In design of the research, training or educational activities, it is the responsibility of the PI to consider and include procedures that minimize animal pain or distress.

As required by the PHS Policy and the AWRs, and reiterated in the *Guide*, the IACUC is mandated to critically evaluate research protocols to ensure that pain and distress are minimized in laboratory animals and assure that appropriate steps will be taken to enhance animal well-being. The AWRs stipulate that the IACUC determine that the principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animal and has provided a written narrative description of the methods and sources used to determine that alternatives were not available. The *Guide* states that the IACUC should ensure the protocol addresses:

- Appropriate sedation, analgesia, and anesthesia;
- Criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and
- Details of post-procedural care.

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.

Examples of procedures that the *Guide* suggests may have the potential to cause pain or distress include:

- physical restraint, survival surgeries,
- food or water restriction, death as an endpoint, noxious stimuli,
- skin or corneal irritancy testing, tumor burdens,
- intra-cardiac or orbital sinus blood sampling, and abnormal environmental conditions.

### 9.1.1 Assessing Pain and Distress

Numerous references indicate that both laboratory animals and humans receive and process noxious stimuli using similar mechanisms. An animal’s response to pain is often adaptive to reduce movement to minimize re-injury and aid recuperation. This response, however, may lead to physiological and behavioral changes which impact negatively on both the animal’s well-being and the research results.
Fundamental to the relief of pain is the ability to recognize its clinical signs in various species of animals. Due to the inability of animals to verbalize, it is essential that animal care staff and researchers receive adequate training on how to recognize clinical signs of pain and distress. 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.

9.1.2 Alleviation of Pain and Distress

Accepted best practices for dealing with the possibility of unrelieved pain and distress should be considered and incorporated into protocols unless there is a sound scientific rationale for deviation from those practices. The investigator must also provide an assurance that unrelieved pain will continue for only the minimum period of time necessary to attain the study objectives.

Protocol methodology should be considered that decreases the potential for pain or distress. In addition to thorough searches of the literature, this can be done through the careful use of pilot studies to determine earlier endpoints or less invasive alternatives.

Pharmacologic treatment of pain or distress should be given as consistent with the type of pain/distress and the needs of the research question. The veterinarian must be consulted for all such protocols and should provide guidance to investigators and the IACUC. Non-pharmacologic treatments should also be employed. This may include special housing considerations, dietary and other environmental enrichments, adjustments and careful supportive care.

It is the responsibility of the investigator to show s/he has considered all the options for minimizing pain and distress that do not compromise the scientific validity of the experiment. The IACUC’s deliberations regarding the management of potential pain and distress in a protocol will be documented. Personnel should be trained in pain and distress management. The IACUC should ensure that there is a mechanism in place for prompt reporting of sick animals to the veterinary staff.