A. Purpose

To define “surgery” versus “procedures”

To define “major” surgery and criteria for multiple “major” surgeries.

To describe standards for consideration for subjecting an individual animal to multiple surgeries and/or procedures.

To describe standards for considerations of the sharing of animals between protocols that involve multiple surgeries and/or procedures.

B. Principle

To ensure that there is consistency between protocols and assist reviewers and researchers in reviewing and writing protocols involving multiple surgeries and procedures.

C. Scope

This applies to all WSU Animal Subjects Approval Forms.

D. Policy Statement

When writing the Animal Subjects Approval form - Researchers are to clearly define surgeries and procedures to be performed and fully justify multiple major survival surgeries. Note: Multiple major survival surgeries on USDA covered species, where the surgeries are not part of a single research protocol, require that the Institutional Official submit a request to the USDA/APHIS and receive specific approval.

E. Definitions

1. Tissue Harvest: If an animal will be euthanatized as per the WSU IACUC policy #28 for the collection of tissues (after confirmation of death), the procedure is defined as a tissue harvest.

2. Surgery: Surgery is defined as the creation of a novel opening in the body or of a pre-existing orifice that involves cutting with a scalpel, scissors, biopsy forceps, punch biopsy, drill, laser, electrocautery, or direct tissue damage by cold (liquid nitrogen) or any comparable device or technique. Biopsies will be considered a surgery as defined below.
3. Types of Surgery:

a. **Biopsy:** The removal of a piece of tissue from a live animal is known as a biopsy.

   If the collection of tissue involves entering a body cavity, then the biopsy shall be considered a major surgery (e.g. liver wedge biopsy), as defined below. The exception is the use of transcutaneous Tru-cut® biopsy needles, fine needle aspirates, or similar techniques of collection samples of organs within a body cavity, which shall be considered a minor surgery. Principal Investigators are encouraged to perform these types of biopsies being guided by ultrasonography.

   The collection of a superficial biopsy may not necessarily require general anesthesia and may only require subcutaneous instillation of a local anesthetic (e.g. lidocaine or bupivacaine), but will be considered a minor surgery.

b. **Non-Survival Surgery:** Non-survival surgery is defined as any surgery in which the animal is euthanized before recovery from anesthesia. This includes any procedure where an incision is created following the administration of a lethal or sub-lethal dose of anesthesia but prior to actual death of the animal. Examples include euthanasia after transcardial perfusion or the removal of a vital organ such as the brain or heart.

c. **Survival surgery:** Any surgery from which the animal recovers consciousness. Aseptic technique must be used for all survival surgical procedures in all species. Please reference WSU IACUC Policy #6 “Aseptic Surgery Techniques for Animals”


d. **Multiple survival surgery:** More than one surgical session is performed and the animal is recovered from anesthesia after each session.

e. **Minor Surgery:** The Guide states that a “minor survival surgery does not expose a body cavity and cause little or no physical impairment (such as wound suturing, peripheral vessel cannulation, castration, dehorning, repair of prolapses, and any procedure routinely done on an “outpatient” basis in veterinary clinical practice).” Other examples of minor surgical procedures include, but are not limited to:

   - Vascular cut-down approach to an artery or vein (e.g. jugular or femoral).
   - Tissue biopsy not involving surgical exposure of a body cavity (e.g. skin, muscle, via endoscopy).
   - Skin or subcutaneous implants.
• Surgical repair of a superficial injury.
• Arthroscopy.
• Oral surgery and tooth extractions not involving bone.
• Closed castrations (age and species dependent)

Minor surgeries require appropriate anesthesia, analgesia, aseptic technique, wound closure (if applicable, to include sutures, staples, tissue glue, and/or bandaging), postoperative wound care, and frequent postoperative monitoring of the animal until healed and/or achieved a normal health status. If post-operative care is necessary, the IACUC protocol or amendment must be clear in regards to who is directly responsible for post-operative care, e.g. appropriately trained laboratory personnel or responsible veterinary clinical staff.

f. **Major surgery**: Both the *Animal Welfare Act* and the *Guide of the Care and Use of Laboratory Animals* (hereafter referred to as The Guide) states that a “major surgery penetrates and exposes a body cavity or produces a substantial impairment of physical or physiologic function.”

• Body cavity is defined as the abdominal, thoracic, cranial, synovial, or bone marrow cavities, i.e. those chambers not immediately associated with the outside world.
• Substantial impairment is defined as the circumstance where the animal is not expected to be normal after a reasonable postoperative recovery period.

Examples include, but are not be limited to those procedures permanently and significantly affecting ambulation, physiology, the immune system, and mentation. Examples of a major surgery include, but are not limited to:

• Laparotomy, including some more invasive laparoscopic procedures.
• Thoractomy.
• Craniotomy.
• Arthrotomy and joint replacement, excluding arthroscopy.
• Orthopedic procedures
• Injury models
- Nerve/muscle transection.
- Eye surgery with cornel incision.
- Significant soft tissue transection.

Major surgeries require appropriate anesthesia, analgesia, aseptic technique, wound closure (sutures, staples, tissue glue, and/or bandaging), postoperative wound care, and more extensive postoperative monitoring of the animal until healed and/or achieved a normal health status. The IACUC protocol or amendment must be clear in regards to whom is directly responsible for postoperative care.

For studies involving mouse tissue sampling for genotyping, please refer to WSU IACUC SOP #2 “Mouse Tissue Sampling Guidelines”:
http://www.iacuc.wsu.edu/documents/forms/pdf/WSU_SOP_2.pdf

4. Procedure:
- A procedure can also be defined as a non-surgical treatment or manipulation of an animal to achieve the goals of the research or educational use of the animal.
- Examples of procedures: blood collection, blood vessel or urinary catheterization, injection (multiple routes), CSF and other body fluid collection and anesthesia or sedation without surgery

F. Justifications for Multiple Major Survival Surgery on a Single Animal

1. **Scientific Purposes:** The justification would need to show how the multiple survival surgeries are necessary for the research being performed and why other methods cannot be utilized to achieve the research goals. The Guide for the Care and Use of Laboratory Animals (the Guide, NRC 2011) states: “Regardless of classification, multiple surgical procedures on a single animal should be evaluated to determine their impact on the animal's wellbeing. Multiple major surgical procedures on a single animal are acceptable only if they are (1) included in and essential components of a single research project or protocol, (2) scientifically justified by the investigator, or (3) necessary for clinical reasons.” (p. 30)

2. **Conservation of a scarce resource:** Major survival surgeries could be performed in separate animals, but this would further reduce the scarce resource by increasing the number of animals used. It needs to be determined that the additional survival surgery does not cause undue stress to the animal.
Application of this reason is discouraged and will be very critically weighed during the review process. Conservation of scarce animal resources may justify the conduct of multiple major surgeries on a single animal, but the application of such a practice on a single animal used in separate protocols is discouraged and should be reviewed critically by the IACUC. When applicable, the IO must submit a request to the USDA/APHIS and receive approval in order to allow a regulated animal to undergo multiple major survival surgical procedures in separate unrelated research protocols (Animal Welfare Act 9 CFR Ch. 1, Part 2 – Subpart C, 2.31 (d) (1) (x)).

3. **Animal Welfare Concerns:** Two surgeries are required that could be performed at the same time, but to do so would sufficiently compromise the animal that it may not survive, whereas if the animal is able to heal from the first before the second, it should survive both procedures.

**G. Justification of Multiple Minor Survival Surgeries and/or Procedures on a Single Animal**

1. **Scientific Purpose:** The justification would need to show how the multiple survival surgeries and/or procedures are necessary for the research or educational use being performed and why other methods cannot be utilized to achieve these goals.

2. **Conservation of a scarce resource:** Multiple minor surgeries and/or procedures could be performed in separate animals, but this would further reduce the scarce resource by increasing the number of animals used. It needs to be determined that the additional survival surgery does not cause undue stress to the animal. Application of this reason is discouraged and will be very critically weighed during the review process.

3. **Animal Welfare concerns:** Two surgeries and/or procedures are required that could be performed at the same time, but to do so would sufficiently compromise the animal that it may not survive, whereas if the animal is able to heal from the first before the second, it should survive both procedures. Some procedures characterized as minor may induce substantial postprocedural pain or impairment and should similarly be scientifically justified if performed more than once in a single animal.

4. **Reducing animal numbers:** Performing multiple minor procedures on a single animal is a method to reduce the use of animals. However, if the research protocols contain procedures with more than momentary pain or distress, a thorough evaluation must be made to determine the impact on the animal’s well-being. This is especially true when there are surgical procedures on the research and teaching protocols.
H. Justification of the Use of Animals on Multiple Research and/or Teaching Projects

1. The sharing of animals between research protocols is a method to reduce the number of animals used in research and teaching in general. However, if the research protocols contain procedures with more than momentary pain or distress, a thorough evaluation of such sharing must be made to determine the impact on the animal's well-being. This is especially true when there are surgical procedures on the research and teaching protocols.

2. If the animal being shared is covered by the USDA Animal Welfare Act and the protocols involve major survival surgery, additional steps must be taken to secure approval. According to the Guide, “When applicable, the Institutional Official must submit a request to the USDA/APHIS and receive approval in order to allow a regulated animal to undergo multiple major survival surgical procedures in separate unrelated research protocols (Animal Welfare Act 9 CFR Ch. 1, Part 2 – Subpart C, 2.31 (d) (1) (x)).

3. Use of animals between protocols should be approved by the IACUC prior to use. If a Principal Investigator intends to transfer and/or share an animal with another Principal Investigator for use in research, testing or teaching, he/she should have this approved by the IACUC on their protocol prior to the transfer. The disposition section of the current protocol covering the animal must indicate the request. In the narrative regarding the chronological use of animals, a justification for the request to transfer/sharing of the animal(s) should be included in both the protocols. The investigator seeking to use the animal transfer should submit an amendment if it has not been approved by IACUC. IACUC will work with the Office of the Campus Veterinarian to ensure that the animal wellbeing is not compromised.

4. The transfer of excess stock animals from WSU rodent colonies is acceptable without prior IACUC approval if the following conditions are met
   - Animals for transfer have not had any research manipulations other than tissue collection for genotyping or breeding
   - There are no material transfer agreements or memorandums of understanding that prohibits transfer to other investigators

I. Use of Analgesics In Surgeries and Procedures:

   The definitions of surgery, major or minor, procedure, or biopsy does not necessarily relate to whether
that particular activity will require analgesics, but in general, the more invasive the surgery/procedure, the more potent, longer lasting, and more frequent dosing of pain medications will be required in order to keep the animal in a pain-free state. The USDA Animal Welfare Act requires that “activities that involve surgery include appropriate provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices.” It is the Principal Investigator’s responsibility to assign a pain category to the protocol (See Guidelines for Pain-levels in Animal Use on the IACUC forms page). The Animal Welfare Act defines a painful procedure as “any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is, pain in excess of that caused by injections or other minor procedures.” Barring specific, scientifically-based and published observations to the contrary, the Principal Investigator must consider the use of analgesics for any potentially painful procedure. The IACUC’s recommendation is for the Principal Investigator to consult with a veterinarian from the Office of the Campus Veterinarian before protocol submission to determine an appropriate pain category and analgesic protocol compatible with welfare of the animal and the science of the protocol. The IACUC will withhold approval on protocols with an inappropriate analgesia regime. If there are any questions regarding this guideline and incorporating its tenets into the research or teaching protocol, then please contact the IACUC or WSU Attending Veterinarian.

J. Responsibility

1. It is the responsibility of the Principal Investigator to conscientiously evaluate the need to perform surgery and procedures. Surgery and procedures which involve more than momentary slight pain and/or distress must be adequately scientifically justified. The Principal Investigator should weigh the potential adverse effects to the animal against the potential benefits to human and/or animal health, the environment and the advancement of science.

2. It is the responsibility of the Principal Investigator to maintain adequate, complete and legible surgical, veterinary and procedure records for all animals involved in the research or teaching protocol. See IACUC Policy #4 “Animal Care Medical Records for Research and Teaching Animals” http://www.iacuc.wsu.edu/documents/forms/pdf/Policy_4.pdf for the record keeping requirements. This record mandate is to ensure the tracking of the use of an individual animal and to document the monitoring of animal welfare and oversight. If animals are transferred or shared between protocols, the records must include all procedures performed on an individual animal and contain veterinary oversight that addresses the wellbeing of the animal and the appropriateness of the multiple uses.
3. It is the responsibility of the IACUC to review the protocol and to perform a Risk-Benefit analysis. The 2011 Guide specifies that the IACUC is obliged to weigh study objectives against animal welfare concerns in accordance with the tenets of the Three R’s. AAALAC International expects that IACUC’s, as part of the protocol review process, will weigh the potential adverse effects of the study against the potential benefits that are likely to accrue as a result of the research. This analysis should be performed prior to the final approval of the protocol, and should be a primary consideration in the review process.

References


Policy #10: Approved by IACUC August 31, 2016