



中国医学科学院-苏州系统医学研究所

Institutional Animal Care and Use Committee

IACUC Guideline # 116.00

- 标题 TITLE :** 动物实验方案的审核标准. Review Criteria of Animal Protocol.
- 目的 PURPOSE :** 指导研究所内动物使用与实验活动的《动物实验方案》的审批规范化、标准化。To facilitate compliance with applicable laws, regulations and policies consistent with the performance of appropriate and productive scientific endeavors.
- 职责 RESPONSIBILITY :** IACUC 委员会. IACUC Committee
- 审核、修订 REVIEW/REVISIONS :** 如有需要 IACUC 负责审核及修订本. SOP IACUC Office Staff will review and revise this SOP as needed.
在 IACUC 委员会批准后执行. Implementation will proceed upon approval of IACUC Committee.

流程 PROCEDURE :

一、替代方法 Alternatives – Replacement, Reduction and Refinement

3R 原则 The “3 Rs”

1. 代替，或使用非动物模型 Replacement, or utilizing non-animal models;
2. 减少使用数量 Reduction of numbers of animals used; and
3. 精化，消除或减少动物痛苦和不安 Refinement, or elimination or reduction of unnecessary pain and distress in animals.

二、安乐方法 Euthanasia

采用的安乐死方法取决于动物品系，年龄，保定状态以及操作人员的技术。方法必须与研究目的相符合。The choice of a method depends on species, age, availability of restraint, skill of the individuals performing euthanasia and other considerations. In a research setting, the method of euthanasia must be consistent with the research goals.



推荐方法的标准：

- 最小程度的痛苦、不安、焦虑或恐惧 minimum pain, distress, anxiety or apprehension;
- 尽快失去知觉 minimum delay until unconsciousness;
- 可靠且不可逆 reliability and irreversibility;
- 人员安全，情感允许 safety of personnel; emotional effect on personnel;
- 与要求和目的兼容，包括组织的后续使用 compatibility with requirement and purpose, including subsequent use of tissue;
- 品种间、年龄间以及健康状态兼容 compatibility with species, age and health status; and
- 药物可实现且避免人员滥药风险 drug availability and human abuse potential.

推荐方法：

AVMA Guidelines for the euthanasia of Animals 2013

可使用的方法 Acceptable：

- 戊巴比妥那 Barbiturates (most species)
- 二氧化碳 Carbon dioxide (CO₂)-bottled gas only (most species)
- 吸入麻醉 Inhalant anesthetics (most species)
- 微波辐射 Microwave irradiation (mice and rats)
- 硫酸三卡因甲烷 Tricaine methane sulfate (TMS, MS222) (fish, amphibians)
- 盐酸苯佐卡因 Benzocaine hydrochloride (fish, amphibians)
- 栓钉贯穿 Captive penetrating bolt (horse, ruminant, swine)
- 乙醚或一氧化碳 Ether and carbon monoxide are acceptable for many species, but relatively dangerous to personnel.

条件使用方法 Conditionally Acceptable (IACUC 要求科学理由 Requires IACUC Approval of Scientific Justification)：

- 脱颈 Cervical dislocation (鸟类，小啮齿动物和兔子 birds, small rodents and rabbits)
- 断头 Decapitation (鸟类，小啮齿动物 birds, rodents, some other species)
- 脑脊髓刺毁法 Pithing (冷血动物 some ectotherms)
- 其他药物及物理方法 Various pharmacological and physical methods

禁用方法 Unacceptable：



- a. 水合氯醛，氯仿和氰化物 Chloral hydrate, chloroform and cyanide
- b. 降压药 Decompression
- c. 神经肌肉阻断药 Neuromuscular blockers
- d. 其他药物及物理方法 Various pharmacological and physical methods
- e. 干冰 Dry ice-generated CO₂

三、人道终点 Humane Endpoints

PHS Policy and AWRs 陈述对于会引起动物暂时或轻微疼痛及不安的操作需要使用适当的镇静镇痛及麻醉药品。The *PHS Policy and AWRs* state that procedures that cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia.

实行人道终点 Developing Humane Endpoints

濒死情况的人道终点 Moribund Condition as a Humane Endpoint

其他科研中人道终点的 Other Humane Endpoints in Research

毒性试验 Toxicity Testing

死亡终点 Death as an Endpoint

四、最小化痛苦和不安 Minimization of Pain and Distress

IACUC 有责任慎重考虑方案中潜在的会引起动物疼痛及不安的因素并考虑如何实现动物的基本福利。It is the responsibility of the IACUC to critically evaluate all research protocols for the potential to cause pain or distress and assess the steps that are to be taken to enhance animal well-being.

- 适当的止痛、镇痛及麻醉措施 appropriate sedation, analgesia, and anesthesia;
- 及时干预或安乐处于试验中承受痛苦及不安的动物的措施 criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and
- 关于术后护理的详细措施 details of postprocedural care.

实验动物方案必须列出动物实验缓解动物的疼痛及不安的措施的详细信息以供 IACUC 审核。涉及重复给药的实验，要求明确的标准。如有任何可能引起动物短暂疼痛和不安的潜在因素，都应提前咨询兽医意见。The protocol must provide adequate information for the IACUC to assess the potential animal pain and/or distress resulting from the study and the effectiveness of the pain- and distress-relieving agents proposed for use. Criteria for re-dosing the animal should also be established. The AV must be consulted for any procedure that has the potential to cause more than



momentary pain or distress.

例如 Examples of procedures which the Guide suggests may have the potential to cause pain or distress, include:

- 保定 physical restraint,
- 存活手术 survival surgeries,
- 一是饮水限制 food or water restriction,
- 处死 death as an endpoint,
- 伤害性刺激 noxious stimuli,
- 皮肤或角膜刺激性实验 skin or corneal irritancy testing,
- 肿瘤实验 tumor burdens,
- 心脏或眼眶采血 intracardiac or orbital sinus blood sampling, and
- 环境异常实验 abnormal environmental conditions.

使用一些合适的有根据的参数和观察方法作为评估项目是非常有必要的。It is necessary to use objective assessments, which means choosing appropriate parameters and quantifying observations.有很多评分模型以供参考。 Numerous models for scoring pain and distress have been published and involve assigning a numeric score to observations with the aid of descriptors. 可以以一些基本的指标作为起步开始制定评估标准，如体重变化，外观、姿态以及无故、诱因行为。之后，评估体系可以印实验项目而修改，更加符合特殊研究。It is often useful to start with a general set of observations for assessing pain and distress such as change in body weight, physical appearance/posture or changes in unprovoked and provoked behavior. The assessment system should then be modified on a case-by-case basis using specific changes that may be anticipated in a particular study.

五、人员资格 Personnel Qualifications

IACUC 需要评估进行实验操作的人员是否有足够的资质并且接受了足够的培训以开展实验操作。The IACUC should assess whether personnel conducting procedures are appropriately qualified and trained in those procedures (IV.C.1.f and 2.31(d)(1)(viii)). 类似的要求见于指南以及美国政府政策第三部分（附件）。A similar requirement can be found in the *Guide* and in U.S. Government Principle VIII (see Appendix).



1. 指南的细化 Developing Guidelines

为了方便评估人员资格和培训水平，IACUC 需要制定一份评估的项目清单，以及参加此类培训的人员的分类列表。To facilitate evaluation of personnel qualifications and training during protocol review, each IACUC should develop a list of items to be assessed as well as a list of classifications of personnel required to participate in such training. 可以是一份根据流程或操作目的所要求的资格和培训项目的清单，或涵盖该机构培训要求的方方面面的清单（详见人员培训指南）。This could be a list of qualifications and training items specific to protocols according to procedures and or manipulations proposed or the list could be broad enough to cover all aspects of the institution's training requirements (see Section Training for members).

系统所人员评估流程中评估项目包括 A procedure specific checklist of ISM include:

- 熟练掌握操作相应种属动物的技能 proficiency in handling specific specie(s),
- 熟练掌握缓解疼痛的方法 proficiency in pain-relieving methods,
- 熟练掌握手术操作 proficiency in surgical manipulations,
- 熟练掌握无菌操作 proficiency in aseptic techniques,
- 熟练掌握痛苦管理 proficiency in pain management,
- 熟练掌握安乐方法 proficiency in euthanasia,
- 熟练掌握术前术后照料 proficiency in pre- and post-operative care,
- 毒品或药品管控执照 Drug Enforcement Administration (DEA) license, and
- 安全部门的检查审批 approval by safety office.

为满足动物方案审查，除以上内容意外，还有一个清单包含以下内容 A checklist of institutional requirements that need to be satisfied as a component of protocol review might include the following in addition to those above:

- 完成职业健康安全风险评估 completion of occupational health and safety risk assessment,
- 相关规章制度的描述 demonstrated knowledge of relevant rules and regulations,
- 参与职业健康安全计划 enrollment in occupational health and safety program,
- 参加合规培训部分 attendance at compliance training session, and
- 观看安全培训视频 viewing of safety training video.

资格评估、培训评估所针对的人员为 Classifications of employees whose qualifications and training



may require assessment include:

- 研究员 investigators,
- 研究技术员 research technicians,
- 动物饲养人员 animal husbandry personnel, and
- 兽医及兽医技术员 veterinarian and veterinary technicians.

IACUC 需要明确的是，所要求的研究人员的培训水平并不是日常的照料动物。An important decision to be made by the IACUC is the level of training required of an investigator not actually involved in the day-to-day manipulation and care of the animals. 如果一名研究人员负责的研究项目涉及动物，他是否如上所述足够专业，是否可以培训其他研究成员。If the investigator is responsible for the research activity and the animals involved, should she or he demonstrate proficiency in the areas indicated above? Is the investigator responsible for training personnel in the lab? 如果是，如何证明，这些需要 IACUC 有明确的政策以避免后续的矛盾。If yes, should she or he demonstrate proficiency in those areas? An IACUC policy on this issue will prevent conflict later.

2. 资格和培训水平评估 Evaluating Qualifications and Training

为避免方案审核过程中出现人员资格以及培训评估的问题，IACUC 可以确定在方案制定以及兽医提供咨询过程中应需要的培训。To prevent problems related to assessment of qualifications and training during protocol review, it is helpful if the IACUC determines any training needs during the protocol development and veterinary consultation. 对新技术、规程或操作的讨论，可以为兽医人员和研究人员提供培训机会，使他们在方案审核之前完成熟练的操作的培训。Discussion of new techniques, procedures, or manipulations at this time can provide the impetus for a training opportunity for both the veterinary staff and the research staff with demonstrated proficiency completed prior to protocol review. 这种培训需要被记录在方案中或被保留记录 This training experience should be so noted in the protocol or otherwise documented.

设施内部人员的培训记录的保留有助于人员资质及培训的评估。Maintaining a database of all participants in the facility's training program who use laboratory animals will facilitate assessment of qualifications and training. 有了这些数据，专业人员的初步评估可由 IACUC 或指定人管理完成。With such a database, preliminary evaluation of an individual's expertise can be an administrative task performed by the IACUC or staff assigned to assist with managing the animal care program. 如果出



现不足，后续备忘将被发送至研究员告知其审核的方案暂停，直到相应的培训完成。If a deficiency is noted, a follow-up memo can be sent to the investigator stating that protocol review is pending until training requirements have been completed.

IACUCs 应该注意到，高发病率或死亡率或动物数量超过最初计划等情况表明需要接受培训，并应立即或者在本年评估中跟踪调查该方案。IACUCs should note that high morbidity or mortality rates or requests for more animals than originally planned may indicate a training opportunity and should be followed up in the context of the relevant protocol, either immediately or during the semiannual review.

新人员以及新技术的使用也是 IACUC 评估的重点。Evaluating the qualifications and training of new personnel or those proposing to use new techniques, procedures, or manipulations will necessitate another approach by the IACUC.

六、兽医意见 Veterinary Review and Consultation

兽医在 IACUC 审查试验方案过程中扮演了十分重要的角色。The veterinarian plays a key role in IACUC protocol review, as described below.

1. 审核动物使用方案 Reviewing Animal Use Protocols
2. 审核存在潜在痛苦及不安的方案 Reviewing Protocols for Potential Pain and Distress
3. 审核涉及手术的方案 Reviewing Protocols Involving Surgery
4. 审核方案确保动物人道安乐 Reviewing Protocols To Ensure Humane Euthanasia of Animals
5. 方案审核及批准后 After Protocol Review and Approval
6. 检查清单 Checklist

参考文献 References

- CCAC (Canadian Council on Animal Care). 1998. CCAC guidelines on choosing an appropriate endpoint in experiments using animals for research, teaching, and testing. Canadian Council on Animal Care. Ottawa, Canada.*
- Carstens E., and O.P.Moberg. 2000. Recognizing pain and distress in laboratory animals. ILAR J 41:62-71.*
- Dennis M. 2000. Humane endpoints for genetically engineered animal models. ILAR J 41:94-98.*
- Hendriksen C.F.M., and D.B. Morton, editors. 1999. Humane Endpoints in Animal Experiments for Research. In: Proceedings of the International Conference, November 22- 25, 1998, Zeist, The Netherlands. London: Royal*



Society of Medicine Press Limited.

Hendriksen C.F.M., and B. Steen. Refinement of vaccine potency testing with the use of humane endpoints. ILAR J 41:105-113.

Montgomery, C.A. Oncologic and toxicologic research: alleviation and control of pain and distress in laboratory animals. Cancer Bulletin 1990; 42:230-237.

Morton D.B. 2000. A systematic approach for establishing humane endpoints. ILAR J 41:80-86.

NRC [National Research Council]. 1992. Recognition and Alleviation of Pain and distress in Laboratory Animals. National Academy Press, Washington, DC.

Olfert E.D., and D.L. Godson. 2000. Humane endpoints for infectious disease animal models. ILAR J 41:99-104.

OECD (Organization for Economic Cooperation and Development). 2000. Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation. Paris, France: Organization for Economic Cooperation and Development.

OECD (Organization for Economic Cooperation and Development). 1998. Harmonized Integrated Hazard Classification System for Human Health and Environmental Effects of Chemical Substances. Paris, France: Organization for Economic Cooperation and Development.

Sass N. 2000. Humane endpoints and acute toxicity testing. ILAR J 41:114-123.

Stokes W.S. 2000. Humane Endpoints for Laboratory Animals Used in Toxicity Testing. In: Proceedings of the 3rd World Congress on Alternatives and Animal Use in the Life Sciences, Bologna, Italy, August 31-September 2, 1999. New York: Elsevier Sciences (Forthcoming).

Stokes W.S. 2000. Reducing Unrelieved Pain and distress in Laboratory Animals Using Humane Endpoints. ILAR J 41:59-61.

批准时间 Approved : 1/3/2018

附件 Appendix :

附件一：动物实验方案审查标准清单 Protocol Review Checklist from IACUC of ISM

附件二：美国政府在测试、研究和培训中使用和照顾脊椎动物的原则 U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training



附件一：动物实验方案审查标准清单

Protocol Review Checklist from IACUC of ISM

Based on government principles,PHS policy,and the guide of IACUC

Protocol Title:

Protocol NO:

A	GENERAL:	Yes/No/NA	Comments
1	Identification of the species and the appropriate number of animals to be used	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
2	A rationale for involving animals,for the appropriateness of the species,and numbers of animal to be used	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
3	A complete description of the proposed use of the animals	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
4	The animals' living conditions are appropriate for their species in accordance with our guideline, and contribute to their health and comfort	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
5	The housing, feeding, and non-medical care of the animals will be directed by the attending veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
6	Medical care for animals will be available and provided as necessary by a qualified veterinarian	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
7	Personnel conducting procedures on the species being maintained or studied are appropriately qualified and trained in those procedures	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
8	The safety of the personnel's working environment has been assessed	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
B	PAIN&DISTRESS ISSUES:		
1	A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
2	Include provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
3	Procedures avoid or minimize discomfort, distress, and pain to the animals	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	



4	The PI has considered alternatives to procedures that may cause more than momentary or slight pain or distress, and has provided a written narrative description of the methods and sources used to determine that alternatives were not available	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
5	The PI has provided written assurance that the activities do not unnecessarily duplicate previous experiments	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
6	Procedures that may cause more than momentary or slight pain or distress to the animals will:	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	a. Be performed with appropriate sedatives, analgesics or anesthetics	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	b. Withholding such agents is justified for scientific reasons, in writing, by the PI and will continue for only the necessary period of time	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	c. Involve, in their planning, consultation with the attending veterinarian	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	d. Not include the use of paralytics without anesthesia	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
7	Animal will be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
C	SURGERY:		
1	Activities that involve surgery include appropriate provision for post-operative care in accordance with established veterinary practices	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
2	All survival surgery will be performed using aseptic procedures, including surgical gloves, masks (when working with regulated species), sterile instruments, and aseptic conditions	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
3	Major operative procedures on non-rodents will be conducted only in facilities intended for that purpose which shall be operated and maintained under aseptic conditions	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
4	Non-major operative procedures and all surgery on rodents do not require a dedicated facility, but must be performed using aseptic procedures	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
5	Operative procedures conducted at field sites not performed in dedicated facilities, are performed using aseptic procedures	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
6	Animal will not be used in more than one major operative procedure from which it is allowed to recover unless:	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	a. Justified for scientific reasons by the PI in writing in the protocol	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	
	b. Required as routine veterinary procedure or to protect the health; OR	<input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> NA	



附件二

U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

- I.- The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et. seq.) and other applicable Federal laws, guidelines, and policies.*
- II.- Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.
- III.- The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.
- IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.
- V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.
- VI.- Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.
- VIII. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.
- IX.- Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

* For guidance throughout these Principles, the reader is referred to the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, National Academy of Sciences.