



## 中国医学科学院-苏州系统医学研究所

### Institutional Animal Care and Use Committee

### IACUC Guideline # 130.00

**标题 TITLE :** 实验动物的人道终点指南. Guidelines for Humane Endpoints on Animals

**目的 PURPOSE :** 为在撰写实验方案时，如何选择可减少动物痛苦和不安的方法提供指导。The purpose of this document is to provide guidelines for selecting an endpoint that reduces animal pain and/or distress, while still meeting research objectives when writing a protocol.

**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、当撰写动物实验方案时，发病率或死亡率的预估以及相应的人道终点必须阐述，并经 IACUC 批准。Human endpoints must be described in the protocol for studies with expected morbidity or mortality and approved by the IACUC. When writing a protocol:
- 可咨询兽医以及查看本文的指南。Consult the Institutional Veterinarian and review this document for guidance (See sections below).
  - 选择与科研目标一致的最早终点。Choose the earliest endpoint that is compatible with the scientific objectives.
  - 在进行大规模试验之前，尽可能的利用预实验评估人道终点，并确保于科研目标一致。Use pilot studies when possible to provide an opportunity to evaluate humane endpoints and assure the scientific objectives are met, before proceeding to large scale studies.



- 可使用一套评分系统，需要咨询兽医，并且在方案书中描述所使用的评分系统。A scoring system can be used. Consult the veterinarian and describe the scoring system to be used in the protocol.
- 如果研究需要继续保留已经濒死的动物，那么就要清楚地描述安乐死的标准并获得 IACUC 的审批。并且符合科研的合理性。Proper approval from the IACUC is required if an investigator wishes to maintain an animal on study ones the animal is moribund and exhibits clear criteria requiring euthanasia. Obtaining such approval requires scientific justification.
- 死亡作为人道终点需要在 IACUC 方案中进行科学的论证以及文档说明，以上的人道终点不能被使用 Death as an endpoint requires scientific justification and documentation in the IACUC protocol that the above humane endpoints cannot be used.

二、如果死亡及濒死在方案中作为终点，那么需要的科学理由包括 If death or moribundity will be used as an endpoint, include in the justification when writing the protocol:

- 有哪些替代方案 What alternatives were considered?
- 为什么不能使用发病作为终点，如何在适合的时候使用替代方案。Why morbidity as an endpoint cannot be used, and how alternatives will be used whenever possible.
- 为何不使用缓解疼痛和不安的方法 Why measures to relieve pain and/or distress cannot be utilized.
- 使用的动物量以及如何确定这是最小数量 Number of animals to be used and why this is the minimal number of animals required.
- 若动物濒死，是否做安乐死处理，如果不，那在濒死以及死亡之间可获得什么数据信息 Whether animals will be euthanized when moribund and if not, what information is to be gained in the interval between moribundity and death.
- 用什么统计或其他方法能确定动物的数量可取得有效的结果 What statistical or other methods were used to determine the number of animals requires to achieve valid results?
- 动物护理及检测流程的计划 A plan for animal care and monitoring procedures:
  - 试验中可能会发生濒死或死亡的动物必须由有识别动物濒死状态经验的（发病，受伤或者异常行为）人员每天至少观察两次，如观察：异常姿势、被毛杂乱、头部蜷缩、眼周鼻周液体渗出、皮肤损伤、异常呼吸、行走困难、饮食饮水减少、脱水以及自残。Animals involved in experiments that may lead to moribundity or death must be monitored at least twice daily by personnel experienced in recognizing signs of morbidity (illness, injury, or abnormal behavior)



for at least the following: abnormal posture, rough hair coat, head tucked into abdomen, exudate around eyes and/or nose, skin lesions, abnormal breathing, difficulty with ambulation, decreased food or water intake, dehydration and self-mutilation.

- 说明观察监测的人员 Indication of who will conduct the monitoring
- 当动物表现出以上的濒死症状时，需要增加监测频率。夜间、周末以及节假日都必须有动物护理或兽医人员监测。一旦动物出现病理症状，应立即通知兽医。并尽快进行动物状态的评估以及建立相应的行动计划。The frequency of observation will be increased when animals exhibit the above or other signs of morbidity. Monitoring at night, weekends and holidays must be provided by the animal care and veterinary staff. The Institutional Veterinarian must be notified as soon as animals show signs of disease. An assessment of the animals' condition should be made as soon as possible and a plan of action established.
- 当动物情况恶化影响其他动物进食进水时，需考虑分笼。濒死或死亡动物要立即移出笼盒。Consideration should be given to moving animals to individual cages when their condition deteriorates to the point that injury from other animals in the cage is likely and/or compromised access to food/water. Moribund and dead animals must be promptly removed from the cage.
- 动物的监测观察记录需要被保存 Written records of monitoring of animals should be kept.

三、当动物实验方案通过 IACUC 审核，实验开始时 Once you have IACUC approval and start your project:

- 当动物出现任何疼痛或不安症状或濒死状态时。通知兽医 Notify the veterinarian when animals exhibit signs of pain and distress or become moribund.
- 当动物出现任何疼痛或不安等作为未预计到的实验症状时，本指南指导兽医咨询 For studies in which morbidity or death is not expected this document should be used as guidance in consultation with the veterinarian when animals exhibit signs of pain and distress.
- 如果濒死以及死亡作为可预计到的终点且通过审核，研究人员需要至少每天观察动物状态，包括周末，节假日。并且要将所有观察记录或治疗记录存档保留。If the study is approved with expected morbidity or death as an endpoint, investigators must monitor animals at least daily, including weekends and holidays, and keep detailed records of any observations and treatments.
- 在发病率和死亡率可能会上升的时期内，研究人员必须至少每天评估动物两次（每 8-12 个小时）。



那些在下一计划评估之前不会存活下来的动物应该被人道地安乐死。During periods in which morbidity and mortality are expected to increase, animals must be evaluated by the investigator a minimum of two times daily (every 8-12 hours). Those animals that are not expected to survive until the next scheduled evaluation should be humanely euthanized.

- 在整个研究过程中，实验动物的健康状况必须与研究的要求相平衡。At all times during the study, the well-being of the research animals must be balanced against the requirement of the study.

#### 四、对于研究中为预计的发病及死亡动物的人道终点 Humane Endpoints for Studies with Expected Morbidity or Mortality

在大部分研究中，根据安乐死标准以及 AVMA 安乐死指南，动物在承受无法缓解的疼痛及不安时应被施以人道安乐死。In most studies, animals must be humanely euthanized if they experience unrelieved pain or distress, based on the euthanasia criteria described below and in accordance with the AVMA Guidance on Euthanasia, 2007.

以下是一般的需要实施安乐死的终点 The following are general humane endpoints that require euthanasia.

- 无法取得饮食饮水超过 24 小时 The inability to reach food or water for more than 24 hours.
- 体重下降达 20% A 20% decrease in normal body weight.
- 身体状态评分大于 5 分（第五部分，评分表） A Body Condition Score typically >5 point (See Section 5)
- 无法被止痛药抑制的明显疼痛症状 Development of conditions that result in significant pain that cannot be alleviated by analgesics.

一般的疼痛和不安评估项目包括体重、外部身体外观、临床症状（例如，无法摄食采水、嗜睡或警觉性降低、呼吸困难、无法保持直立）行为明显改变、外部刺激应答。General observations for assessing pain and distress include change in body weight, external physical appearance, clinical signs (e.g., inability to reach food and water, lethargy or decreased mental alertness, labored breathing, inability to remain upright), significant changes in behavior, and responses to external stimuli. 一般来说，生病的动物应该在垂死的状态之前尽可能早的被识别出来。As a general rule sick animals should be identified as early as possible prior to a moribund state. 实验人员必须要仔细观察动物健康状况、外观、行为的变化，并且了解动物经历的过程以及治疗方法。Laboratory personnel must carefully observe the animals for changes in



health status, appearance, and behavior, and have knowledge of the treatment and procedures that the animals have undergone.

人道终点根据研究内容有所不同。方案会包括很多不同的特殊标准。研究人员必须向收益咨询了解其标准。Humane endpoints will vary depending on the nature of study. Protocols may include more specific criteria. Investigators must discuss this with the Institutional Veterinarian.判断动物在其濒死状态出现之前的最初症状，以避免动物承受额外的痛苦和折磨是更好的施以人道终点的关键。Identifying the initial signs that occur prior to a moribund state in order to avoid additional pain and suffering is key to developing humane endpoints. 评分系统的标准提供了一种很好的、客观的方法来确定安乐死的合适时间，并且可以在机构兽医的帮助下进行单独的项目。Criteria with a scoring system provide an excellent, objective method for identifying the appropriate time for euthanasia, and can be developed with the assistance of the Institutional Veterinarian for individual projects.

如果兽医对动物进行了检查，并确定它不能在存活到下一次检查，那么兽医将会联系 P.I 以获得对该动物进行安乐死的许可。If the veterinarian has examined an animal and determined that it will not survive until the next scheduled examination, a reasonable attempt will be made to contact the Principal Investigator (P.I.) to obtain permission to euthanize the animal.

死亡作为终点要求科学证明以及在 IACUC 方案中的文件说明，但不适用安乐死标准。Death as an endpoint requires scientific justification and documentation in the IACUC protocol that the criteria for euthanasia cannot be used. 这些理由可能包括监管机构的要求的文献证明。Such justifications may include reference to the requirements of regulatory agencies. 以死亡为终点的研究(也称为生存期研究，LD50 等)不能获得 ISM IACUC 的批准，除非该终点在动物使用方案中是科学合理的。Studies with death as an endpoint (also known as survival duration studies, LD50 etc.) are not approved by the ISM IACUC unless this endpoint is scientifically justified in the animal use protocol.

### **人道终点/安乐死标准 Humane Endpoints/Criteria for euthanasia:**

#### 体重下降 Weight loss

成年动物，对比实验前或同龄对照，体重下降 20%。In adult animals, loss of >20 percent of body weight compared to the pre-study weight or to age-matched controls

在生长，或在体重未被记录，或在肿瘤研究中的动物，体重的减少将根据身体状况来评估。In growing animals, or in animals whose body weight has not been recorded, or in tumor studies, weight loss will



be assessed by body condition.

小型啮齿动物厌食 24 小时，大型动物超过 5 天。Decrease anorexia for 24 hours in small rodents, up to 5 days in large animals;

啮齿动物 3 天，大动物 7 天的部分厌食症(低于 50%的热量要求)。Partial anorexia (less than 50% of caloric requirement) for 3 days in rodents, 7 days in large animals

虚弱/无法摄食饮水 Weakness/inability to obtain feed or water

不能或极端不情愿达 24 小时(假定动物已经从麻醉中恢复)。Inability or extreme reluctance to stand which persists for 24 hours (assuming that the animal has recovered from anesthesia).

濒死状态 Moribund state

处于濒死状态的动物，其特征是严重的抑郁，无法移动，An animal found to be in a state of dying characterized by severe depression, nonambulatory,

几乎不可恢复的完全厌食和低温 Complete anorexia and hypothermia with little likelihood of recovery.

感染 Infection

感染(由异常的体温或 WBC 参数引起的), 在一定时间内不能对治疗作出反应。Infection (either overt or indicated by abnormal body temperature or WBC parameters) which fails to respond to therapy within an appropriate time.

肿瘤生长 Tumor growth

超过正常体重 10%的固体瘤。Solid tumors that exceed 10 percent of normal body weight. 假设 1 立方厘米重 1g，肿瘤的质量公式为  $\frac{4}{3}\pi r^3$ ，例如，对于一只 25g 的小鼠，一个直径 1.8cm 的肿瘤等于 2.441 克等于最大允许体积。Assuming  $1\text{ cm}^3 = 1\text{ gm}$ , the formula for the weight of the tumor is  $\frac{4}{3}\pi r^3$ . i.e. for a 25 g mouse, a tumor 1.8 cm in diameter = 2.441 gm = maximum allowable size. 不规则肿瘤使用平均半径计算。For tumors not perfectly round, use the average radius.

身体状况的丧失表明肿瘤生长是由身体和或代谢储备所支持的。Loss of body condition indicating that tumor growth is being supported by body and/or metabolic reserves.

肿瘤生长阻碍了动物摄取食物和饮水的能力以及其他正常的身体机能或者其在笼内移动以保持清洁和干燥的能力。Tumor growth that impedes an animal's ability to ingest food or water and other normal bodily functions or its ability to move about its cage and remain clean and dry.



肿瘤引起的不能通过止痛药或者其他措施缓解的动物疼痛或不安。Tumors that appear to be causing the animal pain or distress that cannot be relieved with analgesics or other palliative measures.

有证据显示肿瘤的坏死及溃疡表明肿瘤已过生长于其血流供应。Evidence of tumor necrosis or ulceration indicating the tumor has outgrown its blood supply.

有证据显示原发性或转移性肿瘤引起器官的紊乱或损坏。Evidence of organ dysfunction and/or failure from either primary or metastasized tumor.

无法缓解的疼痛或不安 Unrelieved pain/distress

对止痛剂或麻醉剂没有任何反应，明显无法缓解的疼痛或不安症状，或者由兽医鉴定的症状。Signs of significant pain and/or distress which are unresponsive to analgesics/anesthetics, or as determined by the ISM veterinarian.

器官的紊乱或损坏 Organ dysfunction/failure

严重的器官系统功能失调的迹象，治疗无效，或者是由一名 ISM 的兽医所确定的预后不良。例子包括但不限于 Signs of severe organ system dysfunction non-responsive to treatment, or with a poor prognosis as determined by a ISM veterinarian. Examples include but are not limited to:

呼吸系统 Respiratory: 呼吸困难以及对适当的治疗没有效果 labored breathing and cyanosis unresponsive to appropriate medical therapy.

心血管系统 Cardiovascular: 急性失血引发的休克或严重贫血；心脏衰竭 acute blood loss resulting in shock or severe anemia; cardiac failure.

胃肠系统 Gastrointestinal: 剧烈呕吐，腹泻，直肠脱垂或肠梗阻 severe vomiting, diarrhea; rectal prolapse or intestinal obstruction.

泌尿生殖系统 Urogenital: 肾衰或肌酸升高，尿道梗阻，膀胱破裂，泌尿障碍，阴道，子宫，阴茎脱垂等 renal failure characterized by elevated BUN or creatinine; urinary tract obstruction; ruptured bladder; uroperitoneum; vaginal, uterine, or penile prolapse.

神经系统 Nervous: 中枢神经系统萧条；癫痫发作；一个或多个肢体瘫痪；神经条件阻碍动物摄取食物或水的能力，或其笼内移动、保持清洁和干燥、进食和饮水的能力。CNS depression; seizures; paralysis of one or more extremities; neurological conditions which impede an animal's ability to ingest food or water or its ability to move about its cage and remain clean and dry inhibiting eating and drinking.



骨骼肌系统 Musculoskeletal: 肌肉损伤或骨折导致无法使用肢体或严重疼痛 muscle damage or bone fracture resulting in inability to use the limb or severe pain.

表皮 Integument: 不愈合的伤口或严重烧伤, 超过体表 10%的烧伤, 反复自残。non-healing wounds or severe burns covering more than 10% of the body; repeated self-trauma.

### 人道终点或安乐死标准 (继上文) Humane Endpoints/Criteria for euthanasia (Continued):

➤ 肿瘤及毒理学研究 Cancer and Toxicological Studies

在癌症研究和毒理学研究选择的临床观察结果。Selected Clinical Observations Used in Cancer Research and Toxicological Studies.

参数 Parameter	观察内容 What to look for
General Appearance/Dehydration	Decreased body weight (>20%) or extreme emaciation, missing anatomy, abnormal posture, hypothermia, fractures appendage, swelling, tissue masses, prolapse, paraphimosis, severe dehydration, labored breathing, diarrhea with weight loss, convulsion, any condition indicating impending death
Movement	Unwillingness to move, lameness, impaired motility preventing the animal from reaching food or water
Body temperature	Decrease in body temperature and severe depression
Reaction	Absence of voluntary responses to external stimuli, cachexia appearance is found
Skin and fur Discoloration	Urine stain, pallor, redness, cyanosis, icterus, wound, sore, abscess, ulcer, alopecia, ruffled fur
Eyes	Exophthalmos, microphthalmia, ptosis, reddened eye, lacrimation, discharge, opacity
Nose, Mouth & Head	Head tilted, nasal discharge, malocclusion, salivation, respiration, sneezing, dyspnea, tachypnea, rales
Urine Discoloration	Blood in urine, polyuria, anuria
Feces Discoloration	Blood in the feces, softness/diarrhea
Locomotor/Hyperactivity	Hyperactivity, coma, ataxia, circling, muscle, tremors
Tumor	Excessive tumor size $\geq 20\%$ body weight

### 五、疼痛及不安的评估 Assessing Signs of Pain and Distress





将评价分配给观察各种动物状态及行为有助于更加客观地评价疼痛及不安。To assess the possibility of pain and distress objectively, it is helpful to assign values to various observations of animal condition and behavior. 以下提供了一个评分系统，基于观察，每一项都会有一个得分，0-3 分。积分动物所承受的痛苦程度。An example of a scoring system is presented below. Based on observations, a score is assigned to each variable, 0 (normal or mild) to 3 (severe changes from normal). The cumulative score gives an indication of the likelihood that the animal is experiencing pain or distress. 人道终点可以根据以下的标准建立 Humane endpoints can be established based on criteria such as:

- 总分 The total score (e.g. a total score >5),or
- 或任何一项得 3 分，视为总分 A score of 3 in any one variable, regardless of the total score.

项目 Variable	
<b>体重变化 Body Weight Changes</b>	
0	Normal
1	< 10 percent weight loss
2	10-15 percent weight loss
3	>20 percent weight loss
<b>外观 Physical Appearance</b>	
0	Normal
1	Lack of grooming
2	Rough coat, nasal/ocular discharge
3	Very rough coat, abnormal posture, enlarged pupils
<b>可测量的临床数据 Measurable Clinical Signs</b>	
0	Normal
1	Small changes of potential significance
2	Temperature changes of 1-2°C, cardiac and respiratory rates increased up to 30 percent
3	Temperature changes of >2°C, cardiac and respiratory rates increased up to 50 percent, or markedly
<b>异常行为 Unprovoked Behavior</b>	
0	Normal
1	Minor changes
2	Abnormal, reduced mobility, decreased alertness, inactive
3	Unsolicited vocalizations, self-mutilation, either very restless or immobile
<b>外部刺激的反应 Behavior Responses to External Stimuli</b>	
0	Normal
1	Minor depression/exaggeration of response
2	Moderately abnormal responses
3	Violent reactions, or comatose
<b>TOTAL</b>	



中国科学院 系统医学研究中心  
Center of Systems Medicine Chinese Academy of Medical Sciences  
苏州系统医学研究所  
Suzhou Institute of Systems Medicine

地址：中国苏州工业园区星湖街218号生物纳米园B5-501,215123  
ADD: 501,B5 Building,218 Xinghu Str.,SIP,China,215123  
电话 / Tel : 0086-512-62873780 | 传真 / Fax : 0086-512-62873779  
网址 / Website : www.ismsz.cn

---

## 参考文献 Reference

*ILAR Journal V41(2) 2000*

*Ullman-Cullere MH, Foltz CJ. Body condition scoring: a rapid and accurate method for assessing health status in mice. Lab Anim Sci 49:319-323, 1999*

**批准时间 Approved : 11/5/2018**