

# Animal Research Protocols 动物研究协定

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# Agenda 议程

- What is an animal research protocol and why do we need them? 什么是动物研究协定，我们为什么需要？
- What common items are found in an animal protocol? 动物协定中哪些是常见的条款？
- Common protocol submission issues 常见的协定申报的问题
- Questions? 问题？

## Disclaimers... 声明。。。

- We are not here to tell you what to do! 我们来这儿不是告诉你该做什么!  
!
- We are here to **share** our experiences on IACUCs 我们要来分享和机构动物管理及使用委员会的经历
- **Share** what we look for when we visit Contract Research Organizations (CROs) 分享我们检查合同研究组织 (CRO)时看些什么
- **IMPORTANTLY...**to give you ideas on how improve your animal care and use program 重要的是：为你们如何改进动物管理及使用方案提供建议

# What is an Animal Research Protocol and Why Do We Need Them?

## 什么是动物研究协定，我们为什么需要？

- Concise description of animal study 对动物研究简明的描述
- Agreement (contract) between Principal Investigator (PI) and the Institutional Animal Care and Use Committee (IACUC) 首席研究员 (PI) 和机构动物管理及使用委员会 (IACUC) 之间的协议 (合同)

## United States Requirements 美国的要求

- Review of proposed animal studies involving the care and use of animals is mandated by: 对涉及动物管理及使用的、所建议的动物研究的审查，是强制性的：
  - Animal Welfare Act (USDA) 动物福利法案（美国农业部）
  - PHS Policy 公共健康服务政策
  - *ILAR Guide for the Care and Use of Laboratory Animals (AAALACi)* 实验动物研究院的《实验动物护理和使用指南》（国际实验动物评估和认可管理委员会）

## Protocol Non-Compliance 协定中的违规

- Denied access to animal facility 不允许进入动物设施
- Report findings to federal agencies 向联邦机构报告所发现的
  - May lose funding! 可能失去研究资金
- Lose privileges to work with animals 失去和动物工作的特权
- Lose your job! 丢了你的工作!

## Other Significant Outcomes 其它重要的结果

- Delayed Studies 研究推迟
- Repeat Studies 研究重做
- Produce “bad” data 产生“坏”数据



# Animal Rights 动物权利

# The “Perfect” Protocol “完美的”协定

- Well thought out 经过缜密考虑
- Well written 写得好
- Submitted on time 按时交
- Everyone is happy 人人都高兴

# What Common Items are Found in an Animal Protocol? 动物协定中哪些是常见的条款?

- Protocol Title 协定题目
- Personnel (PI and secondary investigators) 人员 (首席研究员和下属研究员)
- Animal Information (动物信息)
- Study Objectives 研究目的
- Rationale for Animal Use 动物使用的理由
- Husbandry Requirements 饲养要求
- Experimental Design and Animal Procedures 实验设计和动物操作
- Surgery 手术
- Anesthesia/Analgesia 麻醉/镇痛
- Endpoints 终结点
- Pain and Distress Classification 疼痛和痛苦分类
- Alternatives 替代
- Disposition of animals 动物处理
- Hazardous Agents 危险试剂
- PI Assurances 首席研究员的保证

## Protocol Title 协定题目

- Focuses IACUC on what the study is about 向IACUC 突出到底研究什么
- Clear and concise 清楚而简明
- Species 物种
- Spell out acronyms (e.g., SC, IM, BOT, MRI, etc.) 全拼出缩写 (如 SC, IM, BOT, MRI等)

## Personnel 人员

- Principal Investigator 首席研究员
  - Ultimately responsible for study conduct 对研究行为最终负责
- Study personnel (secondary investigators) 研究人员（下属研究员）
  - Read and follow protocol 阅读并遵守协定
- Contact Information 联系信息
  - Discuss issues 谈问题
  - Emergency procedures 应急预案
- May provide relevant employee background information 可能向相关人员提供背景信息

## Animal Information 动物信息

- Species (common name and/or scientific name) 物种 (常用名和/或专业名称)
  - Monkey vs Cynomolgus (*Macacca fascicularis*) 猴子 对 食蟹猴 (*Macacca* 食蟹猴)
- Strain name 品系名
  - Use correct strain names! 使用正确的品系名!
    - Is it a C57/BL6? Or C57BL/6? Or C57bl6? Or B6? 是C57/BL6? 或 C57BL/6? 或 C57bl6?
    - Give a reference 提供参考
- Number of animals requested annually or every 3 years 每年或每3年需要使用的动物数量

## Study Objectives 研究目的

- Why is this study important? 这个研究为什么重要?
- What is the purpose? 什么目的?
- What are the benefits? 哪些收益?
- Describe in lay person terms 用大众的语言描述

## Rationale for Animal Use 使用动物的理由

- Why must a specific species be used? 为什么必须用某个物种?
- Can a lower species be used? 可以用低一点的物种吗?
- Animal number justification 动物数目的理由
  - Statistics 统计学
  - Historical data 历史数据
  - Group size 组的大小

# Husbandry Requirements 饲养要求

- Special diets: name the diet; who provides it 特殊饮食：名称；谁提供
- Special water: name agents added to water; who will provide it; frequency given; special handling, labeling, disposal, etc. 特殊饮水：水的添加剂名称；谁提供；特殊的处理，标记，处置等
- Fasting: arrangements, duration, frequency 禁食：安排，时限，频率
- Special housing: metabolism caging; altered light cycles, etc. 特殊住宿：代谢笼；改变的光照循环等

# Husbandry Requirements 饲养要求

- Enrichment 生活丰富
- Special handling of caging 笼子的特殊处理
  - Exposed to chemotherapeutics, infectious diseases, isotopes 接触到化疗剂，传染病，同位素

# Experimental Design and Animal Procedures

## 实验设计和动物操作

- Provide details on how study is conducted; tells a clear, concise story of all nonsurgical procedures that will occur (e.g., study design) 提供开展实验的细节：描述一个清楚、简明的所有要发生的、非手术步骤的事情（如，研究设计）
- Give sequence of when procedures will be performed 要进行的步骤按顺序描述
  - Day 0: animal are injected with.... 第0天：动物注射了..
    - Dose, route, volume, frequency 剂量，方式，体积，频率
  - Day 3: Animals are bled 第3天：动物采血
    - Route used, amount to be collected; frequency 方式，收集量，频率

# Experimental Design and Animal Procedures

## 实验设计和动物操作

- Day 7: animals are euthanized 第7天：动物安乐死
  - Method of euthanasia 安乐死方法
  - Euthanized then samples collected 安乐死后样品收集
  - Anesthetized, then perfused, exsanguinated, etc. 麻醉，然后灌注， 放血/抽血

# What Common Items are Found in an Animal Protocol? 动物协定中哪些是常见的条款?

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# Surgery 手术

- Location, personnel performing surgery 地点，手术操作者
- Clear concise description of surgery, species, preparation of surgical site 手术的简明描述，物种，手术地点准备
- Aseptic procedures (use of surgical gloves, masks, sterile instruments, area) 消毒过程（用手术手套，面罩，无菌器皿，地方）
- Major objective procedures on non-rodents only conducted in facilities intended for that purpose 非啮齿类动物大的操作只能在专为此目的设计的设施进行
- Multiple major survival surgeries require scientific justification and approval by IACUC 大的多次存活手术必须有科学理由和IACUC的同意

# Surgery 手术

- Pre-, peri and post-operative care 手术前、中、后护理
  - Anesthetics, Analgesics 麻醉, 镇痛
  - Monitoring equipment 监控仪器
  - Frequency of monitoring and by whom 监控频率及人员
  - Expected signs of pain/distress 预期的疼痛/痛苦的症状
  - Removal of sutures/staples 缝线/钉的拆除
  - Antibiotics 抗生素
  - Documentation in animal medical record 在动物医疗记录中登记

## Non-Survival Surgery 非存活手术

- Level of aseptic technique to be used 使用的无菌技术的层次
  - It may not be a requirement for experiment 也许实验不需要
  - It may be a requirement of experiment to have sterile collection of tissues 也许实验要求在无菌条件下收集组织
  - IACUC policy IACUC的政策
- “Clean” technique “干净”技术
  - Different level of Personal Protection Equipment (PPE) worn 不同层次的个人保护设备的穿戴
    - Face mask, clean lab coat 面罩，干净的实验大褂
    - Non-sterile gloves 非无菌手套
  - Animal Preparation 动物保护
    - May not require shaving or prepping prior to surgical procedure 也许手术前不需要给动物剃毛

## Pain and Distress 疼痛和痛苦

- Describe procedures designed to minimize pain/distress 描述为将疼痛和痛苦降至最小而设计的步骤
- Monitoring of animals 动物监测
  - Frequency of monitoring 监测频率
    - Weekdays, weekends, holidays 平日，周末，节假日
  - Written observations/treatment records 书面的观察/治疗纪录
  - Responsible personnel 责任人

## Pain and Distress 疼痛和痛苦

- IACUC guidelines, literature, previous studies. Define “Endpoints”  
IACUC的指导，文献，过去的研究，定义“终结点”
  - Diarrhea or vomiting – duration 腹泻和呕吐—持续时间
  - Cachexia – duration 恶病体质—持续时间
  - Dehydration 脱水
  - Abnormal postures 异常姿势
  - Tumor size criteria or ulcerations 肿瘤大小标准或溃疡
  - Loss of 20% body weight over a specific time 一段时间内失去20%体重
  - Not eating or drinking 不吃不喝
  - Non-responsive or increase vocalization 无反应和叫声增加
  - Licking, biting, scratching of area (i.e. surgery site)  
舔，咬，挠某些地方（如，手术伤口）

## Alternatives 替代方案

- Principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to animals  
首席研究员考虑过可能导致动物超过瞬间的、较轻微的疼痛或痛苦的替代方案
- Principal investigator has provided written assurance that activities do not unnecessarily duplicate previous experiments  
首席研究员提供书面保证，表示活动不是不必要地重复以前的实验

## Alternatives 替代方案

- Why must alternatives be considered? 为什么必须考虑替代方案?
  - To ensure effective use of the most appropriate research model using the most advanced techniques 为了确保最有效地利用适当的研究模型及最先进的技术
  - Required by Animal Welfare Act 动物福利法案的要求
  - Required by ILAR *Guide* 国际实验动物评估和认可管理委员会《指南》的要求
  - To satisfy public concerns over use of animals 满足公众对过度使用动物的关心

## Alternatives 替代方案

### • The “3 Rs” 三个“R”

- Replacement 替代
- Reduction 减少
- Refinement 优化

## Disposition of Animals 动物的处置

- Euthanasia 安乐死
- Transfer to another IACUC- approved protocol 转移至另一个IACUC批准的协定
- Necropsy (tissue collection) 尸体剖检（组织收集）
- Return to colony then reused after specific washout period 在特定的洗脱期后，回归种群

# Euthanasia 安乐死

- Provide all methods 提供所有的方法
- Ensure compliance with current AVMA Guidelines on Euthanasia or local regulations 确保遵从当前的美国兽医协会对安乐死的指导或当地的法规
  - Provide justification for deviations 对偏差提出理由
- Physical methods 物理方法
  - Examples 举例
    - Cervical dislocation 引颈
    - Decapitation 斩首
  - Provide rationale for withholding drugs 提供不给药的理由
  - Method to ensure death 确保死亡的方法

# Hazardous Agents 危险试剂

- Radioisotopes 放射性同位素
- Chemical hazards (e.g. chemotherapeutic agents, compounds, etc.) 化学危险 (如, 化疗剂, 化合物等)
- Biohazards (e.g. human cell lines, human tissues, infectious agents) 生物危险 (如, 人细胞株, 人的组织, 传染物)
- Carcinogens (e.g., paraformaldehyde) 致癌物 (如, 多聚甲醛)
- Recombinant DNA 重组 DNA
- Provide special handling instructions for animals, caging and equipment, and other special precautions, signage 提供动物特殊处理的指示, 笼子和设备, 及其它特别的预防措施, 标识

## PI Assurances 首席研究员保证

- Requirements of all investigators working on the protocol: 对在这个协定下工作的所有研究员的要求
  - Read and follow the protocol 阅读并遵循协定
  - Perform only *in vivo* procedures in which proficiency has been achieved and documented 当达到熟练程度并有记录后才能进行体内实验操作
  - Keep protocol current (i.e. amendments!) 保持协定的当前性（即，修正文件）
  - Participate in the occupational health & safety program 参加职业健康与安全方案

## Common Protocol Submission Issues

### 常见的协定申报的问题

- Have not completed all sections 没有完成所有部分
- Inadequate alternatives search or not included 替代方案的寻找不充足或没包含
- Procedures not written in clear, understandable manner 步骤没有用清晰易懂的方式写出
- Improper drug dosages, volumes, routes of administration 不合适的药物剂量，体积，给药方式
- Inadequate information on personnel qualifications 人员资质信息不全
- Forget to submit personnel changes (add new personnel) 忘记提交人员更迭（加入新人）
- Forget to submit amendments for changes to project 忘记提交项目改变的修正附件

Questions ???????

问题? ? ? ? ? ?