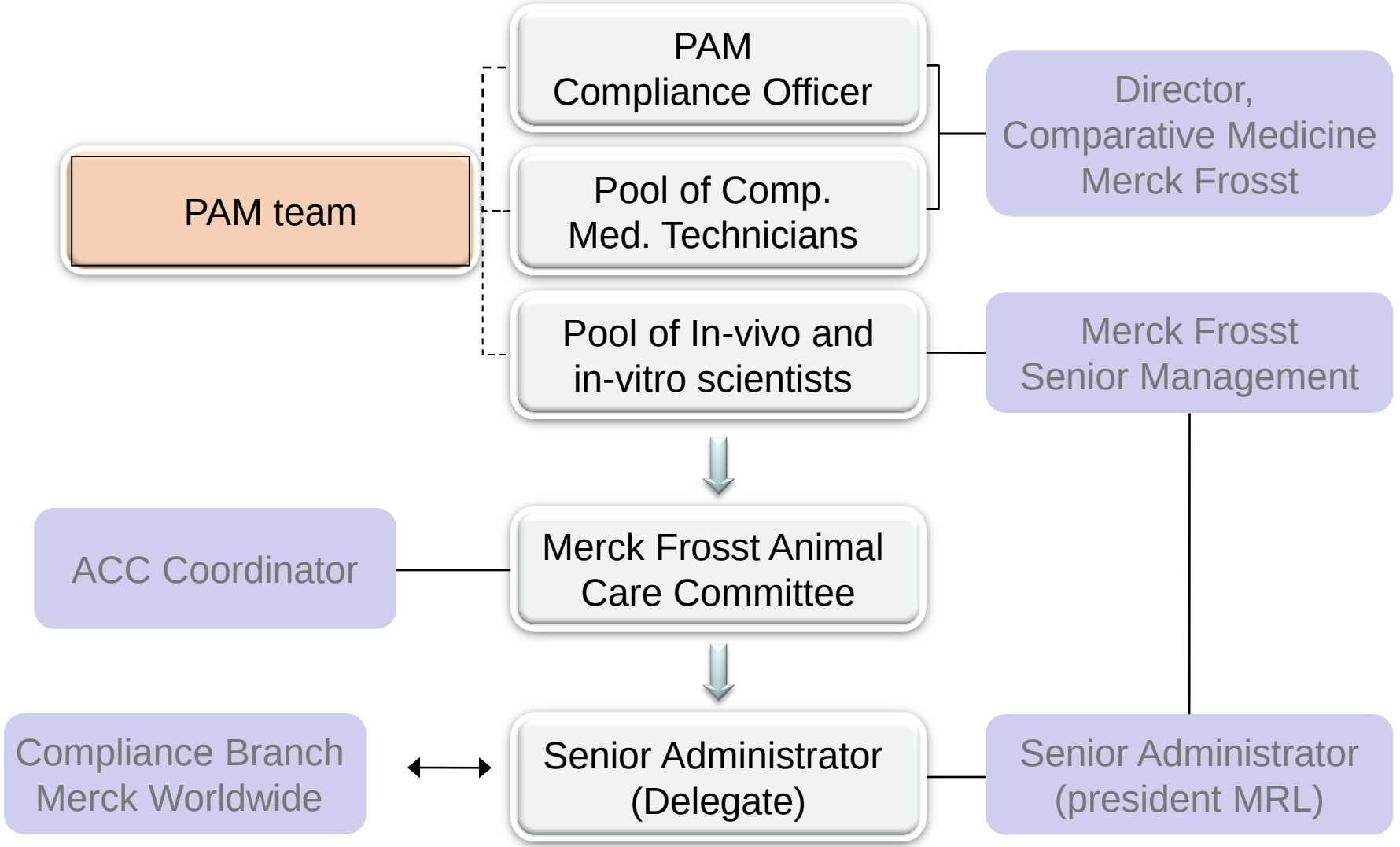
Organizational Structure and Reporting Lines



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Operational Procedure

- The PAM Compliance officer:
  - Selects an appropriate number of approved protocols to review
  - Assigns a 2 member audit team: Lead and Assistant PAM Auditor
  - Other experts (i.e. veterinarians) may be invited as the protocols requires

- The PAM Compliance Audit Team:
  - Sends an e-mail to inform the Principal investigator (PI) and arranges a suitable schedule
  - Reads protocols and other relevant documentation

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Merck Frosst, Montreal
Research Therapeutic Center

Date:

Principal Investigator

SUBJECT: ANIMAL PROTOCOL AUDIT

As you may know, PAM team is performing post approval monitoring of selected protocols throughout MRL-Merck Frosst. [PROTOCOL #] has been selected for review this quarter. In order to monitor for compliance, we will need to meet with you to gain understanding of procedure, data and documents associated with this protocol.

You will be contacted by the Compliance officer, who will set up a meeting with you and your research staff. Prior to this meeting, it is recommended that you review your approved protocol and compare all representations in this document with your current practices. Please provide us the data from a current or ongoing study for our review. The attached protocol audit Checklist will provide a guide to you and your staff as to the specific areas to be addressed.

We anticipate and appreciate your cooperation in this effort to help assure the Canadian on Council animal Care of our continued commitment to the welfare of animals used in research and teaching.

Sincerely,

Stephanie Alleyn
Compliance officer

Operational Procedure (suite)

- The Audit of an Animal Care Committee approved protocol:
  - The PAM audit team, the PI and the in-vivo scientists meet
  - The team assesses the in vivo work, documentation and study protocol and compares it to the ACC approved version using check-list
  - Confirms that the procedures, guidelines and policies are followed

- Reporting by the PAM Audit Team
  - Reviews the finding with the Compliance Officer
  - Categorizes deficiencies and submit findings to ACC for review
  - Inform the PI and his/her supervisor (if deficiencies are found)

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Operational Procedures (suite)

- Follow-up and presentation to the Animal Care Committee
  - PI and his/her supervisor respond to the audit team (if deficiencies are found)
  - PAM audit team writes an executive report summary
  - Report is presented to the Animal Care Committee
  - The PAM audit team performs a follow-up visit (if required by the ACC)
  - Final report and recommendation by the ACC is sent to the Senior Administrator (delegate) and the Director of Comparative Medicine
  - Final report and check- list are archived

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MERCK FROSST RESEARCH LABORATORIES
ANIMAL PROCEDURE STATEMENT AUDIT PLAN

Date of inspection:_____

Building:_____

Principal investigator:_____

Office:_____

Protocol number:_____

Protocol title:_____

Study number:_____

Study dates:_____

Auditors:_____

Animals selected:	
Data reviewed:	
Training records:	
SOP's reviewed:	

Deficiency Categories

- High/Medium Risk Findings
  - There is a real or potential danger or threat to animal welfare and well-being or to the safety of personnel
    - Animal is in pain, analgesic not provided as per protocol
    - End points are exceeded and no action taken
    - Procedures and/or techniques were not approved by the ACC
    - Physical restraint exceeds time limitations specified in protocol
- Low Findings
  - There is no real or potential threat to animals and humans
    - Records incomplete or missing
    - Feeding regimen discrepancy between data and protocol

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Follow up on Deficiencies

- ACC and the Institutional Veterinarian always has the authority to take appropriate action if an animal is in pain or distress
- High/Medium/Low Risk Findings
  - The Principal Investigator and his/her supervisor are notified in writing. Prompt written response are sent to the PAM Audit Team and later submitted to the ACC detailing corrective action, if required
  - If the welfare and well-being of animals and/or safety of humans is compromised with corrective measures difficult to implement, the study may be terminated
  - Repeated offence; in addition to the written response, the Principal Investigator and his/her supervisor must attend the next available ACC meeting to explain the reasons for the deviation and the mechanism put in place to prevent further deviations
- Protocol may be revoked by ACC at any time during its lifecycle
- Merck Frosst ACC institutional appeal mechanism is followed in case of disagreement

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Summary and Conclusion

- The goals of the post-approval monitoring are to :
  - Ensure regulatory compliance throughout Merck Frosst
  - Increase confidence in experimental models
  - Promote animal well-being and safety compliance
  - Assist and support research staff members in an unobtrusive manner
  - Identifies areas where training need to be enhanced
  - Contribute to the continuous refinement of method and practices within Merck Frosst and Merck Research Laboratories

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